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Prediction of fusion and importance of radiological variables for the outcome of anterior cervical decompression and fusion

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Abstract In a prospective randomised study with a 2-year follow-up, 103 patients were randomised to anterior cervical decompression and fusion (ACDF) with a cervical carbon-fibre intervertebral fusion cage (CIFC) or the Cloward procedure (CP). The purpose of the present study was to report predictors for fusion and also to investigate the importance of radiological variables for the clinical outcome. Gender, age, smoking habits, disc height, segmental kyphosis and type of surgical procedure were used as independent (before surgery) variables in a multiple regression model. Male gender, one-level surgery and CP treatment were significant predictors of fusion and explained 14% of the variability of fusion status at follow-up. Number of levels operated on, however, did not influence the clinical outcome. Fifty-two per cent of the women and 17% of the men in the CIFC group, and 25% of the women and 8% of the men in the CP group, had pseudarthrosis. Although patients with a healed fusion had significantly less pain intensity than patients with

pseudarthrosis, radiological variables explained only 4% of the variability of pain at follow-up. Apart from a significant correlation between preoperative kyphosis and neck disability index at follow-up, no significant correlation between either postoperative kyphosis or preoperative or postoperative disc height and clinical outcome was found. Neither degree of segmental kyphosis nor disc height was different between patients with healed fusion and pseudarthrosis. One can conclude that male gender and type of surgery were significant predictors for a healed fusion and that pseudarthrosis affected outcome. In contrast to the commonly held view based mainly on theoretical considerations, no effect on clinical outcome could be demonstrated for segmental kyphosis and disc height at follow-up. Overall, the study shows that the importance of radiological factors as predictors for fusion as well as clinical outcome is limited.

Keywords Predisposing factors · Treatment outcome · Radiology · Radiculopathy · Surgery

Introduction

Many authors have reported the results of anterior cervical decompression and fusion (ACDF) in cervical radiculopathy [4, 19, 20, 24]. Young age, male gender, soft-disc disease, one-level fusion, radicular pain without additional

neck or lumbar pain, correlation between radiological and clinical findings, and short duration of symptoms have been reported to predict a good outcome [2, 6, 8, 9].

In previous studies the outcome has been determined by pain quantification, Odoms criteria [2, 6, 8, 9] and the neck disability index (NDI) [12, 18, 24]. Except for number of levels operated on [24], predictive factors for a

healed fusion after ACDF have not previously been reported. Also, the importance of pseudarthrosis for the clinical outcome after spinal surgery is still highly controversial [5, 10, 22]. The importance of various radiological factors for the clinical outcome is often discussed but with limited scientific support. Restoration and maintenance of a physiological disc height and fusion in lordosis is often claimed to be of importance for the clinical outcome. However, the literature support for this commonly held view is poor.

All previous reports on predictive factors for outcome and fusion, except those by Eriksen et al. [6] and Peolsson et al. [18], were based on bivariate analysis with no control of the possible influence by confounding variables. In the present study a multivariate analysis technique was used that allowed quantification of the importance of each variable studied.

The purposes of the present study was to determine predictive factors for the healing of ACDF and also to investigate the importance of radiological variables for the clinical outcome as measured by pain intensity, NDI, and a global assessment (Odoms criteria).

Patients and methods

After their informed consent had been obtained, 103 patients were randomised to either a cervical carbon-fibre intervertebral fusion cage (CIFC) (AcroMed, Cleveland, Ohio, USA) [24] or the Cloward procedure (CP) [4] with autograft. The inclusion criteria were at least 6 months duration of neck pain and radiculopathy of degenerative origin, with compatible MRI and clinical findings. All patients had preoperative MRI and clinical findings showing cervical nerve root compression. Exclusion criteria were myelopathy, psychiatric disorder, drug abuse and previous spine surgery. All patients asked to take part agreed to participate. In the outpatient clinic 52 patients were randomly assigned to the CIFC and 51 patients to the CP by the attending nurse who picked one of two notes; each pair of notes stated CP or CIFC. Thus, through the investigation, each patient had a 50% likelihood of being operated on by CIFC or the CP.

Preoperatively and at annual follow-ups all patients had a standard clinical examination, radiographs, and answered questionnaires. An independent observer, a junior doctor who was not involved in the treatment of the patients, assisted the patients with filling out the questionnaires.

At both the 1-year and the 2-year follow-ups 89 patients (86%) remained, 47 in the CIFC group and 42 in the CP group, 44 women and 45 men, with a mean age of 47 years (SD 8, range 30–67). Radiological outcome data were obtained for all 89 patients (86%) at the 2-year follow-up. Complete clinical outcome data (pain intensity, NDI and Odoms) were available at the 1-year or 2-year follow-up (mean 19 months, SD 6) in 74 patients (72%). The 1-year data point was used if the 2-year data point was missing, in accordance with the technique of last observation carried forward [7]. Patients for whom complete data sets could not be obtained by this method were excluded. The reason for that was that multivariate analysis presupposes completeness of the data sets. The surgery was performed in a standardised fashion as previously described [24]. Fifty-eight of the 89 patients were operated on at one level, 27 patients at two and four patients at three levels. Postoperatively, a Philadelphia collar was used for 6 weeks. Most patients received general physiotherapy in primary care after removal of the collar.

Background factors

Background data included: gender, age and smoking habit (yes or no).

Radiological evaluation

Radiographs (anterioposterior and lateral) were obtained preoperatively and at annual follow-ups. A radiologist and a spine surgeon independently assessed fusion status, with no knowledge of the clinical outcome. In case of a differing opinion between the two observers, a combined assessment was made and classification agreed upon. The fusion was classified into four types according to the presence or not of bridging bone anterior and/or through the disc space. Type 1A was defined as bridging bone anterior and through disc space; 1B as bridging bone anterior but not through disc space; 2A as no bridging bone anterior but through disc space; and 2B as no bridging bone at all. The treatment was classified as having resulted in a pseudarthrosis if a 2B healing was observed at any level, and otherwise as fused. The disc height was measured with a ruler at the most anterior aspect of the disc. Relating the disc height to the height of C2 or C7 controlled for variations in the magnification. The segmental lordosis/kyphosis was measured with a protractor and defined as the angle between the cranial and caudal endplates of the upper and lower vertebrae, respectively, in the motion segment operated on. If several adjacent segments were treated the segmental lordosis/kyphosis was defined as the angle between the end plates cranially and caudally to the levels operated on [24].

Pain

Pain was quantified by a horizontal 100-mm (0 = no pain, 100 = worst imaginable pain) VAS for pain right now [21].

Disability

Neck specific disability was quantified by the NDI. The ten items of the NDI (pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping, and recreation) are each scored from 0 to 5, added together and transformed to a percentage (0% = no pain or difficulties, 100% = highest score for pain and difficulty on all items) [26].

The independent observer evaluated the outcome of the surgery with regard to the criteria by Odom and classified the outcome into excellent, good, fair or poor [16].

The Ethics Committee at the Faculty of Health Sciences, Linköping University, approved the study.

Statistical methods

Correlations between the preoperative values and healing status at follow-up were determined by Spearman rank correlation coefficient analysis. For age, gender, smoking, disc height, kyphosis, and type of surgery, number of levels operated on (independent variables) that were correlated ($P \leq 0.1$) with the postoperative healing status (dependent variable), a standard linear multiple regression analysis, followed by a statistic step-wise (forward selection) regression analysis, was performed. For the regression model adjusted R^2 , beta, b value, and standard error b were calculated. The adjusted R^2 is the proportion of variation in the dependent variable that is explained by the independent variables, adjusted for number of variables assigned in the analysis. The beta value is the standardised regression coefficient, which reflects the importance of respective independent variable to predict the dependent variable,

and is calculated as if all of the independent variables had variance 1 [23]. Because there were no differences in clinical outcome variables between patients operated on by the CP and the CIFC method, neither before nor after the surgical procedure [24], the CP and the CIFC groups were analysed together as a common group.

Possible differences in segmental kyphosis and disc height, preoperatively and at follow-up, between patients with healed fusion and pseudarthrosis were analysed for statistical significance by the chi-square test. Similarly, differences in fusion rate between the two surgical techniques were analysed by the chi-square test. The importance of healing status and number of levels operated on (one/more than one) for clinical outcome (pain intensity, NDI, and Odom) were also analysed by the chi-square test.

The correlations between kyphosis and disc height preoperatively and at follow-up, on one hand, and healing status and clinical outcome (pain intensity, NDI, and Odom) at follow-up, on the other hand, were analysed by the Spearman rank correlation coefficient analysis followed by a standard multiple regression analysis and a statistic step-wise (forward selection) regression analysis.

A P value ≤ 0.05 was considered to be statistically significant. Descriptive statistics of the patient material was previously published by Vavruch et al. [24].

Results

Prediction of healing status

Bivariate analysis

In bivariate analysis, three preoperative variables (independent variables), male gender, CP treatment and one-level surgery correlated ($P \leq 0.1$) with osseous fusion at follow-up (Table 1).

There was no collinearity (intercorrelation ≥ 0.8) [23] between these independent variables (Table 2).

In the total group of 89 patients there were 24 (27%) patients with pseudarthrosis, six men (13%) and 18 women (41%) ($P=0.003$). In the CP group there were six patients (14%) with pseudarthrosis at least at one level, compared with 18 patients (38%) in the CIFC group ($P=0.01$). In the CP group two men (8%) and four women (25%) had pseudarthrosis (NS). In the CIFC group three men (17%) and 15 women (52%) had pseudarthrosis ($P=0.05$).

Table 1 Bivariate correlation ($P \leq 0.1$) between predictive factors and the outcome healing status for patients operated on by anterior cervical decompression and fusion

Variable	Healing status	
	r-value	P
Gender	0.54	0.004
Treatment	0.51	0.01
N:o levels	0.48	0.06

Table 2 Inter-correlation between preoperative variables which were significantly correlated (tied P value ≤ 0.1) to healing status

Variable	Gender	Treatment	N:o level
Gender	1.0	0.41	0.26
Treatment		1.0	0.41
N:o level			1.0

Table 3 Multiple regression analysis (forward step-wise) of osseous fusion at follow-up for patients operated on by anterior cervical decompression and fusion

Variable	Cumulative adjusted R ² by step	Beta	b	Standard error b
Gender	0.09	0.32	0.29	0.09
N:o operating level	0.12	0.22	0.17	0.08

Table 4 Multiple regression analysis (forward step-wise), split by gender, of predictive factor for osseous fusion at follow-up after anterior cervical decompression and fusion

Variable	Cumulative adjusted R ² by step	Beta	b	Standard error b
Men				
N:o operating level	0.02	0.19	0.10	0.1
Women				
Treatment	0.22	0.54	0.55	0.26

Multivariate analysis

The adjusted R² of the standard multiple regression model for prediction of fusion was 0.14 ($P=0.001$), which means that male gender, one-level surgery and CP treatment explained 14% of the variability in healing status. Gender ($P=0.007$) was significant as a single independent variable in the model. In the forward stepwise regression analysis the best predictor of the postoperative healing status was gender, followed by number of levels operated on (Table 3).

The best predictor in men was the number of levels operated on (adjusted R²=0.02), whereas type of treatment was the strongest predictor of healing status in women (adjusted R²=0.22) (Table 4).

Importance of the radiological outcome for the clinical outcome

Bivariate analysis

The 65 patients with a healed fusion had a mean pain intensity of 33 mm (SD 30) at follow-up, compared with 49 mm (SD 30) in the 24 patients with pseudarthrosis ($P=0.04$). However, the NDI and Odom's criteria were not significantly different between patients with healed fusion and pseudarthrosis (Table 5).

There was a significant correlation between preoperative kyphosis and NDI ($r=-0.23$, $P=0.05$), but not between preoperative kyphosis and pain intensity or Odom at follow-up. There was no significant correlation between preoperative disc height and clinical outcome. Similarly, there were no significant correlations between postoperative kyphosis or disc height and clinical outcome.

Table 5 Kyphosis, disc height, pain, NDI and Odom preoperatively and at follow-up in patients with a healed fusion and with a pseudarthrosis. Values are given as mean (SD)

Parameter	Before surgery		Follow-up	
	Healed	Pseud-arthrosis	Healed	Pseud-arthrosis
Kyphosis	-1.0 (6.4)	-1.6 (5.7)	-0.5 (7.2)	-2.8 (7.7)
Disc height	47.3 (14.3)	51.4 (16.7)	46.9 (15.0)	50.8 (16.6)
Pain	67.0 (20.9)	66.5 (23.4)	32.6 (30.5)	49.2 (30.0)
NDI	34.0 (8.1)	34.5 (8.5)	26.1 (11.2)	28.4 (9.0)
Odom			2.3 (1.1)	2.4 (0.9)

There were no differences in segmental kyphosis or disc height for patients with healed fusion compared to pseudarthrosis (Table 5).

Number of levels operated on and the type of treatment had no importance for outcome on pain intensity, NDI or Odom.

Multivariate analysis

Preoperative kyphosis and disc height had minimal predictive power of clinical outcome. They explained 5.5% of the variability of NDI, 4.0% of the variability of pain intensity and 0.5% of the variability of Odom. Similarly, kyphosis, disc height and healing status at follow-up minimally explained the variability in clinical outcome (NDI 1.5%, pain intensity 7.3% and Odom 0.0%). The most important preoperative radiological factor for NDI and pain intensity at follow-up was kyphosis with an adjusted R^2 of 0.05 for both variables. The most important postoperative variable for pain intensity at follow-up was healing status, with an adjusted R^2 of 0.05. No postoperative radiological variable had any significant predictive value for NDI or Odom at follow-up.

Discussion and conclusion

In a previous report [18] on the same patients we reported that male gender was a predictor for a good clinical outcome after surgery for cervical disc disease, which is in agreement with Eriksen et al. [6]. Male gender has, in several previous studies, been shown to be a positive predictor for outcome of ACDF. The main reason for this is probably factors other than the higher fusion rates in men. In the present study we found significant lower initial pain intensity and a less widespread pain on pain-drawings in men, factors that previously have been suggested to be important for the outcome of ACDF. We also found in other patients (unpublished work), a lower score, by the distress and risk assessment method, for men than for women.

In the present study, surprisingly, male gender was also found to be a positive predictor for fusion. An explanation could be a different basic healing potential in men and women [13, 14, 25]. Other reasons could be men's stronger neck muscles [17], which give compressive forces, and also gender differences in loading conditions; men have a heavier head and larger vertebrae. Even when the patients were split into treatment groups, there were more women with pseudarthrosis in each of the groups.

Contrary to reports that showed a negative effect of smoking on fusion of the lumbar spine [1] we could not document any effect of smoking on fusion rate. Most likely, the reason for this is that pseudarthrosis was seen mainly in the CIFC group and explained by stress shielding by the cage [24].

In this study, as well as in other studies, one-level surgery was associated with a higher fusion rate than multiple-level surgery [3, 11]. This is, however, what one would expect from the pure mathematical viewpoint. The clinical outcome, however, was not influenced by the number of levels operated on [24], which is contrary to the reports by Lunsford et al. [15].

We found that patients with fusion reported less pain. This was, however, not true for the NDI or the overall outcome, as measured by Odom's criteria. Pain must, however, be considered a major outcome variable, and the results of the study support the importance of obtaining fusion in ACDF.

Disc height was not correlated with the clinical outcome. This implies that restoration of disc height and indirect foraminal decompression is not the mechanism by which ACDF improves radicular pain in patients with degenerative disorders. The most likely explanation for improved radicular pain after ACDF is decompression of the nerve root by direct removal of disc tissue or osteophytes from the uncovertebral joint. Extensive foraminotomy was not performed in the patients in this study. The immobilisation of the motion segment by the fusion may also contribute to the improved radicular pain.

Similarly, segmental lordosis at follow-up was not correlated with a better outcome. Thus, the study lends no support to the commonly held view that restoration of lordosis is of importance for the outcome of ACDF. Somewhat the contrary was found: an increased preoperative kyphosis predicted a better outcome. A simple explanation for this may be that a kyphotic segment represents a truly painful segment, and, thus, the correct level was operated on. The results are in accordance with our previous report, which used univariate analysis to show that preoperative kyphosis predicted an improved NDI [18]. In this more comprehensive study using multivariate analysis of the same patients, preoperative kyphosis was correlated to less pain at follow-up. Thus, the results suggest that the correlation of preoperative segmental kyphosis with outcome is not by means of any correlation with other radiological variables at follow-up.

The fact that segmental kyphosis and disc height at follow-up were not correlated with outcome, and that the difference in outcome between fusion and pseudarthrosis was modest, implies that other factors, such as indications for surgery and psychological aspects, not documented in the present study, may be of greater importance for outcome than radiological variables.

Even if the power of the study is a borderline case [23] according to the number of independent variables included in the multiple regression models, the predictive models were stable, and the forward and backward stepwise analysis showed the same results: findings that support the conclusions drawn.

Since one cannot exclude that patients with specific characteristics may have omitted to fill in the questionnaires properly, the missing outcome data points at the 2-year follow-up may have influenced the results. By using the technique, however, of last observation carried forward, we obtained a reasonably high follow-up rate. Furthermore, we could observe no difference in clinical outcome between the 1-year and 2-year follow-up, and there were no preoperative or 1-year differences in those pa-

tients who filled in the 2-year questionnaire and those who did not. This justifies our using 1-year outcome data when 2-year data were missing. It should also be emphasized that the results of the study, and the conclusions, are based on a model that assumed a linear relationship between independent and dependent variables. This may be a simplification of the reality, and the correlations between variables may, therefore, have been underestimated.

In conclusion, the study shows that male gender is an important predictor of fusion in ACDF. The study further shows that obtaining fusion is of importance for pain relief. We found no support, however, for the common concept of the importance of obtaining lordosis and indirect foraminal decompression for a good clinical outcome. The observed low predictive power of preoperative as well as postoperative radiological variables suggests factors other than radiological ones to be major determinants of the outcome of ACDF.

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