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THE VALUE OF ARTIFICIAL DISC REPLACEMENT IN CERVICAL RADICULOPATHY

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Dedicated to my family

The answer my friend is blowin' in the wind
The answer is blowin' in the wind.

- *Bob Dylan*

ABSTRACT

Background; Artificial disc replacement (ADR) is a motion-preserving implant and a further development of existing surgical implants for the treatment of cervical radiculopathy. Theoretically, an artificial disc could decrease stress on adjacent segment and thereby prevent rapid progression of degenerative changes in surrounding segments. ***Aims***; To compare a cervical ADR to fusion in terms of outcome and the most common complications associated with the surgical treatment. To evaluate motion and stability of implanted ADRs with a high accuracy 3DCT method. To develop and validate a questionnaire for the assessment of dysphagia after anterior cervical spine surgery and, to evaluate any difference in dysphagia between the treatment groups.

Patients and methods; 153 patients who met inclusion criteria were included and randomized to either treatment with the Discover artificial disc or fusion with iliac crest bone graft and plating. Randomization was concealed from both patient and caregivers until time for reconstruction of the segment. The patients were followed up for two years and outcome was primarily measured with neck disability index and secondarily with EQ-5D and VAS. Reoperations and complications were also registered in both groups. A subgroup of patients was also investigated with a 3DCT technique for evaluation of motion and stability in the artificial discs. A questionnaire for the assessment of dysphagia was constructed and validated in a group of 45 patients with manifest dysphagia. The questionnaire was then used for the evaluation of postoperative dysphagia after cervical spine surgery.

Results; Data on 137 (91%) patients was available at the follow-up at two years. Nine patients in the disc replacement group and three in the fusion group underwent revision surgery for various reasons during the follow-up. Both treatment groups improved significantly after surgery in all outcome variables. No statistically significant difference in any outcome variable could be seen when the two treatment groups were compared. The motion evaluation showed that a majority of the discs were stable and maintained motion. However, 8% were classified as instable and 5% as ankylotic. Dysphagia was common the first weeks after surgery, but declined and was on group level back to baseline one year postoperatively. When the treatment groups were compared, higher levels of dysphagia were associated with the fusion group.

Conclusion; There was no statistical superiority in any outcome variable in favour of the artificial disc replacement group. Reoperation rates were higher among patients with disc replacement and complications associated to surgery more frequent in the fusion group, but not statistically significant. Dysphagia was common during the first postoperative period, but back to baseline levels after one year. Long-term dysphagia had a higher association with the fusion group.

LIST OF PUBLICATIONS

I. The Discover Artificial Disc Replacement versus Fusion in Cervical Radiculopathy – A Randomized Control Trial with Two Years Follow-Up.

Skeppholm M, Lindgren L, Henriques T, Vavruch, L, Löfgren H, Olerud C.

Submitted for publication

II. In *Vivo* Analysis of Motion and Implant Stability – Evaluation of 38 Discover Artificial Discs using three dimensional CT data.

Skeppholm M, Svedmark P, Noz ME, Maguire Jr GQ, Olivecrona H, Olerud C.

Submitted for publication

III. The Dysphagia Short Questionnaire: an instrument for evaluation of dysphagia: a validation study with 12 months' follow-up after anterior cervical spine surgery.

Skeppholm M, Ingebro C, Engström T, Olerud C.

Spine (Phila Pa 1976). 2012 May 15;37(11):996-1002. doi: 10.1097/BRS.0b013e31823a7a5b.

IV. Comparison of dysphagia between cervical artificial disc replacement and fusion: data from a randomized controlled study with two years of follow-up.

Skeppholm M, Olerud C.

Spine (Phila Pa 1976). 2013 Nov 15;38(24):E1507-10. doi: 10.1097/BRS.0b013e3182a516ef.

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LIST OF ABBREVIATIONS

ACDF	Anterior Cervical Decompression and Fusion
ACSS	Anterior Cervical Spine Surgery
ADR	Artificial Disc Replacement
BMP-2	Bone Morphogenic Protein 2
CI	Confidence Interval
CR	Cervical Radiculopathy
CT	Computed Tomography
DOS	Duration Of Surgery
DSQ	Dysphagia Short Questionnaire
EQ-5D	EuroQol 5 Dimensions
FDA	Food and Drug Administration
HAD	Hospital Anxiety and Depression Scale
HRQoL	Health Related Quality of Life
IDE	Investigational Device Exemption
ICC	Intra Class Correlation
ITT	Intention To Treat
MDADI	MD Anderson Dysphagia Inventory
MCID	Minimal Clinically Important Difference
MRI	Magnetic Resonance Imaging
NDI	Neck Disability Index
NSAID	Non Steroid Anti Inflammatory Drug
OR	Odds Ratio
PP	Per Protocol
QoL	Quality of Life
RCT	Randomized Controlled Trial
RSA	Radiostereometric Analysis
SEM	Standard Error of Measurement
SLP	Speech Language Pathologist
SRD	Smallest Real Difference
TDR	Total Disc Replacement
US	United States (of America)
VAS	Visual Analog Scale

1 INTRODUCTION

1.1 BACKGROUND

Cervical radiculopathy (CR) is defined as a set of symptoms that can occur when one or several nerve roots are affected due to compression in the cervical spine. Pain in the neck combined with radiating pain in one or both arms is the most common reason for the patients to seek care [1]. The condition was first described by Parkinson (1817), although he assumed it was a rheumatic affection of the deltoid muscle [2]. Turner and Oppenheimer published a paper (1936) in which they theorized that the degenerative changes in the structure of the disc and joints were the explanation of the nerve root affection. The annual incidence of CR has in a study by Radakrishnan (1994) been shown to be 83.2/100 000 overall and peaking in the age interval 50-54 years with an incidence of 202.9/100 000. There was a difference between male and female gender with an incidence of 107.3 and 63.5/100 000 respectively. The most frequently affected nerve roots were C7 (46.3%) and C6 (17.6%) and the most common reasons for nerve root entrapment were spondylosis (68.4%) and disc protrusion (21.9%) [3]. Surgery may be considered if non-surgical treatment is not satisfactory and if investigation with magnetic resonance imaging shows findings that correlate to the symptoms. There is no high level evidence that surgical treatment is better than non-surgical in the long term, but seems to give a more rapid improvement in the short term [4-7]. The gold standard surgery technique is anterior cervical decompression and fusion (ACDF), which in a majority of patients leads to reduction of pain and increased quality of life. The main purpose with ACDF is to decompress the nerve tissue and to restore the alignment of the segment in a fixed position [8]. Concerns about how the decreased motion in the fused level is affecting the adjacent segments has given rise to the concept of motion-preserving implants with the aim to decrease stress on adjacent segments [9-11]. The number of different artificial disc replacement (ADR) devices has increased considerably during the past decade and all major manufactures of spinal implants have at least one design on the market. The findings of adjacent level problems after performing ACDF may have accelerated the ADR concepts in hopes of reducing the problem. However, the development of adjacent segment disease is still a controversy and there is no clear evidence that motion-preserving implants prevent adjacent segment disease [12].

1.2 ANATOMICAL AND BIOMECHANICAL ASPECTS OF THE SUBAXIAL CERVICAL SEGMENTS

Subaxial spine includes the levels C3-C7 and a segment is the functional unit consisting of two adjacent vertebras and the mobile anatomic structures that link them together. Motions in the subaxial segments are complex and can be divided into flexion-extension, lateral bending, and rotation. Except for angulation in flexion-extension, there is also always a certain degree of translational motion between the vertebras.

These complex and highly functional biomechanics largely depends on coupled interaction between three main anatomical structures: the disc, the two uncovertebral joints and the two facet joints of each segment. The vertebras are also linked together with stabilizing ligaments and joint capsules, which also affects the motion [13, 14]. Movement is controlled by the muscles that surround the cervical spine with a greater proportion of muscles posterior to the vertebral column. The muscles also have a balancing and stabilizing effect, important for the posture and alignment of the cervical spine.

1.3 DEGENERATIVE CHANGES OF SUBAXIAL CERVICAL SEGMENTS

Degeneration of the spine is largely a normal process that is related to aging, with an uneven distribution, however, between different individuals. The cause of progressing degenerative changes is unclear and probably dependent on several different factors. Genetics, hypoxia, growth factors, inflammatory response and pathology in biomechanics have been proposed as contributing factors for the development of degenerative disc changes and arthritic changes in the cervical joints [15-17]. The most common theory is that degeneration begins in the disc due to morphological and cellular changes leading to decreased content of proteoglycans and water in the nucleus and reduced strength in the surrounding annulus fibrosus [18, 19]. These morphological changes are manifested as decreased disc height and altered motion pattern with a conceivable increased load on the joints [20]. The nerve roots are affected by the degenerative changes either by a herniation in annulus fibrosus, causing a direct mechanical pressure of disc content, or that the collapse of the disc space leads to bulging of the disc and narrowing of the cervical foramina. In later stages of degeneration, osteophytic outgrowths will develop in proximity of the joints and the disc space, which can further affect the neural elements.

1.4 SYMPTOMS AND DIAGNOSIS OF CERVICAL RADICULOPATHY

1.4.1 Clinical manifestations

The main symptom of CR is pain, usually in both neck and upper extremity. Radiating pain is an important symptom as it indicates that one or several nerve roots are affected. Other common associated symptoms are sensory disturbance and numbness in the dermatome supplied by the affected nerve or muscle weakness in the associated myotome. There are considerable overlaps between the roots after exiting the spinal column into the cervical plexus, and, therefore, the symptoms may not always have a clear anatomical distribution [21-23]. A physical examination may also reveal decreased tendon reflexes, inability to use specific groups of muscles or even atrophy of muscles in upper extremity.

There are no universally accepted criteria for the diagnosis of cervical radiculopathy, but in most cases the patients history and the typical clinical findings are sufficient to make the diagnosis. The typical findings associated to the most common nerve root affections are listed in table 1.

Disc level	Root	Pain distribution	Weakness	Sensory loss	Reflex loss
C4-C5	C5	Medial scapular border, lateral upper arm to elbow	Deltoid, supra- and infraspinatus	Lateral upper arm	Supinator reflex
C5-C6	C6	Lateral forearm, thumb and index finger	Biceps, brachioradialis, wrist extensors	Thumb and index finger	Biceps reflex
C6-C7	C7	Medial scapula, posterior arm, dorsum of forearm, 3rd finger	Triceps, wrist flexors, finger extensors	Posterior forearm, 3rd finger	Triceps reflex
C7-T1	C8	Shoulder, ulnar side of forearm 5th finger.	Thumb flexors, abductors, intrinsic hand muscles	5th finger	-

Table 1.

In addition to the neurological examination, there are some provocative tests that can be performed for possible strengthening of the diagnosis. Examples of these are Spurling test, shoulder abduction test, distraction test and the upper limb tension test. The sensitivity and specificity for these tests vary in literature [24]. Differential diagnoses for CR should always be considered and conditions that sometimes will be present with similar symptoms are peripheral nerve entrapment (e.g. carpal tunnel syndrome), disorders of the shoulder, ischemic heart disease, infection (e.g. herpes zoster), neuritis and tumours.

1.4.2 Imaging of the cervical spine

Magnetic resonance imaging (MRI) is the best option for visualizing the typical degenerative changes in discs and joints that may cause nerve root compression, regardless of whether the compression is caused by bony osteophytes or disc. MRI is also appropriate to visualize other spine pathology as tumours, infection and changes caused by trauma [25]. Computed tomography (CT) alone is of limited value in assessing compression of nerve roots, but can be very useful in visualizing bone in cases where bone and soft tissue cannot be clearly differentiated with MRI. Under certain circumstances, such as when the patient has a pacemaker, it is not possible to perform a MRI. In such cases, performing a CT with intrathecal administration of contrast fluid (CT myelography) can be justified. However, because it is an invasive procedure, it should only be considered when there are no alternatives. Plain x-rays do not have any significance in the imaging diagnostics but can still be used to evaluate overall alignment and motion when flexion-extension images is carried out. It should be pointed out that radiological findings must always be interpreted cautiously since pathological findings are very frequent in asymptomatic individuals [26].

1.4.3 Complimentary investigations

Difficulties of an accurate diagnosis can occur in cases where there is doubt about the correlation between the MRI/CT findings and the clinical manifestations. In such cases it can sometimes be helpful to perform selective nerve blocks with local anaesthesia. However, the sensitivity and specificity of selective nerve root blocks are not known and the diagnostic value is debated [27-29]. Nerve-conduction studies can in some cases be helpful, especially when it is doubtful where the nerve lesion is located. One example of this is to distinguish between nerve entrapment in the elbow or the cervical spine [30].

1.5 TREATMENT OF CERVICAL RADICULOPATHY

1.5.1 Non-surgical treatment

Non-surgical therapies are aiming to relieve pain and prevent recurrences. First line therapy usually includes some kind of analgesics such as non-steroid anti inflammatory drugs (NSAID), paracetamol or opioids. Other pharmaceuticals used are steroids, antidepressants, muscle relaxants and neuro-modulating medication. The evidence for medication in the treatment of CR ranges from low to moderate depending on different literature. The current recommendations from The International Association for the Study of Pain (IASP) are that neuropathic pain initially should be treated with neuro-modulators such as gabapentin, pregabalin, tricyclic antidepressants or serotonin norepinephrine reuptake inhibitors [31, 32]. Opioids and Tramadol are recommended as good second-line options and in many patients the side effects will also have an influence on which drugs are chosen [33]. For other non-surgical treatments such as physiotherapy, manipulation by chiropractics and transcutaneous electrical nerve stimulation (TENS), the existing evidence is low [34, 35]. The concept of immobilisation in a neck collar or physiotherapy compared to non-intervention was compared in an RCT and showed significantly better results in both intervention groups, even though the group with no intervention also improved significantly during the follow-up at 26 weeks [36]. The results might to some extent reflect the natural history of CR with acute onset, which to a large extent is unknown. Most of the recommendations for non-surgical treatment are derived from experience or case series studies and the prevailing consensus is that they should be tried of an initial period of at least 6-12 weeks.

1.5.2 Surgical treatment

Surgical treatment of CR can be justified if non-surgical treatment is not satisfactory [37, 38]. If the patient experiences intense, disabling radiating pain that does not show any tendency to disappear within three months of onset, or if there is a rapid progression of neurological deficits, it is generally accepted in Sweden today that the patient consult a spine surgeon to discuss surgical treatment . A condition for this is that findings corresponding to the symptoms are seen on an MRI or CT. The aims with surgery are to decompress the affected nerve root and as far as possible restore normal anatomy. Decompression can be performed with an anterior or posterior approach to the portion of the foramina where the nerve root is affected. Before the 1950s, the posterior approach with decompression by removing a portion of the medial facet joint was the most common way to treat CR surgically [39]. The anterior approach was first described by Robinson and Smith in 1955 and modified in 1958 [40]. The technique gained popularity during the 1960s and are today the most common procedure for decompression of cervical nerve roots. The operation aims at decompressing the neural elements from the anterior side of the vertebral column and at achieving a bony healing between the vertebral bodies. To reach the spinal canal, the disc of the affected segment is removed, and to restore alignment and facilitate bone healing; a bone graft from the iliac crest is inserted in the disc space.

1.5.3 Anatomical considerations and complications

Several important and sensitive anatomical structures must be taken into account when performing surgery in the cervical spine. Damage or pressure on these structures in association with surgery are the most common reasons for unwanted postoperative side effects. The exposure of the anterior cervical column is commonly performed with a longitudinal or transverse entrance medial to the sternocleidomastoideus muscle from the right or the left side. It has by some authors been proposed that the risk for damage to the recurrent laryngeal nerve is lower with a left sided approach since the nerve has a less exposed course than on the right side [41-43], but this also has been contradicted by other authors [44, 45] Damage to the recurrent laryngeal nerve can cause paralysis of vocal cords with voice disturbances and also prolonged dysphagia [43, 46]. Further dissection to expose the vertebral column is done by separating the longitudinal muscles. The carotid artery and vein are identified and retracted laterally, and the oesophagus, which is retracted medially. Damage to the major vessels or oesophagus can result in very serious and even life-threatening consequences [47]. For full exposure of the anterior part of the disc, the longus colli muscle must usually be released in its medial attachment. More laterally, but in proximity to the muscle, the sympathetic trunk is located and damage to it can cause Horners syndrome with miosis, ptosis and sometimes anhidrosis [48]. There is also a risk of damage to the vertebral artery when the posterior elements and the exiting nerve roots are decompressed [49, 50].

Damages to the medulla and nerve roots are also possible with consequences depending on the extent of damage. Another complication associated to bleeding is postoperative hematoma that can cause airway obstruction and be life-threatening [51, 52]. However, despite all the possible risks with this approach, serious complications are not common [53, 54].

1.5.4 Artificial disc replacement

Concerns about the development of progressive degeneration in the adjacent segments of a fusion have led to ideas of motion-preserving devices with the intention to decrease the stress in adjacent levels. In theory, the concept could decrease the development of adjacent segment disease (ASD). The idea of motion-sparing devices for the cervical spine is not new and experiments with different implants and materials have been conducted since the 1950s. The Swedish surgeon Ulf Fernström published the first report on implanted devices with the intention to maintain motion in a series of patients in 1960. He implanted metal balls into the disc space in the treatment of CR with the intention to maintain alignment and motion between the vertebras [55]. The results were discouraging with subsidence of the implants and failure of continued motion of the operated segments. The ideas of motion-preservation were rejected and lay fallow for many years. During the 1980s, there was a new wave of interest in lumbar disc arthroplasty. Encouraging results from studies with the lumbar Charité prosthesis led to the development of the cervical Bristol-Cummings prosthesis, which was presented in 1989 [56]. The first outcome study was presented in 1998 and with more encouraging results than previous experiments. Since then, there has been an explosive development and marketing of various artificial disc replacements. Several randomized trials have been conducted as investigation device exemption (IDE) studies for the approval of the device by the food and drug administration (FDA) in the US [57-62]. A possible bias in the analysis of these studies can be assumed as a majority of them were designed and analysed in cooperation with the manufacturers [63, 64]. There are reports on device related complications as heterotopic bone formation, implant migration and implant failure, although the numbers seems to be small [65-68]. Designs vary between different brands and the artificial disc used in this study is a ball-and-socket construction with unconstrained motion in all directions.

1.6 EVALUATION OF MOTION IN THE CERVICAL SPINE

Most methods for evaluating spinal motion are radiological and focused on measuring motion between spine segments. Studies to evaluate normal range of motion in the cervical spine have previously been conducted showing that factors such as age and pain influence the outcome [69-73]. It is desirable to use a method of high accuracy in order to obtain reliable results. Radiostereometric analysis (RSA) is performed by insertion of tantalum markers into the vertebra and requires a special laboratory equipment setup, but it has been shown to be the most accurate method [74-77].

However, as it is an invasive technique, it is not suitable for routine examination in clinical practice. An alternative non-invasive method previously validated by Svedmark et al. shows almost as high accuracy as RSA, but has the advantage of being performable with an ordinary CT-machine [78, 79]. After that, the motion analysis can be done with 3D imaging in all three planes (sagittal, coronal and transverse). The method is not dependent on implanted markers and can even be used in patients that are not treated surgically where landmarks are chosen in the bone structure. However, the accuracy in the study by Svedmark was obtained by using landmarks on the same artificial disc that was used in this study. We therefore assumed that the accuracy is the same for the evaluation of motion in paper II. See table 2.

Plane	**Rotation** *Degrees*	**Translation** *mm*
Sagittal	0.7	0.4
Coronal	0.4	0.2
Transaxial	0.2	0.5

Table 2.

1.7 POSTOPERATIVE IMPAIRMENT IN SWALLOWING

1.7.1 Normal swallowing

The ability to swallow is dependent on several anatomical structures and a complex innervation from five cranial nerves and the cervical plexus. Swallowing is controlled from the brain stem, largely by reflexes initiated by chewing and food or liquid transport into the oropharynx. Normally, a person swallows about 600 times a day including 200 times when eating. Swallowing can be divided into three separate phases; the oral, the pharyngeal and the oesophageal phase [80]. All of the phases are dependent on normal nerve and muscular function, as well as normal motion in the cervico-cranial junction and subaxial cervical spine [81]. It also requires an absence of obstacles along the anatomical structures involved.

1.7.2 Dysphagia

Dysphagia is defined as an experience of discomfort or difficulty swallowing. It is not a disease-specific diagnosis, rather a diagnosis based on symptoms that can be derived from a variety of conditions [82]. The most common side effect of anterior cervical

spine surgery is dysphagia to some extent. In most patients the dysphagia is transient but there are also reports on more longer-lasting problems [83, 84]. The aetiology of post-operative dysphagia is largely unknown but the short-term dysphagia experienced by almost all patients the first weeks can probably be explained by swelling and deviation of anatomical structures due to retraction during surgery. The cause for long-term problems is more obscure but conceivable reasons are nerve damage, scar tissue formation around the oesophagus, intrinsic muscular impairment in the oesophageal wall, bulk of implants and decreased or altered motion of the cervical spine [85-88].

1.7.3 Evaluation of dysphagia

There are several objective methods for evaluating dysphagia, but they are most commonly used in patients with established or severe problems to determine which phases and anatomical structures that are impaired. Examples of such methods are videofluoroscopy and electrodiagnostics. For evaluation of a patients experience of dysphagia, it is better to use self-evaluation questionnaires [89, 90]. Bazaz et al. developed a questionnaire for the assessment of dysphagia after spine surgery, which has been used in several studies [91]. However, the Bazaz scoring system has never been validated. There are other well-validated questionnaires, mostly developed with the intention to assess dysphagia in malignant and neurological disease [92, 93]. Common to these tools are that they contain a large numbers of questions as to why they are cumbersome to use together with other questionnaires. For the studies III and IV, a shorter questionnaire (DSQ) was developed. We used the MD Anderson Dysphagia Inventory (MDADI) as a gold standard to compare with [93].

2 AIMS

The overall aim of this thesis was to compare artificial disc replacement against fusion in treating cervical radiculopathy, both in terms of outcomes and complications. Objectives with each study were:

I

To compare outcomes between the concept of an artificial disc to gold standard treatment and to register complications associated with the two treatments during a follow-up time of two years.

II

To evaluate in vivo motion and stability of the implanted artificial discs with a non-invasive 3D technique, and also to determine the reliability of this method between independent observers and independent investigations.

III

To test validity and reliability of the Dysphagia Short Questionnaire (DSQ), and also to determine levels of dysphagia over time after anterior cervical spine surgery.

IV

To determine and explain any differences in self-reported dysphagia between patients treated with artificial disc replacement and fusion.

3 PATIENTS AND METHODS

3.1 PATIENTS

All patients, except for the patients in the first validation study in paper III, are from the same cohort. They were included in the RCT for comparison of treatment with ADR or ACDF in cervical radiculopathy. Inclusion was carried out after informed consent during the years 2007-2010. Inclusion and exclusion criteria for the study are listed in table 3.

Inclusion criteria	**Exclusion criteria**
Age 25-60 years	Previous cervical spine surgery
Symptoms of radiating arm pain with a duration of at least 3 months.	More than 2 cervical levels requiring treatment
Correlating findings on MRI on 1 or 2 cervical levels.	Marked osteoarthritis of the facet joints
Eligible for both treatments.	Marked radiological signs or symptoms of myelopathy
Ability to understand and read Swedish language.	Drug abuse, dementia or other obvious reasons for poor compliance
	Cervical malformation or marked cervical instability
	History of whiplash-associated disorder (WAD) or severe cervical trauma
	Pregnancy
	Rheumatoid arthritis, known malignancy, active infection or other systemic disease
	Known allergy or hypersensitivity to any of the constituent materials of the implants or to NSAIDs.

Table 3. Inclusion and exclusion criteria.

3.1.1 Study I

153 patients were initially included in the study. Two patients allocated to ADR did not get the intended treatment and were excluded from further analysis. Due to skewness in the randomization, 81 patients were allocated to the ADR group and 70 to the ACDF group. At the two-year follow- up, five patients in the ADR group and nine patients in the ACDF group were lost to follow-up. Among the nine patients lost in the ACDF group, two died of malignancies during the time of follow-up. Of the remaining 137 patients, nine patients (11%) in the ADR group and three (4%) in the ACDF group underwent secondary surgery. The basic demographics of the included patients at baseline are shown in table 4 and baseline data of outcome variables are shown in table 5.

	ADR n=81	ACDF n=70	p
Men/Women	40/41	33/37	0.79
Age (years) mean (SD)	46.7 (6.7)	47.0 (6.9)	0.81
Smokers n (%)	25 (31)	21 (31)	0.98
Unemployed n (%)	8 (10)	10 (14)	0.37
Weight (kg) mean (SD)	79 (18)	78 (14)	0.69
BMI	26	26	
Sick leave n (%)			
Full time	31 (38)	25 (36)	0.26
Part time	16 (20)	12 (17)	
Other reason	6 (7)	3 (4)	
Not on sick leave	28 (35)	30 (43)	
Analgesic medication n (%)			
Regularly	34 (42)	36 (51)	0.63
Irregularly	34 (42)	25 (36)	
No analgesics	13 (16)	9 (13)	
Neck pain duration n (%)			
<3 months	2 (3)	1 (1)	0.64
3-12 months	15 (21)	19 (27)	
1-2 years	20 (29)	18 (26)	
>2 years	40 (57)	29 (42)	
No neck pain	4 (6)	1 (1)	
Arm pain duration n (%)			
<3 months	3 (4)	3 (4)	0.62
3-12 months	20 (25)	23 (33)	
1-2 years	31 (38)	17 (24)	
>2 years	26 (32)	24 (34)	
No arm pain	0 (0)	0 (0)	
HAD A mean (SD)	7 (4.2)	7 (4.1)	0.93
HAD D mean (SD)	5 (3.5)	5 (3.7)	0.52

Table 4. Demographics at baseline. “Other reason” for sick leave is defined as not being able to work as a result of other ill health. “Analgesic medication” includes all forms of medicaments to ease pain. HAD A is level of anxiety and HAD D level of depression.

	ADR	n=81	ACDF	n=70	p-value
NDI	64.6 (16.2)	64 (26-100)	61.4 (14.2)	61.2 (0-92)	0.25
EQ-5D	0.36 (0.32)	0.25 (-0.18 -0.8)	0.47 (0.30)	0.69 (-0.24 -0.8)	0.03
VAS Neck	57.6 (26.4)	62 (0-100)	58.2 (23.1)	62 (0-100)	0.97
VAS Arm	57.1 (27.5)	60 (0-100)	56.9 (23.0)	62 (0-97)	0.73

Table 5. ITT-analysis of outcome variables at baseline shown as means (SD) and median (range).

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3.1.2 STUDY II

The patients included were the first 28 consecutive patients from the RCT treated with ADR. Resources to do the survey on all patients in the study were not available and the number of patients was based on calculations to perform the ICC between two observers. For practical reasons, they had to live within the Stockholm area for easier accessibility to the investigations that were carried out at Löwenströmska Hospital. 16 were women and the mean age was 46.6 (range 37-57). One patient underwent secondary surgery 13 months after the index operation because of adjacent segment disease (ASD) and another patient 14 months after the index operation because of a persistent root canal stenosis at the index level. The patient with symptoms associated to ASD was treated with ADR at the overlying segment and the patient with root canal stenosis with a unilateral posterior foraminotomy. Both 1- and 2-level ADR were included and the distribution of surgically treated levels is shown in table 6.

Levels	**One-Level ADR (n=18)**	**Two-Level ADR (n=10)**
C4-C5	2	
C5-C6	8	
C6-C7	8	
C5-C7		10

Table 6. Shows distribution of surgical levels.

3.1.3 Study III

3.1.3.1 Validation of the Dysphagia Short Questionnaire (DSQ)

For the validation of the DSQ, 45 patients with known dysphagia were included. They were contacted by two speech language pathologists at a special clinic (ENT, Karolinska Hospital) treating patients with dysphagia. 22 were women and their average age was 64.8 (SD 10.4). Their various diagnoses are listed in table 7.

DIAGNOSIS	No. of patients
Malignancy of the neck region	21
Neurological disease	14
Miscellaneous	4
Xerostomia	2
Unknown	4

Table 7.

3.1.3.2 Evaluation of dysphagia after anterior cervical spine surgery

The patients in this study were all surgically treated for CR with ADR or ACDF at one or two cervical levels. 111 patients were included and they were all operated with an anterior approach. 56 were women and average age was 46.9 (SD 6.7).

3.1.4 Study IV

The patients included in this study were all of the patients included in the RCT with follow-up of DSQ from baseline to two years postoperative, 136 patients in total. 73 were women and the average age was 46.7 (SD 6.7). The distribution between the groups and surgical levels are shown in table 8.

Levels	ADR n (%)	ACDF n (%)
C3-C4	0 (0)	1 (2)
C4-C5	3 (4)	1 (2)
C5-C6	26 (34)	21 (35)
C6-C7	24 (32)	21 (35)
C7-T1	1 (1)	0 (0)
C4-C6	3 (4)	2 (3)
C5-C7	19 (25)	14 (23)
N (% of all)	76 (56)	60 (44)

Table 8. Shows distribution of surgical levels in both groups.

3.2 METHODS

3.2.1. Study I

3.2.1.1 Inclusion

The patients were included after meeting inclusion criteria and informed consent. Inclusion was done at three different spine departments in Sweden; Stockholm Spine Center, Neuro-Orthopaedic Center in Jönköping and the Department of Orthopaedics at Uppsala University Hospital. If the patients did not want to participate in the study, gold standard surgery with ACDF was offered.

3.2.1.2 Randomization process

Randomization was conducted on the basis of a computer-generated list of randomly assembled allocation-numbers. These numbers were transferred to closed envelopes, which were kept in a locker. When a patient was included in the study, a consecutive envelope was linked to that patients personal ID-number. The envelope was kept sealed until it was time for reconstruction of the exposed spine segment and was therefore opened in the operating theatre.

3.2.1.3 Surgery

Surgery was performed according to the Smith-Robinson approach, which has been described earlier. In the ACDF group, an iliac crest bone graft was harvested and inserted in the disc space and thereafter stabilized with an anterior plate of the surgeon's preference. In the ADR group, the Discover artificial disc (DePuy Spine, Ryanham, MA, USA) was implanted. The patients in the ACDF group received bupivacaine via a catheter at the iliac crest bone donor site on the first postoperative day and the ADR group was given ketorolac for ten days postoperatively. Otherwise, the groups were treated similarly with free mobilisation.

3.2.1.4 Clinical outcome measures

Neck Disability Index (NDI) was used as primary outcome variable and was also used for the power analysis. NDI is a well-established and validated outcome score and has also been validated and translated into Swedish [94]. It contains ten main items with multiple-choice questions and is focuses mainly on the evaluation of neck pain and physical function. Adding up the responses provides a total score that will be between 0-100. Higher values indicate more pain and poorer functional status. The Minimal Clinically Important Difference (MCID) for NDI has been set to 7.5 points.

EQ-5D, a non-disease specific questionnaire for the evaluation of health related quality of life (HRQoL), was used as a secondary outcome variable [95]. It contains five questions regarding mobility, self-care, activities, pain and anxiety/depression. The responses are summed up in a formula and will give a result ranging from -0.594 up to one. One represents a very good health status and zero should be interpreted as very bad or deceased. Negative scores should thereby be interpreted as worse than deceased.

Arm and neck **VAS** (visual analogue scale) was used for the evaluation of pain at the different follow-ups. It ranges from 0-100 where 0 is no pain and 100 is the worst imaginable pain.

These outcome measures are the same that are used in the Swedish Spine Register from which we also took other data concerning patient demographics.

3.2.1.5 Data collection and handling

The questionnaires were sent to the patients by mail preoperatively, and after four weeks, three months, one year, and two years. If no reply was received after two reminders, the patient was considered as a loss of follow-up. All data was collected in a database, which was handled by a research nurse. Additional data, such as operating time, blood loss and complications were also entered in the same database.

3.2.2 Study II

Two CT scans of each patient was obtained, one in full voluntary flexion and one in full voluntary extension, providing two separate CT volumes. To achieve this, the patients were positioned on their left side with support for the head (Fig 1.). For the nine patients included in the test-retest evaluation, the procedure was repeated with approximately ten minutes between the investigations. The investigations were carried out according to a low-dose radiation protocol with an estimated radiation of 0.33 mSv/scan and slices were reconstructed at 0.6 mm increments. The image analysis was performed using a 3D image fusion tool, which provides landmarked-based fusion of the two CT volumes. The kinematics analysis measured two motions: 1) movement of the lower prosthetic component relative to the upper prosthetic component, 2) movement between any prosthetic component and adjacent vertebra indicating loosening of the implant. Motion is expressed as rotation and translation in all three planes. Two independent observers evaluated all the images to enable calculation of reliability.

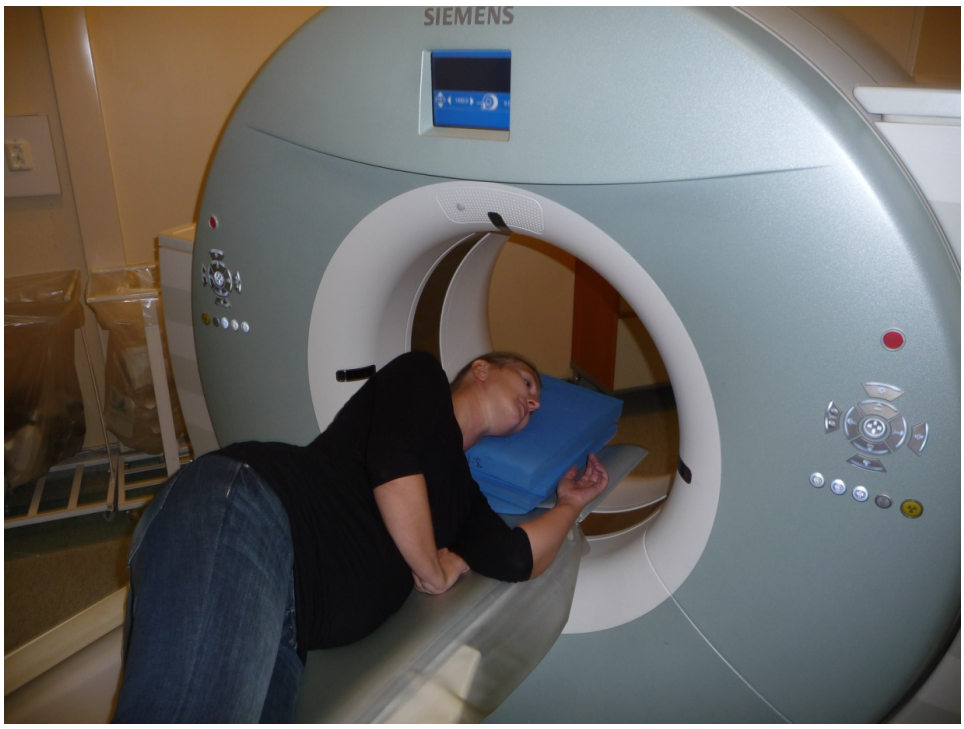

Figure 1. Shows positioning of the patient during the CT-scan.

3.2.3 Study III and IV

3.2.3.1 Development and validation of DSQ

The questionnaire was developed in collaboration with physicians working at the Department for Ear, Nose and Throat diseases with clinical experience from dysphagia. The most common symptoms of dysphagia were captured and the severity of these were weighed and classified with numbers. The questionnaire was translated into English by a qualified translator and retranslated to Swedish by another translator. The questionnaire was also tested on ten test patients to ensure that it was understandable and not too time consuming. The enrolled patients who visited the clinic were asked to answer three forms: DSQ, MDADI and Bazaz at the first visit (T1). A test-retest of the DSQ was also performed with a follow-up, with filling in the DSQ a second time (T2). The EQ-5D for measure of Health Related Quality of Life was also answered at T2. The DSQ questionnaire is shown in fig. 2.

3.2.3.2 Use of DSQ to evaluate dysphagia after anterior cervical spine surgery

The patients from the main study filled in the DSQ preoperatively, at four weeks, three months and one year. The questionnaires were sent to and answered by the patients by mail. Patients with symptoms of severe dysphagia or hoarseness were referred to an ENT-clinic for examination of the vocal cords and swallowing function.

3.2.3.3 Use of DSQ to compare dysphagia between ADR and ACDF

A larger cohort than in the previous study was evaluated with the DSQ preoperatively, at four weeks, three months, one and two years. The questionnaires were distributed in the same way. The ADR and ACDF groups were analysed comparatively

3.3 ETHICAL CONSIDERATIONS

All studies were conducted in conformity with the Helsinki Declaration. All patients received both written and oral information about the studies and inclusion was only done after consent. All patients had the right at any time to discontinue participation in the study. The study protocol was approved by the Regional Ethics Committee in Stockholm (2006/1266-31/3 and 2007/336-31/3).

Ability to swallow	
I have no difficulty in swallowing	0
Food occasionally gets stuck in my throat if I have not chewed it thoroughly enough	1
I find it hard to swallow liquid food	2
I find it hard to swallow solid food	3
I find it hard to swallow saliva	4
Incorrect swallowing	
I do not feel that I swallow incorrectly	0
I sometimes feel I'm swallowing incorrectly, though it does not cause me to cough	1
I sometimes cough in connection with swallowing	2
I frequently cough in connection with swallowing	3
I always get a fit of coughing when I swallow	4
Lump feeling	
I do not have the feeling there is a lump in my throat	0
I sometimes have the feeling there is a lump in my throat	1
I always have the feeling there is a lump in my throat	2
Involuntary loss of weight	
I have not lost weight recently	0
I have lost three or four pounds recently	2
I have lost more than five pounds recently	4
Pneumonia	
I have not had pneumonia due to swallowing incorrectly	0
I have had the occasional bout of pneumonia due to swallowing incorrectly	2
I have had repeated bouts of pneumonia due to swallowing incorrectly	4

Figure 2. The English version of The Dysphagia Short Questionnaire.

4 STATISTICAL ANALYSIS

A database was created in Statistica 9.0,10.0 and 12.0. (StatSoft Inc., Tulsa, OK, USA). This software was used for all calculations and for the creation of diagrams and figures.

A p-value less than 0.05 was considered significant for all analyses except when Bonferroni correction was used. Data were expressed as mean values (SD) or median values (range or intervals), as appropriate.

Study I; Sample size calculation was performed with NDI and an estimated loss of follow-up of 20%. The sample size calculation was based upon a statistical superiority design. Data in both groups were analysed with descriptive statistics, and comparison between the groups was performed with independent t-test, Mann-Whitney U and Fischer exact tests. Analysis of ordinal data within the groups was performed with Wilcoxon`s test and Friedman`s anova. For analysis of repeated measurements between the groups, Kruskal-Wallis anova was used. For some of the variables there were some occasional missing data and these were replaced with a logistic imputation model to reduce the risk of skewing the data. Patients without any data at the two-year follow-up were considered as patients lost to follow-up and were not analysed. All patients who had secondary surgery were included in an intention to treat (ITT) analysis, and the same subjects were excluded from the per protocol (PP) analysis. A Bonferroni correction was used for the level of significance in the subgroup analyses.

Study II; Descriptive statistics were used for the calculation of means, and standard deviations for the motion levels separately. For comparison of motion between different levels, Fisher exact test and Student`s t-test were used. The Wilson quadratic method was used for calculation of a 95% C.I. risk-interval. Intra Class Correlation (ICC) and Cohen`s Kappa for different observers and independent investigations were calculated. The standard error of measurement and repeatability for motions in all three planes were calculated with a 95 C.I.

Study III; Spearman rank test and Gamma test for non-parametric data were used for calculations of correlation between the different outcome sores. Cronbach's alpha was computed for the test of internal consistency of DSQ and a Bland-Altman diagram with 95 C.I. was constructed. Descriptive statistics were also used, as appropriate.

Study IV; The two investigated groups were compared with parametric and nonparametric statistics, as appropriate. The Wilcoxon test for matched pairs was used for comparison within the groups and Kruskal-Wallis anova was used for comparison between the groups at different times of follow-up times. The Fisher exact test was used for comparison between the groups divided into surgical levels. A logistic regression model was constructed and OR and C.I. were calculated for the variables "Group" and "Level".

5 RESULTS AND DISCUSSION

5.1 STUDY I

Both groups improved in the primary outcome variable between baseline and the two-year follow-up. Mean NDI values changed from 63.1(SD 15.3) to 39.8 (SD 19.4) in the ITT analysis and from 63.0 (SD 15.4) to 38.7 (SD 18.7) in the PP analysis. This change in NDI was statistically significant: $p< 0.01$, as were the changes in secondary outcome variables in both ITT and PP analysis: $p< 0.01$. The results were stable between follow-ups at one- and two years regarding NDI in both groups (Fig. 3), as well as in secondary outcome variables.

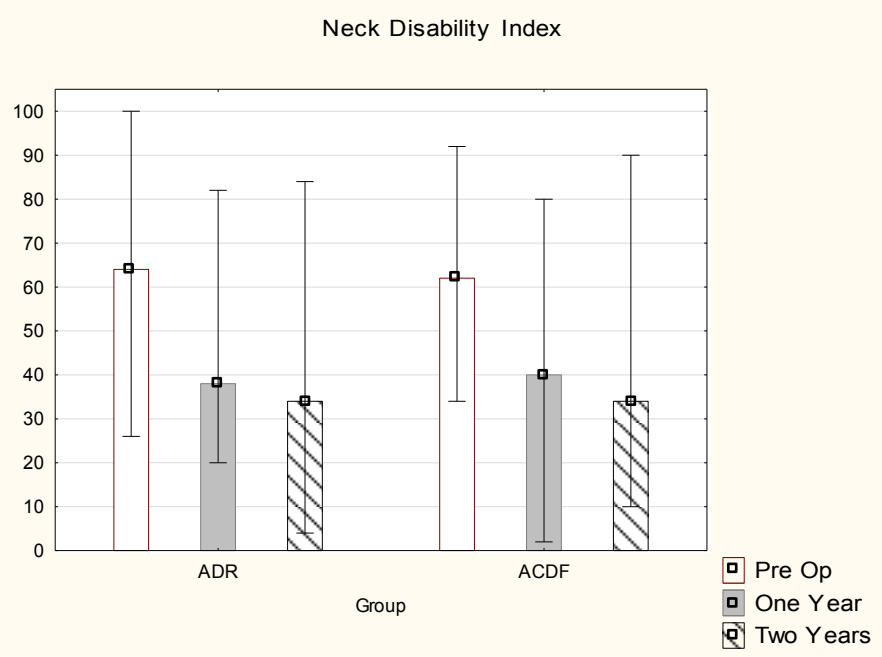

Figure 3. Box shows medians and whiskers range of NDI preoperatively and after one and two years. Per protocol-analysis.

When the two groups were compared, the mean values and medians in the primary and secondary outcome variables were similar in both groups at the two-year follow-up without any statistically significant differences. This was true for both the ITT and the PP analysis and is shown in table 9 and 10.

	ADR	n=76	ACDF	n=61	p-value
NDI	39.1 (20.2)	35.0 (4-94)	40.1 (18.5)	34 (10-90)	0.77
EQ-5D	0.70 (0.30)	0.79 (-0.29 – 1.0)	0.71 (0.26)	0.76 (-0.17 -1.0)	0.92
VAS neck	27.4 (27.3)	18.0 (0-100)	28.6 (24.8)	21.0 (0-73)	0.68
VAS arm	20.7 (23.1)	14.0 (0-90)	20.3 (25.7)	9.0 (0-80)	0.26

Table 9. ITT-analysis of outcome variables shown as means (SD) and medians (range)

	ADR	n=67	ACDF	n=58	p-value
NDI	37.4 (19.3)	34 (4-94)	40.7 (17.9)	34 (10-90)	0.24
EQ-5D	0.72 (0.29)	0.8 (-0.29 – 1.0)	0.71 (0.26)	0.76 (-0.17 – 1.0)	0.50
VAS neck	25.6 (26.6)	16.0 (0-100)	28.7(25.0)	20.5 (0-73)	0.33
VAS arm	19.2 (21.8)	13.0 (0-84)	20.1 (24.9)	9.0 (0-80)	0.75

Table 10. PP-analysis of outcome variables shown as means (SD) and medians (range)

However, the ADR group had a lower mean EQ-5D-value at baseline and this was statistically significant in the ITT analysis, p= 0.03, but not in the PP analysis, p= 0.09. Operating time, blood loss and distribution of surgical levels are listed in table 11.

	ADR	**ACDF**	**p-value**
Op time min (SD)	122 (43)	141 (38)	0.015
Blood loss ml (SD)	212 (159)	218 (178)	0.81
Levels 1/2	58/23	50/20	0.98

Table 11.

The rates of secondary surgery were higher in the ADR group but not statistically significant, p= 0.11. Complications and adverse events, as defined in table 12, were to some extent implant-associated with a higher proportion in the ACDF group, however, not statistically significant, p= 0.16.

Partition of the groups into subgroups of 1- and 2-level treatment groups showed no difference in the ACDF group. The same analysis in the ADR group showed lower mean NDI levels in the 2-level group compared to the 1-level group, 31.3 (SD 16.7) and 41.4 (SD 19.9) respectively. This difference could be clinically relevant but was not statistically significant after Bonferroni correction, p= 0.07. The result is also reflected in EQ-5D with higher mean value in the 2-level group than in the 1-level group, 0.83 (SD 0.2) and 0.67 (SD 0.27) respectively. This difference was statistically significant, p= 0.005, and was found both in the ITT and the PP analysis. It should also be pointed out that no statistical significances were seen between the 1 and 2-level group regarding any of the outcome variables at baseline. The treatment groups were compared regarding sick leave and return to work status during follow-up and the result is presented in table 13. Both groups decreased their consumption of analgesics significantly after surgery, but no significant difference between the groups could be seen at any time during follow-up.

Complication	ADR	ACDF
Postop hematoma[1]	1	0
Infection donor site	n/a	3
Horner´s syndrome	1	0
Donor site pain[2]	n/a	5
Dysphagia[3]	9	12
Implant failure[4]	0	0
C7 palsy	1	0
Wound infection	1	0
Non-union[5]	n/a	1
Dural tear	0	0
Hoarseness[6]	3	4
N (%)	16 (20)	25 (36)

[1] Leading to reoperation.
[2] VAS ≥4 at two-year follow-up.
[3] DSQ ≥4 at two-year follow-up.
[4] Material insufficiency leading to revision surgery.
[5] Leading to reoperation.
[6] First postoperative period.

Table 12.

A comparison between smokers and non-smokers showed unfavourable outcome for the smokers in several outcome variables and was also reflected in the primary outcome variable NDI. Non-smokers improved from a baseline mean NDI of 61 (SD 15.3) to 37.3 (SD 16.7) at the two-year follow-up while corresponding values for smokers was 67.6 (SD 15.3) and 45.8 (SD 24.1). The difference in NDI value between smokers and non-smokers at the two-year follow-up was statistically significant, p = 0.03.

	Four weeks	Three Months	One Year	Two Years
ADR n (%)				
Full time	5 (6)	11 (14)	8 (10)	1 (1)
Part time	30 (37)	14 (17)	8 (10)	1 (1)
Working full time	37 (46)	46 (57)	55 (71)	69 (91)
Other	9 (11)	9 (11)	7 (9)	5 (6)
Total	81	80	78	76
ACDF n (%)				
Full time	6 (9)	9 (14)	9 (14)	1 (2)
Part time	31 (44)	15 (23)	7 (11)	0 (0)
Working full time	26 (37)	30 (45)	40 (62)	52 (85)
Other	7 (10)	12 (18)	8 (13)	8 (13)
Total	70	66	64	61
p-value	0.25	0.85	0.39	0.71

Table 13. Shows return-to-work status at different times of follow-up. ITT-analysis. "Other" means: not working but not on sick leave.

The decisions for reoperation by respective surgeon in both groups were also analysed. Five patients in the ADR group underwent new surgery within the first year, the reason being mostly dissatisfaction with continued neck pain. All of these were 1-level ADR that were converted to fusions at index level. Contributing factors for the decision-making of the surgeon was in three cases a non-optimal implant-positioning and in two cases suspected implant instability or loosening. Two patients underwent a posterior unilateral foraminotomy and the indication for surgery in both cases was arm pain. Another two patients in the ADR group had new symptoms assessed as adjacent segment disease; one was converted to fusions at index level and adjacent level and one had an ADR at adjacent level. Two patients in the ACDF group had secondary surgery with an additional fusion at adjacent level for the same reason and one patient was reoperated because of non-union. All patients who underwent secondary surgery were 1-level procedures, both in the ADR and the ACDF group.

Discussion

Both groups improved significantly after surgery and the interpretation of these data could be that surgery is very effective in a selected group of patients with cervical radiculopathy. However, a weakness with this study, as with many other studies comparing two surgical techniques, is that we do not have a non-surgical control group. Furthermore, knowledge about the natural history of cervical radiculopathy is limited. The results from several RCTs comparing ADR and ACDF have in recent years been published and a majority of these are conducted as IDE-studies, and also with similar designs [57-59, 61].

This study was not part of an IDE study and there are some differences in the design compared to the previous RCTs. First, we included both 1- and 2-level pathology since we believe that this better reflects the mixture of surgery that is usually performed in this group of patients. Secondly, allocation was blinded to both patient and caregiver until time for reconstruction of the vertebral column. The reason for this was to minimize the surgeons' bias in relation to the type of implant and also to prevent non-compliance to allocation. Thirdly, iliac crest bone graft and anterior plating was used in the control group, which was probably the reason for longer operating time in this group. Previously published data indicate that autologous bone graft provides better conditions for bony fusion and, to the utmost, we wanted avoid non-union related complications in the control group [96, 97]. Another difference is that we used a superiority design in contrast to a majority of previous RCTs, which were performed, with non-inferiority designs. The objective with a non-inferiority design is to determine whether the experimental group has an equal or unacceptably worse outcome than the control group. Non-inferiority trials are generally more complex to interpret and can also contain some serious pitfalls in their conclusions [98, 99]. The design can be preferable when the effect size of the active control in comparison to no treatment or placebo treatment is known. Critics of non-inferiority studies have stated that this design may contribute to the introduction of new treatments with equivalent or even inferior effect to existing standard treatment. However, this can sometimes be justified if the new treatment has lower costs or fewer short- or long-term complications. A few studies with longer follow-up time have shown higher rates of secondary surgery in the control group, mostly because of ASD [100]. However, other studies contradict these results and there is still a lack of conclusive evidence for the theory that ADR is protective against ASD [101]. Other possible side effects and complications associated to any of the two treatments have been studied, with ADR showing an advantage, but the impact of these effects will probably not be enough in itself for the new treatment to merit recommendation [102].

In this study, a higher rate of reoperations was performed in the ADR group, which also is somewhat deviant compared to other studies [103, 104]. Even though an analysis of the outcome after secondary surgery is very uncertain – there are varying times for follow-up, too - it seems that the five patients reoperated due to neck pain had a less favourable outcome with very little or no improvement compared to the others who

were reoperated due to other reasons. This could indicate that this subgroup already at baseline had several prognostic factors for a non-favourable outcome. A descriptive analysis of the 12 (8%) patients who underwent secondary surgery revealed a group with a poorer preoperative status. They reported lower HRQoL (mean EQ-5D 0.32, SD 0.33) and somewhat higher NDI (mean 67.1, SD 16.5) compared to the whole study population, but surprisingly enough somewhat lower VAS values. Moreover, 5 (42%) were smokers, 6 (50%) were on full time sick leave because of their neck problems and an additional 3 (22%) were on sick leave for other reasons than neck related disability. They also reported longer duration of symptoms before surgery, 9 (75%) with neck pain and 6 (50%) with arm pain for more than 2 years. A statistical analysis to compare this group to the others in the study was not performed since sample size was too small, but when this group was removed from baseline data, there was not any statistically significant difference in HRQoL between the groups, p= 0.09. The difference is probably clinically relevant and since the levels in EQ-5D were equal in both treatment groups after surgery; the average improvement in HRQoL measured with EQ-5D was greater in the ADR group than in the ACDF group. Patients with poor prognostic factors at baseline were also present in the ACDF group, but these patients were, for some reason, not reoperated to the same extent. One possible explanation is surgeon`s bias in the decision-making process; a combination of uncertainty about a new technology and an opportunity to perform further surgery might have contributed to the rate of reoperations, at least among those patients with predominantly neck pain. We assume that a similar patient in the ACDF group was not offered secondary surgery due to neck pain if the radiographic analysis did not show a clear non-union or implant failure. A non-optimal implant positioning in the ADR group could also have been a factor for poor outcome among these patients. But, in that case, higher improvement values could have been expected after secondary surgery. Revision surgery was not handled as a complication in this study but should still be regarded as a failure of the intended treatment. The results revealed when comparing 1- and 2-level subgroups in the ADR group could be explained by a larger proportion of problems originating from adjacent levels than the index level, initially judged by the surgeon as not being a reason for surgery.

5.2 STUDY II

The mean time between index surgery and CT scanning was 40 months (range 19-50). All prostheses could be successfully evaluated both numerically and visually (Fig. 4). In the sagittal plane, in which the principal movement was performed, mean rotation was 5.1 degrees (SD 3.8) with a range of 0.2 to 15.8 degrees, and a mean translation of 1.0 mm (SD 1.2) with a range of 0.0-5.5 mm. The rotation and translation in the other planes were, as expected, small, and motions in all three planes are presented in table 14. There was a statistically significant difference in mean sagittal rotation with less

motion in level C6-C7 compared to level C5-C6, $p < 0.01$. No significant difference could be seen between C4-C5 level and the other levels. Consideration should be taken regarding the small sample size in this group, which may have affected the result. The mean rotation in the single level ADR group was 5.7 degrees (SD 4.1). In the two level ADR group, the mean rotation in the caudal and the apical ADR were mean 3.3 (SD 2.7) and 5.7 (SD 3.9) degrees respectively, $p = 0.08$.

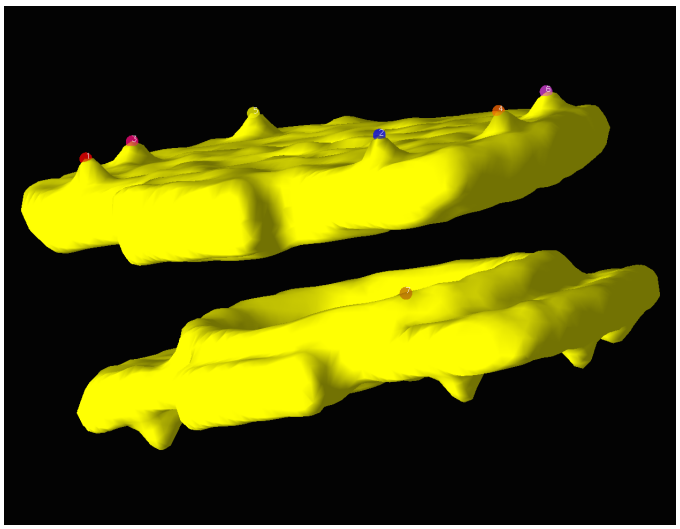

Figure 4.

Evaluation of the registered volumes showed that in two prostheses (5%) there was a clear ankylosis with bridging bone around the ADR and no detectable motion. Three other prostheses had bone masses that bridged the operated segment, but minimal detectable motion and therefore not classified as ankylotic. One of these was the lower level of a two-level replacement with ankylotic upper level and two were one-level replacements. The probability for ankylosis was calculated to be between 1-17% (95% C.I.). In three (8%) of the devices there was a detectable motion between a component of the ADR and the bone. There was also an osteolysis in conjunction with the loose prosthetic component in two of these. The probability of loosening was calculated to be between 3-21% (95% C.I.). All loose components were detected in the one-level group and in the apical part of the two-level ADR. Additionally, there was osteolysis in conjunction with one more apical component without detectable motion between bone and component. No association between ankylosis or loosening and time to follow up could be seen. The repeatability between two observers in the sagittal plane was 1.3 degrees and 1.3 mm (95% C.I.) and the ICC was good or very good except for translation in the coronal plane, which was classed as “fair”. The ICC in the test-retest showed Kappa coefficients varying between 0.31 and 0.93.

Motion	Mean (SD)	Range
Coronal rotation	1.4 (1.5)	0.0 – 5.5
Sagittal rotation	5.1 (3.8)	0.2 – 15.8
Transaxial rotation	1.4 (1.5)	0.0 – 6.2
Coronal translation	0.2 (0.2)	0.0 – 0.8
Sagittal translation	1.0 (1.2)	0.0 – 5.5
Transaxial translation	0.9 (0.8)	0.0 – 2.7

Table 14. Shows mean measured motions in all three planes for all levels.

Discussion

Most previous studies on ADR kinematics have been based on 2D radiographic analyses and focused on segmental motion, either between the components within the ADR or motion in the adjacent level [105]. Stability of the implants has been evaluated, but not to the same extent, and there is a lack of knowledge concerning this [106, 107]. Instability of the implants might theoretically lead to loosening and migration and the consequences of such events could be devastating in the cervical spine. Reports on instable or migrating ADR devices in the literature are quite rare so far and it might not be of any major importance. On the other side, most previous prospective studies have only been presented with two-year data and there is insufficient long-term data for most of the devices on the market. Experiences from other orthopedic implants shows that loosening can be a problem in the longer term and that some implants have led to high frequencies of revision surgery [108-110].The definition of an unstable or loose prosthesis is unclear since there always might be some micro motions between implants and bone. We defined loosening as a detectable motion between bone and prosthesis when comparing the two scans. In one case we found radiographic osteolysis around the spikes of the apical part of the prosthesis without any detectable motion relative to adjacent bone. This is an interesting finding for which there may be various theories. First, there is a possibility that the prosthesis was unstable but that the motion was so small and therefore not detectable with this method. Second, the provocation was inadequate so that the prosthetic part did not move in that specific rotation. In that case, this is a finding of a possible early loosening. However, primary osteolysis is also possible and raises the question of what comes first, osteolysis or loosening? Primary osteolysis caused by micro-particles from wear can be discussed, but support for this cannot be shown in this study. The calculated 95% C.I. for loosening shows a wide range in this material and should be interpreted with caution since the sample size is relatively small.

Another potential problem with the ADR technique, besides loosening, is formation of heterotopic bone. This may cause reduced mobility and even ankylosis. The frequencies in other studies vary and there does not seem to be a clear correlation to patient outcome [111, 112]. We did not further analyze or grade the presence of heterotopic bone but the motion analysis revealed that two prostheses were totally

ankylotic and three were clearly inhibited in motion due to heterotopic bone formation. Theoretically, an ADR that lost motion due to bone formation will function in the same way as a fusion but a new potential problem may occur if the heterotopic bone creates narrowing for the neural and vascular structures. The technique used in this study has been used in other studies and for other implants [113, 114]. It provides 3D information about how the motion is performed in all three planes, which might give a better understanding for the motion. In addition to give a better understanding for how the motion is performed, the method used should have a high accuracy and high reliability. The accuracy for the technique used in this study has previously been evaluated although not as good as RSA *in vitro;* it is almost as good as RSA *in vivo* for the cervical spine [78]. In this study we added reliability tests, both between observers and between scans. The ICC´s between observers are good for most motions but only "fair" for coronal translation [115]. This can be explained by the fact that the range of motion in most patients does not exceed the accuracy of the measurement in that plane. For the motion that the patients performed between the two scans, sagittal rotation, the ICC is very good. This is also the motion with the widest range; the error of the method is relatively smaller in these measurements.

5.3 STUDY III

45 patients answered the DSQ, MDADI and the Bazaz questionnaires at T1. DSQ ranged from 2 to 13 with an average of 6.3 (SD 2.7) and was normally distributed. The MDADI also showed a normal distribution while the Bazaz score showed a more equal distribution of the different alternative answers. There was a significant correlation between the DSQ and the MDADI ($r= 0.59$, $p< 0.01$), but no correlation to the Bazaz score between either the DSQ or the MDADI. There was a weak correlation between DSQ and EQ-5D ($r = -0.27$, $p< 0 .05$) but no correlation between the MDADI and EQ-5D, $r= 0.18$. The Bazaz score showed an inverted correlation to EQ-5D with higher values of HRQoL associated with more dysphagia ($r= 0.31$, $p< 0.05$). Five patients did not participate at T2 and therefore, the test-retest was evaluated on the basis of the 40 patients who attended both visits. The Cronbach's alpha coefficient was calculated to 0.82, indicating very good agreement between T1 and T2. A Bland-Altman diagram with a 95% C.I. was constructed for the DSQ and showed a good agreement between T1 and T2 with no systematic error related to the magnitude of the score (Fig. 5) Preoperatively the DSQ scores were low with a mean value of 1.4 (SD 1.9). 17 patients (15%) had a score of four or higher indicating quite severe dysphagia even before surgery. At four weeks postoperatively, the mean value was 3.2 (SD 2.5) and only 16 (14%) reported a DSQ of zero. 46 (41%) reported a DSQ of 4 or more also indicating a larger group of patients with more severe problems compared to baseline.

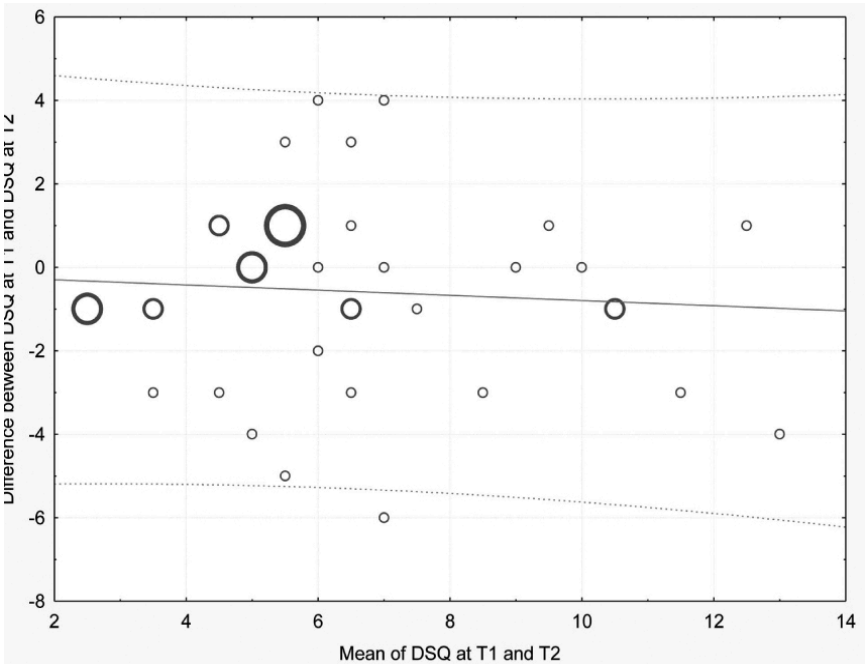

Figure 5. Bland-Altman diagram with 95% C.I. for the DSQ at T1 and T2.

At three months the mean DSQ levels had decreased to 1.7 (SD 2.0) and at one year they were back to baseline levels, 1.2 (SD 1.7). Of the 17 patients who scored four or higher at baseline, 14 improved after surgery with significantly lower DSQ values at one year. The DSQ levels are shown in a box-plot in figure 6.

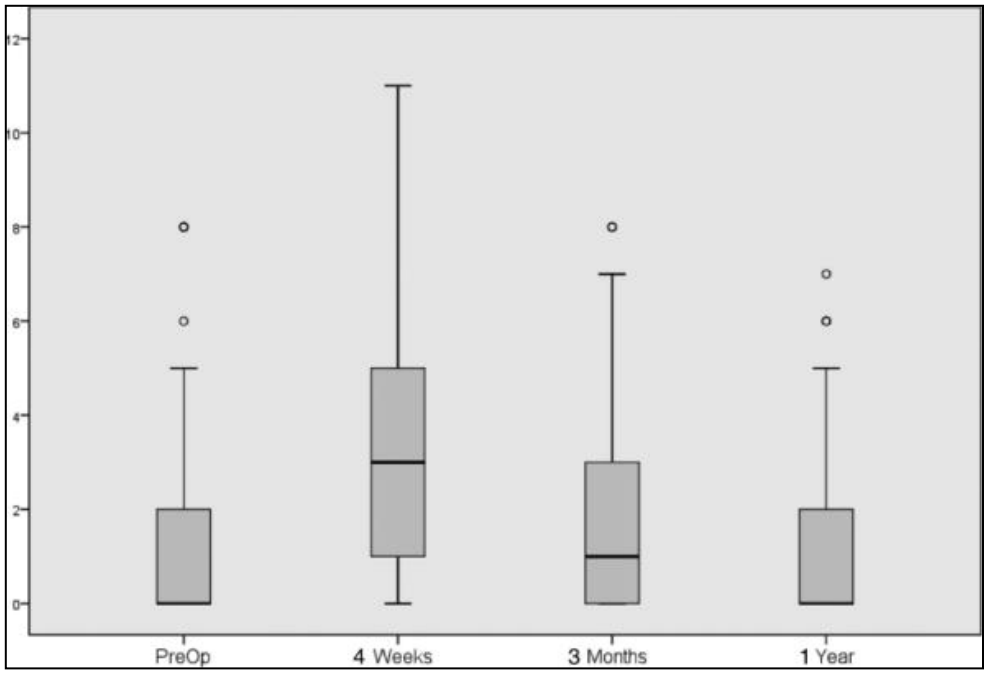

Figure 6. Box-plot of DSQ-values over time. Center equals medians and boxes 1st to 3rd quartiles. Whiskers represent non-outlier range.

Discussion

It may seem unnecessary to develop a questionnaire for swallowing disorders when validated forms already exist. However, the existing questionnaires are probably too extensive to use with a variety of other questionnaires, as in this study. The previously most frequently used questionnaire, the Bazaz score, has not been validated and the reliability of that score may therefore be questioned [91]. Nor could we find any correlation between the Bazaz and the two other questionnaires; this contributes further to uncertainty about its validity. The reasons for this are not clear, but one conceivable explanation could be that it contains too few categories, which may result in an inability to distinguish between patients with different levels of dysphagia. Another reason for criticizing the Bazaz score is how swallowing problems have been classified; for example, inability to swallow liquid always scores higher than problems with solid food. That is not always the case and the reverse situation might be more usual [116-118]. Generally, problems with swallowing liquid are larger problems when there is a neurological dysfunction affecting the oral and pharyngeal phase of swallowing, while problems with swallowing solids may be more affected by obstruction in the oesophageal phase of swallowing. Another problem is how the term "solid" should be defined, as there is probably a quite wide range of different food consistencies between "liquid" and "solid". Speech language pathologists, who are the profession that often examine and evaluate this group of patients, use different kind of foods to test the ability to swallow. Such evaluations may help them to understand which part of swallowing that is impaired and also how the patient can be helped. The patients who were assessed after the anterior cervical spine approach did not have nearly as high levels of dysphagia as the patients included in the first study, which we initially also hypothesized. That was why we wanted to test the questionnaires on a group of patients with established dysphagia since validation on a group of patients from the second study would have resulted in too many patients scoring very low and contributing to considerable floor effects. The good correlation to "the gold standard" MDADI can be seen as a support for progressivity; low values are generated in patients with milder forms of dysphagia and higher values in patients with more severe dysphagia.

In the second part of the study, we found that at least 15% of the patients experienced a non-negligible dysphagia before surgery. The incidence of dysphagia among a normal population is not well known and it is unclear if these levels could be expected or if it should be interpreted as a consequence of cervical spondylosis. One argument for the latter is that a normal function in cervical spine motion, muscular function and nerve function is probably important for the swallowing mechanism to some extent. All of these functions can be affected by changes in cervical spondylosis. Large degenerative osteophytes may sometimes also develop as a consequence of the spondylosis and in severe cases result in a swallowing obstruction in the oesophageal phase. This was not the case in our study population, as this would have rendered exclusion. At the four-week follow-up the DSQ levels were significantly higher, but still, on average lower levels compared to the patients in the first part of the study. This indicates that the patients undergoing cervical spine surgery do not really have the same problem as the patients with dysphagia caused by malignancies or neurological disease. The dysphagia

among the patients after spine surgery was also clearly transient with levels almost back to baseline at three months. In the short term, it seems clear that surgery causes dysphagia in almost all patients to a certain extent. Some patients may also have more prolonged dysphagia but on a group level, there was no difference between baseline and at one year after surgery.

5.4 STUDY IV

Both groups had similar levels of DSQ and similar demographics besides EQ-5D at baseline. As in study III, both groups showed significantly higher levels of dysphagia at the four-week follow-up compared to baseline, $p< 0.01$. There was no statistically significant difference between the groups until the follow-up at two years when there were statistically higher levels of dysphagia in the ACDF group, $p= 0.04$. These calculations were performed as an ITT analysis; and as twelve patients underwent secondary surgery during the follow-up period, a PP analysis was also performed. The PP analysis did not show any statistically significant differences in comparing the groups during the first year; but as in the ITT analysis, there was a statistical difference at two years, $p= 0.03$. To investigate whether higher levels of dysphagia were associated to treatment group or the number of surgical levels, a logistic regression model with a 95% C.I. was constructed. The level of dysphagia was dichotomized thus: a level of four or higher was considered more "severe" and lower levels as "less severe" dysphagia. OR for Levels (1 vs. 2) and Group (ADR/ACDF) were 0.2 ($p= 0.14$) and 0.019 ($p= 0.02$) respectively. A box-plot of mean DSQ for both groups at all follow-ups is shown in figure 7.

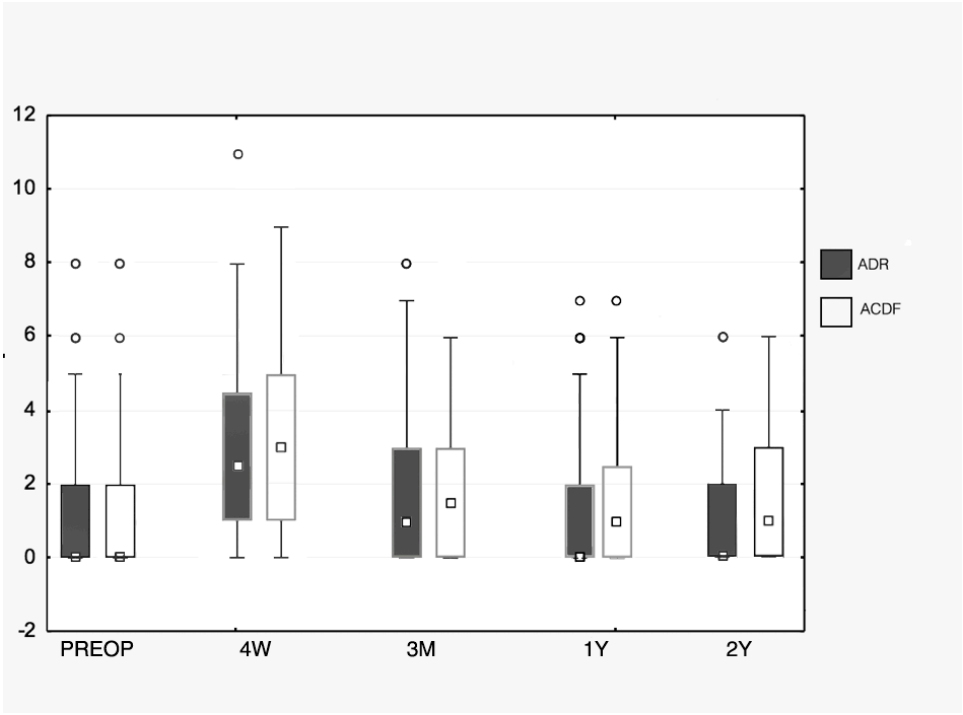

Figure 7. Box-plot of DSQ-values in both groups over time. Center equals median and boxes 1st to 3rd quartiles. Whiskers show range and dots outliers.

Discussion

Several different factors may influence postoperative dysphagia and previous studies have been made, aiming to explain how swallowing is affected by surgery in this area. Possible causes for short-term dysphagia could be postoperative swelling of soft tissues and the esophageal wall, even though a correlation in some previous studies has not been clearly shown. Risk factors for more prolonged dysphagia have also been proposed in previous studies: multilevel surgery, long DOS, gender (women), bulk of implants, use of BMP-2, psychiatric disorders, mal-alignment and nerve damage[119-123]. The question of whether patients undergoing surgery with TDR have less dysphagia compared to patients undergoing ACDF has previously been studied. McAfee et al. showed less dysphagia in the ADR group both after-short time follow-up and after one and two years; 251 patients were included and were evaluated with the Bazaz score [102]. One possible explanation for the different outcomes, according to the authors, could be a less traumatic surgical technique in the patients treated with ADR. Some doubts can be raised as to the results of the study by McAffee et.al since the evaluation of dysphagia was performed with a non-validated instrument and as to the fact that 16% of the patients had had previous surgery. In contrast to the study by McAffee et al., our study design with randomization after decompression but before reconstruction, minimizes the risk for differences in pressure on esophagus and nerve damage which both can theoretically have an impact on dysphagia.

We could not see any statistical differences between the treatment groups until two years after surgery even though the absolute values in the ACDF group were higher at all times during follow-up. Since both groups were treated similarly during surgery, it is more likely that dysphagia in a longer term is associated to the effects of the implants or the number of surgical levels. The logistic regression analysis showed a stronger association to the type of implant than to the number of surgical levels, and the significant difference in DSQ at two years was found in both the one- and two-level group. This finding indicates that the risk for higher levels of dysphagia in the long term is reduced in the ADR group. Two conceivable factors affecting long-term dysphagia can be highlighted in this study. First, decreased motion of the cervical spine, and secondly, bulk of anterior plate fixation. One limitation in this study is that we cannot determine which one of these two factors contributes most to the development of long term dysphagia in the ACDF group. It is also conceivable that altered alignment may contribute to disturbances in the swallowing mechanism in the ACDF group. However, these factors were not analyzed in this study. Even though we found a statistically significant difference between the groups at the two-year follow-up, the differences in DSQ on a group level were unobtrusive. In an attempt to obtain the MCID for the DSQ, the smallest real difference (SRD) was calculated using the ICC from study III and the standard error of measurement (SEM). This is a mathematical method to find the limits for what the smallest clinically relevant difference could be and should be interpreted cautiously [124]. The MCID is usually calculated with other methods including testing in a cohort of patients. The calculated

SRD cannot directly be regarded as the MICD for the DSQ, but can provide an indication of the approximate value. Taking this into account, the statistically significant difference on group level cannot uncritically be transferred to, or interpreted as, a clinically significant difference.

6 GENERAL DISCUSSION

Clinical randomized trials comparing different surgical treatment options are always difficult to conduct, as it can be both ethically indefensible and impracticable to perform them in a blinded fashion. Moreover, to interpret the results accurately, knowledge about the natural history of the disease or knowledge about placebo treatment options is also required. To conduct studies comparing surgery to non-surgery can be even more cumbersome as the design might deter patients from participating. Such a design also excludes all forms of blinding to treatment. Placebo or "sham" surgery can be performed in a randomized fashion blinded to patients but the design is hard to implement for patients seeking care in surgical departments. The patients in this study were blinded to treatment before surgery, which minimized dropouts after allocation and thereby also minimized a serious selection bias. If inclusion criteria were fulfilled it was not difficult to include patients in this study, which can be attributed to the patients` generally having a positive attitude to the concept of an artificial disc, as patients who did not participate were offered treatment with ACDF. A more positive attitude to one of the treatment options might also result in a bias. Totally blinded studies comparing ADR to ACDF have not yet been conducted but would be desirable. When the results from this study are interpreted, it should be pointed out that the primary treatment effect most likely is a consequence of the neural decompression and not of the implant. Possible significant differences between the implants will probably not show before longer-term follow-up, even though trends in differences in complications and revision surgery could be seen in this study after two years.

How to measure outcome is also essential, as outcome measures must be validated and used in other studies for comparison. We choose NDI as primary outcome variable and EQ-5D and VAS as secondary outcomes. NDI is validated in Swedish and has also been used in several earlier outcome studies evaluating both surgical and non-surgical cervical treatments. All of the outcome variables are also used in the Swedish spine register and comparison to larger groups of patients is therefore possible. The results of NDI are usually normally distributed and statistically easy to use while the EQ-5D gives a bimodal distribution, which might cause some pitfalls in the calculations and interpretation. EQ-5D is widely used for evaluation of quality of life in normal population subgroups and for comparison between different treatments, but the results might also be affected by other factors.

Introduction of new techniques are often associated with new side effects and complications. Conceivable complications from ADR treatment are loosening with migration, wear of different components and heterotopic bone formation. There are some reports of migration, but according to existing literature it seems to be quite rare [125-127]. Wear does not generally seem to be a problem but might become more evident in the future when longer-term outcomes are available. Several reports on heterotopic bone formation have been published, but the correlation to patient-reported outcome is still unclear [128]. Progressive bone formation can possibly result in

decreased range of motion or new neurological impairment due to narrowing of root canals. The radiological CT technique used in paper II has the advantage of being non-invasive - in contrast to RSA that requires implantation of tantalum markers - and of being more accurate than 2D x-ray methods used in other studies. Accuracy is very important when evaluating very small motions, especially as in the case with the initial phase of prosthetic loosening. We therefore believe that the 3D CT method will be of great value not only in scientific work but also in clinical practice in the evaluation of ADR patients in the future.

Dysphagia as a consequence of the anterior approach to the cervical spine is well known and has been described and evaluated previously. Bazaz et al. were the first to publish a prospective study and they concluded that postoperative dysphagia was common during the first postoperative period and that a fraction of patients still reported dysphagia one year after surgery. However, no baseline data was collected and the follow-up was performed by telephone interview, using a non-validated dysphagia score. Theoretically, dysfunction in the cervical spine due to spondylosis might cause problems with swallowing even before surgical intervention. The purpose of the studies in paper III was to evaluate dysphagia with a more reliable tool and also to investigate the impact of surgery alone. As in other studies, a small fraction of patients with dysphagia remains even after long-term follow-up. This study shows that this fraction is not larger nor has higher values of dysphagia than the group of patients reporting dysphagia before surgery. On the other hand, it does not seem to be the same individuals in the group reporting late dysphagia as those reporting dysphagia before surgery; this raises two questions. First, does surgery of cervical spine pathology decrease dysphagia in some individuals? Secondly, what is the aetiology of long-term dysphagia in patients undergoing anterior spine surgery? As the patients in the main study were treated similarly regarding surgical exposure and had a similar distribution of surgical levels, a possible impact from implant could be evaluated. The bulk of anterior plating and decreased motion of the cervical spine as a result of fusion could theoretically contribute to more chronic problems with swallowing. Statistically, there was no significant difference between the groups until the two-year follow-up and this can possibly be explained by the fact that early and late dysphagia partly have different causes. The early phase is probably caused more by the surgical trauma to soft tissue, while the later phase could be caused by permanent nerve damage, scar tissue, bulk of implant and decreased or altered motion.

When new treatment alternatives are introduced, it is always important to evaluate the benefits in comparison to already existing alternatives. Besides direct effects, other factors, such as costs and complication rates, must also be considered. The idea of ADR as a technique to prevent ASD could not be confirmed in this study and it is also very dubious to assert that ACDF is causing ASD, as this might be an effect of ongoing degeneration of cervical spine segments. Lower frequencies of ASD after ADR have to some extent been confirmed by studies showing lower revision surgery rates due to ASD problems [100], but it should be pointed out that reoperation rate is not an outcome measure, rather a decision by the surgeon who might also be influenced by different treatment options and requests from the patient, thus not without considerable risk of bias.

7 CONCLUSIONS

STUDY I

No significant superiority in neck disability index or in secondary outcome variables could be seen in the disc replacement group compared to the control group. Reoperation rates were higher among patients with disc replacement; however, they were not clearly associated to implant-related events. A higher proportion of complications associated to surgery were detected in the ACDF group, mostly associated to bone harvesting and postoperative dysphagia. The differences in secondary surgery and complications between the two groups were not statistically significant. No differences in secondary surgery caused by adjacent segment disease could be seen between the two treatments after two years. Treatment with artificial disc replacement did not result in better outcome compared to fusion measured with Neck Disability Index two years after surgery.

STUDY II

The majority of the Discover artificial discs continue to be mobile up to 40 months after implantation, and also to be properly attached. However, 8% of the Discover discs in this study exhibited clear signs of loosening and 5% were ankylotic. Reliability between independent observers was high for all motions larger than the expected measurement error.

STUDY III

The DSQ measures the experience of dysphagia as it correlates well to the MD Anderson Dysphagia Inventory, used as gold standard for dysphagia measurements. The DSQ also showed a good reproducibility which is why it can be considered as a validated tool for measuring dysphagia.

Already at baseline a proportion of patients reported dysphagia. Postoperative dysphagia after ACSS is very common during the first weeks after surgery, but the levels of dysphagia are relatively mild and the dysphagia resolves over time. One year after surgery the levels were back to baseline levels.

STUDY IV

Long-term postoperative dysphagia could possibly be explained by factors like bulk of implants and decreased or altered motion of the cervical spine. The results in this study should be interpreted with caution because of uncertainty in clinically significant differences between the groups.

8 FUTURE STUDIES

Artificial disc replacement is still a relatively new technique in the treatment of cervical radiculopathy. Many studies have shown encouraging results regarding outcome and lower rates of secondary surgery of ADRs, but long-term follow-ups of larger cohorts from non-corporate performed studies are desirable. For this study, a five-year follow-up is planned with the aim to evaluate if there is a difference in ASD between the treatment groups and, in that case, if this will be reflected in outcome data. There is also an ongoing evaluation of the radiological material and the main issues are whether the findings will correlate to any of the outcome variables. As a majority of previous RCTs comparing ADR to ACDF have shown slightly better results for ADR, it is conceivable that studies comparing different prosthesis designs will be conducted in the future. There might be differences in motion pattern, wear and long-term stability, factors that could all affect the outcome.

9 SVENSK SAMMANFATTNING

Studie 1

Cervikal radikulopati är ett tillstånd som kännetecknas av smärta orsakad av att en eller flera nervrötter i nacken är påverkade. Smärtan kan vara mycket intensiv och förläggs typiskt till nacke och med utstrålning i en eller båda armarna. Förutom smärta finns ofta andra associerade symptom som känselrubbningar och muskelsvaghet. Utbredningen av besvären beror på vilken eller vilka nervrötter som är påverkade. Orsaken till att nerverna blir påverkade är degenerativa förändringar i diskar och facettleder som kan resultera i att utrymmet för nerverna minskar till en sådan grad att de komprimeras.

Vanligtvis är besvären intensiva vid debuten och under flera veckor för att sedan minska och därefter helt avklinga. I början syftar behandlingen till att lindra smärtan och detta kan göras med olika analgetika, tillfällig immobilisering eller försök med manuella terapimetoder. Kirurgisk behandling kan övervägas om besvären inte förbättras under de första tre månaderna och är funktionsnedsättande. Den vanligaste tekniken är att dekomprimera de aktuella nervrötterna genom att frilägga kotpelaren framifrån, avlägsna disk och benpålagringar som inskränker utrymmet för nerverna. Förutom att frilägga nerverna syftar operationen till att göra segmentet orörligt med bibehållen distans mellan kotorna, s.k. steloperation. Resultaten efter steloperation är generellt goda med minskade smärtor och ökad livskvalitet. Den förändrade biomekaniken i det stelopererade området gör att en större del av rörelse och belastning istället överförs till intilliggande segment som möjligen kan påskynda utveckling av degenerativa förändringar och ge en potentiell risk för nya besvär. Dessa teorier har gjort att det har skett en utveckling av konstgjorda diskar med syfte att bevara rörligheten i det opererade området och därmed minska belastningen på intilliggande diskar och leder. I studien inkluderades 153 patienter där 81 patienter randomiserades till operation med diskprotes och 70 till steloperation. Det var en likartad fördelning av patienter mellan grupperna avseende basdata samt kön och ålder. Det enda som skiljde grupperna åt var att diskprotesgruppen skattade lägre livskvalitet och denna skillnad var statistiskt signifikant. Randomiseringen var blindad för både kirurg och patient fram till det tillfälle då implantatet skulle sättas in. Två patienter i diskprotesgruppen uteslöts från vidare analys före randomisering då kirurgen under operationen bedömde att de aktuella nivåerna var för degenererade för att behandla med diskprotes. Nio patienter i samma grupp blev reopererade av olika anledningar och fem avbröt studien. Av de patienter som randomiserades till steloperation blev tre reopererade, två avled under uppföljningen och nio avbröt studien. Totalt följdes 137 patienter (91 %) upp efter två år. Båda grupperna förbättrades efter behandlingen och skillnaden var statistiskt signifikanta i alla utfallsvariabler. Däremot fanns inga statistiskt signifikanta skillnader mellan behandlingsgrupperna i någon av utfallsvariabler efter två år och värdena var jämna mellan grupperna. Komplikationsfrekvensen var något högre i steloperationsgruppen men inte statistiskt signifikant.

Studie 2

För att mäta de konstgjorda diskarnas rörlighet krävs någon form av radiologisk teknik. Noggrannheten i mätningen till stor del beror på vilken teknik som används. I många av de tidigare studierna har konventionella röntgenmetoder använts. De är enkla att använda men har en relativt mycket sämre noggrannhet jämfört med t.ex. röntgenstereofotogammetri analys (RSA) som har den högsta uppmätta noggrannheten *in vivo.* Nackdelen med den senare är att tantalumkulor måste sättas in i patienten för att undersökningen ska kunna utföras och att den därför inte lämpar sig i klinisk praxis. I studie 2 har rörelseanalys gjorts med en relativt ny metod som är baserad på en tredimensionell bildanalys och har hög nogrannhet.. Undersökningarna görs med datortomografi och är icke-invasiv. 28 patienter ur diskprotesgruppen undersöktes med datortomografi och rörelsemätning, dels mellan de ingående proteskomponenterna och dels mellan protes och intilliggande kota. Sammanlagt undersöktes 38 proteser (10 patienter hade två) och alla undersökningar gick att använda i rörelseanalysen. Mellan de flesta proteskomponenter fanns det rörlighet även om rörelseomfånget varierade ganska mycket mellan olika individer och olika nivåer. Två (5 %) av proteserna var helt orörliga och tre (8 %) uppvisade tydlig rörlighet mellan protes och ben och klassades därmed som lösa.

Studie 3

En vanlig komplikation till främre friläggning av kotpelaren är sväljsvårigheter, dysfagi, som oftast är mest markanta första veckorna efter operationen för att sedan försvinna hos de flesta. Omfattningen av den postoperativa dysfagin har studerats tidigare men har då utvärderats med objektiva mätmetoder eller icke-validerade frågeformulär. Orsakerna till postoperativ dysfagi är inte helt klarlagda men operationstraumat i sig är sannolikt en del av förklaringen till besvär med sväljning den första postoperativa perioden. Orsaker till de sena besvären är mer oklara men tänkbara faktorer skulle kunna vara nervskador, ärrbildning, minskad eller ändrad rörlighet i kotpelaren samt att stora implantat kan komprimera matstrupen bakifrån. För att mer tillförlitligt sätt kunna värdera de upplevda sväljbesvären efter operation konstruerades ett frågeformulär i samarbete med läkare och logopeder på en öron-näsa-hals-klinik. Detta formulär testades på en grupp patienter med känd dysfagi och jämfördes mot en redan validerad och mer omfattande skala. Överensstämmelsen mellan skalorna var god och den nya användes sedan för att utvärdera dysfagi på 111 patienter det första året efter operation. Sväljbesvär var vanligt första tiden efter operation och efter fyra veckor rapporterade 85% av patienterna någon grad av sväljproblematik men besvären var lindriga på gruppnivå. Ett år efter operation var värdena på samma låga nivå som före operation.

Studie 4

I denna studie användes samma frågeformulär för skattning av dysfagi som i studie 3 för att utvärdera om det fanns skillnader i upplevda sväljproblem mellan de patienter som behandlats med diskprotes och de som stelopererats. Inga statistiskt signifikanta skillnader kunde påvisas vid uppföljningar upp till ett år. Vid uppföljning efter två år fanns en statistiskt signifikant skillnad med mer dysfagi i gruppen som genomgått steloperation. Högre värden av dysfagi var också statistiskt signifikant associerat till samma grupp.

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Errata

Paper IV, page 3

~~There were no differences in mean surgical duration (DOS) between the ADR group and the ACDF group, 125 minutes (SD 42.6) compared to 141 minutes (SD 38.0), p=0.18.~~

There were differences in mean surgical duration between the ADR group and the ACDF group, 125 minutes (SD 42.6) and 141 minutes (SD 38.0) respectively. The difference was statistically significant, p=0.018.