School of Physiotherapy

The role of functional, radiological and self-reported measures in predicting clinical outcome in spondylotic cervical radiculopathy

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This thesis is presented for the degree of
Doctor of Philosophy
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DECLARATION

To the best of my knowledge and belief this thesis contains no material previously published by any other person except where due acknowledgment has been made.

This thesis contains no material which has been accepted for the award of any other degree or diploma in any university.

Signature: ………………………………………….

Date:………………………...

ABSTRACT

Background

Cervical radiculopathy (CR) results in significant disability and pain and is commonly treated conservatively with satisfactory clinical outcomes. However, a considerable number of patients require surgery to prevent irreversible neurological damage or when pain is unremitting. Both conservative and surgical treatments are characterised by a plethora of strategies and interventions, making comparisons between treatment groups a difficult task.

The ability to predict the likely outcomes of treatment is important to clinicians involved in treatment and serves as an important basis for health policy, resource management and core knowledge essential for patients to have an informed consent when being offered both conservative and surgical interventions. Generic and condition specific measures in clinical conditions may have a role in predicting clinical outcome after treatment. Common measures employed in the examination and evaluation of cervical radiculopathy patients include self reported measures of pain and disability, measures of impairment and function, neurological and radiological evidence of the disease. Unfortunately, few studies exist that provide knowledge in understanding factors associated with the presentation of cervical radiculopathy and the ensuing long-term clinical outcome.

The objective of this thesis was to address the limited understanding of the impairment measures and prognostic outcomes associated with cervical radiculopathy in an Indian population for both surgical and conservative treatment strategies. In these aspects, this thesis was original.

Aim

The principal aim of this thesis was to evaluate the role of clinical (pain, disability), functional (posture, cervical ROM), radiological (radiographic segmental curvature and segmental movements in the sagittal plane), socio-demographic and lifestyle factors (age, gender, BMI, work characteristics, physical activity, smoking, life-style changes, duration of symptoms, co-morbidities and number of previous episodes) in predicting clinical outcome (pain and disability) at one year in a cervical

radiculopathy cohort which was treated conservatively or surgically. To support and substantiate the primary aim, associations, relationships, differences between the outcome variables at different measurement times, and effects of treatment were determined. Furthermore, a series of studies were undertaken examining key assessments of cervical spine impairment to further support the primary clinical outcome study.

Methods

The main element of the thesis derived clinical data from a sample of convenience of 163 patients (109 patients in the conservative group and 54 in the surgical group). All measurements were done at baseline, that is, prior to any form of intervention, and then at pre-determined intervals until a one year follow-up period in both treatment groups. After baseline assessments, the conservative group underwent medical treatment and physiotherapy whereas the surgery group underwent surgery, and post-surgery, were given ergonomic advice and exercises. An intention to treat analysis approach was adopted for dropouts (14% at 12 months).

A large series of other studies were undertaken prior to and in parallel with the main clinical trial (Agarwal et al. 2005 a,b,c; Agarwal et al. 2006). Emphasis was placed on tester reliability for each measure used in this study and consequently methodological studies establishing reliability and validity of measures were carried out and published. Cervical range of motion, a key measure of impairment and neck functions, frequently used by physiotherapists as an assessment tool, was analysed to determine the effects of age, gender and repeat measurements over time in asymptomatic individuals (n = 219) as well as differences in range of motion between asymptomatics and patients with cervical radiculopathy. During the initial course of this research, it became evident that the pain and disability questionnaire (Neck Pain and Disability scale) in the English language was not applicable to a section of the patient population. This was therefore translated into Hindi (the national language of India).

The outcome variables with their respective measuring instruments were neck pain and arm pain (101 Numerical Pain Rating Scale), pain and disability (NPAD), depression (NPAD factor 3 scores), posture (head neck angle), cervical range of movement (Spin-T goniometer), radiographic sagittal segmental curvature (Posterior Tangent Method) and radiographic sagittal segmental motion (Penning's method).

Demographics and lifestyle factors consisted of either continuous or dichotomous variables.

A range of parametric and non-parametric tests analysed the correlations and differences between outcome variables at different times of measurements as well as determined treatment efficacy. The Clinical Prediction Rule (CPR) analysis was used to determine the group of predictor variables which could result in a successful outcome in a CR cohort, following conservative or surgical intervention. The NPAD (English and Hindi) was the outcome criterion for the CPR analysis of this study with a score of <22 (minimal or no pain and disability) used as a responder threshold.

Results

The Hindi version of the NPAD was tested as valid and reliable. The maximum typical error values between repeat measurements of radiographic segmental curvature (levels C2-7), radiographic segmental flexion-extension motion (levels C2-7) and composite active cervical ROM did not exceed 3°. However, when composite cervical ROM was tested for reliability of repeat measurements at 3 months intervals (total 6 months from baseline), typical error values were slightly higher (not exceeding 5°). Similarly, typical error values for Head-neck angle were 4° for same day measurements, but higher, reaching up to maximum 8°, for repeat measurements at 3 weeks.

The effects of age, gender and clinical condition on composite active cervical ROM showed that within a normal population, for both genders, a systematic change in cervical ROM was noted with the rate of range of motion loss varying between 3° to 5° per decade from age 20 to 80 years. Differences in composite active cervical ROM between a cervical radiculopathy group and matched controls measurements suggested that flexion and extension range of motion were more likely reduced in the CR cohort. Similarly, patients with CR had systematically decreased radiographic sagittal flexion-extension motion of the cervical spine (C2- 7) compared to an asymptomatic cohort.

At baseline, the two treatment groups were comparable for age, gender, BMI, marital status, duration of symptoms (in weeks) and co-morbidities, radiographic segmental curvature (C2-7) as well as head-neck angle measurements whilst the surgery group patients showed more severity with higher levels of pain and disability and neurological deficits. Simultaneously, the surgery group also demonstrated more radiological segmental flexion-extension motion and composite active cervical ROM when compared to the conservative group.

Outcome at 12 months showed a statistically significant improvement in both groups for neck pain, arm pain and disability measures. The surgery group with higher baseline scores demonstrated a larger reduction in pain scores than the conservative group. For repeat measurements following intervention, the conservative group demonstrated a systematic pattern suggesting improvements for radiographic sagittal segmental curvature and flexion-extension motion values and composite range of motion in all directions. However, this consistency for the same variables was not so in the surgical group during repeat measurements following surgery. Head – neck angle was neither sensitive nor responsive over the treatment period for either group. Both treatment groups showed improvement from baseline to final measurements for all neurological scores. Hundred percent improvement at final follow-up was not achieved for any neurological sign in either group.

Significant bivariate correlations were consistent in establishing a negative relationship between radiographical sagittal segmental curvature values at symptomatic levels and arm pain scores, between composite active cervical ROM and pain and disability measures and between radiological segmental flexion-extension motion at the diagnosed symptomatic level/s and final neck pain scores. This implies that reduced radiographic curvature and flexion-extension motion as well as composite range of motion are correlated with increased pain and disability or vice-versa.

Further, to test the principal hypothesis, the combination of baseline factors that predicted good clinical outcomes at different time points in Indian CR patients, treated conservatively and surgically were:

Conservative (3 months): Age < 40 years, BMI <24.4, No recent lifestyle changes, Duration of symptoms ≥ 33 weeks, NPAD factor 1 < 18, Neck flexion < 40°, Number of previous episodes <2. Three of the seven predictors generated an 8.54 fold increase [likelihood ratio 95% Confidence Interval (CI) 4.17 to 17.48] for the individual to be a responder. With three predictors, post-test probability of success increased to 82% from a pre-test probability of success of 35%.

Conservative (12 months): Education level ≥ post graduate, PTM C2-7 ≥ 11°, PTM (symptomatic level) ≥ 2.5°, Rotation (right) > 55°. Three of the four predictors generated a 9.8 fold increase (likelihood ratio 95% CI 3.3 to 29.8) for the individual to be a responder, with a post-test probability of success at 93%.

Surgery (3 months): Age < 40 years, Head neck angle < 40°, NPAD scores < 55. Two of the three predictors generated a positive likelihood ratio of 10.15, which is a 10 fold increase (likelihood ratio 95% CI 3.4 to 30.7) for the individual to be a responder, increasing the post-test probability of success from 31% to 82%.

Surgery (12 months): Duration of symptoms ≥ 33 weeks, NPAD scores < 55, Neck flexion < 40°, Rotation (right) > 55°. Two of the four predictors generated a 16-fold increase (likelihood ratio 95% CI 2.3 to 112) for the individual to be a responder and the post test probability of success increased to 94% from a pre-test probability of success at 50%.

Conclusion

In conclusion, this study was able to provide original and long-term assessments of cervical spine movement characteristics as well as translating the primary outcome into Hindi. The clinical finding was able to identify predictor clusters that provide level IV evidence of predicting outcomes at different timelines for cervical radiculopathy for both conservative and surgically treated patients. The use of these predictors in future studies may help in decision making for the appropriate type of treatment and expected outcome in CR patients.

STATEMENT OF ORIGINALITY

This thesis is presented for the degree of Doctor of Philosophy at the Curtin University of Technology. The research project was undertaken between 2002 and 2007 at Belle Vue Clinic, Kolkata and Bombay Hospital, Mumbai.

The research project was developed in association with my supervisors, Associate Professor, Garry T Allison and Dr Steve Edmondston who have been involved in editing the thesis and associated publications.

I have independently collected and processed data, performed analysis, and compiled this thesis and its associated publications.

I declare that all the material presented in this thesis is original, apart from work which is acknowledged from other sources within the text.

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DEDICATION

To Shiv

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PUBLICATIONS AND PRESENTATIONS ARISING FROM THIS THESIS

JOURNAL PUBLICATIONS

Agarwal S, Allison GT, Singer KP 2005 Validation of the Spin-T Goniometer – A cervical range of motion device. **J Manip Physiol Ther** 28(8): 604-9

Agarwal S, Allison GT, Agarwal A, et al. 2006 Reliability and validity of the Hindi version of the Neck Pain and Disability Scale in cervical radiculopathy patients. **Disabil Rehabil** 28(22): 1405-12

Agarwal S, Allison GT, Singer KP 2005 Evaluation of cervical range of motion in a cervical radiculopathy patient group and a matched control group using the Spin-T Goniometer. **Journal of Musculoskeletal Research** 9(2): 93-101

Agarwal S, Allison GT, Singer KP 2005 Reliability of the Spin-T cervical Goniometer in measuring cervical range of motion in an asymptomatic Indian population. **J Manip Physiol Ther** 28(7): 487-92

CONFERENCE PRESENTATIONS

Agarwal S, Allison GT, Singer KP (2008). Segmental radiographic hypomobility- role in degenerative cervical radiculopathy. **46th annual conference of the Indian Association of Physiotherapists**, Dehradun, India.

Agarwal S, Allison GT, Agarwal A, Singer KP (2006). Reliability and validity of the Hindi version of the Neck Pain and Disability Scale in cervical radiculopathy patients. **In Intercommat**, New Delhi, India.

Agarwal S, Allison GT, Singer KP (2004). Evaluation of cervical range of motion in a cervical radiculopathy patient group and a matched control group using the Spin-T goniometer. **Neptacon (annual conference of the Nepal Physiotherapy Association)**, Kathmandu, Nepal.

Agarwal S, Allison GT, Singer KP (2003). Validation of the Spin-T goniometer – a cervical range of motion device. **41st annual conference of the Indian Association of Physiotherapists,** Mumbai, India

AWARDS

CP Nair Oration award for professional contribution and excellence in research and academics by the IAP, 2009 at the **4th WCPT -AWP and IAP Congress**, Mumbai, 25th January, 2009. Oration topic 'Outcome measures in cervical radiculopathy research.'

Agarwal S (2008). Segmental radiographic hypomobility- role in degenerative cervical radiculopathy. Senior category Science Paper Award (2nd). In **46th annual conference of the Indian Association of Physiotherapists**, Dehradun, India

Agarwal S (2003). Validation of the Spin-T goniometer – a cervical range of motion device. Senior category Science Paper Award (1st). In **41st annual conference of the Indian Association of Physiotherapists**, Mumbai, India

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LIST OF ABBREVIATIONS AND TERMS

CR – cervical radiculopathy
C- cervical
T - thoracic
TENS – transcutaneous electrical nerve stimulation
CSRS – Cervical Spine Research Society
MRI – magnetic resonance imaging
CT – computerised axial tomography
VAS – visual analog scale
NPRS – numerical pain rating scale
NDI- neck disability index
PSFS- patient specific functional scale
ADL- activities of daily living
DRAM- distress and risk assessment management
ROM – range of motion
ACD/F – anterior cervical discectomy/fusion
BMI – body mass index
NPAD – neck pain and disability
LR+ - positive likelihood ratio
LR - negative likelihood ratio
Sn – sensitivity
Sp – specificity
DRI- disability rating index
CPR- clinical prediction rule
PLL- posterior longitudinal ligament
ALL- anterior longitudinal ligament
PTM- posterior tangent method
PLL – posterior longitudinal ligament
ALL- anterior longitudinal ligament
ULTT - upper limb tension test
VAS – visual analogue scale
RCT – randomised controlled trials
DTR- deep tendon reflex
NT – not testable
EMG – electromyography
NCV – nerve conduction velocity
OPD – out-patients department
Sym – symptomatic
Flex – flexion
Ext - extension
NS – not significant

CHAPTER 1

INTRODUCTION

1.0 Introduction

Cervical spondylotic radiculopathy occurs when one or more degenerative segments cause impingement of the exiting nerve root in the intervertebral foramen. Cervical radiculopathy (CR) presents as neck and upper limb pain causing significant distress and anxiety to the patient (Persson et al. 1997a; Persson et al. 1997b; Sampath et al. 1999; Persson and Lilja 2001; Peolsson et al. 2006b). The resultant levels of pain and disability in cervical radiculopathy are very high and therefore it represents a significant clinical population (Saal et al. 1996; Sampath et al. 1999; Wainner et al. 2003; Peolsson et al. 2006b).

Epidemiology

Limited epidemiological data on CR is available. Although CR does not have a high incidence (0.8 case per 1000 persons) (Radhakrishnan et al. 1994) or prevalence rate (3.5 per 1000) (Salemi et al. 1996), the associated pain and disability pose a challenge to any clinician attempting to provide relief to the patient. It is the treatment of this condition which generates interest and forms a basis for clinical research and the foundation of this thesis.

Treatment of Cervical Radiculopathy

Cervical radiculopathy can be managed conservatively (Moeti and Marchetti 2001; Constantoyannis et al. 2002; Waldrop 2006; Cleland et al. 2007a) or surgically (Smith and Robinson 1958; Bohlman and Emery 1988; Vavruch et al. 2002). Conservative treatment options include non-steroidal anti-inflammatory drugs and muscle relaxants (Saal et al. 1996; Murphy et al. 2006), corticosteroids (Murphy et al. 2006) and a range of collars (hard, soft, Philadelphia) (British Association of Physical Medicine 1966; Saal et al. 1996; Persson and Lilja 2001). Physiotherapy plays a major part in conservative management approaches. These may include various types of cervical traction that can be delivered in different ways (Saal et al. 1996; Olivero and Dulebohn 2002; Murphy et al. 2006); manual traction (Persson and Lilja 2001), mechanical traction from overhead (Constantoyannis et al. 2002) or in the supine position (British Association of Physical Medicine 1966). Exercises in a wide range of formats have been used in studies using a non-surgical treatment approach in CR patients (Saal et al. 1996; Persson and Lilja 2001; Murphy et al. 2006). Posture and ergonomic advice form an important component (Saal et al. 1996; Persson et al. 1997a). Passive therapies for pain relief include transcutaneous electrical nerve stimulation (TENS) (Saal et al. 1996; Persson and Lilja 2001), cold (Valtonen and Kiuru 1970; BelEliyahu 1996; Saal et al. 1996), superficial heat (Persson and Lilja 2001; Murphy et al. 2006), deep heat (Valtonen and Kiuru 1970; Honet and Puri 1976) and ultrasound (Persson and Lilja 2001). Medical interventions such as periradicular/epidural corticosteroid injections which have been shown to provide significant pain relief (Saal et al. 1996; Vallee et al. 2001; Murphy et al. 2006), are further conservative management options.

Surgical procedures for CR can be divided into anterior and posterior approaches. Anterior procedures are currently more popular because they avoid exposure of the spinal canal and involve less soft tissue damage (Smith and Robinson 1958; Fraser 1995). Surgical procedures can vary according to the type of graft used (material and shape of the graft), and the number of cervical segment involved in the surgery (Hacker et al. 2000; Vavruch et al. 2002). Few patients with CR require surgery at more than two levels of the cervical spine. Higher non-union rates have been reported for multi-level discectomy and fusion compared to single levels (Emery et al. 1997; Bolesta et al. 2000). Non-union rates are often a measure of a successful operating technique but are not necessarily a reflection of the clinical outcome for the patient with CR.

Outcome of treatment for Cervical Radiculopathy

The different methods of conservative and surgical management, makes the evaluation of clinical outcomes from single or multi-modal interventions (surgery or conservative) (Radhakrishnan et al. 1994; Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001; Cleland et al. 2005; Peolsson et al. 2006b) difficult to evaluate. A review of trials that include conservative and surgical interventions suggests that the outcomes at one year of the different management approaches are not significantly different (Persson et al. 1997a; Persson and Lilja 2001). The strength of the evidence supporting the inference “no differences in clinical outcomes following conservative or surgical interventions” needs careful deliberation. Of the limited studies reported in the literature, low sample size in each group and the large number of outcome variables may contribute to inferential statistical errors (type I & II). Similarly, there are conflicting results from studies examining outcomes from the same treatment approaches. For example, a Cervical Spine Research Society (CSRS) multicenter clinical trial of CR patients (non-randomised) (Sampath et al. 1999) reported patient satisfaction and neurological improvement as being higher in the surgery group. In contrast, Heckmann et al (1999), demonstrated that more patients in the conservative group had pain relief compared to the surgical group at the 5.5 year follow-up. The limited range of outcome measures and retrospective design are limitations of this study. The results of a large population based epidemiologic study (Radhakrishnan et al. 1994) indicated that 90% patients improved with conservative treatment, at a median follow-up of 4.9 years. Honet and Puri (1976) found 70% patients exhibited good or excellent outcomes following conservative management at a 2 year follow-up. Improvement between the 2 and 5 year follow-up periods suggests that there may be an influence of spontaneous recovery of CR (Spurling and Segerberg 1953; Vinas et al. 2001).

Overall, the results of intervention studies show definite but varying improvement for both surgical and conservative interventions. However, many questions remain regarding treatment outcomes, and the ability to predict which individuals are more likely to respond to the different approaches to management. To date few studies have examined the factors that may influence the response to conservative or surgical management of CR.

Outcome and prognostic measures

The focus in current healthcare is to provide guidelines and rationale for the type and duration of treatment. In evidence based practice, there are four domains of investigation. The most common form of evidence based research is treatment efficacy. A less common area of investigation for evidence based practice is prognostic studies. Factors that define the success or failure of an intervention are outcome measures, which provide clinicians an opportunity to measure changes in clinical status. Prognostic factors that can be used to predict the treatment outcome in an objective manner are often not studied. Both outcome and prognostic measures should ideally be reliable, valid, practical, and cost effective.

Predictive studies

Although there are few studies of high quality that report clinical outcomes for CR, only four studies have examined the baseline factors that may be prognostic of patients with CR. Important methodological factors in prognostic studies include clear diagnostic criteria, adequate sample size, an adequate follow-up period, use of reliable and valid outcome measures. It has also been recommended that prognostic and risk factors should be expressed in terms of the likelihood of the outcome occurring (Laupacis et al. 1994). These factors have been analysed in four published studies, which have attempted to determine the baseline variables that may predict a successful outcome in patients with CR (Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b; Cleland et al. 2007a).

Cleland et al (2007a) chose the diagnostic test item cluster (Wainner et al. 2003) to identify patients with CR. Wainner et al (2003) had relied on standardised electrophysiological examination as a reference criterion for diagnosis of CR. The diagnostic value and accuracy of neurophysiolgical studies is debatable (van der Bent et al. 1995; Nardin et al. 1999; Slipman et al. 2005) and the utility is directed more towards exclusion of conditions such as median or ulnar nerve entrapment, that may share common clinical signs and symptoms with radicular disorders (Fisher 2002). The diagnostic criteria for CR adopted by Peolsson and co-workers (2003; 2004; 2006b) was based on a clinical neurological assessment and verified by magnetic resonance imaging (MRI). MRI sagittal, oblique and axial images are ideal for viewing disc protrusions and cervical radiculopathy (Brown et al. 1988; Wilson et al. 1991), whilst T2 weighted images provide differentiation between herniated disc material and osteophytes. Although MRI are associated with false positive results in asymptomatic individuals (Boden et al. 1990; van Rijn et al. 2006), MRI provides valid results when interpreted in conjunction with the patient’s history and clinical presentation (Shah and Rajshekhar 2004).

A second criterion that is important in developing prognostic studies is the duration of the follow-up period of assessment, and the number patients lost to follow-up. Peolsson et al. (2006b) reported a 33% dropout at 2 to 3 years, where the initial sample size was 34 patients. In contrast, Cleland et al (2007a) reported a 5% dropout from 101 patients, where the follow-up period was only 1 month. The other two studies (Peolsson et al. 2003; Peolsson et al. 2004) had 48% and 28% drop-out at the two years follow-up. In conclusion, there is limited inference that may be drawn from previous prognostic studies, as the long-term follow-up has been associated with a high drop-outs rate Peolsson et al (2003; 2004; 2006b), while those with a low number of drop-outs have had a short duration of follow-up (Cleland et al. 2007a). This is a significant deficiency in this area of clinical research.

Another important issue in prognostic studies is the reliability and validity of outcome measures used in previous research. Prognostic studies should include outcome measures (with established reliability and validity) evaluated in previous research. A wide range of outcome measures have been used in previous studies (Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b; Cleland et al. 2007a). These include socio-demographics (age, gender, smoking, family situation, education level, type of work, work status), symptom analysis [pain intensity – Visual Analog Scale (VAS), Numerical Pain Rating Scale (NPRS), pain distribution], duration of current episode, number of previous episodes, dominant arm affected, use of analgesics, presence of low back pain; radiological measures (disc height*, fusion status, segmental lordosis / kyphosis *), neck pain-related disability [Neck Disability Index (NDI), Patient Specific Functional Scale (PSFS), ADL*], psychological factors [distress and risk assessment management (DRAM)]; impairments (cervical range of motion, grip strength); general health (VAS), and patient satisfaction (expectations of treatment*, symptom satisfaction), global rating of change, posture assessment*, cervical and thoracic range of motion (ROM) assessment*, neurological assessments*, muscle strength of the deep cervical flexors* and scapulothoracic muscles*. These variables were analysed for prediction of outcome. Unfortunately, not all outcome measures listed have been examined for reliability (*) which makes the inclusion of these difficult in future studies, without further evaluation.

The methods of analysis used in prognostic studies are another criteria to review in these studies. Peolsson et al (2006b) used a Spearman rank correlation analysis between baseline variables (independent variable) and pain, disability and general heath (dependent variables) at last follow-up, followed by a forward step-wise regression analysis to identify the most important predictors. Cleland et al (2007a) used the NDI, PSFS, NPRS and the Global Rating of Change scores to determine a successful outcome. Patients were dichotomised into 'successful' or 'unsuccessful' based on scores greater or less than the minimal clinical important change (MCIC). Univariate analyses were used to identify potential predicting variables which were significantly different ($p < 0.10$) between the 'successful' and 'unsuccessful' groups.

These variables were entered into a stepwise logistic regression model to determine the most accurate set of variables for predicting a successful outcome. The likelihood ratio, sensitivity and specificity of these variables were calculated. The positive likelihood ratio (LR+) indicates how much a given prediction model could raise the probability of obtaining the outcome (Sackett 1992) as compared to a step wise regression analysis where the regression coefficient (R^2) indicates the percentage of the dependent variable explained by an independent variable measured at baseline examination. The Clinical Prediction Rule (CPR) used by (Cleland et al. 2007a) may help improve clinical decision making by matching a treatment to a sub-group of patients, using variables which predict the outcome

1.1 Statement of the Problem

Concern about escalating health costs, impact of this cost on the healthcare system, number of work-days lost, and related disability has made it imperative for health care professionals to investigate prognostic factors for specific disorders (Kjellman et al. 2002; Wainner et al. 2003; Tseng et al. 2006; Waldrop 2006; Raney et al. 2009). The concern of many patients about their treatment relates to the prognosis of the disorder and the impact of possible treatments. In order to provide patients with more information, clinicians should be aware of factors that can affect treatment outcome. To date, there is limited information on factors that can predict outcome for patients with cervical radiculopathy, and how this may be modified by treatment. Methodological issues in previous predictive literature include high patient drop-out rate Peolsson et al (2003; 2004; 2006b), low duration follow-up (Cleland et al. 2007a), less than optimal statistical analysis (Peolsson et al. 2006b) and reliability of outcome measures not being completely established (Peolsson et al. 2003; Peolsson et al. 2004; Cleland et al. 2007a). A further issue is the low prediction value (R^2 = 0.05) of key variables (Peolsson et al. 2004) which results in poor clinical utility. It also indicates that the un-explained variance in such studies may be indicative of the necessity to include other variables for prediction. Planning a predictive study should include correlated variables along with the variables of interest (Altman 2001).

It is important to note that all the studies by Peolsson et al (2003, 2004, 2006b) examined outcomes of a surgical intervention cohort. Furthermore, the post hoc predictive models used in these studies have not been validated in prospective cohort analyses. Cleland et al (2007a) presented a prognostic study but so far the model has not been validated in further studies, and included only patients who were managed conservatively. No predictive model study has examined both surgical and conservatively treated patient groups and examined the same prognostic factors. In order to evaluate appropriate and effective treatment outcomes in patients with cervical radiculopathy, both treatment options should be evaluated in a single study using the same outcome variables in the prediction analysis.

1.2 The significance of the study

This longitudinal cohort study of patients with medically diagnosed CR will provide new information in relation to the prognostic factors for surgical and conservative management.

It is significant that this study will be conducted in India as cervical radiculopathy and management outcomes have not been examined in this population. Previous studies in this population have examined neck pain and related conservative and surgical management (Deopujari and Bhagwati 1996; Sambasivan 1996) but clinical research trials have not been adequately reported. The cost, risks and loss of workdays associated with anterior cervical fusion surgery are high, and difficult to sustain in a country like India. Therefore, a study undertaken in India to evaluate the utility of clinical, functional and radiological measures to predict the management outcome for patients with cervical radiculopathy will provide important new information about this patient group.

To date, no previous studies have concurrently examined both surgically and conservatively management patient cohorts using the same outcome measures. This will be the first study to be able to compare outcomes and prognostic factors between these different methods of treatment for cervical radiculopathy.

The research makes a further significant contribution by comparing methods of measuring cervical range of motion and segmental mobility.

Finally, the study also makes a significant contribution to neck pain research in India by validating the Hindi translation of the Neck Pain and Disability scale, one of the primary outcome measures used to measure neck pain-related disability.

1.3 Study aims

This study will provide a unique assessment of outcomes of medically and surgically treated Indian patients who have been diagnosed with cervical radiculopathy. These patients will have multiple domains of assessments on repeated occasions with up to average 12 months follow-up. Clinical outcomes will be made for socio-demographic factors, lifestyle factors, pain measures, cervical range of motion, postural assessments, and radiological segmental assessments. The principal aim will be to determine if clinical, radiological and functional variables of CR patients at baseline will predict clinical outcome at one year, following either conservative or surgical management. In order to fulfil the primary aim of this study, this study will determine:

The intra-tester reliability of measuring instruments to be used in this study. These include a cervical range of motion goniometer (the Spin-T goniometer), radiological measure of sagittal segmental flexion-extension motion (Penning's method), radiological measure of sagittal segmental curvature (Posterior Tangent Method) and posture measurement (Head – neck angle).

The reliability and validity of the NPAD, translated into Hindi, in a CR patient cohort.

The reliability and validity of the Spin- T goniometer as a measuring instrument for cervical ROM.

Differences between an asymptomatic group and a CR patient group in active cervical range of motion in all three planes as well as in segmental flexion-extension motion.

The effect of age, gender and time on active cervical ROM in an asymptomatic population.

Differences in composite sagittal plane active cervical ROM measurements with segmental radiographic flexion-extension motion of the cervical spine in the same plane.

The association between clinical outcome measures at one year with baseline measures of pain, disability, depression, radiographic sagittal cervical segmental curvature and flexion-extension motion, head neck angle, active cervical range of motion), patient socio-demographics and lifestyle details.

Overall, the research thesis will contribute to the limited knowledge in the clinical, functional and radiological assessment of CR and in the management of CR.

CHAPTER 2

REVIEW OF LITERATURE OF CERVICAL RADICULOPATHY: BACKGROUND, TREATMENT OPTIONS AND OUTCOME MEASURES

2.0 Introduction

The review of the normal cervical spine anatomy is presented prior to discussing changes associated with cervical spine degeneration. Degenerative changes in the cervical spine are important in the development of CR, which literally means ‘pathology of the cervical nerve root’. The severe pain and disability associated with CR provide the motivation for new research into the management of this disorder. The literature review examines the current methods of assessment and treatment of CR. The importance of measures which can predict the clinical outcome of CR is highlighted given the range of measures used to evaluated treatment outcome described in literature. The literature review concludes with an appraisal of measures which will be used in this research. The selected outcome measures, their associations with each other, and their ability to predict clinical outcome at a one year follow-up formed the hypotheses of this research.

2.1 The anatomy of the normal cervical spine

The curvature of the cervical spine, viewed in the sagittal plane is lordotic, and in the frontal plane appears straight or mildly tilted to one side (Cailliet 1991b). The cervical spine supports the head and allows controlled and specific movements.

The cervical spine consists of seven cervical vertebrae (C1 - C7), subdivided into the occipito-atlanto-axial complex (C0-C1-C2), known as the upper cervical spine. The atlas (C1) and axis (C2) vertebrae are morphologically distinct. The third through the seventh (C3- C7) follow a typical morphology with minor variations (Mercer and Bogduk 2001).

A typical vertebra consists of a vertebral body anteriorly and a bony ring (neural arch) posteriorly. The posterior elements continue from the posterior surface of the vertebral body, that is at the base of the pedicle and extend laterally into the transverse process and then posteriorly towards the midline as the laminae which join at the midline to form bifid spinous processes. The transverse and the spinous processes serve as bony attachments to numerous ligaments and muscles. Projecting upwards and downwards from the junction area of the laminae and pedicle are the superior and inferior articular processes. These articulate to form the zygapophyseal joints (Penning 1989; Panjabi et al. 1991; Bland 1998).

2.1.0 The cervical vertebral body

The vertebral body is roughly a cylindrical mass of cancellous bone, contained in a thin shell of cortical bone. Its superior and inferior surfaces, slightly concave, are the vertebral endplates (White and Panjabi 1990b). The presence of uncinate process, a postero-lateral bony projection from the sides of the vertebral end-plate, deepens the concave superior surface of a vertebral body in the coronal plane. A prominent inferior lip projects from the postero-inferior surface of the vertebral body which articulates with the uncinate process of the subjacent vertebral body, forming the joints of Luschka or the uncovertebral joints.

2.1.1 The cervical intervertebral disc

Each vertebral body is separated from the subjacent vertebral body by a fibrocartilaginous intervertebral disc, caudal to the C2 level. In a normal population with no evidence of disc degeneration, the discs contribute to 22% of the cervical spine length and the cervical disc height to vertebral body height is at a ratio 2:5 (Kapandji 1974). Each disc consists of a central nucleus pulposus and surrounding it the annular fibrosus.

As per cadaveric studies the nucleus pulposus present at birth becomes indistinct by the fourth decade (Taylor and Twomey 1994; Bland 1998). The fibrocartilaginous structure of the cervical disc makes cervical disc protrusion unusual, other than in young individual subjected to significant trauma. Horizontal clefts which extend from the uncovertebral joints transect the posterior annulus and the nucleus and give rise to bipartite discs (Tondury 1958; Bland 1994; Mercer and Bogduk 1999). However, one of the established causes of radiculopathy is cervical nuclear disc herniation (Saal et al. 1996; Heckmann et al. 1999; Constantoyannis et al. 2002; Goffin et al. 2003), diagnosed using MRI (Magnetic Resonance Imaging) (Ashkan et al. 2002; Shah and Rajshekhar 2004).

The disc is bound superiorly and inferiorly by the hyaline cartilage end plates of the vertebral bodies. Collagen fibres join the vertebral end plate with the annulus fibrosus and small perforations in the end plate permit vascular communications between the discs and vertebral bodies. The annulus is thick anteriorly and progressively thinner towards the uncinate processes and posteriorly (Mercer and Bogduk 1999). When viewed from the top, the annulus almost appears crescentic (Mercer and Bogduk 1999; Tonetti et al. 2005). The most superficial fibres of the annulus blend with the anterior and posterior longitudinal ligaments.

The intervertebral discs allow movements of vertebral bodies and permit weight bearing and equal distribution of load.

2.1.2 The cervical spine curvature

Viewed in the sagittal plane, normal lordosis in the cervical spine results from wedge shaped inter-vertebral discs that are thicker anteriorly than posteriorly (DePalma and Rothman 1970). Although cervical lordosis extends from superior C1 vertebral body to inferior T1 vertebral body, sagittal cervical spine curvature has been traditionally measured from C2- C7 levels using a variety of methods (Williams and Warwick 1973). Using a geometric model Harrison et al (1996), estimated a mean lordotic angle from C2 to C7 of 34° (range 16.5° to 66°) in the adult population.

Cervical spine segmental curvature values vary in an asymptomatic population. Penning (1978) provided radiological evidence that wide variation exists in cervical spine postures in the sagittal plane in subjects who had never sustained an injury to the cervical spine. Reasons for such differences may include individual genetic composition, body type, activity thoracic and cervical muscles, occupational demands, cultural and environmental factors, nutrition and emotional influences (Janda 1988; Penning 1988).

2.1.3 The zygapophyseal joints

The cervical zygapophyseal joints or facet joints are formed by the articulation of the inferior articular process of one cervical vertebra with the ipsilateral superior articular process of the vertebra below. The articular facets may be round or oval, and there is often right-left asymmetry (Pal et al. 2001). As typical synovial joints, the articular surfaces are lined by articular cartilage, synovial folds about the periphery and enclosed by a joint capsule. The synovial folds are liable to project into the joints, and have a tendency to proliferate in a fibrous like pannus in diseases of the zygapophyseal joints (Bland 1994).

The capsule consists of well-oriented collagen and elastic fibres. The elastic fibres of the medial aspect are oriented like the ligamentum flavum, projecting vertically from one articular process to the other and may join with the ligamentum flavum. Antero-laterally, the elastic fibres are less concentrated, are oriented obliquely in the transverse and sagittal planes and appear to provide an important barrier to the posterior to anterior shear (Tonetti et al. 2005). In the neutral position, the capsule of the facet joint is lax allowing for the large range of gliding that occurs between the articular facets during all movements. At the extremes of range, the capsule is taut and functions as a stabilising or resisting ligament and has been referred to as a capsular ligament (Oatis 2001).

2.1.4 Anatomy of the spinal canal

Ligaments play a very important role in cervical spine stability and function. The posterior longitudinal ligament (PLL) in the cervical spine attaches and descends from the posterior surface of the vertebral body, anterior to the spinal cord. The anterior longitudinal ligament (ALL) descends along the anterior surface of the vertebral body (Cailliet 1991b). The PLL is thicker and more developed in the cervical spine than in the thoracic or lumbar spines (Bland 1998). The ALL is attached firmly to the vertebral bodies, but only loosely at the disc area. Conversely, the PLL is firmly attached to the disc but loosely to the vertebral body surface. This anatomical fact may explain why osteophytes are larger and more common anteriorly than posteriorly, considering there is minimal resistance anteriorly (Bland 1998; Mercer and Bogduk 1999). The ligamentum flavum extends from the antero-inferior border of the lamina above to the postero-superior border of the lamina below, is discontinuous in the midline, and laterally merges with the medial capsule of the facet joints. Also called the yellow ligament, it represents pure elastic tissue when young, with increased amounts of fibrous tissue with aging (White and Panjabi 1990c).

The osseous wall of the spinal canal of the cervical spine at each level is formed by the posterior cortex of the vertebral body, and the neural arch, defined by the pedicles and laminae. The soft tissue structures contributing to the boundary are the annulus fibrosus, PLL and paired ligamentum flavum (Heller 1992).

The average antero- posterior dimension of the spinal cord in the sub-axial cervical spine is 10cm and that of the bony spinal canal 17cm, providing ample space for the neural elements (Heller 1992). It is also known that the spinal cord volume and the spinal canal area are variable amongst individuals. A wide spinal cord and a small bony canal is easily predisposed to spinal cord compromise in degenerative changes of the spine (Bland 1998).

Race, gender and body habitus may contribute to variations in spinal canal dimensions (Panjabi et al. 1991; Tan et al. 2004). Linear, angular and area dimensions were quantitatively smaller in Singapore Chinese cadavers (Tan et al. 2004) compared to Caucasian populations (Panjabi et al. 1991). Similar differences in cervical vertebral dimensions between races and gender have been described (Grave et al. 1999; Lim and Wong 2004). This has an implication in the choice of surgical hardware, which is dependent on depth and height of the recipient cervical spine site (Wood and Hanley 1992).

2.1.5 The intervertebral neural foramen

The neural foramen in the cervical spine extends obliquely anteriorly and inferiorly from the spinal canal. The boundaries of the foramen superiorly and inferiorly are the pedicles, posteriorly the medial aspect of the facet joint and anteriorly the postero-lateral portion of the disc, the uncovertebral joints and the vertebral artery (Heller 1992; Tanaka et al. 2000). The foramen shape resembles a funnel, divided into medial and lateral zones, with the medial zone narrow and the lateral zone wide (Tanaka et al. 2000). Paired spinal nerves formed by the union of the dorsal and ventral roots exit through the neural foramina at each level. The narrow medial zone predisposes to nerve root compression subject to pathology.

2.1.6 The nerve roots

Each spinal nerve is assigned the number of the vertebra whose pedicle forms the inferior wall of the foramina being passed through (Heller 1992). At the exit of the foramen, each nerve occupies one third to one fourth of the foramen diameter, and bifurcates into dorsal and ventral branches (Tanaka et al. 2000). The dorsal branch has a pre-dominant sensory role and innervates the para-cervical musculature, facet joints and has a cutaneous representation in the upper limbs whereas the ventral branch provides segmental innervations to muscle groups in the para-cervical region and the upper limbs (Bogduk 1994). Tanaka et al (2000) demonstrated that the ventral branch lies in a more caudal position than the dorsal branch within the foramen and compression of the nerve root and symptoms produced will depend upon the specific anatomical site around the nerve root producing the compression.

From cranial to caudal, the nerve roots emanating from the neural foramen of the cervical spine are angled downwards and laterally to reach their respective inter-vertebral foramen (Tanaka et al. 2000). This occurs due to the rapid growth of the spine at a faster rate than the cord, which may also cause a physiological traction to the cord and the nerve roots (Bland 1994). Because of this obliquity, the nerve roots can be compressed at one disc above that of the corresponding intervertebral foramen. A high incidence of intra-dural connections among the dorsal nerve rootlets of C5, C6 and C7 were also found which is considered a normal variation (Tanaka et al. 2000). In degenerative spondylosis, loss of disc height may affect the anatomic relationship between inter-vertebral disc and neural roots in the foramen (Tanaka et al. 2000).

2.2 Cervical spine movements

The classic spinal motions are flexion, extension, lateral rotation and lateral flexion. Motion in the cervical spine may be divided into the upper cervical spine (occiput to C2) and the lower cervical spine (C3 to T1). Movements of the upper cervical spine include flexion-extension and lateral rotation with minimal lateral flexion whereas in the lower cervical spine all four movements occur (White and Panjabi 1990b). Movements of the complex series of multi-axial joints in the cervical spine are determined by the orientation of the facets, passive tension of the ligaments, muscles, joint capsule and fibres of the annulus fibrosus (White and Panjabi 1990b) and controlled by numerous segmental and multi-segmental muscles (Youdas et al. 1991).

Cervical muscles can be broadly classified based on function as anterior (flexors) and posterior (extensors) muscles. Muscles in both groups may attach obliquely and on independent contraction of one side are capable of lateral movements. A clinical model (White and Panjabi 1990b; Vernon et al. 1992; Watson and Trott

1993), classifies spinal muscles as superficial and deep, where the superficial muscles function as mobilisers and the deep muscles function as stabilisers of the spine. The deep muscles originate and insert segmentally (for example: Rectus capitis anterior, Rectus capitis lateralis, Longus colli, Interspinalis, Multifidus). Superficial muscles include the Sternocleidomastoid, Scalene and Trapezius.

2.3 Cervical spondylotic radiculopathy

2.3.0 Incidence and prevalence

The incidence of a disorder is the number of new cases which occur during a specific period of time whereas prevalence is the number of cases present at any one time (normally one year) (Gore et al. 1986). Thus, incidence conveys information about the risk of developing the disorder, whereas prevalence indicates how widespread the disorder is in a specific population. A population based study conducted in Minnesota USA during 1976 to 1990, reported an annual incidence rate of CR of 107.3 per 100,000 men (1 case per 1000 men) and 63.5 per 100,000 women (0.6 case per 1000 women) with a peak incidence at 50-54 years of age (Radhakrishnan et al 1994). An annual prevalence of 3.5 per 1000, with a peak at age 50-59 years, was reported from a door to door survey in Italy (Salemi et al, 1996). Despite the fact that CR does not have a high incidence or prevalence rate, the resultant pain and disability associated with this condition forms an important basis for continued clinical research.

Most epidemiological surveys and clinical studies of CR have been conducted in Western countries. Since there is no available information about this disorder in India, the epidemiology of CR in that country is largely unknown. This provides a stimulus for conducting new studies of CR in India.

2.3.1 Aetiology

Radiculopathy refers to signs and symptoms of nerve root compression. This may involve one or more nerve roots and be present unilaterally or bilaterally. Any of the hard or soft tissues that define the spinal canal or intervertebral foramen can contribute to the cluster of symptoms associated with radiculopathy (Connell and Wiesel 1992).

Nuclear disc herniation is classified as ‘soft disc’ whereas ‘hard disc’ refers to an osteophyte within the foramen. The nucleus may protrude through weak points in the annulus fibrosus and this may be posterior, intra-foraminal, lateral or anterior (Connell and Wiesel 1992). Postero-lateral protrusion, near the entrance zone of the foramen, is due to the relative inadequacy of the annulus (Mercer and Bogduk 1999) and the PLL laterally (Heller 1992). Degenerative changes in the disc cause loss of disc height, resulting in reduction in size of the neural foramen, making the emerging nerve roots more vulnerable to compression. Degeneration combined with instability in the spine can result in hypertrophy of the supporting ligaments and formation of osteophytes (Sampath et al. 1999). Osteophyte arising from the posterior vertebral body, a prolapsed fibro-cartilaginous annulus or uncovertebral osteophytes can compress the nerve root anteriorly. Similarly, osteophytes arising from the superior articular process, hypertrophy of the ligamentum flavum and the peri-radicular fibrous tissue affect the nerve root posteriorly (Tanaka et al. 2000). Although cadaveric and population studies (Taylor and Twomey 1994) indicate that disc protrusion is more common in individuals less than 40 years of age, cervical disc protrusion in people older than 40 years has been reported in clinical studies. (Heckmann et al. 1999; Hacker et al. 2000)

Nerve root irritation in the cervical spine may be acute, sub-acute or chronic (Connell and Wiesel 1992). Acute radicular symptoms more commonly have a traumatic origin. Sub-acute radiculopathy is more common in patients with pre-existing cervical spondylosis and chronic radiculopathy is a progression of acute or sub acute-radiculopathy which has not responded to conservative management. Based on the nerve root level and anatomical structures involved, the presenting signs and symptoms of CR vary.

2.3.2 Clinical findings and symptoms

Cervical radiculopathy normally occurs in people ranging in age from 24 – 65 years (Grob et al. 2001; Persson and Lilja 2001), although it is more common between 40 - 60 years (Radhakrishnan et al. 1994; Salemi et al. 1996). Gender bias towards male has been described in some clinical studies (Yoss et al. 1957; Radhakrishnan et al. 1994; Heckmann et al. 1999) although more recent studies show equal gender distribution (Vavruch et al. 2002) or a higher prevalence females (Cleland et al. 2007a).

Cervical radicular pain presents as excruciating unremitting pain, predominantly in the arm and hand. Neck pain may not necessarily be present or can occur with a variable level of severity. The pain is a result of mechanical pressure on the nerve root exerted by disc protrusion, spondylotic osteophyte or both, and is associated with a local inflammatory response (Ahlgren and Garfin 1996; Autio et al. 2006).

Activities of daily living (Heckmann et al. 1999; Sampath et al. 1999) have been known to be affected due to pain in cervical radiculopathy. Disability levels have been frequently measured in previous studies (Persson and Lilja 2001; Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b).

Classical neurological deficits including sensory, motor and reflex changes are primary clinical features of CR, occurring in the regions of the arm innervated by (Radhakrishnan et al. 1994) the affected nerve root(s). However, despite the dermatomal mapping of the upper limb, considerable overlap often exists in the sensory innervations and symptom patterns of patients with CR affecting the same spinal nerve root. Sensory symptoms may not exist in the entire dermatome and sometimes do not follow a classical dermatomal distribution at all (Takeshima et al. 2002) (Table 2.0). The fact that symptoms do not follow a particular dermatomal distribution does not exclude the existence of a symptomatic nerve root (Heller 1992). The reflex and motor deficits accompanying a radiculopathy vary depending on the relative contribution of the root to the musculotendinous unit being tested (Table 2.0). Given the known variations in the brachial plexus as well as numerous intradural and extradural anastomoses between nerves, such variability is expected (Connell and Wiesel 1992).

Table 2.0 Neurological findings associated with CR

Disc Level	Root	Pain Distribution	Weakness	Sensory Loss	Reflex Loss
C4-C5	C5	Tip of shoulder, neck, anterior arm	Deltoid, biceps	Lateral upper arm	Biceps
C5-C6	C6	Neck, shoulder, medial border scapula, Lateral arm, dorsal forearm	Biceps, wrist extensors	Thumb and index finger	Biceps
C6-C7	C7	Neck, shoulder, medial border scapula, Lateral arm, dorsal forearm	Triceps, wrist flexors, finger extensors	Middle finger	Triceps
C7-T1	C8	Neck, medial border scapula, medial aspect arm and forearm	Intrinsic hand muscles	Little finger	-

Modified from (Boden et al. 1991) and (White and Panjabi 1990a)

Clinical neurological examinations are a routine component of most studies (Saal et al. 1996; Sampath et al. 1999; Wainner et al. 2003; Cleland et al. 2005), assist diagnosis (Moeti and Marchetti 2001; Vavruch et al. 2002; Waldrop 2006), and have been used to monitor change in neurological status in response to treatment (Saal et al. 1996; Heckmann et al. 1999; Grob et al. 2001). The reliability (Viikari-Juntura 1987) and validity (Viikari-Juntura et al. 1989) of clinical neurological tests has been reported with the tests showing moderate reliability (kappa coefficients = 0.40 – 0.64). Using an analysis based Clinical Prediction Rule (CPR), Wainner et al (2003) determined that Viikari Juntura et al (1989) had achieved sensitivity (Sn) and specificity (Sp) ranging from 0.59 to 0.80. Used as outcome measures by Cleland et al (2007a), none of the neurological tests emerged as predictors of treatment outcome. Consequently, clinical neurological tests form part of clinical examination aiding diagnosis, but may not necessarily be used as outcome measures or prognostic factors.

Neural provocation tests decrease or increase symptoms in the affected arm and are indicative of nerve root pathology. Some of the commonly used tests in cervical radiculopathy include the Upper Limb Tension Test (ULTT 1, 2A & B, 3) (Magee 2002), Spurling's test and the shoulder abduction test. The first two tests cause exacerbation of pain by stretching or compressing the involved nerve root, whereas a positive shoulder abduction test is characterised by reduction or elimination of symptoms. The reliability and accuracy of these tests vary in previous published literature (Viikari-Juntura 1987; Viikari-Juntura et al. 1989). The reliability of the ULTT and shoulder abduction test has been reported as being poor, while the reliability of the Spurling's test has been shown to be fair to good (Viikari-Juntura 1987). Better reliability for the Spurling's test (kappa 0.60) and the ULTT (kappa 0.76) was reported by Wainner et al. (2003). The sensitivity and specificity values of the Spurling's test was calculated as 0.36 (sensitivity), 0.96 (specificity) (Viikari-Juntura et al. 1989). Similarly, lower sensitivity 0.50 (95% CI = 0.27 to 0.73) and higher specificity 0.86 (95% CI = 0.77 to 0.94) of Spurling's test were reported by Wainner et al (2003). With a higher specificity, the Spurling's test is likely to be negative when the condition is absent (Laupacis et al. 1997). Shah and Rajshekhar (2004) reported sensitivity of 0.83 to 1.00 and specificity of 0.85 to 1.00, of Spurling's test when applied to patients with soft cervical disc protrusion.

The chronic and high level pain and disability associated with CR can lead to adoption of abnormal postures (Constantoyannis et al. 2002). Abnormal posture may be defined as imbalance at the pelvic, shoulder and neck, giving rise to asymmetry in alignment in the coronal or sagittal plane. Adoption of extreme cervical posture by patients may occur in response to pain, in order to accommodate activities of daily living, workplace or professional demands. Further, this adoption of faulty posture leads to adaptation in spinal alignment leading to changes in muscle activity, increased load on the surrounding soft tissue and deeper structures (Darnell 1983). Over time, these factors may in turn predispose patients to on-going pain and disability, and poor recovery of the related pathology. So far, measurement of abnormal posture has been reported from only one CR clinical study (Cleland et al. 2007a). Future studies need to explore the association between cervical posture and pain and disability measures, in patients with CR.

Radicular pain is exacerbated by any movement which influences the involved nerve root (Connell and Wiesel 1992). Flexion may be associated with increased radicular pain if the disc has herniated into the neural foramen, and more so if the nerve root is already less elastic due to aging (Cusick and Yoganandan 2002). Extension causes narrowing of the foramen, which if already compromised by a osteophyte will cause or exacerbate symptoms of pain (Cailliet 1991a). Increased pain with extension also occurs due to pressure on an inflamed disc which can cause further herniation of the disc into the intervertebral foramen causing irritation to the nerve root (White and Panjabi 1990c). The biomechanical reasoning is that normal intra-discal pressure increases with extension, ranging from 440 kPa in an upright position to 910 kPa in an extended position. Ipsilateral rotation of the neck at 40° can result in foramen narrowing up to 23% when compared with the neutral position (Muhle et al. 1998). Pain-limited cervical rotation of less than 60° has been used as a clinical variable for the diagnosis of CR (Wainner et al. 2003), although other factors may contribute to limitation of cervical motion (Constantoyannis et al. 2002). Examination of the range of neck movement and associated symptoms forms part of the clinical examination in CR because of the importance of neck movement in activities of daily life. Reduced range can result in significant impairment of function, for example, rotation of the neck while crossing the road or driving, looking down for writing or cooking, looking up to reach out for objects placed on high shelves or hanging the washing.

Although CR can occur at any level of the cervical spine, surgical studies have shown that nerve root compression occurs most commonly at C5-6 (C6 nerve root), C6-7 (C7 nerve root) and C4-5 levels (C5 nerve root), respectively (Brown 1971; Gore et al. 1986; Fukusaki et al. 1995; Persson et al. 1997a). This was further supported by a large surgical study (n=525) which found the most common level involved as C5-6 (54.7%) followed by C6-7 (44.8%) (Thorell et al. 1998). However, some studies have shown C7 radiculopathy to be more common than C6 (British Association of Physical Medicine 1966; Honet and Puri 1976; Radhakrishnan et al. 1994).

Conventional radiography can detect loss of disc height, facet joint arthritis, bony osteophytes, curvature changes, and segmental motion. Radiographic studies have shown that patients with cervical spondylosis can have concomitant deformity in the form of kyphosis or kyphosis-lordosis, either from degenerative or iatrogenic instability (Rushton and Albert 1998). Segmental kyphotic deformities and segmental laxity occur in severe disc degeneration or post surgery (Peolsson et al. 2004). Advances in radio-diagnosis for cervical spine patients have come from improvements in diagnostic imaging, in particular Computerised Axial Tomography (CT) and MRI. In CR, CT is considered superior for evaluation of bony osteophytes causing foraminal stenosis, whilst MRI is normally used to document nerve root compression and assess the morphology of the intervertebral disc (Garvey et al. 2002). However, the MRI may be superior because sensitivity for the detection of nerve root compression is higher than for the CT scan (Brown et al. 1988), and the

T2-weighted MRI images allow better differentiation between disc material and osteophytes. Limitations of MRI are expense, availability, claustrophobia, movement artefacts, presence of metal in the body and the scan time. Imaging findings needs to be correlated with clinical signs and symptoms as they yield false positives in asymptomatic people (Boden et al. 1990; van Rijn et al. 2006).

2.4 Treatment options in CR

CR is a complex clinical condition with a variety of specific causes. During clinical assessment, clinicians should attempt to correlate physical findings with imaging information to assist identification of the specific pathology relating to the disorder. A clear understanding of the natural history of CR assists treatment recommendations as well (Connell and Wiesel 1992). In management of a clinical syndrome such as CR, the procedure should consider the pathology underlying the symptoms while preventing morbidity. These principles should be adhered to strictly or it may result in unpredictable clinical outcomes (Rushton and Albert 1998).

Despite advances in understanding of the aetiology, patho-physiology and treatment of CR, there still remain many unresolved questions about what constitutes optimal treatment. Some studies suggest that the natural history of the disorder is generally favourable and spontaneous recovery occurs over time (Spurling and Segerberg 1953; Radhakrishnan et al. 1994; Vinas et al. 2001). Conservative interventions, used in the management of CR include: rest, heat, cold, cervical collars, medication (analgesics, muscle relaxants, oral steroids, non-steroidal anti-inflammatory drugs (NSAIDs)) and physiotherapy (Vin Gijn 1995; Saal et al. 1996; Murphy et al. 2006). Although surgical intervention may be indicated when neurological signs persist, CR patients with neurological deficits have been shown to respond favourably to conservative treatment. However, some other conservative studies (Olivero and Dulebohn 2002; Murphy et al. 2006) have used neurological deficits (especially motor weakness) as exclusion criteria.

The point at which conservative therapy is deemed to have failed is a matter of controversy and is defined differently in different institutions (Radhakrishnan et al. 1994; Gore and Sepic 1998; Shah and Rajshekhar 2004). The average duration of conservative treatment in previous studies has ranged from 13 months (range 1 week to 15 years) (Gore and Sepic 1998) to 4.9 years (Radhakrishnan et al. 1994) prior to the patients being managed with surgery. The duration of symptoms, and the nature of the underlying pathology, affects the surgical outcome marking the timing of the surgical intervention. Surgery for chronic CR in patients with osteophytes in the intervertebral foramen has been associated with less complete recovery (Yamamoto et al. 1991), whereas patients with soft lateral disc protrusion responded well to surgery (Pointillart et al. 1995). In summary, surgical options have been explored when neurological signs begin to show signs of non-recovery, and have failed to respond to conservative therapy (Aldrich 1990; Radhakrishnan et al. 1994; Gore and Sepic 1998; Shah and Rajshekhar 2004). However, patients with unremitting pain in the distribution of a nerve root for more than six weeks, in the absence of a specific neurological deficit, and who have not recovered with conservative management, may also warrant surgery (Jones 1998). A recent trend towards greater use of surgical management of CR may be due to the development of new surgical procedures, development of new imaging techniques, an increase in the prevalence of the disease and an increase in the number of spinal surgeons (Davis 1994; Ciol et al. 1996; Angevine et al. 2003). Surgery variables include type of surgery, graft material, shape of the graft and levels of surgery (Hacker et al. 2000; Vavruch et al. 2002). Socio-economic issues (social or family support, cost of surgery, number of working days lost) and the health care system in a country also influence the incidence of surgery for CR.

2.4.0 Conservative treatment

Oral drugs: Non-steroidal anti-inflammatory drugs and muscle relaxants (Saal et al. 1996; Murphy et al. 2006) are used in the management of CR, in isolation or in combination with other physical therapy modalities. Oral corticosteroids (Murphy et al. 2006) and opioids (Mazanec and Reddy 2007) are options if symptoms are not controlled by NSAIDs.

Cervical collar: A range of collars (hard, soft, Philadelphia) have been used in the conservative management of CR. A hard cervical collar worn for 2 weeks (Saal et al. 1996) did not provide significant relief in pain, whereas shoulder resting rigid collars for day use, and a soft collar at night, for 3 months had a significant impact on pain intensity at a one year follow-up (Persson et al. 1997a; Persson and Lilja 2001). When used in combination with home based halter traction for between 2-6 weeks, a cervical collar (type not mentioned) was effective in providing complete or significant pain relief in 68 out of 81 patients (Olivero and Dulebohn 2002). The authors do not mention any specific outcome measures of pain. Results of two randomised clinical trials (RCT) (Persson et al. 1997a; Persson and Lilja 2001) showed no difference in improvement between patients treated with a collar, and a control group, whereas, Fukusaki et al (1995) demonstrated that patients treated with a nerve root sleeve injection had a faster recovery than the patients treated with a collar. Short duration use of a collar does not seem to yield significant improvement, whereas long use appears more effective. However, the use of a collar is a passive process and the adverse effects of prolonged immobilisation on tissues must be considered.

A range of physiotherapy modalities have been used in previous studies including traction, exercises, heat, cold, electrotherapy modalities and ergonomic advice.

<u>Cervical traction:</u> Variables in traction administration include the type of traction; home (Saal et al. 1996; Olivero and Dulebohn 2002; Murphy et al. 2006), manual (Persson and Lilja 2001), overhead (Constantoyannis et al. 2002) and supine (British Association of Physical Medicine 1966). The neck position, angle of pull, traction force, duration of traction and total duration of treatment are all factors that may vary the type and dose of any traction intervention (Wong et al. 1997).

A systematic review by Van der Heijden et al (1995) could not form a strong conclusion about the efficacy of traction due to non-homogenous patient groups and poor methodological qualities of the reviewed studies. Results from studies published since the review, support both manual traction (Persson and Lilja 2001) and home traction (Saal et al. 1996; Olivero and Dulebohn 2002; Murphy et al. 2006) as effective methods of pain reduction in CR. However, Saal et al (1996) and Olivero and Dulebohn (2002) did not use any validated outcome measures and therefore the true benefits cannot be determined. When used in combination with other modalities, the treatment has been effective (Saal et al. 1996; Moeti and Marchetti 2001; Constantoyannis et al. 2002; Cleland et al. 2005). Moeti and Marchetti (2001) and Constantoyannis et al (2002) emphasise the importance on early intervention as one of the reasons for successful treatment using traction. Four single cases (Constantoyannis et al. 2002) of large volume herniated discs were successfully treated with vertical door traction for 6 to 8 hours a day (45 minutes every hour with 15 minutes rest), together with muscle relaxants and anti-inflammatory medicines and a Philadelphia cervical collar for 3 weeks. Compliance to adhere to this regime was identified as a practical issue related to this treatment protocol.

Exercise: Initially supervised, and subsequent home exercises, have been used in studies using a non-surgical treatment approach in patients with CR (Saal et al. 1996; Persson and Lilja 2001; Murphy et al. 2006). Exercise programmes in different studies vary and yet they share some common aspects. These include strengthening exercises for the shoulder girdle and chest (Saal et al. 1996; Cleland et al. 2005; Cleland et al. 2007a), upper and lower body strength and endurance exercises (Saal et al. 1996; Persson and Lilja 2001), isometric neck exercises, and shoulder flexibility and stretching exercises (Persson and Lilja 2001), strengthening deep neck flexors (Cleland et al. 2005), improving endurance of deep neck flexors (Waldrop 2006) cervical stabilisation exercises (Ylinen et al. 2003), end-range loading to correct derangement (McKenzie 1983; Murphy et al. 2006), sensori-motor training, aerobic exercise (Persson and Lilja 2001; Murphy et al. 2006) and weight training (Murphy et al. 2006). Descriptions of exercise intensity and protocol vary widely. Petersen et al (2000) describe a strengthening program for the deep neck flexors where the patient is asked to maintain a nod in supine with the head supported. Ylinen and co-workers (2003) used exercises to increase the endurance of the deep cervical flexors, where the patient was asked to lift the head off the plinth and hold the upper neck in flexion. Ylinen et al (2003) used this exercise protocol in chronic non-specific neck pain and its use in a CR cohort may be questionable if the patient has not been trained with the head supported method previously. Most studies have used a combination of exercises. Hence, the efficacy of any one particular exercise cannot be ascertained. Moreover, exercises have been used in combination with other methods of treatment.

Posture and ergonomic advice: Ergonomic instructions and postural correction form an essential part of the physiotherapy programme (Saal et al. 1996; Persson et al. 1997a). Training included postural control (Saal et al. 1996; Persson and Lilja 2001; Waldrop 2006) and body mechanics training (Saal et al. 1996).

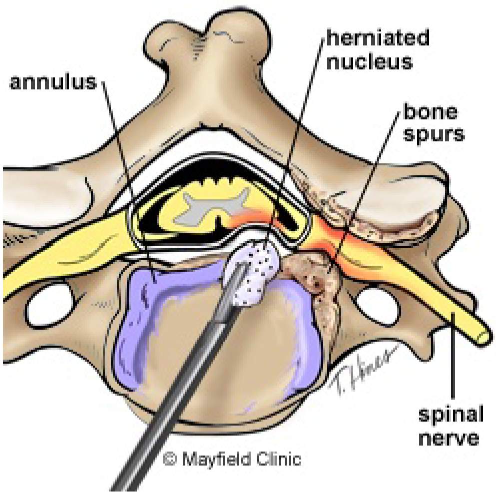
Mixed therapies: Passive therapies for pain relief include TENS (transcutaneous electrical nerve stimulation) (Saal et al. 1996; Persson and Lilja 2001), cold (Valtonen and Kiuru 1970; BelEliyahu 1996; Saal et al. 1996), superficial heat (Persson and Lilja 2001; Murphy et al. 2006), deep heat (Valtonen and Kiuru 1970; Honet and Puri 1976) and ultrasound (Persson and Lilja 2001). The rationale for the use of a single physiotherapy modality has not been ascertained and most modalities have been used in conjunction with other treatments. Although this reflects common clinical practice, the drawback is that treatment guidelines are unable to comment on the efficacy of a single modality.

Epidural nerve root steroid injection: Periradicular/epidural corticosteroid injections are known to provide significant pain relief (Saal et al. 1996), both in chronic (Vallee et al. 2001) and acute CR conditions (Murphy et al. 2006). Although Fukusaki et al (1995) demonstrated significant reduction in pain compared to a control group, the results of the other three studies (Saal et al. 1996; Vallee et al. 2001; Murphy et al. 2006) are limited because of the lack of a control group. Complications of this treatment may include nausea, bloating of the abdomen, shortness of breath and pain/infection at the injection site (Cicala et al. 1989).

2.4.1 Surgical treatment

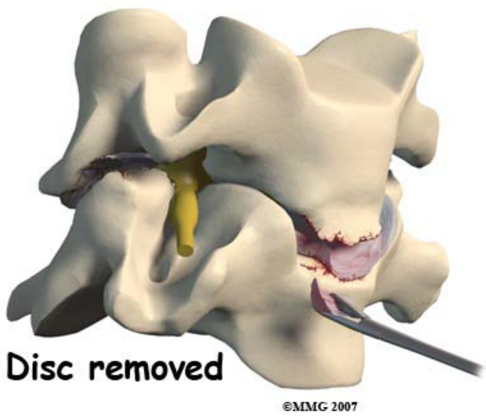
The goals of surgical treatment should be decompression, restoration of alignment and stability, reduction in symptoms, improvement in function and high patient satisfaction. Decompression involves removal of the soft disc or osteophytes from the compressed neural elements. Maintenance of alignment involves restoration of the disc space height and foraminal height (Jacobs et al. 2004). Stability involves elimination of motion which is considered to prevent formation of osteophytes.

Surgical procedures for CR can be divided into anterior and posterior approaches. Anterior procedures are more popular because they avoid exposure of the spinal canal and involves less soft tissue damage (Fraser 1995) (Figures 2.0 A & B). The earliest description of anterior cervical discectomy was by Smith and Robinson (1958). This technique uses a left anterior approach, with a longitudinal incision along the anterior border of the Sternocleidomastoid muscle. By dissecting the superficial cervical fascia and passing medially from the carotid sheath and laterally from the oesophagus and trachea, the anterior aspect of the cervical spine can be reached. After identification of the correct level, the ALL is explored and cut, and the disc is excised. Non-union remains a concern with a 12.3% pseudoarthrosis rate using the classic Smith-Robinson technique (Bohlman and Emery 1988). Several modifications to the classic technique have been developed with the aim of improving fusion rates. One technique is burring of endplates down to the subchondral bone. This technique improved the fusion rate to 95.6% without producing notable deformity due to settling (Emery et al. 1994). Another modified technique involved burring the end plates, distraction of the segments, placement of a tricortical autologous iliac crest graft in a reverse position such that the cortical cross-section faced posteriorly, creating a stabilising strut in the middle column (Brodke and Zdeblick 1992). The removal of cartilage from the endplates induces fusion with the bone graft (Bohlman and Emery 1988; Zdeblick and Bohlman 1989). Some surgeons choose not to resect the end-plate because thinning of the end plate can cause biomechanical weakening (An et al. 1993).



A

Image source: www.mayfieldclinic.com/PE-ACDF.htm



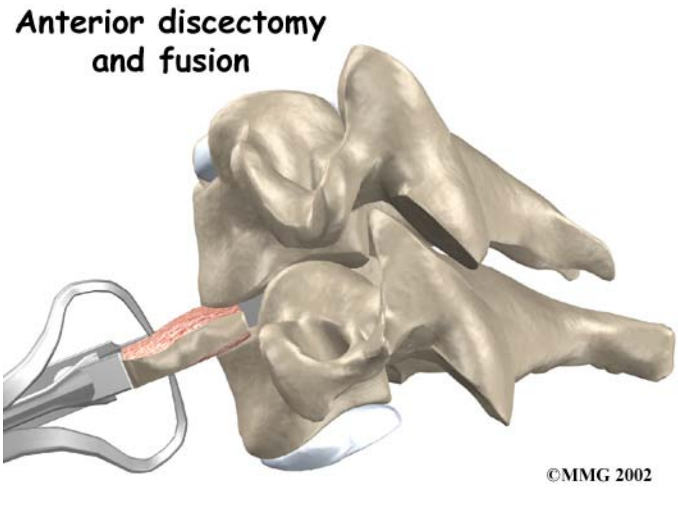
B

Image source: www.eorthopod.com/public/patient -education

Figures 2.0 A & B The anterior approach for anterior cervical discectomy

The Cloward technique uses a 10-12 mm tri-cortical bone graft harvested from the iliac crest. The graft is in the shape of a round bone dowel and the anterior vertebral bone structure is drilled into a reciprocal shape (Cloward 1958). In theory, the graft should be oversized several millimetres if the foramen is narrowed, to restore original disc height and decompress the neural foramen (Figure 2.1 A). Realistically, graft resorption and collapse may lessen this effect as healing occurs (An et al. 1993). Using the anterior approach, both the value of filling the disc space, and the graft material used are issues of on-going discussion (Thorell et al. 1998).

Fusion materials generally include an autograft, an implant material derived from the same individual (Figures 2.1 A & B), or an allograft, which is an implant material derived from another individual (usually from cadavers) other than the individual (Jacobs et al. 2004). Advantages of a fusion procedure following decompression of the neural structures are maintenance of disc height, avoidance of vertebral settling and improved stability at the fusion site, reducing the potential for recurrent foraminal stenosis (Cloward 1958; Bailey and Badgley 1960; Zdeblick et al. 1993). The most common source of autograft tissue is the iliac crest. Complications of harvesting a graft from the iliac crest include chronic donor site pain, pelvic fracture, lateral femoral cutaneous nerve palsy and a longer hospital stay (McGuire and St John 1994).



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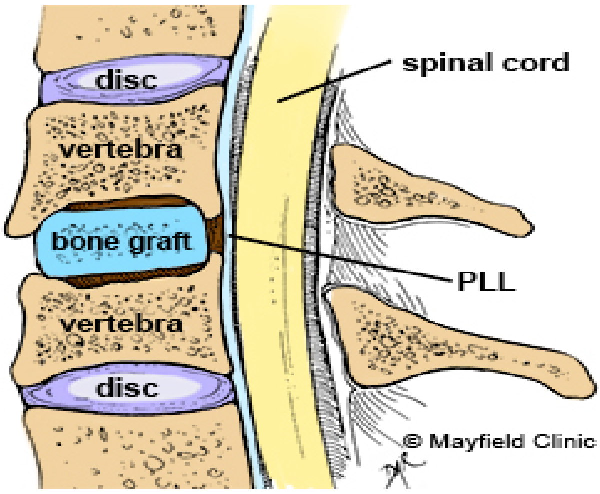

B

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Figures 2.1 A & B Anterior cervical discectomy and fusion with autograft

Advantages of both discectomy alone (Figures 2.0 A & B &2.2) and discectomy with bone graft (Figures 2.1 A & B) have been described (Abd-Alrahman et al. 1999). Discectomy alone is associated with a shorter hospital stay and reduced duration of surgery (Abd-Alrahman et al. 1999; Dowd and Wirth 1999). Anterior cervical discectomy and fusion (ACDF) leads to greater pain relief initially, but long term results have been shown to be comparable to those of discectomy without fusion (Abd-Alrahman et al. 1999; Dowd and Wirth 1999). A loss of segmental lordosis or healing in kyphosis (Figure 2.2) is relatively common following both surgical procedures.

Figure 2.2 Post surgery radiograph. Anterior cervical discectomy at C5-6. Fusion with mild kyphosis at C5-6.

The usual candidate for anterior cervical fusion has pathology affecting 1 or 2 spinal segments. Very few patients require surgery at more than 2 levels. Multiple level procedures have been associated with higher non-union rates compared with single level fusion (Emery et al. 1997; Bolesta et al. 2000). Radiological evidence of graft dislodgement is reported in between 2.1% to 4.6% of single-level fusions compared with 10% to 29% of multilevel fusions (Zdeblick and Bohlman 1989). In multi-level degeneration, the dominant pain generator level/s should be isolated. The surgical technique used is usually dependent upon the number of levels which require fusion and the experience and preference of the surgeon. The choice of surgical technique used should be based on both evidence derived from clinical studies as well as the judgement of the surgeon (Jacobs et al. 2004).

It is evident from this review of the treatment methods for CR, that the outcome of either both conservative and surgical management is variable both between studies, and individuals managed with the same treatment approach (Saal et al. 1996; Heckmann et al. 1999; Moeti and Marchetti 2001; Peolsson et al. 2003; Cleland et al. 2005; Peolsson et al. 2006b; Waldrop 2006; Cleland et al. 2007a). Furthermore, it is difficult to compare outcomes between studies as studies use different inclusion criteria, and importantly have different approaches to outcome measurement.

2.4.2 Comparison of treatment outcome

Some researchers have included conservatively and surgically managed patient groups in the same study and used the same measures to compare treatment outcomes between groups (Persson et al. 1997a; Persson et al. 1997b; Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001).

A Cochrane review (Fouyas et al. 2002) (currently withdrawn due to update not being available) of the role of surgery for cervical spondylotic radiculo-myelopathy involved a MEDLINE (1966 – 2000) and EMBASE (1980 – 2000) search of 13,209 citations. The trial selected for CR was (Persson et al. 1997a) (n=81) which compared ACDF (n=27) with physiotherapy (n=27) and collar (n=27). This only single randomised controlled study compared different treatments in homogenous sub-groups of patients with CR. The results (Persson et al. 1997a) indicated that the short-term response was superior in the group managed surgically with respect to pain, parasthesia or sensory loss. However, at the one year follow-up, no significant differences between the groups were observed. In a follow-up report of the same study (Persson and Lilja 2001), patient centred outcome measures (Mood Adjective Check list, the Hospital Anxiety and Depression scale, Disability rating index) were reported as being no different between groups at the 1 year follow-up. As per the Cochrane review, the selected study (Persson et al. 1997a) as well as the subsequent publication (Persson and Lilja 2001) scored well on methodological quality (sub-group homogeneity, randomisation, and appropriateness of outcome measures, selection criteria and follow-up). Acceptability of the results of this study requires consideration of the low sample size and the large number of outcome variables.

A Cervical Spine Research Society (CSRS) multicenter clinical trial (non-randomised) (Sampath et al. 1999), compared surgical (anterior and the posterior approach as applicable) and conservative treatment of patients with CR, and reported significant improvement in pain, following treatment in both groups. Patient satisfaction and neurological improvement were reported as higher in the surgery group although the outcome measures used (6 point descriptive pain rating scale, 5 point patient satisfaction scale, 6 point neurologic outcome scale, 5 point functional status scale and a 5 point scale to record specific activities of daily living) were of questionable reliability and validity.

A long-term follow-up (5.5 years) study, which is one of the longest follow-up periods reported in CR studies, demonstrated that more patients in the conservative group had relief in pain than in the surgical group (Heckmann et al. 1999). The limited number of outcome measures and a retrospective design were limitations of this study.

Studies which have explored both treatment methods (Persson et al. 1997a; Persson et al. 1997b; Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001) provide valuable information on outcomes of treatment. At the same time, any future study should ideally be conducted with improved research methods, valid and reliable outcome measures and adequate sample size. Further, many questions remain regarding identification of individuals at risk of a poor outcome. What need to be identified are factors which may assist in predicting which patients are likely to have a successful outcome from a specific method of treatment.

2.5 Outcome measures in predictive cervical radiculopathy studies

Prediction of success or failure of an intervention or evaluation of change in clinical status in response to treatment requires the use of clinical outcome measures. Few studies have tried to determine which baseline variables are capable of predicting a successful outcome in patients receiving treatment for CR (Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b; Cleland et al. 2007a). A typical predictive study will include prognostic factors and risk factors as variables to predict outcome. Prognosis is the possible outcome of a disease over a given time period, and the rate of occurrence of the outcome (Laupacis et al. 1994). Prognostic factors refer to intrinsic characteristics of an individual such as age, gender, and BMI. Risk factors relate to external variables contributing to the development of the disease (lifestyle, work style, smoking, and co-morbidities). This literature review attempted to follow the guidelines of Laupacis et al (1994) in the review of previous prognostic studies. These include well defined diagnostic criteria, a sufficiently long follow-up, and low subject drop-out. Other important guidelines include objective, patient-centred outcome measures, and prognostic and risk factors expressed in terms of the likelihood of the condition occurring. Using similar principles, Beneciuk et al (2009) formed an eighteen item list of criteria to assist the review of methodological quality of physical therapy intervention studies which have used a Clinical Prediction Rule.

One of the main factors in developing a predictive outcome study is to ensure that the patient group included in the study has a valid and specific diagnosis. The diagnostic criteria for CR adopted by Peolsson and co-workers (2003; 2004; 2006b) included at least 6 months of neck and arm pain with a neurological deficit, and cervical degenerative disc disease verified by MRI. Exclusion criteria included myelopathy, cervical fracture or subluxation, cervical tumour, psychiatric disease and drug abuse. Cleland et al (2007a) chose the diagnostic test item cluster (Wainner et al. 2003) to identify patients with CR and did not establish any exclusion criteria in their study. The four criteria (Wainner et al. 2003) included cervical rotation toward the symptomatic side of less than 60°, positive responses to the Spurling's test, upper limb tension test and cervical distraction test. Operational definitions were provided to standardise the tests and improve reliability. Using the criteria described by Wainner et al (2003), the presence of all 4 variables was associated with a positive likelihood ratio (LR+) of 30.3 (95% CI = 1.7 to 538.2), sensitivity of 0.24 (95% CI = 0.05 to 0.43), and specificity of 0.99 (95% CI = 0.97 to 1.0) for detecting CR, when compared with neuro-diagnostic testing. Although a LR+ of 30.3 raised the post-test probability of success of diagnosis to 90%, the 95% CI was very wide. As this could compromise the accuracy of the diagnosis, the presence of three variables with a LR+ of 6.1 (95% CI = 2.0 to 18.6) would probably result in a more accurate diagnosis. Further, Wainner et al (2003) used a standardised electro-physiologic examination (electromyography and nerve conduction studies) as a reference criterion to divide patients with and without CR. The diagnostic value of neuro-physiological studies in isolation is debatable. The accuracy of such tests during blinded studies with verification from surgery, MRI or clinical examination has been reported as being 30% to 95% (van der Bent et al. 1995; Nardin et al. 1999; Slipman et al. 2005). Neuro-physiological examinations, such as nerve conduction tests, are important to rule out other conditions such as median or ulnar nerve entrapment, that may share clinical signs and symptoms with radicular pathologies (Fisher 2002).

Further important features of prognostic studies are long term follow-up and a low drop-out rate. Although both elements are important, a long duration follow-up is typically associated with a higher drop-out rate (Peolsson et al. 2006b) compared to studies with only short-term follow-up (Cleland et al. 2007a). Peolsson et al (2006b) reported an initial sample size of 34 but had a 33% drop out at 3 year follow-up. In contrast, Cleland et al (2007a) reported a drop-out rate of only 5% (n=101) of patients at the short-term (28 day) follow-up in their conservative intervention study. Similarly, Peolsson et al. (2003) reported an initial sample size of 103 and a drop-out rate of 29% at 1 year, and 42% at 2 years. Although these studies (Peolsson et al. 2003; Peolsson et al. 2004; Cleland et al. 2007a) used an 'intention to treat analysis' which increases the number of patients included in the final analysis, the high number of drop-outs (Peolsson et al. 2003; Peolsson et al. 2004) and short follow-up duration (Cleland et al. 2007a) impact on the results of this type of study. It is important that future predictive studies evaluating surgical and conservative treatment of CR, have an appropriate follow-up period and low drop-out rate (Beneciuk et al. 2009).

The use of standardised questionnaires or measurements of pain intensity, disability, general health, and depression is important in the design of predictive studies (Beneciuk et al. 2009). The use of standardised self reported outcome measures is evident in previous studies of CR (Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b; Cleland et al. 2007a). These included scales for pain intensity [visual analog scale (VAS), numerical pain rating scale (NPRS)], pain and disability [neck disability index (NDI), patient specific functional scale (PSFS)], and distress [distress and risk assessment management (DRAM)]. Other risk and prognostic factors which have been included in CR management studies related to socio-demographics (age, gender, smoking, family situation, education level, type of work, work status), pain distribution, symptom duration, number of previous episodes, dominant arm affected, use of analgesics, and presence of low back pain/ co-morbidities. Appropriate analysis (Beneciuk et al. 2009) of these outcome variables was included by Cleland et al. (2007a). Some variables included in the prediction of outcome analysis were not tested for reliability or validity. These include the radiological disc height measurement, radiological evaluation of segmental deformity (Peolsson et al. 2003; Peolsson et al. 2004), activities of daily living (ADL) (Cleland et al. 2007a), expectations of treatment, posture assessment, cervical and thoracic range of motion, neurological assessments, (Cleland et al. 2007a) and muscle strength (Cleland et al. 2007a). This makes the interpretation of the results difficult and suggests selection of appropriate outcome measures is important in the development of prognostic studies.

The first step in statistical analysis used in predictive studies involves a univariate analysis where one predictive variable is compared to the outcome at one time. The advantage of this kind of analysis is that it allows the researcher to determine which individual predictive variables are associated with the outcome. The next step involves a multi-variate analysis to explore the relationship of predictor variables with each other, as well as with the outcome (Laupacis et al. 1997). The multivariate analyses commonly used for this purpose include logistic regression, discriminant function analysis, and recursive partitioning (Laupacis et al. 1997). Logistic regression analysis is the most commonly used.

The statistical analysis employed by Peolsson et al (2003; 2004; 2006b) included a rank correlation test (bivariate analysis) between baseline variables (independent) and outcome variables (dependent) at the final follow-up. The significant correlations ($p<0.05$) were analysed further using multiple linear regression analysis, followed by a forward step-wise regression analysis to reveal the most important predictors. Further, to check the stability of the test, Peolsson et al (2006b) conducted analysis by backward selection to remove redundant variables (related factors), selected early in forward step wise regression. Cleland et al (2007a) conducted the univariate analysis (Laupacis et al. 1997), and then the significant variables ($p<.10$) were entered into a logistic stepwise regression model to determine the most accurate set of variables for predicting success. The outcome in this case is a dichotomous variable of success or failure (non-success).

The statistical method adopted by Cleland et al (2007a) using the dichotomous outcome scoring is more appropriate because it produces accuracy statistics such as sensitivity, specificity, positive likelihood ratio (LR+) and negative likelihood ratio (LR-). Sensitivity reflects the ability of a test to identify when the condition is present whereas specificity reflects the ability of a test to identify when the condition is absent (Sackett 1992). The LR+ and the LR- are calculated using the combined information provided by sensitivity and specificity. A LR+ value is high when both the sensitivity and specificity of a test is high. The value of the LR+ indicates how much a prediction model could raise the probability of obtaining the outcome (Sackett 1992) as compared to a stepwise regression analysis where the purpose of regression is to suggest a possible explanation of the variation in the dependent variable (y), by demonstrating a systematic covariation in a logically related variable (x). For example, Peolsson et al (2006b) chose arm pain, neck pain, neck specific disability and general health to evaluate clinical success at a three year follow-up

(Table 2.1). Non-smoking and normal Distress and Risk Assessment Method (DRAM) were predictors (R^2 = 0.48) of low arm pain, low baseline pain frequency, absence of low back pain and normal DRAM ratings were predictors (R^2 = 0.69) of low neck pain, and normal DRAM rating, low usage of pain killers and low pain intensity (R^2 = 0.73) were predictors for a low NDI score.

In the study by Cleland et al (2007a) four predictor variables (age < 54 years, dominant arm not affected, looking down does not worsen symptoms, multimodal physical treatment) were identified as the best predictors of short-term outcome for patients with CR (Table 2.1). With all 4 variables present, the LR+ was 8.3 (95%CI= 1.9 to 63.9) and the post-test probability of success was 90%. This form of analysis helps practitioners determine when a particular treatment approach may be beneficial and therefore can contribute to the clinical decision-making process. The fundamental weakness of this specific prediction rule however was that one of the predictive factors was ‘a course of physical therapy treatment’. Therefore, the rule may not be useful prior to the commencement of treatment of this nature and therefore the ability to use this prediction rule cluster for prognostic clinical reasoning is highly questionable. Nevertheless, to date this is the only CR treatment study which has included the development of a Clinical Prediction Rule.

The utility of CPRs primarily lies in improved decision making, whether it is for diagnosis, prognosis or matching patients to optimal interventions. For the same reasons, the CPRs need to be developed and validated as per rigorous methodological procedures. The first step involves creation of the rule by developing a list of predictor variables which are likely to predict the occurrence of the outcome (Laupacis et al. 1997). Univariate and subsequent multivariate data analysis results in the formation of the most parsimonious group of predictors, which maximises the accuracy of the CPR to determine a positive or successful outcome. Before this CPR can be actually used in clinical practice, it is necessary to ‘prospectively validate’ it to ensure that similar results are obtained in a different patient population with the same condition (Laupacis et al. 1997; Childs and Cleland 2006). This eliminates variables which may have entered phase 1 by chance or were particular to the population or clinicians of the previous study. The final step involves ‘conductance of an impact analysis’ to study the impact of the CPR on cost, outcomes of implementation and patient satisfaction (Childs and Cleland 2006).

To date there is only one CPR developed for CR outcomes (at 28 days) for conservative treatment. This rule includes factors that reflect the type of treatment therapy and therefore is not able to be easily generalised.

Table 2.1 Predictors of outcome in previous studies – a summary of results

Study	Outcome	Variables
Cleland et al. (2007a)	good outcome	1. Age < 54 years 2. Dominant arm is not affected 3. Looking down does not worsen symptoms 4. Multimodal treatment in at least 50% visits
Peolsson et al. (2003)	reduced pain	1. Increased segmental kyphosis 2. Male gender 3. Older age 4. No smoking 5. Increased right rotation neck ROM 6. Low NDI
Peolsson et al. (2003)	reduced disability	1. Reduced current pain 2. No smoking 3. Increased flexion neck ROM 4. Higher education levels 5. Increased segmental kyphosis 6. Increased right hand grip
Peolsson et al.(2004)	good fusion	1. Male gender 2. Cloward's procedure
Peolsson et al. (2004)	reduced pain and disability	1. Increased kyphosis
Peolsson et al. (2006b)	reduced arm pain	1. No smoking 2. Normal DRAM rating
Peolsson et al. (2006b)	reduced neck pain	1. Reduced pain frequency 2. Absence of low back pain 3. Normal DRAM rating
Peolsson et al. (2006b)	reduced disability	1. Normal DRAM rating 2. Reduced pain killers 3. Reduced pain intensity
Peolsson et al. (2006b)	general health	1. Reduced pain intensity

Central to every clinicians practice are the diagnosis of disorders, and consideration of the likely prognosis. A clinicians experience and knowledge guide the interpretation of the history, symptoms, physical examination and radiological investigations and contribute to making an accurate interpretation of a patient's disorder. Predictive studies use the same approach in a more quantified way, to assess the likely response to treatment. The results of predictive studies aid in clinical decision making, and may create efficiencies in healthcare delivery, without compromising patient care. Consequently, predictive research is important in a country like India with has a vast population and a requirement to optimise healthcare expenditure.

2.6 Review of outcome measures

A range of outcome measures relevant to patients with neck pain and CR will be discussed in the following review. This review of outcome measures includes items socio-demographic factors, patient history, clinical measures, measures of impairment and disability and radiological measures.

2.6.0 Pain

Remission of neck or radicular pain is the outcome most desired by the patient (Zoega et al. 2000; Lim and Wong 2004; Murphy et al. 2006). Trials examining effects of conservative management (Murphy et al. 2006; Cleland et al. 2007a), anterior cervical fusion surgery (Zoega et al. 2000; Grob et al. 2001; Murphy et al. 2006), or both (Persson et al. 1997a; Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001) have shown a decrease in pain in response to the intervention (Table 2.2). Similar results have been reported from a number of case series reporting treatment of CR (Moeti and Marchetti 2001; Vavruch et al. 2002; Cleland et al. 2005; Waldrop 2006). Table 2.2 summaries the CR treatment studies which have included pain intensity as an outcome measure.

A review of studies to determine which method of treatment (surgical and conservative) provided better long term pain relief was possible where both treatment methods were evaluated using the same outcome measures. However, the specific pain measurement approach has been inconsistent between studies, which makes direct comparison difficult (Persson et al. 1997a; Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001). Heckmann et al (1999) calculated the proportion of patients who had an improvement in neck pain and arm pain within each treatment group. Significant improvement in radicular pain was reported in both patient groups (100% in the conservative, 95% in the surgery group) but there was no significant improvement in neck pain. Sampath et al (1999) reported a significant improvement in pain (overall pain rating, worst pain rating) in both treatment groups. Although the difference in pain scores was higher in the surgery group, no between groups statistical test was conducted to determine whether this difference was statistically significant.

Persson et al. (1997a) and Persson and Lilja (2001) reported changes in pain intensity (current pain, worst pain last week) in patients with CR treated in a rigid collar, compared to those treated with physiotherapy and surgery. There was a significantly greater improvement in pain intensity scores in the surgery group than in the group treated in a rigid collar at three months, but this difference was no longer evident at the one year follow-up. In summary, current studies suggest that all treatment methods evaluated result in a long-term decrease in pain. However, it remains unclear as to which treatment method is more effective with respect to pain relief.

Pain may be evaluated with respect to distribution, intensity and quality (Peolsson et al. 2006b) (Table 2.2). Although intensity (Persson et al. 1997a; Sampath et al. 1999; Persson and Lilja 2001; Vavruch et al. 2002; Murphy et al. 2006; Cleland et al. 2007a) and quality (Sampath et al. 1999) have been evaluated frequently, the distribution of pain has been less frequently reported (Persson and Lilja 2001; Peolsson et al. 2006b). Only one study (Peolsson et al. 2006b) has used pain distribution as an outcome measure. The distribution of pain in CR may be of dermatomal distribution or follow a less distinct distribution, and may include neck pain with referral to the paraspinal, on the medial scapular border and occasionally it is presented as neck pain with acute spasms arising from stimulation of the sinu-vertebral nerve fibres that may or may not occur in conjunction with cervical radicular patterns (Sampath et al. 1999). Since CR may present with varied combinations of neck and arm pain, future assessment of pain intensity should include neck and arm pain separately.

Table 2.2 Summary of CR studies demonstrating reduction in pain intensity following treatment (surgery, conservative, both)

Study	(n)	Age (yrs) Mean (range)	Gender M/F	Treatment	Pain scale	Pain measure	Pain score (Pre) Mean ± SD(range)	Pain score (post)/last FU Mean ±SD (range)	Difference of means/ statistical significance (post vs. pre)
Cleland et al. (2007a)	96	50.8	35/61	Con	11 NPRS	Current, best & worst in last 24 hours	6.5 ± 2.4	2.8 ± 2.5	3.8 (2.1)
Murphy et al. (2006)	35	47.2 (24-68)	14/21	Con	NRS		6.4 ± 2.4	1.7 (2.1)	4.9 (5)
Zoega et al. (2000)	46	25-60	22/ 24	CSLP vs. no plate (1,2 levels)	VAS (median values)	Combination of current pain and max & min pain in last 3 days	Without plates neck: 6.3 (4.4-9.1), arm 6.3 (2.9-8.6)	Neck: 5.6 (0 - 8.2), arm 5.9 (0-7.8)	Neck: p> 0.3; Arm: p = 0.04
Vavruch et al. (2002)	99	47	45/44	CIFC & CP	VAS 100mm	Present pain; worst pain last week	Present pain CP = 69, CIFC = 65	CP = 28 CIFC = 38	p<0.01
Sampath et al. (1999)	246	48.1 (23-83)	55/45	Surgery; conservative	Pain severity on a 5 point scale, descriptive on a 6 point scale	Most severe pain rating; avg pain rating. Avg used for calculation	Surgery: 3.4 Con: 3.08	Surgery: 1.8 Con: 2.04	Surgery: 1.6 Con 1.04, p<0.001
Persson and Lilja (2001)	81	47.5 (28-64)	44/ 37	Surgery vs. physio vs. collar	VAS 100mm	Present pain; worst pain last week	Present pain surgery 47 ± 26 physio 50 ± 21 collar 49 ± 51	surgery 30 ± 28 physio 39 ± 26 collar 35 ± 24	not calculated

M= male; F= female; yrs = years; SD = Standard deviation; FU = follow-up; Con = conservative; pre= pre-treatment; post = post treatment; CSLP = cervical spine locking plate; CIFC = carbon fibre intervertebral fusion cage; CP =Cloward procedure; vs. = versus; NRS/NPRS = Numerical Pain Rating Scale; VAS = Visual Analog scale; Avg = average, physio = physiotherapy. For surgical studies, pain scores have been presented for single level surgery only.

2.6.1 Pain and Disability

Functional disability and psychological distress play a more important role in prediction of chronic pain than initial pain intensity (Hunter 2001). Pain and disability have both been used as outcome measures in CR studies (Peolsson et al. 2003). High pain intensity has been shown to be associated with a high level of disability, lengthy symptom duration (Persson and Lilja 2001) and previous similar symptoms. High levels of disability has been associated with high pain intensity, low general health, low expectation of treatment and lengthy symptom duration (Kjellman et al. 2002).

The relationship between pain and disability has been explored in two ways: (i) where both the variables have been measured during the same time (Persson and Lilja 2001) and (ii) where one variable has been measured at baseline and correlated with the other at follow-up. Persson and Lilja (2001) reported that at the 3 and 12 month follow-up, all items in the disability scale (Disability Rating Index) showed significant positive correlations with pain, independent of the prescribed treatment, whereas at baseline there was a positive correlation between only some items of the DRI and pain intensity. The second type of association was explored by Peolsson et al (2003; 2004; 2006b). Low correlations (r =0.26, p= 0.02) were reported between pain intensity (VAS) at baseline, used as a predictive variable, and disability (NDI) at follow-up (Peolsson et al. 2003) where (Persson and Lilja 2001;Persson and Lilja 2001)(Persson and Lilja 2001; Persson and Lilja 2001)pain, the best predictor for disability at one year, explained only 13% of the total variance of disability (Peolsson et al. 2003). In another study by the same group of authors (Peolsson et al. 2006b), a stronger association between NDI at three years and baseline measures of pain intensity (r = 0.65, p=0.003) and neck pain (r=0.47, p = 0.04) respectively was reported. Using a stepwise linear regression analysis, 73% of variance in disability scores (NDI) at three years was explained by DRAM scores, pain medication intake and pain intensity at baseline (Peolsson et al. 2006b). The relationship between pain and disability has been explored so far in two studies and reported in multiple publications (Persson et al. 1997a; Persson and Lilja 2001; Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b). The results have been variable as the authors have analysed data from sub-groups of the same patient population and reported these results in different publications. These results may have further been influenced by the variable drop-out rates at different follow-up points. Long-term disability in CR can lead to low patient satisfaction with treatment and since this relationship has been explored in very few studies, further evaluation of this relationship would be a good inclusion in future studies.

2.6.2 Depression

Studies of psychological distress and depression have shown that these factors may impact on treatment through reduced patient participation and compliance (Harkapaa et al. 1991; Moeti and Marchetti 2001). Factors such as pre-existing psychological stress, depression and anxiety may increase the reaction to pain and alter pain behaviours. Conversely, the functional limitation associated with pain in CR may be a cause of emotional disturbance (Persson and Lilja 2001). These authors reported significant correlation between depression and pain at the completion of treatment in CR patients treated with surgery or a cervical collar. The explanations for this finding related to either a feeling of hopelessness in relation to the disorder, or low expectations of treatment (Persson and Lilja 2001). In a surgical study (Peolsson et al. 2006b), the baseline DRAM score was significantly correlated with neck pain, arm pain, disability scores at a three years follow-up and was a predictor of these outcomes. Depression is an important factor that needs to be considered in predictive intervention studies (Beneciuk et al. 2009). Depression as a baseline variable has been used in only one previous CR study (Peolsson et al. 2006b) and therefore its inclusion as a predictive variable in future prospective CR studies is important.

2.6.3 Scales for pain, disability and depression/anxiety used in previous CR studies

Pain evaluation is difficult because of its subjective nature and the reliability of pain scales in the clinical setting is underscored here. Further, the intensity of pain has been measured in various ways in different studies. Pain was assessed for intensity (by modifying a 5 point scale developed by Melzack and Torgerson (1971)), and quality (a descriptive score which was later assigned numerical values, 0 to 5) (Sampath et al. 1999). 'Average pain' and 'worst pain' scores were derived from these and an 'overall score' was calculated from the mean of 'worst pain' and 'average pain' scores. The reliability of this method of pain measurement was not reported (Sampath et al. 1999). Pain has also been assessed with respect to 'current pain' and 'worst pain' (Persson et al. 1997a; Persson and Lilja 2001; Peolsson et al. 2006b) using a VAS. Cleland et al (2007a) used an11 point Numerical Pain Rating Scale (NPRS) to assess pain by calculating the average of current, worst and lowest pain intensity reported in the past 24 hours.

Both the 10cm Visual Analogue Scale (VAS) (Hacker et al. 2000; Zoega et al. 2000; Persson and Lilja 2001; Garvey et al. 2002; Peolsson et al. 2003; Peolsson et al. 2004) and the 11 point NPRS (Cleland et al. 2005; Tseng et al. 2006; Cleland et al. 2007a; Raney et al. 2009) are reliable pain assessments and have commonly been used to measure pain intensity. Cleland et al (2005; 2007a) used the 11 point NPRS, based on the findings of Jensen et al. (1994) who found that the 11 point scale provided a pain measurement of equal value to the original 101 point scale. An earlier study Jensen et al (1986) compared the utility of the 10 cm VAS, the 101-point NPRS (101-NRS), the 11–point Box Scale (BS-11), the 6 point Behavioural Rating Scale (BRS-6), the 4-point Verbal Rating Scale (VRS-4) and the 5-point Verbal Rating Scale (VRS-5). They concluded that the 101-NRS was the most preferred pain measurement technique with respect to reliability, validity, responsiveness, ease of administration and sensitivity to statistical analysis.

The neck pain disability questionnaires such as the Neck Pain and Disability scale (NPAD) (Wheeler et al. 1999), Neck Disability Index (NDI) (Vernon and Silvan 1991) and the Northwick Park Questionnaire (NPQ) (Leak et al. 1994) have been developed to assess aspects of neck pain-related disability. Pain is acknowledged as being a complex perceptual experience, with sensory, affective, and intensity dimensions. The NDI is a single dimension scale and pain intensity accounts for 59% to 65% of the total variation. The NPAD has four factors: neck problems, pain intensity, emotion and cognition, interference with activities of daily living. The NDI and the NPQ are based on the Oswestry questionnaire (Pietrobon et al. 2002), while the NPAD was designed using the Million Visual Analogue Scale template. Both the NPQ and the NDI have been reported as reliable and valid scales (Pietrobon et al. 2002; Wlodyka-Demaille et al. 2002). The face, criterion, and construct validity, and test-retest reliability of the NPAD have been established in two independent studies (Wheeler et al. 1999; Goolkasian et al. 2002). Both NDI and the NPAD have been tested in a range of neck pain disorders (Goolkasian et al. 2002; Tseng et al. 2006; Raney et al. 2009). Limitations of the NDI include poor responsiveness (Cleland et al. 2006) especially for detecting small changes in disability (Hoving et al. 2002). The advantage of the NPAD is the multi-dimensional nature of the questionnaire, and the responsiveness of each factor with respect to treatment (Goolkasian et al. 2002; Pietrobon et al. 2002).

The NPAD has been reliably translated into French (Wlodyka-Demaille et al. 2002) and Turkish (Bicer et al. 2004). Disability scales developed in a country reflect the language expressions of that country and its socio-cultural way of life (Bicer et al. 2004). There is no neck disability questionnaire currently available in Hindi, the national language of India. This is a major disadvantage when neck pain research is conducted in the local population who do not understand or speak English. Since the NPAD translation into French and Turkish was reliable and valid, it seems a suitable choice of scale to be translated into Hindi. To be relevant to the Indian population, adaptation to local expressions and lifestyle factors would be required. Further testing of the reliability and validity of the translated version would be required prior to introduction into clinical studies. Furthermore, the cognitive and emotional domain of the NPAD correlates well with the Beck Depression Inventory (BDI) (Wheeler et al. 1999). Therefore, the added advantage of a Hindi version of the NPAD would be that not only would it provide a comprehensive measure of pain and disability but would also measure anxiety and cognition.

2.6.4 Cervical spine radiographic segmental angle and sagittal curvature

Degenerative changes in the spine can cause changes in sagittal segmental curvature or sagittal plane curvature (lordosis) (Pointillart et al. 1995; Das et al. 2001; Pickett et al. 2004). Surgical treatment of the cervical spine (ACDF) has been associated with kyphotic deformity and graft collapse in the early post-operative phase and at longer-term follow up (Abd-Alrahman et al. 1999; Wang et al. 1999; Hacker 2000) Fusion in segmental kyphosis increases the load on adjacent disc segments, leading to accelerated degeneration (Katsuura et al. 2001). The development of post-surgical segmental kyphosis may not necessarily change the total cervical lordosis, possibly due to compensation in other regions of the neck (Troyanovich et al. 2002; Pickett et al. 2004). Radiological segmental alignment measurements have been used to assess morphological changes at the affected level, the effect on adjacent segments (Oda et al. 1999), and the influence of segmental kyphosis on long term pain and disability (Peolsson et al. 2003; Peolsson et al. 2004).

The interpretation of segmental alignment and cervical lordosis measurements as outcome variables requires consideration of the variability of these measurements in the normal population. Cervical sagittal curvature values have been described in an asymptomatic population in which significant variability was evident (Penning 1978). Pain may further contribute to variability in these measurements (Table 2.3) particularly at segments in the lower cervical spine in which CR is more prevalent. In clinical studies, differences in sagittal cervical curvature have been identified in patients with similar pain scores. The C2-7 (2 line Cobb’s method) values of five alignment types were lordosis (17.5° ± 7), straight (2.8° ± 6.7), kyphosis (-16.5° ± 6.4), upper lordotic and lower kyphotic (-1.6° ± 6.1) and upper kyphotic and lower lordotic

(4° ± 6.4) (Takeshima et al. 2002). The C2-7 sagittal curvature measurement (Cobb angle) ranged from 30.2° lordosis to -17.2° kyphosis patients (n =14) with CR and cervical myelopathy (Pickett et al. 2004) (Table 2.3). Using the same method of curvature analysis, considerable variation in patients (n=30) with degenerated discs was reported (lordotic: mean = 21.7° (95% CI 17.5 to 25.8), straight: mean = 7.3° (95% CI 1.6 to 13.1) and kyphotic: mean= -9.7° (95% CI –22.5 to -3.2) (Cote et al. 1997). However, the radiographs included in the analysis were those with more significant degenerative change and cervical curvature, and may therefore be representative of more advanced cervical degeneration.

Cervical segmental radiological alignment has been measured in surgical studies and correlated with successful fusion, pseudoarthrosis, pain and disability (Emery et al. 1997; Das et al. 2001; Peterson et al. 2003; Peolsson et al. 2004). Contemporary surgical techniques strive to maintain the original segmental alignment reflecting the importance of maintaining the normal load bearing mechanics of the cervical spine (Pickett et al. 2004). However, some surgical studies have shown no statistical difference between patients with preserved and abnormal segmental alignment with respect to clinical outcomes at one year post-surgery (Pointillart et al. 1995; Heidecke et al. 2000; Laing et al. 2001). In contrast, other studies have demonstrated an association between segmental alignment and clinical outcomes. Interestingly, increased segmental kyphosis was associated with a better functional outcome at the one year follow-up (Vavruch et al. 2002). Similarly, Peolsson et al. (2003) observed that a pre-operative segmental kyphosis was correlated with a lower post-operative disability (NDI) score.

The segmental kyphosis has also been included in studies attempting to predict surgical outcome in patients with CR (Peolsson et al. 2003; Peolsson et al. 2004). Pre-operative segmental kyphosis was found to explain between 4 and 9% of the variance in post-operative pain and disability (Peolsson et al. 2003; Peolsson et al. 2004). Unfortunately, this is of little value in relation to prediction of the response to treatment, as more than 90% of the variance in outcome is not accounted for. This is a consistent finding in the publications of the Peolsson and co-workers. Statistically significant univariate associations are reported which reflects the confidence of the variables being associated. Due to the large sample size and narrow confidence limits, the magnitude of the covariance however needs to be considered in the clinical interpretation.

Table 2.3 A review of studies for measurement values of mean (SD) values of radiographic cervical curvature (C2-C7) in asymptomatics and different clinical population

	Harrison et al. (2004)	**Harrison et al. (2004)**	**Harrison et al. (2004)**	**Pickett et al. (2004)**	**Harrison et al. (2000)**	**Harrison et al. (2000)**
Method used	PTM	PTM	PTM	Cobb's	Cobb's	PTM
Population type	asymptomatic	Acute pain	Chronic pain	Myelopathy/ radiculopathy	Patient (type not mentioned)	Patient (type not mentioned
n	72	52	70	14	30	30
Age group mean ± SD (range)	40.6 ± 10.4	34 ± 11	44 ± 15.1	41.8 (30-56)	Not mentioned	Not mentioned
Levels						
C2-3	6.4 ± 5.3	6.5 ± 4.2	5.6 ± 5.4		1.60 ± 4.6	5.84 ± 5.1
C3-4	6.9 ± 5.0	5.7 ± 5.6	3.5 ± 5.5		4.35 ± 5	5.07 ± 5.5
C4-5	6.8 ± 4.9	6.3 ± 6	4.7 ± 5		1.87 ± 6.4	5.50 ± 6.9
C5-6	6.6 ± 5.3	5.2 ± 12	3.1 ± 5.1	4.09 ± 10.7	3.94 ± 6.4	2.66 ± 7.9
C6-7	7.8 ± 5.9	4.7 ± 13	5.1 ± 8.	4.83 ± 16.15	5.45 ± 4.9	6.67 ± 5.2
C2-7	34.5 ± 9.8	28.6±10.6	22.0±14.5	12.20 ± 13.4	17.20 ± 14.6	25.77 ± 13.4

n = number of patients; PTM = Posterior Tangent Method

All measurements are in degrees

2.6.5 Methods of cervical spine radiographic sagittal curvature measurement

Sagittal curvature of the cervical spine is usually measured from lateral cervical spine radiographs (Hacker 2000; Zaveri and Ford 2001; Peolsson et al. 2004). The most common measurement is the Cobb angle which was originally described for the measurement of thoracolumbar scoliosis from antero-posterior radiographs (Emery et al. 1997; Kawakami et al. 2000; Zaveri and Ford 2001). The angle is formed by the intersection of perpendiculars from lines drawn through the end-plates of the vertebral bodies at each end of the spinal region being measured. Measurement of cervical spine curvature using this method involves drawing lines parallel to the inferior endplate of the C2 vertebral body and the inferior vertebral endplate of the C7 vertebral body. Perpendiculars drawn from these lines form the angle of cervical curve from C2/C3 to C7 (Figure 2.3).

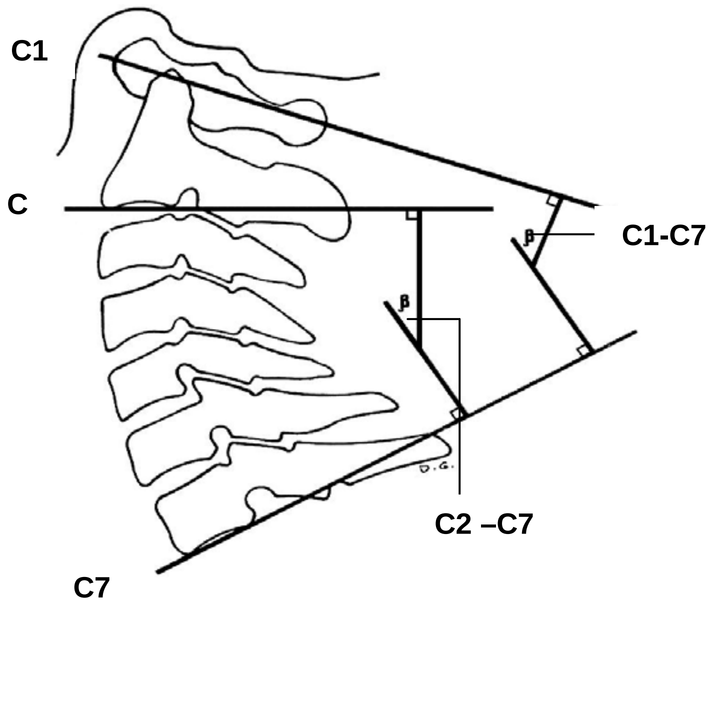


Figure 2.3 The four line Cobb's method on lateral cervical radiograph. C1- 7 angle formed by perpendiculars dropped from line C1 (line joining C1 anterior and posterior tubercles) and C7 (line drawn along inferior C7 vertebral body endplate). Similarly, angle formed between C2- 7.

The suggested advantages of the Cobb's method are that it has been traditionally used and comparisons of normative values can be made with previous literature. Using the Cobb angle for cervical spine measurements, the inter-examiner error has been reported as being 8.3° (ICC = 0.96, 95% CI = 0.88 to 0.98) (Cote et al. 1997). The intra-examiner error values reported in other studies are 4.5° for the thoracic spine (Singer et al. 1990) and 10° in the lumbar spine (Polly et al. 1996). In longitudinal studies of cervical curvature, changes recorded in follow-up examinations that are less than measurement error cannot be attributed to change in the status of the disease or the effects of treatment.

The method of cervical curvature measurement proposed by Gore et al (1986) uses the posterior vertebral body as the reference landmark. This method was compared with the Cobb angle method for C3 to C7 cervical curvature in 20 asymptomatic individuals and 20 cervical patients with cervical spondylosis (Silber et al. 2004). The standard deviations of the intra-observer measurements were lower using Gore's method compared to the Cobb angle in both groups. Intra-observer error values were significantly lower for the Gore method but descriptive data and unit of error were not reported (Silber et al. 2004).

Similar to the curvature analysis technique of Gore is the Posterior Tangent Method (PTM) (Harrison et al. 1996) (Figure 2.4). Harrison developed the technique using engineering analysis (Harrison et al. 2000) and applied the PTM to measure segmental and global angles from lateral cervical radiographs. High intra - examiner reliability values for the C2 to C7 curvature were reported (Pearson's r = 0.82 to 0.95, 95% CI = 0.80 to 0.99), with intra and inter-tester error of less than 2°, for hand drawn (Figure 2.4) and computer generated angles (Jackson et al. 1993) (Table 2.3). Harrison et al. (2000) described the total C2 to C7 curvature values obtained by the Cobb's of less than 17° compared to the PTM which were up to 26°(Table 2.3) (Harrison et al. 2000). The Cobb angle is not an optimal method in the cervical spine as the inferior end-plate does not form a perpendicular with the posterior vertebral body (Harrison 1986; Harrison et al. 1998). This is further compounded in the degenerative cervical spine, where the presence of osteophytes makes it difficult to identify true anatomical borders.

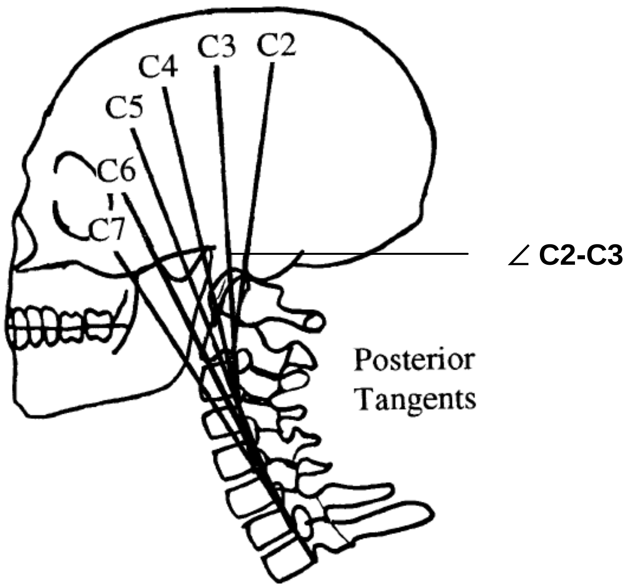


Figure 2.4 The Harrison's Posterior Tangent method (PTM) on a lateral cervical radiograph image from C2-C7. Posterior tangents are drawn along the posterior margin of each vertebral body, joining the postero-superior and postero-inferior vertebral body corners. Angle formed between C2-C3 posterior tangent lines is demonstrated above.

The variability of cervical segmental curvature measures in a normal population is large; however, clinical studies have demonstrated that this variability is accentuated in the presence of pain and pathology. Harrison et al (2004), demonstrated significant differences in C2 to C7 segmental alignment measurements between patients with pain and asymptomatic subjects (Table 2.3). Measurement error should be minimised in order for measures of cervical segmental curvature to be included with confidence in studies which seek to monitor change in these variables over time, or include them in predictive outcome models.

2.6.6 Cervical spine radiographic sagittal segmental motion

Abnormal segmental motion has been used as an indicator of mechanical instability which, when associated with pain, may require medical or surgical intervention (Dvorak et al. 1993). Analysis of cervical segmental motion in the sagittal plane may be conducted using functional radiographs obtained with the spine at the extremes of flexion and extension.

Radiological methods have been used extensively to study segmental kinematics of the cervical spine. Segmental motion in the sagittal plane is a combination of sagittal rotation, together with postero-anterior and superior-inferior translation (Dvorak et al. 1993). Comparison of translational motion between studies is possible when measurements are conducted using the same anatomical landmarks on the vertebral body. In normal individuals, translational movements have a linear association with rotational movements (Frobin et al. 2002; Kristjansson et al. 2003). Translation is dependent on the magnitude of physiological forces used to produce the motion. In cadaveric studies, Moroney et al (1988) calculated maximum antero-posterior translation of 0.52mm in response to a physiological load of 19.6N. In response to a force of 50N, antero- posterior translations of up to 2.5 mm have been described (White et al. 1975). Consequently, sagittal translation ranges or motion is small, and dependent on the applied forces, the magnification of the radiograph and the measurement technique. Segmental sagittal rotation measurements are reported more consistently, despite different methods of measurements used. They are more commonly used in clinical studies (Penning 1978; Dvorak et al. 1993).

Variability in sagittal segmental rotation in the cervical spine can be due to the segmental level and age. Segmental rotational motion has been reported as being smallest at C2-3 and greatest at C4-5 and C5-6, followed closely by C6-7 (Penning 1978; Dvorak et al. 1988a; Dvorak et al. 1993; Takeshima et al. 2002) (Table 2.4A). Total motion from C2-3 to C6-7 tends to decrease with age (Qi et al. 2000). The maximum segmental sagittal rotation is generally greatest at C5-6 in younger individuals and at C4-5 in older people, possibly due to the greater prevalence of degenerative change in the lower cervical disc segments (Holmes et al. 1994; Qi et al. 2000).

Analysis of normal sagittal segmental rotation (flexion-extension range of motion) has been reported in a number of radiological studies using different measurement techniques (Penning 1978; Dvorak et al. 1988a; Ordway et al. 1999; Puglisi et al. 2004). A review of these studies is presented in Tables 2.4 A & 2.4 B.

Table 2.4 A Segmental range (in degrees) of flexion-extension range of motion values in the middle and lower cervical spine in asymptomatic populations. All segments show a large spread of normal values.

Author/s	**Lysell (1969)** *	**Penning (1978)**	**Dvorak et al. (1988b)**	**Dvorak et al. (1993)**	**Ordway et al. (1999)**	**Puglisi et al. (2004)**
Number of subjects	28	020	28	45	20	126
Age in years Mean ± SD (range)	52 (11-67)	Young adults	22-47	31 (23-49)	31 (20-49)	31± 7
Active/passive	cadaver	active	active	passive	active	active
Levels	Mean (range)	Mean (range)	Mean (range)	Mean ± SD	Mean ± SD	Mean ± SD
C2-3	10 (5-16)	12 (5-16)	10 (5- 15)	12.0 ± 3.0	13 ±5	10.0 ± 3
C3-4	15 (7-26)	18 (13-26)	15 (7 –23)	17.2 ± 3.9	17 ± 4	15.7 ± 3.5
C4-5	20 (13-29)	20 (15-29)	19 (13-26)	21.1 ± 3.5	19 ± 4	17.9 ± 4
C5-6	20 (13-29)	20 (16-29)	20 (13-28)	22.6 ± 4.2	19 ± 3	18.9 ± 4.6
C6-7	17 (6-26)	15 (6 –25)	19 (11-26)	21.4 ± 3 7	17 ± 5	16.2 ± 4.9

Methods used: Radiograph & co-ordinatograph (Lysell 1969); Radiograph superimposition (Penning 1978), (Dvorak et al. 1988b); Radiograph superimposition and software analysis (Puglisi et al. 2004), (Dvorak et al. 1993); Digitised radiographs & software analysis (Ordway et al. 1999)
* Cadaver study

When compared to a reference population, patients with neck pain tend to have decreased segmental translation and flexion-extension rotational motion in the cervical spine. Postero-anterior translation in three patient groups (radicular, degenerative and traumatic) was significantly decreased compared to an asymptomatic control group, with this difference most evident in the C6-7 segment. Furthermore, 40% of all cervical segments in the patient groups were hypomobile in superior–inferior translation (Dvorak et al. 1993). In patients with whiplash associated disorders (WAD), and using a different measurement method, the C5-6 segment was significantly hypomobile compared to the range measured in individuals without pain (Kristjansson et al. 2003). Similar impairments of segmental rotation have been reported in patients with WAD (Dvorak et al. 1993; Puglisi et al. 2004) (Table 2.4 B). Patients with WAD have also been shown to have significantly less total flexion-extension motion measured from spinal radiographs, compared to healthy matched control subjects (Puglisi et al. 2004).

Very few studies have analysed total sagittal range, or sagittal segmental motion in patients with CR. The total active pre-operative flexion-extension range of motion measured from C2-7 in patients with CR was reported as being $45.4 \pm 15.6°$ (Ishihara 1968). This value is lower than the same flexion-extension range measured in asymptomatic subjects. Motion in the C6-7 segment was reported as being decreased in patients with disc degeneration and CR, compared to an asymptomatic group (Dvorak et al. 1993) (Table 2.5 B). This is in contrast to the study of Lysell (1969) who reported that degenerative changes in the cervical spine had no effect on sagittal segmental motion. It must be noted that the study by Lysell (1969) was a cadaveric study and the method of measurement significantly different to that used in clinical studies.

Table 2.4 B Segmental flexion-extension range of motion values (in degrees) in the middle and lower cervical spine in a symptomatic population. A brief review of four studies

Author/s	**Dvorak et al. (1993)**			**Takeshima et al. (2002)**	**Kristjansson et al. (2003)**	**Puglisi et al. (2004)**
Type of patients/subject	Degenerative	Radicular	Whiplash	Chronic WAD	Neck pain	WAD (grades I & II)
Number of patients	13	16	35	129	48	32
Age (years) Mean ± SD	41	40	38	36.7 ± 7.2	33 ± 12.9	29.3 ± 8.5
Active/passive	passive	passive	passive	active		passive
Levels						
C2-3	10.2 ±3	9.7 ±3.6	10.7 ± 3.7	9.7 ± 2.8	6.5 ± 3.9	
C3-4	16.5 ±2.5	16.4 ±5.6	18.4 ± 4.5	14.4 ± 3.7	11.8 ± 4.4	19.3 ± 3.7
C4-5	19.2 ±4.	18.7 ± 3.6	21.6 ± 5.1	16.9 ± 3.8	14.3 ± 4.8	21.1 ± 4.0
C5-6	16.7± 6	19 ±6.1	21.3 ± 5.5	16.8 ± 4.4	16.1 ± 4.7	21.3 ± 4.6
C6-7	15.9± 4.5	13.8 ± 4.7	17.4 ± 6.1	12.7 ± 5.2	11.1 ± 4.8	

Method used by all authors: Radiograph superimposition and software analysis

In cervical spine degeneration, hypomobility evident at the affected levels suggests a limiting mechanism, which could be active, or reflexogenic muscular restraint caused by pain, or the effect of degenerative change on segmental motion (Dvorak et al. 1993). Degenerative disc disease results in loss of disc height and desiccation of the disc material. Segmental motion in the sagittal plane is influenced by structural factors such as disc height, and the antero-posterior dimension of the vertebral bodies. Segmental motion is also influenced by the stiffness of the disc, with increased stiffness being associated with decreased motion (White and Panjabi 1990b). Segmental hypomobility has been identified radiologically in individuals with cervical disc pathology compared to individuals without disc degeneration (Good and Mikkelsen 1992). To date, comparative data is limited with respect to segmental motion and the influence of pathology in well controlled clinical studies. A large study comparing patients with CR with an asymptomatic group would provide useful information about the influence of pain and pathology on cervical sagittal segmental motion.

The influence of cervical segmental hypomobility on clinical outcome in individuals with neck pain or CR is not known. Although hypomobility can be due to disc degeneration or pain (Dvorak et al. 1993), the relationship between segmental motion and pain has not been explored in previous literature. A frequent diagnostic aid in spondylotic radiculopathy, the utility of radiographs can be enhanced if segmental motion is associated with pain or predictive of the long term pain outcome.

2.6.7 Methods of measurement of cervical spine radiographic sagittal motion

Measurement of cervical segmental motion in the sagittal plane is usually achieved using lateral radiographs. One of the earliest known methods for this analysis is that described by Buetti Buamel (1954). Another popular method (Penning 1978) (Figure 2.5) requires superimposition of the extension radiograph over the flexion film, in order to examine changes in segmental orientation at the extremes of the sagittal range. From these tracings of the vertebral bodies, movement is represented in the form of a movement diagram. The Penning (1978) method has been found to be more reliable than that of Buetti Buamel (1954) in asymptomatic subjects, and in patients with soft tissue injury of the neck (Dvorak et al. 1988b). Dvorak et al (1991) developed a technique which involved the superimposition of the flexion over the extension radiograph, then using a digitising system (Digikon DK2020, Kontron, Germany) to measure the segmental rotation values. Puglisi et al (2004) used the Penning method of drawing lines along the radiograph edge after superimposition of the vertebral bodies of each segment using the flexion and extension lateral radiographs. To improve reliability, the authors chose to scan the image formed by the lines and analyse the angles using a software programme. The inter-examiner reliability has been reported as being between 1.5° to 2° (Puglisi et al. 2004). Reliability of the Penning method has been reported correlation coefficients of between r=0.60 to 0.80, based on paired comparisons from measurements derived by 5 examiners (Schop et al. 1999).

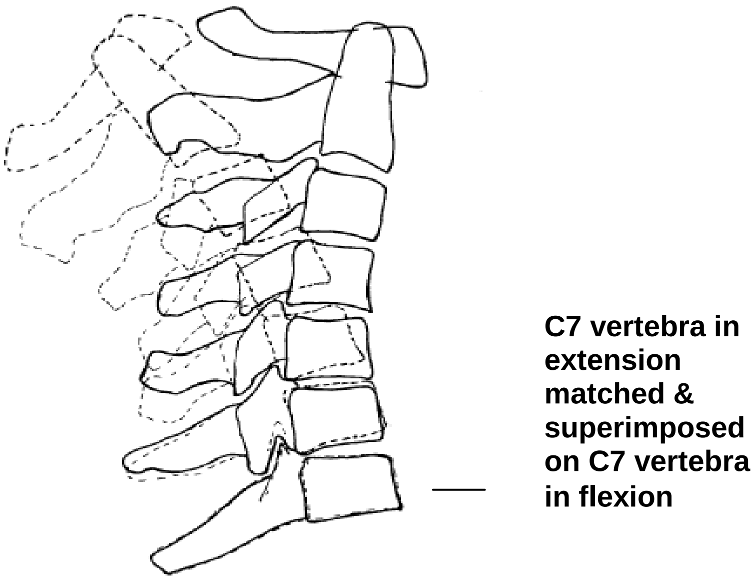


Figure 2.5 Penning's method of superimposition of lateral extension radiograph (solid lines) over the lateral flexion radiograph (interrupted lines) to calculate flexion-extension motion.

The Penning method of flexion-extension segmental motion analysis is an inexpensive method that can be used in routine clinical practice. This method is useful in a country like India, where expensive and sophisticated software analysis may not be available in all regions of the country.

2.6.8 Clinical measurement of cervical spine range of motion

The cervical spine is the most mobile region of the spine, affording the head a large range of motion. Composite cervical spine movement is difficult to investigate accurately because of the complex anatomy and variable movement patterns that may be associated with habit, posture or pain. In spite of this, the assessment of cervical range of motion is a fundamental component of clinical examination, contributing to clinical reasoning, diagnosis and evaluation of treatment efficacy.

Clinical disorders of the spine are associated with symptoms of pain, disability and, in many cases, an impairment of range of motion (Jordan et al. 1997; Dall'Alba et al. 2001; Lee et al. 2004). Neck mobility is influenced by pain (Cassidy et al. 1992; Jordan et al. 1997), trauma (Osterbauer et al. 1996), disease (Viitanen et al. 1998) and whether the movement is measured actively or passively (Table 2.5). Pain and stiffness during, or at the extremes of motion, consistent with the patients symptoms, is indicative of abnormal mechanics of the cervical spine. Significant reduction in primary and conjunct ROM was observed for patients with degenerative cervical spine disorders (Dvir et al. 2006) and whiplash associated disorders, compared to matched asymptomatic individuals (Dall'Alba et al. 2001). A significant reduction in active neck extension has been seen in patients with chronic neck pain (Jordan et al. 1997), degenerative disc disease (Dvir et al. 2006) and whiplash associated disorders (Dall'Alba et al. 2001) (Table 2.5).

Although clinical conditions of the cervical spine are commonly associated with a decrease in range of motion (Jordan et al. 1997; Dall'Alba et al. 2001; Lee et al. 2004), composite cervical range of motion measurements have not been commonly employed as outcome measures in surgical studies. Cervical spine range of motion is linked to function, and the loss of some movement due to surgical fusion is not considered significant unless it hampers the quality of the patient’s life. Grob et al (2001) reported an increase in cervical ROM following a single or double level cervical fusion. Peolsson et al (2003) examined the association between neck range of motion and pain and disability, and reported a negative correlation between NDI scores at follow-up at two years and baseline active neck flexion ($r = -0.33$, $p=0.005$) and right rotation ($r= -0.40$, $p = 0.0009$). In the same study, significant correlations between pain intensity (VAS) and range of motion were not found. Further, a step-wise regression analysis found that 23% of the variance in NDI scores was explained by low baseline pain intensity, non- smoking and higher active neck flexion mobility (Peolsson et al 2003).

Conservative management studies have used composite cervical movements for the purpose of diagnosis of CR. Cervical rotation to the involved side of less than 60° (LR+ 1.8, 1.3 to 2.4) and cervical flexion of less than 55° (LR+ 1.5, 1.2 to 2.0) were two of eleven variables to have diagnostic accuracy for CR. Of these, cervical rotation of less than 60° was one of the four cluster items for the most accurate diagnosis of CR, when compared to a reference standard of neurodiagnostic testing (Wainner et al. 2003). Following this study, Waldrop (2006) used the Clinical Prediction Rule (CPR) proposed by Wainner et al (2003) to assist the diagnosis of patients with CR.

Following treatment with multi-modality physiotherapy, five out of six patients achieved an increase in cervical range of motion including rotation of greater than 60° bilaterally. Cleland et al (2005) used the CPR in their study, but did not report the cervical ROM outcome. Cleland et al (2007a) is the single conservative study which has explored the capacity of cervical ROM to predict outcome in patients with CR. They identified variables ‘looking down does not worsen symptoms’ (LR+ 1.3, 0.93 to 1.8) and ‘flexion greater than 30°’ (1.4, 0.89 to 2.1) as significant predictors of short term success of conservative management in patients with CR. Although the two individual variables were significant predictors, the LR+ values close to 1 indicate a post-test probability of a successful outcome as being nearly equal to the pre-test probability of a successful outcome. The two variables are similar with respect to neck function and therefore the flexion range variable was not included in a logistic regression analysis to identify the best set of predictive variables for treatment outcome. ‘Looking down does not worsen symptoms’ formed one of the four predictors which maximised the likelihood of a person achieving a successful outcome. Inter-tester reliability of these measures was not established by the authors.

Both surgical and conservative management studies are limited (number of studies, analysis used, reliability of outcome measure) in providing evidence on the association of cervical range of motion measures with pain and disability measures, in CR. Future research is required to study the association between these two measures. The role of functional limitations in the persistence of pain and disability should be studied further.

Table 2.5 Summary of review of studies for composite cervical range of motion (in degrees) comparing patients with neck pain disorders, with asymptomatic subjects. Variability in measurements in asymptomatic subjects and error values between repeat measurements are presented where available.

Author	Instrument used	(n)	Gender M/F	Age (years)	Sample type	Flexion	Extension	LR (R)	LR (L)	LF (R)	LF (L)	Error (SEM)
Dall'Alba et al. (2001)	Fastrak, Polhemius	89	41/48	39	Normal	47 ± 9	52	67 ± 8	68 ± 9	37 ± 8	38 ± 8	
Dall'Alba et al. (2001)	Fastrak, Polhemius	114	22/93	37	Whiplash	35 ± 11	37 ± 12	53 ± 13	54 ±14	31 ± 9	31 ± 10	
Sterling et al. (2002))	Fastrak, Polhemius	19	7/12	30 ± 11	Normal	41±11	56 ± 14	61 ± 13	65 ± 10	35 ± 5	35 ± 9	3 to 6
Sterling et al. (2002))	Fastrak, Polhemius	19	6/13	32 ± 11	Chronic Neck pain – traumatic/ non-traumatic origin	41 ± 11	53 ± 14	59 ± 8	60 ± 8	33 ± 7	34 ± 8	2 to 7
Tousignant et al. (2002)	CROM instrument	24	6/18	19-69	Neck pain					29 ± 10	28.2 (8.9)	
Lee et al. (2004)	CROM instrument	26	13/13	27 ± 7	Normal	58	74	73	74	45	46	
Lee et al. (2004)	CROM instrument	14	7/7	29 ± 7.	Sub-clinical neck pain	58	74	70	70	44	44	
Dvir et al. (2006)	Zebris CMS 70P	25	14/11	48 (28-70)	Degenerative changes	40 ± 15	35 ± 12.	47 ± 16	53 ± 16	30 ± 9	28 ± 10	4 to 9

M = males; F= females; LR = lateral rotation, LF = lateral flexion, R = right, L= left, SEM = Standard Error of Measurement, CROM = Cervical-Range -of -Motion instrument

2.6.9 Methods of composite cervical range of motion measurement

In clinical practice, an objective measurement of cervical range of motion is important, with measurement techniques requiring clinical utility and reliability. Reliability of the measuring instrument, with respect to inter- or intra-tester reliability, is an issue that require consideration in clinical trials. The universal goniometer has been shown to have a moderate inter-tester reliability for the measurement of cervical range of motion (Youdas et al. 1991). High on reliability and accuracy, Peolsson et al (2003) used the cervical measurement system (CMS) equipment, which had demonstrated excellent reliability and accuracy, to measure cervical ROM in a surgical patient cohort. Using the CA-6000 spine motion analyser, typical error of less than 3.9° for all motions was reported by Petersen et al. (2000) and coefficients of variance of between 2.4% to 10.9% by Christensen and Nilsson (1998a). Sophisticated and modern equipment such as the CA 6000 spine motion analyser (Petersen et al. 2000), FASTRAK (Jordan et al. 2000), and Ultrasound-based motion analysers (CMS 70P) (Dvir and Prushansky 2000), are capable of reliably measuring natural combinations of planes of movements. The disadvantage of these tools is that they are expensive and non-portable, and therefore confined to dedicated research laboratories or institutions. The cervical-range-of-motion (CROM) instrument (Performance Attainment Associates, Roseville, MN) has been repeatedly tested for its reliability and showed a high intra-tester (ICC > 0.84) and inter-tester (ICC > 0.73) reliability for all neck movements (Youdas et al. 1991). However, the CROM system measurements can be influenced by needle drag and geometric errors if the device is tilted during rotational movement. A more recent method is both non-invasive and easy to operate, and provides data that is clinically accurate and reliable. The Spin-T goniometer, designed and developed by Haynes and Edmondston (2002), is capable of measuring composite cervical movements. It has been found to be a reliable for measuring both primary and coupled movements of the cervical spine (Haynes and Edmondston 2002).

2.6.10 Composite sagittal ROM and radiographic sagittal motion of the cervical spine

Surface measurements of composite cervical flexion and extension have been frequently compared to measurements obtained from sagittal plane cervical radiographics (Dvorak et al. 1991; Ordway et al. 1997; Tousignant et al. 2000). As discussed earlier, radiological methods of cervical sagittal range of motion provide reasonably accurate and reliable measurements, and have normally been in research (Penning 1978; Dvorak et al. 1988b). The effect of cervical spine pain disorders and pathology on segmental mobility and surface measurements have been discussed earlier (Dvorak et al. 1993; Dall'Alba et al. 2001; Lee et al. 2004; Puglisi et al. 2004; Cleland et al. 2007a).

Total sagittal mobility from the occiput to C7, measured using a radiological technique (Dvorak et al. 1991) was compared to measurements derived using a computerised motion tracking device (Polhemus, Colchester, VT) and the CROM device (Ordway et al. 1997). Significant differences in range were identified between the CROM and the radiographic method ($p<0.05$), whereas there was better measurement agreement between the motion tracking device and the radiological measurements (Ordway et al. 1997). The reasoning provided by the authors was that measurement with the CROM device does not exclude thoracic movements entirely and this may have contributed to the difference. Accounting for thoracic spine movements Tousignant et al (2000) (n=31) measured cervical spine sagittal mobility using lateral radiographs and reported a significant correlation ($r= 0.97$ for flexion and $r = 0.98$ for extension) with measurements obtained using the CROM. Further, the CROM was able to explain 94% of the variance in the radiographic measures of cervical flexion and extension (Tousignant et al. 2000). Herrmann Bredenkamp (1990) compared measurements of cervical sagittal range of motion obtained using a pendulum goniometer with those obtained from lateral radiographs. Differences between the two methods were not significant, and the Pearson correlation between measures was strong ($r = 0.98$).

Safety concerns related to repeat exposure to radiation, together with financial constraints and availability, provide an incentive to establish a relationship between external cervical ROM and radiological measurements (Herrmann Bredenkamp, 1990). Results of studies in asymptomatic individuals (Herrmann Bredenkamp, 1990; Ordway, 1997), which have compared surface and radiological measurements, have shown that the two methods of measurement provide results which are not significantly different.

2.6.11 Posture evaluation

A consistent relationship between surface posture measurements and the presence of spinal pain has been difficult to establish, despite being the focus of a number of studies (Darnell 1983; Trott 1988; Kogler et al. 2000). However, there is evidence from some previous studies which suggests that neck posture is affected by pain or trauma. Patients with neck trauma have been found to have significantly lower postural performance than normal subjects (Kogler et al. 2000), whereas muscular pain (Trapezius muscle) did not cause significant posture differences compared to an asymptomatic group (Refshauge et al. 1994b).

The variability in this association between posture and pain is due to the departure from a well-balanced posture (relative to a vertical reference line) in individuals without neck pain (Grimmer 1997; Masse et al. 2000). This is due to the large number of factors which can influence spinal posture and sagittal curvature. Different whole body sitting postures can have an influence the posture of the cervical spine (Black et al. 1996). Similarly, thoracic spine curvature can influence head and neck posture, with hyper-kyphosis being associated with a larger atlanto-cervical angle than thoracic hypo-kyphosis (Zepa et al. 2000). Gender differences and body shape have an effect on posture as well (Hanten et al. 2000). Assessment of symmetry between the right and left sides of the body as well as increased or reduced spinal curvatures are common clinical observations. Despite the variability in the normal population, posture evaluation continues in clinical practice which provides the rationale to include posture analysis in cervical spine research. A forward head posture has previously been associated with altered tempero mandibular joint (TMJ) mechanics, thoracic outlet syndrome, cervical spondylosis, facial pain, neck pain and poor deep cervical flexor endurance (Darnell 1983; Rocabado 1983; Ayub et al. 1984; Grimmer 1996; Cleland et al. 2007b). A forward head posture is not always (Trott 1988) associated with an extended or hyperlordotic upper cervical spine, but previous studies have found this posture to be associated with a more flexed lower cervical spine (Darnell 1983; Ordway et al. 1999).

Cervical spine posture has not been used an outcome measure in clinical studies related to CR. Surgical studies reporting results of various spinal fusion techniques, do not typically measure the association with pain or degeneration. In a recent single case series study (Waldrop 2006), five out of six conservatively managed patients with CR presented with a forward head posture. Although Cleland et al (2005) evaluated posture in eleven patients with CR, the association with pain, and changes in response to treatment was not reported. Cleland et al (2007a) evaluated posture visually and categorised each subject into a postural group according to defined criteria. The authors (Cleland et al. 2007a) did not provide any reliability analysis of the measurement technique, and posture was not a predictor of short term outcome following conservative intervention. Conservative management studies have examined this association, but no conclusive results can be drawn with respect to the relationship between posture and pain. Posture evaluation may be included in a CR management study in order to determine whether the posture of the individual can influence the short or long-term pain or whether specific postural characteristics are indicative of the presence of pain.

2.6.12 Methods of posture evaluation

Head and neck postures are usually evaluated clinically by visual inspection. Quantitative methods include position of the head position in relation to a vertical reference line (Kendall et al. 1952; Ayub et al. 1984). A frequently used method of evaluating head on neck posture (Watson and Trott 1993; Raines and Twomey 1994; Grimmer et al. 1999) is the cranio-vertebral angle, first described by Wickens and Kiputh (1937). The head neck angle is a measure of the position of the tragus relative to the C7 spinous process, in the sagittal plane. The head-neck angle measures the external head and neck alignment. It is the angle formed by a line from the tragus to C7 intersecting with the horizontal. The average value of head-neck angle in normal adults is 49 ° ± 4° (Johnson 1998) and similar values were measured for children between the ages of 8 and12 years (Grimmer et al. 1999). The head neck angle measure provides a simple measure of forward head posture which has been associated with CR (Cleland et al. 2005). Further, the reliability of the cranio-vertebral angle measurement when measured on two occasions is good with reliability co-efficients of $r > 0.80$ (Rheault et al. 1989; Watson and Trott 1993).

The head neck angle measure is a reliable method of assessment of head on neck posture. Using this instrument, the relationship between surface angle markers and pain can be evaluated in the clinic.

2.6.13 Cervical Radiculopathy: Demographic and Lifestyle factors

Demographic information and lifestyles factors of patients with CR (Tables 2.6 & 2.7) have been reported in some studies (Dowd and Wirth 1999; Heckmann et al. 1999; Hacker 2000; Zoega et al. 2000; Grob et al. 2001). Some studies have examined the role of socio-demographic and lifestyle factors in predicting outcome in patients with CR (Persson and Lilja 2001; Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b; Cleland et al. 2007a).

Peolsson et al (2003) reported a non-significant negative correlation between age and post-surgery pain intensity (VAS) (-0.20, $p = 0.07$). They also used a step-wise regression model to show that increased kyphosis, male gender and older age could predict 24% variance of pain intensity at the long-term follow-up. A history of smoking explained a further 4% of the variance in the long-term pain outcome. An interesting observation from that study was that older age predicted greater decrease in pain intensity after surgery. This result is similar to Raney et al (2009) who reported that a patient age of greater than 55 years was a predictor of a successful outcome for neck pain treated with traction and exercises. Although, age of less than 54 years emerged as an individual predictor variable (LR+ = 1.5, 95% CI = 1.2 to 2.1) the associated likelihood ratio was low (Cleland et al. 2007a). Paradoxically, however, 'age < 54 years' was one of 4 variables that maximised the ability to identify subjects likely to experience a successful outcome after conservative management of CR (Cleland et al. 2007a). Future research is necessary to examine if age as a prognostic factor varies according to the type of intervention (surgical or conservative) within the CR population.

Gender has been similarly analysed with respect to outcome in patients with neck pain and CR (Table 2.6). At 3 year follow-up, gender has been shown to correlate significantly with arm pain (r= 0.59, p=0.02), neck pain (r= 0.59, p=0.02) and disability (r= 0.69, p=0.004) although gender did not emerge as a predictor of long-term outcome (Peolsson et al. 2006b). The authors stated that males were associated with a better outcome than females although no analysis was presented to substantiate this. Other studies have found that gender did not have a significant influence on pain and disability outcome in patients with CR (Thorell et al. 1998; Palit et al. 1999).

The role of BMI as a predictor for neck pain has been assessed in a population survey (Webb et al. 2003) as well as in clinical trials (Tseng et al. 2006; Raney et al. 2009). High BMI has been shown to predictor low back pain, although was not an independent predictor of neck pain (Webb et al. 2003). Raney et al (2009) reported that a high BMI was a significant predictor of a successful outcome following cervical traction in patients with neck pain. BMI has been reported in only one previous study of patients with CR (Heckmann et al. 1999). The study reported the proportion of individuals in each study group that had a BMI of greater than 28 (Table 2.6).

A survey of the determinants of upper limb pain in patients with neck pain revealed that pain was frequently bilateral or in the dominant arm (Walker-Bone et al. 2004). Since CR presents upper limb pain as a common symptom, the role of the dominant arm was explored by Cleland et al (2005) in a case series of 11 patients, and found that 6 patients had radicular pain in the dominant arm. In a later study (Cleland et al. 2007a) the role of the dominant arm was again evaluated. The 'dominant arm not affected' emerged as one of the four predictor variables of long-term outcome.

Individually, the LR+ value was 1.5 (95% CI = 1.1 to 2.2), with a post-test probability of success of 62.9% for a successful outcome which was not much higher to a pre-test probability of success as 53%.

The work characteristics (heavy work and light work) were assessed as part of the Disability Rating Index (DRI) of patients with CR (Persson and Lilja 2001), in order to compare patients treated conservatively with those treated surgically. After treatment and at the 12 months follow-up, the surgery group had improved scores for heavy work compared to the conservative group. Peolsson et al (2003) reported that greater pain and disability was found in blue-collar workers compared to white-collar workers although no data was presented to support this statement. Education levels may reflect a difference in work load which in turn may affect function (Peolsson et al. 2003). Very low but statistically significant negative correlations were found between baseline education levels (elementary school, vocational school, high school and university) and disability outcomes, implying that people with higher education will be more likely to have a lower level of disability. Vavruch et al (2002) calculated the percentage of patients with college education as 20% but did not discuss the implication of education as a variable. Other studies have examined employment status (Saal et al. 1996; Heckmann et al. 1999; Sampath et al. 1999) pre- and post-intervention to study the effects of treatment on employment. Categories of employment (Table 2.7) in the study of Sampath et al (1999) included employed, housewife, retired, unable to work.

Physical activity during leisure time was categorised by Waal et al. (2003), as an extra-individual determinant of musculo-skeletal pain. Leisure-time physical activity has not been examined with respect to outcome in any other studies examining CR and related management.

Marital status was recorded by Vavruch et al (2002) and Peolsson et al (2003) and Persson and Lilja (2001) reported living arrangements (Table 2.7). However, the implications of these variables on clinical status or treatment outcome with respect to CR were not discussed.

‘Well being at work’ with categories of positive, neutral and negative was recorded by Persson and Lilja (2001) as well as ‘transfer to another post due to neck pain’. There were no significant differences in these variables between the different treatment groups. Anxiety/distress (work-related or otherwise) have been recorded by others in this patient group (Persson and Lilja 2001; Peolsson et al. 2006b). Further, interpreting distress with the DRAM questionnaire (a psychosomatic and psychological assessment), Peolsson et al (2006b) concluded that normal DRAM scores were most important in predicting a successful outcome, measured as low pain and disability outcome.

Cigarette smoking has been shown to be a risk factor for developing disc disease (An et al. 1994), associated with a higher risk of spinal pain (Palmer et al. 2003) and lower rates of successful fusion in the lumbar (Andersen et al. 2001) and cervical spine (Persson and Lilja 2001). Although India's vast population makes it the second largest number of smokers in the world, the prevalence is lower (20-29%) compared to the majority of European countries (30-39%), China and Russia (60% and above) and comparable to the USA, UK and Australia (20-29%) (World Health Organization 2004). A lower prevalence rate was recorded in a study (Jindal et al. 2006) conducted in India which estimated a 15.6% 'ever smokers' (people with current or past smoking habit) in a sample of 73,605 subjects from different parts of the country. Indians smoke cigarettes as well as 'bidis'. 'Bidis' are more common in the lower socio-economic group as well as rural India. These are hand rolled cigarettes in temburni leaf tied with a string. Although they contain one-quarter tobacco compared to a full size cigarette, they are more lethal as larger quantities of tar and carbon-monoxide are delivered in each puff (World Health Organization 2004). Smoking correlated significantly with arm pain severity ($r= 0.56$, $p=0.03$) in patients with CR, and was included in a step-wise regression model, as a predictor of arm pain (adjusted $R^2 = 0.24$) (Peolsson et al. 2006a). Persson and Lilja (2001) detected no significant correlation between pain intensity and number of cigarettes per day, before or after treatment. However, non-smokers had significantly less pain before treatment ($p = 0.01$) and after treatment ($p = 0.03$) compared to smokers. This was more evident in the surgical group at the 6 months follow-up (Table 2.7).

Table 2.6 Demographic data of patients in previous CR treatment studies

Authors	**Treatment**	**Age in yrs Mean ± SD (range)**	**Gender n, %**	**BMI values N, %**
Dowd and Wirth (1999)*	surgery	50	M= 40% F = 60%	
Grob et al. (2001)*	surgery	49 (24-74)	M= 11 F= 15	
Heckmann et al. (1999)	surgery	50	M= 11, 52% F= 10, 48%	BMI >28 n=11 (52.3%)
Heckmann et al. (1999)	conservative	50	M= 21, 54% F= 18, 46%	BMI >28 n=11 (28.2%)
Hacker (2000) Φ	surgery	44 ± 9	M= 41% F= 59%	
Persson and Lilja (2001) Φ	surgery	45 (28-56)	M=16, 59% F= 11, 41%	
Persson and Lilja (2001)	conservative	48 (31-61)	M= 11, 41% F= 16, 59%	
Vavruch et al. (2002) Φ	surgery	47	M= 25, 61% F= 16, 39%	
Shah and Rajshekhar (2004)	surgery and conservative	42 (22 –60)	M= 37 F= 13	

* ACD, Φ ACF; BMI = Body Mass Index; n = number of patients

Table 2.7 Social data of patients in CR studies. Method of data analysis and choice of variables varies in different studies.

Study	**Work characteristics N (%)**	**Smoking N (%)**	**Living arrangements N (%)**
Dowd and Wirth (1999)		30%	
Heckmann et al (1999) (surgery)	Occupation with strenuous work 4 (19%)	9 (42.9%)	
Heckmann et al (1999) (conservative)	Occupation with strenuous work 6(15.4%)	8 (20.5%)	
Hacker (2000) Φ		47%	
Persson and Lilja (2001) (surgery)	Well being at work: positive 19 (70%), negative 1 (4%), neutral 7 (26%)	53 (65%)	Living arrangements: living with others 18 (66%)
Persson and Lilja (2001) (conservative)	Well being at work: positive 21 (78%), negative 1 (4%), neutral 5 (18%)		Living arrangements: living with others 22 (81%)
Vavruch et al. (2002) Φ	Blue collar 32 (78%)	20 (49%)	Married 95(39%)

* ACD, Φ ACF, N = number of patients

In studies evaluating both surgically and conservatively managed patients with CR, the symptom duration of the patients with CR has varied considerably with examples being from 2 months to 27 years (mean 26 $\pm$ 53 months) (Sampath et al. 1999) and between 6 months and 10 years (Heckmann et al. 1999; Persson and Lilja 2001). Surgically managed patients with CR treated in a medical facility in India reported a duration of symptoms ranging between 2 weeks and 3 years (Shah and Rajshekhar 2004). In contrast, patients treated conservatively with multi-modal physiotherapy, have had symptom durations of 18 weeks (median) (Cleland et al. 2005), 6 weeks (mean) (Murphy et al. 2006), 8 weeks (mean) (Cleland et al. 2007a) and between 6 days and one year (Waldrop 2006) or 2 years (Sampath et al. 1999). A longer duration of symptoms has been shown to impact on recovery (Yamamoto et al. 1991), as well pain intensity and emotional responses to the disorder (Andersson et al. 1993). The number of previous episodes of CR prior to recruitment into a management study was on average 3 with a range of between 0 and 8 episodes (Sampath et al. 1999). Cleland et al (2007a) measured the number of patients who had prior episodes and not the number of previous episodes.

The presence of co-morbidities has been evaluated in relation to clinical measures. Pain frequency and low back pain explained 58% of the variance in neck pain in a surgically managed cohort of patients with CR (n = 23) (Peolsson et al. 2006b). The presence of co-morbidities and the influence on treatment outcome has not been reported in other studies of patients with CR. The presence of co-morbidities and the association with pain, disability and response to treatment appears to be an important issue to examine in future studies of patients with CR.

Variables (risk factors and prognostic factors) have been combined to review their role in outcomes in CR studies. Data from available literature is not sufficient to evaluate the roles of these factors and their influence on outcome. A large sample study to investigate the role of these factors is required. Further, many of these factors have different prevalence and inter-relationships in different cultural settings. No studies have been undertaken examining these specific questions in a large Indian cohort. Consequently, any future studies in this area will be the first to report if findings in the Western literature can be generalised to the Indian population.

2.7 Summary of literature review

The purpose of this literature review was to review the variables reported in the literature related to CR, and examine their value as predictive variables for treatment outcome.

The range of measures and outcomes from different studies highlights the multi-dimensional nature of CR, and provides a good background for the development of future studies. There are many types of measures that can be used to describe the impact of CR on the patient, both before and after treatment. There are different domains of outcome assessment, and in earlier studies, the emphasis was primarily on measures of surgical success, for example, a successful fusion. However, it is well recognised in evidence based practice that such measures are not a reflection of the clinical outcome, or of patient satisfaction. The literature review revealed that treatment efficacy should also be measured using assessments of pain intensity, quality of life and functional status. Measures of impairment are important in circumstances where specific impairments correlate with function (such as pain free range of motion).

The literature highlights the importance of further studies to include clinical, functional, radiological, socio-demographic and lifestyle factors as outcome measures in patients treated surgically or conservatively for CR. The limited number of studies related to CR, conducted in India, underscores the importance of further evaluation of CR, and related management in that country.

CHAPTER 3

METHODS

3.0 Introduction

Based on the review of the related literature the principle focus of the planned research was to document the outcomes of a conservatively and surgically treated cohort of individuals with a medical diagnosis of cervical radiculopathy. The documentation of primary outcome measures of these patient populations and then the development of a CPR was the final data analysis of the thesis. From the literature, however it was clear that there were some fundamental questions to be answered in terms of what factors were associated with outcomes or even in differences between individuals with and without cervical radiculopathy. Furthermore, to contribute to the derivation of the CPR analysis it was necessary to undertake preliminary (but significant) research to validate and establish the reliability of specific methods of assessment. The thesis made particular focus on the assessment of radiological spinal curvature and flexion-extension motion and composite active cervical ROM.

Finally, the primary outcome variable of a responder non-responder status at 12 months following the specific intervention was established using the NPAD. It was felt necessary that this scale should be translated into the Hindi language, so this was undertaken to further validate the main clinical focus in the Indian context. These preliminary studies have in part been reported in the literature, however will also be reported in the following chapters.

The methods chapter is divided into three sections. The first section identifies the objectives, hypotheses and ethics of the research thesis. The second section is the preliminary study elements and the third the main clinical outcome study with the univariate and multivariate analysis for the data to develop a CPR for positive outcomes.

The methods of specific assessments are described and it should be noted that these methods were kept constant across the different elements of the series of independent research projects.

3.1 Objectives and Hypotheses

3.1.0 Objectives

The objectives of this research project are:

I. To test the accuracy and reliability of a cervical range of motion goniometer, the Spin-T goniometer, in a normal population.
II. To determine differences in active cervical range of motion in all three planes between an asymptomatic group and a CR patient group in an Indian population using the Spin-T goniometer.
III. To evaluate the reliability and validity of the NPAD, translated into Hindi, in a CR patient cohort.
IV. To establish intra-tester reliability of measures (PTM, Penning's method, head neck angle) which will be subsequently used as measuring instruments in a CR treatment outcome study.
V. To determine the effects of age, gender and time on active cervical range of motion (ROM) in an asymptomatic population in order to provide a normative database for longitudinal clinical trials intending to use active cervical ROM as an impairment measure.
VI. To record clinical outcomes from conservatively and surgically treated CR patients for a follow-up period of one year.
VII. To determine differences in segmental flexion-extension motion between a CR patient cohort and an asymptomatic population.
VIII. To compare composite sagittal plane active cervical ROM measurements with segmental radiographic flexion-extension motion of the cervical spine in the same plane.
IX. To explore the association between clinical outcome measures at one year with baseline measures of pain, disability, depression, cervical segmental curvature, head neck angle, active cervical range of motion (composite and segmental), patient socio-demographics and lifestyle details.

3.1.1 Alternative Hypothesis

It is hypothesised that clinical, radiological and functional variables of CR patients at baseline will predict clinical outcome at one year, following either conservative or surgical management.

Independent variables: Clinical, radiological, functional assessment; socio-demographic and lifestyle factors (all at baseline)

Dependent variables: NPAD score (at 12 months)

3.1.2 Sub –hypotheses

I At a one year follow-up, change in arm pain scores and neck pain scores will be similar in both treatment groups (conservative management or surgery) in a CR patient cohort.

II High pain intensity will correlate with disability before and after treatment in both treatment groups.

III Baseline assessments of radiological measures of cervical spine curvature and active cervical ROM will significantly correlate with pain and disability at baseline in both treatment groups.

IV Increased Head neck angle at baseline will be positively associated with increased pain at baseline.

V Radiographic segmental flexion-extension motion of the cervical spine will be hypomobile in a CR cohort, compared to a matched asymptomatic control group.

VI Reduced radiographic segmental flexion-extension motion of affected levels in the cervical spine, at baseline, will correlate with final neck pain scores in both treatment groups.

VII Measurements of active cervical spine flexion-extension (sum of flexion and extension) range of motion will correlate positively with radiographic measures (C2-7) of cervical spine segmental flexion-extension motion in both treatment groups.

VIII Baseline clinical, functional, radiological, socio-demographic measures and life-style factors will be associated with final neck and arm pain scores in conservatively and surgically treated CR patients.

IX Baseline clinical, functional, radiological, socio-demographic measures and life-style factors will be predictive of outcome at one year based on final NPAD scores in conservatively and surgically treated CR patients.

3.1.3. Human Research Ethics committee

Institutional Human Research Ethics Committee approval for this research project was received on 27.10.2003; reference number RA/4/1/0828.

3.1.4 Ethical considerations

All participants of this study were given a university approved consent form. In addition, information about the research and the importance of follow up was explained in full (Appendix 3.0). Research was started only after receipt of a signed consent form (Appendix 3.0) from the subject/patient according to institutional policy of the University of Western Australia. Candidates were free to withdraw their participation without prejudice.

3.1.5 Confidentiality

The confidentiality of identity, diagnosis and therapeutic records has been kept for all participants in this study.

3.1.6 Originality of the project

A structured literature search was undertaken during the development of this proposal. The search design identified and included all designs of studies (literature review, case studies, case series, clinical trials, cohort studies, randomised clinical trials, laboratory experiments and cadaveric studies). The search was conducted in the electronic databases of Medline, Embase, CINAHL and PEDro and Cochrane Collaboration (Back review group up to 2005) from 1982 – 2004 (citations from 2006 – 2008 were subsequently added during the course of the research trial) for published literature in English and foreign languages using the key words and MESH terms: cervical radiculopathy, surgery cervical radiculopathy, treatment cervical radiculopathy, predictive variables, predictive factors, Clinical Prediction Rule, Odd’s ratio, Likelihood ratio, neck pain, cervical radiculopathy pain, radicular pain, neck disability, radiographic cervical spine curvature, radiographic segmental spine movements/ motion, Penning, posterior tangent method, cervical range of motion, cervical goniometer, anterior cervical fusion, anterior cervical discectomy, outcome measures in anterior cervical discectomy, anterior cervical fusion and outcomes, neck posture, neck pain scales, neck disability scales, pain scale, scales for depression and anxiety, Neck Pain and Disability, 101 Numerical Pain Rating Scale, Smith Robinson, Cloward, cervical radiculopathy medical management/ physiotherapeutic management, heat, traction, corticosteroid injection, exercises, collar. In addition to electronic databases, personal communication with experts in India and abroad and a comprehensive search for articles in journals not indexed was carried out. A systematic approach (journal and thesis search and consultation with experts) was taken to determine lack of published reports on outcome measures in anterior cervical fixation and conservative management with emphasis on Indian publications.

From this review process, it was considered that the primary focus of the thesis was original in context and scope.

3.2. Preliminary Studies

A series of preliminary studies were undertaken to improve the overall scale and validity of the research methods and data assessment processes in the context of the Indian hospital study.

3.2.0 Study 1

Objective

The objective of this study was to examine the accuracy and reliability of the Spin-T goniometer. The findings of this section have been reported in the following two publications (full text in Appendix 3.1) and are summarised in the text below.

> ***Agarwal S**, Allison GT, Singer KP 2005 Validation of the Spin-T Goniometer – A cervical range of motion device. J Manip Physiol Ther 28(8): 604-9*
>
> ***Agarwal S**, Allison GT, Singer KP 2005 Reliability of the Spin-T cervical Goniometer in measuring cervical range of motion in an asymptomatic Indian population. J Manip Physiol Ther 28(7): 487-92*

Study Design

The validity study was an experimental design study. The concurrent validity of the Spin-T goniometer was tested against a gold standard, the Motion star, a 3D position sensor. This was undertaken in an experimental laboratory in Western Australia. The reliability study was a repeat measurement study in an asymptomatic Indian population.

Sample size

Validity study: 72 paired data sets were generated for the Motion-Star and the Spin-T goniometer on a foam head model, for movements in all 3 cardinal planes. Subsequently, 234 readings were taken for successive increments in angles in all 3 cardinal planes with the Spin-T mounted on the subjects (n=4) and simultaneous position information from the Motion-Star.

Reliability Study: 30 adults were tested three times in each direction, flexion, extension, lateral rotation (both sides) and lateral flexion (both sides).

Test protocol

Composite cervical range of motion

Composite active cervical ROM was measured using the Spin-T goniometer (Haynes and Edmondston 2002). The participant was seated upright on a straight-back chair facing a wall, trunk stabilised and feet on the ground (Figure 3.0). The Spin-T goniometer was mounted on the head of the participant. The wall served as a reference surface for the T-square of the Spin-T during measurements of rotation and flexion/extension. The participants were instructed to sit upright, trunk in contact with the back of the chair, grasp the rear leg of the chair with each hand. The upper trunk was strapped to the back of the chair at mid thoracic level. All measurements were taken in this position (Figure 3.0).

For the validity study, participants were instructed to move their head in one direction with small successive increments until s/he had achieved end range. This was similarly followed in all other five directions.

In the reliability study, the participants were given instructions to move their head in one direction as far as possible without causing any pain or discomfort. On reaching their end-range of movement, the participant was asked if that was their maximum range. Measurements were taken at that angle of neck movement. Verbal instructions were the same and uniform for all participants. Each movement was measured only once in each direction. Prior to strapping on the Spin-T goniometer, the participant was asked to move the head in rotation and flexion-extension, twice in each direction, for practice of the correct movement pattern and which served the purpose of a warm-up and familiarisation. Measurements with the Spin-T were taken in the following sequence: flexion, extension, lateral rotation right and left, lateral flexion right and left for all participants. This cycle was repeated three times in the same sequence for reliability of measurement testing. These procedures are consistent with previously reported use of the Spin-T instrument (Haynes and Edmondston 2002).

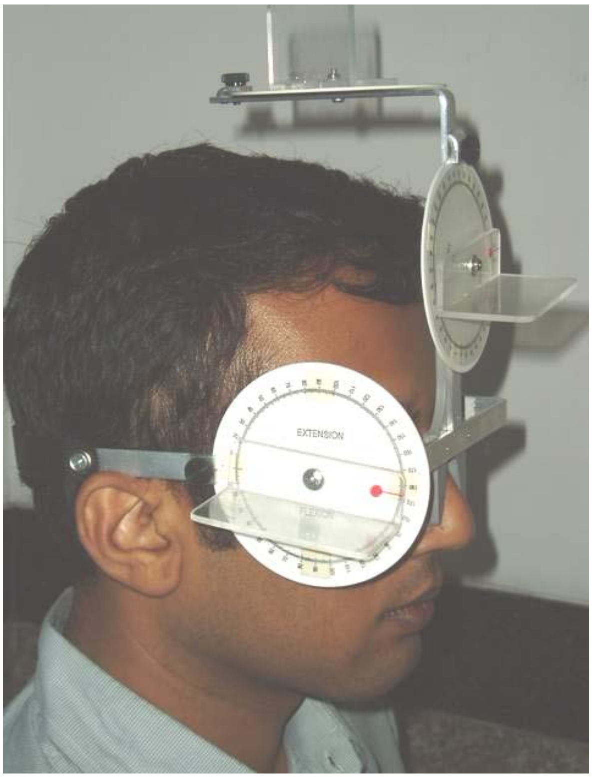


Figure 3.0 The Spin-T goniometer strapped on a subject's head. The sagittal plane dial is marked for flexion and extension measurements. The coronal plane dial (front facing) for lateral flexion to both sides, and the axial plane dial (top of the head) for rotation to both sides.

Statistical analysis.

Validity study: A repeat measures design using a linear regression model was employed. Simultaneous data acquisition of cervical spine ROM was performed for a series of ranges of motion in all cervical movements, namely, flexion-extension, lateral flexion (left and right) and rotation (left and right). Paired data sets of movements in all six directions were compared for the Motion-Star data and the Spin-T data using first a linear regression model analysis and secondly 95% limits of agreement (Hopkins 2000). Coefficients of determination (R^2) were calculated and confidence intervals assessed for systematic change in the intercept.

Reliability study: All descriptive data are reported as means and standard deviation (SD). Reliability coefficients, Intra-class correlation coefficient (ICC 2,1 – a two-way random effects single measure reliability) (Shrout and Fleiss 1979) and 95% CI were derived from repeated measures ANOVA. Where differences in ANOVA were detected, post hoc paired T tests were undertaken to document trial-to-trial differences. The typical error (Hopkins 2000) and the Coefficient of Variation (CV), which expresses the variance as a percent of the mean, were calculated to determine the degree of error. A probability of $p<0.05$ was adopted as the criterion for accepting statistical differences.

3.2.1 Study 2

Objective

To determine differences in cervical ROM in all three planes between an asymptomatic group and a CR group. The findings have been published (full text in Appendix 3.2).

> ***Agarwal S**, Allison GT, Singer KP 2005 Evaluation of cervical range of motion in a cervical radiculopathy patient group and a matched control group using the Spin-T Goniometer.* ***Journal of Musculoskeletal Research*** *9(2): 93-101*

Study Design

Gender and age matched clinical cohort analysis

Sample size

89 (46 CR patients and 43 age and gender matched controls)

Test protocol

Composite cervical ROM

This was assessed using the same protocol as described in Study 1 except that because a patient cohort was involved, patients were specifically asked to move their heads within pain free limits.

Statistical analysis

Descriptive statistics were used to report average pain levels. Differences between groups for age, gender, height, weight, BMI, and composite cervical movements; flexion, extension and rotation both sides were compared using an independent samples t-test. Within group differences between rotation left and right were calculated using a paired t-test. Probability (p) was considered significant at less than 0.05.

3.2.2 Study 3

Objective

To establish the reliability of the NPAD, translated into Hindi for research in an Indian population. The research has been published (full text in Appendix 3.3A).

***Agarwal S,** Allison GT, Agarwal A, et al. 2006 Reliability and validity of the Hindi version of the Neck Pain and Disability Scale in cervical radiculopathy patients. Disabil Rehabil 28(22): 1405-12*

Study Design

A pilot study was conducted using the original English version and based on feedback, adaptations were made in the original as well as the translated version. The second step involved translation of the NPAD by the forward and backward procedure (Fukuhara et al. 1998; Wlodyka-Demaille et al. 2002). Three pairs of bilingual professionals, two bilingual patients and one professional translator were involved in this process. The third step tested the reliability of the translated version in a CR patient cohort. The final step to determine the validity involved asymptomatic individuals.

Sample size

Pilot study: 15 patients
Translation process: 9 individuals
Reliability testing of the NPAD- 64 Indian patients with CR
Face validity: 38 asymptomatic Indian individuals

Test protocol

The NPAD scale:

The NPAD, a region specific scale was used to quantify pain and disability (Appendix 3.3B). The NPAD (Wheeler et al. 1999) is based on the Million Visual Analogue Scale (VAS) template and consists of 20 items/questions. Each question has a 10 cm visual analogue scale graded from 0 (no disability) to 5 (total disability) (Wlodyka-Demaille et al. 2004). The total score is a maximum of 100. Solid vertical lines indicate whole points (0 to 5), vertical grids placed in between two solid lines represent half points. A whole or a half score entails marking on the vertical line or grid, whereas a quarter score requires marking in the space between the vertical line and the grid. Modifications to this design and translation into Hindi were made and consequently only whole scores were employed in the current study (0 to 5).

The four characteristics of the NPAD scores have been identified as disabling neck problems (factor 1, maximum score = 20), pain intensity (factor 2, maximum score = 30), the effect of neck pain on emotion and cognition (factor 3, maximum score = 15) and the degree to which neck pain interfered with functional activities (factor 4, maximum score = 35).

Participants were encouraged to read the questionnaire prior to marking. Assistance to complete the questionnaire, where required, was provided by a Physiotherapist with 5 years of clinical experience, not involved in the research, and who understood and spoke the language of the participants. The assistance was provided for instructions purposes and not to provide any contextual support related to interpreting the question. The time taken to complete the NPAD (Hindi and English) was maximum 8 minutes.

Statistical analysis.

Reliability: Test- retest measurements were compared using the Intra-class Correlation Coefficient ($ICC_{2,1}$) for total and factor scores. A linear regression analysis was used to compare between day NPAD scores and the regression slope was compared to the line of identity (slope m =1). Typical error values were determined and the 95% confidence limits reported. Item–factor score correlations and factor-total score correlations were analysed with the Pearson product moment correlation test.

Validity: Face validity compared NPAD scores of the patient group with the asymptomatic group using an independent samples t-test. Construct validity was assessed with the Pearson product moment correlation between NPAD scores and external measures.

Statistical significance was set at the 95% level of confidence.

3.2.3 Study 4

Objective

To determine the effects of age and gender on active cervical ROM in an asymptomatic population in a longitudinal study. This study remains unsubmitted (full text in Appendix 3.4).

Study Design

A longitudinal study – repeat measurements design. Asymptomatic Indian subjects (age range 20-89 years) were recruited for measurements of active cervical ROM with the Spin-T goniometer. Approximately 30 subjects were measured per decade for the 7 decades 20+yrs to 80+yrs. The measurements were conducted at baseline with repeat measurements at 3 months and 6 months. The entire study was conducted over duration of 11 months.

Sample size

219 (110 males; 109 females)

Test protocol

Composite cervical range of motion

This was assessed using the same protocol as described in Study 2.

Statistical analysis

All descriptive data were reported as means and standard deviation (SD). Differences between genders were calculated with an un-paired t test. Intra-class correlation coefficient (ICC 3, 1) was used to calculate variance between repeat measurements of cervical ROM, baseline to 3 months to 6 months. The typical error, and the Coefficient of Variance (CV%), which expresses the variance as a percent of the mean (Hopkins 2000), were calculated to determine the degree of error between repeat measurements. Statistical significance was set at the 95% level of confidence.

3.2.4 Studies 5-7

The next three studies were reliability studies on three of the main measures. These have not had reliability data reported previously or the reliability is highly dependent on user /experimenter skills according to literature.

The research study design and statistical analysis principles are the same for all three and have been described in one summary.

Objective

Intra-rater reliability of measuring instruments, namely, segmental radiological curvature, segmental radiological flexion-extension motion, head neck angle

Study designs.

Repeat measurement studies to measure intra-tester reliability of the researcher

Sample size

30 (15 males, 15 females)

Test protocols

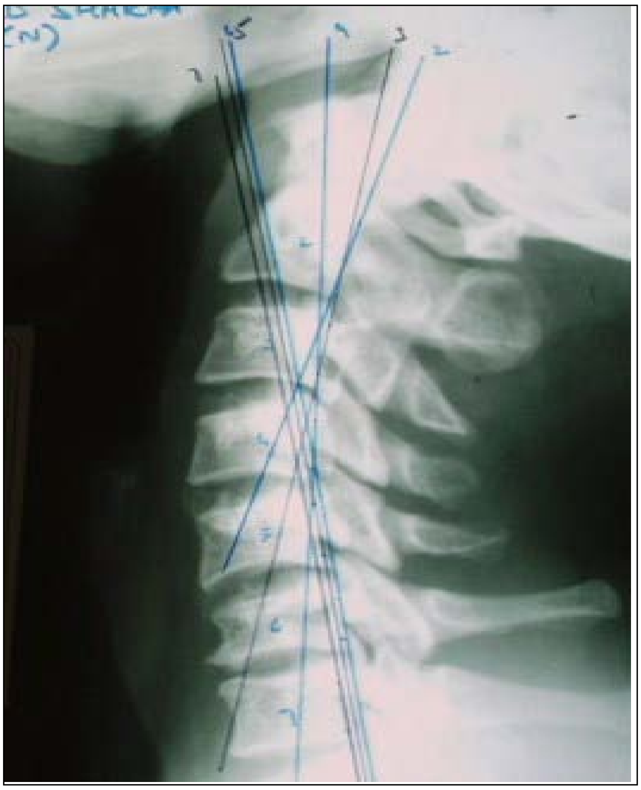
Study 5 Radiographic curvature of the cervical spine

Sagittal cervical segmental curvature was measured on lateral cervical radiographs in the neutral position with the PTM (Harrison et al. 2000). Instructions to radiographers were provided to ensure uniformity in positioning during X-ray (Clark 1986) (Appendix 3.5). The method involved manually marking the postero-superior and postero-inferior vertebral body endpoints (Figure 3.1 A). The line connecting these points represented the posterior vertebral body line. The posterior vertebral body lines at C2 and C7 intersected to form the angle of sagittal curvature from C2 to C7. Segmental curvature between C2-3, C3-4, C4-5, C5-6 and C6-7 were measured using the same method.

Although, the PTM has been analysed using a computer technique (Harrison et al. 2000), a personal communication (Appendix 3.6) with the developer (Harrison 2005) of the technique confirmed that both the manual and the digitised methods were reliable and provided similar results

A

Figure 3.1 A Harrison PTM in a cervical spine radiograph of an asymptomatic person. Manual lines drawn along points on the posterior vertebral margins from C2-7 enable angular intersections to be measured between C2-3, C3-4, C4-5, C5-6 and C6-7.



B

Figure 3.1 B Harrison PTM in a cervical radiograph of a CR patient. Proximity of lines between C5, C6 and C7 suggests straightening of curvature between these levels.

The intra-tester reliability of the PTM (n=30) was determined by using two copies of lateral digital radiographs of each patient (total 2 copies /patient). A second person (physiotherapist 1 with 5 years of clinical experience) coded the paired sets. The images were presented in a blinded random order to the researcher. The researcher measured segmental curvature from C2 to C7 of each set without any knowledge about the sequential order of the paired sets. Measurements of paired sets were compared later for intra-tester reliability.

Study 6 Radiographic segmental flexion-extension motion of the cervical spine

These radiographs were measured for segmental flexion-extension motion in the sagittal plane as per the Penning method (Penning, 1978b). Radiographer instructions were standardised (Appendix 3.5). Patients were instructed to perform active movements only and passive overpressure was not used. Dvorak et al (1988b) demonstrated that active assessments were more likely to uncover hypo-mobile segments than passive movements. Active movements thus seemed to be a more appropriate method of assessment in degenerative conditions.

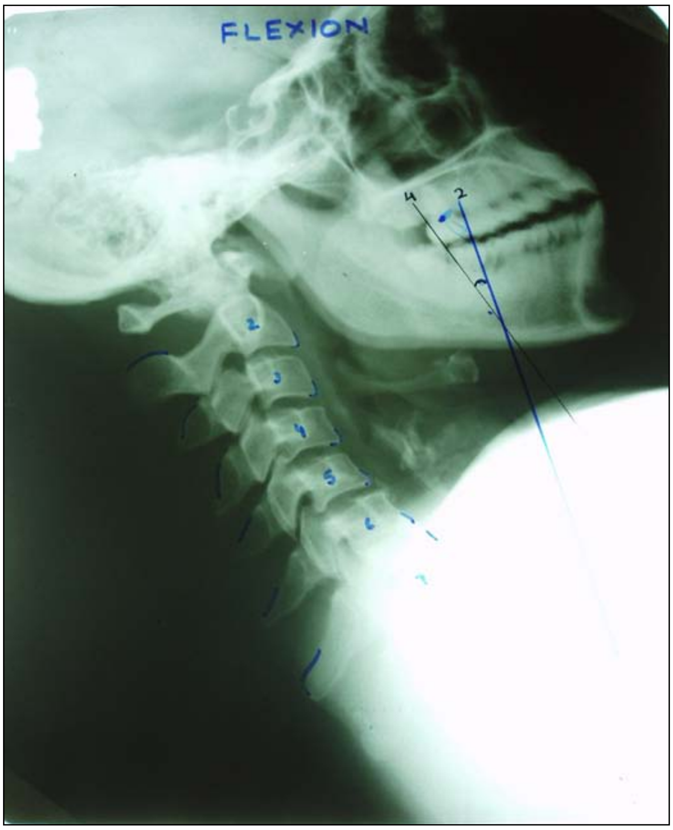
The limits of measurement for radiological flexion-extension motion were between C2 and C7 vertebral bodies. The method involved the superimposition method, where a flexion view film was taped on a radiological view-box and the matching extension view film superimposed. It was ensured that both images had the same radiological enlargement factor (Appendix 3.5). Standard procedure and instructions to radiographer included that the central ray should be directed horizontally at C4-5 and the images had to have the same magnification (Clark 1986). This was ensured by setting the distance of the film cassette from the tube at 72 inches. Where the radiographs were digital, same magnifications could be obtained with the software. Some radiographs were too dark for superimposition. In such cases, an alternative method was to outline the contours of the vertebral bodies and spinous processes of the X ray films on tracing paper and perform the measurement. Although known to increase chances of error (Penning 1998), this method was essential in some cases.

To assess the range of motion of any one segment, for example C2-4, the extension film was superimposed on the flexion film, with the outline of C2 vertebral body in extension completely matching C2 in flexion (Figure 3.2 A). A line was drawn along the edge of the extension film on the underlying flexion film. The next vertebral body, C4, was subsequently superimposed and matched, and a new line drawn along the extension film (Figure 3.2 B). The angle between the two lines was the flexion to extension range of motion for segment C2-4 (Dvorak et al. 1993; Penning 1998) (Figure 3.2 C).

A

Figure 3.2 A Extension cervical spine film superimposed on a flexion film, matching the outline of the C2 vertebral bodies.

Figure 3.2 B Lines drawn along the edge of the extension film corresponding to superimposition of C2 and C4 vertebral bodies in flexion and extension.



C

Figure 3.2 C Flexion-extension motion obtained between C2 and C4 vertebral bodies.

In this method, source of error can occur due to differences in lateral projection (due to concomitant rotation and/ or lateral bending) that interferes with reliable superimposition and increases chances of error (Penning 1998).

Two copies of flexion and extension radiographs per person (total 4 copies/person) were used to ascertain intra-tester reliability of the Penning method (n=30). Method for blinding was the same as curvature measurement.

Study 7 Cervical – Head Neck Posture

Posture was measured using the head neck angle measurement (Refshauge et al. 1994a). Participants were advised to adopt their relaxed natural posture in standing and look straight ahead. To control the visual gaze and to ensure that the posture was indeed a natural relaxed posture, a series of 1-inch diameter coloured dots were stuck vertically on a wall in front of participants. The head position was standardised by asking the participant to focus on a dot in front, at eye level (Black et al. 1996). The participants were made to flex and extend their necks fully thrice before coming back to their natural posture. They were asked if the eye was at the same dot level. If not, the entire exercise was repeated until the eyes focussed on the same dot level on consecutive occasions. The rationale was that participants were most likely to replicate their natural posture and not any other. Feet were at a comfortable width apart on a horizontal line marker on the floor to replicate similar positioning for each participant. A free hanging plumb line defined the true vertical in the photographs (Figure 3.3).

A camera (Olympus, model no. µ 400 digital, 4 megapixels, autofocus at 3X, with an optical zoom 5.8 –17.4mm) was mounted on an adjustable tripod at a set distance of 3 feet from the participant, with the lens of the camera orthogonal to the sagittal plane to ensure a pure orthogonal image of the participant. The camera height was adjusted to approximately the middle of the neck such that when the focus was adjusted, it incorporated an image from the eyebrow to 2 inches below the shoulder joint. A left sagittal image of the head and neck of each patient was taken (Figure 3.3). Participants were asked to wear clothing appropriate to expose the seventh cervical vertebra. The spinous process of C7 was chosen because it can easily be seen and palpated and the position confirmed by palpating for movement of C6 and the relative lack of movement at C7 during cervical extension (Grimmer 1997). An adhesive marker was placed on the spinous process of C7 (Figure 3.3). Digital images were converted to 24-bit Bitmap images (2272 by 1704 pixels) and the head neck angle was determined by drawing an angle formed by the tragus, C7 and the vertical. The head neck angle measures the forward inclination of the cervical spine. The larger the angle formed, the more forward the tragus is to C7. The angle was measured on digital images using the Scion Image (Release Beta 4.0.2) software. The average value of head neck angle in normal adults is 49 ° ± 4° (Johnson 1998; Grimmer et al. 1999) when measured from the horizontal. This study measured the head neck angle with the vertical resulting in normal values at 41°.

Figure 3.3 Head neck angle measurement in a CR patient. Adhesive marker placed on the C7 spinous process. The angle was measured between lines from the tragus to C7 and C7 to the vertical (green line in the figure). The thick white line was the hanging plumb line.

Two digital photographs of each patient (n = 30) were taken during the same session and one after 3 weeks (total 3 photographs/person). A physiotherapist who had a clinical experience of 5 years coded each image of a participant. The image was edited such that the face was masked. The same tester measured the coded photographs for head neck angle.

<u>Statistical analysis</u>

For reliability of repeat measures with instruments (PTM, Penning's method and the head neck angle), the descriptive data was expressed as mean and standard deviation. The typical error was calculated for differences between two measurements because of its applicability and utility in clinical trials. The typical error (Hopkins 2000) provides error values in the same unit and allows calculating actual gain from treatment by taking into account the basic error between measures. Another analysis conducted was the retest correlation by using the intraclass correlation coefficient or ICC 2,1 – a two-way random effects single measure reliability (Shrout et al. 1979).

3.3 Main clinical cohort investigation

3.3.0 Study design

This study was a prospective clinical cohort study over a $4^{1/2}$ years period (2003 to 2007). This study has been documented along the recommendations of the CONSORT (Consolidated Standards of Reporting Trials) statement (Begg et al. 1996; Moher et al. 2001) noting however that this is not a randomised controlled trial - (abstract, introduction, methods, objectives, outcome measures, sample size, assessment, inclusion/exclusion criteria, recruitment, participant flow, interventions, baseline data, statistical methods, results, outcomes and estimation, discontinued intervention, numbers analysed, discussion).

3.3.1 Sample size-clinical cohort analysis

Initially 100 participants were considered for the study. This was based on prior studies that exist within the literature. Previous clinical trials reporting outcomes of individuals under different surgical treatments for cervical radiculopathy have utilised sample sizes of n = 74 (Peolsson et al. 2003), n = 89 (Peolsson et al. 2004) and n = 23 (Peolsson et al. 2006b). A recent study (after this research was started) (Cleland et al. 2007a) reported a final sample size of 96 in a conservative CR cohort. No studies had examined two cohorts concurrently over a substantial period of time and therefore on examination of the power of the study, it was considered that 50 subjects would allow a 95% confidence of detecting a change in scores of 0.4SD between repeated test occasions with a power of 80% (http://www.stat.uiowa.edu/~rlenth/Power/index.html). To increase the power of the study and the robustness of the clinical predication rule it was decided to double the conservative numbers. This reflected the greater availability of the cohort in the same sampling period of the surgical population and difficulty recruiting participating surgeons. This increased the sensitivity of the changes in the means over time to 0.28 SD with the same level of confidence and statistical power.

The respective sample sizes of 50 and 100 allowed between group differences to be detected with 95% confidence and 80% power of 0.48SD assuming a pooled equal variance model. A 10% over-recruitment was allowed for dropouts. In the clinical assessments it was planned that approximately 110 patients in the conservative group would be recruited and 55 in the surgical cohort. Thus, process objectives were met by targeting 172 consecutive patients (in total) with a final recruitment of 163, with 109 and 54 subjects in different treatment groups.

Assessed for eligibility (n = 172 consecutive patients)

Excluded (n=9). Refused/inability to participate

Sample of convenience (n = 163)

Allocated to Conservative treatment

(n= 109).

All 109 were analysed & treated.

At 3 months (n=98)
Lost to follow-up = 6
Reasons: Outstation patients, denied follow-up

Discontinued intervention = 5
Reasons: Dissatisfied, no improvement; underwent surgery.

At 6 months
No follow up

At 12 months (n=93)
Lost to follow-up = 5
Reasons: Refused to participate.

Allocated to Surgical treatment

(n = 54).

All 54 were analysed & underwent surgery.

At 3 months (n = 51)
Lost to follow-up = 2
Reasons: Moved to another place

Discontinued intervention = 1
Reasons: death

At 6 months (n=50)
Lost to follow-up = 1
Reasons: death

At 12 months (n=48)
Lost to follow-up = 2
Reasons: Refused to participate

Figure 3.4 Flow diagram of the number of patients through the phases of this clinical trial {http://consort-statement.org/www.consort-statement.org, (Begg et al 1996, http://consort-statement.org/www.consort-statement.org,(Begg et al)

3.3.2 Subjects

3.3.2A Inclusion Criteria

Normal subjects above the age of 18 years were recruited for the reliability, validity and comparative studies (details provided in Appendices 1-4). Patients presenting symptoms of neck pain with radicular symptoms, of cervical spondylotic origin, diagnosed by clinical findings (pain intensity and distribution, neurological deficits, clinically provocative test, radiographs) correlated with MRI findings (Persson et al. 1997a; Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001; Vavruch et al. 2002; Peolsson et al. 2003; Peolsson et al. 2006b), were recruited for the main study.

3.3.2B Exclusion Criteria

The following criteria were used to exclude patients.

Neck tumour, spinal deformities, arthritis, mental illness, neck trauma, past surgery, obesity, major illness in the past six months, cerebro-vascular accident, myocardial infarction, chronic obstructive pulmonary disease, renal disease, recent pregnancy, cervical rib, congenital cervical deformities and brain atrophy.

3.3.2C Withdrawal Criteria

Subjects were withdrawn from the study if:

1. They withdrew their consent
2. If they sustained further concomitant injuries or severe illness (or death)
3. If they had further surgery

3.3.3 Treatment Groups

The clinical cohort comprised of patients from selected hospitals in the cities of Kolkata and Mumbai. Both cities are large metropolitan cities of India with population figures calculated in 2009 as more than 14 million (http://www.world-gazetter.com). The selection of the hospital venue for this study was due to logistics and convenience. Bombay Hospital (Mumbai) is an 830 bed, multi-speciality hospital of Mumbai. Belle Vue Clinic, Kolkata, is a premier multi-speciality institution of the city, with approximately 300 beds. Given the population estimates of the cities and their suburbs, a huge number of patients throng the outpatients departments. Further, patients from the Middle East countries come to Bombay Hospital frequently, where as patients from Bangladesh frequent the Kolkata hospitals. These are besides patients from other states of India.

172 consecutive patients who met the inclusion and exclusion criteria were eligible for the study (Figure 3.4). 163 agreed to participate in the study. Of these 12 consecutive surgery patients were from Bombay Hospital. Patients were recruited from the surgery and physiotherapy outpatient department if they fulfilled the inclusion and exclusion criteria. Patients with CR were recruited into either treatment group depending on the severity of condition (pain, disability, neurological deficiencies), the form of management considered most appropriate by the treating spinal surgeon/ neuro-physician in consultation with the patient. The researcher did not directly influence the allocation of the treatment group and no attempts were made to influence group allocation. This therefore was not a randomised clinical trial and the researcher had no input into the group allocation.

Patients who underwent conservative management formed the conservative group whereas patients undergoing anterior cervical surgery formed the surgical group.

3.3.4 Measures and instruments

Separate assessment sheets were used to document the following:
A detailed patient history inclusive of socio-demographics (Appendix 3.7) and lifestyle factors (Appendix 3.8) were recorded once at baseline. Clinical history, background to current problem, duration of symptoms and co-morbidities, pain, pain and disability, functional measures (cervical ROM and posture), radiological measures (segmental curvature and segmental flexion-extension motion), neurological signs, MRI reports, clinically provocative tests (Spurling's test, ULTT, Arm abduction test), length of brace use (Waal et al. 2003) were measured/ assessed, recorded and reported in assessment sheet Appendix 3.9, as per a timeline (Tables 3.1 A & B). These were documented for each patient in separate assessment sheets.

Selected reliable and valid measures with important socio-demographics and lifestyle factors were selected to predict outcome (Table 3.0).

Table 3.0 List of measures and respective measuring instruments employed in this study to predict outcome

	Measures	Instruments
I	Pain	101-NPRS; NPAD scale
II	Disability	NPAD Scale
III	Depression	NPAD factor 3
IV	Radiographic Curvature	PTM
V	Composite cervical ROM	Spin-T goniometer
VI	Radiographic segmental flexion-extension motion	Penning's method
VII	Posture	Head neck angle
VIII	Socio-Demographic factors, Lifestyle factors, duration of symptoms, co-morbidities, number of previous episodes	

Table 3.1 A Timeline of frequency of repeated measures and corresponding measuring instruments in a CR cohort treated surgically

Measure	Scale/Instrument	Baseline	Post		
			3 months	6 months	1 year
Pain	101 NPRS	✓	✓	✓	✓
Disability	NPAD	✓	✓	✓	✓
Depression	NPAD factor 3	✓	✓	✓	✓
Posture	Head neck angle	✓	✓	✓	✓
Radiographic segmental curvature	PTM	✓	✓	✓	✓
Composite cervical ROM	Spin-T goniometer	✓	✓	✓	✓
Radiographic segmental flexion-extension motion	PENNING	✓	✓	✓	✓
Brace use	TIME	✓	✓	✓	✓
MRI, lifestyle details, socio-demographics and co-morbidities		✓			
Duration of symptoms, number of previous episodes		✓	✓	✓	✓
Neurological signs		✓	✓	✓	✓
Clinically provocative tests		✓	✓	✓	✓

Table 3.1 B Timeline of frequency of repeated measures and corresponding measuring instruments to predict outcome in a CR cohort treated conservatively

Measure	Scale/ Instrument	Baseline	Post	
			3 months	1 year
Pain	101 NPRS	✓	✓	✓
Disability	NPAD	✓	✓	✓
Depression	NPAD factor 3	✓	✓	✓
Posture	Head neck angle	✓	✓	
Segmental radiographic curvature	PTM	✓	✓	
Composite cervical ROM	SPIN-T goniometer	✓	✓	
Radiographic segmental flexion-extension motion	PENNING	✓	✓	
Brace use	TIME	✓	✓	
MRI, lifestyle details, socio-demographics and co-morbidities		✓		
Duration of symptoms, number of previous episodes		✓	✓	
Neurological signs		✓	✓	
Clinically provocative tests		✓	✓	

I Pain

Pain intensity was measured using the 101 NPRS (Jensen et al. 1986) for patients to record their perceived level of pain intensity on a numerical scale from 0–100, (0 = no pain and 100 representing maximum pain) (Figure 3.5). The number stated by the patient represented current pain intensity for neck pain and arm pain separately (Heckmann et al. 1999; Peolsson et al. 2006b).

101 NUMERICAL PAIN RATING SCALE

NECK PAIN

The 101 – point Numerical Pain Rating Scale (NPRS – 101)

Please indicate on the line below the number between 0 and 100 that best describes your neck pain. A zero (0) would mean "no pain", and a one hundred (100) would mean "pain as bad as it could be."

Please mention/write only one number.

____

ARM PAIN

The 101 – point Numerical Pain Rating Scale (NPRS – 101)

Please indicate on the line below the number between 0 and 100 that best describes your arm pain. A zero (0) would mean "no pain", and a one hundred (100) would mean "pain as bad as it could be."

Please mention/write only one number.

____

Figure 3.5 101 NPRS – Instructions to participants on how to record their Neck and arm pain intensity

II Disability

Disability and pain were quantified using a region specific scale, the NPAD. Both the English and Hindi versions of the NPAD (Appendices 3.3A & 3.3B) were used, as applicable, in a CR cohort, treated conservatively or surgically (description of the NPAD has been provided in Study 3). The effect of neck pain on disability has been demonstrated by the use of region specific disability scales in previous studies (Murphy et al. 2006; Peolsson et al. 2006b; Cleland et al. 2007a).

Participants were encouraged to read the questionnaire prior to marking. A physiotherapist with 5 years of clinical experience (Physiotherapist 1) not involved in the research, helped patients complete the assessment sheets/ questionnaires. The time taken to complete the NPAD (English and Hindi) was maximum 8 minutes.

III Depression

NPAD Factor 3 (Appendix 3.3A), was analysed separately to study the impact pain has on emotion and cognition. Factor 3 scores were correlated with pain scores. Factor 3 comprises of questions 13, 14, 15 out of the 20 questions which form the NPAD questionnaire. These questions query about feeling of depression, hopelessness and if emotions and ability to think have been affected by pain. Although factor 3 of the NPAD is not an established scale for assessment of depression, the NPAD showed a strong correlation with the Beck Depression Inventory (BDI) which may be explained by the identification of Factor 3 accounting for 12% of the variance of the factor –total score analysis (Wheeler et al. 1999). As Factor 3 was part of a reliable and valid questionnaire, as well as translated into a local language, it was justified to use the factor 3 scores to screen depression. It is acknowledged that this may not be a valid measure of depression.

IV Radiographic curvature measurement

The radiographic segmental curvature measurements were measured with the PTM (Harrison et al. 2000; Harrison et al. 2004). (Description of the method employed have been reported in Study 5, Figures 3.1 A & B)

V Composite cervical ROM

Active cervical ROM was assessed using techniques described in study 3 (Figure 3.0). Measurements with the Spin-T were taken in the axial and sagittal planes, that is, lateral rotation (right and left) and flexion/ extension, specifically in this order for all patients. The reason why movements in only two planes were chosen was because results of previous literature suggests movements in these planes affected by neck pain (Jordan et al. 1997; Dall'Alba et al. 2001; Lee et al. 2004), or movements in these planes associated with pain and disability (Peolsson et al. 2003) and success of outcome (Cleland et al. 2007a).

VI Radiographic segmental flexion-extension motion:

Radiographic segmental flexion-extension motion was measured using the Penning method (Dvorak et al. 1993; Penning 1998) (Figures 3.2 A,B,C). The methods are reported in study 6.

Lateral cervical radiographs in flexion and extension followed composite measurements of flexion and extension ROM with the Spin-T, to retain patient positioning and enable comparative analysis.

VII Posture

The Head neck angle method was used to measure posture. Details of the technique and subsequent measurement have been described in Study 7.

VIII Socio-Demographics

Socio-demographic details (Appendix 3.7) included age (years), gender (male, female), weight (kg), height (metres), dominant hand (right, left), mother tongue, marital status and educational level. Information on height (measured by a wall-mounted tape measure) and weight (digital weighing scale accurate to the nearest 0.1kg) were used to calculate the BMI with the formula (weight in kg/height in metres squared). The BMI (Hasvold et al. 1996; Heckmann et al. 1999) was categorised according to the World Health Organisation definitions (<20 underweight; 20-24.99 normal; 25-29.99 overweight; >30 obese).

Patients were asked to fill the socio-demographic form, with their age, and mark the applicable gender (Dowd and Wirth 1999; Heckmann et al. 1999; Persson and Lilja 2001). Dominant arm was noted in order to assess if CR was more prevalent in the upper limb which strained more in life activities (Cleland et al. 2007a).

Education levels were categorised as high school, graduate, post-graduate and doctorate. For analysis these were categorised as ‘up to high school’, and ‘graduates and above’. Education levels have been associated with the kind of work an individual performs (Peolsson et al. 2003).

Marital status or living with others was noted to study its implications on treatment response. The categories recorded were single, married, widowed and divorced, which for the purpose of analysis were grouped: single, divorced and widowed as one group and married as another. ‘Living with others’ has been noted by Persson and Lilja (2001) and Peolsson et al (2003). ‘Living with others’ is a description of an individual who does not live alone. The people or person in the ‘others’ category may be anyone. A more conventional description was used in the Indian context for clarity of explanation.

Lifestyle details included questions (Appendix 3.8), some which had been used in previous studies (Borghouts et al. 1998; Heckmann et al. 1999; Vavruch et al. 2002) and were therefore used in this study to predict outcome. Some information (occupation, recent change in body weight > 10kg, and if patient had refused surgery for his/her present conditions) was gathered as a routine practice as well as to give any pertinent advice to the patient. Lifestyle data information used to predict outcome included work characteristics categories (Heckmann et al. 1999; Vavruch et al. 2002) (active = blue and brown collar workers, sedentary = white collar, skilled professional workers); Leisure physical activity (yes, no); recent change in lifestyle ('yes' = death of a relative/ friend, increased work load, work related stress (Persson and Lilja 2001), depression, change of residence, family tension; 'no' = no change); smoking behaviour (Heckmann et al. 1999; Persson and Lilja 2001) (1= smoking every day, smoking now and then ; 2= not smoking but previously every day, not smoking but previously now and then, never smoked) (Persson and Lilja 2001; Palmer et al. 2003).

Blue-collar workers comprise working class people who typically perform manual labour. Brown collar workers are those who do physically demanding jobs – construction, manufacturing, delivery services, coolies, gardening and waste removal. White collar comprise of salaried professionals or an educated worker who performs semi-professional office work, administration and sales co-ordination task. Skilled professional workers include skilled professionals (doctors, designers) performing some deskwork as well. Leisure physical activity was a method to assess general non-work levels of activity. It asked if individuals did any sporting activities, physical games or regular exercises. Lifestyle questions were generated from previous studies (Hasvold et al. 1996; Borghouts et al. 1998).

Questions on duration of symptoms (Yamamoto et al. 1991; Heckmann et al. 1999; Waal et al. 2003; Shah and Rajshekhar 2004), number of previous episodes (Sampath et al. 1999) and co-morbidities (Peolsson et al. 2006b) were part of Appendix 3.9. Duration of symptoms was measured in days/ weeks/ months or years as applicable. The number of previous episodes of same or similar symptoms was noted. The question on co-morbidities was asked 'if you suffer from any ailment?' Patients were further asked to specify the treatment and drug/dosage of each co-morbidity reported.

3.3.5 Measures and modalities used for diagnosis and to record progression

I Neurological Signs

Neurological tests have been used as part of routine clinical examination in CR, for diagnosis of level (Moeti and Marchetti 2001; Vavruch et al. 2002; Waldrop 2006), and to ascertain change in clinical status (Saal et al. 1996; Grob et al. 2001; Persson and

Lilja 2001). Neurological deficits were measured at baseline and during follow-up in both groups to record changes and improvement. In this study they were not used as outcome measures as have been reported in some previous recent research (Wainner et al. 2003; Cleland et al. 2007a). Diagnosis of radiculopathy was based on a radicular pattern of pain, sensory, motor and Deep Tendon Reflex (DTR) deficits. A standard format of neurological signs (Figure 3.6, Appendix 3.9) was used for evaluation of neurological status at baseline and subsequent measurements.

Sensations tested included light touch and pin prick; graded 0 = absent, 1 = impaired, 2 = normal, NT = not testable (American Spinal Injury Association 1996). Total 8 levels were assessed (C2 levels to T1) resulting in a maximum (unaffected) score 16 for each sensation on each side. Definitions of the grading system were adopted from (American Spinal Injury Association 2003), having high intra and inter-rater reliability of the sensory and motor methods of testing (Marino et al. 2008).

For motor deficits; C4-5 to T1-2 levels reflecting total 5 neurological motor levels, were tested. Motor scores were tested on a 0-5 scale (Medical Research Council of the United Kingdom 1978). Unaffected motor performance resulted in a maximum motor score of 25 for each limb, the scoring system method of calculation was adapted from (American Spinal Injury Association 1996). The following muscles were used to test the specific motor nerve root function (Boden et al. 1991).

- C5 for elbow flexors
- C6 for wrist extensors
- C7 for elbow extensors
- C8 for finger flexors muscle (distal phalanx of middle finger)
- T1 for little finger abductor.

Deep tendon reflex (DTR) for biceps (C5); triceps (C7) supinator (C6) (Boden et al. 1991) were tested and scored with the following grades as per the Reflex Grading System (Nolan 1996) :

- 0 = no reflex elicited or absent
- 1 = impaired/ hypo reflexive response elicited
- 2 = normal reflex or equal to sound side

Score 3 was not used in this study as it was meant for a hyper-responsive reflex. Conditions generating hyper-responsive reflex (i.e. upper motor neurone lesions) were part of the exclusion criteria of this study. The maximum scores for reflexes were 6 on each side. Therefore, for one side, sensory scores of 16, motor scores of 25 and DTR scores of 6 implied no deficits.

Although the ASIA scale is used to determine the level and extent of spinal cord injury, in this study the format was used to measure neurological deficits arising from the cervical spine. Neurological signs were tested and documented by the referring neuro-physician/ spinal surgeon as well as the researcher. In case of any discrepancy, the patient was referred back to the consultant for a final decision.

MOTOR		SCORE	
MUSCLES		R	L
C_5	Elbow Flexors		
C_6	Wrist Extension		
C_7	Elbow Extension		
C_8	Finger Flexors		
T_1	Finger Abductor (Little Finger)		
TOTAL			
(maximum)		25	25
REFLEXES			
Biceps			
Triceps			
Supinator			
TOTAL			
(maximum)		6	6

Dates	SENSORY			
	LIGHT TOUCH		PIN PRICK	
	R	L	R	L
C_2				
C_3				
C_4				
C_5				
C_6				
C_7				
C_8				
T_1				
TOTAL				
(maximum)	16	16	16	16

Figure 3.6 Format of neurological (motor, DTR, sensory) test scoring. Scores for each side and each level were added to calculate the total score.

II Radiographs

Plain radiographs were used to evaluate degenerative changes of the cervical spine. Since some changes are universal, radiographic findings were used for clinical correlation. Radiographs included antero-posterior, lateral and oblique views. Antero-posterior views were viewed to detect reduction in disc space, uncal osteophytes and lateral asymmetry. Lateral view showed cervical curvature, anterior and posterior osteophytes, end plate degeneration and facet arthropathy (Figure 3.7). Oblique views were useful to detect narrowing of the neural foramen. Radiograph findings were noted in Appendix 3.9.

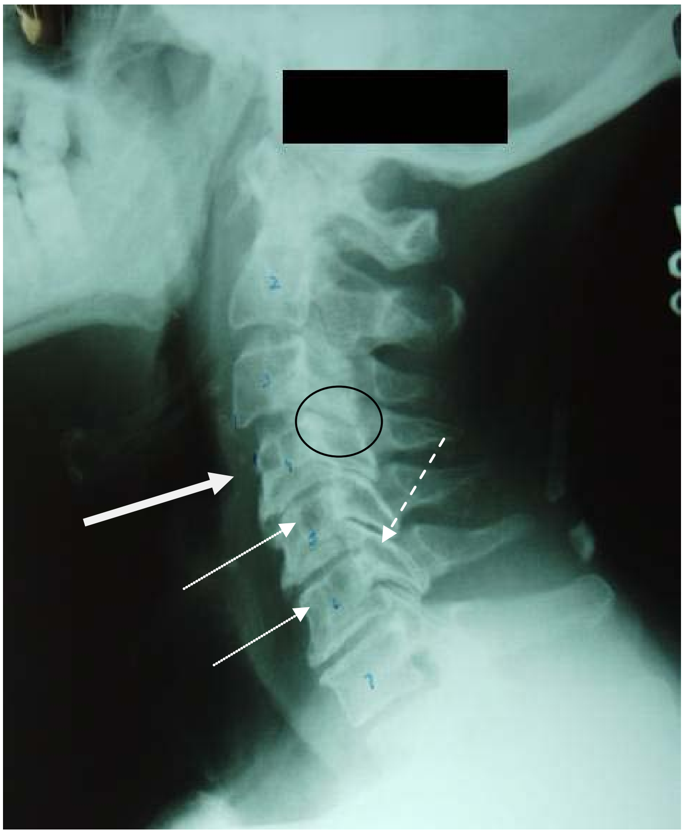
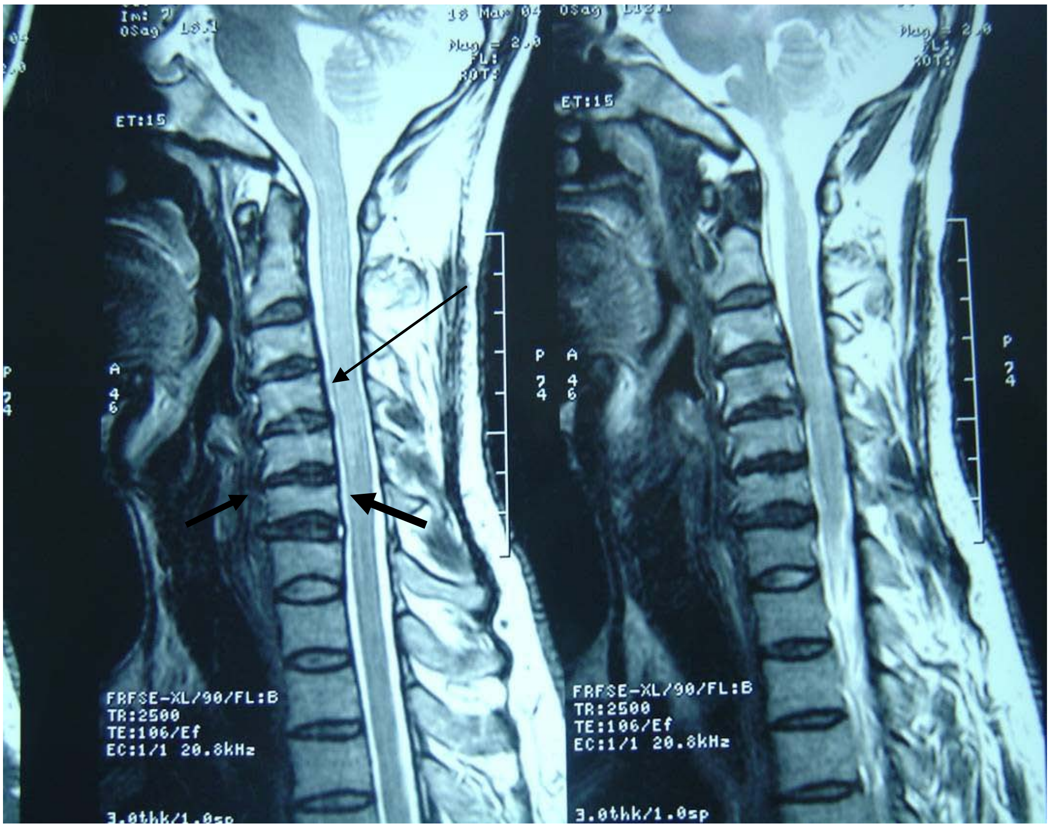


Figure 3.7 Lateral radiograph of a CR patient showing degenerative changes. Anterior bridging osteophyte (thick white arrow), reduced disc height (thin white arrow) and facet joint arthropathy (circle), posterior osteophyte (dotted arrow) are changes seen on this radiograph

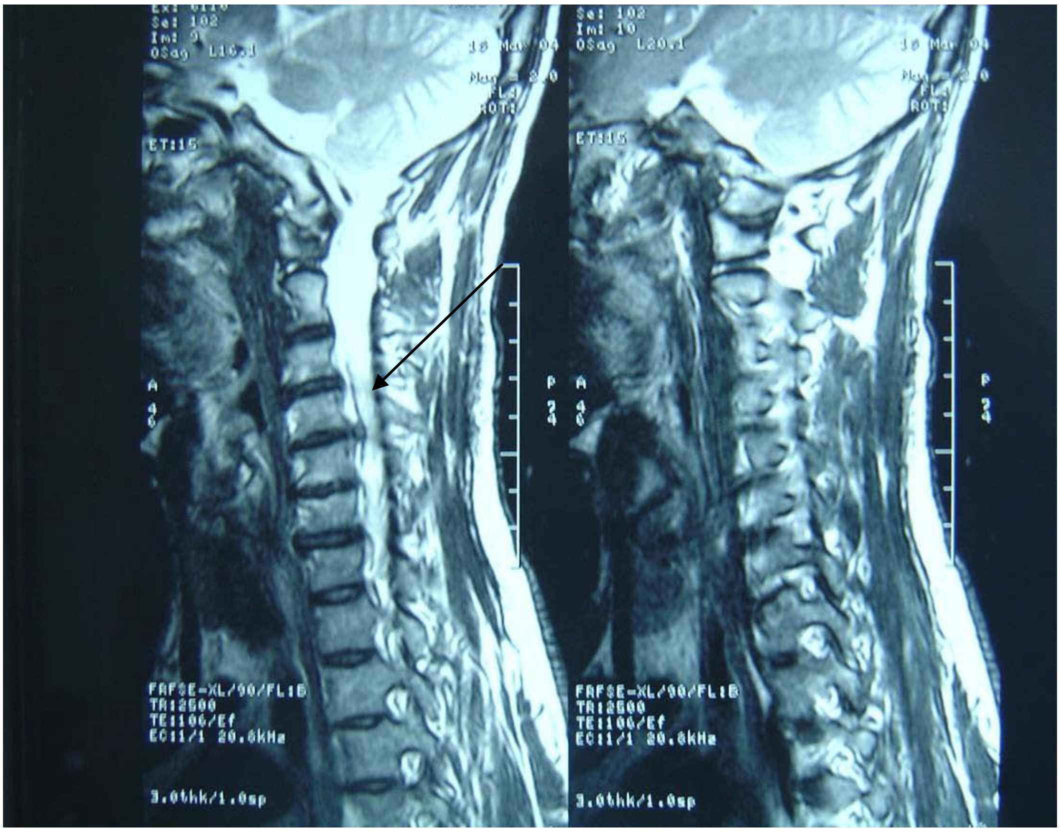
III Magnetic Resonance Imaging (MRI)

MRI were routinely done for confirmation of clinical diagnosis (Figures 3.8 A, B, C). Both T1 and T2 MRI images were screened for curvature, canal and neural foramen diameter, osteophytes and disc degeneration (Brown et al. 1988; Wilson et al. 1991; Garvey et al. 2002). For the final confirmation of diagnosis, MRI findings were correlated with clinical assessments. MRI findings were noted in Appendix 3.9.



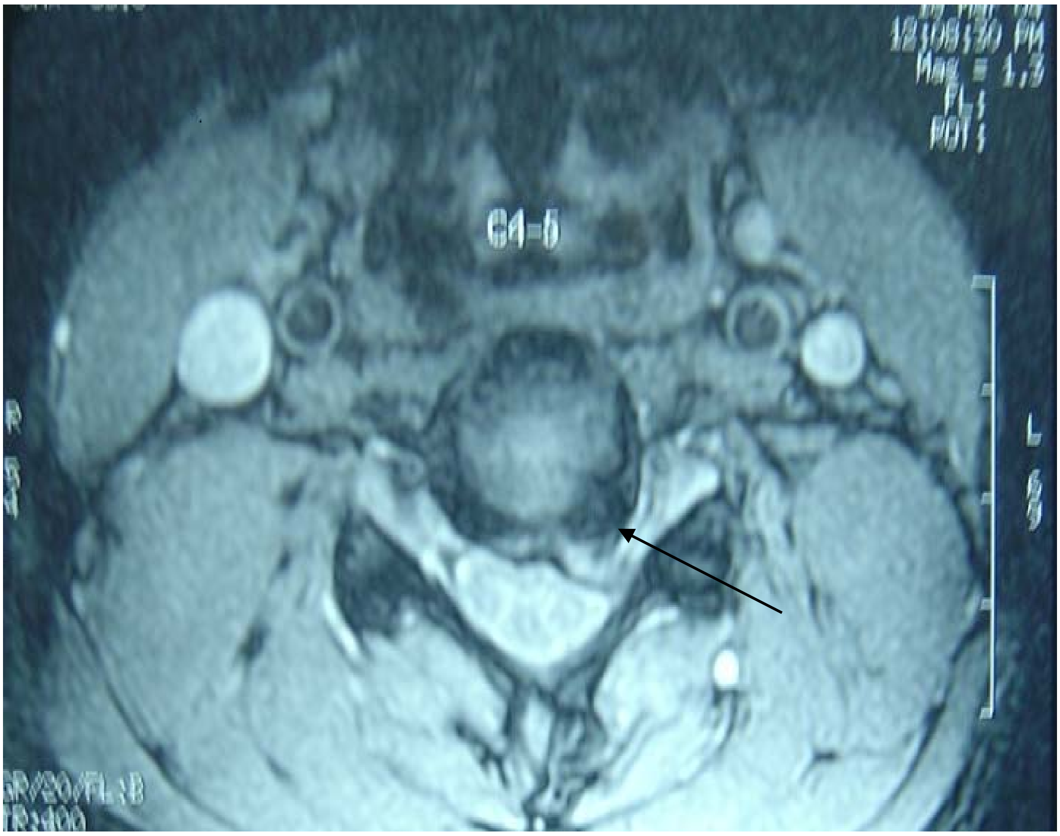
A

Figure 3.8 A Cervical spine MRI sagittal view. Multi-level degenerative changes in the cervical spine C4-5, C5-6, C6-7, with mild posterior disc bulge at C4-5 (thin arrow), anterior and posterior disc bulge C6-7 (thick arrow).



B

Figure 3.8 B Cervical spine MRI oblique views. C4-5 posterior disc protrusion (arrow)



C

Figure 3.8 C Cervical spine MRI axial view. Prolapsed disc at C4-5 causing bilateral neural foramen narrowing, left > right (black arrow)

IV Clinically provocative tests

(Findings of all tests were noted in Appendix 3.9)

Clinically provocative tests decrease or increase symptoms in the affected upper limb and are useful to determine nerve root pathology.

1VA Spurling's test

Spurling's test is the reproduction of the patient's nerve symptoms by movements of the neck. It is performed by extending the neck, rotating the head, and then applying downward pressure on the head. The test is considered positive if pain radiates into the limb ipsilateral to the side the head is rotated to. The test was conducted as described by Wainner et al (2003).

IVB Upper Limb Tension Test (ULTT)

The ULTT stretches the involved nerve root and is characterised by exacerbation of radicular symptoms. The ULTT procedural methods are described here.

Patient in supine. Position: Shoulder abducted and laterally rotated and depressed, elbow extended, forearm supinated, wrist extended and fingers extended. Neck flexed to the contra lateral side. Positive neurological findings indicated a median, axillary and or a musculo-cutaneous nerve lesion. Positioning and testing as described by Magee (2002).

Patient in supine. Position: Shoulder abducted, medially rotated and depressed, elbow extended, forearm pronated, wrist flexed (with ulnar deviation) and fingers flexed. Neck flexed to the contra lateral side. Positive neurological findings indicated a radial nerve lesion (Magee 2002).

Patient in supine. Position: Shoulder abducted (90 degrees), laterally rotated and depressed, elbow flexed, forearm pronated and, wrist extended (radial deviation) and fingers extended. Neck flexed to the contra lateral side. Positive neurological findings indicated an ulnar nerve lesion (Magee 2002).

IVC Shoulder abduction test

Patient's hand (symptomatic side) was placed (actively or passively) on top of the head. This action relieves the nerve from the traction effect of the weight of the arm hanging by the side of the body. Relief of symptoms suggests nerve root compression (Viikari-Juntura et al. 1989).

3.3.6 Pre-intervention testing procedure

After signing an informed consent (Appendix 3.0), pre-intervention, all patients in both groups underwent a pre-set, standardised assessment procedure. Patients completed standardised assessment sheets and questionnaires: socio-demographic information (Appendix 3.7), lifestyle details (Appendix 3.8), 101 NPRS (Figure 3.5) and NPAD (Hindi or English) (Appendix 3.3A & 3.3B). All patients were assisted by an independent observer (physiotherapist 1), not involved in treatment, to complete the assessment sheets/ questionnaires. For diagnosis, experienced neuro-physicians and spine surgeons used a detailed clinical assessment, backed by radio-diagnostic imaging (X-Ray and MRI) and electrophysiological tests (EMG/NCV) (only if considered essential). Further, the researcher also examined the clinical assessments and had the opportunity to discuss the medical diagnosis with the treating medical physician/surgeon to verify any potential discrepancy in diagnosis. Additionally, all outcome measures as described earlier Table 3.0 formed the baseline data for all 163 patients. For all radiological and clinical assessments, the assessor was blinded to the patients' treatment and therefore the group allocation.

3.3.7 Intervention

3.3.7A Surgical Group

Anterior cervical discectomy without fusion (ACD), anterior cervical discectomy with fusion (ACD/F), performed at 1-2 levels (Abd-Alrahman et al. 1999; Dowd and Wirth 1999; Bolesta et al. 2000) were included in this group (Appendix 3.10). All patients were advised to wear a hard collar immediately post-surgery for minimum 6 weeks and maximum 12 weeks. Initial follow-up visits to the surgeon involved removal of sutures, attention to the scar tissue/ wound if required and if the patient developed any symptoms. After these initial visits, the patient was required to follow-up with the surgeon once after 8 weeks and then after 12 weeks. From the physiotherapist, patients received an initial advice on correct posture and ergonomics (during the hospital stay) (Saal et al. 1996; Persson et al. 1997a). Later, exercises were started for the neck muscles, varying between 2 - 6 weeks post –surgery. Advice on exercise programmes were provided for 12-13 weeks which coincided with the 3 months follow-up assessment. Exercises initially involved scapular exercises, upper limb exercises (especially if there was motor involvement) and sub-maximal isometric neck exercises (Persson and Lilja 2001). The intensity and duration of exercises varied with the individual patient's recovery, discomfort at the time of treatment and presenting symptoms. Isotonic neck exercises and deep neck flexors exercises (Cleland et al. 2005) were started after removal of the collar. During follow-up visits patients were asked about compliance to the exercise programme and in the absence of exercise aggravating any symptoms, further emphasis was placed on the importance of performing the on-going exercises.

3.3.7B Conservative Group

Patients underwent conservative management for a maximum duration of 3 months. Conservative management included (Appendix 3.10):

Oral drugs: Non-steroidal anti-inflammatory drugs and muscle relaxants (Saal et al. 1996; Murphy et al. 2006), singly or in combination. Oral corticosteroids (Murphy et al. 2006), opioids (Mazanec and Reddy 2007) and epidural nerve root steroid injections (Saal et al. 1996) were administered when symptoms were unrelenting. The attending physician / neuro-physician or spinal surgeon dispensed medication advice.

Cervical collar: Hard and soft cervical collar were used in the conservative management of CR depending upon the symptoms of the patient. Duration was minimum 3 weeks to a maximum of 5 weeks. The collar was an adjunctive therapy. The duration was noted in Appendix 3.10.

Various physiotherapy modalities were used in a multimodal approach that matched the clinical practice of the rehabilitation department. These included: traction, various types of exercises, heat, cold, electrotherapy modalities to reduce pain and ergonomic advice. These are briefly described below:

Posture and ergonomic advice: Ergonomic instructions and postural correction instructions (Saal et al. 1996; Persson et al. 1997a) were provided to every patient in the first visit and emphasised upon during every follow-up.

Cervical traction: Some patients were treated with manual traction (Persson and Lilja 2001) and subsequently overhead intermittent cervical traction. Intermittent electrical traction was only used when patients had responded positively to 4-5 sessions of manual traction.

Exercises: Initially supervised isometric neck exercises and scapular exercises, neck muscle stretching exercises (Persson and Lilja 2001) and neural tissue mobilisation (Magee 2002) were done. Deep neck flexors strengthening to improve endurance of deep neck flexors (Cleland et al. 2005), sensori-motor training, and weight training (Ylinen et al. 2003; Murphy et al. 2006) were added at later stages. Intensity, duration and number of repetitions were dependent on the severity of symptoms.

Mixed therapies: For pain relief TENS (transcutaneous electrical nerve stimulation) (Saal et al. 1996; Persson and Lilja 2001) was used along the radiating pain. Superficial heat (Persson and Lilja 2001; Murphy et al. 2006) and deep heat (Valtonen and Kiuru 1970; Honet and Puri 1976) were applied before exercises or traction.

Ultrasound was used (Persson and Lilja 2001) over tender myofascial regions and spinal levels as deemed necessary.

3.3.8 Post-intervention testing and follow-up

The post-intervention time-line of assessments for both treatment groups is listed in Figures 3.1 A & 3.1 B. The first post intervention assessment of all outcome measures was done at 12 weeks from the date of surgery and in the conservative group at 12 weeks from completion of treatment. Subsequent assessments in the surgical group were conducted at six months and one year (Figure 3.1 A) and in the conservative group at one year (Figure 3.1 B).

3.3.9 Data Management

At the end of one year, complete data was available for 48 patients in the surgery group and 93 patients in the conservative group. Patients (n = 163) were analysed with the intention to treat analysis (Begg et al. 1996). For patients whose data was not available at 1 year, the 6 months/3 months data was carried forward for analysis.

Descriptive statistics was used to summarise baseline data in both groups: cohort socio-demographics, lifestyle details, duration of symptoms, co-morbidities, number of previous episodes, clinical, functional and radiological measurements, levels involved, site of pain, length of brace usage and neurological signs.

Change score analysis for differences in neck and arm pain (baseline versus 12 months) within each group was calculated. This allows the raw data at one year to be converted into absolute change scores when compared with baseline scores.

Between group comparisons (asymptomatic versus symptomatic and surgical versus conservative) were done using an un-paired t-tests or a non–parametric equivalent – Mann Whitney U test, as indicated by data type or distribution.

Significant change in pain and disability scores between each measurement (baseline, vs. 3 months vs. 6 months vs. 12 months) was calculated using the Wilcoxon signed rank test (the non-parametric equivalent to a paired sample t test) to determine the effect of treatment in each group.

Segmental radiographic flexion-extension motions (C2-7) were correlated with sagittal plane active composite movements using the Spearman's Rank-Order Correlation Coefficient test.

Segmental flexion-extension motions were compared between a patient group and a matched asymptomatic group using an un-paired t test.

Correlation between pre-intervention factors (pain scores, disability scores; depression, radiological measures of curvature and flexion-extension motion, composite ROM, head neck angle, demographics and lifestyle details) and post intervention pain scores at a one year follow-up, were determined by Spearman's rank-order correlation coefficient analysis. Spearman's Rank-Order Correlation Coefficient is the non-parametric analog of the Pearson product-moment correlation coefficient. The results of the former and latter are closely similar, as the Spearman correlation is calculated in a very similar manner as Pearson, except that Spearman first ranks the data.

Significance for all measurements was accepted at $p < 0.05$ and no alpha level corrections were undertaken.

Patients were classified as having successful outcomes/responder, if during their last follow-up at 12 months they achieved a NPAD score of ≤ 22. This was the operational definition of a 'Responder', individuals who reported more than 22 (i.e. mild problems or worse was operationally defined as a 'Non-responder'). This made the NPAD the outcome criterion for the CPR analysis of this study. The clinical distribution of the NPAD total scores were appropriately analysed from a neck pain group, where the clinical significance of this grouping was identified (Wheeler et al. 1999). Scores were normally distributed around a mean score of 61 ± 16 (Wheeler et al. 1999). The scores were categorised as: 0 – 22 = none to minimal pain; 23- 40 = mild; 41-57 = moderate pain; 58-74 = moderate to severe pain; 75 – 92= severe pain; 93 – 100 = extreme pain, suffering and disability.

Similar to previous studies which used predictor variables for treatment success (Childs et al. 2004; Cleland et al. 2007b), this study chose the region specific pain and disability measure, the NPAD to judge a patient's successful outcome. The NPAD is a valid reference standard for identifying clinically important change in patients' status (Goolkasian et al. 2002; Pietrobon et al. 2002). Further, the NPAD, translated into Hindi (Agarwal et al 2006), was proven a valid and reliable scale in a CR cohort.

Patient variables at baseline (socio-demographics, lifestyle details, self-reported pain scores, neurological examination and other continuous variables) were dichotomised within each treatment group for a successful outcome/responder or an unsuccessful outcome/non-responder based on the treatment response, as indicated on the NPAD score at 3 months and 12 months. Univariate analyses were used to identify potential predicting variables, which were significantly different between the 'responder' and 'non-responder' groups. Independent samples t test for continuous variables and Chi Squared test for nominal/categorical variables were used. Variables with a significance level of less than 0.10 were retained as potential predictor variables. A lower significance of 0.10 was chosen to minimise the likelihood of excluding potentially helpful variables.

The mean 101 NPRS neck and arm pain change scores as well as the mean NPAD total and factor change scores (and their 95% CI) were calculated for both groups and differences analysed with an independent t test to validate that a difference existed between groups based on the NPAD score grouping.

For all variables with significant univariate relationships, the specificity, sensitivity, LR+ and LR- were calculated for potential predictor variables. Sensitivity expresses the 'true positive rate'. It is the proportion of patients with the condition or outcome of interest who are positive on the Clinical Prediction Rule (CPR). Specificity denotes the 'true negative rate'. It is the proportion of patients who do not have the condition and report negative on the CPR. The likelihood ratios (LR) combine the information from sensitivity and specificity. A LR+ expresses the change in odds favouring the outcome when the patient satisfies the criteria of the CPR, whilst the LR- expresses the change in odds favouring the outcome when the patient does not satisfy the criteria of the CPR (Sackett 1992). An accurate CPR would have a large LR+ to rule in the diagnosis or a small LR- to rule out the diagnosis (Sackett 1992) In cases where the sensitivity or specificity was 0 or 1 then 0.5 was added or subtracted from the value to generate a likelihood ratio (Wainner et al. 2003; Raney et al. 2009). In such cases, this is noted in the results and the 95% CI are estimated.

Another method used was the receiver operator characteristic curve for some variables, which is a graphical representation of the trade-off between plotting sensitivity vs. 1- specificity, using different cut-points in the data (Laupacis et al. 1997). The 'y' axis shows the sensitivity whilst the 'x' axis represents '1-specificity'. In the case of continuous variables, dichotomous thresholds were determined by an optimisation function that determined the threshold that had the highest sensitivity and specificity (equal weighted contribution).

Additionally, all predictor variables were entered into a step wise logistic regression analysis to determine the most accurate set of variables for predicting success. In logistic regression, the outcome variable is a binary event (responder versus non-responder). The risk of developing an outcome is given as logarithmic odds (Laupacis et al. 1997). For the prognostic purpose, the variables retained in the regression model were used as the most optimal cluster of variables for predicting optimal outcomes for CR patients treated conservatively or surgically. The specificity, sensitivity, LR+ and LR- and corresponding 95% CI were calculated for all variables that were retained in the model. The pre-and post test probability of success was calculated for the predictor variables.

The number of responders and non-responders at 3 months and 12 months in both groups and additionally at 6 months in the surgery group, for each successful predictor was calculated.

4.0 Summary of methods

The methods section of this thesis was divided into three sections:

Section 1 listed all objectives, which laid the foundation to the methods section of this study to determine variables, which can predict a successful outcome in a CR cohort. To fulfil the objectives, based on the literature review, the principal hypothesis and sub-hypotheses were formed.

Section 2 consisted of conductance of 7 studies which established the reliability and validity of variables, for their use in the main research in CR patients, treated either conservatively or surgically. These studies were original, and a necessary support to the main clinical study.

Section 3 comprised a unique clinical cohort of CR patients (n= 163) treated either conservatively or surgically. It is the first study to examine outcome measures in such a large cohort of both treatment types and follow-up until 12 months. Further, it explored sub-hypotheses, some which have not been explored earlier in medical literature. The main hypothesis employed analysis of Clinical Prediction where baseline factors influenced the outcomes of a responder.

Most of these findings are unique to the current medical literature and all are unique in the Indian setting.

CHAPTER 4

RESULTS

THE PREDICTIVE ROLE OF BASELINE VARIABLES IN A CERVICAL RADICULOPATHY PATIENT COHORT, TREATED CONSERVATIVELY OR WITH ANTERIOR CERVICAL DISCECTOMY/ FUSION

4.0 Introduction

The aim of this study was to determine if baseline measures of pain, disability, depression, radiological cervical segmental curvature and flexion-extension motion, composite active cervical range of motion, posture, patient demographics and lifestyle have a predictive role in determining outcome in CR patients at one year.

This led to the principal hypothesis of this study: that 'clinical, radiological and functional assessment of CR patients at baseline will predict clinical outcome at one year, following either conservative or surgical management'.

To address this main hypothesis a series of studies and parallel analyses were undertaken to contribute to the understanding and knowledge in clinical outcomes in CR in the Indian setting for both conservative and surgical interventions.

A large sample of convenience was recruited for this study (N=163) with 109 patients in the conservative and 54 in the surgical treatment groups. All patients were assessed once pre-intervention (baseline) and at 12 months. The conservatively treated group had an interim assessment of primary outcomes at 3 months and the surgical group had two interim assessments at 3 and 6 months. The primary outcome assessment was the NPAD score at 3 and 12 months and baseline assessments were used to consider their univariate and predictive merit in the outcome of CR patients treated conservatively and by surgery.

The results from this study are presented in this chapter in five sections. The first section comprises of tables and figures illustrating socio-demographic data and baseline measurements of all outcome variables used in the two groups. It brings into focus any differences that existed at baseline between the two treatment groups. Section two provides descriptive data display of some key variables on repeat measurements. It documents the progress of each group until the final follow-up at one year. Section three analyses and illustrates each research sub-hypothesis. Section four comprises the published (4 papers) and unpublished results of the preliminary study elements. Section five illustrates the results of the main clinical outcome study which includes the univariate and multivariate analysis of the data and the final CPR analysis for positive outcomes.

4.1 Baseline data analysis

Initial measurements were analysed using descriptive statistics. Between group differences were calculated using parametric or non-parametric tests, based on data distribution.

4.1.0 Socio-demographic and Lifestyle factors analysis

Descriptive data analysis of baseline socio-demographic and lifestyle details of the total group and separate treatment cohorts are reported in Table 4.0. Between group comparisons are reported later (Table 4.3) and in general conservative and surgery groups were comparable for age, gender, BMI and marital status, but not for dominant hand, education levels, work type, physical activity, annual income, lifestyle changes and smoking.

Table 4.0 Demographics and lifestyle details upon entry to the trial of two treatment groups of CR patients (n = 163)

Variables	Conservative (n= 109)	Surgical (n= 54)	Total (n= 163)
Age (years)			
Mean ± SD	45 ±11	45 ±10	45 ± 11.24
Range	23-66	27-69	23 - 69
Gender			
Male (N, %)	62 (57)	31 (57)	93 (57)
Female (N, %)	47 (43)	23 (43)	70 (43)
BMI			
Mean ± SD	25 ± 4	25 ± 4	25 ± 4
Range	(17-37)	(18-40)	(17-40)
Dominant hand			
Right (N, %)	108 (99)	48 (89)	156 (96)
Left (N, %)	1 (1)	6 (11)	7 (4)
Education levels (N, %)			
Up to High School	12 (11)	26 (48)	38 (23)
Graduates and above	97 (89)	28 (52)	125 (77)
Work Characteristics (N, %)			
Active	47 (43)	32 (59)	79 (48)
Sedentary	62 (57)	22 (41)	84 (52)
Physical activity (N, %)			
Yes	52 (48)	16 (30)	68 (41)
No	57 (52)	38 (70)	95 (59)
Annual Income (N, %)			
Less than Rs.50,000	11 (10)	16 (30)	17 (11)
50,000 – 1 lac	12 (11)	8 (15)	20 (13)
1-2 lacs	17 (16)	5 (9)	22 (15)
2-5 lacs	24 (22)	15 (28)	39 (25)
More than 5 lacs	45 (41)	10 (19)	55 (36)
Marital status (N, %)			
Single	9 (8)	3 (6)	12 (7)
Married	100 (92)	46 (85)	146 (90)
Widowed	0	5 (9)	5 (3)
Divorced	0	0	0
Life style changes (N, %)			
Yes	70 (64)	28 (52)	98 (60)
No	39 (36)	26 (48)	65 (40)
Smoking (N, %)			
Yes	34 (31)	8 (15)	42 (26)
No	75 (69)	46 (85)	121 (74)

1 lac = 100000, Exchange rate= Rupees 40 = 1 US $ (variable) N = number of patients

4.1.1 Duration of Symptoms, Co-morbidity, and Number of previous episodes

Although the range of duration of symptoms (in weeks) recorded for the each group was different (conservative 2-240 weeks and surgery 1-52 weeks), this can be explained by some chronic extreme cases in the conservative group. The median values were not significantly different (z= 0.22, p = 0.82), and the inter-quartile ranges (25 to 75 percentile) for both groups were equal (4-32 weeks) (Table 4.1).

Table 4.1 Median and IQR (25th – 75th percentile) values of duration of current symptoms prior to treatment in both groups

Duration of symptoms (weeks)	Conservative	Surgical	z	p
Median	8	9.5	0.22	0.825
IQR (25% -75%)	4-32	4-32		

IQR = Inter-quartile range; z = Mann Whitney U test

The number of previous episodes recalled by the participants differed between cohorts (z= 3.35, p = 0.001). The surgical group had a larger number of previous episodes with about one quarter of participants reporting three or more prior episodes compared to 10% of conservative treated patients. Consistent with this, the conservative group reported more first episode presentations (50% vs. 26%) (Table 4.2). The number of co-morbidities was similar between groups (z= -0.09, p = 0.929) (Table 4.2)

Table 4.2 Number and percentage of previous neck pain episodes and associated co-morbidity in a CR patient cohort (n = 163) on entry to the trial. The patients were treated either surgically or conservatively.

Frequency	Conservative Frequency (%)	Surgical Frequency (%)	Z	p
No. of previous episodes				
0	54 (49)	14 (26)	3.35	0.001**
1	40 (37)	19 (35)		
2	5 (4)	8 (15)		
3	7 (7)	12 (22)		
4	2 (2)	1 (2)		
5	1 (1)	0 (0)		
Median (IQR)	1 (0-1)	1 (0-2)		
Co-morbidity	28 (26)	14 (26)	0.09	0.929
0	35 (32)	19 (35)		
1	34 (31)	13 (24)		
2	9 (8)	7 (13)		
3	2 (2)	1 (2)		
4	1 (1)	0 (0)		
5				
	1 (0-2)	1 (0-2)		
Median (IQR)				

Z = Mann Whitney U test. The inter-quartile range (IQR) represents the 25th and the 75th quartile values. **p <.01

4.1.2 Baseline pain and disability measurements

Pain and disability scores were significantly different at baseline (Table 4.3), with the surgical group consistently demonstrating higher mean value (Figures 4.0 and 4.1).

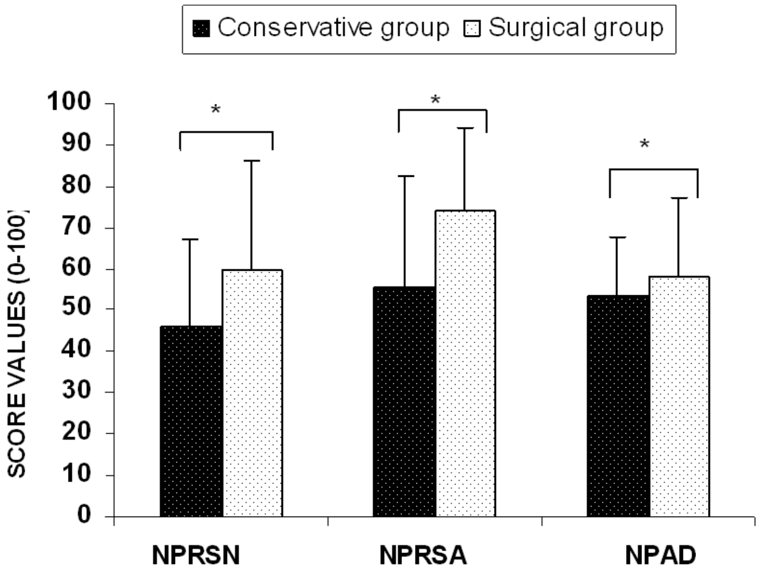


Figure 4.0 Mean and standard deviation (SD) values of baseline pain scores, NPRS N (neck), NPRS A (arm) and NPAD of a CR patient cohort treated conservatively and surgically. Statistical significance* p<0.05

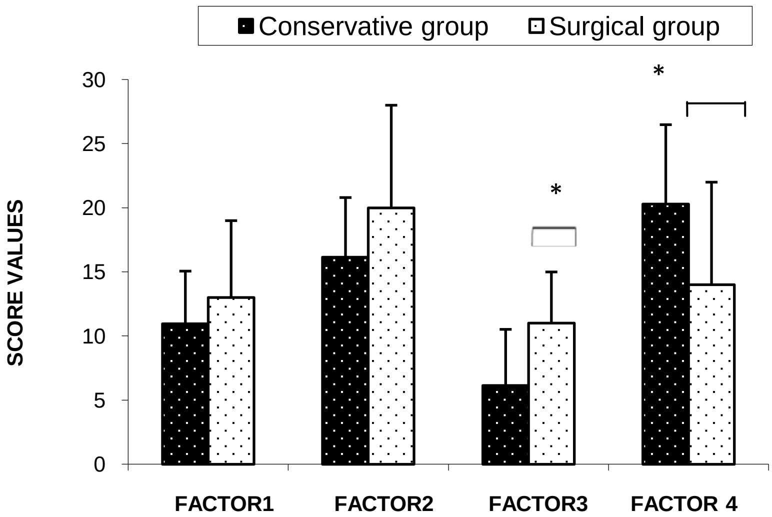


Figure 4.1 NPAD factor scores (mean, SD): Comparison between surgical and conservative groups at baseline. NPAD factors: 1 (neck pain, maximum (max) score 20); 2 (pain intensity, max score 30); 3 (effect of pain on emotion and cognition, max score 15); 4 (life activities interfered, max score 35). Statistical significance* p<0.05

4.1.3 Levels of Involvement

In both groups, the highest prevalence of involvement was the C5-6 level (Figures 4.2 A and B). In the conservative group, this level was involved in 68.7% of cases. This comprised most commonly of a single level involvement (58.7%) and less frequently two levels (9%). In the surgery group, the C6-7 level (41%) singly was most involved but when single and double levels were both considered, the C5-6 was involved in 45% patients.

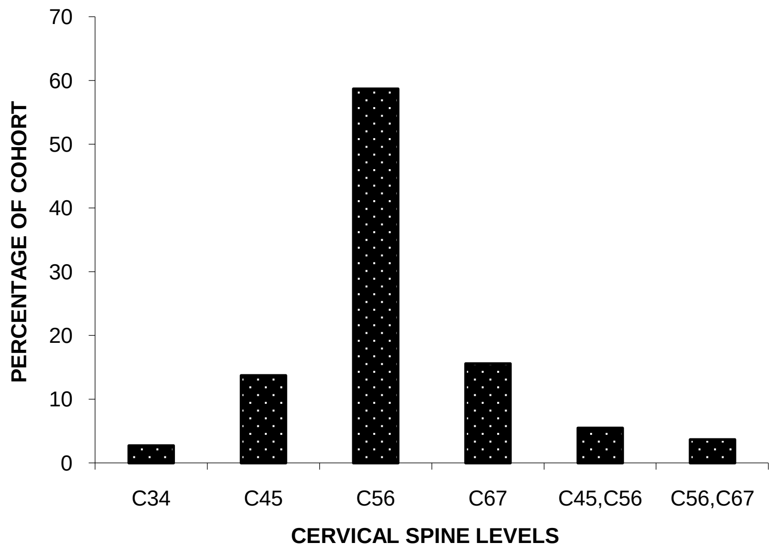


Figure 4.2 A Diagnosed levels: conservative group. Maximum involvement C5-6 (59%), followed by C6-7 (16%) and C4-5 (14%). Double level involvement in 9% patients.

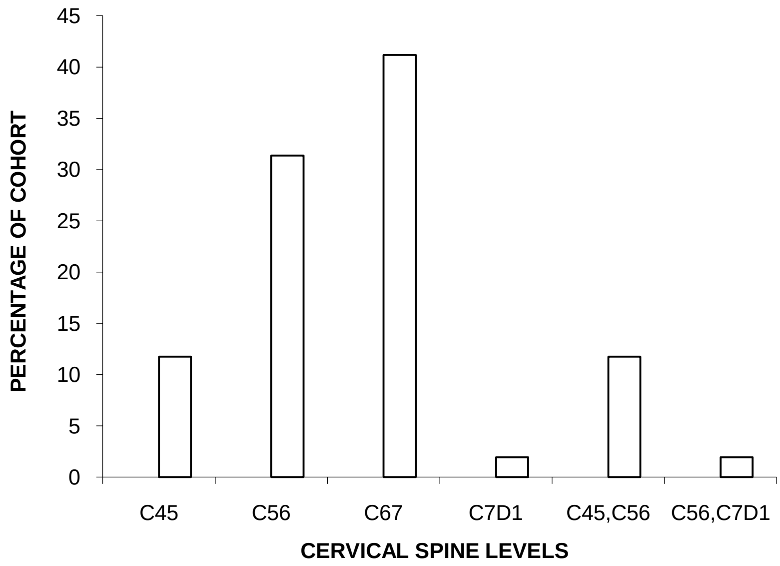


Figure 4.2 B Diagnosed levels: surgery group. C6-7 (41%), C5-6 (31%) and C4-5 (12%). C5-6 double level with C4-5 (12%) and C7-D1 (2%).

4.1.4 Baseline radiographic segmental curvature measurements

Figure 4.3 illustrates baseline measures of segmental kyphosis where the mean values in the surgical group were significantly higher at C2-3, C3-4, and lower at C5-6, than the conservative group (Table 4.3). The mean curvature value at C5-6 ($-1\pm 5°$) and at the identified symptomatic levels (csym) ($–1 \pm 4°$) in the surgery group were negative, implying over half of the patients had segmental kyphosis. Although the total mean value at C2-7 was higher in the surgical group implying comparative more lordosis, the difference was not statistically significant. Examining all the means of the segmental levels, it was noted that the conservative group had a relatively consistent level of segmental lordosis (between 2-4 degrees). In comparison, the surgical group demonstrated extreme values (significantly greater or significantly less) when compared to the conservative group.

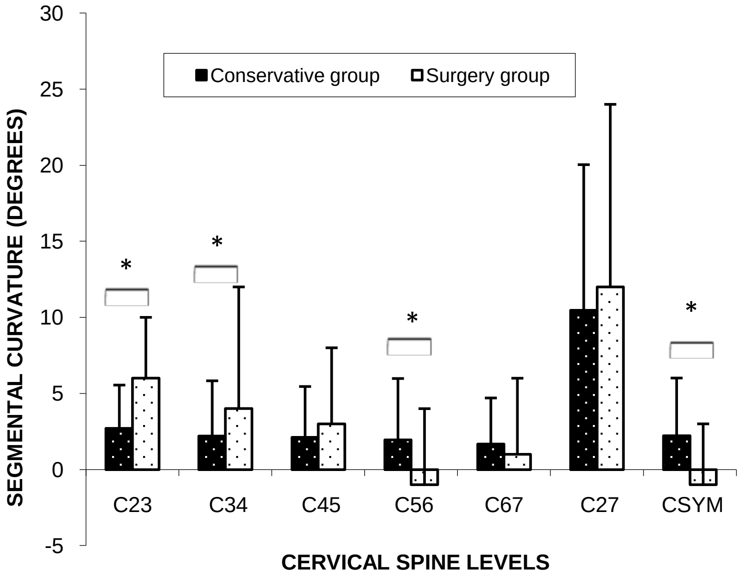


Figure 4.3 Sagittal radiological curvature using PTM, C2 to C7 levels, (mean, SD) at baseline. Involved diagnosed level (Csym). Kyphosis (negative value) at C5-6 and csym levels in the surgical group. Significant differences* p<0.05.

4.1.5 Baseline radiographic segmental flexion-extension motion measurements

At baseline, the surgical group demonstrated statistically ($p<0.05$) greater radiological segmental flexion-extension motion at 3 of the 5 levels (except C2-3 and C6-7) as well as the symptomatic level and total lordosis (C2-7) when compared to the conservative group (Figure 4.4, Table 4.3).

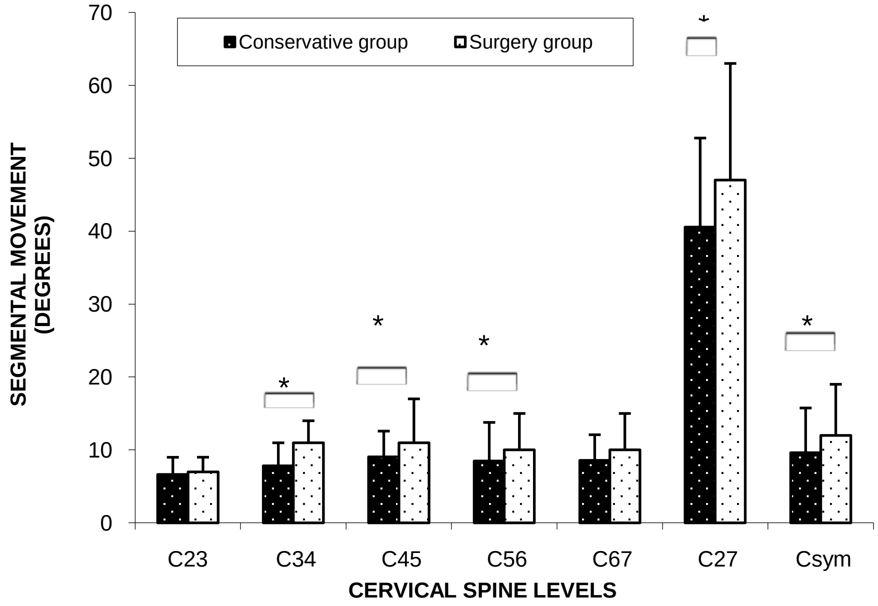
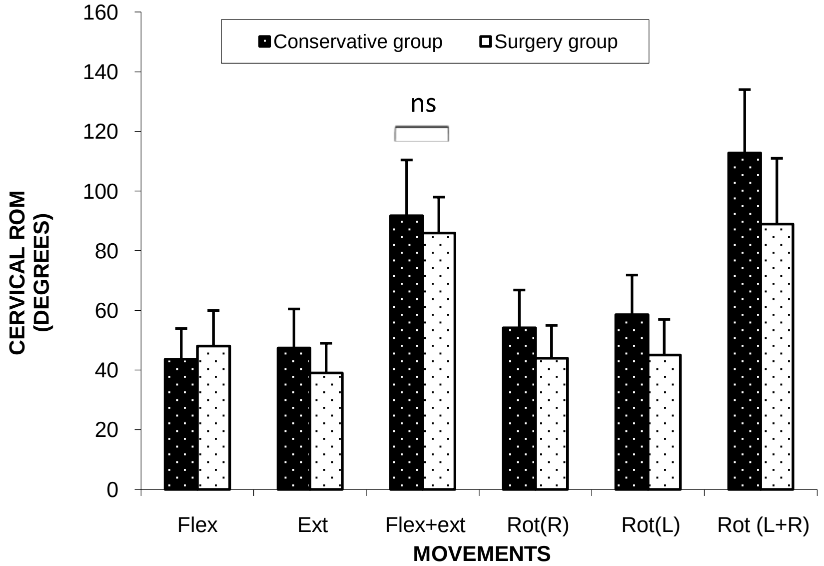


Figure 4.4 Baseline segmental radiological flexion-extension motion (mean and SD), levels C2 to C7, using Penning's method. Involved level = Csym. Between groups significant differences* p<0.05.

4.1.6 Baseline composite active cervical ROM measurements

Mean values for baseline composite active cervical ROM were less in the surgical group compared to the conservative group, in all directions except flexion which was greater in the surgical group (Figure 4.5). Further, all comparisons were statistically significantly different between groups except sum of flexion and extension (Table 4.3).



Flex = flexion; Ext = extension; Rot (R) = rotation right, Rot (L) = rotation left, ns = non significant

Figure 4.5 Baseline composite active cervical ROM measured with the Spin-T goniometer in sagittal and axial planes. Comparison of mean (SD) between surgical and conservative groups. All comparisons different at p<.05 except for combined Flexion and Extension

4.1.7 Baseline head-neck angle measurements

No statistical differences were detected between the treatment groups at baseline for Head-neck angle. Both groups had a mean value of around 40 degrees (Figure 4.6).

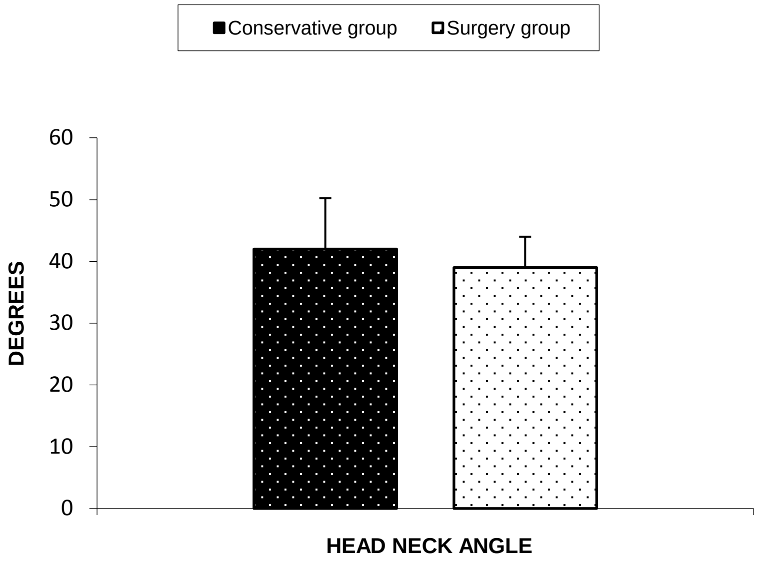


Figure 4.6 Mean (SD) values of head- neck angle in a cervical radiculopathy cohort measured at baseline. No significant differences were detected between groups.

4.1.8 Pain distribution in conservative and surgery groups at baseline

The surgery group had 59% of patients with left arm pain and 37% with right arm pain whereas the conservative group had 41% of patients with left arm pain and 40% with right arm pain. Neck pain had a much higher reported prevalence in the surgical group (90%) when compared to the conservative group (40%) (Figure 4.7). No significant association was determined linking arm dominance with the predominant side of reported symptoms.

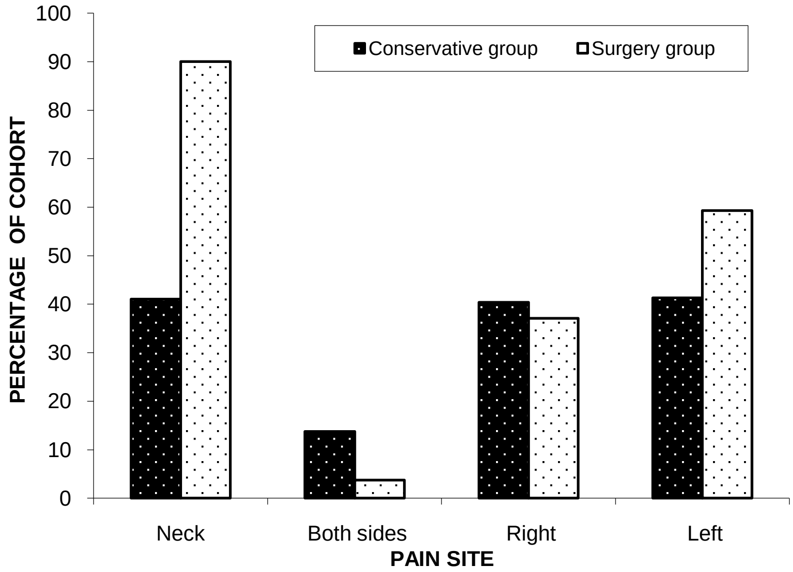


Figure 4.7 Frequency of pain site distribution in surgical and conservatively managed groups. Cumulative values exceed 100% due to multiple sites of pain (neck and arm).

4.1.9 Neurological signs measured at baseline

Baseline neurological deficits as tested clinically were more prominent in the surgery group as compared to the conservative group. Comparing right and left sides, the sensory and DTR were more affected on the left in the surgical group. Similar distribution was not apparent in the conservative group.

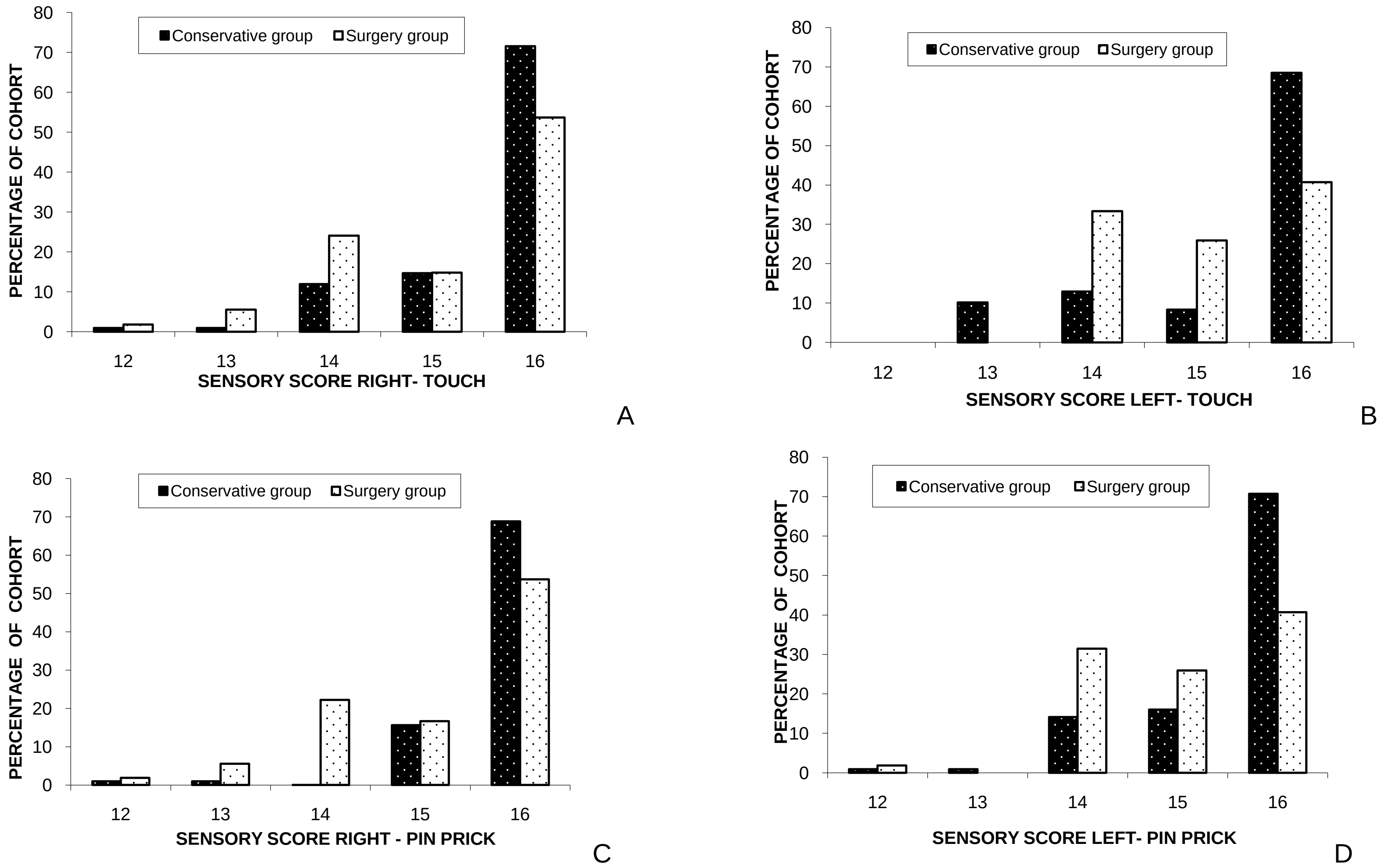
Sensory assessments of 'light touch' and 'pin prick' are illustrated in Figures 4.8 (A – D). A higher percentage of individuals in the surgery group have scores 14 and 15, and a lesser number score 16 when compared to the conservative group. This is indicative of greater sensory deficits in the surgical group.

Motor scores (Figures 4.8 E and F) demonstrate a higher percentage of surgical patients reporting scores 22, 23, 24 indicating greater motor deficits in the surgical group, as compared to the conservative group.

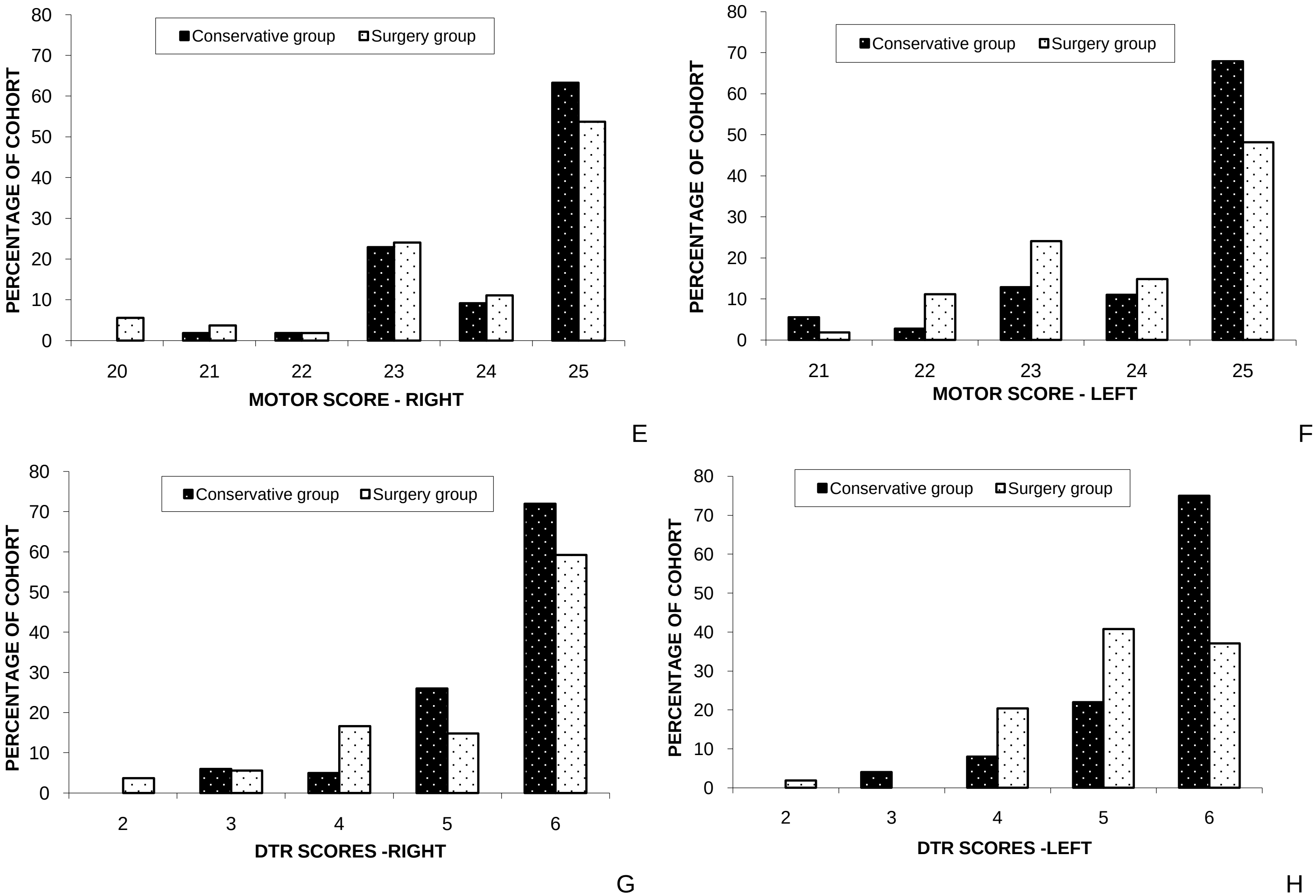
Baseline measures of DTR scores indicate normal responses for 60% right sided and 37% left sided surgical patients. This indicated more reflex deficits of the left side in the surgical group. Normal response scores were documented in more than 70% for both right and left sides in the conservative group (Figures 4.8 G and H).

In this study, the surgery group demonstrated a left side bias evident by higher number of patients reporting left side pain and greater percentage reporting sensory and DTR deficits on the same side. Differences in pain presentation or neurological deficits between sides reflected the asymmetry of the unilateral pathology presentations typical of cervical radiculopathy.

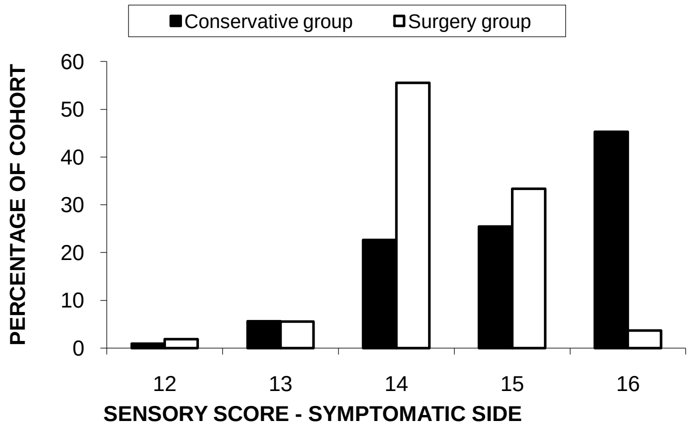
When only the symptomatic side was compared (Figures 4.8 I-K), the surgery group demonstrated a strong indication that it had much greater evidence of a nerve root pathology resulting in larger sensory, motor and DTR deficits when compared to the conservative group.



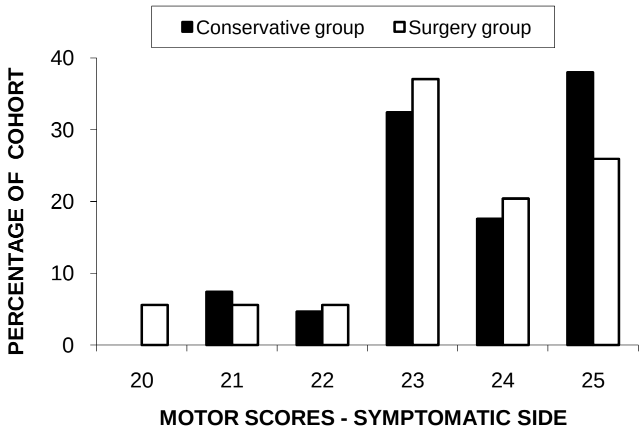
Figures 4.8 A – D Comparison of baseline sensory scores for light touch and pin prick (right and left sides) between conservative and surgery treatment groups of CR. Note: a maximal score of 16 suggests no obvious deficit.



Figures 4.8 E – H Comparison of baseline motor and DTR scores (right and left sides) between conservative and surgery treatment groups of CR. Note: a maximal score of 25 (motor) and 6 (DTR) suggests no obvious deficit.



I



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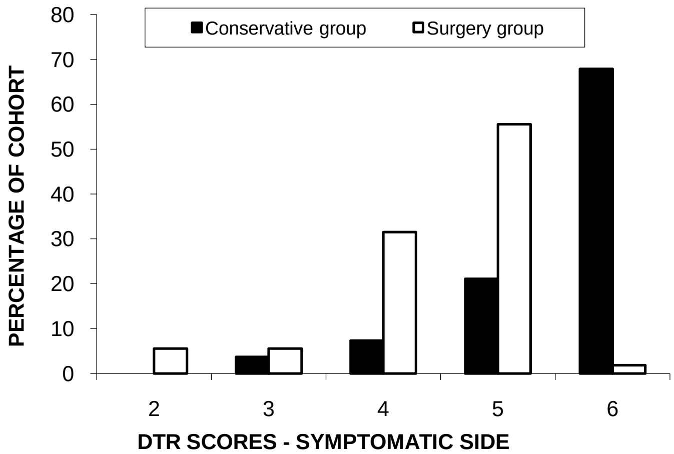


K

Figures 4.8 I-K Comparison of baseline sensory, motor and DTR scores (symptomatic side) between conservative and surgery treatment groups of CR.

4.1.10 Types of surgical procedures

In the surgery cohort 30 (56%) underwent anterior cervical discectomy whereas 24 (44%) underwent discectomy and fusion. Seven patients went through double level surgery whilst the remaining patients were treated for single level. Data for levels and procedure were pooled for analysis as no significant difference was detected between the two groups at baseline.

Table 4.3 Baseline differences of key variables between surgically and conservatively treated groups. Parametric (un-paired t-test) and non-parametric (Mann-Whitney U test) analysis based on data distribution.

Variables	Conservative (n=109)	Surgical (n=54)	T/Z	p
	Mean ± SD / Median (IQR)#	Mean ± SD / Median (IQR) #		
Age	45 ± 11	45 ± 10	0.11	0.907
BMI#	25 (22-27)	25 (23-28)	-0.12	0.906
NPRS (Neck)	46 ± 21	60 ± 26	-3.44	0.001**
NPRS (Arm) #	50 (39-76)	80 (60-90)	4.07	0.001**
NPAD#	53 (46-59)	57 (45-70)	4.07	0.001**
PENNING				
C2-7	41 ±12	47 ±17	-2.85	0.004*
C23#	7 (5-8)	7 (5-9)	0.29	0.769
C34	8 ± 3	11 ± 3	-5.96	0.001**
C45#	9 (7-11)	11 (9-15)	3.00	0.002**
C56	9 ± 5	10 ± 5	-2.28	0.023
C67	9 ± 4	10 ± 5	-1.77	0.077
Penning Csym level#	9 (5-12)	12 (7-15)	2.41	0.015**
PTM				
C2-7	10 ±10	12 ±12	-1.06	0.290
C23	3 ± 3	6 ± 4	-6.60	0.001**
C34#	3 (0-5)	5 (0-8)	2.47	0.013**
C45#	2 (0-4)	3 (0-6)	1.02	0.308
C56#	2 (0-4)	0 (-5 to 2)	-4.23	0.001**
C67	2 ± 3	0.54 ±5	1.86	0.063
PTM Csym level#	2 (0 to 4)	0 (-4 to 2)	-4.75	0.001**
Cervical ROM				
Flexion#	45 (39-50)	49 (40-56)	1.96	0.049
Extension	47 ± 13	39 ± 10	4.14	0.001**
Flexion +Extension	92 ± 19	86 ± 12	1.89	0.060
Rotation (Right)	54 ± 13	44 ± 11	5.04	0.001**
Rotation (Left)	59 ± 13	45 ± 12	6.25	0.001**
Rotation (Right +Left)	113 ± 21	89 ± 22	6.62	0.001**
Head Neck angle#	40 (36-50)	39 (35-43)	-1.67	0.094

Median values with 25th and 75th Inter-quartile range values. Significance at **p <.01, * p <.05

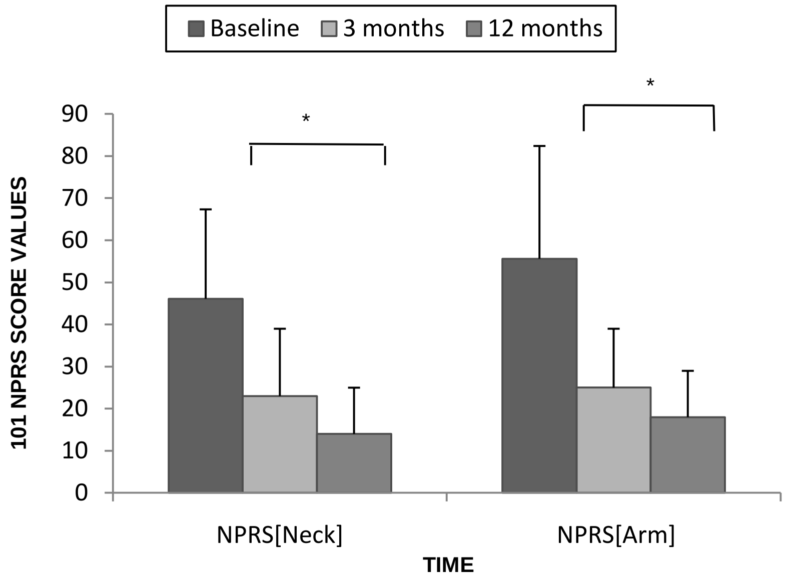
4.2 Repeat measurements of key variables– descriptive data analysis

4.2.0 Repeat Measurements of Pain and Disability

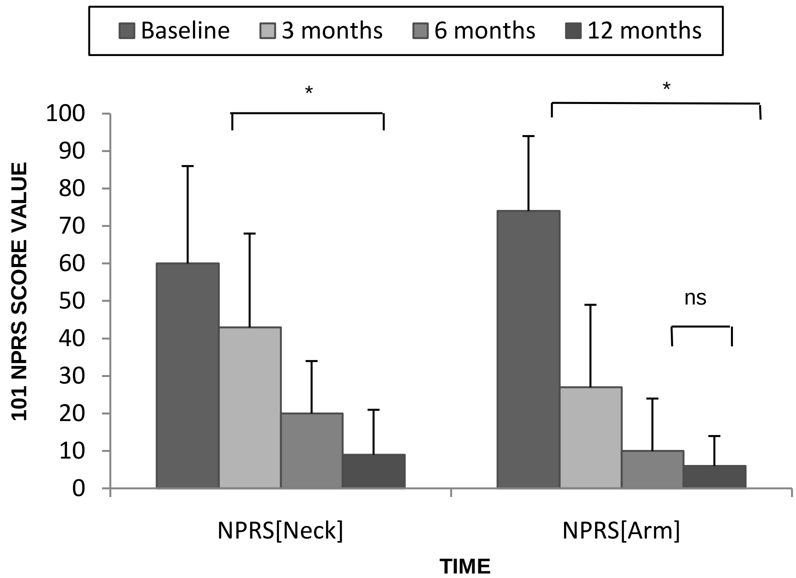
Both groups demonstrated statistically significant improvement for 101 NPRS neck and arm pain measures, when baseline scores were compared to scores at 3 months , and final scores at 12 months (Figures 4.9 A and 4.9 B). The surgery group demonstrated no statistically significant reduction for arm pain between 6 months and 12 months (Figures 4.9 B). In both groups, the initial arm pain score was higher than the initial neck pain score, typical of radicular pain.

In the conservative group, there was a steady decline in the total NPAD scores from baseline to final follow-up. However, when individual factors were analysed, mean Factor 3 score values (effect of pain on emotion and cognition) showed no statistical difference between 3 months and 12 months (Figure 4.10B).

In the surgery group, the mean total NPAD scores showed a mild increase in mean scores from 6 months to 12 months. This increase was probably caused by NPAD Factor 4 scores, (Figure 4.11B), which showed a significant increase in mean score value (Wilcoxon signed rank test $z = -4.96$, $p<0.01$) between 6 months to 12 months. Further, the difference in the mean values of factor 3 scores between 6 months and 12 months were not statistically significant (Figure 4.11B).

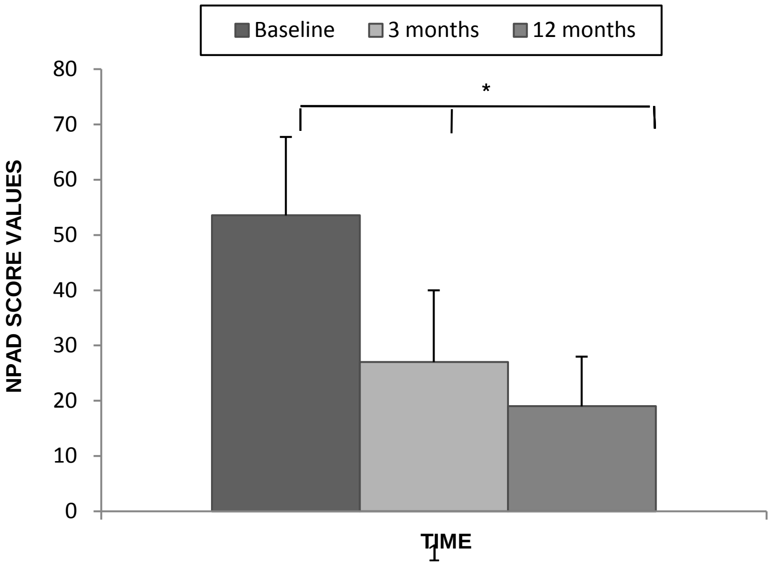


A

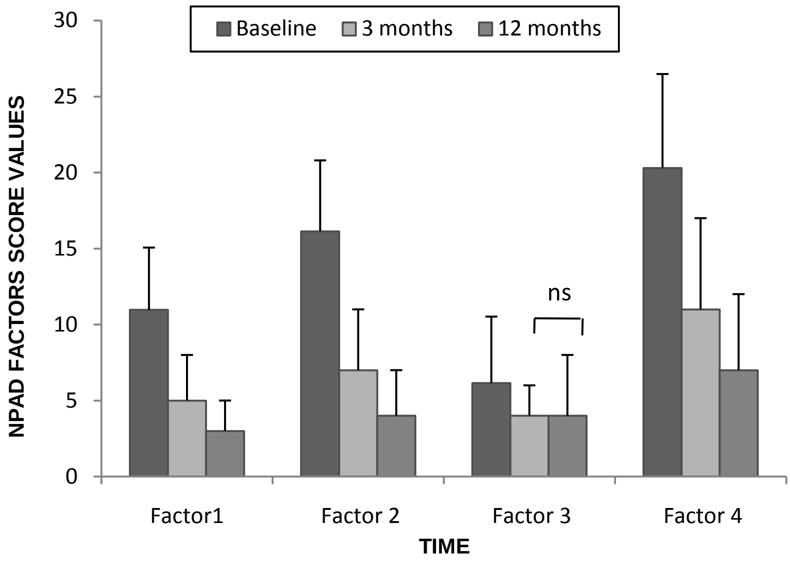


B

Figure 4.9 A & B 101 NPRS neck and arm scores in the conservative group (A) (baseline, 3 months, 12 months) and surgical group (B) (baseline, 3 months, 6 months, 12 months). Scores were statistically different* ($p < 0.05$) at all time measurements, except NPRS arm scores between 6 months and post-treatment in the surgical group (not significant = ns).

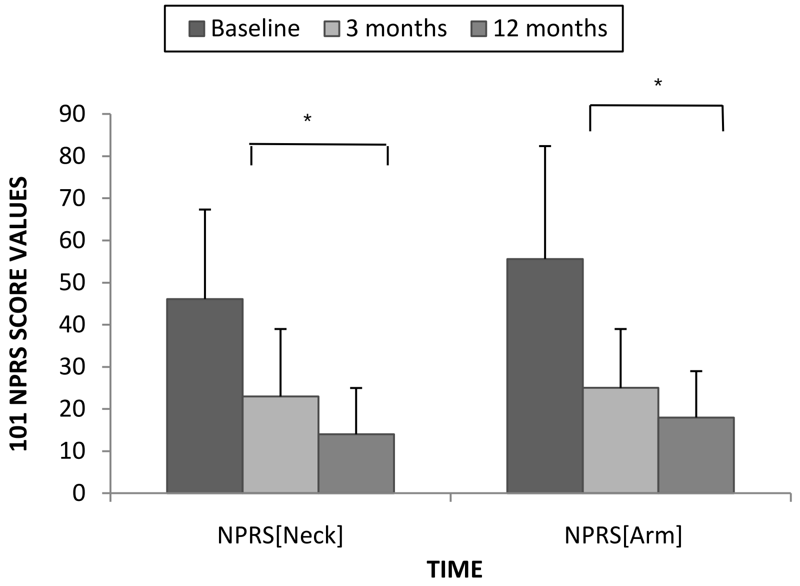


A

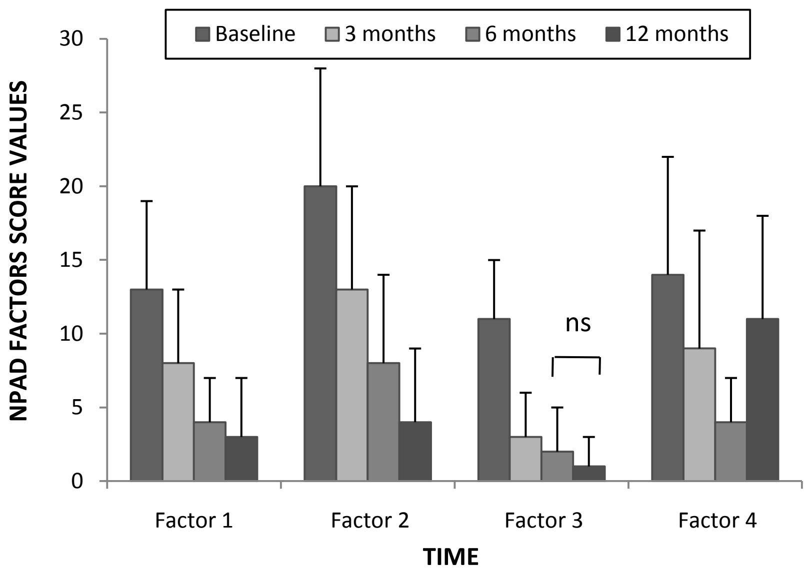


B

Figures 4.10 A & B Baseline, 3 months and 12 months scores for NPAD total (A) and NPAD Factor scores (B) in the conservative group treated for CR. Scores were statistically different* ($p < 0.05$) at all time comparisons for all factors with the exception of the Factor 3 (ns) between 3 months and 12 months.



A



B

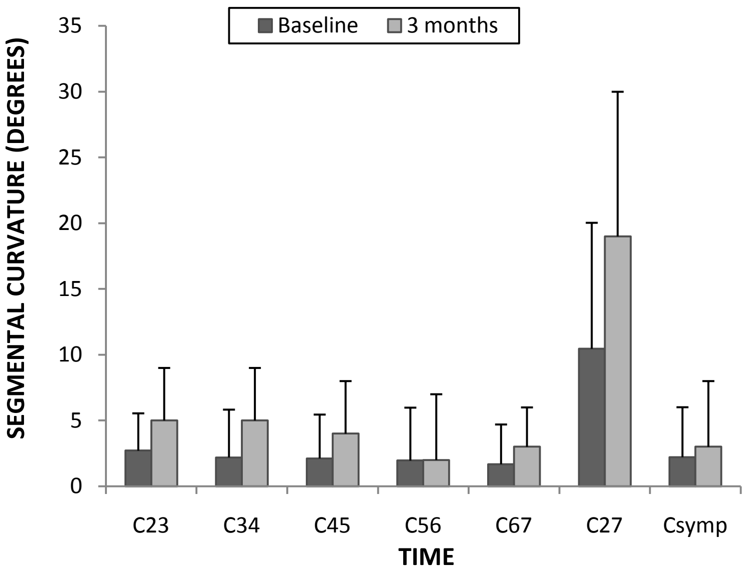
Figures 4.11 A & B Baseline, 3 months, 6 months and 12 months, repeat measurements, NPAD total (A) and factor scores (B) in the surgical group (ACD/F). Scores were statistically different* (p <0.05) at all time comparisons for all factors with the exception of the Factor 3 (ns) between 6 months and 12 months.

4.2.1 Repeat measurements of sagittal segmental radiographic curvature

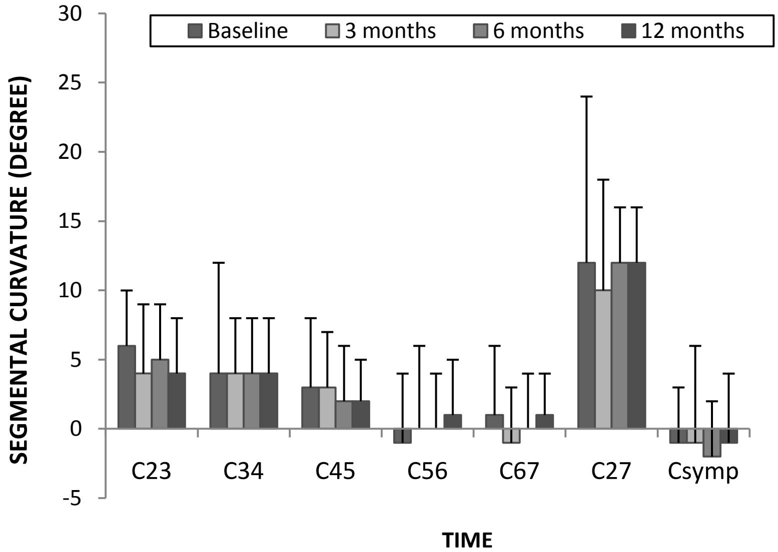
At short-term (3 months), in the conservative group (Figure 4.12 A), the mean radiographic segmental curvature values suggest a trend for increase in curvature values. Non-parametric rank analysis (Wilcoxon) was able to detect statistical difference ($p<.001$) observed at C2-3 ($z = -5.25$), C3-4 ($z = -4.30$), C4-5 ($z = -5.27$), C6-7 ($z = - 3.42$) and C2-7 ($z = -5.53$) but not at C5-6 ($z = -1.50$, $p = 0.13$) or the symptomatic levels ($z = -1.66$, $p = 0.096$).

The surgery group (Figure 4.12 B) demonstrated varied changes for different levels over a 12 months repeat assessment period. Compared to baseline values, mean C2-3 segmental curvature values reduced at 3 months ($z = -3.03$, $p = 0.02$) and 12 months ($z = -2.45$, $p = 0.01$). The C3-4 level mean values remained largely unaltered from baseline to 12 months. At the C4-5 level, the mean segmental curvature value reduced (reduction in lordosis) from 6 months onwards, although the difference was not statistically significant during any of the repeat measurements. At baseline, the mean C5-6, measured -0.54° ± 5.4, whereas at 12 months, the mean value was positive 1.54° ± 4.57, the difference being statistically significant ($z = -2.45$, $p < 0.05$).

The C6-7 mean value which was positive at baseline (0.56° ±4.68) became negative at 3 months (-0.48° ± 4.70) ($z= -2.05$, $p <0.05$), positive from 6 months to 12 months ($z = -2.06$, $p < 0.05$) and at one year the mean values were the same as baseline measurements. Mean curvature values at the symptomatic level/s remained negative during all repeat measurements in this group (mean –2°, range –22° to 10°). C2-7 mean curvature values remained grossly unchanged despite other segmental variations.



A

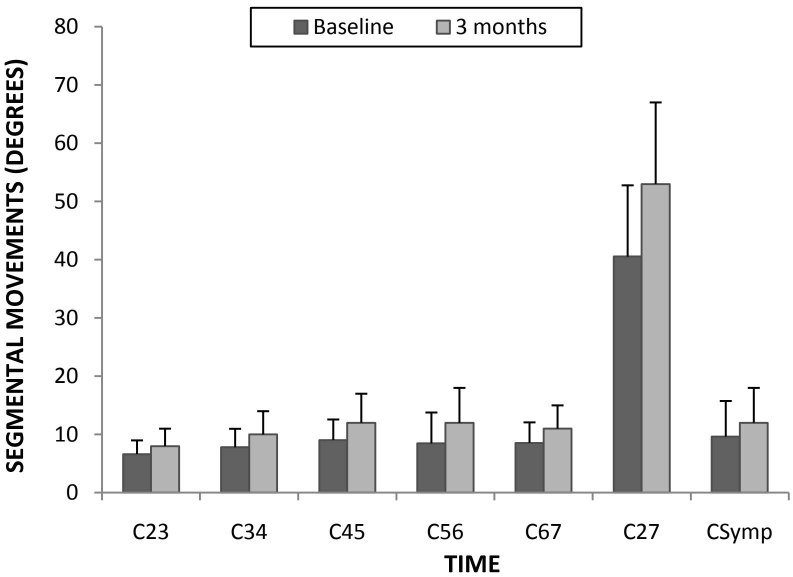


B

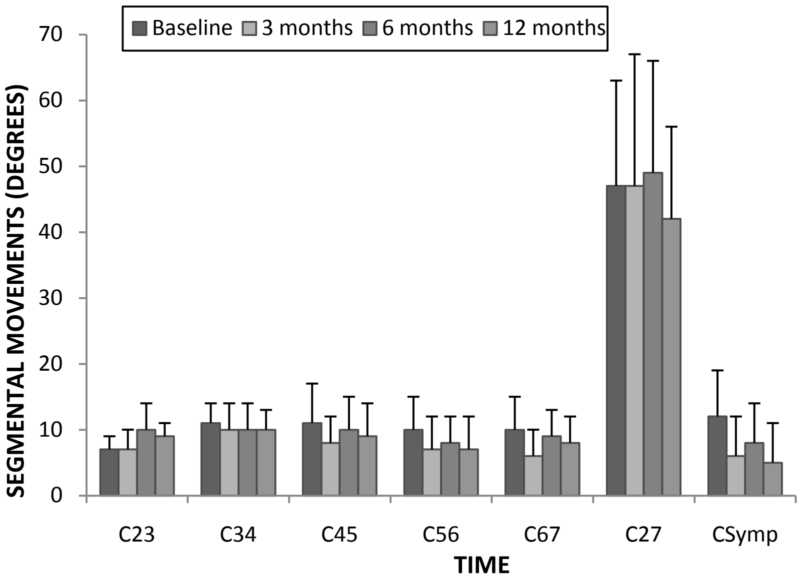
Figures 4.12 A & B Mean (SD) of repeat measurements of sagittal segmental radiographic curvature in the (A) conservative (0-3 months) and (B) surgical cohorts (0-12 months).

4.2.2 Repeat measurements of radiographic sagittal segmental mobility

Over time, from baseline to 3 months, the conservative group demonstrated an increment in mean values for sagittal segmental flexion-extension motion at all levels (Figure 4.13A). Non-parametric rank analysis (Wilcoxon) was able to detect statistical difference ($p<.001$) at C2-3 ($z = -4.74$), C3-4 ($z = -5.34$), C4-5 ($z = -6.62$), C5-6 ($z = -5.50$), C6-7 ($z = -6.15$), C2-7 ($z = -7.62$) and at the symptomatic levels ($z = -3.96$). On the contrary, in the surgery group, from baseline to 3 months, statistically significant mean reduction was observed at C3-4, C4-5, C5-6, and C6-7 and at the symptomatic level. At 12 months, mean reduction in segmental flexion-extension motion was observed for all levels except C2-3, which showed an increase (Figure 4.13 B). From baseline to 12 months, statistically significant differences ($P<0.05$) were detected at C2-3 ($z = -3.81$), C5-6 ($z = -3.33$), C6-7 ($z= -3.16$), C2-7 ($z = -2.76$) and the symptomatic level ($z = -5.58$).



A

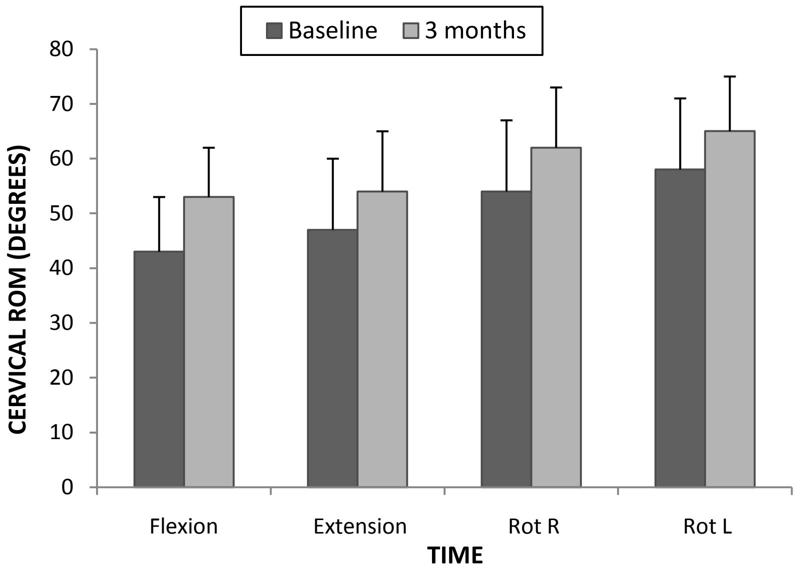


B

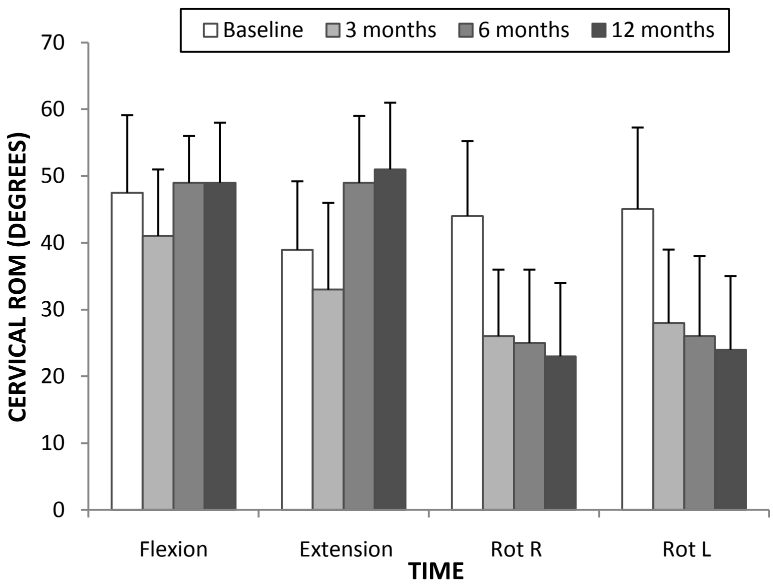
Figures 4.13 A & B Mean (SD) of repeat measurements of sagittal segmental radiographic flexion-extension motion in the (A) conservative (0-3 months) and (B) surgical cohorts (0-12 months).

4.2.3 Repeat measurements of composite active cervical ROM

At 3 months, statistically significant ($p<0.05$) increase in range of motion in all directions was seen in the conservative group: Flexion ($z = -7.94$), extension ($z = -6.27$), sum of flexion + extension ($z = -8.03$), rotation right ($z = -5.94$), rotation left ($z = -4.42$) rotation left and right (z = - -6.32) (Figure 4.14 A) whereas the surgery group at 3 months showed a statistically significant ($p< 0.05$) reduction in range of motion in all directions compared to baseline (Figure 4.14 B). Flexion and extension mean values increased ($p < 0.05$) 6 months onwards, whereas rotation to both sides remained persistently reduced ($p < 0.05$) compared to baseline. At 12 months, compared to baseline, flexion remained nearly unchanged ($z = -0.887$, $p = 0.375$). Extension ($z= -5.53$), and sum of flexion and extension ($z = -5.53$) increased significantly ($p<0.05$). Statistically significant reduction ($p <0.05$) were demonstrated for rotation right (Rot R) ($z = -5.88$), rotation left (Rot L) ($z= 5.82$) and sum of rotation ($z = -5.87$).



A

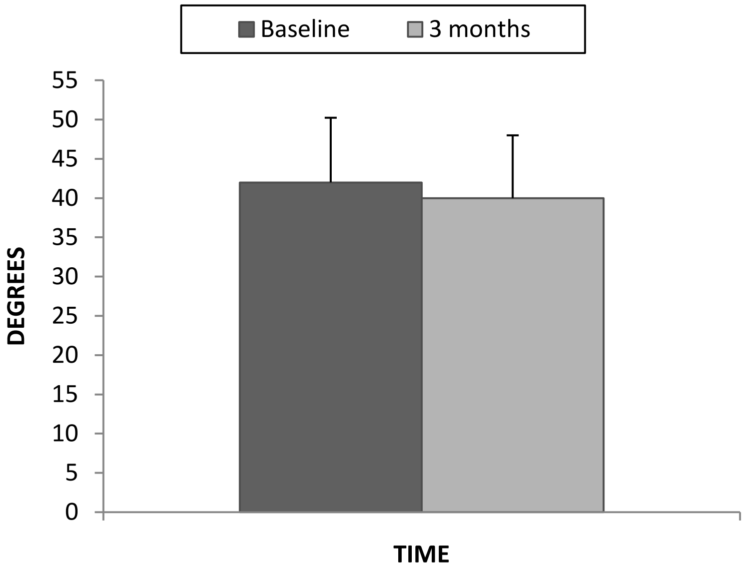


B

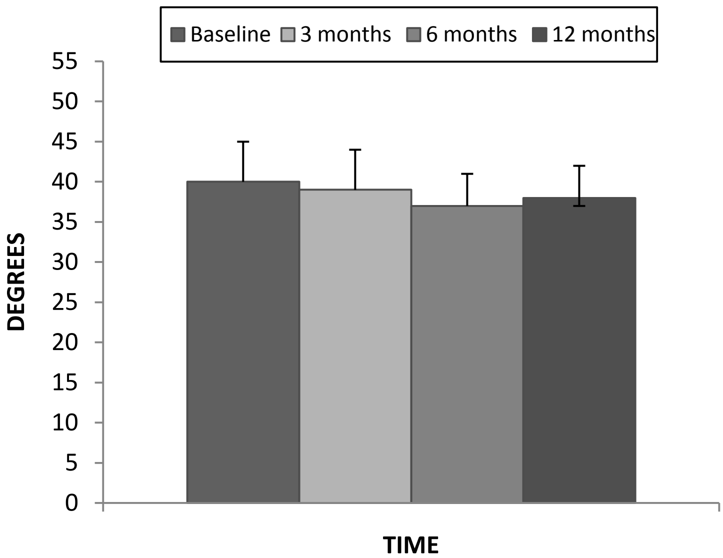
Figures 4.14 A & B Mean (SD) of repeat measurements of sagittal and axial plane active composite cervical range of motion in (A) conservatively (0-3 months) and (B) surgically (0-12 months) treated CR cohort

4.2.4 Repeat measurement of head neck angle

The mean values of head neck angle in both groups remained relatively constant from baseline to final follow-up in both groups. There was no statistical difference seen between any two measurements (p>.05).



A



B

Figures 4.15 A & B Mean (SD) of repeat measurements of head neck angle in a (A) conservatively (0-3 months) and (B) surgically (0-12 months) treated CR cohort

4.2.5 Repeat neurological scores

The conservative group showed improvement from baseline to 3 months for all neurological scores, although no neurological sign showed 100% improvement when a deficit was noted in the baseline assessment. The surgery group too showed improvement for all neurological signs when baseline measurements were compared to final measurements at 12 months. However, maximum motor scores (score 25), right side, achieved at 6 months (89% patients) showed a slight deterioration (80%

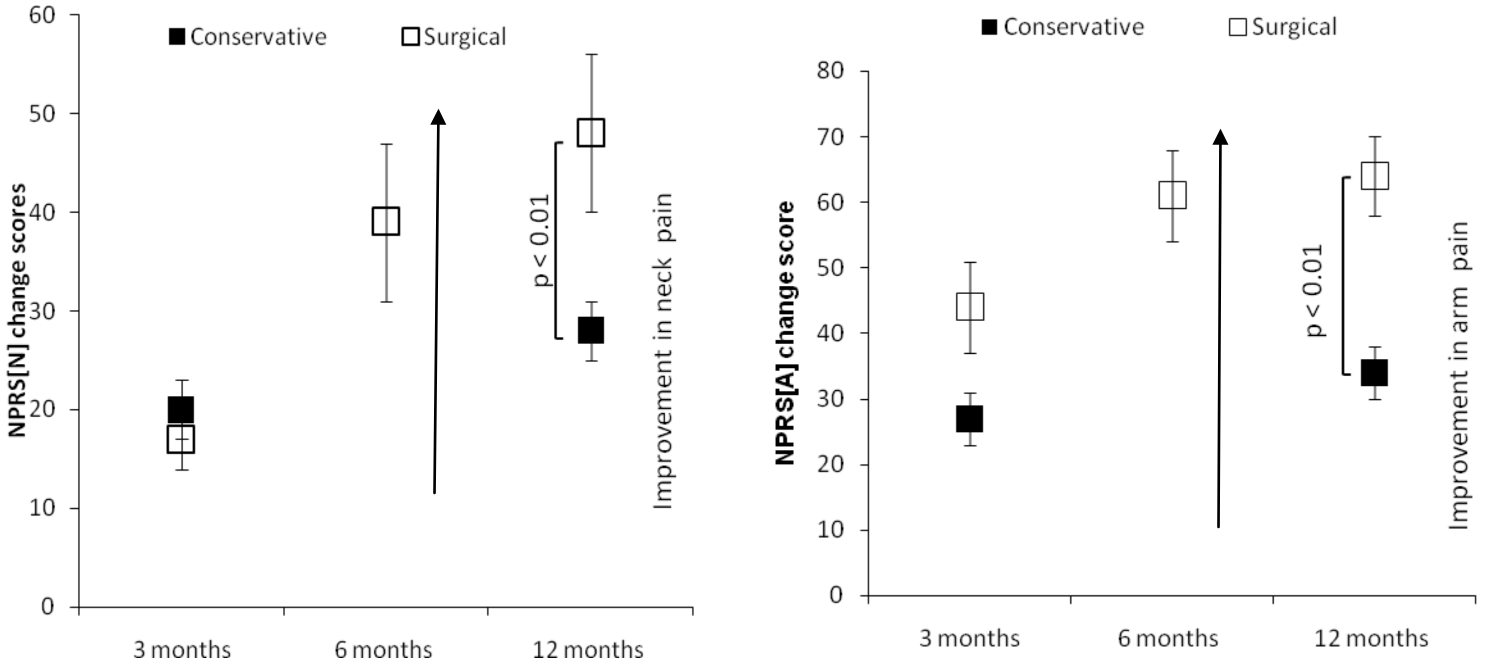
patients at 12 months. A similar observation was made for the DTR scores, right side, (from 91% to 87% patients) from 6 months to 12 months. 100% improvement at 12 months was not achieved for any neurological sign in the surgery group.

4.3 Hypotheses analyses

4.3.0 Change in neck and arm pain from baseline to 12 months in conservative and surgically treated groups

At 3 months, the surgical group demonstrated a greater change score than the conservative group with arm pain. For neck pain, similar change scores were reported for both groups. At 12 months, change scores for both neck ($z = 3.82$, $p<0.001$) and arm pain ($z = 6.38$, $p <0.001$) were significantly greater in the surgical group compared to the conservative group. One factor that may have contributed to greater change scores is a significantly higher baseline score in the surgery group (Figures 4.16A and B).

The first sub-hypothesis stated that at a one-year follow-up, change in arm pain, neck pain scores would be similar in both treatment groups (conservative management or surgery) in a CR patient cohort. The first sub-hypothesis is therefore rejected.



A B

NPRS [N] = NPRS neck; NPRS [A] = NPRS arm

Figures 4.16 A & B Change score values (95%CI) of NPRS neck and arm pain at 3 and 12 months to highlight differences between conservative and surgery groups. Improvement in change score for both neck and arm pain evident in both groups at 12 months.

Table 4.4 Change score analysis (baseline to 12 months) of neck and arm pain within conservative and surgery groups.

	Change scores between baseline and final scores within group [Median (IQR)]		**Difference in change scores between surgery and conservative group (Mann Whitney U test)**	
Pain scale	Conservative group (n=109)	Surgery group (n=54)	z	p
NPRS (Neck)	30 (20-40)	52 (30-75)	3.82	<0.00**1
NPRS (Arm)	35 (25-55)	70 (55-80)	6.38	<0.001**

**p <.01

4.3.1 Relationship between pain and disability, before and after treatment (at 12 months follow-up) in both groups

In the conservative group, neck pain and arm pain demonstrated a consistent relationship with disability scores at baseline and at 12 months (Table 4.5). Positive moderate correlations were seen between variables arm pain and disability, both at baseline and at 12 months, whereas neck pain was weakly correlated with disability scores at baseline which increased to moderate values at 12 months.

In the surgery group (Table 4.5), significant weak correlations were determined at baseline between arm pain and NPAD scores, which at 12 months became a strong positive correlation. Figure 4.17 illustrates a positive correlation between the two variables. Neck pain scores were not significantly correlated with disability scores at baseline or at 12 months. The second sub-hypothesis stated that high pain intensity would correlate with disability before and after treatment in both treatment groups.

This sub-hypothesis is accepted for the conservative group, but can be only partially accepted for the surgery group.

Table 4.5 Spearman rank correlation coefficient (r) between measurements of pain (101 NPRS neck /arm) and disability (NPAD), at baseline and 12 months follow-up, in the conservative and surgical groups.

	Baseline		**12 months**	
	Conservative r	Surgery r	Conservative r	Surgery r
101 NPRS (neck) with NPAD	0.19*	0.20	0.44*	0.08
101 NPRS (arm) with NPAD	0.45*	0.29*	0.47*	0.58*

* p <0.05

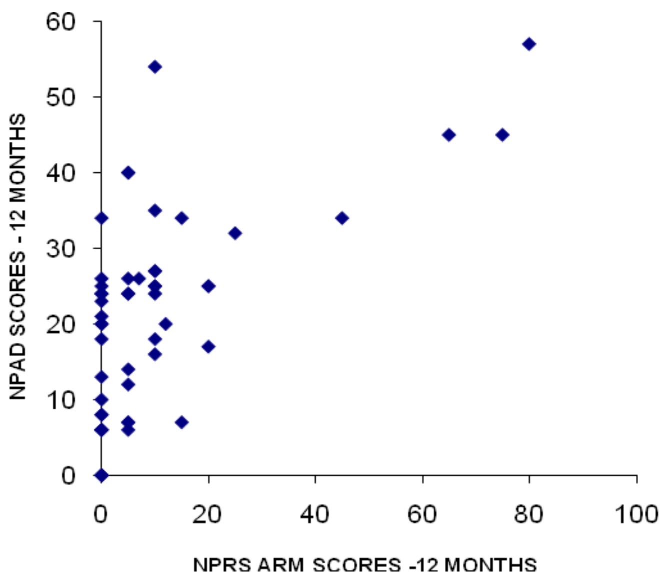


Figure 4.17 Scatter diagram illustrating positive correlation between final 101 NPRS arm scores and final NPAD scores in the surgical group

4.3.2 Association between baseline curvature measurements and measures of neck pain, arm pain, disability at baseline

The third sub-hypothesis states: Baseline radiological measures of curvature of the cervical spine, total (C2-7) and at the symptomatic level/s will negatively correlate with pain and disability at baseline in either treatment group.

The results of correlation between radiological measures of curvature at baseline and neck pain, arm pain and disability scores at baseline revealed a negative relationship between paired variables which were significantly correlated. This implied that lower curvature values (suggesting reduced lordosis or relative kyphosis) resulted in higher pain and disability levels (Table 4.6). The third sub-hypothesis is partially accepted.

Table 4.6 Spearman rank correlation coefficient (r) showing negative correlations between significantly correlated variables **p <.01, * p <.05. Radiological curvature measures using the posterior tangent method (PTM) at baseline with pain and disability scores at baseline in the conservatively and surgically treated groups.

	Total Curvature C_2-C_7		Symptomatic level(s) curvature	
Conservative	**r**	**p**	**r**	**p**
Neck pain	-0.10	0.300	-0.07	0.440
Arm pain	-0.31	0.001**	-0.22	0.017*
Disability	-0.17	0.070	-0.20	0.031*
Surgical	**r**	**p**	**r**	**p**
Neck pain	0.09	0.474	0.18	0.186
Arm pain	-0.08	0.552	-0.60	0.001**
Disability	-0.08	0.535	-0.31	0.023*

From all the paired comparisons, baseline curvature at the symptomatic level demonstrated the greatest rank correlation with baseline arm pain (Table 4.6). Figure 4.18 shows the scatter plot for baseline arm pain and curvature at the symptomatic level for the surgical group.

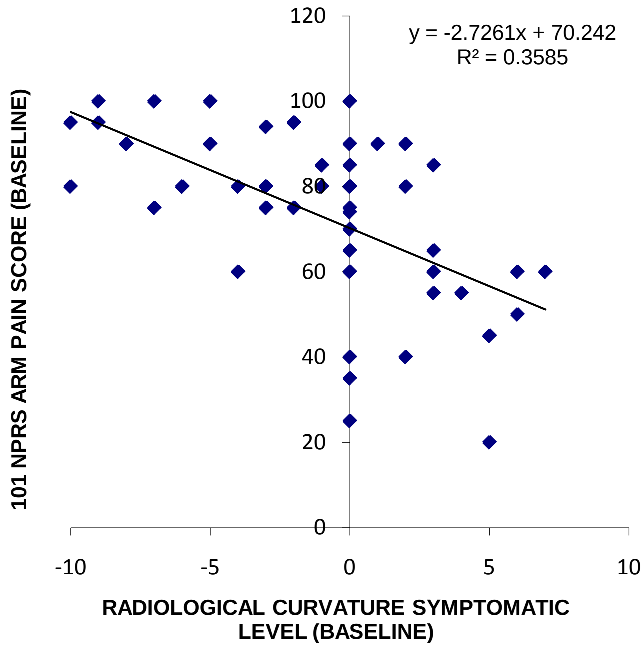


Figure 4.18 Scatter diagram illustrating negative correlation between baseline radiological curvature at the symptomatic level (measurement in degrees) and baseline NPRS arm scores in the surgery group

4.3.3 Active cervical ROM and measures of pain and disability at baseline

Negative significant correlations between baseline composite active cervical ROM and pain and disability measures at baseline were determined. This implies that reduced range of motion was correlated with increased pain and disability (Table 4.7). Significant correlations (r >0.40) were observed only in the surgical group with the maximum negative correlation seen between baseline extension and NPAD scores (r= -0.60) (Table 4.7). All movements were not correlated to all measures of pain and disability and therefore the fourth sub-hypothesis, that 'Baseline cervical ROM, flexion, extension and lateral rotation (R and L) will correlate with measures of pain (101 NPRS) and disability at baseline, in both treatment groups' is partially accepted.

Table 4.7 Correlation between composite active cervical ROM [flexion, extension and rotation (right and left)] with measures of neck and arm pain (101 NPRS) and disability (NPAD), at baseline in both groups.

Variables		Conservative		Surgical	
Baseline		r	p	r	p
Flexion	NPRS Neck	-0.11	0.215	-0.42	0.001**
	NPRS Arm	0.09	0.317	-0.48	0.001**
	NPAD	0.01	0.854	0.11	0.420
Extension	NPRS Neck	-0.22	0.018*	-0.06	0.631
	NPRS Arm	0.00	0.943	-0.47	0.001**
	NPAD	-0.01	0.879	-0.60	0.001**
Rotation right	NPRS Neck	-0.19	0.046**	0.01	0.996
	NPRS Arm	-0.28	0.001**	-0.45	0.001**
	NPAD	-0.21	0.024	-0.28	0.038*
Rotation left	NPRS Neck	-0.19	0.038	-0.05	0.684
	NPRS Arm	-0.16	0.085	-0.27	0.046
	NPAD	-0.09	0.345	-0.19	0.156

r = Spearman rank correlation coefficient; **p <.01, * p <.05

4.3.4 Relationship between measures of head-neck posture and pain

A positive correlation (r= 0.56, p=0.001) was seen between head neck angle measures and neck pain scores at baseline in the surgery group which implied higher values of head neck angle was associated with increased neck pain. This association did not reach statistical significance in the conservative group. Head neck angle measures did not correlate with arm pain in either group (Table 4.8). The fifth sub-hypothesis that increased head neck angle is positively associated with pain can only be partially accepted.

Table 4.8 Spearman rank correlation coefficient (r) between head neck angle with measures of neck and arm pain (101 NPRS), at baseline, in both groups. Significant levels calculated at **p <.01, * p <.05.

Variables		Conservative		Surgical	
		r	p	r	p
Head neck angle	NPRS (Neck)	0.02	0.830	0.56	0.001**
	NPRS (Arm)	0.05	0.550	-0.17	0.198

4.3.5 Differences in radiographic segmental flexion-extension motion between an asymptomatic group and a CR cohort.

The results of this analysis show a statistical difference in radiological flexion-extension range of motion between a CR patient cohort (n = 35) and an asymptomatic group (n = 35) (age and gender matched) for all segments between C2 and C7 except for the C2-3 segment (p=0.09) (Table 4.9). The findings suggest that the hypothesis that patients with CR have systemically decreased segmental and total flexion-extension motion of the cervical spine was supported for the total curvature C2- 7 and all segmental measures with the exception of the C2-3 level.

Table 4.9 Differences in mean, standard deviation (SD) values between groups (asymptomatics versus CR cohort) for radiological segmental flexion-extension motion.

Level	Asymptomatics Mean ± SD	Patients Mean ± SD	t	p
C_2C_3	8 ± 3	7 ± 3	1.70	0.093$^{n.s.}$
C_3C_4	15 ± 5	10 ± 4	4.30	0.001
C_4C_5	19 ± 5	12 ± 4	6.12	0.001
C_5C_6	19 ± 5	12 ± 6	5.52	0.001
C_6C_7	15 ± 5	10 ± 4	4.01	0.001
C_2C_7	75 ±19	47 ± 9	7.82	0.001

t = unpaired t test, p = significance value, n.s. = non-significant >0.01. All measurements in degrees

4.3.6 Association of neck pain with hypo-mobility of diagnosed levels

Significant negative correlation was seen between baseline radiological segmental rotational flexion-extension motion (Penning method) at the diagnosed symptomatic level/s and final neck pain scores in both groups. The negative correlation (Surgical r = -0.58, conservative r = -0.57, both p<.0001) implies that lower values of segmental mobility were correlated with higher levels of pain at 12 months in a CR group who had received treatment. The seventh sub-hypothesis which states that ‘ hypomobility of affected levels in the cervical spine measured radiologically in the sagittal plane will correlate with final neck pain scores in both treatment groups’ is accepted.

4.3.7 Radiographical segmental flexion-extension motion and composite active range of motion in the sagittal plane

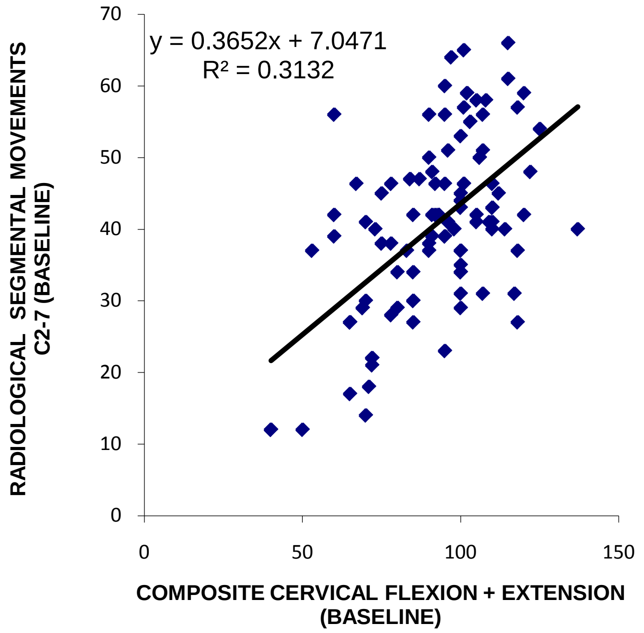
Analysed for measurements at baseline and 3 months (in both groups), 6 months and 12 months (surgery group), radiological segmental flexion-extension motion demonstrated a positive significant correlation with sum of composite active flexion and extension range of motion in both groups. Correlations were strong in the conservative group and weak in the surgical group. Measurements at 12 months in the surgery group (p=0.24) (Table 4.10) were not significantly correlated. Based on the above analysis, the eighth sub-hypothesis that 'Measurements of active cervical spine flexion-extension (sum of flexion and extension) range of motion will correlate positively with radiographic measures (C2-7) of cervical spine sagittal segmental motion in both treatment groups' is partially accepted.

Table 4.10 Spearman rank correlation coefficient (r) between segmental radiological flexion-extension motion (Penning's method) of the cervical spine (C2-7) and sum of composite active flexion and extension of the cervical spine, in both groups treated for CR.

	Conservative		**Surgical**	
	r	p	r	p
Baseline	0.51	0.001**	0.37	0.006**
3 months	0.53	0.003**	0.39	0.004**
6 months	NA	NA	0.26	0.052
12 months	NA	NA	-0.16	0.243

**p <.01, * p <.05
NA – There was no radiological data collected at 6 months and 12 months in the conservative group.

Scatter graphs were plotted to illustrate the association between the two variables. The independent variable (sum of flexion and extension) could predict 31% and 14% variance of the dependent variable (radiological segmental flexion-extension motion C2-7) (Figures 4.19A and B).



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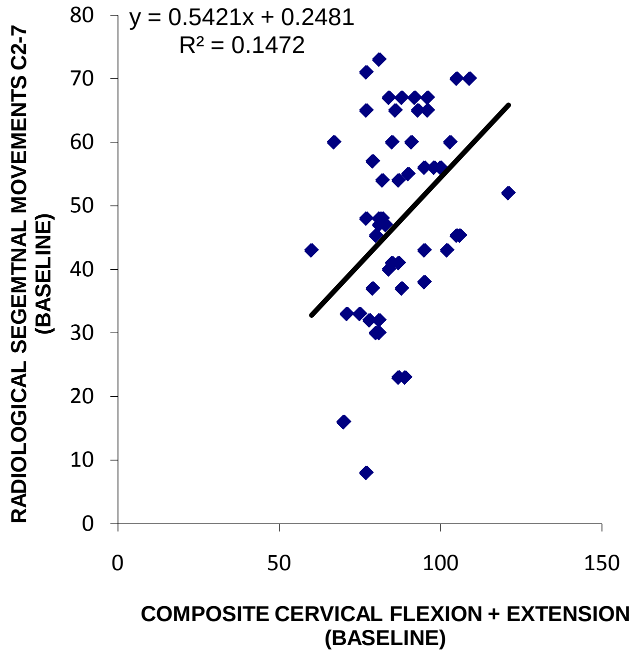

B

Figures 4.19 A & B Scatter diagram with a linear regression analysis between active composite cervical spine flexion + extension range of motion and segmental radiographic sagittal motion (C2-7) of the cervical spine in the conservative group (A) and surgery group (B) at baseline.

4.3.8 Association of baseline variables with neck pain at 12 months using bivariate correlation analysis

Correlation between neck pain as final outcome and variables measured at baseline in the conservative group (Table 4.11) showed significant moderate to high correlations for arm pain (r= 0.67), segmental radiological flexion-extension motion (C4-5 r= -0.56, C5-6 r= - 0.63, C6-7 r= -0.51, C2-7 r = -0.74, symptomatic level r= - 0.57), and active work style (r= 0.60).

For the surgical group significant strong correlation were calculated between final neck pain scores and baseline segmental radiological flexion-extension motion C3-4 (r= - 0.50), C6-7 (r= -0.58), C2-7 (r= - 0.62) symptomatic levels (r= - 0.58); and age (r= 0.55) (Table 4.12).

4.3.9 Association of baseline variables with arm pain at 12 months using bivariate correlation analysis

In the conservative group, the result of Spearman rank correlation analysis showed moderate to strong positive correlation between final arm pain scores and baseline arm pain (r=0.59). Other significant correlations analysed (r < 0.50) are presented in Table 4.11.

In the surgery group, Spearman rank correlation coefficient (r) values between baseline variables and final arm pain scores (Table 4.12) did not yield r values > 0.50. Significant moderate correlations were however determined between final arm pain and baseline variables; arm pain (r = 0.44), PTM C4-5 (r = -0.40), rotation range of motion (left) (r =-0.45) and rotation sum (r = -0.43).

4.3.10 Association of baseline variables with disability scores at 12 months using bivariate correlation analysis

In the conservative group, radiological segmental curvature value (PTM C2-7) was the only variable that had a moderate to strong significant negative correlation (r = -0.59) with disability outcome at 12 months (Table 4.11).

In the surgical group, moderate to strong significant correlations (r>0.50) were observed between final follow-up NPAD scores and pre-op arm pain (r = 0.75), radiological segmental curvature at the symptomatic level PTM C2-7 (r = -0.54) and extension (r = -0.58) (Table 4.12).

Table 4.11 Conservative group: Spearman rank correlation coefficient analysis (r) between baseline measures (grouped as clinical, radiological, functional and demographics/lifestyle data/others) and outcome of neck pain, arm pain and disability at 12 months in the conservative group.

Baseline	**Final outcome**					
	Neck pain		**Arm pain**		**Disability**	
	r	**p**	**r**	**p**	**r**	**p**
Clinical measures						
Neck pain	0.21	0.024*	0.25	0.007*	0.15	0.105
Arm pain	0.67	0.001**	0.59	0.001**	0.37	0.001**
Disability	0.14	0.122	0.38	0.001**	0.33	0.001**
NPAD factor1	0.10	0.292	0.13	0.163	0.11	0.247
NPAD factor2	0.07	0.416	0.11	0.224	0.26	0.006*
NPAD factor3	0.09	0.338	0.40	0.001**	0.28	0.002*
NPAD factor4	0.08	0.385	0.23	0.013*	0.17	0.063
Radiological measures						
PTM C2-3	-0.24	0.011*	-0.25	0.008*	-0.44	0.001**
PTM C3-4	-0.02	0.814	-0.05	0.543	-0.34	0.001**
PTM C4-5	-0.01	0.902	-0.117	0.225	-0.33	0.001**
PTM C5-6	-0.29	0.002*	-0.33	0.001**	-0.47	0.001**
PTM C6-7	-0.28	0.002*	-0.23	0.016*	-0.37	0.001**
PTM C2-7	-0.18	0.052	-0.25	0.007*	-0.59	0.001**
PTM symptomatic level	-0.10	0.255	-0.19	0.039*	-0.42	0.001**
Penning C2-3	-0.36	0.001**	0.02	0.792	0.01	0.843
Penning C3-4	-0.38	0.001**	0.00	0.983	-0.03	0.730
Penning C4-5	-0.56	0.001**	-0.15	0.109	-0.22	0.019*
Penning C5-6	-0.63	0.001**	-0.34	0.001**	-0.26	0.006*
Penning C6-7	-0.51	0.001**	-0.16	0.082	-0.30	0.001**
Penning C2-7	-0.74	0.001**	-0.23	0.014*	-0.25	0.007*
Penning symptomatic level	-0.57	0.001**	-0.28	0.002*	-0.21	0.025*
Functional measures						
Head neck angle	0.16	0.088	0.09	0.322	0.15	0.111
Flexion	-0.24	0.011*	0.03	0.695	0.03	0.690
Extension	-0.39	0.001**	-0.08	0.399	-0.18	0.049*
Flexion + Extension	-0.38	0.001**	0.01	0.903	-0.063	0.510
Rotation right	-0.33	0.001**	-0.22	0.020*	-0.27	0.004*
Rotation left	-0.29	0.002*	-0.08	0.369	-0.32	0.001**
Rotation right + left	-0.38	0.001**	-0.21	0.023*	-0.41	0.001**
Demographics/Lifestyle/ others						
Age	0.43	0.001**	0.14	0.132	0.30	0.001**
Gender	0.04	0.663	0.05	0.544	0.15	0.107
BMI	0.12	0.202	0.14	0.121	0.15	0.105
Lifestyle changes	-0.14	0.135	-0.01	0.845	-0.29	0.002*
Smoking	-0.09	0.322	-0.02	0.776	0.15	0.097
Work style	0.60	0.001**	0.47	0.001**	0.34	0.001**
Duration of symptoms	-0.11	0.245	-0.30	0.001**	-0.24	0.012*
No. previous episode	-0.09	0.330	0.14	0.132	0.181	0.059
Co-morbidity	0.18	0.053	0.21	0.029*	0.34	0.001**

** $p \leq 0.001$, * $p \leq 0.05$

Table 4.12 Surgery group: Spearman rank correlation coefficient analysis (r) between baseline data (grouped as clinical measures, radiological measures, functional measures and demographics/lifestyle data) and outcome of neck pain, arm pain and disability at 12 months.

Baseline	**Final outcome**					
	Neck pain		**Arm pain**		**Disability**	
	r	**p**	**r**	**p**	**r**	**p**
Clinical measures						
Neck pain	-0.25	0.063	-0.09	0.498	-0.139	0.313
Arm pain	-0.06	0.614	0.44	0.001**	0.75	0.001**
Disability	-0.22	0.101	0.16	0.238	0.40	0.003*
NPAD factor1	-0.08	0.544	0.24	0.073	0.34	0.012*
NPAD factor2	-0.17	0.208	0.14	0.305	0.33	0.016*
NPAD factor3	-0.08	0.556	-0.00	0.949	0.055	0.686
NPAD factor4	-0.12	0.370	0.17	0.205	0.38	0.005*
Radiological measures						
PTM C2-3	0.10	0.468	0.10	0.431	0.09	0.490
PTM C3-4	-0.30	0.027*	0.08	0.537	-0.03	0.790
PTM C4-5	-0.27	0.048*	-0.40	0.003*	-0.19	0.147
PTM C5-6	-0.11	0.397	0.04	0.772	-0.11	0.415
PTM C6-7	0.02	0.848	-0.16	0.222	-0.38	0.005*
PTM C2-7	-0.26	0.053*	-0.08	0.555	-0.09	0.487
PTM symptomatic level	0.06	0.659	-0.30	0.029*	-0.54	0.001**
Penning C2-3	0.12	0.350	0.03	0.793	0.23	0.082
Penning C3-4	-0.50	0.001**	-0.13	0.319	-0.06	0.617
Penning C4-5	-0.36	0.008*	-0.04	0.722	0.16	0.234
Penning C5-6	-0.46	0.001**	-0.02	0.857	0.24	0.070
Penning C6-7	-0.58	0.001**	-0.19	0.148	0.02	0.839
Penning C2-7	-0.62	0.001**	-0.07	0.582	0.22	0.106
Penning symptomatic level	-0.58	0.001**	-0.09	0.475	0.148	0.282
Functional measures						
Head neck angle	-0.22	0.100	0.08	0.544	-0.07	0.579
Flexion	-0.18	0.182	0.14	0.307	0.43	0.001**
Extension	0.04	0.719	-0.39	0.004*	-0.58	0.001**
Flexion+ Extension	-0.15	0.251	-0.07	0.596	0.04	0.725
Rotation right	-0.06	0.639	-0.38	0.005*	-0.46	0.001**
Rotation left	-0.19	0.155	-0.45	0.001**	-0.23	0.094
Rotation right + left	-0.16	0.228	-0.43	0.001**	-0.33	0.014*
Demographics/Lifestyle/others						
Age	0.55	0.001**	0.35	0.010*	0.15	0.249
Gender	0.33	0.014*	0.07	0.563	-0.11	0.405
BMI	0.26	0.057	0.12	0.356	0.11	0.410
Lifestyle changes	0.15	0.260	-0.05	0.716	0.00	0.993
Smoking	0.22	0.107	0.11	0.421	0.16	0.241
Work style	0.09	0.478	0.01	0.933	0.05	0.672
Duration of symptoms	-0.12	0.371	-0.23	0.081	-0.27	0.049*
No. previous episode	-0.21	0.112	-0.14	0.277	-0.28	0.037*
Co-morbidity	-0.25	0.065	-0.20	0.145	-0.07	0.594

** $p \leq 0.001$, * $p \leq 0.05$

4.4 Results of published and unpublished preliminary studies

The following are a summary of the results of the manuscripts published from this thesis. Each paper is published in full in the corresponding appendices where full data sets and figures are provided.

4.4.0 Study 1- The reliability and validation of the Spin-T Goniometer – A cervical range of motion device.

Agarwal S, Allison GT, Singer KP 2005 Validation of the Spin-T Goniometer. A cervical range of motion device. J Manip Physiol Ther 28(8): 604-9
See Appendix (3.0).

Results

This study found that the cervical ROM technique utilised throughout this thesis is valid. The coefficient of determination (R^2) for all planes of cervical ROM for both model and human data sets were >0.997. The regression equations for the model data demonstrated no significant intercept for flexion-extension and lateral rotation except for lateral flexion (mean = -0.350 degrees , 95 % CI = -0.642 to -0.057). Following a similar trend, the slope for only lateral flexion was significantly different from the line of unity (gradient = 1.0). Human data showed statistically significant offset for flexion-extension (mean = -0.527 degrees, 95% CI = -0.793 to - 0.261) and lateral flexion range of motion s (mean = 0.812 degrees, 95%CI = 0.466 to 1.58). The regression slope for flexion-extension and lateral rotation was significantly different from 1. The regression equations identify systematic changes in the intercepts that are well within the clinical limits of significance <1.5 degrees.

Agarwal S, Allison GT, Singer KP 2005 Reliability of the Spin-T cervical Goniometer in measuring cervical range of motion in an asymptomatic Indian population. **J Manip Physiol Ther** 28(7): 487-92 (Appendix 3.1)

Results

This study found that the cervical ROM technique utilised throughout this thesis was reliable. All repeated measures demonstrated high ICCs (All > 0.96, p < 0.01). The ANOVA detected no differences between trials for all range of motions except rotation. The typical error values for the rotation trials did not exceed 2.5° and the CV did not exceed 4 %, which is clinically acceptable considering the normally variable cervical range of motion.

4.4.1 Study 2 – Range of motion in cervical radiculopathy and normal controls

Agarwal S, Allison GT, Singer KP 2005 Evaluation of cervical range of motion in a cervical radiculopathy patient group and a matched control group using the Spin-T Goniometer. **Journal of Musculoskeletal Research** 9(2): 93-101 (Appendix 3.2)

Results

The results showed that the mean cervical spine ROM in the cervical radiculopathy group was reduced compared to matched controls for flexion ($t = 2.26$, $p = 0.02$), extension ($t = 2.30$, $p = 0.02$) and full cycle rotation (sum of left and right rotation) ($t = 2.01$, $p = 0.04$). Differences calculated between normal controls and patients for paired rotation range of motion did not reach statistical significance. The findings suggest that flexion and extension range of motion are more likely to demonstrated systematic differences between cohorts of cervical radiculopathy and match controls.

4.4.2 Study 3 - Reliability and validity of the Hindi version of the Neck Pain and Disability Scale

Agarwal S, Allison GT, Agarwal A, et al. 2006 Reliability and validity of the Hindi version of the Neck Pain and Disability Scale in cervical radiculopathy patients. Disabil Rehabil 28(22): 1405-12
(See Appendix 3.3A)

Results

This study was used to validate the use of this instrument in the clinical trial conducted in the Indian cohort in this thesis. No other clinical assessments tools for neck pain and disability are available that would be recognised and comparable by experts in the western English literature. Therefore, this study needed to be undertaken and therefore justifies in part the use of this instrument as the primary outcome measure in this thesis.

It was found that in a similar cohort of patients that were the focus of this theses, the ICC values for test-retest NPAD total and factor scores were >0.92 and R^2 values

>0.912. Pearson product moment correlation of item versus factor scores varied from 0.17 to 0.91 and for factor versus total scores 0.72 to 0.91. Differences in NPAD scores between the patient and the asymptomatic group were significant ($t = 30.90$, $p<0.05$). Convergent validity was explained when Factor 2 (minus item 20) was correlated ($r = 0.67$) with NPRS maximum value scores. Divergent validity was illustrated by low correlation with VAS Activity ($r = 0.15$) and negative correlation with VAS Depression ($r = - 0.80$) scores. These results are consistent with other research in the translation and validation of the NPAD scores into other languages (i.e. Turkish) (Bicer et al. 2004).

4.4.3 Study 4 -The effects of age and gender on active cervical ROM in an asymptomatic Indian population in a longitudinal study.

Agarwal S, et al. The effects of age and gender on active cervical ROM in an asymptomatic Indian population in a longitudinal study.
This study is currently under review and remains unpublished (Appendix 3.4).

Results

The results of this study demonstrated that active cervical ROM had a significant relationship with age but not with gender. For both genders, a systematic change in cervical ROM was noted with the rate of range of motion loss varying between 3° to 5° per decade with advancing age. Baseline measurements of active cervical ROM were predictive of cervical ROM accounting for a minimum 72% variance (lateral flexion right) to maximum 85% variance (extension) for measurements at 6 months. Reliability of repeat measurements at 3 months intervals (total 6 months from baseline) of cervical ROM yielded typical error values not exceeding 5°. Few studies have undertaken repeated testing over a large cohort over such a period. The findings of this part of the thesis provide evidence of the expected changes in ROM over time for age, direction and gender.

4.3.4 Studies 5-7- Reliability studies of principle measures utilised in the thesis.

These three studies remain unpublished and will be a focus once the thesis is submitted. These three studies were reliability studies of three principal measures used in the main study. The findings support the research utility in the context of the study thereby improving the internal validity of the thesis findings.

Study 5 Reliability study of radiographic curvature assessments of the cervical spine

Results

The maximum typical error values between two measurements of radiographic segmental curvature for levels C2-7 was 1.84° (not exceeding 2.47°) (Table 4.13). The repeated measures demonstrated high ICC, ranging between 0.82 to 0.99.

Table 4.13 Repeat measurement reliability analysis of segmental radiographic curvature measurements, levels C2 to C7.

Level	Measurement 1 Mean (SD)	Measurement 2 Mean (SD)	Typical error (95%CL)	ICC (95%CL)
C2-C3	3.47 (2.54)	3.70 (2.69)	0.78 (0.62 – 1.05)	0.91 (0.82 – 0.95)
C3-C4	2.07 (4.11)	1.97 (4.17)	0.78 (0.62 – 1.05)	0.91 (0.82 – 0.95)
C4-C5	1.53 (3.53)	1.77 (3.70)	0.48 (0.38 – 0.65)	0.98 (0.96 – 0.99)
C5- C6	2.90 (3.32)	3.13 (3.36)	0.78 (0.62 – 1.05)	0.94 (0.88 – 0.97)
C6-C7	2.42 (3.06)	2.30 (3.01)	0.76 (0.61 – 1.02)	0.93 (0.87 – 0.97)
C2-C7	12.46 (9.35)	12.09 (8.55)	1.84 (1.47 – 2.47)	0.95 (0.91 – 0.98)

n = 30, ICC = Intra class correlation coefficient, CL: Confidence Limits

Study 6 Reliability study of radiographic segmental mobility assessments of the cervical spine

Results

The maximum typical error values between two measurements of radiographic segmental mobility for levels C2-7 was 1.83° (95% Confidence Limit = 1.45 to 2.60) (Table 4.14). The repeated measures demonstrated high ICC, ranging between 0.85 to 0.98.

Table 4.14 Repeat measurement reliability analysis of segmental radiographic mobility measurements, levels C2 to C7.

Level	Measurement 1 Mean (SD)	Measurement 2 Mean (SD)	Typical error (95% CL)	ICC (95%CL)
C2-C3	6.91 (2.74)	6.73 (2.86)	0.74 (0.59 – 0.99)	0.93 (0.85 – 0.93)
C3-C4	10.23 (4.10)	10.83 (4.08)	0.76 (0.60 -1.02)	0.96 (0.92 – 0.98)
C4-C5	12.57 (3.36)	13.37 (4.06)	1.04 (0.83 -1.40)	0.93 (0.90-0.96)
C5- C6	12.87 (5.43)	13.40 (5.61)	0.78 (0.62 -1.05)	0.98 (0.95 – 0.99)
C6-C7	10.60 (4.20)	11.35 (4.71)	0.75 (0.59 -1.00)	0.97 (0.94 – 0.98)
C2-C7	53.20 (11.68)	55.70 (12.44)	1.83 (1.45 – 2.60)	0.97 (0.95 – 0.98)

n = 30, ICC: Intra class correlation coefficient, CL: Confidence Limits

Study 7 A reliability study (same day and at 3 weeks) of the assessment of Cervical – Head Neck Posture

The typical error values for same day measurements of the Head-neck angle were maximum 4° and at 3 weeks interval were maximum 8° (Table 4.15). The ICC values were low for measurements after 3 weeks versus baseline measurements

Table 4.15 Repeat measurement reliability analysis of head neck angle measurements, same day and after 3 weeks

	Change in Means	Typical error (95%CL)	ICC (95%CL)
Measurement 1 vs. 2 (same day)	0.85 (-1.04 to 2.75)	3.58 (2.85 to 4.49)	0.61 (0.33- to-0.80)
Measurement 3 vs. 1 (after 3 weeks)	0.89 (-2.32 to 4.10)	6.08 (4.84 to 8.17)	-0.13 (-0.47 to -0.24)

n = 30, ICC = Intra class correlation coefficient, CL: Confidence Limits

4.5. Predictors of outcome at one year in a CR cohort, treated conservatively or surgically

The key results of this thesis in terms of clinical outcomes and predicting responders relates to the data derived from the clinical prediction rule (CPR). The 3 and 12 month predictive variables are presented in Table 4.16. The four sets of predictor variables at 3 months and 12 months, are presented for the responder and non responder status at 3 and 12 months for both conservative and surgically treated individuals with CR.

Table 4.16 Key results: clinical, radiological and functional measures, socio-demographic and lifestyle factors predicting neck pain and disability outcomes in a CR study group

Predictors for responding to conservative intervention (n=109)	
3 months	**12 months**
Age < 40years	Education ≥ postgraduate level
BMI <24.4	PTM C2-7 ≥ 11°
No recent lifestyle changes	PTM symptomatic level ≥ 2.5°
Duration of symptoms ≥ 33 weeks	Neck Rotation (right) > 55°
NPAD factor 1 > 18	
Neck flexion < 40°	
Number of previous episodes < 2	
Predictors for responding to the surgery intervention (n=54)	
3 months	**12 months**
Age < 40 years	Duration of symptoms ≥ 33 weeks
Head neck angle > 40°	NPAD scores < 55
NPAD scores < 55.	Neck Flexion < 40°
	Neck Rotation (right) > 55°

4.5.0 Mapping of clinical outcome

The outcome of intervention in both groups was mapped by grouping the NPAD scores according to clinical significant changes as defined by (Wheeler et al. 1999) (Table 4.17).

Baseline scores show a maximum frequency distribution between scores 41- 74. Initially, by 3 months, more patients in the conservative group (76%) compared to the surgery group (65%) had achieved scores < 40 (none to mild pain). In contrast, at 12 months, the conservative group achieved score < 40 in 85% patients whereas the surgery group had 93% patients who had scores <40. It was noted that patients who persisted with moderate pain (scores 41-57) in the conservative group as well as in the surgery group mainly comprised of drop-out at 3 months (6 drop-outs in the conservative group and 2 in the surgery group) and 12 months (5 drop-outs in the conservative group and 2 in the surgery group). At 12 months, when the two groups were compared, only the conservative group had 5 patients with moderate to severe pain (score 58-74). Again, these patients comprised of those who dropped out at 3 months and may reflect the principles of intention to treat analysis.

Table 4.17 Distribution of the number (percentage) of patients split by clinical significance of NPAD scores at 3 and 12 months in both conservative (n=109) and surgery (n=54) groups

	None – minimal	**Mild**	**Moderate**	**Moderate to severe**	**Severe**	**Extreme pain, suffering and disability**
	0-22	23-40	41-57	58-74	75-92	93-100
Baseline						
Conservative	1 (0.9)	15 (13.8)	64 (58.7)	22 (20.2)	5 (4.6)	2 (1.8)
Surgical	3 (5.6)	7 (12.9)	19 (35.2)	14 (25.9)	9 (16.7)	2 (3.7)
3 months						
Conservative	38 (35)	44 (40)	20 (18)	6 (6)	1	0
Surgical	17 (31)	18 (34)	12 (23)	6 (11)	1 (1)	0
12 months						
Conservative	64 (59)	28 (26)	12 (10)	5 (5)	0	0
Surgical	27 (50)	23 (43)	4 (7)	0	0	0

Clinical significance of NAPD score derived from (Wheeler et al. 1999)

4.5.1 Baseline socio-demographic and lifestyle characteristics of responders and non-responders

In the conservative group at 3 months (n = 109), 38 patients were categorised as having successful outcomes based on their NPAD scores at 3 months (scores <22). These were categorised as responders. 71 did not meet the threshold and were categorised as non-responders (Tables 4.17 and 4.18A). In the conservative group at 12 months, based on the final NPAD scores, there were 64 responders and 27 non-responders. In the surgical group at 3 months (n = 54), 17 patients were responders whereas 37 were non-responders, whilst at 12 months there were 27 responders and 27 non-responders (Tables 4.17 and 4.19A). Clearly, both cohorts demonstrated improved responses in the 9 months between 3 months and 12 months follow-up.

Subject socio- demographics, lifestyle details and initial baseline variables from the subject history and self-report measures for all patients in both groups (conservative and surgery), and responders and non-responders within each group are shown in Tables 4.18A and B, 4.19A and B.

In the conservative group, significant differences between responders and non-responders were obtained for age, gender, education levels, work characteristics, lifestyle changes, smoking, duration of symptoms, co-morbidity, arm pain levels, NPAD total scores and NPAD factors 2 and 3 scores (Table 4.18 A and B). It was noted, that NPAD factor 1 and 4 scores were not significantly different between responders and non-responders. Factor 1 scores were related to neck problems (looking up and down, looking left and right) and Factor 4 scores (pain interfering with socialising, recreation, work, personal relationships) related to pain interfering with life activities. One plausible reason could be that pain scores were not high enough for patients in the conservative group to have limitations in necessary life activities. The responders had a lower mean age compared to non-responders. The responders included a higher percentage of people who had postgraduate education when compared to non-responders. The non-responders included a greater percentage of people who had recent life changes. Responders had a longer median duration of symptoms, whilst the number of co-morbidities was higher in the non-responder group. For all self-reported pain scores which were significantly different between the two groups, the non-responders, as by definition, had a higher mean score.

In the surgery group, responders and non-responders were significantly different in education levels, annual income, duration of symptoms, side of pain, arm pain levels, NPAD total score and NPAD factors 1, 2 and 4 (Tables 4.19 A and B). There were a larger percentage of graduates in the non-responder group compared to the responders, and yet a larger percentage of non-responders belonged to a lower annual income groups (≤ 1 Lac). The median duration of symptoms was longer in the responder group. For all self-reported pain scores which were significantly different between the two groups, the non-responders had a higher mean score.

In both treatment groups, there was no significant difference in baseline NPRS (neck) scores between responders and non-responders.

Table 4.18 A Comparison of patients' baseline socio – demographics and lifestyle details between responders and non-responders at 12 months follow-up in the conservative group

Variables	All subjects (n= 109)	Responder (n=64)	Non responde r (n=45)	p
Age (years)				
Mean ± SD	45 ± 10.96	40 ± 10.11	49 ± 9.35	0.010*
Gender				
Male (N, %)	62 (57)	40 (66)	22 (45)	0.071*
Female (N, %)	47 (43)	19 (34)	28 (55)	
BMI				
Mean ± SD	25 ± 3.75	24 ± 3.45	25 ± 3.92	0.239
Dominant hand				
Right N (%)	108 (99)	64 (100)	44(98)	0.231
Left N (%)	1(1)	0	1 (2)	
Education levels (N, %)				
1 Up to High School	12 (11)	4 (6)	8 (18)	
2 Graduates	81 (74)	46 (72)	35 (78)	0.030*
3 Post graduates	14 (13)	12(19)	2 (4)	
4 Doctorate	2 (2)	2 (3)	0	
Work Characteristics (N, %)				
Active	47 (43)	35 (55)	12 (27)	0.004*
Sedentary	62 (57)	29 (45)	33 (73)	
Physical activity (N, %)				
Yes	53 (49)	30 (47)	23 (51)	0.612
No	56 (51)	34 (53)	22 (49)	
Annual Income (in Rupees) (N, %)				
< 50,000	11 (10)	4 (6)	7 (16)	
50,000 – 1 lac	12 (11)	6 (9)	6 (13)	
1-2 lacs	17 (16)	11 (17)	6 (13)	0.109
2-5 lacs	24 (22)	19 (30)	5(11)	
>5 lacs	45 (41)	24 (38)	21 (47)	
Marital status (N, %)				
Single Widowed/Divorced/	9 (8)	7 (11)	2 (4)	0.225
Married	100 (92)	57 (89)	43 (96)	
Life style changes (N, %)				
Yes	70 (64)	36 (56)	34 (76)	0.038*
No	39 (36)	28 (44)	11 (24)	
Smoking (N, %)				
Yes	34 (31)	25 (39)	9 (20)	0.034*
No	75 (69)	39 (61)	36 (80)	

Significance level* at p< 0.10

Table 4.18 B Comparison of patients' baseline self reported variables between responders and non-responders at 12 months in the conservative group. Significance level* at p <0.10

Variables	**All subjects (n= 109)**	**Responder (n=64)**	**Non responder (n=45)**	**p**
Duration of symptoms (weeks) Median (IQR)	8 (4-32)	12 (4 – 46)	8 (4 – 16)	0.010*
No. of previous episodes, (N, %)				
0	54 (54)	34 (53)	20(44)	
1	40 (37)	23(36)	17 (38)	
2	5 (5)	2 (3)	3(7)	0.755
3	7 (6.42)	3 (5)	4 (9)	
4	2 (2)	1 (2)	1 (2)	
5	1 (0.91)	1 (2)	0	
Co-morbidity (N %)				
0	28 (26)	23 (36)	5(11)	
1	35 (32)	23 (36)	12 (27)	
2	34 (31)	11 (17)	23 (51)	0.003*
3	9 (2)	5 (8)	4 (9)	
4	2 (5)	1 (2)	1 (2)	
5	1 (1)	1 (2)	0	
Pain sites (N, %)				
Neck	45 (41)	25 (39)	15 (13)	0.541
Both sides	15 (14)	6(13)	11 (17)	0.842
Right	44 (40)	19 (42)	27 (42)	
Left	45 (41)	20 (45)	26 (41)	
101 NPRS Neck Mean ± SD	46 ±21.23	43 ± 20.75	49 ±21.84	0.168
101 NPRS Arm Mean ± SD	56 ±26.79	45 ±20.91	66 ± 24.08	0.001*
NPAD (total score) Mean ± SD	54 ±14.21	49±8.13	57 ± 16.23	0.006*
NPAD (factor 1) Mean ± SD	11 ± 4.10	11 ± 3.56	11 ± 4.58	1.00
NPAD (factor 2) Mean ± SD	16 ± 4.66	15 ± 2.68	17 ± 5.47	0.010*
NPAD (factor 3) Mean ± SD	6 ± 4.37	5 ± 3.86	8 ± 4.42	0.001*
NPAD (factor 4) Mean ± SD	20 ± 6.18	19 ± 4.51	22 ± 6.87	0.600

Table 4.19 A Comparison of patients' socio – demographics and lifestyle details between responders and non-responders at 12 months follow-up in the surgery group

Variables	All subjects (n= 54)	Responder (n = 27)	Non responder (n=27)	p
Age (years)				
Mean ± SD	45 ±9.64	44 ± 8.37	46 ± 10.56	0.390
Gender				
Male (N, %)	31(57)	14 (52)	17(63)	0.409
Female (N, %)	23 (43)	13 (48)	10(37)	
BMI				
Mean ± SD	25 ± 4.16	25 ± 3.86	25 ± 4.51	0.921
Dominant hand				
Right (N, %)	48 (89)	24(89)	24 (89)	1.00
Left (N, %)	6 (11)	3 (11)	3 (11)	
Education levels (N, %)				
1 Up to High School	26 (48)	18 (67)	8 (30)	
2 Graduates	25 (46)	7 (26)	18 (67)	0.010*
3 Post graduates	3 (6)	2 (7)	1 (4)	
4 Doctorate	0			
Work Characteristics				
(N, %)	32 (59)	18 (67)	14 (60)	0.268
Active	22 (41)	9 (33)	13 (48)	
Sedentary				
Physical activity (N, %)				
Yes	16 (30)	6 (22)	10 (37)	0.233
No	38 (70)	21 (78)	17 (63)	
Annual Income (N, %)				
Less than Rs.50,000	16 (30)	7 (26)	9(33)	
50,000 – 1 lac	8 (15)	2 (7)	6 (22)	
1-2 lacs	5 (9)	1 (4)	4 (15)	0.051*
2-5 lacs	15 (27)	12 (44)	3 (11)	
More than 5 lacs	10 (19)	5 (18)	5 (18)	
Marital status (N, %)				
Single/ Widowed/		5 (18)	3 (11)	
Divorced	8 (15)	22 (82)	24 (89)	0.44
Married	46 (85)			
Life style changes (N,				
%)	28 (52)	14 (52)	14 (52)	1.00
Yes	26 (48)	13 (48)	13 (48)	
No				
Smoking (N, %)				
Yes	8 (15)	5 (19)	3 (11)	0.44
No	46 (85)	22(81)	24 (89)	

Significance level* at p< 0.10

Table 4.19 B Comparison of patients' self reported variables between responders and non-responders at 12 months follow-up in the surgery group.

Variables	All subjects (n= 54)	Responder (n = 27)	Non responder (n=27)	p
Duration of symptoms (weeks) Median (IQR)	9.5 (4 – 32)	22 (6 – 36)	8 (4 – 24)	0.052*
No. of previous episodes (N, %)				
0	14 (26)	5 (19)	9 (33)	
1	19 (35)	8 (30)	11 (41)	
2	8 (15)	5 (19)	3 (11)	0.191
3	12 (22)	9 (33)	3 (11)	
4	1 (2)	0	1 (4)	
Co-morbidity (N, %)				
0	14 (26)	7 (26)	7 (26)	
1	19 (35)	10(37)	9 (33)	
2	13 (24)	6 (22)	7 (26)	0.866
3	7 (13)	3 (11)	4 (15)	
4	1 (2)	1 (4)	0	
Pain site (N, %)				
Neck	49(90)	24(89)	25(93)	0.639
Both sides	2(4)	1(4)	1(4)	
Right	20(37)	15(56)	5(19)	
Left	32(60)	11(41)	21(79)	0.017*
101 NPRS Neck Mean ± SD	60 ± 26	59 ± 28.76	61± 23.99	0.823
101 NPRS Arm Mean ± SD	74 ± 20	62 ±19.42	85 ±11.48	<.0001*
NPAD (total score) Mean ± SD	58 ± 19.25	49 ±19.99	66 ±14.61	0.002*
NPAD (factor 1) Mean ± SD	13 ± 63	11 ± 6.06	15 ± 4.42	0.009*
NPAD (factor 2) Mean ± SD	20 ± 8	16 ± 9.40	23 ± 5.83	0.006*
NPAD (factor 3) Mean ± SD	11 ± 4	11 ± 2.94	11 ± 4.60	0.653
NPAD (factor 4) Mean ± SD Range	14 ± 8	10 ± 7.75	17 ± 7.49	0.003*

Significance level* at p< 0.10

4.5.2 Baseline neurological scores of responders and non-responders

The baseline measurements for neurological examination of the symptomatic side (myotomes, dermatomes and reflexes) for all patients in both treatment groups, as well as responders and non-responders within each treatment group are shown in Tables 4.20 and 4.21. Within both treatment groups, the responders and non-responders were different for motor scores, whereas the deep tendon reflex (DTR) scores significantly differed within the surgery group only. In both treatment groups, for motor and DTR scores, a larger percentage of non-responders had lower scores, implying greater neurological deficits at baseline.

Table 4.20 Findings from neurological examination (ASIA scores) for the conservative group at baseline: responder vs. non-responders at 12 months.

Variable	Responders (n=64)	Non-responders (n = 45)	Chi square	p
Sensory score – symptomatic side				
10	0(0)	1(2)		
11	1(2)	1(2)		
12	1(2)	0(0)	6.993	0.321
13	1(2)	5(11)		
14	15(23)	9(20)		
15	16(25)	11(24)		
16	40(47)	18(40)		
Motor score - symptomatic side				
20	0(0)	1(2)		
21	2(3)	6(13)		
22	1(2)	4(9)	16.051	0.007*
23	19(30)	16(36)		
24	17(27)	2(4)		
25	25(39)	16(37)		
DTR score – symptomatic side				
2				
3	2(3)	2(4)		
4	3(5)	5(11)	5.570	0.135
5	18(28)	5(11)		
6	41(64)	33(73)		

NOTE: The scores above are derived from American Spinal Injury Association neurological form. Sensory scores (0 = no response, 1 = impaired, 2 = normal, NT = not testable) are calculated from levels C2 to T1 (total score = 16). Motor scores (1-5) from C5 to T1 (total score 25). DTR (0= absent, 1= impaired, 2 = equal to sound side), for biceps, triceps and supinator (total score = 6). Significance level* at $p < 0.10$

Table 4.21 Findings from neurological examination (ASIA scores) for the surgery group at baseline: responder vs. non-responders at 12 months.

Variable	Responders (n=27)	Non-responders (n = 27)	Chi-square	p
Sensory score – symptomatic side				
12	1(4)	0(0)		
13	1(4)	2(7)		
14	15(56)	15(56)	3.556	0.469
15	8(30)	10(37)		
16	2(7)	0(0)		
Motor score - symptomatic side				
20	1(4)	2(7)		
21	2(7)	1(4)		
22	1(4)	2(7)	10.026	0.075*
23	10(37)	10(37)		
24	2(7)	9(33)		
25	11(41)	3(11)		
DTR score – symptomatic side				
2	2(7)	1(4)		
3	2(7)	1(4)		
4	4(15)	13(48)	8.56	0.073*
5	19(70)	11(48)		
6	0(0)	1(4)		

NOTE: The scores above are derived from American Spinal Injury Association neurological form. Sensory scores (0 = no response, 1 = impaired, 2 = normal, NT = not testable) are calculated from levels C2 to T1 (total score = 16). Motor scores (1-5) from C5 to T1 (total score 25). DTR (0= absent, 1= impaired, 2 = equal to sound side), for biceps, triceps and supinator (total score = 6). Significance level* at p< 0.10

4.5.3 Differences in baseline continuous variables between responders and non-responders within conservative and surgery groups

Continuous variables from baseline clinical examination, including angular measurements of sagittal segmental vertebral movement and curvature, posture and composite active cervical ROM, were analysed for all patients and for differences between responders and non-responders within each treatment group (Tables 4.22 and 4.23). The responders and non-responders within the conservative group differed for segmental radiological flexion-extension motion (Penning's method of evaluation) at C2-7 (composite range) and levels C4-5, C5-6 and C6-7 whereas in the surgery group, the responders and non-responders were different at C2-7 composite range and C2-3 level. In the conservative group, the non-responders had lower mean segmental flexion-extension motion for total (C2-7) and lower cervical segments (C4-7). In contrast, in the surgery group the non-responders had higher mean segmental flexion-extension motion values for total C2-7 and differed significantly at only C2-3 level. For segmental radiological curvature evaluations (PTM), in the conservative group, the responders and non-responders were significantly different at all levels whereas the surgery group differed at C6-7 and symptomatic levels only. In both treatment groups, for all levels which were significantly different, the non-responder group had lower mean segmental curvature values. Extension and rotation range of motions were significantly lower in the non-responders in the conservative group, and similarly in the surgery group. Contrarily, the responders had lower mean flexion range of motion values in both groups, albeit significant only in the surgery group.

Table 4.22 Continuous variables from baseline clinical examination: responders vs. non-responders at 12 months in the conservative group.

Variable	All patients (n= 109)	Responder (n= 64)	Non-responder (n = 45)	p
PENNING	(degrees)	(degrees)	(degrees)	
C2-7	41±12.22	44± 11.91	37 ± 13.21	0.016*
C2-3	7 ±2.34	7 ± 2.47	7 ± 2.19	0.748
C3-4	8 ±3.16	8 ± 3.40	8 ± 2.89	0.768
C4-5	9 ±3.53	10 ± 3.08	8 ±3.97	0.030*
C5-6	9 ± 5.30	10 ± 6.10	7 ± 4.88	0.041*
C6-7	9 ± 3.51	10± 3.26	7 ± 3.55	0.002*
Penning sym level	10 ±6.12	10 ± 6.10	9 ± 6.65	0.227
PTM				
C2-7	10 ±9.57	18 ± 4.20	5 ± 9.01	0.001*
C2-3	3 ±2.84	4 ± 2.14	1 ± 2.82	0.001*
C3-4	2 ±3.63	4 ± 3.09	0.8 ± 3.82	0.001*
C4-5	2 ±3.33	4 ± 2.63	1 ± 3.39	0.001*
C5-6	2 ±4.02	4 ± 3.90	0.3 ± 3.60	0.001*
C6-7	2 ±3.02	2.62 ± 2.44	1 ± 3.38	0.004*
PTM sym level	2 ±3.79	4 ± 4.41	1 ± 2.56	0.001*
Cervical ROM				
Flexion	44 ±10.29	43 ± 8.82	44 ±11.29	0.84
Extension	47 ±13.09	50±15.05	44 ±10.71	0.02*
Flexion +Extension	92 ±18.73	93 ±19.72	89±18.43	0.228
Rotation (Right)	54 ±12.62	58 ±13.86	50 ±10.32	0.001*
Rotation (Left)	59 ±13.30	64 ±12	54 ±12.91	0.01*
Rotation (Right +Left)	113 ±21.24	122±21.72	103±17.85	0.01*
Head Neck angle	42±8.24	42±8.02	44±9.44	0.264

Table 4.23 Continuous variables from baseline clinical examination: responders vs. non-responders at 12 months in the surgery group.

Variable	All patients (n= 54)	Responders (n= 27)	Non-responders (n = 27)	p
PENNING	(degrees)	(degrees)	(degrees)	
C2-7	47±16	43±16.27	51±15.85	0.061*
C2-3	7±2	6±2.42	7±1.97	0.076*
C3-4	11±3	11±2.27	11±3.56	0.769
C4-5	11±6	10±5.56	11±5.64	0.193
C5-6	10±5	9±4.96	11±4.81	0.177
C6-7	10±5	9±5.24	11±4.58	0.213
Penning sym level	12±7	11±5.69	13±7.14	0.160
PTM				
C2-7	12±12	14±12.92	10±11.38	0.139
C2-3	6±4	6±3.37	7±4.19	0.540
C3-4	4±8	5±8.24	3±8.20	0.491
C4-5	3±5	3±4.86	2±5.10	0.184
C5-6	-1±5	0±5.73	-1±5.13	0.308
C67	1±5	2±4.69	-1±3.98	0.004*
PTM sym level	-1±4	1±4.26	-3±3.55	0.001*
Cervical ROM				
Flexion	48±12	43±11.21	52±10.29	0.002*
Extension	39±10	45±8.36	33±7.62	0.001*
Flexion +Extension	86±12	88±12.63	85±10.58	0.249
Rotation (Right)	44±11	48±11.64	40±9.56	0.016*
Rotation (Left)	45±12	47±13.70	43±10.55	0.271
Rotation (Right +Left)	89±22	95±24.66	84±18.02	0.066*
Head Neck angle	40±4.99	40±5.39	39±4.61	0.688

Significance level* at p< 0.10

4.5.4 Differences in change score between responders and non-responders, for pain and disability measures, calculated between baseline and final measurements in conservative and surgical groups

Baseline, assessments and change scores for the NPAD, NPRS A and NPRS N are shown in tables 4.24 and 4.25. In both treatment groups, the initial pain and disability scores were higher in the non-responders compared to the responders for all pain and disability scores. In the conservative group, change scores were significantly higher in the responder group for NPAD total scores, factors 1, 2 and 4 and neck pain scores when compared to the non-responder group. In the surgery group, change scores were significantly different between the responders and non-responders for NPAD factor 3 scores and arm pain scores. For arm pain scores, the non-responder group had a higher change score compared to the responder group.

Table 4.24 Mean (SD) Change Scores for the Neck Pain and Disability Scale, NPRS N (neck) and NPRS A (arm) in the conservative group for responders and non-responders at 12 months.

Scale	Responder (n= 64)	Non-Responder (n = 45)	z	p
NPAD (total)				
Initial	51(12.23)	57(16.24)	-5.70	0.001*
Final	14(6.12)	37(14.28)		
Change score	38(11.16)	20(17.25)		
NPAD (factor 1)	11(3.75)	11(4.59)		
Initial	2(2.09)	6(4)	-4.46	0.001*
Final	9(4.47)	4(5)		
Change score				
NPAD (factor 2)	13 (3.88)	17 (5.48)		
Initial	3 (2.22)	9 (5.05)	-4.122	0.001*
Final	12 (3.74)	8 (6.98)		
Change score				
NPAD (factor 3)	5 (4.11)	8 (4.43)		
Initial	3 (3.04)	6 (5.36)	-0.146	0.884
Final	2 (4.37)	1 (5.10)		
Change score				
NPAD (factor 4)	20 (5.62)	21 (6.87)		
Initial	5 (3.13)	14 (4.48)	-5.24	0.001*
Final	14 (5.82)	7 (7.45)		
Change score				
NPRS Neck	44 (10.93)	49 (21.84)		
Initial	11 (9.46)	28 (23.22)	-3.44	0.001*
Final	33 (16.57)	21 (16.86)		
Change score				
NPRS Arm	49 (26.51)	66 (24.09)		
Initial	16 (9.92)	31 (24.91)	-0.84	0.420
Final	32 (21.83)	35 (25.01)		
Change score				

Table 4.25 Mean (SD) of Change Scores for the Neck Pain and Disability Scale, NPRS N (neck) and NPRS A (arm) in surgery group for responders and non-responders at 12 months.

Scale	Responder (n = 27)	Non-Responder (n= 27)	z	p
NPAD (total)			-1.030	0.303
Initial	49±19.99	66±14.61		
Final	10±7	31±9.59		
Change score	40±18.85	34±17.83		
			-0.373	0.709
NPAD (factor 1)	11±6.06	15±4.42		
Initial	1±1.95	6±4.90		
Final	10±6.27	9±7.00		
Change score				
			-0.182	0.856
NPAD (factor 2)	16±9.40	23±5.83		
Initial	2±2.48	8±6.06		
Final	15±9.22	15±8.52		
Change score				
			-1.877	0.060*
NPAD (factor 3)	11±2.94	11±4.60		
Initial	1±1.56	3±4.41		
Final	10±3.44	7±5.62		
Change score				
			-0.321	0.749
NPAD (factor 4)	10±7.75	17±7.49		
Initial	7±6.41	13±5.81		
Final	3±9.10	4±8.32		
Change score				
			-0.442	0.658
NPRS Neck	59±28.76	61±23.99		
Initial	10±11.51	14±20		
Final	50±31.81	47±31.60		
Change score				
			-2.64	0.008*
NPRS Arm	62±19.42	85±11.48		
Initial	3±5.47	17±22.70		
Final	59±18.76	69±26.94		
Change score				

4.5.5 Baseline predictor variables in the conservative group

Individual variables from self –reported measures, socio-demographics and lifestyle details, functional and radiological measures were tested for univariate relationship with the NPAD outcome criterion at 3 months and at 12 months, using independent t test for continuous variables and chi-square tests for categorical variables. Variables with a significant relationship with the NPAD outcome criterion ($p \leq 0.10$) were retained as potential prediction variables. The accuracy for group allocation (and 95% CI) of all predictor variables at 3 and 12 months in the conservative group are shown in tables 4.26 and 4.29 respectively. The significant baseline variables were entered into a logistic step-wise regression analysis to determine the best set of variables to predict a successful outcome in the conservative group at 3 months (Table 4.28) and 12 months (Table 4.31).

4.5.5A Predictor variables for outcome at 3 months in the conservative group

19 baseline individual variables exhibited a significance level ($p < 0.10$) for analyses for a successful outcome at 3 months. Out of 19, 6 variables were obtained from socio-demographic and lifestyle background, 5 from self reported clinical measures, 3 from radiological measures, and 5 from functional measures. The accuracies with 95% CI of all 19 variables are shown in Table 4.26. The cut-off values determined from the receiver operating characteristic curves for continuous variables are shown in Table 4.26. The positive likelihood ratios ranged from 0.16 to 2.80, which explain a small probability range for a subject to experience a positive outcome. However, the further logistic regression analysis of these variables generated a set of variables that maximises the potential to identify subjects who are likely to have a positive outcome (Table 4.28).

Table 4.26 Sensitivity, specificity and likelihood ratios for variables with a significant* univariate relationship (p <0.10) for identifying successful outcomes in a conservatively managed cervical radiculopathy cohort at 3 months

Variable	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	p*
Age < 40years	0.55 (0.39,0.69)	0.80 (0.69,0.87)	2.80 (1.61,4.85)	0.55 (0.38,0.80)	0.002
BMI <24.4	0.57 (0.42,0.72)	0.66 (0.54,0.76)	1.71 (1.12,2.61)	0.63 (0.42,0.95)	0.015
No recent Lifestyle change	0.23 (0.12,0.39)	0.14 (0.07,024)	0.27 (0.15,0.49)	5.41 (2.97,9.88)	0.001
Number previous episodes < 2	0.36 (0.23,0.52)	0.43 (0.32, 0.55)	0.65 (0.41,1.04)	1.44 (1.01,2.07)	0.052
No Co-morbidity	0.44 (0.30,0.60)	0.84 (0.74,0.91)	2.88 (1.51,5.52)	0.65 (0.48,0.88)	0.001
Symptoms < 33 weeks	0.60 (0.44,0.74)	0.05 (0.02,0.13)	0.64 (0.49,0.83)	7.00 (2.50,19.62)	0.001
NPRS (neck) < 56	0.84 (0.69,0.92)	0.35 (0.25,0.46)	1.29 (1.04,1.61)	0.44 (0.20,0.99)	0.032
NPAD < 55	0.71 (0.55,0.83)	0.49 (0.38,0.60)	1.40 (1.03,1.90)	0.58 (0.33,1.01)	0.040
NPAD factor 1 < 18	0.89 (0.75,0.95)	0.01 (0.01,0.07)	0.90 (0.81,1.01)	7.47 (0.86,64.52)	0.030
NPAD factor 2 <17	0.76 (0.60,0.87)	0.43 (0.32,0.55)	1.35 (1.03,1.77)	0.54 (0.28,1.01)	0.039
NPAD factor 3 <13	1.00 (0.90,1)	0.14 (0.07,0.24)	1.16 (1.05,1.27)	0.09 #	0.015
PTM C2-7 < 11°	0.21 (0.11,0.36)	0.45 (0.34,0.56)	0.38 (0.2,0.73)	1.75 (1.29,2.37)	0.001
PTM (sym. level) < 2.5°	0.31 (0.19,0.47)	0.39 (0.28,0.51)	0.52 (0.31,0.86)	1.73 (1.21,2.48)	0.003
Penning C2-7 <25°	0.02 (0.004, 0.13)	0.85 (0.75,0.92)	0.18 (0.02,1.40)	1.13 (1.01,1.26)	0.058
Flexion < 40°	0.36 (0.23,0.52)	0.80 (0.69,0.87)	1.86 (0.99,3.49)	0.78 (0.60,1.02)	0.050
Flex+ ext <70°	0.21 (0.11,0.36)	0.91 (0.82,0.96)	2.49 (0.93,6.65)	0.86 (0.72,1.03)	0.060
Rotation (left) <55°	0.10 (0.04,0.24)	0.59 (0.47,0.69)	0.25 (0.09,0.67)	1.51 (1.21,1.88)	0.001
Rotation (sum) < 110°	0.21 (0.11,0.36)	0.50 (0.39,0.61)	0.42 (0.22,0.82)	1.55 (1.17,2.06)	0.004
Head neck angle <40°	0.60 (0.44,0.74)	0.60 (0.48,0.71)	1.53 (1.04,2.25)	0.65 (0.42,1.00)	0.030

This is an estimate of the LR where the zero value in the 2 x 2 contingency table was replaced by 0.5. (Raney et al. 2009)

Seven variables were retained in the 3 month regression model for predicting a successful outcome following conservative treatment. With 3 predictors, 53% patients were in the responder group, whilst only 7% were present in the non-responder group. When 4 or more predictors at baseline were present, there were no patients in the non-responder group. Although the total number of predictors were 7, there were no patients meeting more than 5/7 criteria who experienced a successful or un-successful outcome (Table 4.27). The LR+ was calculated as near 1 because the equation resulted in a zero in the denominator. 0.5 was added to this cell in the table to enable a LR+ calculation (Table 4.28).

Table 4.27 The 7 variables forming the clinical prediction rule and the number of subjects in each group at each level, at 3 months in a cervical radiculopathy cohort treated conservatively

Number of predictors present	Responders (% of patients)	Non-responders (% of patients)	Total patients (% of patients)
1	38%	60%	98%
2	38%	31%	69%
3	32%	7%	37%
4	15%	0%	15%
5	6%	0%	6%
6	0%	0%	0%
7	0	0	0

The combination of 7 variables retained in the final regression model to predict responders at 3 months in the conservative treatment group include:

- Age < 40years
- BMI <24.4
- No recent lifestyle changes
- Duration of symptoms ≥ 33 weeks
- NPAD factor 1 >18
- Neck flexion < 40°
- Number of previous episodes < 2

The results of the accuracy analysis, which includes sensitivity, specificity, positive (LR+) and negative (LR-) likelihood ratio and the post-prediction probability of success for each level of the model are shown in Table 4.28. The LR+ was calculated by the formula sensitivity/ 1- specificity. The value of the LR+ indicated how much a given prediction model could raise the probability of obtaining the outcome. The pre-test probability of having a successful outcome was 35% as calculated by the percentage of responders at 3 months (38 out of 109.patients) (Go 1998; Cleland et al. 2007a;

Raney et al. 2009) With 3 out of 7 predictors, the LR+ value was 8.54 (95% CI =4.17 to 17.48) increasing the likelihood of success with conservative management from 35% to 82%. With 4 predictors from the seven, the LR+ of a responder in this cohort was 56.44 (95% CI = 3.46 to 919.03). In this cohort, this had 100% post-test probability of success at 3 months. With 5 predictors, the post test probability of success dropped to 90% because of a lower LR+ 22.57 (95% CI = 1.29 to 393.48)(Fagan 1975). The reason why the LR+ dropped was because the sensitivity or the true positivity of the analysis reduced to 0.15. With ≥ 6 variables, the LR+ was equal to 1.85, indicating minimal change (10%) from pre-test probability of success (Laupacis et al. 1997).

Table 4.28 Combination of predictor variables identified in the logistic regression analysis and associated accuracy statistics with 95% confidence intervals (CI) for each level of the prediction model, for identifying successful outcome in the conservative group at 3 months

Number of predictors present	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Probability of success with conservative management
1	0.98 (0.88,0.99)	0.15 (0.08,0.25)	1.16 (1.05,1.29)	0.08 (0.00,1.38)	39%
2	0.98 (0.88,0.99)	0.56 (0.44,0.67)	2.26 (1.73,2.95)	0.02 (0.01,0.36)	55%
3	0.84 (0.69,0.92)	0.90 (0.81,0.95)	8.54 (4.17,17.48)	0.17 (0.08,0.36)	82%
4	0.39 (0.25,0.55)	0.99 (0.93,0.99)	56.44 (3.46,919.03)	0.60 (0.47,0.78)	100%
5	0.15 (0.07,0.30)	0.99 (0.93,0.99)	22.57 (1.29,393.48)	0.84 (0.73,0.97)	90%
6	0.01 (0.00,0.11)	0.99 (0.13,0.99)	1.85 (0.03,91.77)	0.99 (0.95,1.03)	45%
7	0.01 (0.00,0.11)	0.99 (0.13,0.99)	1.85 (0.03,91.77)	0.99 (0.95,1.03)	45%

4.5.5B Predictor variables for outcome at 12 months in the conservative group

18 baseline variables were analysed for a successful outcome at 12 months in the conservative group ($p < 0.10$) (Table 4.29). Accuracy statistics for all 18 variables with their 95% CI and the cut-off values determined from the receiver operating characteristic curves for continuous variables are shown in Table 4.29. The individual

LR+ varied from 0.15 to 3.39. Of these 18 variables, 11 variables were common to the 3 months predictors. These included age, lifestyle changes, duration of symptoms, co-morbidities, NPAD scores, NPAD factor 3 score, PTM C2-7, PTM at the symptomatic level, Penning C2-7, rotation range of motion to the left and rotation (both sides). Age had the maximum LR+ value of 3.39.

Table 4.29 Sensitivity, specificity and likelihood ratios for variables with a significant* univariate relationship (p<0.10) for identifying successful outcomes in a conservatively managed cervical radiculopathy cohort (12 months)

Variable	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	p*
Age < 40 years	0.45 (0.33,0.57)	0.86 (0.73,0.93)	3.39 (1.53,7.5)	0.63 (0.49,0.81)	0.001
Male gender	0.64 (0.51,0.74)	0.53 (0.39,0.67)	1.37 (0.95, 1.97)	0.67 (0.44,1.03)	0.070
No lifestyle changes	0.56 (0.44, 0.67)	0.24 (0.14, 0.38)	0.74 (0.56, 0.97)	1.78 (0.99, 3.20)	0.038
No Smoking	0.39 (0.28, 0.51)	0.80 (0.66, 0.89)	1.95 (1.01, 3.77)	0.76 (0.59, 0.97)	0.034
Education ≤post graduate	0.78 (0.66,0.86)	0.04 (0.01, 0.14)	0.81 (0.70, 0.94)	4.92 (1.17, 20.60)	0.011
Active work characteristic	0.54 (0.42, 0.66)	0.73 (0.58, 0.84)	2.05 (1.20, 3.49)	0.61 (0.44, 0.85)	0.003
Duration ≤ 33 weeks	0.73 (0.61, 0.82)	0.04 (0.01, 0.14)	0.76 (0.65, 0.90)	5.97 (1.45, 24.59)	0.002
Co-morbidity <1	0.35 (0.25,0.48)	0.88 (0.76,0.95)	3.24 (1.33,7.86)	0.72 (0.58,0.89)	0.003
NPRS (arm) <56	0.67 (0.55, 0.77)	0.60 (0.45, 0.72)	1.67 (1.13, 2.49)	0.54 (0.35, 0.83)	0.004
NPAD < 55	0.67 (0.55, 0.77)	0.55 (0.41,0.69)	1.51 (1.04,2.18)	0.59 (0.38,0.91)	0.017
NPAD factor 3 <13	0.95 (0.87, 0.98)	0.15 (0.07, 0.28)	1.12 (0.98, 1.29)	0.30 (0.08,1.10)	0.052
PTM C2-7 ≤ 11°	0.20 (0.12, 0.31)	0.24 (0.14, 0.38)	0.26 (0.16, 0.44)	3.25 (1.92, 5.52)	<.0001
PTM (sym level) ≤ 2.5°	0.34 (0.23, 0.46)	0.26 (0.14, 0.39)	0.46 (0.31, 0.67)	2.46 (1.52, 4.51)	<.0001
Penning C2-7 < 25°	0.03 (0.01, 0.10)	0.80 (0.66, 0.89)	0.15 (0.03, 0.68)	1.21 (1.04, 1.41)	0.003
Extension < 50°	0.37 (0.26, 0.49)	0.40 (0.27, 0.54)	0.62 (0.42, 0.92)	1.56 (1.04, 2.34)	0.020
Rotation (right) < 55°	0.32 (0.22, 0.45)	0.26 (0.15, 0.41)	0.44 (0.30, 0.66)	2.51 (1.50, 4.21)	<0.0001
Rotation (left) < 55°	0.17 (0.09, 0.28)	0.51 (0.32, 0.65)	0.35 (0.19, 0.65)	1.62 (1.19, 2.20)	0.001
Rotation (sum) <110°	0.25 (0.16, 0.36)	0.40 (0.27, 0.54)	0.41 (0.25, 0.67)	1.87 (1.27, 2.75)	0.001

At 12 months, the predictors for the conservative group included a combination of 4 variables for a successful outcome. There were no patients in the non-responder group when all 4 criteria were met (Table 4.30).

Table 4.30 The 4 variables forming the clinical prediction rule and the number of subjects in each group at each level, at 12 months in a cervical radiculopathy cohort treated conservatively

Number of predictors present	Responders of conservative management (% of patients)	Non-responders of conservative management (% of patients)	Total patients (% of patients)
1	58.7%	35.8%	94.5%
2	54.1%	17.4%	71.6%
3	38.5%	2.8%	41.3%
4	4.6%	0%	4.6%

The 4 predictor variables generated by the logistic regression analysis to predict responders at 12 months in the conservative treatment group included 1 variable from socio-demographic background (education ≥ postgraduate level), 2 radiological assessment variables (PTM C2-7 ≥ 11°, PTM symptomatic level ≥ 2.5°) and 1 functional assessment variable (rotation right > 55°) (Table 4.31).

Accuracy statistics were calculated based on the number of predictors present (Table 4.31). The pre-test probability of a successful outcome was 59%. When 3 out of 4 variables were present, the LR+ value was 9.84 (95% CI = 3.25, 29.79), and the post-test probability of success increased to 93%. When all 4 variables in the final model were present, the LR+ value reduced to 7.10 (0.39, 126.92) due to lack of non-responders who met the criteria. This led to a reduction in the post-test probability of success to 90% (Fagan 1975). Presence of 3 out of 4 variables comprised the most parsimonious combination of predictors for identifying subjects likely to have a successful outcome at 12 months following conservative management of cervical radiculopathy.

Table 4.31 Combination of predictor variables identified in the logistic regression analysis and associated accuracy statistics with 95% confidence intervals (CI) of individual predictor variables for identifying successful outcome in the conservative group at 12 months

Number of predictors present	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Probability of success with conservative management
1	0.99 (0.93,0.99)	0.13 (0.06,0.26)	1.14 (1.01,1.28)	0.05 (0.00,1.01)	62%
2	0.92 (0.82,0.96)	0.57 0.43,0.71)	2.18 (1.54,3.09)	0.13 (0.05,0.32)	76%
3	0.65 (0.53,0.76)	0.93 (0.82,0.97)	9.84 (3.25,29.79)	0.36 (0.26,0.52)	93%
4	0.07 (0.03,0.17)	0.98 (0.90,0.99)	7.10 (0.39,126.92)	0.93 (0.86,1.00)	90%

4.5.6 Baseline predictor variables in the surgical group

Individual variables from self –reported measures, socio-demographics and lifestyle details, functional and radiological measures were tested for univariate relationship with the NPAD outcome criterion at 3 months, 6 months and at 12 months, using independent t test for continuous variables and chi-square tests for categorical variables. Variables with a significant relationship with the NPAD outcome score ($p \leq 0.10$) were retained as potential prediction variables. The accuracies (and 95% CI) of all predictor variables at 3 and 12 months in the surgery group are shown in tables 4.32 and 4.35 respectively, whereas the accuracy analysis of the 6 months variables were put in an appendix 4.0. The significant baseline variables were entered into a logistic step-wise regression analysis to determine the most accurate set of variables to predict a successful outcome in the surgery group at 3 months (Table 4.34) and 12 months (Table 4.37).

4.5.6A Predictor variables for outcome at 3 months in the surgery group

9 variables from baseline were identified through the univariate analysis ($p < 0.10$) for a successful outcome at 3 months (Table 4.32). Accuracy statistics with 95% CI, for all variables are shown in table 4.32. The cut-off values determined from the receiver operating characteristic curves for continuous variables are shown in Table 4.32. The

LR+ values ranged from a minimum 0.38 (95% CI 0.13, 1.13) for NPRS (neck) scores, to a maximum 3.99 (95% CI 1.77, 8.98) for age. The 9 potential predictor variables were entered into a logistic regression analysis which maximised the ability to identify people who were likely to achieve success at 3 months from surgery (Table 4.34).

Table 4.32 Sensitivity, specificity and likelihood ratios for variables with a significant* univariate relationship (p<0.10) for identifying successful outcomes in a surgically managed cervical radiculopathy cohort at 3 months

Variable	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	p*
Age < 40years	0.64 (0.41-0.82)	0.83 (0.68-0.92)	3.99 (1.77-8.98)	0.42 (0.21-0.81)	0.001
Smokers	0.29 (0.13-0.53)	0.91 (0.78-0.97)	3.62 (0.97,13.45)	0.76 (0.55, 1.05)	0.040
Active work characteristics	0.76 (0.52, 0.90)	0.66 (0.47,0.81)	2.29 (1.29, 4.16)	0.48 (0.14, 0.86)	0.081
NPRS (neck) <56	0.17 (0.06, 0.41)	0.54 (0.38,0.68)	0.38 (0.13,1.13)	1.52 (1.05,2.20)	0.045
NPRS (arm) <56	0.35 (0.17,0.58)	0.89 (0.75,0.95)	3.26 (1.05,10.07)	0.72 (0.50,1.04)	0.031
NPAD <55	0.58 (0.36, 0.78)	0.67 (0.51,0.80)	1.81 (0.98,3.34)	0.60 (0.33,1.12)	0.066
PTM C2-7 ≤ 11°	0.23 (0.09,0.47)	0.40 (0.26,0.56)	0.39 (0.16,0.97)	1.88 (1.17,3.02)	0.014
Rotation (right) < 55°	0.58 (0.36,0.78)	0.13 (0.05,0.27)	0.68 (0.44,1.03)	3.04 (1.12,8.23)	0.023
Head neck angle <40°	0.17 (0.06,0.41)	0.29 (0.17,0.45)	0.25 (0.08,0.71)	2.77 (1.61,4.76)	0.003

At 3 months (Table 4.34), a combination of 3 baseline variables were retained in the final regression model (1) age less than 40 years (2) head neck angle greater than 40° (3) NPAD scores less than 55. Table 4.33 shows that 26% patients were present in the responder group when 2 out 3 predictors were present, whilst only 5.6% were present in the non-responder group. When all 3 predictors were present, the 9.3% patients were in the responder group, whereas there were none in the non-responder group (Table 4.33).

Table 4.33 The 3 variables forming the clinical prediction rule and the number of subjects in each group at each level, at 3 months in a cervical radiculopathy cohort treated surgically.

Number of predictors present	Responders (% of patients)	Non-responders (% of patients)	Total patients (% of patients)
1	29.6	48.1%	77.8%
2	25.9%	5.6%	31.5%
3	9.3%	0%	9.3%

Accuracy statistics were based on the number of predictors present (Table 4.34). The pre-test probability for the likelihood of having a successful outcome was 31%. Having 3 out of 3 predictors present resulted in a LR+ equal to 21.76 (95% CI 1.25, 376.19), thereby increasing the likelihood of success with surgical management to 95%.

Table 4.34 Combination of predictor variables identified in the logistic regression analysis and associated accuracy statistics of individual predictor variables for identifying successful outcome in the surgery group at 3 months

Number of predictors present	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Probability of success with surgical management
1	0.94 (0.73,0.98)	0.29 (0.17,0.45)	1.33 (1.05,1.70)	0.19 (0.02,1.41)	38%
2	0.82 (0.58,0.93)	0.91 (0.78,0.97)	10.15 (3.35,30.72)	0.19 (0.06,0.53)	82%
3	0.29 (0.13,0.53)	0.98 (0.88,0.99)	21.76 (1.25,376.19)	0.71 (0.52,0.97)	95 %

4.5.6B Predictor variables for outcome at 12 months in the surgery group

For a successful outcome at 12 months, 10 baseline variables exhibited a significance level $p > 0.10$ in a univariate analysis and were identified as predictor variables (Table 4.35). Of these 10, 2 variables were common to individual predictor variables at 3 months (NPRS arm score < 56; rotation range of motion to the right >55°). The accuracies and the 95% CI are shown in Table 4.35. The cut-off values determined from the receiver operating characteristic curves for continuous variables are shown in Table 4.35. The positive likelihood ratios ranged from 0.59 to 4.

Table 4.35 Sensitivity, specificity and likelihood ratios for variables with a significant* univariate relationship (p<0.10) for identifying successful outcomes in a surgically managed cervical radiculopathy cohort at 12 months

Variable	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	P
Duration < 33 weeks	0.62 (0.44,0.78)	0.11 (0.03,0.28)	0.70 (0.51,0.97)	3.33 (1.03,10.79)	0.025
NPRS (arm) <56	0.37 (0.21,0.55)	1 (0.87,1)	20.37 #	0.62 (0.47,0.84)	0.001
NPAD < 55	0.59 (0.40,0.75)	0.77 (0.59,0.89)	2.66 (1.23,5.77)	0.52 (0.31,0.86)	0.005
NPAD Factor2 < 17	0.55 (0.37,0.72)	0.77 (0.59,0.89)	2.5 (1.14,5.46)	0.57 (0.35,0.91)	0.784
NPAD Factor 4 < 13	0.59 (0.40,0.75)	0.70 (0.51,0.84)	2.0 (1.03,3.87)	0.57 (0.34,0.97)	0.020
PTM Symptom level ≤ 2.5°	0.59 (0.40,0.75)	0 (0,0.12)	0.59 (0.43,0.81)	22.4 #	0.001
Flexion <40°	0.29 (0.15,0.48)	0.92 (0.76,0.97)	4.0 (0.93,17.13)	0.76 (0.58,0.99)	0.035
Extension < 50°	0.62 (0.44,0.78)	0 (0,0.12)	0.62 (0.47,0.84)	20.37 #	0.001
Rotation (right) < 55°	0.62 (0.44,0.78)	0.07 (0.02,0.23)	0.68 (0.5,0.92)	5.0 (1.20,20.71)	0.008
Rotation (left + right) <110°	0.70 (0.51,0.84)	0.07 (0.02,0.23)	0.76 (0.58,0.99)	4.0 (0.93,17.13)	0.035

this is an estimate of the LR where the zero value in the 2 x 2 contingency table was replaced by 0.5 (Raney et al. 2009)

No patient was positive for all 4 predictors. 9.3% patients were present in the responder group when 3 predictors were present (Table 4.36).

Table 4.36 The four variables forming the clinical prediction rule and the number of subjects in each group at each level, at 12 months in a cervical radiculopathy cohort treated surgically

Number of predictors present	Responders (% of patients)	Non-responders (% of patients)	Total patients (% of patients)
1	42.6%	22.2%	64.8%
2	29.6%	1.9%	31.5%
3	9.3%	0%	9.3%
4	0%	0%	0%

For a successful outcome at 12 months after surgery (Table 4.37), the baseline predictor variables included a combination of 4 variables.

- Duration of symptoms ≥ 33 weeks
- NPAD score < 55
- Flexion < 40°
- Rotation (right) > 55°

If 1 out of 4 variables were present, the post- test probability of success was 66% from a pre-surgical likelihood of success of 50%. The maximum LR+ was achieved with 2 variables (LR+ = 16, 95% CI = 2.28 to112.3), increasing the post-surgical probability of success to 94%. When 3 out of 4 variables were present, the LR+ value reduced to 10.18 (95% CI 0.58 to 177.52), correspondingly reducing the post –surgical likelihood of success to 85% (Table 4.37). When all 4 predictors were present the model became unstable since no patients in this cohort had all 4 variables (Laupacis et al. 1997).

Table 4.37 Combination of predictor variables identified in the logistic regression analysis and associated accuracy statistics of individual predictor variables for identifying successful outcome in the surgery group at 12 months

Number of predictors present	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Probability of success with surgical management
1	0.85 (0.67,0.94)	0.55 (0.37,0.72)	1.91 (1.22,3.00)	0.26 (0.10,0.70)	66%
2	0.59 (0.40,0.75)	0.96 (0.81,0.99)	16 (2.28,112.3)	0.42 (0.26,0.67)	94%
3	0.18 (0.08,0.36)	0.98 (0.84,0.99)	10.18 (0.58,177.52)	0.82 (0.68,1)	85%
4	0.01 (0.00,0.15)	0.98 (0.84,0.99)	1.0 (0.02,48.62)	1.0 (0.93,1.07)	NA

4.6 Summary of results

At baseline, the two treatment groups were comparable for age, gender, BMI, marital status, duration of symptoms (in weeks) and co-morbidities, but different for other socio-demographic and life-style variables. The surgery group patients showed more severity in terms of statistically significant higher mean values for pain (neck and arm), disability scores as well as neurological deficits. Simultaneously, the surgery group also demonstrated more radiological segmental flexion-extension motion and composite active cervical ROM when compared to the conservative group. For radiographic segmental curvature (C2-7) as well as head-neck angle measurements, no statistical differences were detected between the treatment groups at baseline.

Outcome at 12 months showed a statistically significant improvement in both groups for neck pain, arm pain and disability measures. The surgery group demonstrated a larger reduction in pain scores than the conservative group. One factor, which could have influenced this, is higher baseline scores in the surgery group. At 3 months compared to baseline, in the conservative group, the mean radiographic sagittal segmental curvature and flexion-extension motion values suggested a trend for increase in values at nearly all levels. Following a similar pattern, statistically significant increase in composite range of motion in all directions was seen in the conservative group. However, this consistency was not so in the surgical group, which demonstrated changes varying from ‘reduction’ to ‘no change’ in radiographic sagittal segmental curvature and flexion-extension motion at different cervical levels over a 12 month, repeat assessment period. This was probably due to the effects of surgical intervention at 1-2 levels of the cervical spine after baseline measurements. An initial reduction in composite active cervical ROM was seen at 3 months in the surgery group, whereas at 12 months, flexion and extension significantly increased. Rotation range of motion to both sides remained persistently low for all repeat measurements. The mean values of head neck angle in both groups remained relatively constant from baseline to final follow-up in both groups. Both treatment groups showed improvement from baseline to final measurements for all neurological scores. 100% improvement at final follow-up was not achieved for any neurological sign in either group.

Several studies were conducted prior to the main research to ascertain the reliability and validity of variables to be eventually used as outcome measures. The principle outcome measure, the NPAD was translated into Hindi, the national language of India, and successfully tested for its reliability and validity. This was deemed important for the results of this study to be recognised and compared with studies using similar outcome measures in populations of other countries. The Spin-T goniometer, used for measuring composite cervical ROM was tested as valid. All outcome measures were tested for repeat measurement reliability. The maximum typical error values between two measurements of radiographic segmental curvature for levels C2-7, radiographic segmental flexion-extension motion for levels C2-7 and composite active cervical ROM did not exceed 3°. However, when composite cervical ROM was tested for reliability of repeat measurements at 3 months intervals (total 6 months from baseline), typical error values were slightly higher (not exceeding 5°). Similarly, typical error values for Head-neck angle were 4° for same day measurements, but higher, reaching up to maximum 8°, for repeat measurements at 3 weeks.

Further, the effects of age, gender and clinical condition on composite active cervical ROM was ascertained. Within a normal population, for both genders, a systematic change in cervical ROM was noted with the rate of range of motion loss varying between 3° to 5° per decade from age 20 to 80 years. This emphasised matching of age between cohorts, and further, composite active cervical ROM measurements were tested for differences between a cervical radiculopathy group and matched controls. The results suggested that flexion and extension range of motion were more likely to demonstrate systematic differences between cohorts.

Correlations between measures of pain and disability (at baseline, at final follow-up) with socio-demographic measures, lifestyle factors, radiographic measures, measures of impairments (at baseline, at final follow-up) were analysed. Although varied relationships were ascertained between sets of variables, it was demonstrated that the significant correlations between pairs of variables tested were consistent in establishing a negative relationship between radiographical sagittal segmental curvature values at symptomatic levels and arm pain scores. Similarly, at baseline, negative significant correlations between composite active cervical ROM and pain and disability measures and between radiological segmental flexion-extension motion (Penning method) at the diagnosed symptomatic level/s and final neck pain scores in both groups were determined. This implies that reduced radiographic curvature and flexion-extension motion as well as composite range of motion are correlated with increased pain and disability or vice-versa. Conversely, a positive correlation between head neck angle measures and neck pain scores at baseline in the surgery group implied that as head neck angle values increased/reduced there was a corresponding increase/decrease in neck pain.

Similar to the findings of composite active cervical ROM between an asymptomatic population with a CR cohort, patients with CR had systematically decreased radiographic sagittal segmental and total flexion-extension motion of the cervical spine (C2- 7).

Further, to test the principal hypothesis, factors that would predict clinical outcome at one year in CR patients, treated conservatively and surgically, were analysed using the CPR method in both groups at 3 months and 12 months. In the conservative group (n = 109), 64 patients were categorised as having successful outcomes whilst 45 were categorised as non-responders. In the surgical group (n = 54), 27 patients were responders whereas 27 were non-responders. The outcome criterion was the NPAD score, where score <22 were responders. In both treatment groups, the initial pain and disability scores were higher in the non-responders compared to the responders for all pain and disability scores. When scores at 12 months were compared to baseline scores, in the conservative group, change scores were significantly higher in the responder group for NPAD total scores and neck pain scores despite the non-responders having a higher baseline score. The surgery group demonstrated a higher change scores for arm pain in non-responders. In both treatment groups, the univariate analysis revealed significant characteristics of responders and non-responders. The two treatment groups differed on variables between responders and non-responders but were similar for some. In both treatment groups, there was no significant difference in NPRS (neck) scores between responders and non-responders and in both treatment groups. For motor and DTR scores, a larger percentage of non-responders had lower scores, implying greater neurological deficits at baseline.

Significant (univariate analysis) baseline variables were entered into a logistic step-wise regression analysis to determine the best set of variables to predict a successful outcome in the conservative group at 3 months and 12 months and surgery group at 3 and 12 months.

The combination of variables retained in the final regression model to predict responders of conservative and surgical treatment in a CR cohort include:
Conservative (3 months): Age < 40 years, BMI <24.4, No recent lifestyle changes, Duration of symptoms ≥ 33 weeks, NPAD factor 1 < 18, Neck flexion < 40°, Number of previous episodes <2.

Conservative (12 months): Education level ≥ post graduate, PTM C2-7 ≥ 11°, PTM (symptomatic level) ≥ 2.5°, Rotation (right) > 55°.
Surgery (3 months): Age < 40 years, Head neck angle < 40°, NPAD scores < 55.
Surgery (12 months): Duration of symptoms ≥ 33 weeks, NPAD scores < 55, Neck flexion < 40°, Rotation (right) > 55°

Results of this study have been discussed in the following chapter.

CHAPTER 5

DISCUSSION OF CLINICAL TRIAL OUTCOMES IN CERVICAL RADICULOPATHY

5.0 Introduction

Insight and understanding of factors which can indicate or predict a good outcome in a clinical condition like CR is imperative for both clinicians and researchers. Although surgery is recommended to those patients in whom symptoms persist, worsen or conservative interventions have failed, it is difficult to ascertain from previous studies what factors contribute to a level of response that does not necessitate continued conservative treatment or progression to a surgical intervention. Of the studies that are reported in the literature, there are no studies within the context of the Indian population. In this aspect, the findings of the thesis are unique. However, in many aspects, this study also contributes to the general question of prognosis in both conservative and surgical interventions due to the lack of information in the Western literature. The principal issue in this study was whether pre-intervention factors could predict outcome based on a large number of baseline assessments including previously reported risk and prognostic factors. Knowledge of predictive factors can assist clinicians in the clinical reasoning process and also assist in future research by controlling for confounding factors which may increase the statistical power of subsequent efficacy studies by improving study group homogeneity. Both these aspects may allow more high quality evidence to be reported with greater confidence in optimising the management of cervical radiculopathy.

Factors used to predict outcomes should be derived from valid and reliable assessment tools, and need to provide clear evidence on the balance of risk and benefit, from intervention for cervical spondylosis (Fouyas et al. 2002). Most individual items of the clinical examination in this study were found to have at least a fair level of reliability and accuracy. The pain intensity measure, the 101 NPRS, was reported previously as being reliable, valid, responsive to change, ease of administer and sensitivity to statistical analysis (Jensen et al. 1986). Similarly, the NPAD, was selected as the primary outcome because it had, face, criterion and construct validity, and test-retest reliability previously established by Wheeler et al. (1999) and later by Goolkasian et al. (2002). Furthermore, the scale had been successfully translated from English into other languages (Wlodyka-Demaille et al. 2002; Bicer et al. 2004).

This study chose the NPAD to measure disability in a CR cohort of the Indian population and as part of this thesis the NPAD was translated into the national language of India, Hindi. An important finding of this thesis was that the translation process was successful with demonstration of acceptable test-retest reliability, face, convergent and divergent validity (Agarwal et al 2006). No other neck pain-related disability scale covering similar clinical domains relevant to cervical radiculopathy is available in Hindi. Previous studies examining the management of neck pain in the Indian population have used English language outcome measures without cultural validation.

The NPAD scores (from the English as well as the Hindi versions as necessary) were subsequently used as the outcome criterion in the Clinical Prediction Rule statistical analysis of this study. This helped determine predictor variables for successful outcome the surgically and conservatively managed treatment groups.

Many researchers report the reliability of outcome measures as established in previous studies. Where possible, the reliability and validity of key outcome measures was evaluated in preliminary studies to improve the quality of the results of the main study. The radiographic curvature measurement technique selected for this study was the Posterior Tangent method. Its high intra- tester reliability values and low typical error values (Jackson et al. 1993) made it an ideal choice for segmental radiographic curvature analysis. For the purpose of this thesis, the intra-tester reliability was calculated in 30 subjects in preliminary studies (5-7). Low typical error values (1.84°) (study 5) were comparable to the results of Jackson et al. (1993) which established this measurement technique as suitable for repeat measurements in the clinical setting. Similarly, a careful literature review identified Penning's method as a reliable method of radiological measurement of segmental sagittal motion (Dvorak et al. 1991; Puglisi et al. 2004). In the present study, the intra-tester reliability, calculated as the mean typical error for repeat measurements, was 1.83° (study 6), which was comparable to that reported by Puglisi et al. (2004). Although hand drawn measurements were used in this thesis for both radiographic measurements, deliberate standardisation during measurements yielded clinically useful low typical error, which supports the use of these measures in a longitudinal study. The intra-tester reliability of posture measurement for within and between day analysis was examined as well (study 7).

To measure cervical ROM, with the purpose of using a function based outcome measure, a new measuring instrument, the Spin-T goniometer was used. Although the reliability was evaluated by Haynes and Edmondston (2002), the validity of the Spin-T was established in the present study (Agarwal et al. 2005c), as was the reliability in an Indian population (Agarwal et al. 2005b). Differences in cervical ROM between an asymptomatic Indian population and patients with CR were also reported (Agarwal et al. 2005a). The influence of age and gender on cervical ROM was examined in a longitudinal study (unpublished, study 4). The typical error values for testing between 0 and 6 months had a 95% CL of between 2.12° and 4.51°, which was acceptable with respect to typical error values of about 2.5° for testing on the same day (Agarwal et al. 2005b). Evaluating the magnitude of the between test errors for each movement over time assisted the interpretation of changes observed in the clinical study over the 12 months follow up. No other studies have undertaken such a rigorous approach to establishing the changes in range of motion over time. One reason for this is that most clinical efficacy studies utilise a Randomised Controlled Trial (RCT) design. Using the RCT design, the effects of natural history are controlled by the randomisation process. Within the clinical setting in which this study was conducted, it was not possible to undertake a randomised controlled trial for the management of patients with cervical radiculopathy. The efforts to document the changes over time, however do contribute to the strength of the thesis finding and the clinical literature in general.

The focus of this study was to predict outcomes of intervention in a cohort of Indian patients with CR. Based on recommended methodological standards (Laupacis et al. 1997; Beneciuk et al. 2009) this study established the reliability of all outcome measures to assess outcome. Previous CR predictive studies (Peolsson et al. 2003; Peolsson et al. 2004; Cleland et al. 2007a) have used outcome measures, some for which they established the reliability and for others they did not. In this study, the importance of establishing reliability was further emphasised by not using the results of neurological assessments and provocative clinical tests, because their intra-tester reliability was not well ascertained.

To date, no previous studies have examined surgical and conservative interventions for patients with CR using the same set of reliable outcome measures and conducted longitudinal evaluation of each group for 12 months. The design of this study intended to improve decision making for the management of patients with cervical radiculopathy, by identifying predictive factors related to treatment outcome for surgical or conservative treatment.

5.1 Baseline data: socio-demographic, lifestyle and continuous variables in a CR cohort

The following sections identify the baseline information that was collected in this study and discussed in comparison with the reported literature. For some variables, there have only been one or two previous studies that have addressed these issues and therefore discussion is rather limited. In summary, the populations of this study tended to have common traits with the previous literature.

5.1.0 Age and Gender

Age and gender are the most common patient descriptors for any clinical study. Few studies (Peolsson et al. 2003; Peolsson et al. 2006b; Cleland et al. 2007a) have examined whether these are significant prognostic factors for any of the primary outcomes. The present study included a longitudinal evaluation of active cervical ROM, which demonstrated that there was a small decline in active ROM with age (assessed as a few degrees per year). Furthermore, the upper limit of the measurement error was in the order of 5 degrees over a 6 month period. With this understanding in the Indian population, it was evident that age (or more correctly the duration between the testing sessions) was likely to have a significant systematic influence on the active range of motion outcome in either patient group.

The age of the respective cohorts in this study was consistent with previous studies of patients with the same diagnosis (Persson et al. 1997a; Abd-Alrahman et al. 1999; Palit et al. 1999; Garvey et al. 2002; Peolsson et al. 2003; Shah and Rajshekhar 2004; Murphy et al. 2006). This suggests that any difference in outcomes between the studies is unlikely to be due to differences in the age of the subjects. The mean age of the patient groups in the present study (mid 5th decade) suggests that CR is a pathology of middle age, and associated with the onset of degenerative changes in the cervical spine (Tondury 1958; Bland 1994).

Gender ratios in CR groups have been varied in previous studies with some studies having a greater number of males than females (Heckmann et al. 1999; Shah and Rajshekhar 2004), while others have more females than males (Dowd and Wirth 1999; Hacker 2000; Cleland et al. 2007a). In the present study, higher percentage of men was evident in both treatment groups (57% conservative, 57% surgical), which is similar to the gender ratio of (52-54% male in both treatment groups) reported by Heckmann et al (1999). Due to the limited numbers of studies examining the management of CR, it is unclear whether the gender ratio of patient groups has an impact on the clinical outcomes.

5.1.1 BMI

The World Health Organisation categorises BMI as (<20 underweight; 20-24 normal; 25-29 overweight; >30 obese). The mean BMI score of patients in this study was 25 in both groups, which is lower than previous reports of BMI in patients with neck pain (mean BMI = 28.13) (Raney et al. 2009) and CR (Heckmann et al. 1999). The only previous CR study (Heckmann et al. 1999) which provides BMI values of its surgical and conservatively managed patients, categorised BMI values > 28 as overweight. In order to compare BMI values of the Indian population, this study calculated the number of patients with BMI values > 28. The percentage of persons with BMI values > 28 in this study, in both treatment groups was much lower (20% surgery and 18% conservative) than the 52% of surgically treated patients and 28% of conservatively treated patients reported by (Heckmann et al. 1999).

5.1.2 Education levels and work characteristics

Since this study was undertaken in the Indian setting, it is interesting to note that the majority of participants had a graduate degree qualification (85% in the conservative group; 94% in the surgery group). This is much greater than the 20% of patients with a graduate degree reported in a previous reported study (Vavruch et al. 2002). This may reflect the fact that the present study was conducted in private hospital settings where it may be expected that individuals from middle to high socio-economic group are over represented. This observation however was not consistent with the assumption that this educated class would undertake less strenuous or physically demanding (blue/brown collar) work. The proportion of participants in this study who reported strenuous or physically demanding work in both treatment groups (43% in the conservative group and 59% in the surgery group) was substantially higher than that reported by Heckmann et al. (1999) (19% in the surgery group and 15% in conservative group) but lower than the percentage of blue collar workers (78%) included in the study of Vavruch et al (2002).

5.1.3 Marital status and Life style changes

The majority of patients in this study were married (>85%). This was much larger than the proportion of married patients (39%) reported in previous similar studies (Vavruch et al. 2002). This is probably a reflection of the social structure of the Indian society. The conservative group had a higher number of patients who reported lifestyle change (64%) than the surgical group (52%). Previous studies (Persson and Lilja 2001) had recorded no such differences between the treatment groups. Future research may consider the significance of these “life changes” on the impact of treatment for CR.

5.1.4 Dominant arm

Previous studies not only determined a relationship between dominant arm and radicular pain but also determined that patients’ whose dominant arm was not affected were more likely to respond to specific interventions (Cleland et al. 2005; Cleland et al. 2007a). With 99% of the conservative patients and 89% of the surgery patients being right handed, this type of analysis in this study cohort was not likely to have sufficient numbers to be sensitive and therefore yield any useful information.

5.1.5 Smoking and co-morbidities

In this study, 31% of the conservative group were smokers and 15% of the surgery group. Heckmann et al (1999) reported a lower percentage in the conservative group (21%) and a higher percentage in the surgery group (43%). Overall, a larger percentage of smokers have been reported in previous surgical studies; 49% (Vavruch et al. 2002), 30% (Dowd and Wirth 1999) and 47% (Hacker 2000). The association of cigarette smoking with disc disease (An et al. 1994) or higher risk of spinal pain (Palmer et al. 2003) may explain the higher percentage of smokers in previous studies. Although a lower percentage of current smokers compared to previous clinical studies are reported here, it is consistent with the prevalence of smokers (with or without spinal conditions) (World Health Organization 2004) in India. In fact, they are slightly higher than reported by Jindal et al (2006) who has reported 15.6% ‘ever smokers’ (current and past smokers) whereas this study classified ‘smokers’ as those who currently smoke. This study did not investigate the impact of smoking on co-morbidities. Generally, the presence of co-morbidities (1 to 5) recorded in this study was higher (74%) in both treatment groups compared to Heckmann et al (1999) where 56% of the conservatively treated patients and 52% surgically treated patients had co-morbidities.

5.1.6 Duration of symptoms and number of previous episodes

The health-care and referral system prevalent in India was reflected in the 'duration of symptoms' data. Previous studies have reported symptom durations ranging from 2 months to 10 years (Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001). Surgical intervention at a much shorter duration of symptoms may be prevalent in India. A previous study of patients with CR (Shah and Rajshekhar 2004), reported a mean symptom duration of 7.2 months before surgical treatment, which is similar to the mean of 5 months in this study. Patients participating in this study were part of a private (non-government) healthcare system and had direct access to the surgeon. Surgery was performed based on the clinical and radiological signs presented by each patient.

In many western countries, there are varying levels of public supported healthcare. In most public healthcare systems, there is a waiting list for consultation with a medical specialist and the related treatment services. This may in part explain the extended duration of symptoms prior to treatment being reported in some studies. Furthermore, the literature reflects some degree of publication bias where studies are only published if the investigators are associated with a research Institute or funded clinical setting. In western countries, many of these institutions are publicly funded and public healthcare and the related issues of service delivery and waiting times may influence cohort studies. Conversely, having direct access to the spine-surgeon may have resulted in some surgeries being performed earlier than may have occurred in a different medical system.

Sampath et al (1999) merged data of the surgical and conservative treatment groups and described a mean number of previous episodes of 3.24 (0-8). This study recorded a lower median number of previous episodes (1.0) in both groups. When the two treatment groups were compared in the present study, the inter-quartile range was higher in the surgical group (0-2) compared to conservative group (0-1). The finding that the surgical group patients had a significantly higher number of previous episodes than the conservative group reflects the common practice of attempting to manage episodes conservatively prior to surgery. This is consistent with western literature.

Fifty-one percent of the conservative treatment group patients reported previous episodes. This is much higher than the percentage of patients with previous episodes (28%) reported by Cleland et al (2007a). However, Cleland et al (2007a) do not provide any detail of the number of previous episodes. Not reporting the actual number of prior episodes makes it difficult to make comparisons with this study. For example, although the number of previous episodes in this study ranged from 0-5, the conservative group included 49% patients with no previous episodes, 37% with one previous episode and only 1% with 5 previous episodes. Therefore, a comparison of percentage of individuals with previous episodes is not adequate to define the previous history and progression of the CR disorder. This issue is further complicated by the recall of patients with chronic pain and their expectations of appropriate illness behaviour, which may vary in different cultural settings.

5.1.7 Pain distribution

This study identified a significantly higher prevalence of neck pain in the surgically treated group (90%) compared to the conservative group (41%). Although Heckmann et al. (1999) reported a high prevalence of neck pain in the surgery group (95.2%), the neck pain prevalence was similar in their conservative group (92%). In the present study, within the surgery group, the prevalence of left arm pain was higher than that of right arm pain, which discounted any possible association between arm dominance and the presence of pain. In the conservative group, pain was equally prevalent in the right and left upper limbs.

5.1.8 Disability scores

At baseline, the surgically treated group had a higher level of disability than the conservatively treated group. This was more evident for factors 3 and 4 of the NPAD scale. Since factor 3 measures the effect of pain on emotion and cognition and factor 4 scores measure the impact of the disorder on activities of daily life, it is possible that these factors played a role in the preference for surgical treatment. Heckmann et al. (1999) did not determine the effects of pain on emotion and cognition or life activities at baseline. However, after treatment the surgically treated group had a higher percentage of patients with severely impaired activities of daily living (ADL) compared to the conservative group.

5.1.9 Cervical spine radiographic segmental curvature

The results of this study indicated lower radiographic segmental curvature values at baseline compared with those reported from previous studies. It is unclear whether these differences reflect selection bias with respect to clinical management preferences, or differences in spinal morphology related to race and genetic factors in the respective study populations.

The total radiographic segmental curvature (C2-7) values were comparable to those reported in a previous study of a similar patient population (Pickett et al. 2004). However, the segmental curvature values at the most affected levels (C5-6, C6-7) was lower in the present study in both treatment groups. The lower mean value in the present study was despite the fact the Pickett et al. (2004) used Cobb's method of measurement which has been shown to underestimate cervical curvature values (Harrison et al. 2000). All segmental curvature values were lower in the present study than those reported previously for patients with acute and chronic neck pain (Harrison et al. 2004). It is possible that pain may have had a significant influence on sagittal segmental curvature in the present study. Pain can affect curvature values as evident in the study of Harrison et al (2004), where the acute and chronic neck pain patients had lower segmental curvature values than the asymptomatic group.

Comparing curvature values between the two treatment groups, significantly higher mean curvature values at C2-3 and C3-4, were identified in the surgery group compared to the conservative group, whilst at C5-6, the segmental curvature was significantly lower in the surgery group. There was no difference in mean total curvature values between the two groups suggesting that differences between segments may cancel each other out resulting in no between group differences in total segmental curvature (C2 to C7).

5.1.10 Cervical spine composite ROM

The only previous study which looked at the effect of disc degeneration on cervical ROM was that of Dvir et al. (2006). In the present study, ranges of motion in flexion, extension and rotation to both sides in the conservative group were higher than those reported by Dvir et al. (2006). The surgery group had a significantly lower range of rotation compared to the conservative group in this study and that reported by Dvir et. al. (2006). The extension range was low in the surgery group and similar to results of previous studies (Dall'Alba et al. 2001; Dvir et al. 2006). Reduced extension in cervical radiculopathy has been identified in an earlier study (Agarwal et al. 2005a). The reduced range of motion observed in the surgery group could be an effect of higher pain scores and related muscle guarding.

5.2 Sampling

This was not a randomised controlled trial and the sample was one of convenience related to the study setting and the compliance of the therapists and medical practitioners providing the treatments. Therefore, sampling bias may occur due to the nature of the referral system inherent in a private medical system. It was not possible to influence the clinical pathway of management selected by the respective professions.

Although CR does not have a very high prevalence (0.3%), this study recruited 172 consecutive CR patients who met the inclusion and exclusion criteria. One hundred and sixty three patients (95%) agreed to participate in the study. This was a very high rate of recruitment, which was assisted by counselling the patients during their first visit. The risks and benefits of participating in the study were included in the information about both treatment approaches. All patients received this information and the treatment deemed most appropriate for them based on clinical and radiological diagnosis. The recommendation was made and presented to the patients by an independent medical team. Recruitment of consecutive patients was maintained to eliminate selection bias. The nature of the group allocation process may explain in part the between group differences in pain and other factors at baseline.

The surgery group demonstrated significantly higher neck and arm pain and disability scores compared to the conservative group at baseline. The severity of un-remitting pain, disability and neurological deficit was a significant reason for patients to be prescribed surgical treatment. The surgery group also included some patients, who had undergone previous conservative intervention, but the pain had returned and the neurological status had worsened. Sampath et al (1999) described similar circumstances in a multicenter trial, where CR patients who did not respond to conservative treatment were managed surgically.

The percentage of drop-outs in previous surgical studies was higher 29%,(Peolsson et al. 2003), 14% (Peolsson et al. 2004), 16% (Peolsson et al. 2006b) than what was observed in the present study (12%) at a one year follow-up. The conservative group had a 15% drop-out at one year, which was justifiably higher than Cleland et al (2007a) (5%) calculated at 28 days.

The management of CR in India, like in other countries, varies according to the treating team and their respective preferences. Although conducted in India, this study was based on universal standards of western medicine, rehabilitation and research principles. In general, the author is confident that the delivery of treatment was of an appropriately high standard. Although the patients' economic backgrounds ranged from low to high middle class/upper class, the treatment provided was of optimal quality because the consultant surgeons, physicians and physiotherapists were well qualified. This may increase the generalisation to other studies reported in the Western Literature but may not be generalised to all medical systems in India.

5.3 Outcomes of treatment

5.3.0 Reduction in pain

This study demonstrated continuous significant improvements in pain and disability scores following treatment in both groups. Self-reported scores of neck pain, arm pain and disability continued to show improvement even after the end of treatment. This continued improvement may be attributed to the initial intervention (surgery or conservative) and the natural history of the disorder. A Randomised Control Trial is the gold standard for evaluation of each treatment method, independent of that which would occur over time.

The conservative treatment and post-surgical management included elements that are common to other studies. For example, they included combinations of isometric neck exercises, scapular exercises, neck muscle stretching exercises (Persson and Lilja 2001), neural tissue mobilisation (Magee 2002) to maintain nerve root mobility, deep neck flexors strengthening to improve endurance of deep neck flexors (Cleland et al. 2005), sensori-motor training, weight training (Murphy et al. 2006), ergonomic instructions and postural instructions (Saal et al. 1996; Persson et al. 1997a) for a maximum of 13 weeks from baseline/surgery. Although, firm conclusions cannot be drawn for individual treatment modalities, the results of this study confirm that initial or conservative treatment or surgery followed by a planned exercise regime leads to continued improvement for a duration of at least one year. These results may be compared to Ylinen et al (2003) where women with chronic neck pain achieved an effective reduction in pain and disability following one year of neck strengthening and endurance exercise.

During the course of repeat assessments in a one-year follow-up, there was no significant difference in arm pain between 6 and 12 months in the surgery group although there was a significant difference from baseline at both assessment points.

This is consistent with Persson and Lilja (2001) who found that there was no significant change in mean pain intensity between 3 months to 12 months in the surgery group although there was a reduction of mean pain intensity from baseline to one year.

The maintenance of the reduction in pain is often related to the duration of the follow-up assessments. Recent conservative studies have only undertaken follow-up assessments at 1 month (Cleland et al. 2005; Murphy et al. 2006; Cleland et al. 2007a). One issue addressed in the present study is the tendency for conservative treatments to have short follow-ups and surgical interventions having longer periods of follow-up. This partly relates to the requirement of some surgical journals for a longer follow-up for surgical procedures. This also explains a tendency for one cohort to have continuous follow-up with a series of related publications (Persson et al. 1997a; Persson and Lilja 2001; Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b). The repeated reporting of follow-up data needs to be carefully interpreted since it could be that one study may overly influence the literature due to the relatively limited number of studies reporting treatment outcomes. This further demonstrates the importance of the present study in the context of conservative and surgical management of cervical radiculopathy.

In the present study, there was a significant decrease in mean pain scores at each follow-up until 1 year, in the conservative group. Although Persson and Lilja (2001) reported similar data for this length of follow-up, the study compared differences between treatment groups but not within groups at each follow-up. However, the descriptive data shows a reduction in mean pain scores for each treatment group (surgery, physiotherapy, and collar).

From baseline to one year, the surgical group in this study demonstrated a greater decrease in neck and arm pain compared to the conservative treatment group. Similar trends were reported in previous studies although statistical analysis in both studies was not conclusive (Sampath et al. 1999; Persson and Lilja 2001). In this study, the surgical cohort had a significantly higher baseline pain score than the conservative group. This confounds comparisons between treatment outcomes over time. Sampath et al (1999) attributed the larger change in pain in the surgery group to the initial high pain levels. The findings of this study cannot discount a similar conclusion and therefore comparisons of treatments when the groups are different at baseline need to be interpreted with care. The two treatment methods have different clinical indicators and risk profiles thereby questioning the validity of any attempt to control for a common confounding variable. Although a randomised controlled trial may be applicable more desirable research design it would be difficult or possibly impossible to conduct.

5.3.1 Reduction in disability

Disability scores following treatment for CR are not well reported. This may reflect the focus on pain in surgical studies since this is likely to be high (as found in this study) and influence treatment decisions with respect to surgical management.

Some studies have failed to detect a difference in disability following surgery at the 1 and 2 year follow-up (Hacker et al. 2000; Vavruch et al. 2002; Peolsson et al. 2006a). In comparison, the present study demonstrated significant improvement in disability scores at one year in both the surgery and conservatively managed groups which is consistent with the results of Sampath et al (1999). Previous studies have shown that multi-modality physiotherapy treatment resulted in a clinically meaningful decrease in disability at 3 months (Murphy et al. 2006) and 6 months (Cleland et al. 2005) after treatment. Likewise, in the present study, the disability scores improved between baseline and both follow-up intervals in the conservative group

Despite the general improvement in disability scores over time, an interesting observation was made about the factor 3 scores (the impact of pain on emotion and cognition). In both treatment groups factor 3 scores improved between baseline and the 3 month follow-up, after which there was no further significant improvement (at 12 months). It was noted that relatively low scores were achieved for this factor at the 3 month follow-up, reducing the potential for further significant improvement beyond that point. This suggests that the improvements in pain and disability at 3 months were associated with similar improvements in emotion and cognition.

In the surgical group, Factor 4 scores significantly increased between the 6 month and one year follow-up. Factor 4 scores represent how much life activities are restricted, for example socializing, recreation, work activities. Similarly, Persson and Lilja (2001) found that the surgery group did not improve with respect to walking, climbing stairs, or making a bed, for up to one year following treatment. Caution and apprehension about re-injury during daily activities following surgery, may be responsible for the slow recovery in the capacity to resume activities of daily living in the surgically treated patients.

One aspect that warrants discussion of the impact of disability on outcomes is the fact that sample sizes are often determined on the primary outcome measures of pain. It has been shown that pain is reduced following surgery but the literature suggests that disability scales either have less sensitivity to detect change or that the heterogeneity of the disability outcomes is greater following surgery. Therefore, some studies may have insufficient power to detect long-term changes in disability when the primary outcome variable (used to derive sample size) is pain.

5.3.2 Improvement in neurological signs

The results of this study indicated neurological improvement in both treatment groups, when baseline measurements were compared to final measurements. This is similar to the findings of other researchers (Saal et al. 1996; Heckmann et al. 1999; Grob et al. 2001). However, this study did not show 100% improvement for any neurological measure in either treatment group, which is consistent with the results of Saal et al (1996; 1997; 1999; 2001). Comparing the improvement in neurological function between surgery and conservative groups, Heckmann et al (1999) achieved greater improvements in the conservative group, whilst in contrast, Sampath et al (1999) determined the surgical group had statistical improvement in neurological function whilst the conservative group did not. Similarly, in the present study, the surgical cohort fared better than the conservative at final (12 month) follow-up. Approximately 90% patients in the surgical group and 78% in the conservative group at the final follow-up achieved full recovery of motor, sensory and deep tendon reflexes. It is pertinent to mention here that in this study, the conservative group underwent final neurological assessments at 3 months, closer to the completion of their treatment duration, compared to the surgical group who underwent final assessment at 12 months, whilst the surgery was conducted close to baseline. Therefore, some improvement in the surgical group may be attributed to natural recovery. In the surgical patients, a deterioration of motor scores on the right side (6 patients) and deep tendon reflex scores on the right (1 patient) was observed. Of these six, the one patient who had deterioration of both motor and DTR scores had increased NPAD scores between 6 months and one year. Of the other 5 patients who had deterioration of right side motor scores, one had an increase in arm pain score and disability score, whilst the others had increased neck pain scores between the 6 month and 12 month follow-ups.

Since neurological signs and symptoms (including pain and numbness) are a primary aspect of the clinical diagnosis, these should be considered as important aspects of recovery. The recovery of these neurological signs in the majority of participants in both cohorts suggests that both interventions had components that were well suited to the neurological recovery. Since this study is not a randomised clinical trial, the changes over time may be partly due to natural recovery during this period of follow-up. That stated, however since many participants had had continuous symptoms for a substantial period of time prior to the intervention and that the follow-up extended past this period it is likely that some element of the recovery is attributable to the specific and non-specific impact of receiving an intervention.

5.3.3 Repeat measurements for radiographic and functional measures outcome

This is the first study to examine repeat measurements of segmental sagittal radiographic curvature and flexion-extension motion, as well as composite active cervical ROM for different interventions in patients with CR. Consequently, no literature exists against which comparisons can be made. What was noted is that there is a relatively good association between the changes in these outcomes over the course of the study. The responses however were different at different measurement time in the two treatment groups.

The timing of the assessment of radiographic and impairment measures during the study was different in the two treatment groups. The principle difference for repeat measurements was that the conservative group was measured at baseline and then at 3 months, whereas the surgery group was measured at baseline, 3, 6 and 12 months. The following sections discuss these findings.

5.3.3.0 Changes in radiographic segmental sagittal curvature on repeat measurements

In the conservative group, increased curvature values were identified at all levels except C5-6, between baseline and 3 months. Incidentally, the C5-6 level was identified as the most prevalent level for diagnosis of CR in the conservative group (Brown 1971; Gore et al. 1986; Fukusaki et al. 1995; Persson et al. 1997a). This may suggest that the most affected level maintains the baseline curvature change which may have occurred due to pathology. The other levels may have had altered curvature in response to muscle spasm, pain or compensation (Oda et al. 1999) which changed following treatment.

There was no systematic change in segmental sagittal curvature in the surgery group as was seen in the conservative group. Segments C6-7 and C5-6, were the most prevalent symptomatic levels in the surgical group and demonstrated the greatest level of change. This was also because these levels underwent surgical interventions. Measurements at all levels had a large within-group variance (SD). Despite the segmental variations, the total C2-7 curvature values remained unchanged, which further supports the conclusion that in the surgically managed cohort there may be segmental compensation strategies. It is hypothesised that following the surgical intervention, changes to the treated segment cause compensatory adjustments at other segments, negating any overall change in cervical curvature. However, since the compensation of the unaffected levels is not systematic (i.e. they are randomly lordotic or kyphotic responses) it is difficult to validate the compensatory hypothesis.

Interpretation of the segmental sagittal curvature results should consider the typical error values established in Study 5 of this thesis. Changes in repeat measurements for some segments, in both treatment groups, were not much greater than the typical error values, although they were significantly different from baseline. The significant changes in curvature in some segments, especially C2-3 and C3-4 in the conservative group and C2-3, C5-6 and C6-7 in the surgery group, may assist the interpretation of systematic changes within a group. However, these changes when identified in a single assessment fall within the typical error measurements. This suggests that in the clinical setting with individual cases these assessments have limited value.

5.3.3.1 Changes in radiographic segmental flexion-extension motion and sagittal composite active range of motion

From baseline to 3 months, the response of the conservative group was generally uniform. The mean radiographic segmental flexion-extension motion values increased significantly at nearly all levels although the increase at certain levels (C2-3, C3-4, and C6-7) was close to the typical error values established in Study 6. The increase in total C2-7 flexion-extension motion value was considerably higher than the typical error values. The composite active cervical range of motion in the sagittal plane increased significantly as well. These changes were much larger than the typical error values for repeated composite active sagittal motion calculated in an earlier study (Agarwal et al. 2005b).

However, the changes in these measurements was somewhat different in the surgical group over the12 month follow-up period. At 3 months, radiographic segmental flexion-extension motion at all cervical levels (except the non-surgical level, C2-3) showed significantly reduced movement. Similarly, at 3 months, composite active cervical ROM showed a significant decrease in flexion, extension and composite sagittal motion.

At 12 months, the effects of surgical fusion were evident at the more prevalent surgical levels (C5-6, C6-7, symptomatic level) as well as for the total C2-7 range. These levels continued to show significantly reduced motion compared to baseline. This was not the case for composite active cervical ROM where the sagittal plane motion improved significantly. Although previous research has correlated composite active cervical ROM in the sagittal plane with radiographic segmental sagittal motion (Dvorak et al. 1991; Ordway et al. 1997; Tousignant et al. 2000), the effects of surgery and post-surgical management may explain the decrease in motion observed in the present study. Fear of moving and the behavioural adaptations associated with immobilisation in a collar may have contributed to the post-surgical decrease in mobility. It is unclear what proportion of a reduction in movement was behavioural or mechanical (bony or soft tissue).

Assessments of stiffness, where range of motion is assessed while a controlled torque is acting on the spine may be the only way to elucidate the true contribution of mechanical stiffness to the decrease in mobility. A decrease in radiographic flexion-extension motion could be a long-term result of surgery and fusion of the symptomatic segment. The reason for the increase in active composite cervical spine motion may be a direction for future research. Although the surgery increased the mechanical stabilisation and reduced the capacity of the segments to move, the subsequent post surgical rehabilitation may have contributed to reducing pain, improving soft tissue extensibility and improving willingness to move. The different changes in sagittal mobility for the conservative and surgical managed patients with CR may be attributed to the type of intervention. This is the first study to examine longitudinal changes in sagittal mobility in conservative and surgically managed patients with CR.

5.3.3.2 Changes in composite active cervical ROM (axial rotation) on repeat measurements

In the conservative group the range of left and right rotation, motion increased significantly at the 3 month follow-up. In the surgery group, the rotation range decreased significantly at 3 months compared to baseline and remained reduced at 12 months compared to baseline. Patients who underwent surgery did not regain their rotation range of motion in either direction, despite significant improvements in the sagittal range of motion. At baseline, there was a significant difference in rotation range between the two treatment groups, with the conservative group demonstrating significantly more rotation. With repeat measurements, the conservative group increased rotation range at 3 months whereas the surgery group had a significant decrease in rotation. The reason for the persistent decrease in rotation range of motion is not clear as rotation movement occurs primarily in the upper cervical segments (White and Panjabi 1990b) whilst surgery was performed in the lower segments. Pain, fear of pain and persistent loss of extensibility in the cervicothoracic musculature may account for this observation.

5.3.3.3 Changes in head neck angle measurements on repeat measurements

The head neck angle is a common measure of posture in neck pain studies but a large typical error that is related to the behaviour of the individual (Study 7) makes it difficult to detect systematic changes over time unless they are large. The findings of this study suggest that head neck angle is not sensitive to changes over time in patients with CR, or that change in head neck posture is not a significant feature of CR.

In summary, the two treatment groups responded differently to repeat measurement variables. Whereas the conservative group showed a tendency to improve, the surgery group was more mixed during repeat measurements. Of course, one primary reason was a surgical intervention in the surgery group which was bound to impact radiographic and functional outcome variables. The second reason was that the surgery group was measured four times including baseline for radiographic and impairment outcomes whilst the conservative group twice. Finally, it could be that there was a selection bias (the groups were fundamentally different) and this is their normal recovery process.

5.4 Sub-hypotheses

The primary focus of the thesis was to determine whether variables assessed at baseline could predict treatment outcome in patients with CR who were treated conservatively or with surgery. Specific sub-hypotheses were derived from the review of the related literature. The following section discusses issues related to these specific sub-hypotheses.

5.4.0 Association between pain and disability (baseline and 12 months)

The relationship between pain and disability has been investigated in a number of previous studies of patients with CR (Persson and Lilja 2001; Peolsson et al. 2003; Peolsson et al. 2006b). These studies report a consistent positive correlation between pain and disability although the level of association varies between studies, and there are differences in the specific measures, for example, Pain (current pain, worst pain last week, arm pain, neck pain, and pain intensity) and Disability (VAS, NDI, NPRS, DRI). The ability to determine whether these associations change over time is uncertain since the follow-up periods differ and few studies (Peolsson et al. 2003; Peolsson et al. 2006b) have reported longitudinal data for both domains. In the present study, positive correlations were identified between pain (neck and arm) and disability in the conservative group at baseline and at twelve months. In the surgical group, only arm pain correlated with disability both at baseline and at 12 months.

Persistent pain is an important indicator of the level of disability and on-going functional limitation (Persson and Lilja 2001). The results of the present study are very similar to those of Persson and Lilja (2001) where some disability items (Disability Rating Index) were positively correlated with pain intensity at baseline, whilst all items were positively correlated with pain at 12 months. The results of the present study support the association between neck and arm pain, and disability in patients with cervical radiculopathy, and confirm this finding in the Indian population.

5.4.1 Association between radiographic curvature at baseline and clinical measures at baseline and final follow- up

There was a negative correlation between cervical segmental kyphosis and arm pain and disability scores at baseline, signifying an association between the development of segmental kyphosis and the level of pain and disability. It has been suggested that normal physiological lordosis is desirable to maintain mechanical stability, minimise stress within the motion segment (Zaveri and Ford 2001) and maintain normal patterns of motion (Penning and Wilmink 1987). Changes in curvature may lead to increased mechanical loads which can cause disruption to disc nutrition (Buckwalter 1995) and changes in disc biochemistry (Hutton et al. 1998). This may partially explain the previous observation that cervical spine curvature (C2-7) values in patients with acute neck pain were 6° less than in asymptomatic individuals and 13° less than in patients with chronic neck pain (Harrison et al. 2004). These results indicate that patients with neck pain and CR are more likely to have a reduced cervical lordosis than individuals without pain.

In this study, the associations between spinal curvature, arm and neck pain, and disability scores were examined in both patient groups prior to treatment. All statistically significant correlations were negative, implying that reduced radiographic segmental curvature is associated with increased pain and disability. Of interest is that there was a significant negative correlation between arm pain, disability scores and segmental radiographic curvature but not with neck pain. A moderate correlation was identified between the symptomatic level curvature and arm pain. This is the first study to report associations between neck and arm pain, and radiographic segmental kyphosis. This is also the first study, which has looked at this association in patients managed with conservative treatment, and found the strength of association to be lower than in the patients managed surgically.

To date there are no studies that have reported a long-term association between radiographic segmental curvature and clinical measures in patients with CR managed conservatively. It has been suggested that a larger pre-surgery kyphosis is correlated with a higher reduction in pain after surgery (Vavruch et al. 2002; Peolsson et al. 2004). The authors suggest that pre-operative kyphosis was modified by the surgical treatment and therefore confirms the pain source and explains the related improvement. Heidecke et al (2000) and Laing et al (2001) concluded that the presence of a segmental kyphosis following surgery did not influence pain and disability outcomes compared to patients where the segmental alignment was preserved.

Baseline radiological segmental curvature values were analysed for long-term associations with pain and disability measures. Disability and arm pain intensity at 12 months were negatively correlated with baseline C2-7 curvature in the conservative group, and symptomatic level curvature in the surgery group. This result suggests that conservatively managed patients with a reduced cervical curvature may have a higher level of arm pain and disability. In the surgery group, reduced curvature of the symptomatic level is associated with higher arm pain and disability. Neck pain was not correlated significantly either at baseline or at subsequent time measurements. These results have implications on the rehabilitation programme for individuals who present with reduced curvature values at baseline.

5.4.2 Radiographic segmental flexion-extension motion–asymptomatics, symptomatic levels and composite active cervical sagittal plane ROM over repeat measurements

Measurements of segmental flexion - extension motion show that asymptomatic subjects in the current study displayed lower mean values compared to those from previous studies: at all segments compared to Dvorak et al (1993), only at C2-3 compared to Ordway et al (1999) and Puglisi et al (2004) , at C2-3 and C3-4 compared to Penning (1978) and C6-7 compared to Dvorak et al (1988b). Dvorak et al (1988b) used the radiograph manual superimposition method and active movements, as done in this study, whereas the Dvorak et al (1993) had developed a specially designed software to measure passive movements. C2-3 measurements reported in this study were consistently low compared to previous studies. Similarly, when the patient group was compared, the C2-7 mean values in this study (46.4 $\pm$ 9) were less than that of Dvorak et al (1993), but nearly equal to Ishihara (1968). The values were also similar to Holmes et al (1994) who examined Chinese patients with cervical myelopathy. The same authors also studied asymptomatic subjects and reported less segmental mobility in the patients than that reported in previous studies (Penning 1978; Dvorak et al. 1993). The segmental flexion-extension motion in asymptomatic subjects in the present study was not as low as that reported by Holmes et al. (1994) but low enough to suggest that there may be differences between Caucasian and Asian populations in cervical segmental motion.

Segmental hypo-mobility may be due to muscle spasm, soft tissue tightness or mechanical wear of the spinal joints (Dvorak et al. 1993). The results of this study suggest that a limitation of motion was evident at the symptomatic level as well as the remaining segments of the cervical spine. A comparison between asymptomatic subjects and a CR cohort revealed significant differences in segmental motion at all levels except C2-3. Previous studies have shown segmental hypomobility primarily at the affected levels in severe discogenic spondylosis (Good and Mikkelsen 1992), in degenerative radiculopathy from C2 to C7 (Ishihara 1968) and at 1-2 levels only (Dvorak et al. 1993). Some of these results have limited value due to the small sample size (Dvorak et al. 1993) or lack of summary data for all segments analysed (Ishihara 1968). The present study overcame these limitations by using an adequate sample size (n = 35) and reporting of summary data for all segments. Although Lysell (1969) was unable to detect differences between normal and degenerative spines, the present study found systematic differences between asymptomatic subjects and patients with CR. These findings provide good evidence that there are segmental movement differences between asymptomatic subjects and patients with neck pain and CR.

The underlying mechanisms for these differences need further investigation, for example, pain or fear of pain may decrease the active segmental sagittal motion. Patients in the CR group had a mean NPRS score of 60 $\pm$ 20. Pain as a cause of reduced segmental flexion-extension motion was not discussed by Dvorak et al (1993) or Holmes et al (1994). This is the first study to establish an association between pain measures and radiographic segmental flexion-extension motion. A strong negative correlation between radiographic flexion-extension motion at symptomatic level/s at baseline, and neck pain severity at 12 months following treatment was identified in the present study. This suggests that reduced segmental flexion-extension motion at baseline is associated with increased neck pain 12 months later. Although single associations are unable to infer causality, the longitudinal assessments suggest that there is a strong relationship and further long-term studies are required to establish this definitively. The process of degeneration of joints occurs over time, in turn causing muscles and other tissues to slowly adapt and change optimal resting lengths. These changes have been proposed to contribute to long-term neck pain.

This study demonstrated a significant association between radiographic segmental sagittal motion with composite active sagittal cervical motion. Previous studies (Ordway et al, 1997; Herrmann Bredenkamp, 1990; Tousignant et al, 2000) describe a positive association between radiographic measurements and surface measurements of cervical sagittal motion in normal subjects. The present study examined this issue in a clinical population of patients with CR. Strong positive correlations between the two measures at baseline and at 3 months were observed in the conservative group. Significant correlations in the surgery group were weak at baseline and at 3 months, and were not significant at 6 and 12 months. This finding could be due to an on-going segmental fusion phase, a desired outcome of surgery. Post surgical movement restriction as a result of bracing (Askins and Eismont 1997), apprehension about movement, residual pain, or changes in normal kinematics may be other contributing factors.

Factors that may have contributed to the results in both groups are (i) the reliability of the two measuring instruments (ii) evaluation of a clinical population and (iii) analyses of measurements between C2-7 (radiographic) without calculating the contribution of Occipital-C1, C1-2 (Ordway et al. 1997; Ordway et al. 1999) or thoracic movements. Although the surgical intervention did affect movement at the fused segment, the cause of the more general and sustained limitation of sagittal motion may be mechanical or behavioural in nature.

5.4.3 Association between composite active cervical ROM (sagittal and axial planes) and clinical measures

This thesis includes the first study (Agarwal et al. 2005a) to compare composite active cervical ROM in asymptomatic individuals with that of patients with CR, and to demonstrate significant reductions in flexion, extension and full cycle lateral rotation in the CR patients compared to asymptomatic individuals (Agarwal et al. 2005a). The decrease in active cervical ROM may have resulted from altered biomechanics of the cervical spine due to disc degeneration, pain (or fear of pain), or both. Decreased range of motion has been reported in many studies of patients with neck pain (Cassidy et al. 1992; Jordan et al. 1997; Lee et al. 2004).

Negative correlations between disability scores and neck movement have been reported in previous studies (Peolsson et al. 2003), but not between pain scores and neck movements. In this study, significant negative correlations were seen between disability scores, neck pain scores and neck movements at baseline. The strength of association was greatest between baseline extension and disability scores at baseline. During maximal extension, the backward movement of the upper vertebra upon the inclined facet of the lower vertebra may result in laminar impingement, cause increased pressure on the disc or narrow the foraminal space causing irritation of the nerve root (White and Panjabi 1990a). Although rotation motion to both sides was significantly negatively correlated with pain and disability measures in both treatment groups, this did not correlate with the symptomatic side. This may suggest an overall reduction in active motion and it is not possible to determine the specific factors contributing to the restriction.

Two previous studies have reported using reduced rotation as a diagnostic criteria (Wainner et al. 2003) and as being negatively correlated with measures of pain and disability (Peolsson et al. 2003). The results of the present study further develop this concept by demonstrating negative correlations between composite active cervical ROM in all measured directions and measures of pain and disability.

5.4.4 Association of head neck angle with clinical measures

In this study, the surgical group showed a significant positive correlation between head neck angle and neck pain scores at baseline. The pain scores of the surgery group were very high at baseline, which may have resulted in a pain-easing posture being adopted by these patients. Although not directly comparable, a forward head posture has been associated with conditions other than CR, such as altered TMJ mechanics, thoracic outlet syndrome, spondylotic changes, facial pain and poor deep cervical flexor endurance (Darnell 1983; Rocabado 1983; Ayub et al. 1984; Grimmer 1996). However, it is conceded that no direct comparisons with previous studies are possible because previous surgical studies have not reported posture measures, either as a clinical assessment or as an outcome measure. In contrast, no significant correlation between head neck angle and neck pain was identified in the conservative group. The pain scores in the conservative group were lower compared to the surgery group, which suggests the influence of pain on head neck posture was less pronounced than in the surgical.

5.4.5 Associations between baseline variables and the final pain intensity outcome

Due to the large number of factors which were significantly correlated with the pain intensity outcome, only factors that account for more than 25% of the outcome variance ($r > 0.50$) will be discussed. Further, the subsequent development of a clinical prediction rule that used a hierarchical logistic approach to select variables will be used to define the most important baseline predictor variables. It is necessary to examine the univariate associations however, since few if any studies have conducted hierarchical analysis of factors contributing to the outcomes in patients with CR, who have received either conservative or surgical treatment.

Two previous studies specifically examined associations between baseline age and final pain outcome in a surgical cohort (Peolsson et al. 2003; Peolsson et al. 2006b). Neither study reported significant correlations between the two variables. In the current study, significant positive correlations between age and final neck pain scores in the surgery group ($r > 0.50$) were seen. Degenerative changes in the spine associated with aging (Cusick and Yoganandan 2002), may be further accelerated with surgical intervention and may explain why age was associated with the pain outcomes emphatically in the surgery group.

Occupation has been associated with increased pain levels in previous neck pain studies. Cagnie et al (2007) found white collar workers tended to report higher neck pain intensity. In contrast, blue collar workers reported greater pain and disability than white collar workers in a study by Peolsson et al (2003). Ability to do heavy work improved more in the surgery group compared to the conservative group, as assessed by Persson and Lilja (2001). In the present study, the active work style variable comprised of blue and brown collar workers who demonstrated a positive correlation with final neck pain intensity only in the conservative group. Given the nature of work of blue and brown collar workers, and concurrently suffering from CR, the resultant positive association with pain at 12 months following conservative management is consistent with previous studies (Persson and Lilja 2001; Peolsson et al. 2003). It is these individuals who fail conservative treatment who may go onto surgical interventions.

The current study showed a significant positive correlation between baseline arm scores and final neck and arm pain scores in both treatment groups, suggesting that this association exists independent of the intervention. The only previous study (Peolsson et al. 2006b) which explored neck and arm pain separately did not detect any association between baseline arm pain scores with final pain scores. Arm pain is a characteristic symptom of CR, and is associated with increased disability at baseline and 12 months (as discussed earlier), as well as neck and arm pain at 12 months following treatment. The strong correlation with long-term pain and disability outcomes establishes arm pain as an important baseline variable. As previously discussed, strong significant correlations were also analysed between baseline sagittal segmental motion at symptomatic levels and long-term neck pain scores. This suggests a possible interaction between baseline pain and mechanical factors, and long-term pain outcomes in patients with CR.

5.5 Clinical outcome mapped by NPAD scores

At the three month and one year follow-up, patients were categorised according to their level of pain and disability based on their NPAD score (Wheeler et al. 1999). Scores between 0 and 22 implied ‘none to minimal pain and disability’. Based on this criterion, the NPAD scores were used to classify the patients in both treatment groups into responders (< 22) and non-responders (≥ 22). This classification based on NPAD scores has been employed in previous studies which used disability measures to define treatment success (Childs et al. 2004; Cleland et al. 2007b). The NPAD is a clinically responsive scale (Goolkasian et al. 2002; Pietrobon et al. 2002). A preliminary study in this thesis established the validity and test-retest reliability of the Hindi translation of the NPAD in patients with CR (Agarwal et al 2006). Reduction in pain intensity and improvement in disability are accepted as key outcome measures in spinal treatment (Borghouts et al. 1998; Kjellman et al. 2002; Cleland et al. 2007a).

Thirty-five percent patients had a successful outcome at 3 months following conservative intervention. This is lower than the 48% reported by Cleland et al (2007a) at a mean duration of follow-up of 28 days. Categorisation as successful is dependent on the intervention as well as the outcome measure chosen as the outcome criterion. Apart from this, the three months follow-up may have caused some reductions in effects of treatment in the present study whereas the Cleland et al (2007a) study at the shorter follow-up period of 28 days retained positive outcomes following treatment for mean 6.4 sessions. A similar analysis for follow-up at 3 months has not been reported from previous surgical studies. A number of previous studies (Abd-Alrahman et al. 1999; Klein et al. 2000; Zoega et al. 2000) have employed the Odom's criteria to classify clinical outcome. The Odom's criteria, a single rating scale is not sufficient as an outcome measure because it combines aspects of outcomes (signs and symptoms) which may be poorly related (Deyo et al. 1998). However, Odom's scale includes some categories, which can be compared to NPAD score categories. In the surgical group in the present study, the frequency distribution of patients in the 'none to minimal' (50%) and 'mild' (50%) categories were similar to the percentage of patients reported as 'excellent' and 'good' by Abd- Alrahman et al (1999) and Klein et al (2000). When mean disability values were compared, the disability levels at 12 months in the present study were similar to Vavruch et al (2002) but less than Palit et al (1999). On the basis of results generated from the current study, the pain and disability outcomes of Indian patients in this study are comparable to those reported from other parts of the world.

5.6 Clinical Predication Rule analysis

An important aspect of the CPR analysis is the choice of the principal outcome variable. With a different principal outcome variable and different set of 'responders and non-responders' the outcome of this study may be different. It is accepted that although pain reduction is a desirable treatment outcome, it is not the only dimension for a successful outcome. This study therefore used a pain and disability outcome variable which had four factors, (neck problems, pain intensity, emotion and cognition, interference with life activities). Each of these factor scores had a high significant correlation with the total score (Wheeler et al, 1999; Agarwal, 2006). The multi-dimensional aspect of the NPAD made it an ideal choice for translation into Hindi. Previous studies using a CPR analysis have used principal outcome measures based on patient satisfaction and perceived improvement (Tseng et al. 2006; Cleland et al. 2007a; Raney et al. 2009). However, none of these had been validated into Hindi so the Hindi translation of the NPAD was the preferred outcome measure for translation of this form of research into the Indian population.

Many patients' first concern about their treatment relates to prognosis of the disease condition. In order to provide patients with more information, clinicians need to be aware of factors associated with treatment prognosis. Clinical prediction rules (CPR) are commonly used in health-care practice to establish prognosis or to improve decision making by matching a treatment to a specific sub-group of patients.

Prognostic factors for patients with cervical radiculopathy (Wainner et al. 2003) and for patients with neck pain treated with multi-modality physiotherapy interventions have been reported (Cleland et al. 2005; Cleland et al. 2007a). However, there is limited information in relation to long-term prognostic factors for patients with CR treated conservatively with which to compare the results of the present study. The only study of conservative interventions for CR used a 28 day follow-up period on which the CPR was developed (Cleland et al. 2007a).

There are studies that have examined long-term predictive factors for patients with CR who have been managed surgically. These studies used forward step-wise regression analysis using linear modelling to predict the percentage of the dependent variable (pain) explained by an independent variable measured at baseline examination (Peolsson et al. 2003; Peolsson et al. 2004; Peolsson et al. 2006b).
The present study is the first to undertake a comprehensive longitudinal assessment of patients with CR treated either conservatively or surgically, using a combination of impairment and disability measures to predict the clinical outcome 12 months after treatment.

The CPR analysis was conducted for both groups at 3 months, the surgical group at 6 months and for both groups at 12 months. For these analyses, individual predictor variables exhibited LR+ ratios of between 0.15 and 4. It was observed that the baseline neck pain scores and neck pain prevalence was not significantly different between the responders and non-responders at 12 months in both groups. This may be because upper limb pain is so intense that the neck pain was not a significant issue for these patients. This could also be due to the choice of the outcome variable selected to divide the patients into responders and non-responders.

In the conservative management group, change scores for pain and disability were higher in the responder group except for arm pain. The baseline arm pain score in the non-responder group was higher than in the responder group, which is likely to have contributed to this difference. In the surgery group, a higher change score was only seen for NPAD factor 3 (in the responder group) and arm pain scores (in the non-responder group). Consistent with the conservative group, the non-responders in the surgery group had the greater arm pain change score. This can be explained by the fact that they had higher baseline scores for arm pain and therefore had greater potential to change over time. In both treatment groups, high initial arm pain scores suggest that it is more likely this group will have a larger change in pain following intervention, regardless of whether the patients within the group were categorised as responders or non-responders. A smaller sample size (n=27) in the responder and non-responder group may have contributed to a Type 2 error for some of the variables and therefore without hierarchical statistical approaches (see later) one cannot assume Factor 3 is the major predictor of outcome for the surgical group.

This study reported both the positive and negative likelihood ratios (LR+, LR-) for the change in probability that a subject will experience a successful outcome following surgery or conservative treatment when they satisfied the rule's criteria. Further, at different points of repeat measurements, a pre-prediction probability of success was calculated. The logistic stepwise regression analysis identified a small group of predictors for each repeat analysis, which maximised the ability to identify a subject likely to experience a successful outcome. The pre-prediction probability of success was increased with the logistic regression analysis where 'n' number of predictors increased the post-test probability of success. This probability was different at different points. This implied that when those 'n' numbers of predictors are present, the appropriate treatment should be applied because the patient has a chance equal to the post-test probability of responding favourably to the treatment. A total of four Clinical Prediction Rules were created which included one for each treatment group at the 3 and 12 month follow-up periods. These group predictors have been discussed below:

5.6.0 Individual predictor variables common to each patient group and follow-up period.

Some individual predictors were present in the different CPRs for groups and across time. These were age < 40 years (conservative group predictor at 3 months and 12 months and surgical group predictor at 3 months), cervical rotation to the right > 55 degrees (conservative group predictor at 12 months, surgery group predictor at 6 months and 12 months) NPAD score <55 (surgery group predictor at 3 and 12 months), duration of symptoms ≥ 33 weeks (conservative group predictor at 3 months and surgery group predictor at 12 months) and cervical flexion < 40 degrees (conservative group predictor at 3 months and surgery group predictor at 12 months). Clustered together these suggest relatively young patients with flexion affected more than rotation with moderate symptoms (NPAD) and reporting symptoms for longer than 8 months seem to respond to the interventions in this study. These findings form the basis of future studies that may examine the clinical validity of each and grouped factors in predicting the response to surgical or conservative management for cervical radiculopathy.

Cleland et al (2007a), in the only other CPR analysis for patients with CR, found that the response at 28 days was in part determined by age. They reported that individuals younger than 54 years had greater potential for a successful outcome. In the present study there are similar findings in that the younger individuals (albeit <40yrs) were more likely to be responders to either treatment. This was the case for the both treatment groups at the 3 month follow-up, as well as at the 12 months follow-up in the conservative group. In contrast, Peolsson et al (2003) found that, age was positively associated with reduced pain intensity in surgically treated patients with CR at a 2 year follow-up (i.e. older people had less pain). This contrasts with previous clinical studies where older age was associated with increased neck and arm pain following conservative in a treatment (British Association of Physical Medicine 1966), and in a radiculopathy and myelopathy cohort treated surgically (Bertalanffy and Eggert 1988). The interpretation of these results is difficult as the statistical models employed are different in each study. That stated, the individual models are unable to explain the different directions of change with respect to age and pain outcomes. It is known that degenerative changes in the cervical spine have a positive association with age (Penning 1988). Other factors influenced by age are reduced bone mineral density (Marquez et al. 2001) and reduced muscle strength (Peolsson et al. 2001). Therefore, since Peolsson et al examined surgical outcomes and pain reduction rather than a global level of disability, it may be these factors that explain the different impact of age on the long-term outcomes.

It is only with future research using disability scores as outcomes that the influence of these factors and age as a confounder can be determined. What can be concluded from this study is that in the short term (3 months) in both groups and at 12 months in the conservative group, it is likely that individuals who are younger are more likely to respond to treatments for CR.

Symptom duration with a threshold above 33 weeks was a predictor of successful outcome at 3 months in the conservative group and at 12 months in the surgery group. Surgical studies of patients with CR have reported successful outcomes where symptoms durations have ranged from 2 months to 10 years (Heckmann et al. 1999; Sampath et al. 1999; Persson and Lilja 2001) whilst conservative studies have reported a relatively shorter symptom duration prior to treatment (6 days to 6 weeks to one year) (Cleland et al. 2005; Murphy et al. 2006; Waldrop 2006). When we compare the results of the present study with previous surgical studies, then 33 weeks or approximately 8 months (with a maximum duration of symptoms calculated as 52 weeks) is at the lower end of the range symptom duration previously reported. Thus, duration of symptoms (≥ 33 weeks) as a predictor of outcome in the surgery group at 12 months is consistent with previous surgical studies. The range of duration in conservative studies extends to one year (Waldrop 2006) or up to 10 years (Sampath et al. 1999; Persson and Lilja 2001). Although a duration of symptoms > 33 weeks as a positive predictor, suggests that people who had long-term pain were the ones who responded to treatment, comparisons with durations of previous studies clarified that the duration of onset of this study was well within the range reported for CR. CR patients with this duration of symptoms have responded to treatment interventions in previous studies (Sampath et al. 1999; Persson and Lilja 2001; Murphy et al. 2006). Experiencing symptoms of CR for > 33 weeks may have led to the development of muscle tightness, postural changes, reduced range of motion, and other sources of nociceptive input from different spinal segments. It may be that individuals with a long duration of symptoms may have other factors contributing to, and even maintaining, some of the CR symptoms. These additional problems may respond specifically to treatment independently of the symptoms associated with CR. Some improvement may be attributed to the passage of time (Honet and Puri 1976).

Another group predictor for a successful outcome at 3 months in the conservative group, and 12 months in the surgery group, was ‘cervical flexion < 40°. It is well known that cervical flexion is associated with dynamic changes in the spinal canal and may have an effect on the spinal cord (Cusick and Yoganandan 2002). The cervical spinal canal is lengthened in flexion. This may cause traction of a nerve root, compressed at a higher level whilst emerging at a lower level. A significant increase in adjacent intra-discal pressure at C4-5 and C6-7 has been measured when C3-4 was loaded at 20° flexion (Eck et al. 2002). More flexion may cause an increase in load on a degenerated disc. Hence, flexion < 40° may actually be a combination of protective responses as well as movement restriction developed over a period of time. In contrast to the results of this study, Peolsson et al (2003) reported increased neck flexion at baseline as being a predictor of low disability following surgery for CR. Lack of descriptive data from that study makes comparisons with the present study difficult. Cleland et al (2007a) too reported that a successful outcome was related to individuals with greater than 30° cervical flexion. Their sample was slightly older (51 years) than the sample in the present study (45 years). Although we found that age is a confounding factor for active cervical flexion, the 5-6 years is not likely to make any difference.

Right rotation ≥ 55° was an important individual predictor in the conservative group at the 12 months follow-up and in the surgery group at the 6 and 12 month follow-up. A rotation range of motion > 55° in individuals aged 45 to 55 years is towards the upper end of the normal range of motion (average 66 ± 7°) (Youdas et al. 1992; Trott et al. 1996)(study 4). Increased right rotation at baseline has been previously shown to be correlated with lower NDI scores at 12 months (Peolsson et al. 2003). The reason why rotation to only one side (right) is correlated with reduced disability is not clear. However, it is likely to be a manifestation of the hierarchical statistical approach. Right rotation is more strongly correlated with the disability outcome than left rotation. Since these two measures are correlated then the left rotation drops out of the statistical model. In the present study, and that of Peolsson et al (2003), right rotation range is one of the best predictors of outcome. Earlier findings in this thesis found limited association between arm dominance and the side of arm pain in patients with CR. Therefore, these findings suggest that the reason why the movement to the right is the better predictor is that this may be the task that is most comfortably performed by the patient. Therefore, rotation to the dominant side (right) could be a habitual movement pattern and less affected by apprehension and fear of pain. The impact of limb dominance on movement behaviour in patients with chronic neck pain may be an area for future research.

The range of neck rotation was relatively high compared to the normal ranges previously reported. This may be explained in mechanical terms since in CR, the neural foramen can be compromised by osteophytic bone, disc material or hypertrophy of the ligamentum flavum causing compression of the exiting nerve root (Heller 1992; Mercer and Bogduk 2001). Rotation to one side is accompanied by ipsi-lateral lateral flexion, causing narrowing of the neural foramen (White and Panjabi 1990b). In patients with CR where the neural foramen is compromised by pathology, rotation to one side is likely to cause increased symptoms. Therefore, if a patient has the ability to rotate their head and neck beyond 55° without increasing the radiculopathy symptoms, that may be suggest less compromise of the nerve root. In this context, it was noted that there were a significant number of responders with right-sided pain and non-responders with left-sided pain in the surgery group. This difference between right- and left-sided pain was not evident in the conservative group. Cervical rotation mobility also seems to have a role in the diagnosis of CR. Rotation < 60° was one of the four cluster items used to assist the diagnosis of CR in the study of (Wainner et al. 2003). In the present study, the mean baseline rotation range was 56° ± 13 in the conservative group, and 44° ± 12 in the surgery group. Thus, a large proportion of both treatment groups fulfilled the diagnostic criteria of rotation < 60°.

High baseline disability levels can result in a longer duration of symptoms (Kjellman et al. 2002), and low baseline NDI scores (< 11.50) can be a predictor of success of spinal manipulation in the management of neck pain (Tseng et al. 2006). A NPAD score < 55 implies patient subgroups ranging from 'no pain and disability' to 'moderate pain and disability'. Scores > 57 are associated with 'moderate to extreme pain and disability'. NPAD score of < 55 at baseline was one of the group variables, which predicted a successful outcome at 3 and 12 months, in the surgery group. Previous studies provide limited data for comparison of this result, other than that a low disability (NDI) was correlated with greater improvement in pain one year after surgery in patients with CR (Peolsson et al. 2003). In the present study, baseline NPAD scores of <55 were predictive for a successful outcome at 12 months, suggesting that patients with low to moderate disability were more likely to have a successful outcome following surgical treatment. At the face value this seems reasonable, as individuals with lower disability, were more likely to fall below the 'responder' threshold.

5.6.1 Hierarchical analysis of predictors

Few studies have reported multivariate hierarchical models for prediction of treatment outcome in patients with CR. As previously discussed, Peolsson et al. (2003) utilised a stepwise linear regression, and Cleland et al (2007a) reported a CPR for short-term outcomes.

The key feature of the hierarchical models (such as stepwise regression analysis or the CPR) is that the factors included in the model are those which best determine the outcome (variance in a linear model or group allocation for a CPR). They are not a set of the best individual predictors. Therefore, the interpretation of the cluster of factors is often difficult to explain, and specifically within this thesis, where there are no previous studies for comparison.

The next 4 sections discuss the specific CPR for each cohort and for each follow-up interval.

5.6.1.1 Predictors of a successful outcome: conservative group, 3 months

The CPR results suggested that younger patients (age < 40 years), with low to moderate BMI (<24.4), with no recent lifestyle change, with a symptom duration of more than 33 weeks, less than two previous episode, neck flexion range of motion of not more than 40° and who had problems with neck activities at baseline (NPAD factor 1 > 18), are more likely to have a successful short term outcome (3 months) after conservative treatment. When a sub-set of these factors is present, the predicted likelihood ratio of being a responder changes. For example, when three variables were present, the likelihood (LR+ 8.54, 95% CI 4.17, 17.48) of responding to treatment at three months increased the post-test probability of success to 82%. With four variables present, the LR+ value increased to 56.44, raising the post-test probability of success to 100%. However, the 95% CI for this LR+ was wide (3.46, 919.03). Although the post-test probability of success increased to 100% with four out of seven variables, better prediction accuracy was achieved with three out of seven variables because the confidence limits for four of seven are wider. This is a manifestation of the small numbers in specific cells when calculating the LR values. Similar inferences with predictor numbers have been drawn in previous studies (Cleland et al. 2007a; Raney et al. 2009).

High BMI levels have been associated with low back pain (Webb et al. 2003), weakly associated with neck pain (Makela et al. 1991) and a successful outcome following traction treatment in patients with neck pain (Raney et al. 2009). In the present study, BMI of< 24.4 as one of the predictors of a successful outcome at three months, which suggests that for patients with CR, not being overweight, increases the chances of a good response to multi-modality conservative management. The literature provides no evidence that individuals with CR who have a normal BMI are more likely to have successful treatment outcomes.

At baseline, a larger number of patients in the conservative group reported lifestyle changes compared to the ones who did not. This could be one of the factors which may have influenced ‘no lifestyle change’ as one of the predictors in this treatment group. No recent lifestyle change implied that the patient did not have a recent bereavement among family or friends, there was no increased work load or stress at work, recent change of residence nor reported clinical depression. Lifestyle change was assessed as nominal data, using multiple choice questions as part of lifestyle details and not an established scale or questionnaire. ‘No changes in lifestyle’, was one of the predictors for a successful outcome at three months in the conservatively managed group of this study. Although direct comparisons cannot be made, Peolsson et al (2006b) reported that normal ratings of the DRAM were most important in predicting a successful response to surgical treatment for CR where outcome was measured as changes in disability, as well as arm and neck pain. The DRAM, a measure of distress, is an integration of psychosomatic and psychological assessments. The scores distinguish between ‘depressed distressed’ or ‘somatic distressed’. The questions which comprise the ‘lifestyle change’ variable in the present study are similar to ‘depressed distressed’ classification of the DRAM.

Less than one previous episode was one of the conservative group predictors for a successful outcome at three months following treatment. This suggests that patients reporting fewer previous episodes may have a CR disorder where the underlying pathology is less severe and less likely to cause recurrent episodes. Descriptive data of the ‘number of previous episodes’ in the conservative group identified 86% patients with less than one previous episode. This large number of patients with a low number of previous episodes could have influenced the data analysis. Documenting the recall accuracy of previous episodes is an interesting issue, which would be a topic for further study.

Factor 1 of the NPAD measures functional problems associated with neck movement. NPAD factor 1 scores >18, was one of the predictors of a successful outcome three months after conservative treatment. In contrast, increased neck mobility has been associated with successful outcomes in previous studies. Cleland et al (2007a) reported that ‘looking down does not worsen symptoms’ was one of the group predictors for a successful outcome following conservative treatment for CR. Further, in patients with neck pain, Tseng et al (2006) found that predictors of a successful treatment outcome were ‘feeling better with neck movements’ and ‘without feeling worse on neck extension’. NPAD factor 1 has maximum score of 20, and therefore a score of >18 implied a high level of movement limitation was present in the responders. Limitation of movement could have been due to pain, apprehension or structural pathology. Alternatively, the initial limitation of movement may have protected the neck from further injury and contributed to the successful outcome. The NPAD factor 1 score of > 18, which reflects neck movement restriction, was effectively treated with conservative management, and such that patients with this high level of movement limitation became responders at 3 months.

Although the list of predictors was large, it took only three of seven predictors to increase the post-test probability of success to 82%. The predictors as a group raise the likelihood of post-treatment success. This is the first stage of the development of a CPR rule for the treatment of CR, and therefore requires further validation in future CPR studies.

5.6.1.2 Predictors of a successful outcome: conservative group, 12 months

The CPR analysis of the conservative group at twelve months suggested that individuals who were likely to have a successful outcome were those with a post-graduate educational qualification. Along with this, their radiographic cervical spine curvature could be straight or lordotic, but not kyphotic, for total curvature as well as curvature at the symptomatic level. Further, the range of right rotation should be greater than fifty-five degrees. There were a total of four variables in the group which could predict a successful outcome at twelve months. However, there was a small number of non-responders who did not meet all 4 criteria and a wide CI associated treatment success when the 4 variables were present (95% CI = 0.39, 126.92). Consequently, clinicians should interpret the change in prediction of treatment success from three to four predictors with caution. This may be a function of the statistical analysis, and that similar outcomes may be seen with 3 or 4 of the predictors present (post-test probability of success 93%).

Although 59% of patients in the present study reported a successful outcome at twelve months following conservative treatment, limited long-term follow-up in previous conservative management studies of CR makes it difficult to interpret this response in relation to previous studies. This is the first study to develop a CPR for conservative treatment of CR with a follow-up period of longer than 28 days.

Peolsson et al (2003) reported that higher education was associated with lower disability outcomes following conservative management of CR. In the present study, a post-graduate education qualification was one of the group variables, which predicted a successful outcome at twelve months in the patients with CR who were managed conservatively.

Normal lateral cervical curvature values between C2 and C7 have been reported previously as being on average 34° (range 16° - 66°) (Harrison et al. 1996) and average segmental values as being 6° ± 5°. These values are variable in asymptomatic individuals (Takeshima et al. 2002) and reduced in degenerative conditions (Pointillart et al. 1995; Das et al. 2001; Pickett et al. 2004). At the 3 month follow-up, radiological curvature between C2 and C7 of greater than 11° and curvature greater than 2.5° at the symptomatic segment were individual predictors of a successful outcome in the conservative group, suggesting that curvatures tending towards lordotic values were likely to respond to conservative interventions. However, both variables were included in the final group of predictors of successful outcome in the conservative group only at the twelve month follow-up. Previous conservative management studies have not explored these variables for predicting outcome.

This study has the longest follow-up period and sample size of any conservative treatment study for CR using this method of analysis. The results indicate that responders to conservative treatment did not have severely altered sagittal curvature at baseline. Although curvature values are variable (Penning 1978; Takeshima et al. 2002), and alterations not necessarily linked to the presence of pain (Heidecke et al. 2000; Laing et al. 2001), in the present study, the predictor variables were related to the alignment of the symptomatic segment as well as the cervical spine as a whole. Cervical degeneration as a cause of segmental kyphosis has been reported in previous studies (Pointillart et al. 1995; Das et al. 2001; Pickett et al. 2004). The results of the present study may reflect the less significant changes in sagittal alignment and related degenerative changes in the responders.

The above results and the limited impact of rotation motion impairment suggest that the responders in the conservative treatment group did not have advanced degenerative changes in the cervical spine at baseline. In the surgery group, C2-7 curvature greater than 11° was an individual predictor of a positive outcome at three months, whereas the symptomatic curvature value of greater than 2.5° was an individual predictor at six months and twelve months. These results suggest that lordotic or straight sagittal curvature at baseline is predictive of a successful long-term outcome (12 months).

Repeat radiographs were not performed in the conservative group patients at 12 months. Since the conservative group did not undergo any surgery that may cause the curvature values to change, it is assumed that the curvature values would be unlikely to change over the 12 month follow-up, other than minor changes related to degeneration. Of the 4 variables in the CPR, two were segmental curvatures which suggest spinal alignment and related patterns of load transfer may be important with respect to prognosis in conservatively managed CR. Since the issue of impact of sagittal curvature values on a successful conservative treatment outcome have not been explored in a CR cohort in previous studies, this could well be a topic for future research.

5.6.1.3 Predictors of a successful outcome following surgery: 3 months

The CPR for a successful outcome at three months for the surgery group included the following variables: younger patients (age < 40 years), patients with head neck angle more than 40° and with disability levels < 55 on the NPAD. The absence of non-responders fulfilling all three criteria for a successful outcome, and inclusion of 10% of responders meeting all three criteria resulted in a high LR+ (21.76) but with a wide CI (1.25, 376.19). For clinicians intending to use this CPR to predict the short-term response to surgical treatment in patients with CR, prediction based on two criteria is recommended (LR+ 10.15, 95% CI = 3.35, 30.72) which suggests a likelihood of successful outcome of 82% (compared to pre-test probability of success of 31%).

Head-neck angle of greater than 40° (normative value of head neck angle = 41°) was one of the group predictors for a successful outcome at three months following surgical treatment. This implies that having a forward head posture may increase the likelihood of a successful outcome following surgical treatment for CR. The mean head-neck angle value at 3 months in the responder group was 42 ± 6°. The median value for the responders was 42°, which implies that half the responders had head-neck angle values less than 42°. Although this finding suggests a forward head posture predicts a favourable treatment response, half the responders had head-neck angles less than the normal mean value. However, a forward head posture is not an individual predictor of a successful outcome, but is one of the group predictors. Direct comparisons with other studies cannot be made, as posture measurements have not been included in previous studies of CR. In patients with neck pain, Cleland et al (2007b) found a large percentage of the patient group had a forward head posture, with no significant difference between the responders and non-responders.

Younger patients with lower levels of pain-related disability are more likely to have a better short-term response to surgical treatment for CR. This is supported by the CPR at the 3 month follow-up. Long-term follow-up is necessary to evaluate the success of surgical intervention in the group as a whole.

5.6.1.4 Predictors of a successful outcome following surgery: 12 months

The CPR for the surgery group suggested that lower than moderate disability levels at baseline, cervical flexion less than the normal range (< 40°), cervical rotation range of motion > 55° and a duration of symptoms >33 weeks were the best predictors of a successful outcome at twelve months. Although four predictor variables were included in the model, none of the non-responders met more than 2 of the 4 criteria. The CI of the LR+ (10.18) when three out of four criteria were present was large (95% CI = 0.58, 177.52). Therefore estimating the long-term response to surgical treatment for a patient with CR may be achieved when a minimum of two out of four criteria are present (post-test probability of success 94%).

Summary of discussion

This discussion highlights the limited number of studies reporting treatment outcomes and predictors of outcomes for patients with CR. Comparison of some of the results of this thesis with previous reports was not possible because of absence of comparative data. This thesis covered a range of issues relevant to treatment and evaluation of clinical outcomes in patients with cervical radiculopathy. Normally, a list of predictors is developed with reference to previous research and clinical experience. The predictor variables in the present study were drawn from clinical, functional, radiological, socio-demographic and lifestyle factors. These were measured at baseline and repeated over a period of one year following treatment. Associations between variables were determined at different time-points, and baseline variables were used to predict the clinical outcome at one year. These analyses were conducted in conservative and surgically managed treatment groups. The scope of this study was large and makes a significant contribution to this area of medical research.

The original nature of this study is emphasised with respect to the following issues. This is the first study to (i) study both conservative and surgically treated patients with CR over a period of 12 months in an Indian population (ii) translate the NPAD to Hindi (iii) conduct repeat measurements of cervical ROM in a longitudinal study to determine effects of age and gender (iv) conduct repeat measurements of sagittal radiographic measures of segmental curvature and flexion-extension motion (v) determine differences in segmental radiographic flexion-extension motion data between asymptomatic subjects and patients with CR (vi) compare segmental radiographic and composite active cervical ROM measures in patients with CR and (vii) analyse data using a CPR in patients with CR treated either conservatively or surgically.

For the CPR analysis, the outcome criterion for a successful treatment outcome used in this study was the NPAD score. It is accepted that a different method of defining treatment success may have generated different predictor variables from those identified in this study.

Although the principal objective of this thesis was the development of the CPR, this study is classified as Level IV in the hierarchy of CPR studies (McGinn et al. 2002), which is the lowest level. For the results of this study to be implemented in clinical practice, the CPR will need to be validated in a different clinical setting with different clinicians conducting the research (Level III). If the results can be validated in several clinics, it will attain a level II. The impact analysis study will qualify it for Level I evidence. This study is the essential first step towards the development of the CPR for treatment outcome in patients with CR.

CHAPTER 6

6.0 Conclusions

Results of predictive analysis in a clinical cohort inform our clinical judgement and have the potential to change clinical decisions and reduce unnecessary costs while maintaining quality of care and patient satisfaction. The challenge to clinicians is to evaluate the applicability and impact of the rule and to find ways to capably incorporate the predictors into their daily practice. This study provides the first step (at Level IV of the hierarchy of CPR studies, which is the lowest level) in the formation of the clinical prediction rule. It informs researchers to consider the most powerful predictors in their research.

From the finding of this thesis and in conjunction with the review of the related literature the following conclusions can be drawn:

The Hindi version of the NPAD has test-retest reliability, face, convergent and divergent validity. This opens up opportunities of continued research in the Indian population.

The Posterior Tangent Method is a reliable measure for radiographic sagittal segmental curvature with low typical error values for repeat measurements. Similarly, the Penning's method is a reliable method for measurement of radiographic segmental flexion-extension motion with typical error for repeat measurements calculated as mean 1.83°.

The typical test retest error of head neck angle was large enough for no significant changes to be ascertained during repeat measurements for this measure over a period of twelve months. The typical error suggests that for an individual clinical case study this measure may not be sensitive to document anything except large changes in posture.

The Spin-T goniometer is a reliable and valid measuring instrument of cervical ROM in the Indian population. There are differences in cervical ROM between an asymptomatic and CR population and these are not explained by test error or age or gender. Furthermore, active cervical ROM has a significant relationship with increasing age but not with gender. A longitudinal data suggests however, that over a

6 month period there is a less than 5% chance that normal cohorts have a change in cervical ROM greater than 5 degrees.

Both forms of treatment (surgery and conservative) cause significant reductions in pain and disability scores in a CR cohort. Yet, higher baseline scores can influence an apparent improvement in neck pain and arm pain. This may account for greater changes in the surgery group when compared to the conservative group at twelve months follow-up. Pre intervention pain (independent of treatment strategy) correlates with levels of disability and post treatment levels of pain.

Independent of the type of intervention provided in this study, complete neurological recovery is not a certainty at 12 months follow-up.

Systematic changes during repeat measurements (0-3 months) are likely to occur in association with conservative treatments as assessed by radiographic measures as well as composite active cervical range of motion. In the surgery group at 12 months follow-up, this change in radiological measures was not observed.

Reduced radiographic segmental flexion-extension motion is associated with increased neck pain in a CR cohort, pre and post intervention. Similarly, reduced radiographic segmental curvature is associated with increased neck pain, arm pain and disability measures in a CR cohort, pre and post-intervention. It is also clear that, radiographic segmental flexion-extension motion is reduced in CR compared to an asymptomatic cohort.

On presentation, reduced active composite cervical movements are associated with increase disability and neck pain scores. Prior to any intervention, a positive correlation exists between composite active cervical motion in flexion and extension and radiographic segmental flexion-extension motion in a CR cohort. This association changes when individuals undergo a surgical intervention showing that there are mechanical changes following surgical fusion methods.

Univariate analysis suggest that increased pain at 12 months is more likely in older participants and following conservative treatment in blue and brown collar workers, however the development of CPRs for the different time period and treatment interventions suggest combinations of factors contribute to good or poor outcomes. For example, the predictive CPR generated in different treatment cohorts had common elements of age, duration of symptoms, NPAD scores, active composite neck rotation and neck flexion movements. If a therapist is planning conservative intervention then a good outcome is likely to occur at three months in the presence of a combination of seven variables. Of these seven, 3 to 4 of them, show an increased likelihood of the individual being a responder to treatment. The number of variables suggests that there are multiple factors that contribute to the clinical response in this population. At 12 months, however the main predictors came down to 4 variables.

If a client is planning a surgical intervention pathway for CR, then the outcome at three and 12 months is related to a cluster of three and four variables respectively. In each case, the presence of 2 variables increases the probability of being a responder to about around 80% or higher.

It is now concluded that these predictive models be validated in a similar cohort study program. The use of these predictors in future studies may help in decision making for the appropriate type of treatment and expected outcome in CR patients.

6.1 Limitations

Patients in this study could not be randomised into the treatment groups. This was due to ethical reasons and the prevalent healthcare system in India. Non-randomisation may have caused a sampling bias.

The treatment methods in the conservative group or post surgery did not follow a standardised protocol. A multi-modality treatment method was followed, based on presenting symptoms and underlying pathology.

A larger sample group would contribute to statistical analysis especially considering the number of predictors chosen in this study. However, given the low prevalence of CR, the pre-test probability of achieving a successful outcome at each repeat measurement was higher. This allowed for a comparatively smaller sample size because fewer cases were required to observe a successful outcome to depict the accuracy of the decision making within acceptable confidence limits.

To determine responders of treatment and a successful outcome, this study did not use scales which measured patient satisfaction or global perceived effects. Perceived improvement is important because different patients have different concerns about their recovery, and they consider a treatment successful if their individual concern has improved or recovered. However, it is appropriate to mention that reduction of pain and disability could not be very different from patient satisfaction and perceived improvements.

The clinical assessment at one year in the conservative group was partially done over the phone, some had to be mailed and some patients filled up the questionnaire in person. This may have an implication on the reliability of results.

A control group was not ethically possible. The role of intervention to spontaneous recovery therefore could not be explored.

Although at baseline, the assessor was blinded to the treatment group of the patient, for subsequent assessments, it was not possible for the assessor to be blinded to the surgical patients. The superficial and radiological evidence of the type of treatment was obvious. This may have resulted in a bias of post-surgery assessments.

The follow-up duration was limited to a mean 12 months. For surgical patients a longer follow-up (3-5 years) would be ideal considering fusion of the operated level and its implication on adjacent levels.

The CPR analysis conducted in this study was at Level IV of the category of CPR studies, which is the lowest level. The predictors generated in this study are required to be validated in another patient sample in another setting.

Cultural differences may limit the external validity (generalisability).

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Appendices

Appendix 3.0
Patient/ subject consent form for PhD research project

Title of Project: Functional, radiological and self-reported measures predicting clinical outcome in Indians with a diagnosis of cervical radiculopathy.

I, ____, freely and voluntarily consent to participate in a research project to be conducted by Shabnam Agarwal, a PhD candidate at the University of Western Australia. I understand that the project is being undertaken in order to test the effectiveness of a treatment approach / a method of assessing patients and is part of the candidate's PhD research project.

The procedures have been fully explained to me, including the number of times I will be required to attend the department/ be measured or treated in connection with the project. I understand that my treatment will continue as usual after the study if it is necessary.

I authorise the candidate to keep, preserve, use and dispose off the findings from this research with the provision that my name will not be associated with any of the results.

I understand that I may withdraw my consent and discontinue participation in this research at any time without prejudice to me.

All questions have been answered to my satisfaction and I have read and understood the contents of this form.

Participant _________________________________
Date___________________________

Witness____________________________________Date___________________

I have explained and defined in detail the research procedure to which the subject/patient has consented to participate.

Signature_________________________________
Date____________________________

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STUDY 4

THE EFFECTS OF AGE AND GENDER ON ACTIVE CERVICAL ROM IN AN ASYMPTOMATIC POPULATION IN A LONGITUDINAL STUDY.

ABSTRACT

Objective

To determine the effects of age, gender and time on active cervical range of motion (ROM) in an asymptomatic Indian population in order to provide a normative database for longitudinal clinical trials intending to use cervical ROM as an impairment measure.

Design

Longitudinal cohort study with repeat measurements of cervical spinal range of motion.

Methods

219 (110 males; 109 females) asymptomatic Indian participants (age range 20-89 years) were recruited for measurements of active cervical ROM. Approximately 31 subjects were measured per decade with assessments of cervical ROM (flexion, extension, lateral flexion and rotation bilaterally) conducted at baseline, 3 and 6 months. An experienced physiotherapist used the Spin-T goniometer (intra-tester reliability and validity previously demonstrated) for all assessments of ROM.

Results

Active cervical ROM had a significant relationship with age but not with gender. For both genders, a systematic change in cervical ROM with advancing age, was noted with the rate of movement loss varying between 3° to 5° per decade.

Baseline measures of active cervical ROM were strongly related to assessments at 3 and 6 months – explaining between 72% and 85% of the population variance. Reliability of repeat measurements at 3 months intervals (total 6 months from baseline) of cervical ROM yielded an upper 95% confidence limit for typical error not exceeding 5°.

Conclusion

This study is the first to provide normative data on cervical AROM in an asymptomatic Indian population (2^{nd} to 8^{th} decade). Further, this is the first reliability study to perform repeat measures of cervical AROM three times, over a span of 6 months.

It was concluded that active cervical ROM had a significant relationship with age but not with gender. Changes over a 6 month period would not be expected to be any greater than 5 degrees at the 95% confidence limits.

Implications

The use of ROM impairment would expect a small decline in ROM with age with no more than a 5 degree change in any 6 month period. This change over time is valuable information since it is within the measurement error of expected clinical changes on test re-test assessments during shorter period between assessments.

Key words

Neck, ROM, cervical spine, age, gender, measurement, goniometer, spine movements

Introduction

Cervical range of motion (ROM) is a common measure of impairment in neck pain and the extent of impairment can only be evaluated when compared with normal data. Variability of cervical ROM is an issue, being dependent on examiner, instrument, age, gender and time of the day and time interval between two measurements. These issues were reviewed and discussed in details in studies by (Agarwal et al. 2005c; Agarwal et al. 2005b), who examined the use of the Spin-T goniometer for the assessment of cervical spine ROM. Reliability of cervical ROM have been assessed in previous studies with the Standard Error of Measurement (SEM) <4° (Petersen et al. 2000; Lantz et al. 2003); <5° (Solinger et al. 2000; Haynes and Edmondston 2002), 3-6° for asymptomatic subjects and 2-7° for chronic neck pain patients (Sterling et al. 2002). The period between repeated measurements in reliability studies vary within the literature. For example, reliability assessments have been investigated during the same session (Petersen et al. 2000; Solinger et al. 2000; Haynes and Edmondston 2002) or at a one week interval (Sterling et al. 2002; Lantz et al. 2003). The role of evidence based practice and the longer-term follow-up suggest that a longer duration of test –retest assessments may be warranted. To date, no studies were found that examined long-term test retest data of a large cohort population study.

The effect of age and gender on cervical ROM using reliable measuring instruments have been reported by various authors. (Youdas et al. 1992; Kuhlman 1993; Trott et al. 1996; Sforza et al. 2002). These measurements however were only tested on a single session of testing and the results are summarised in Table 1.

These cohort data sets illustrate a decrease in cervical ROM with progressing age although the results of Sforza et al (2002) cannot be generalised for both genders as the cohort included only males. Previous calculated reductions of active cervical ROM were 5° per decade for extension and 2-3°/ decade for other movements for both genders (Youdas et al. 1992). Loss in extension range of motion for both genders was greater than other movements when an older group was compared to a younger age group (Kuhlman 1993). Although, the generally observation was that both genders demonstrated a significant extension loss from the 2nd through the 5th decade, surprisingly an increase in extension was observed in the 6th decade (Trott et al. 1996). This one off variation may be associated with a small sample size in each decade (n=15). Similar associations with extension were not achieved for the males in the same study or any of the other studies.

The females demonstrated significantly greater range of motion than males for all movements except flexion (Youdas et al. 1992; Kuhlman 1993) although such findings were not demonstrated by Trott et al (1996).

A detailed literature search revealed no available normative data of an Indian population for measures of active cervical ROM. The ability to document the systematic change in normal control Indian subjects over a 6 month period and if gender and age are significant factors in the range of motion adds value to the utility of using cervical ROM as an ongoing assessment of cervical impairment. The purpose of this study was therefore, to document the cervical ROM at 3 month intervals on three occasions within an age cohort of 7 decades for both genders.

Methods

219 (110 males; 109 females) asymptomatic Indian subjects were recruited for measurements of cervical ROM to assess the effect of age, gender and time (Table 2). Subjects were recruited from staff of Belle Vue Clinic, Kolkata, India, and comprised brown, blue and white collar employees, relatives of employees, professionals, as well as persons accompanying patients. The sample represented people from different

states of India and socio-economic backgrounds, thereby contributing to the applicability of the results to the general population. The purpose and procedure of the study was fully explained to the subjects and a signed consent was obtained. Measurements were taken by one physiotherapist with 15 years of clinical experience.

The entire duration of the study was 11 months. The Spin-T goniometer conceived, designed and developed by Haynes and Edmondston (2002) was used to measure cervical ROM in an asymptomatic Indian population in this study. Its reliability and details of the measuring instrument were established (Haynes and Edmondston 2002). The concurrent validity was confirmed in an experimental design study (Agarwal et al. 2005c), where the Spin-T goniometer was tested in all 3 cardinal planes against a gold standard, the Motion star, a 3D position sensor. The results indicated the coefficient of determination (R^2) for all planes of cervical ROM were >0.997. Next a reliability study, a repeat measurement study in an asymptomatic Indian population was conducted (Agarwal et al. 2005b). Important methodological aspects included stabilisation of the participants, familiarisation of the process, warm- up movements, uniformity of instructions and ensuring the same neutral start position for each movement. The reliability of the Spin-T was good where all repeated measures demonstrated high ICCs (All > 0.96, $p < 0.01$) and the typical error values for all trials did not exceed 2.5° and the CV did not exceed 4 %.

The measurements in this study were conducted at baseline with repeat measurements at 3 months and 6 months. Measurements with the Spin-T were taken in the following fixed sequence: flexion, extension, lateral rotation right and left, lateral flexion right and left for all participants in consistency with previous reports (Haynes and Edmondston 2002; Agarwal et al. 2005b). All measurements were taken only once in each direction. The patient distribution is shown in Table 2.

An average of 31 subjects were recruited for baseline measurements in each of the seven age decades (2nd – 8th). Approximately 11% subjects failed to return on each test occasion (Table 2).

All descriptive data were reported as means and standard deviation (SD). Differences between genders were calculated with an un-paired t test (Table 3). Intra-class correlation coefficient (ICC 3,1) was used for repeat measurements of cervical ROM, baseline to 6 months (Table 5). The ICC reflects the inter-trial variance relative to the population variance. The Typical Error, also known as within-subject standard deviation, is the standard deviation in each subject's measurements between tests, after any shifts in the mean have been taken into account (Hopkins 2000) and the Coefficient of Variance (CV%), which expresses the variance as a percent of the group mean, were calculated to determine the degree of error between repeat measurements. Paired data sets of movements for baseline measurements and 6 months measurements in all six directions were compared using a linear regression model analysis (Hopkins 2000) (Figures 1A – 1F). Coefficients of determination (R^2) were calculated as well as systematic change in the intercept. Probability of $p < 0.05$ was considered significant. SPSS for Windows version 11.5 was used for all analyses.

Results

Raw data of active cervical ROM (mean, SD, range) in six directions for each decade (2^{nd} to 8^{th}), measured at baseline, 3 months and 6 months have been presented as an appendix *.

Baseline measures (Table 3) showed gender differences for lateral flexion (left) only. Negative values for mean differences suggested higher cervical mean ROM values in the female gender for flexion, extension, lateral flexion (right and left sides) and lateral rotation (left).

Since the genders did not differ significantly for five out of six movements (Table 3), data for subsequent analysis were pooled to represent age related changes and repeat measurement errors in an asymptomatic Indian population (Tables 4).

For both male and female gender, a systematic change over the age groups for all movements was noted. Cervical ROM reduced with advancing age, the rate of movement loss varying between 3° to 5° per decade. Females had slightly greater ROM mean values when compared to males, but this was demonstrated for some of the measures only (Figures 1A –F).

The results (Table 5) suggested low inter-trial variance ICC > 0.83 which is clinically acceptable and projects high consistency between repeat measures by the same examiner. The ICC values declined when baseline measures were compared with measurements at 6 months implying mild increased variability over the 6 month period between testing. The regression analysis, for the same set of variables, illustrated a moderate coefficient of determination R^2, maximum for extension 0.852, followed by rotation (left) 0.850, rotation (right) 0.806, flexion 0.804, lateral flexion (right) 0.728 and minimum for lateral cervical flexion (left) 0.722. Further analysis including calculation of typical error values were done to delineate changes that reflected repeat measurement errors to differentiate from clinical improvement related to treatment intervention (Table 6). Typical error values were within 5° and the maximum CV% 13% for repeat measures spanning 6 months for movement in each direction in an asymptomatic Indian population (n=166).

Discussion

The discussion of this study on longitudinal analysis of active cervical ROM places emphasises on a reliable and valid measuring instrument for data collection to maximise correlation and minimise error between repeat measurements. Lack of differences in cervical ROM between genders enabled the results of this study to be pooled for further discussions. Thus mean pooled values of active cervical ROM generated in this study were discussed with results of previous studies. Analysis of correlations and differences between measurements of baseline, 3 months and 6 months generated values which deemed cervical ROM a stable measure in future longitudinal studies. Moreover, this is the first longitudinal study to perform a repeat measurement of active cervical ROM from baseline to 6 months. The effect of age on active cervical ROM, well illustrated in the results section, was in tandem with results of previous research.

The Spin-T goniometer has been demonstrated as an accurate and reliable measuring instrument. Intra-tester reliability of repeat measurements during the same session varied between ICC >0.87 (Haynes and Edmondston 2002) and ICC >0.96 (Agarwal et al. 2005b). Typical error values did not exceed 4° (Agarwal et al. 2005b), 5° (Haynes and Edmondston 2002). This study used the Spin-T goniometer for repeat measurements over 6 months. The ICC (3,1) for repeat measures at 3 months interval (baseline vs 3 months) was > 0.91, 3 months vs 6 months > 0.88. ICC values of repeat measurements at 6 months interval (baseline vs 6 months) were lower > 0.84 (Table 4). Typical error values did not exceed 5° and the lower and upper limits of the 95% CL did not exceed 6.5°. (Sterling et al. 2002) had reported a repeat measurement error of 3-6° at 7 days interval. Considering the repeat measurement duration of 6 months in this study, and the normal variability of the cervical spine, a typical error value of maximum 5° spanning age groups (20 – 89 years) for both genders establishes a suggested clinical threshold for detecting real change. The magnitude of the changes observed in this study compare favourably with the clinical threshold generally used within a test sessions of 5°-8° using standard neck ROM assessments (Haynes and Edmondston 2002; Sterling et al. 2002)). Its implication in clinical studies directs longitudinal experimental designs using cervical ROM as an impairment measure to consider the error value prior to declaration of change due to intervention/treatment efficacy/disease.

This study observed no gender differences as seen in previous studies (Youdas et al. 1992; Kuhlman 1993) except for lateral flexion (left). Difference of movement in one direction is not suggestive of an overall trend. Differences may reflect the repeated testing and therefore could reflect a type I error. The clinical magnitude of the changes as observed in this study however were generally small in magnitude and therefore for a clinical interpretation changes of less than 5 degrees over 6 months or between each decade are the upper expected limit of normal variance.

The mean values of range of motion calculated in this study (Table 2, raw data in Appendix) were similar to previous studies (Youdas et al. 1992; Kuhlman 1993; Trott et al. 1996; Sforza et al. 2002). Detailed inspection revealed active flexion range of motion assessed in this study was more than compared to (Youdas et al. 1992; Trott et al. 1996). Flexion range of movement for age group 20-29 was similar to (Kuhlman 1993). Extension for both genders was less than assessed by (Youdas et al. 1992; Trott et al. 1996) Overall, the mean ROM varied between a few degrees more or less as compared to previous studies establishing the natural variability of cervical ROM in a normal population. It would seem from mean data that there is no string indication that the Indian population has a large variability in active cervical ROM when compared to western cohorts.

Descriptive data comparisons of individual ranges of motion revealed mean cervical extension and rotation (both sides) had maximum range followed in descending order by flexion and lateral flexion (both sides) similar to (Sforza et al. 2002)and (Youdas et al. 1992). In the latter study, cervical extension as maximum range was followed by right rotation, left rotation, flexion, right lateral flexion and left lateral flexion. This difference in mean values between left and right was analysed in the current study for lateral flexion only, but not for lateral rotation. Although mean values differ between left and right lateral rotation in previous studies (Dall'Alba et al. 2001; Agarwal et al. 2005a), the differences were not significant.

Reduction of cervical ROM with age for both genders was witnessed for all movements. The rate of reduced ROM and is consistent with previous research (Youdas et al. 1992; Trott et al. 1996; Sforza et al. 2002) although (Lantz et al. 1999)I calculated a larger difference between active cervical ROM in the third decade compared to the fourth, 11.6° for flexion-extension and 8.4° for axial rotation. In this study the movement loss with age was gradual and progressive with no sudden dip or rise.

Age related degeneration can cause changes in the mechanical character and the morphology of the spine (Heller 1992; Debois et al. 1999). In the cervical spine normal motion is usually coupled with motion about at least one other axis (White and Panjabi 1990). This is proposed to lead to universal loss of cervical movement with degeneration associated with aging (White and Panjabi 1990; Bland 1998). The findings of this study are generally consistent with this global decline.

A close analysis of reduction of individual movements visavis increase in age showed that in females maximum loss occurred in mean cervical extension (6°/decade) followed by mean lateral rotation right (5.4°/decade) whereas the male gender showed maximum losses in mean rotation (average 5°/decade), followed by both extension and flexion (4°/decade each). Kuhlman (2003) and Youdas et al (1992) reported similar findings with extension movement. Larger losses of extension in females with aging were attributed to increased dorsal kyphosis and resultant forward head posture (Kuhlman 1993). Extension and rotation movements of the cervical spine display larger range in the 2nd and 3rd decades compared to flexion and lateral flexion. It may be speculated that increased wear and tear in these directions explain larger losses in movement in these directions with aging.

Conclusion

This study is the first to provide data on cervical active ROM in an asymptomatic Indian population (2nd to 8th decade). Active cervical ROM had a significant relationship with age but not with gender. Reliability of repeat measurements at 3 months intervals (total 6 months from baseline) yielded typical error values not exceeding 5°. It is suggested therefore that changes in active cervical ROM of magnitudes of 5 or less degrees would allow the clinician to consider that this is within normal variation of testing changes. Similarly changes in 6 months are not expected to be any larger than 5° and over time there is a slight decline in active ROM. These changes however in terms of the clinical context of follow up (1 -2 years max) would be well within measurement errors of less than 3°.

The results of this study have implications on longitudinal clinical trials aiming to use cervical ROM as a measure for impairment outcome or determine treatment strategies.

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Table 1 Descriptive data (mean ± SD) from previous studies of cervical ROM in asymptomatic subjects – age and gender distribution

				Age groups (in years: decade distribution)						
Author/s	**Sample(n)**	**Gender**	**Mov**	**20-29**	**30-39**	**40-49**	**50-59**	**60-69**	**70-79**	**80-89**
1. (Youdas et al. 1992)	avg 40/decade	M & F	Flex	54±8	47±9	49±11	45±9	41± 8	39±8	40±8
		M	Ext	76±12	68±12	62±12	59±10	57±10	53±14	49±11
		F	Ext	85±10	78±13	77±13	65±16	65±13	54±10	50±14
		M	Rot (R)	69±6	67±7	64±9	61±7	53±7	50±10	46±8
		F	Rot (R)	74±5	71±5	70±6	61±8	65±9	53±8	52±10
		M	Rot (L)	69±7	65±9	62±7	58±8	56±6	49±8	46±9
		F	Rot (L)	71±5	65±8	64±7	62±8	59±9	50±7	50±10
		M	LF (R)	44±7	42±8	38±11	36±5	30±5	26±7	24±6
		F	LF (R)	44±7	46±8	42±9	37±7	33±10	28±7	26±6
		M	LF (L)	41±7	41±10	36±8	35±7	30±5	25±8	23±7
		F	LF (L)	42±5	44±8	41±9	35±6	34±8	27±6	23±7
2. Kuhlman 1993)	Diff 15 >n <25	M	Flex	69±6					58±10	
		F	Flex	70±10					64±8	
		M	Ext	70±6					51±12	
		F	Ext	81±6					52±8	
		M	Rot (R)	90±3					71± 9	
		F	Rot (R)	95±3					73±7	
		M	Rot (L)	90±3					71±9	
		F	Rot (L)	95±4					75±10	
		M	LF (R)	46± 5					34±6	
		F	LF (R)	51±4					37±5	
		M	LF (L)	48±4					36±5	
		F	LF (L)	50±5					39±5	
3. (Trott et al. 1996)	30/decade	M/F	Flex	57	47	47	45			
			Ext	76	65	61	60			
			Rot (R)	78	77	74	70			
			Rot (L)	72	71	64	63			
			LF (R)	48	45	39	35			
			LF (L)	45	40	39	32			
4. (Sforza et al. 2002)	Diff 20> n < 30	M	Flex	60±12	47±5					
			Ext	69±12	70±9					
			Rot (R)	79±7	76±6					
			Rot (L)	75±8	76±8					
			LF (R)	40±8	38±8					
			LF (L)	36±8	40±9					

Measuring Instruments used in different studies : 1. CROM 2. Gravity goniometer 3. 3 space Isotrak system 4. Opto-electric instrument

All measurements are in degrees.

N= number of persons; M = males; F = females; Mov= movement; Flex = flexion; Ext = extension; Rot (R)= rotation right; Rot (L) = rotation left; LF (R)= lateral flexion right; LF (L)= lateral flexion left

Blank spaces in decades imply measurements for those decades not done

Table 2 **Distribution (n) of an asymptomatic Indian population, by age (2nd –8th decade) and gender, measured for cervical ROM at baseline, 3 months and 6 months.**

Age range (years)	Baseline n		3 months n		6 months n	
	male	female	male	female	male	female
20-29	14	16	12	15	11	13
30-39	19	17	18	17	16	15
40-49	17	19	14	14	14	13
50-59	18	17	17	15	13	14
60-69	16	15	15	13	14	13
70-79	16	14	13	14	10	10
80-89	10	11	8	9	5	6
Total	**110**	**109**	**97**	**97**	**83**	**83**

n= number of subjects

Table 3 **Unpaired t-test to analyse differences between genders for cervical ROM measurements in all directions (flexion, extension, lateral rotation right and left, lateral flexion right and left) at baseline in an asymptomatic Indian population (n= 219)**

	Mean difference	95% Confidence Interval of the Difference		t	df	p
		Lower	Upper			
FLEX(M) – FLEX(F)	-0.41	-3.51	2.67	-0.26	217	0.79
EXT(M) – EXT(F)	-0.72	-4.50	3.06	-0.37	217	0.70
LRR(M) – LRR(F)	0.02	-3.34	3.40	0.01	217	0.98
LRL(M) – LRL(F)	-2.58	-5.70	0.53	-1.63	217	0.10
LFR(M) – LFR(F)	-1.87	-4.55	0.79	-1.38	217	0.16
LFL(M) – LFL(F)	-2.99	-5.41	-0.57	-2.44	217	0.01*

Flex = flexion, Ext= extension, LFR = Lateral flexion right, LFL = Lateral flexion left, LRR = Lateral rotation right, LRL = Lateral rotation left, M= Male, F= Female

Table 4 **Repeat measurement values of composite cervical movements (data pooled for age and gender) at baseline, 3 months and 6 months in an asymptomatic Indian population (n=166). Mean (in degrees) and (SD) values.**

	Baseline	**3 months**	**6 months**
Flexion	50 (11)	50 (10)	50 (10)
Extension	59 (13)	60 (13)	60 (13)
LR (R)	60 (12)	60 (13)	61 (12)
LR (L)	60 (11)	60 (10)	61(11)
LF (R)	38 (9)	38 (9)	39 (9)
LF (L)	37 (9)	36 (7)	37 (8)

LR (R)= lateral rotation right, LR (L) = lateral rotation left, LF(R) = lateral flexion right, LF(L) = lateral flexion left

Table 5 **Intra-observer ICC (3,1) values for correlation of measurements between baseline and 3 months, 3 months and 6 months, 6 months and baseline of cervical ROM in all directions, in an asymptomatic Indian population (n=166).**

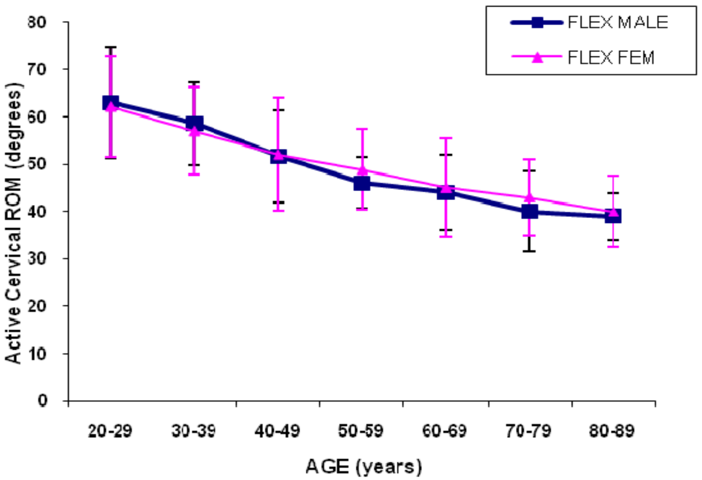
	ICC (3,1)		
	Baseline and 3 months	**3 and 6 months**	**6 months and baseline**
Flexion	0.920	0.949	0.893
Extension	0.964	0.970	0.923
Lateral rotation (R)	0.952	0.952	0.898
Lateral rotation (L)	0.942	0.940	0.922
Lateral flexion (R)	0.913	0.945	0.851
Lateral flexion (L)	0.933	0.882	0.846

R = right, L = left

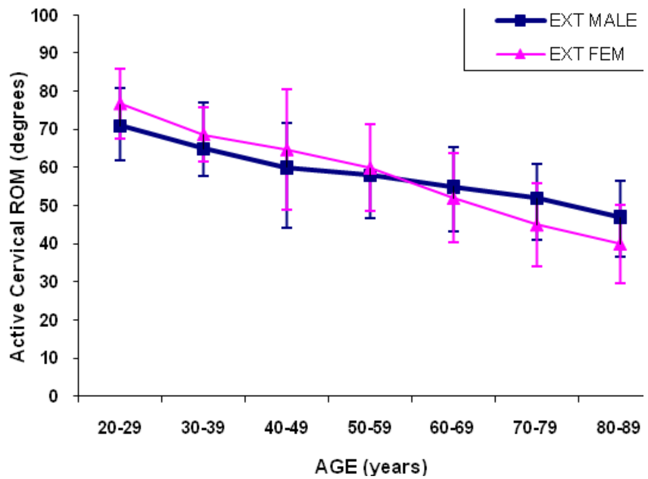
Table 6 **Typical error values with 95% confidence limits (CL) and the CV% to determine error between repeat cervical ROM measurements in all 6 directions (baseline vs 3 months vs 6 months) in an asymptomatic Indian population.**

Movement	**Change in mean**	**Typical error**	**95 % CL**		**CV %**	**95% CI**	
			Lower	Upper		Lower	Upper
Flexion							
Baseline vs 3 months	0.00	3.14	2.84	3.52	6.5	6.1	7.6
3 months vs 6 months	0.23	2.38	2.15	2.67	5.2	4.8	6.0
6 months vs Baseline	-0.23	3.66	3.31	4.11	7.8	7.3	9.1
Extension							
Baseline vs 3 months	0.99	2.61	2.36	2.93	4.7	4.4	5.5
3 months vs 6 months	-0.07	2.35	2.12	2.63	4.2	3.9	4.9
6 months vs Baseline	-0.92	3.79	3.42	4.24	7.0	6.6	8.2
Lateral Rotation (R)							
Baseline vs 3 months	0.27	2.81	2.54	3.15	5.5	5.1	6.4
3 months vs 6 months	0.99	2.81	2.54	3.15	5.6	5.2	6.5
6 months vs Baseline	-1.26	4.02	3.63	4.51	8.0	7.5	9.3
Lateral Rotation (L)							
Baseline vs 3 months	0.03	2.58	2.33	2.89	4.7	4.3	5.4
3 months vs 6 months	0.81	2.60	2.35	2.91	4.9	4.5	5.6
6 months vs Baseline	-0.84	3.12	2.82	3.50	5.8	5.4	6.7
Lateral flex (R)							
Baseline vs 3 months	0.43	2.90	2.61	3.25	8.6	8.1	10.1
3 months vs 6 months	0.08	2.21	2.00	2.48	6.4	6.0	7.5
6 months vs Baseline	-0.52	3.65	3.30	4.09	10.7	10.1	12.7
Lateral flex (L)							
Baseline vs 3 months	-0.28	2.20	1.99	2.47	6.3	5.9	7.4
3 months vs 6 months	0.25	2.77	2.50	3.10	8.1	7.6	9.5
6 months vs Baseline	0.02	3.46	3.12	3.87	10.2	9.7	12.2

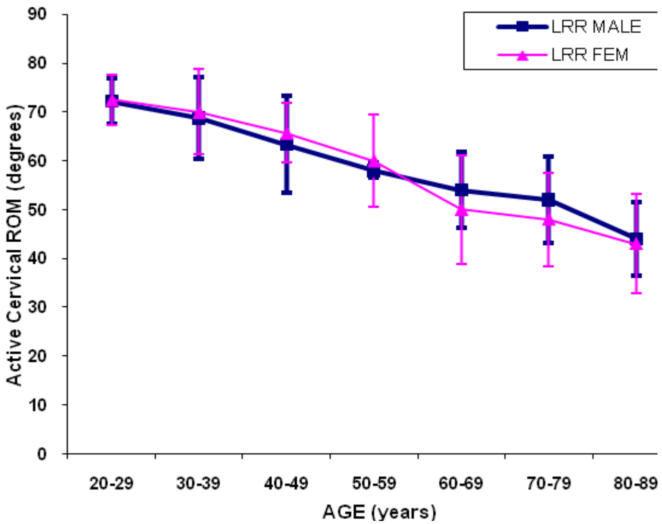
CV = Coefficient of variance


FLEX MALE
FLEX FEM
Active Cervical ROM (degrees)
80
70
60
50
40
30
20
10
0
20-29
30-39
40-49
50-59
60-69
70-79
80-89
AGE (years)

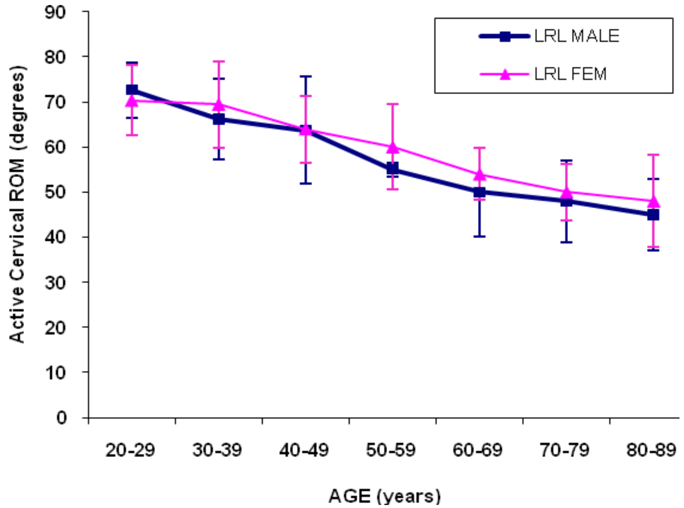
1A


EXT MALE
EXT FEM
Active Cervical ROM (degrees)
100
90
80
70
60
50
40
30
20
10
0
20-29
30-39
40-49
50-59
60-69
70-79
80-89
AGE (years)

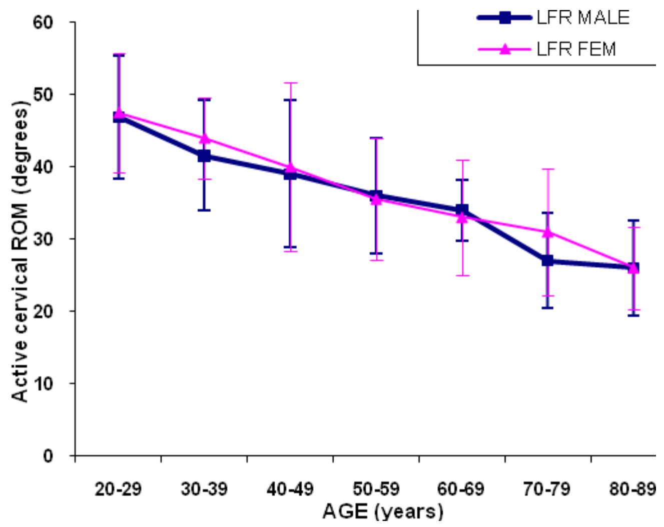
1B


LRR MALE
LRR FEM
Active Cervical ROM (degrees)
90
80
70
60
50
40
30
20
10
0
20-29
30-39
40-49
50-59
60-69
70-79
80-89
AGE (years)

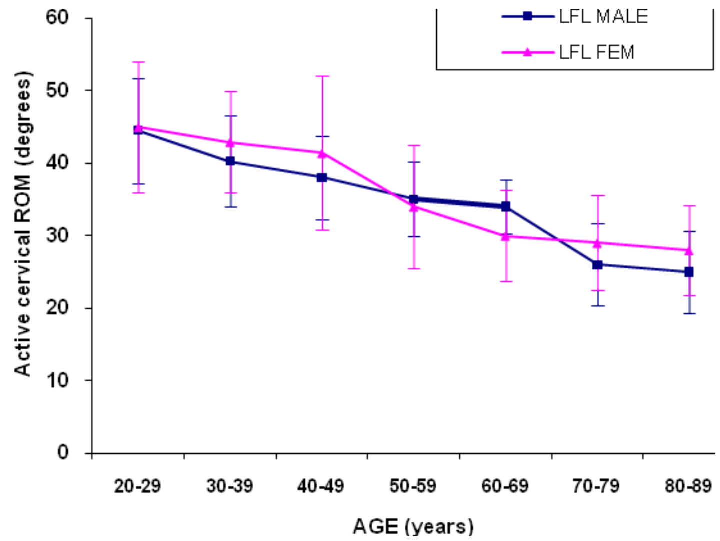
1C


LRL MALE
LRL FEM
Active Cervical ROM (degrees)
90
80
70
60
50
40
30
20
10
0
20-29
30-39
40-49
50-59
60-69
70-79
80-89
AGE (years)

1D



1E



1F

Fem = female, Flex = flexion, Ext= extension, LFR = Lateral flexion right, LFL = Lateral flexion left, LRR = Lateral rotation right, LRL = Lateral rotation left

Figures 1A,B,C,D,E,F The mean (SD) values of cervical ROM in all six directions (flexion, extension, lateral rotation right and left, lateral flexion right and left) for decades 2nd to 8th, in asymptomatic Indian males (n=110) and females (n=109).

Appendix 3.5

Information to radiographers

CERVICAL SPINE RADICULOPATHY RESEARCH

**INFORMATION TO RADIOGRAPHERS FOR X-RAY,
CERVICAL SPINE, LATERAL VIEW
PATIENT POSITIONING (Clark 1986)**

- Patient should be advised to look forward, straight ahead, drop shoulders and be relaxed as much as possible.
- Please do not extend the neck for the lateral view of the cervical spine.
- For uniformity of all X-Rays, the central ray should be directed horizontally at C4-5.
- Please try and ensure C7 vertebral body is visible. In case of a short neck, please use weights if the patient can tolerate.
- Please avoid rotation of the vertebral column.
- Images of each patient should have the same magnification.
- Positioning for flexion and extension views: If the patient is very flexible, 10” × 12” film may be turned sideways for flexion view.

NEUTRAL VIEW

Shabnam Agarwal
Chief Physiotherapist
Belle Vue Clinic
Kolka

Dr RN Sain
Director Radiology

Appendix 3.6
Personal communication with the developer of the posterior tangent method on reliability of the hand drawn method

----- Original Message -----

From: Deed E. Harrison, D.C.
To: shabnam
Sent: Wednesday, February 09, 2005 10:38 PM
Subject: Re: Posterior tangent method

Shabnam Agarwal,

Thank you for your email. It is always pleasant to see that other researchers are interested in utilizing and/or advancing the methodology that we have developed and tested. Currently, we have a computer based digitization program for stored x-ray images in digital format but it is not commercially available yet.

To answer your queries:

1) In some of our recent papers we have digitized vertebral body x-y locations using a sonic digitizer mounted on an x-ray view box. Then using a customized computer program have calculated sagittal plane rotation angles, translation distances, and modeled the sagittal plane geometry of the posterior cervical curve:

1. Harrison DE, Harrison DD, Cailliet R, Troyanovich SJ, Janik TJ, Holland B. Cobb Method or Harrison Posterior Tangent Method: Which is Better for Lateral Cervical Analysis? Spine 2000; 25:2072-78.
2. Harrison DE, Cailliet R, Harrison DD, Janik TJ, Holland B. Radiographic Analysis of Lumbar Lordosis: Centroid, Cobb, TRALL, or Harrison Posterior Tangents? Spine 2001; 26(11): E235-E242.
3. Harrison DD, Harrison DE, Janik TJ, Cailliet R, Haas JW, Ferrantelli J, Holland B. Modeling of the Sagittal Cervical Spine as a Method **to** Discriminate Hypo-Lordosis: Results of Elliptical and Circular Modeling in 72 Asymptomatic Subjects, 52 Acute Neck Pain Subjects, and 70 Chronic Neck Pain Subjects. Spine 2004; 29:2485-2492

2) In past studies we have performed line drawing by hand and in reference #2 below we have compared this to our sonic digitization methods. In summary, both methods are reliable and lead to similar results:

1. Harrison DE, Holland B, Harrison DD, Janik TJ. Further Reliability Analysis of the Harrison Radiographic Line Drawing Methods: Crossed ICCs for Lateral Posterior Tangents and AP Modified Risser-Ferguson. J Manipulative Physiol Ther 2002; 25(2): 93-98.
2. Troyanovich SJ, Harrison DE, Harrison DD, Holland B, Janik TJ. A Further Analysis of the Reliability of the Posterior Tangent Lateral Lumbar Radiographic Mensuration Procedure: Concurrent Validity of Computer Aided X-ray Digitization. J Manipulative Phsyiol Ther 1998;21(7): 460-467.
3. Jackson BL, Harrison DD, Robertson GA, Barker WF. Chiropractic Biophysics Lateral Cervical Film Analysis Reliability. J Manipulative Physiol Ther 1993; 16(6): 384-391.
4. Harrison DD, Janik TJ, Troyanovich SJ, Holland B. Comparisons of Lordotic Cervical Spine Curvatures to a Theoretical Ideal Model of the Static Sagittal Cervical Spine. Spine 1996;21(6):667-675.

Recent studies have begun using computerized enhanced digitization of films either scanned, photographed, or CR/DR x-ray technology already in digital format. These digitization programs have shown similar reliability and in some cases better reliability due to enhanced and enlarged images on the screen. However, you must have customized software to account for magnification of distances--angles will remain constant.

I hope this is of help to you and answers questions. I have attached a few of the pertinent articles for you.

Deed E. Harrison, DC

Appendix 3.7

Patient Socio-demographics

NAME

AGE

SEX Female / Male

WEIGHT

HEIGHT

RIGHT OR LEFT HANDED

MOTHER TONGUE

MARITAL STATUS Single/ Married/ Widowed/ Divorced

EDUCATIONAL LEVEL High School/ Graduate/ Post-Graduate/ Doctorate

REFERRED BY

INPATIENT/ OUT PATIENT

Date of 1st Visit

Date of 2nd Visit

Date of 3rd Visit

Date of 4th Visit

Date of 5th Visit

ADDRESS

PHONE No. Residence

Office

Mobile

E.MAIL

Appendix 3.8

Lifestyle details (Note: not formatted for this appendix)
Please tick (√) the answer considered most appropriate.

Name **Date**

1. **YOUR OCCUPATION (you can tick more than one if applicable)**
   - ☐ Student ☐ Housewife
   - ☐ Computer professional ☐ Accountant
   - ☐ Carpenter ☐ Surgeon
   - ☐ Architect ☐ Doctor
   - ☐ Designer ☐ Self Employed
   - ☐ Other (please specify)
2. **WORK CHARACTERISTICS**
   - ☐ Active (blue/brown collar) ☐ Sedentary (white collar, professional)
3. **WORK INVOLVES?**
   - ☐ Neck bending work ☐ Involves repetitive work
4. **DO YOU EXERCISE/PLAY GAMES REGULARLY?**
   - ☐ Yes ☐ No
5. **ANY CHANGE IN YOUR LIFESTYLE RECENTLY?**
   - ☐ Death of a relative/friend ☐ Increased work load
   - ☐ Work/job related problems ☐ Change of residence
   - ☐ Family tension ☐ No change
6. **HAS THERE BEEN ANY CHANGE IN YOUR BODY WEIGHT (> 10 KGS) IN THE LAST 6 MONTHS ?**
   - ☐ Yes ☐ No
7. **SMOKING BEHAVIOUR.**
   - ☐ Smoking everyday ☐ Smoking now and then
   - ☐ Not smoking now but previously everyday ☐ Never smoked
8. **HAS SURGERY BEEN RECOMMENDED TO YOU FOR YOUR PRESENT CONDITION?**
   - ☐ Yes ☐ No
9. **IF YES, HAVE YOU AGREED OR REFUSED.**
   - ☐ Agreed ☐ Refused
10. **IF YOU HAVE REFUSED, WHY? PLEASE SELECT ANY OF THE FOLLOWING?**
    - ☐ Fear of surgery ☐ Lack of job support
    - ☐ Lack of family support ☐ You believe you will do well with conservative management
    - ☐ Any other reason
11. **ANNUAL INCOME**
    - ☐ Less than Rs. 50,000 ☐ Rs. 50,000- 1 lac
    - ☐ Rs. 1-2 lacs ☐ Rs. 2-5 lacs
    - ☐ More than Rs. 5 lacs

Appendix 3.9 (Note: format altered for Thesis appendix)

Clinical, functional & radiological assessment (pre and post treatment)

NAME: **DATE**

Chief complaint

Onset of current problem (DD/MM/YY)

No. of previous episodes
History & duration of current problem

Any history of injury to the neck? : Yes / No

PREVIOUS MEDICAL HISTORY
Do you suffer from any ailment ? : Yes / No

If yes, specify treatment / drug and dosage

DATE

Chief complaint

Onset of current problem (DD/MM/YY)

No. of previous episodes
History & duration of current problem

Any history of injury to the neck? : Yes / No

Section repeated for repeated visits.

SIGNS AND SYMPTOMS

Morning stiffness

Tenderness

Parasthesia tingling numbness Pins and needles

Muscle spasm

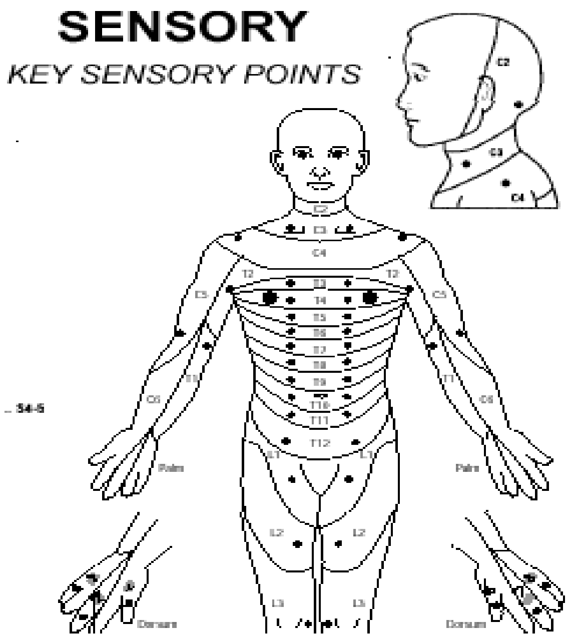
Spurling's test

Arm abduction test

ULTT

Any particular work / activity which increases symptoms

Section repeated for repeated visits.



SENSORY

Dates																
	LIGHT TOUCH		PIN PRICK		LIGHT TOUCH		PIN PRICK		LIGHT TOUCH		PIN PRICK		LIGHT TOUCH		PIN PRICK	
	R	L	R	L	R	L	R	L	R	L	R	L	R	L	R	L
C_2																
C_3																
C_4																
C_5																
C_6																
C_7																
C_8																
T_1																
TOTAL																
(maximum)	16	16	16	16	16	16	16	16	16	16	16	16	16	16	16	16

0 = Absent, 1 = Impaired, 2 = Normal, NT = Not Testable.

MOTOR AND REFLEXES

Dates									
MUSCLES		R	L	R	L	R	L	R	L
C_5	Elbow Flexors								
C_6	Wrist Extension								
C_7	Elbow Extension								
C_8	Finger Flexors								
T_1	Finger Abductor (Little Finger)								
TOTAL									
(maximum)		25	25	25	25	25	25	25	25
REFLEXES 0 = no reflex, 1 = hyporeflexive , 2 = Normal reflex, equal to sound side.									
Biceps									
Triceps									
Supinator									
TOTAL									
(maximum)		6	6	6	6	6	6	6	6

CERVICAL ROM WITH SPIN-T GONIOMETER

Dates				
Flexion				
Extension				
Lat rot (R)				
Lat rot (L)				

CURVATURE MEASUREMENT (PTM)

Dates				
C_2–C_7				
C_2C_3				
C_3C_4				
C_4C_5				
C_5C_6				
C_6C_7				

CERVICAL ROM: FLEXION TO EXTENSION [C2-C7] Penning's ∠

Dates				
$C_2 – C_7$				
Involved segments				
C_2 C_3				
C_3 C_4				
C_4 C_5				
C_5C_6				
C_6 C_7				

POSTURE ASSESSMENT

Dates				
HEAD NECK ∠				

Dates				
MRI				
Curvature				
Level of degeneration				
Disc				
Osteophyte				
Canal diameter				
Facet joint				
Indenting				
Side				
X- Ray				
Curvature (subjective)				
Level of degeneration				
Disc height				
Osteophyte				
Neural foramen				
EMG/ NCV				
Diagnosis				

Appendix 3.10

Treatment record sheet

MEDICAL TREATMENT

PHYSIOTHERAPY TREATMENT
Posture care advice

1. Avoid forward neck bending for long
2. Avoid lifting heavy objects
3. Avoid sleeping with arm under head
4. Avoid hooking telephone between ear and shoulder
5. Avoid jerks while commuting
6. To use a contour pillow
7. To try and sit with head support
8. Avoid turning head to one side for long

TREATMENT	**DOSE/DURATION**
TENS	
Traction	
Muscle Stretching	
Diapulse/ SWD/ IR	
Manual therapy	
Exercises	
Ultrasound	
Others	

TYPE OF BRACE:

LENGTH OF BRACE USAGE:

SURGICAL TREATMENT

Anterior cervical discectomy without fusion.
Type
Anterior cervical discectomy with fusion
Type

SURGERY DETAILS

Levels

No. of levels

Instrumentation used

Instrument details

Graft harvested

Appendix 4.0

Predictor variables for outcome at 6 months in the surgery group

13 baseline individual variables exhibited a significance level (p <0.10) for analysis for a successful outcome at 6 months. The accuracies with 95% CI of all 13 variables are shown in Table A4.1. The cut-off values determined from the receiver operating characteristic curves for continuous variables are shown in Table A4.1. The positive likelihood ratios ranged from 0.45 to 2.29.

Table A4.1 Sensitivity, specificity and likelihood ratios for variables with a significant univariate relationship for identifying successful outcomes in a surgically managed cervical radiculopathy cohort at 6 months

Variable	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	P
Male Gender	0.48 (0.33,0.64)	0.23 (0.09,0.47)	0.63 (0.41,0.97)	2.18 (0.87,5.43)	0.054
NPRS (neck)< 56	0.27 (0.15,0.42)	0.41 (0.21,0.63)	0.45 (0.23,0.89)	1.77 (0.97,3.23)	0.024
NPRS (arm) < 56	0.27 (0.15,0.42)	1.0 (0.81,1)	9.6 #	0.72 (0.6,0.88)	0.017
NPAD <55	0.48 (0.33,0.64)	0.76 (0.52,0.90)	2.06 (0.82,5.18)	0.67 (0.44,1.01)	0.081
NPAD Factor4 <13	0.54 (0.38,0.68)	0.76 (0.52,0.90)	2.29 (0.92,5.69)	0.60 (0.38,0.93)	0.036
PTM (Sympt level) ≤ 2.5°	0.70 (0.54,0.82)	0.0 (0,0.18)	0.70 (0.57,0.86)	10.4 #	0.011
Penning C2-7 ≤ 25°	0.18 (0.09,0.34)	1.0 (0.81,1)	6.6 #	0.81 (0.69,0.94)	0.054
Flexion < 40°	0.27 (0.15,0.42)	1.0 (0.81,1)	9.6 #	0.72 (0.6,0.88)	0.017
Extension < 50°	0.72 (0.57,0.84)	0.0 (0,0.18)	0.72 (0.6,0.88)	9.6 #	0.017
Flexion + extension < 70°	0 (0,0.09)	0.88 (0.65,0.96)	0.113 #	1.13 (0.95,1.34)	0.033
Rotation (right) < 55°	0.70 (0.53,0.82)	0.05 (0.01,0.28)	0.74 (0.58,0.96)	5.05 (0.64,39.61)	0.050
Head neck angle < 40°	0.43 (0.28,0.59)	0.23 (0.09,0.47)	0.56 (0.35,0.89)	2.41 (0.97,5.94)	0.022

this is an estimate of the LR where the zero value in the 2 x 2 contingency table was replaced by 0.5.

The 13 potential predictor variables were entered into a logistic regression analysis which maximised the ability to identify people who were likely to achieve success at 6 months from surgery (Table A4.2). The results of the accuracy analysis, which includes sensitivity, specificity, positive (LR+) and negative (LR-) likelihood ratio and the post-prediction probability of success for each level of the model are shown in Table A4.2. The value of the LR+ indicated how much a given prediction model could raise the probability of obtaining the outcome. The pre-test probability of having a successful outcome was 69% as calculated by the percentage of responders at 6 months (37 out of 54 patients)

At 6 months (Table A4.2), a combination of 2 baseline variables were retained in the final regression model (1) Female gender (2) NPAD scores less than 55. With 1 out of 2 predictors, the LR+ value was 2.01 (95% CI 1.20, 3.34) increasing the likelihood of success with conservative management from 69% to 81%. With 2 of 2 predictors, the LR+ of a responder in this cohort was 6.89 (95% CI = 0.98, 48.01). This had 94% post-test probability of success.

Table A4.2 Combination of predictor variables identified in the logistic regression analysis and associated accuracy statistics of individual predictor variables for identifying successful outcome in the surgery group at 6 months

Number of predictors present	Sensitivity	Specificity	Positive likelihood ratio	Negative likelihood ratio	Probability of success with surgical management
2	0.40 (0.26,0.56)	0.94 (0.73,0.98)	6.89 (0.98,48.01)	0.63 (0.47,0.84)	94%
1	0.94 (0.82,0.98)	0.52 (0.30,0.73)	2.01 (1.20,3.34)	1.02 (0.02,0.42)	81%

Discussion of predictors of surgery group at 6 months

Analysis of outcome measures at six months in the surgery group indicated female gender and a cervical rotation range of motion to the right > 55°as group predictors for a successful outcome. Based on the pre-test probability of 69%, and that patients would respond successfully to a surgical intervention, if patients exhibited both predictors (LR+ = 6.89), the post-test probability of success increased to 94%. It must be conceded that the 95% CI was wide (0.98, 48.01) and for acquiring a greater accuracy in determining a successful outcome, only one out of two predictors should be used (LR+ 2.01, 95% CI = 1.20,3.34; post – test probability of success = 81%).

Female gender was one of the group predictors for a successful outcome at the six months follow-up in the surgical group. Gender has not influenced pain or disability outcome in several previous studies (Thorell et al. 1998; Palit et al. 1999; Zoega et al. 2000). Male gender was a predictor for reduced current pain intensity (Peolsson et al. 2003) although in a later study (Peolsson et al. 2006) gender was not predictive of arm pain, neck pain or disability. Significant percentage improvement in pain was more in females than males at 3-4 weeks but the same was not demonstrated at 3 months (Murphy et al. 2006) in a conservative study. This study is the first to have female gender as a predictor for a successful outcome in a CR surgical cohort at 6 months. Interesting results from previous studies show that females had a significantly greater range of motion than males for all movements except flexion (Youdas et al. 1992; Kuhlman 1993), although results of (Trott et al. 1996) contradict these findings. While the CPR analysis is conducted using a very specific method, one can speculate if the presence of one variable influenced the other.

Considering that only a single variable can successfully predict a successful outcome at 6 months following surgical intervention, the utility of the CPR analysis at 6 months is limited.

References:

Clark, KC (1986). Positioning in Radiography. R. Swallow and Naylor E. London, William Heinemann Medical Books.

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Murphy, DR, Hurwitz, EL, Gregory, A, et al. (2006). "A nonsurgical approach to the management of patients with cervical radiculopathy: a prospective observational cohort study." J Manip Physiol Ther **29**(4): 279-87.

Palit, M, Schofferman, J, Goldthwaite, N, et al. (1999). "Anterior discectomy and fusion for the management of neck pain." Spine **24**(21): 2224-8.

Peolsson, A, Hedlund, R, Vavruch, L, et al. (2003). "Predictive factors for the outcome of anterior cervical decompression and fusion." Eur Spine J **12**: 274-80.

Peolsson, A, Vavruch, L and Oberg, B (2006). "Predictive factors for arm pain, neck pain, neck specific disability and health after anterior cervical decompression and fusion." Acta Neurochir (Wien) **148**(2): 167-73; discussion 173.

Thorell, W, Cooper, BS, Hellbusch, L, et al. (1998). "The long-term clinical outcome of patients undergoing anterior cervical discectomy with and without intervertebral bone graft placement." Neurosurgery **43**(2): 268-74.

Trott, PH, Pearcy, MJ, Ruston, SA, et al. (1996). "Three-dimensional analysis of active cervical motion: the effect of age and gender." Clin Biomech (Bristol, Avon) **11**(4): 201-206.

Youdas, JW, Garrett, TR, Suman, VJ, et al. (1992). "Normal range of motion of the cervical spine: An initial goniometric study." Phys Ther **72**(11): 770-80.

Zoega, B, Karrholm, B and Lind, B (2000). "Outcome scores in degenerative cervical disc surgery." Eur Spine J **9**: 137-43.