



# Clinical course and prognostic models for the conservative management of cervical radiculopathy: a prospective cohort study

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## Abstract

**Purpose** To describe the clinical course and develop prognostic models for poor recovery in patients with cervical radiculopathy who are managed conservatively.**Methods** Sixty-one consecutive adults with cervical radiculopathy who were referred for conservative management were included in a prospective cohort study, with 6- and 12-month follow-up assessments. Exclusion criteria were the presence of known serious pathology or spinal surgery in the past. Outcome measures were perceived recovery, neck pain intensity and disability level. Multiple imputation analyses were performed for missing values. Prognostic models were developed using multivariable logistic regression analyses, with bootstrapping techniques for internal validation.**Results** About 55% of participants reported to be recovered at 6 and 12 months. All multivariable models contained 2 baseline predictors. Longer symptoms duration increased the risk of poor perceived recovery, whereas the presence of paresthesia decreased this risk. A higher neck pain intensity and a longer duration of symptoms increased the risk of poor relief of neck pain. A higher disability score increased the risk of poor relief of disability, and larger active range of rotation toward the affected side decreased this risk. Following bootstrapping, the explained variance of the models varied between 0.22 and 0.30, and the median area under the curve varied between 0.75 and 0.79.**Conclusions** The clinical course of cervical radiculopathy appears to be long, with most of the reduction in symptoms occurring within the first 6 months. All prognostic models showed an adequate predictive performance with modest diagnostic accuracy and explained variance.**Graphical abstract** These slides can be retrieved under Electronic Supplementary Material.

**Key points**

1. Cervical radiculopathy
2. Conservative management
3. Clinical course
4. Prognostic models
5. Recovery

Predictor	OR (95%CI) <sup>†</sup>	Beta <sup>‡</sup>	Adjusted Beta <sup>‡</sup>
Paresthesia (Yes) <sup>§</sup>	0.18 (0.03-1.10)	-1.72	-1.21
Duration of symptoms (weeks)	1.01* (1.00-1.02)	0.012	0.008

Performance measures	Median (IQR) R <sup>2</sup>	Median (IQR) AUC
Initial <sup>†</sup>	0.37 (0.29-0.43)	0.82 (0.80-0.85)
Bootstrap <sup>‡</sup>	0.22 (0.14-0.29)	0.75 (0.70-0.77)

\*p-value <0.05. <sup>†</sup>Reference category is 'no' (OR=1) <sup>‡</sup>acquired from the imputed datasets. <sup>§</sup> performance measure acquired from bootstrapping procedure on the imputed datasets. <sup>||</sup> regression coefficients multiplied by the shrinkage factor of 0.70 retrieved from bootstrapping procedure.

**Take Home Messages**

1. The clinical course of patients with cervical radiculopathy appears to be long, with only approximately half of the patients recovered at 6 and 12 months.
2. A longer duration of symptoms, absence of paresthesia, a higher neck pain intensity at baseline, a higher baseline disability score and a lower active rotation towards the affected side were related to poor perceived recovery, poor relief of neck pain and/or disability.

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Extended author information available on the last page of the article

## Introduction

Cervical radiculopathy occurs when a cervical nerve root is compressed or inflamed [1, 2]. Patients with cervical radiculopathy typically report arm pain, neck pain and sensory deficits along the distribution area of the affected nerve root(s) [1, 3]. Although there are no universally accepted diagnostic criteria for cervical radiculopathy [4], the diagnosis is usually based on a combination of clinical signs and symptoms, combined with magnetic resonance imaging (MRI). Most patients are initially treated conservatively, but when conservative treatment fails or in severe conditions, surgery is considered [5, 6].

Knowledge of the course and prognostic factors is imperative to provide accurate information to patients with cervical radiculopathy about the prognosis. Several, mostly older studies, describe the course of cervical radiculopathy [2, 3, 7]. Generally, cervical radiculopathy appears to have a favorable but lengthy course, with 70–90% of patients reporting no or mild symptoms after 5–10 years [2, 3, 7]. A recent systematic review revealed that 83% of patients with cervical radiculopathy due to cervical disk herniation recovered within 24–36 months. Most of the improvement occurred within 4–6 months after onset [7]. As conservative management is usually the initial treatment for patients with cervical radiculopathy, it is important to have a better understanding of the clinical course of the disorder and prognostic factors which may influence this course [5, 6].

There is a paucity of information on prognostic factors for cervical radiculopathy [7]. A recent systematic review reported that patients with a workers' compensation claim appeared to have a poorer prognosis [7]. One study identified several factors to be predictive for successful short-term recovery following physiotherapy [8]. However, to date, no study has described a prognostic model for long-term outcome in conservatively managed patients with cervical radiculopathy. Therefore, this study aimed to describe the clinical course, and develop and internally validate prognostic models for poor prognosis in conservatively managed patients with cervical radiculopathy.

## Methods

### Design

This is a prospective cohort study with a 6- and 12-month follow-up. The Medical Ethics Committee of the Elisabeth Hospital in Tilburg, The Netherlands, approved the study.

All participants provided written informed consent prior to participating.

### Participants

Participants were recruited between July 2013 and October 2014. Consecutive patients with cervical radiculopathy who were referred to a multidisciplinary clinic in The Netherlands by their general practitioner or medical specialist were eligible for participation. All participants underwent MRI scanning before entering the study. A neurosurgeon with extensive (i.e., > 10 years) clinical experience in managing patients with cervical radiculopathy reached the diagnosis of cervical radiculopathy if clinical findings from the history and physical examination (e.g., pain, numbness, paresthesia, muscle strength, and reflex changes) corresponded with nerve root compression observed on MRI. Inclusion criteria for this study were: diagnosis of cervical radiculopathy due to disk herniation, stenosis or a combination, at least 18 years of age, referred for conservative management and adequate understanding of the Dutch language to complete the questionnaires. Patients were excluded in case of known serious pathology (such as malignancies, fractures, (rheumatoid) arthritis, infections or myelopathy), multiple sclerosis, diabetes mellitus, polyneuropathy, complex regional pain syndrome or a history of spinal surgery.

### Procedure

At baseline, patients provided information regarding demographics and potential prognostic factors via electronic questionnaires. The neurosurgeon performed a clinical neurological examination. After 6 and 12 months, patients completed a digital survey of questions regarding the current level of recovery (Global Perceived Effect scale [9]); questions regarding their level of symptoms (including Numeric Pain Rating Scales for neck pain, arm pain and disability [10]); sick leave due to the cervical radiculopathy (duration in weeks); treatment received (i.e., physical therapy, manual therapy, injections, medication, other) and medication use (type and amount). A copy of the digital survey is provided in Appendix 1. Participants who did not respond to the electronic questionnaire, received a reminder after 1 and 2 weeks, followed by a final reminder via a telephone call.

### Outcomes

The course of cervical radiculopathy was described in terms of perceived recovery, neck and arm pain intensity and perceived disability at 6 and 12 months. Additionally, we determined the proportion of participants with a high pain intensity at 6 and 12 months, i.e., a score of 7 or higher on an 11-point Numeric Rating Scale (NRS) [10, 11].

The primary outcome measure for the prognosis was the perceived recovery at 12 months, measured on a 7-point Global Perceived Effect (GPE) scale [9]. Patients were considered recovered if they scored ‘completely recovered’ or ‘much improved’ [9]. Secondary outcome measures were neck pain intensity and disability level at 12 months. Patients were considered recovered if they scored  $\leq 2$  for neck pain intensity and disability on an 11-point NRS, ranging from 0 to 10 [12].

### Potential predictors

We determined which factors to include in the multivariable analyses for each outcome measure separately [13, 14]. Because there is a lack of knowledge about prognostic factors for cervical radiculopathy, we included prognostic factors for non-specific neck pain, such as duration of symptoms (weeks), previous episodes of neck pain (yes/no), pain intensity (0–10) and presence of low back pain (yes/no) [15, 16]. Additionally, because we were interested in physical factors that could be influenced by conservative management, the following potential prognostic factors were included: active range of motion of the neck (measured with a Cervical Range or Motion device (CROM; Performance Attainment Associates, Lindstrom, MN, USA)) [17]; deep neck flexor endurance (measured with a clinical muscle endurance test as described by Harris et al. [18]); the level of disability (measured with an 11-point NRS, ranging from 0 (no disability) to 10 (total disability)) and the presence of neuropathic pain (measured with the Dutch language version of the PainDETECT Screening questionnaire) [19]. The factors needed to be easily obtainable and reliable to measure in clinical practice, to ensure that the factors can be widely used in clinical practice. Table 1 provides an overview of the selected potential predictors per outcome measure.

### Statistical analysis

#### Missing values

We performed several missing value analyses: First, we performed Little’s MCAR test, to determine whether values were missing (completely) at random. Then we compared the main baseline characteristics of participants with and without missing data, to determine if there were any relevant differences between the groups. We compared the characteristics both visually and statistically with independent sample *t* tests and Mann–Whitney *U* tests.

#### Clinical course

The clinical course of cervical radiculopathy at 6 and 12 months was described using descriptive statistics. We

**Table 1** Overview of predictors included in the multivariable logistic regression analyses per outcome

#### *Poor recovery*

1. Presence of neck pain (yes/no)
2. Presence of low back pain (yes/no)
3. Presence of paresthesia in the arm or hand (yes/no)
4. Arm pain worse than neck pain (yes/no)
5. Duration of symptoms (weeks)
6. Active rotation to the affected side (degrees)

#### *Neck pain*

1. Presence of neck pain (yes/no)
2. Neck pain intensity (0–10 NRS)
3. Presence of low back pain (yes/no)
4. Duration of symptoms (weeks)
5. Arm pain worse than neck pain (yes/no)
6. Prior episode of neck pain (yes/no)

#### *Disability*

1. Active rotation to the affected side (degrees)
2. Level of disability (0–10 NRS)
3. Presence of low back pain (yes/no)
4. PainDETECT Screening Questionnaire (0–38)
5. Prior episode of neck pain (yes/no)
6. Deep neck flexor endurance (s)

used complete-case analyses to determine the clinical course of cervical radiculopathy.

### Prognostic models

Multiple imputation methods were performed on the predictor and outcome measures with missing values. We used the Multivariate Imputation by Chained Equations (MICE) method with linear method imputation, and the number of imputations was related to the amount of missing data [13, 14, 20]. Demographic variables, predictor variables and the 6- and 12-month outcome variables were included in the imputation models [20].

We performed multivariable logistic regression analyses for each primary and secondary outcome in the imputed dataset. A priori, we aimed to include six factors in our models. The common rule of thumb states that the sample size for multivariable regression should be approximately 10 events in the smallest group per factor included in the analyses [13]. Therefore, we aimed to include a minimum of 60 participants in the smallest group (i.e., either recovered or non-recovered at 12 months) [13]. However, the final dataset was smaller than anticipated, because of the strict criteria we used to diagnose cervical radiculopathy. The recruitment period could not be extended, but initiatives were taken to maximize enrollment of suitable patients within the predefined time frame. This restricted

the number of possible predictors per outcome. Because it was difficult to determine the three most relevant predictors for each outcome based on theoretical plausibility, we decided to include all six predefined predictors and apply strict bootstrapping techniques to correct for overfitting.

We used a manual backward selection procedure in the pooled analysis model, in which the factor with the highest significance level was removed, until all variables in the model had a  $p$  value  $< 0.157$  [13, 21]. The predictive influence of the predictor was estimated by the odds ratio (OR). Performance of the model was determined by the explained variance and the accuracy of the model. The explained variance is described in terms of the Nagelkerke  $R^2$ . The accuracy of the prognostic models was determined by the area under the curve (AUC). An AUC  $< 0.6$  means that the prognostic model has no discriminatory value, an AUC  $> 0.8$  reflects good discriminatory value [22]. Since no universal method has been described, the pooled AUC and Nagelkerke  $R^2$  were acquired by determining the median of the individual AUCs and Nagelkerke  $R^2$  of the imputed datasets [14].

The internal validity of the models was assessed through bootstrapping techniques with 500 repetitions. Bootstrapping is the preferred method for internal validation to determine the optimism in the initially developed model, based on the model's performance in numerous (i.e., 500) bootstrap samples derived from the complete dataset. It determines a shrinkage factor that can be used to adjust the regression coefficient and performance indicators to correct for any optimism and to better reflect the actual performance of the model [13]. The models were internally validated in terms of explained variance and accuracy. The statistical analyses were performed in IBM SPSS, version 23 (IBM Corp, Armonk, NY, USA) and the bootstrap techniques in R statistics. All methods are reported in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) guideline [13, 14].

## Results

### Participants

Sixty-one patients with cervical radiculopathy enrolled in the study. The mean (SD) age was 49.5 (9.0) years, 54% were female and the median duration of symptoms was 26 (IQR 8.5–104.0) weeks. The baseline characteristics are described in Table 2.

### Missing value analyses

There were missing data for one predictor variable at baseline (active rotation toward the affected side) ( $N = 5$ ; 8.2%)

**Table 2** Baseline characteristics and follow-up measures at 6 and 12 months

	Baseline	6 months	12 months
Age in years	49.5 (9.0)		
Female	54%		
Duration of symptoms in weeks*	26 (96)		
<i>Education level</i>			
Low	13%		
Middle	71%		
High	16%		
<i>Work</i>			
Part-time	31%		
Fulltime ( $\geq 36$ h/week)	54%		
Not applicable	15%		
<i>Cause of nerve root compression**</i>			
Disk herniation	43%		
Stenosis	14%		
Combination of both	43%		
<i>Location disk herniation**</i>			
Foraminal	48%		
(Para)median	17%		
Lateral	5%		
Other (e.g., broad based)	16%		
Not applicable (e.g., stenosis)	14%		
<i>Symptoms</i>			
Neck pain	74%	61%	66%
Arm pain	98%	42%	55%
Paresthesia arm and/or hand	82%	39%	42%
Numbness arm and/or hand	64%	42%	32%
Neck pain intensity*	5 (6)	3 (6)	3 (5)
Arm pain intensity*	6 (2)	1 (5)	3 (4)
Disability*	5 (4)	3 (5)	2 (5)
PainDETECT screening questionnaire	12.6 (5.4)		
Sick leave during last 6 months	36%	27%	13%
Duration of sick leave in weeks*	0 (3)	0 (4)	0 (0)
<i>Treatment received (excl. medication)‡</i>		56%	45%
Physiotherapy		29%	32%
Manual therapy§		34%	32%
Corticosteroid injection therapy		42%	40%
Other (e.g., acupuncture, diet)		24%	14%
<i>Current medication use†</i>	59%	34%	26%
Paracetamol	31%	44%	29%
NSAIDs	33%	24%	18%
Tramadol	16%	12%	5%
Morphine	8%	2%	0%
Antidepressants	5%	5%	3%
Anti-epileptics	3%	0%	3%
Other	7%	7%	8%
<i>Global perceived effect</i>			

**Table 2** (continued)

	Baseline	6 months	12 months
Completely recovered		12%	13%
Much improved		44%	42%
Slightly improved		24%	24%
Not changed		17%	13%
Slightly worsened		2%	5%
Much worsened		0%	3%
Worse than ever		0%	0%
<i>Recovered (dichotomized)</i>			
GPE recovered		56%	55%
Neck pain recovered		42%	47%
Arm pain recovered		59%	47%
Disability recovered		46%	58%

Values are presented as mean (SD) for continuous data and as percentages for categorical data unless stated otherwise

Education level: low=lower vocational education; middle=high school and/or secondary vocational education; high=higher professional education and/or university; GPE=global perceived effect; N.A.=not available; NRS=Numeric Rating Scale; NSAIDs=non-steroidal anti-inflammatory drugs

\*Data presented as median and interquartile range (IQR). \*\*Data available on  $N=58$  participants. †Some participants used more than one type of medication. ‡Some participants were treated with more than one intervention. §The manual therapy treatment contained at least some form of joint mobilization or high velocity thrust manipulation

and for outcome data at 6 months ( $N=20$ ; 32.8%) and 12 months ( $N=23$ ; 37.7%) follow-up. Missing value analyses indicated that missing values were missing (completely) at random. Visual comparison of the baseline characteristics of responders and non-responders at 12 months revealed a larger proportion of females in the complete case group compared to the group with missing data; however, this between-group difference was nonsignificant (See Table 3).

## Clinical course

At 6 months and at 12 months, ~55% of patients reported to be recovered on the GPE scale. At 6 months, 42% reported to be recovered in terms of neck pain and 47% at 12 months. The median neck pain intensity decreased from 5 to 3 at 6 months and remained 3 at 12 months. Fifty-nine percent of patients reported no or only slight arm pain at 6 months, which decreased to 47% at 12 months. The median arm pain intensity decreased from 7 to 1 at 6 months, and increased to 3 at 12 months. The proportion of patients who experienced high-intensity neck pain was 24% at 6 months and 18% at 12 months. For high-intensity arm pain, the proportions were 17% (6 months) and 11% (12 months). At 6 months, 46% reported to be recovered in terms of disability, which

**Table 3** Baseline characteristics of patients with complete data compared to patients with missing data

12-months follow-up	Complete data	Missing data
Age <i>in years</i>	51 (13)	48 (12)
Female	63%	39%
<i>Education level</i>		
Low	13%	13%
Middle	71%	70%
High	16%	17%
Prior neck pain	68%	65%
Muscle weakness	61%	61%
Paresthesia	82%	83%
Duration of symptoms <i>in weeks</i>	24 (95)	26 (96)
Sick leave duration* <i>in weeks</i>	0 (1)	0 (6)
Neck pain intensity*	5 (6)	5 (7)
Arm pain intensity*	7 (3)	6 (2)
Disability level*	5 (5)	5 (3)

Values are presented as mean (SD) for continuous data and as percentages for categorical data unless stated otherwise

Education level: low=lower vocational education; middle=high school and/or secondary vocational education; high=higher professional education and/or university

\*Data presented as median and interquartile range (IQR)

further improved to 58% at 12 months. The median level of disability reduced from 5 at baseline, to 3 at 6 months and 2 at 12 months. The proportion of patients experiencing high-level disability was 15% (6 months) and 13% (12 months).

With respect to management, 59% of patients used medication at baseline, which decreased to 34% at 6 months and 26% at 12 months. Approximately 30% of patients received physiotherapy, ~33% manual therapy and ~40% corticosteroid injections. Some participants underwent more than one intervention. Table 2 provides a detailed overview of the clinical course.

## Multivariable logistic regression analyses

Results for the multivariable backward logistic regression analyses of the imputed data for the three outcome measures are shown in Tables 4, 5 and 6.

## Prognostic models

The prognostic model for perceived poor recovery contained two baseline predictors: 'presence of paresthesia' and 'duration of symptoms'. People with a longer duration of symptoms had a higher risk for persistent symptoms, and people with paresthesia had a reduced risk (Table 4). The prognostic model for poor relief of neck pain consisted of two baseline factors: 'neck pain intensity' and 'duration of symptoms,' indicating a higher risk of persistent neck pain

**Table 4** Final model for poor perceived recovery at 12 months ( $N=61$ )

Predictor	OR (95% CI) <sup>†</sup>	Beta <sup>†</sup>	Adjusted beta <sup>‡</sup>
Paresthesia (yes) <sup>‡</sup>	0.18 (0.03–1.10)	– 1.72	– 1.21
Duration of symptoms (weeks)	1.01* (1.00–1.02)	0.012	0.008
Performance measures	Median (IQR) $R^2$	Median (IQR) AUC	
Initial <sup>†</sup>	0.37 (0.29–0.43)	0.82 (0.80–0.85)	
Bootstrap <sup>§</sup>	0.22 (0.14–0.29)	0.75 (0.70–0.77)	

95% CI = 95% confidence interval; AUC = area under the curve; IQR = interquartile range; OR = odds ratio;  $R^2$  = Nagelkerke  $R^2$

\* $p$  value < 0.05. <sup>‡</sup>Reference category is ‘no’ (OR = 1). <sup>†</sup>acquired from the imputed datasets. <sup>§</sup>Performance measure acquired from bootstrapping procedure on the imputed datasets. <sup>‡</sup> Regression coefficients multiplied by the shrinkage factor of 0.70 retrieved from bootstrapping procedure  
ORs reported are acquired from the imputed datasets, prior to bootstrapping. An AUC < 0.6 indicates that the prognostic model has no discriminatory value, an AUC > 0.8 reflects good discriminatory value

**Table 5** Final model for poor recovery of neck pain at 12 months ( $N=61$ )

Predictor	OR (95% CI) <sup>†</sup>	Beta <sup>†</sup>	Adjusted beta <sup>‡</sup>
Baseline neck pain intensity (0–10)	1.42* (1.04–1.95)	0.35*	0.26
Duration of symptoms (weeks)	1.01 (1.00–1.03)	0.01	0.01
Performance measures	Median $R^2$ (IQR)	Median AUC (IQR)	
Initial <sup>†</sup>	0.45 (0.40–0.49)	0.84 (0.82–0.86)	
Bootstrap <sup>§</sup>	0.30 (0.25–0.36)	0.79 (0.77–0.81)	

95% CI = 95% confidence interval; AUC = area under the curve; IQR = interquartile range; OR = odds ratio;  $R^2$  = Nagelkerke  $R^2$

\* $p$  value < 0.05. <sup>†</sup>Acquired from the imputed datasets. <sup>§</sup>Performance measure acquired from bootstrapping procedure on the imputed datasets. <sup>‡</sup>Regression coefficients multiplied by the shrinkage factor of 0.73 (retrieved from bootstrapping procedure)

ORs reported are acquired from the imputed datasets, prior to bootstrapping. An AUC < 0.6 indicates that the prognostic model has no discriminatory value, an AUC > 0.8 reflects good discriminatory value

**Table 6** Final model for poor recovery of disability level at 12 months ( $N=61$ )

Predictor	OR (95% CI) <sup>†</sup>	Beta <sup>†</sup>	Adjusted beta <sup>‡</sup>
ROM rotation affected side (degrees)	0.94* (0.88–1.00)	– 0.07*	– 0.05
Baseline disability score (0–10)	1.40 (1.00–1.95)	0.33	0.22
Performance measures	Median $R^2$ (IQR)	Median AUC (IQR)	
Initial <sup>†</sup>	0.41 (0.36–0.49)	0.83 (0.80–0.87)	
Bootstrap <sup>§</sup>	0.25 (0.19–0.35)	0.76 (0.73–0.82)	

95% CI = 95% confidence interval; AUC = area under the curve; IQR = interquartile range; OR = odds ratio;  $R^2$  = Nagelkerke  $R^2$

\* $p$  value < 0.05. <sup>†</sup>Acquired from the imputed datasets. <sup>§</sup> performance measure acquired from bootstrapping procedure on the imputed datasets. <sup>‡</sup>Regression coefficients multiplied by the shrinkage factor of 0.68 retrieved from bootstrapping procedure

ORs reported are acquired from the imputed datasets, prior to bootstrapping. An AUC < 0.6 indicates that the prognostic model has no discriminatory value; an AUC > 0.8 reflects good discriminatory value

for patients with a higher baseline neck pain intensity and a longer duration of symptoms (Table 5). For disability, the prognostic model also contained two baseline factors: ‘active rotation toward the affected side’ and ‘baseline disability score.’ Patients with a greater active rotation toward the affected side had a lower risk for persistent disability, and

patients with a higher baseline disability score had a higher risk (Table 6).

The median explained variance ( $R^2$ ) varied between 0.37 and 0.45 for the three prognostic models. The median AUC varied between 0.82 and 0.84. Following bootstrapping, the explained variance decreased and varied between 0.22 and 0.30, and the median AUC varied between 0.75 and 0.79 for the three models (Tables 4, 5 and 6).

## Discussion

This study aimed to describe the clinical course of cervical radiculopathy for those patients who are managed conservatively and to derive prognostic models to identify patients at risk for poor recovery.

### Clinical course

According to the findings regarding perceived effect, approximately half of the patients indicated to be recovered at 6 and 12 months. Similar proportions were observed for neck and arm pain recovery. Although the mean reported pain intensities (3/10 NRS) and level of disability (2/10 NRS) were fairly low at 12 months, the variability between patients was rather large. Approximately 20% of patients still experienced high-intensity pain and high level of disability at 6 months, and ~15% at 12 months. In addition, ~20% of patients took medication typically prescribed for moderate to severe (neuropathic) pain at 6 months, and ~10% at 12 months (opioids, antidepressants and anti-epileptics). It is noteworthy that recovery, pain and disability levels were similar at 6 and 12 months, indicating that further improvement between 6 and 12 months was limited.

A recent systematic review summarizing two studies revealed that most improvement occurs in the first 4–6 months and that 83% of patients recovered completely within 2–3 years [7]. In our study, the long-term recovery (12 months) was less favorable, possibly because we included a larger proportion of patients with a longer history of symptoms. This seems a plausible explanation, since longer duration of symptoms was associated with poor recovery in our multivariable prognostic models.

### Prognosis

The multivariable logistic regression analyses generated plausible prognostic models containing a combination of predictors that are commonly captured and easily obtainable in clinical practice. A longer duration of symptoms, absence of paresthesia, a higher neck pain intensity at baseline, a higher baseline disability score and a lower active rotation toward the affected side were related to poor perceived recovery, poor relief of neck pain and/or disability at 12 months. After bootstrapping, all prognostic models showed an adequate predictive performance with modest diagnostic accuracy and explained variance. The results indicate that the models may potentially be useful to identify patients with a less favorable prognosis.

Some of the identified variables have previously been identified as univariable predictors for other musculoskeletal conditions, and some may be more unique to cervical radiculopathy

[16, 23]. High initial pain intensity and a long duration of symptoms are known to be predictive of a poor recovery in various musculoskeletal disorders [16]. High levels of initial disability have been associated with poor recovery in musculoskeletal disorders [16] and lumbar radiculopathy [23]. For lumbar radiculopathy, sensory changes, including paresthesia, were not associated with outcome [23], whereas our study revealed that presence of paresthesia at baseline was associated with a lower chance of a poor perceived recovery. This seems counterintuitive. However, based on the finding that the presence of paresthesia decreased from 82% of patients at baseline to 42% at 12 months, one could argue that resolution of paresthesia may be an important factor in perceived recovery. The association between a larger active rotation toward the affected side and a reduced risk of persistent disability was in line with prior research indicating that movement restrictions are negative prognostic factors for musculoskeletal disorders [16].

It would have been informative to perform subgroup analyses based on type of nerve root compression (i.e., disk herniation, stenosis or a combination), or more specifically on the level, type and site of the disk herniation. However, we were unable to perform subgroup analyses because of the small dataset for these items. We recommend that the characteristics of the nerve root compression are taken into account in future research into the prognosis of cervical radiculopathy.

### Study limitations

Our study has some limitations. Possible predictors were selected based on theoretical plausibility. Given the finite number of possible predictors that can be considered, we had to limit the selection to the most plausible predictors for each outcome variable. Since little is known about the prognostic factors for cervical radiculopathy, we made a priori assumptions about which predictors would be most valuable to determine the prognosis. We focused on possible predictors that were widely available to health practitioners in various settings. We therefore selected predominantly signs and symptoms as possible predictors. Including other factors, such as results from electrodiagnostic test or imaging, or psychosocial factors (e.g., anxiety and depression) may have yielded different results.

The nature of physiotherapy (e.g., type of exercises) and manual therapy (e.g., type of mobilization) were not recorded in detail. Hence, we cannot draw conclusions about the influence of different types of interventions on the prognosis. Given that studies of the effectiveness of physiotherapy and manual therapy in patients with cervical radiculopathy have shown comparable results, we assume that the influence of specific characteristics of the treatment on prognosis would be limited [5, 24].

To resolve the issue of missing data, we performed multiple imputations on the predictor variables with missing data and the outcome variables. Multiple imputation is used increasingly to account for missing data, and it is reported to be more valid than using complete-case analysis only [13, 25, 26].

Due to the strict diagnostic criteria we used for cervical radiculopathy, the number of patients we could recruit in the available time frame was smaller than anticipated. This resulted in a lower number of cases per event than preferred [13]. However, we accounted for possible overfitting by combining the multiple imputations with a strict bootstrap procedure [27]. In line with expectations, the bootstrap procedure showed a shrinkage factor of approximately 0.70 in all models. Consequently, the diagnostic accuracy and the explained variance were slightly lower in all models. Given the multiple imputation methods used and the internal validation procedure, we believe that these results adequately reflect the prognostic value of the models and correct for the optimism in the initial models. However, considering the smaller dataset to derive the models and the relatively large amount of missing data, it is important that these findings are validated in a larger external dataset. Until these prognostic models have been confirmed, the results should be interpreted with caution.

## Conclusion

The clinical course of patients with cervical radiculopathy appears to be long, with only approximately half of the patients recovered at 6 and 12 months. A longer duration of symptoms, absence of paresthesia, a higher neck pain intensity at baseline, a higher baseline disability score and a lower active rotation toward the affected side were related to poor perceived recovery, poor relief of neck pain and/or disability. Confirmation of the prognostic models through external validation is necessary.

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## Compliance with ethical standards

**Conflict of interest** The authors declare that they have no conflict of interest.

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## Appendix

See Table 7.

**Table 7** Digital follow-up survey at 6 and 12 months

6 and 12 months digital follow-up survey	
Global perceived effect	7-item Global Perceived Effect scale
Treatment	During the past 6 months, have you received treatment for your neck and/or arm pain? If so, which treatment did you receive for your neck and/or arm pain? Medication Physiotherapy Manual therapy Corticosteroid injections Other (please define)
Treatment satisfaction	How satisfied were you with the results of your treatment? (0–6)
Sick leave	Have you experienced sick leave due to your neck and/or arm pain? (yes/no) If so, what was the duration of the sick leave? (weeks)
Neck pain	Are you currently experiencing pain in your neck? (yes/no) What is the pain intensity of your neck pain? (NRS 0–10)
Arm pain	Are you currently experiencing pain in your arm? (yes/no) What is the pain intensity of your arm pain? (NRS 0–10)
Disability	Are you currently experiencing limitations in your daily activities? (yes/no) How bothersome are these limitations in your daily activities? (NRS 0–10)
Paresthesia	Are you currently experiencing paresthesia in your arm and/or hand? (yes/no)
Numbness	Are you currently experiencing numbness in your arm and/or hand? (yes/no)
Medication use	Are you currently using any form of medication for your neck and/or arm pain? (yes/no) Which medication do you use? None Paracetamol NSAIDs Tramadol Morphine Opioids Anti-depressives Anti-epileptics Other (please define)

*NRS* Numeric Rating Scale; *NSAIDs* nonsteroidal anti-inflammatory drugs



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