Effects of preoperative mental distress versus surgical modality, arthroplasty, or fusion on long-term outcome in patients with cervical radiculopathy

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OBJECTIVE Several efforts have been made to investigate the long-term efficacy of artificial disc replacement surgery compared with that of fusion after decompression for the treatment of cervical degenerative disc disease and radiculopathy. However, research on the impact of mental distress on surgical treatment outcome has been sparse. The aim of the authors was to investigate the potential predictive value of preoperative risk factors in determining long-term outcome.

METHODS A total of 153 patients (mean age 47 years) with single- or double-level cervical degenerative disc disease and radiculopathy were randomly assigned to undergo either anterior cervical discectomy and fusion ($n = 70$) or artificial disc replacement ($n = 83$). The primary outcome was the Neck Disability Index (NDI) score, a patient-reported function score that ranges from 0% to 100%; higher scores indicate greater disability. Preoperative variables such as sex, age, smoking status, employment status, having a strenuous job, neck pain duration, arm pain duration, amount of regular exercise, Hospital Anxiety and Depression Scale (HADS) score, NDI score, whether surgery was performed on 1 or 2 levels, and allocated treatment were analyzed in multiple linear regression models with the 5-year NDI score as the outcome.

RESULTS A total of 47 (31%) patients had either a HADS anxiety or HADS depression score of 10 points or higher. High values on the preoperative HADS were a negative predictor of outcome ($p = 0.009$). Treatment allocation had no effect on 5-year NDI scores ($p = 0.32$).

CONCLUSIONS Preoperative mental distress measured with the HADS affects long-term outcome in surgically treated patients with cervical radiculopathy.

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KEYWORDS artificial disc replacement; Hospital Anxiety and Depression Scale; treatment outcome; Neck Disability Index; cervical radiculopathy

CERVICAL radiculopathy is characterized by radiating pain from the neck to the shoulder, shoulder blade, arm, or hand and is typically the consequence of degenerative changes such as disc herniation and osteophyte formation; lower cervical segments are affected most frequently.¹⁹ Most patients with cervical radiculopathy recover after nonsurgical treatment, but persistent pain and patient expectations can motivate surgical intervention.³⁹ The most common surgical treatment procedure

is anterior decompression and fusion (more than 100,000 patients in the United States undergo such surgery each year).²⁶ However, in recent years, artificial disc replacement (ADR) has become an alternative approach.⁸ Several investigational device exemption studies have found clinical noninferiority in comparisons of ADR devices and fusion surgery.^{6,9,31} Even after surgery with decompression of the affected nerve, some patients do not improve or benefit from it. Studies of predictive factors have reported differ-

ABBREVIATIONS ADR = artificial disc replacement; EQ-5D = EuroQol-5 Dimensions; HADS = Hospital Anxiety and Depression Scale; ITT = intention to treat; MCID = minimum clinically important difference; NDI = Neck Disability Index; PROM = patient-reported outcome measure; RCT = randomized controlled trial; VAS = visual analog scale.

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ent variables that affect treatment outcome,^{3,11,16} such as preoperative mental distress, which has been found to be a predictor of negative short-term outcome after surgical treatment for cervical radiculopathy.³⁷ Long-lasting pain can affect psychological/psychosocial factors and can be a mental burden to patients, which predisposes them to developing anxiety and/or depression.¹⁴ In contrast, anxiety and depressive disorders, as well as passive coping, can affect patient perception of and susceptibility to pain.^{4,25,41} For lumbar conditions, comprehensive research has established emotional dysfunction, depression, anxiety, fear, and heightened anger as risk factors for poor surgical outcome,⁵ but for the cervical spine, such research has been sparse. To our knowledge, the role of anxiety and depression assessed using the Hospital Anxiety and Depression Scale (HADS) as the screening tool in long-term outcome after surgical treatment of cervical radiculopathy has not been investigated.

The aim of our study was to investigate the potential predictive value of preoperative risk factors in 5-year outcomes after surgery for cervical radiculopathy.

Patients and Methods

Trial Design

We conducted a multicenter randomized clinical superiority trial in which patients with cervical radiculopathy were assigned randomly to undergo either unconstrained ADR using a Discover cervical disc prosthesis (DePuy Spine, Johnson & Johnson) or fusion using autologous iliac crest graft and plate fixation after decompression. We enrolled patients with cervical radiculopathy aged 25–60 years who met the inclusion criteria (Table 1). According to company guidelines, an ADR device is not recommended for patients with osteoporosis. Therefore, patients with a known diagnosis of osteoporosis or previous osteoporotic fractures and elderly patients (> 60 years old) were excluded. Enrollment of patients took place at 3 Swedish study centers between 2007 and 2011.

Details of the randomization process and results from the 2 years of follow-up have been published previously.³⁶ In brief, after surgical exposure and decompression were

completed, simple 1:1 randomization without blocks was performed using a closed-envelope technique. Hence, both the patient and the surgeon were blinded until decompression was completed and instruments for both ADR and fusion were prepared in the operating room. The ADR group was treated with nonsteroidal anti-inflammatory drugs for 10 days after surgery; otherwise, the postoperative regime was the same in both groups. No collar or restrictions were used in either group. All the participating surgeons were highly experienced in performing both trial interventions.

Trial Oversight

The trial was approved by the local Swedish ethics review board, and each participant provided oral and written informed consent. This study was based on data from the original randomized controlled trial (RCT). The study was registered in the ISRCTN registry (No. 44347115).

Data Collection and Outcomes

The patients completed baseline characteristic questionnaires, postal follow-up questionnaires, and validated patient-reported outcome measures (PROMs) without any assistance from the surgeon. Preoperative data collected included age, sex, length, weight, smoking habits, exercising habits, working status, sick leave status, duration of neck pain, use of analgesics, and PROMs, including Neck Disability Index (NDI) score,²⁸ EuroQol-5 Dimensions (EQ-5D), and the 10-point visual analog scale (VAS)-neck and VAS-arm. The surgeons recorded data including diagnosis, surgical treatment method, surgical levels involved, neurological impairment, Ranawat scale score,³³ Frankel grade,¹³ instability of the cervical spine, type of implant, and eventual perioperative complications. Follow-up and PROM questionnaires were sent to the patients 4 weeks, 3 months, and 1, 2, and 5 years after surgery.

The primary outcome, NDI score, is a 10-item self-administered questionnaire that measures disability in patients with neck pain. The questions measure the ability to perform daily activities (e.g., to dress, lift heavy objects, read, work, drive a car, sleep, and perform leisure-time activities), concentration abilities, and severity of pain and

TABLE 1. Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Age 25–60 yrs	Previous cervical spine surgery
Symptoms of radiating arm pain with a duration of at least 3 mos	>2 cervical levels requiring treatment
Correlating findings on MRI on 1 or 2 cervical levels	Visible or severe osteoarthritis in facet joints evaluated preoperatively on plain radiographs and MRI
Eligible for both treatments	Marked radiological signs or symptoms of myelopathy
Ability to understand and read Swedish language	Drug abuse, dementia, or other reason to suspect poor adherence to follow-up
	Cervical malformation or marked cervical instability
	History of whiplash-associated disorder 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 nonsteroidal antiinflammatory drugs

FIG. 1. Consort diagram.

headache. Each item is scored from 0 to 5. The maximum score is 50 points, which indicates severe disability, and the minimum score is 0, which indicates no disability. The score we used was transformed to a percentage (score of 100) by doubling the total score (range 0%–100%). The minimum clinically important difference (MCID) is 15%–17.3%.^{7,44}

Secondary outcomes were the EQ-5D (range 0.0–1.0, higher scores reflect better quality of life)⁴⁰ and VASs for neck and arm pain²³ (range 0–100 mm, higher scores indicate more severe pain). The MCIDs are 21 mm for the VAS-neck and 29 mm for the VAS-arm.²³

The HADS was used to assess the prevalence of anxiety (HADS-a) and depression (HADS-d) before surgery. The HADS⁴⁵ is a 14-item instrument with 7 questions that

concern anxiety (HADS-a) and 7 that concern depression (HADS-d). Every item is scored on a 4-point scale from 0 to 3, and scores for each subscale range from 0 to 21; the highest total score is 42. It is a validated tool in medical practice for screening psychological distress in non-psychiatric patient populations.^{18,27} Falavigna et al.¹² found that a HADS-d cutoff score of ≥ 10 points in patients undergoing spine surgery resulted in a sensitivity of 71% and a specificity of 95%.

Statistics

We calculated that a minimum of 102 patients would be required for a superiority trial to have 80% power with $\alpha = 0.05$ to detect an MCID in the NDI scores between the treatment groups of at least 10 points.^{22,32,38} To make up for

TABLE 2. Baseline patient demographics stratified according to randomized group

Patient Characteristics	No.	ADR (n = 83)	Fusion (n = 70)	Total (n = 153)
Sex (no. [%])	153			
Female		41 (49.4)	37 (52.9)	78 (51.0)
Male		42 (50.6)	33 (47.1)	75 (49.0)
Age in yrs (mean $\pm$ SD)	153	47 $\pm$ 6.8	47 $\pm$ 6.9	47.0 $\pm$ 6.9
Treatment (no. [%])	153	83 (54.2)	70 (45.8)	153
Body mass index (mean)	151	26 [2]	26	26
Smoker (no. [%])	149	26 (31.7) [1]	21 (31.3) [3]	47 (31.5) [4]
Pension (no. [%])	148	1 (1.2) [1]	0 (0.0) [4]	1 (0.7) [5]
Unemployed (no. [%])	149	8 (9.8) [1]	10 (14.9) [3]	18 (12.1) [4]
Sick leave (no. [%])	148	56 (68.3) [1]	44 (66.7) [4]	100 (67.6) [5]
Disability pension (no. [%])	143	42 (53.8) [5]	31 (47.7) [5]	73 (51.0) [10]
Heavy work (no. [%])	148	72 (87.8) [1]	54 (81.8) [4]	126 (85.1) [5]
Neck pain duration (no. [%])	149			
<3 mos		2 (2.4) [1]	1 (1.5) [3]	3 (2.0) [4]
3–12 mos		15 (18.1)	19 (27.1)	34 (22.2)
1–2 yrs		20 (24.1)	18 (25.7)	36 (24.2) [4]
>2 yrs		40 (48.2)	29 (41.4)	69 (46.3) [4]
Arm pain duration (no. [%])	149	[1]	[3]	[4]
<3 mos		3 (3.6)	3 (4.3)	6 (4.1)
3–12 mos		20 (24.1)	23 (32.9)	43 (28.9)
1–2 yrs		31 (37.3)	17 (24.3)	48 (32.2)
>2 yrs		26 (31.3)	24 (34.3)	50 (33.6)
Regular exercise (no. [%])	147	35 (42.2) [3]	18 (25.7) [3]	53 (36.1)
HADS score (mean $\pm$ SD)	149			
Depression		5.0 $\pm$ 3.5 [3]	4.7 $\pm$ 3.7 [1]	4.9 $\pm$ 3.6
Anxiety		7.0 $\pm$ 4.2 [3]	7.0 $\pm$ 4.1 [1]	7.0 $\pm$ 4.1
Total		12.0 $\pm$ 7.0 [3]	11.8 $\pm$ 7.1 [1]	11.9 $\pm$ 7.0
NDI score (mean $\pm$ SD)	149	63.9 $\pm$ 16.6 [1]	61.5 $\pm$ 14.5 [3]	62.8 $\pm$ 15.7
Levels (no. [%])	153			
1		55 (66.3)	50 (71.4)	105 (68.6)
2		28 (33.7)	20 (28.6)	48 (31.4)

Percentages were computed by group. Values in square brackets indicate the number of missing patients.

crossovers and noncompliance, the final sample included 153 patients.

PROMs were analyzed primarily as intention to treat (ITT) and included all randomly assigned patients. Missing values were imputed with multiple imputation using chained equations as implemented in the R package MICE⁴³ with 20 iterations. A multiple linear regression model was fit to imputed data by using the 5-year NDI score as the outcome and variables from the baseline data as predictors. The predictors were selected based on present knowledge and the directed acyclic graph¹⁷ approach: sex, age (continuous), allocated treatment (fusion vs arthroplasty), smoking status (current vs no present smoking), retirement pension status (yes vs no), unemployment status (yes vs no), sick leave status (yes vs no), disability pension status (yes vs no), having a strenuous job (yes vs no based on the patients own opinion [strenuous was defined as heavy lifting]), neck pain duration (< 3 months, 3–12 months, 1–2 years, or > 2 years), arm pain duration

(< 3 months, 3–12 months, 1–2 years, or > 2 years), amount of exercise (regular exercise > 1/week, yes vs no), preoperative HADS-a score (continuous), preoperative HADS-d score (continuous), preoperative NDI score (continuous), and levels of surgery performed (1 or 2). A second analysis was made in which the HADS-a and HADS-d scores were replaced with the HADS-total score but otherwise with the same variables. Regression coefficients together with 95% confidence intervals (CIs) and p values were calculated for the null hypothesis of no predictive effect on outcome (coefficient = 0).

HADS scores were dichotomized into the high-HADS group if either the anxiety or depression score was ≥ 10 points and the low-HADS group if the anxiety and depression scores were < 10 points, based on Falavigna et al.^{12,37} Using ANCOVA (analysis of covariance), we calculated the mean 5-year outcome value for each HADS group (high and low) adjusted for baseline values of the outcome. The mean differences of the 5-year values between the

TABLE 3. Patient demographics at baseline stratified according to HADS score group

Patient Characteristics	No.	High-HADS Group (n = 47)	Low-HADS Group (n = 102)	Total HADS Score (n = 153)
Sex (no. [%])	149			
Female		27 (57.4)	50 (49.0)	77 (51.7)
Male		20 (42.6)	52 (51.0)	72 (48.3)
Age in yrs (mean $\pm$ SD)	149	46.2 $\pm$ 6.4	47.3 $\pm$ 6.9	47.0 $\pm$ 6.7
Treatment (no. [%])	149			
ADR		26 (55.3)	54 (52.9)	80 (53.7)
Fusion		21 (44.7)	48 (47.1)	69 (46.3)
Smoker (no. [%])	146	19 (40.4) [0]	27 (27.3) [3]	46 (31.5)
Pension (no. [%])	145	1 (2.1) [0]	0 (0.0) [4]	1 (0.7)
Unemployed (no. [%])	146	10 (21.3) [0]	8 (8.1) [3]	18 (12.3)
Sick leave (no. [%])	144	29 (61.7) [0]	43 (46.2) [9]	72 (51.4)
Disability pension (no. [%])	143	30 (63.8) [0]	60 (61.9) [5]	90 (63.0)
Heavy work (no. [%])	145	32 (69.6) [1]	92 (92.9) [3]	124 (85.5)
Regular exercise (no. [%])	146	13 (27.7) [0]	40 (40.4) [3]	53 (36.3)
HADS score (mean $\pm$ SD)	149			
Depression		8.3 $\pm$ 3.1	3.3 $\pm$ 2.5	4.9 $\pm$ 3.6
Anxiety		11.7 $\pm$ 2.8	4.9 $\pm$ 2.5	7.0 $\pm$ 4.1
Total		20.0 $\pm$ 4.4	8.2 $\pm$ 4.3	11.9 $\pm$ 7.0
NDI score (mean $\pm$ SD)	146	68.1 $\pm$ 16.5 [0]	60.8 $\pm$ 14.6 [3]	63.2 $\pm$ 15.6
Levels (no. [%])	149			
1		35 (74.5)	69 (67.6)	104 (69.8)
2		12 (25.5)	33 (32.4)	45 (30.2)

Percentages were computed by group. Patients with missing HADS scores were removed from the study; values in square brackets indicate the number of missing patients.

groups are also presented with a 95% CI. A positive mean difference corresponds to higher values in the high-HADS group than in the low-HADS group. In contrast to NDI scores, lower values for the EQ-5D indicate a worse quality of life; hence, a negative mean difference corresponds to lower values, which reflect a worse quality of life for the high-HADS group than for the low-HADS group.

As a complement, the Spearman rank correlations between the variables we identified as interesting predictors, HADS-total (including HADS-a and HADS-d) and the preoperative outcome measurement, the NDI score, are reported with the Spearman coefficient together with a p value for the null hypothesis of no association. The purpose of this subsection was to study the association between these predictors by determining if the same patients had high values for both scores.

All statistical analyses were performed in R 3.1.0 (2014), packages x86_64, w64, and mingw32 (<http://www.R-project.org>).

Results

The patient-inclusion flow chart is presented in Fig. 1. We randomly assigned 153 patients to undergo ADR (n = 83) or fusion (n = 70). There were 78 women and 75 men with a mean age of 47 years (range 31–60 years) (Table 2). Five patients had a comorbidity (hypertension alone was not accounted for); 3 patients had heart disease, and 2 had been treated for cancer. The mean follow-up duration was

TABLE 4. Results (regression coefficients) from the prediction analysis with HADS-a and HADS-d separately, imputed data

Variable	Reference	Level	Regression Coefficient (95% CI)	p Value
Sex	Female	Male	1.05 (–5.93 to 8.02)	0.77
Age		By 1 unit	–0.27 (–0.80 to 0.26)	0.31
Allocated treatment	Fusion	ADR	3.45 (–3.41 to 10.32)	0.32
Smoking	No	Yes	2.10 (–6.24 to 10.44)	0.62
Pension	No	Yes	2.44 (–38.57 to 43.44)	0.91
Unemployed	No	Yes	–0.68 (–13.07 to 11.69)	0.91
Sick leave	No	Yes	–0.47 (–9.25 to 8.32)	0.92
Disability pension	No	Yes	3.50 (–6.18 to 13.18)	0.47
Strenuous job	No	Yes	–2.79 (–15.82 to 10.24)	0.67
Neck pain duration		By 1 unit	5.17 (–0.34 to 10.67)	0.066
Arm pain duration		By 1 unit	0.92 (–5.35 to 7.19)	0.77
Regular exercise	No	Yes	–3.82 (–11.26 to 3.61)	0.31
HADS-a score		By 1 unit	0.74 (–0.39 to 1.87)	0.20
HADS-d score		By 1 unit	0.79 (–0.53 to 2.11)	0.24
NDI score		By 1 unit	0.25 (–0.01 to 0.50)	0.063
Levels, 1/2	1	2	–0.75 (–8.41 to 6.90)	0.85

TABLE 5. Results (regression coefficients) from the prediction analysis with HADS total, imputed data

Variable	Reference	Level	Regression Coefficient (95% CI)	p Value
Sex	Female	Male	1.05 (−5.89 to 7.99)	0.76
Age		By 1 unit	−0.27 (−0.80 to 0.25)	0.31
Allocated treatment	Fusion	ADR	3.45 (−3.39 to 10.29)	0.32
Smoking	No	Yes	2.11 (−6.20 to 10.42)	0.62
Pension	No	Yes	2.46 (−38.48 to 43.39)	0.91
Unemployed	No	Yes	−0.68 (−13.02 to 11.65)	0.91
Sick leave	No	Yes	−0.46 (−9.22 to 8.31)	0.92
Disability pension	No	Yes	3.50 (−6.15 to 13.15)	0.47
Strenuous job	No	Yes	−2.79 (−15.78 to 10.20)	0.67
Neck pain duration		By 1 unit	5.19 (−0.19 to 10.57)	0.059
Arm pain duration		By 1 unit	0.90 (−5.29 to 7.09)	0.77
Regular exercise	No	Yes	−3.82 (−11.24 to 3.59)	0.31
HADS total score		By 1 unit	0.76 (−0.19 to 1.33)	0.009
NDI score		By 1 unit	0.25 (−0.01 to 0.50)	0.060
Levels, 1/2	1	2	−0.77 (−8.37 to 6.83)	0.84

66 months (range 57–77 months). Nine patients in each group failed to report their NDI score at the 5-year follow-up visit. The cervical levels involved were allocated within the patient groups as follows: C4–C5, 4 (3%); C5–C6, 50 (33%); C6–C7, 50 (33%); C7–T1, 1 (1%); C4–C6, 4 (3%); and C5–C7, 44 (29%).

The high-HADS group included more patients who were smokers (19 of 47 [40%]) and who exercised less (13 of 47 [28%]) than the low-HADS group (27 of 102 [27%] and 40 of 102 [40%], respectively) (Table 3). The HADS-a (Spearman coefficient = 0.74, 95% CI −0.39 to 1.87; $p = 0.20$) and HADS-d (Spearman coefficient = 0.79, 95% CI −0.53 to 2.11; $p = 0.24$) scores separately and treatment allocation (Spearman coefficient = 3.45, 95% CI −3.41 to 10.32; $p = 0.32$) had no effect on the 5-year NDI scores (Table 4). High values on the preoperative HADS-total (Spearman coefficient = 0.76, 95% CI 0.19–1.33; $p = 0.009$) were a negative predictor of outcome (Table 5).

There were 47/153 patients (31%), 26/83 (31%) in the ADR group and 21/70 (39%) in the fusion group, with either a HADS-a or HADS-d score of ≥ 10 points; ≥ 10 points is the cutoff value for indicating significant anxiety/depression for patients undergoing spine surgery.¹² The high-HADS group improved in NDI scores from a mean of 68.1 (95% CI 63.3–73.0) to 45.8 (95% CI 39.2–52.5), and the low-HADS group improved from a mean of 60.4 (95% CI 57.5–63.3) to 29.1 (95% CI 25.0–33.3) (Fig. 2); the mean difference in improvement between the groups was 13.4 (95% CI 5.7–21.2; $p < 0.001$) (Table 6). We also found differences between groups in EQ-5D (−0.16, 95% CI −0.29 to −0.03; $p = 0.014$) and VAS-neck (13.3, 95% CI 3.7–22.9; $p = 0.007$) scores but no difference between groups in VAS-arm scores (7.0, 95% CI −2.3 to 16.4; $p = 0.14$) (Table 6).

The correlation analysis revealed that the patients with higher HADS-total (Spearman coefficient 0.44), HADS-a (Spearman coefficient 0.34), and HADS-d (Spearman coefficient 0.50) scores also had higher preoperative NDI scores ($p < 0.001$); hence, the mentally distressed patients scored the same as the more disabled patients. We found a correlation between the anxious and the depressed patients, indicating that it was more likely to have high scores on both scales (Spearman coefficient 0.67; $p = 0.001$).

FIG. 2. Imputed data, ITT analysis of the high versus low HADS scores. The time-plot diagram shows the mean values of the NDI (left) and VAS-neck (right) scores at each time point. Error bars, 95% CIs.

Discussion

The post hoc analysis of our RCT revealed that anxiety and depression but not treatment modality had a negative effect on surgical treatment outcome even after 5 years of follow-up. Variables that have been reported previously^{11,16} to be important predictors (e.g., smoking and sex) did not affect long-term outcomes in our study, even though the mentally distressed patients in our study were more likely to be smokers.

In a previous post hoc study, which investigated the association between patients with a high HADS score and female sex, we did not find women to be more depressed than men.²³ Conflicting results among previous studies regarding the role of women/men and positive/negative outcomes have been found.^{11,16} One theory is that sex might be a confounder and we instead need to investigate something else, such as mental distress.⁴² Mutual mechanisms and comorbidity between pain and depressive disorders seem to exist.¹⁴ Passive coping has been reported to be a risk factor for disabling neck pain.²⁵ Hence, finding these patients with risk factors before surgery might enable early interventions to enhance treatment success.³⁵

The results from our study suggest that more attention should be paid to the mental distress of patients, because they had an inferior outcome after long-term follow-up. The high-HADS patients also improved after surgical treatment and therefore should not be denied this treatment option, but other resources such as multidisciplinary care should be considered. The fact that most study reports on fusion versus arthroplasty did not present any convincing differences in long-term outcomes among treatment modalities^{6,9,31} indicates that further research about additional treatment and intervention regarding psychological/mental factors in the pain experience and coping mechanisms might be more useful for improving outcome.^{1,10,35}

Most studies on patients with a cervical spine condition have reported associations between mental disability and less improvement after surgical treatment, even though the follow-up periods were short.^{2,15,21,30} Interesting to note is that Mayo et al.²⁴ failed to find such associations, which could be explained by the very short follow-up period (only 6 months) in that study. Persson and Lilja²⁹ discovered that although the patients in their study used active coping before surgery, they developed passive coping mechanisms after surgery to treat cervical radiculopathy; the authors therefore recommended a multidisciplinary rehabilitation program that includes cognitive behavioral therapy groups.

Vadivelu et al.⁴² summarized the relationship between pain and psychology and explained that pain and mood have comparable neuroanatomical substrates and neurobiological mechanisms. The regions in the brain associated with the emotional and sensory responses to pain and the regions affected by depression overlap anatomically. The same dysregulation of dopamine and serotonin is common with both chronic pain and depression. Depressed patients show greater emotional reactivity, which can lead to a diminished ability to regulate pain. Hence, patients with pre-operative depression need more analgesics after surgery than nondepressed patients. Also, anxiety seems to play an important role in pain perception and triggers the same

TABLE 6. Imputed data for the ITT analysis: high-HADS versus low-HADS groups at baseline and after 5 years of follow-up

Score	High-HADS Group					Low-HADS Group					ANCOVA	
	Baseline			5 yrs		Baseline			5 Yrs		Estimate (95% CI)	p Value
	Mean (95% CI)	Median (range)	Mean (95% CI)	Median (range)	Mean (95% CI)	Mean (95% CI)	Median (range)	Mean (95% CI)	Median (range)	Estimate (95% CI)		
NDI	68.1 (63.3 to 73.0)	68 (0 to 92)	45.8 (39.2 to 52.5)	48 (2 to 88)	29.1 (25.0 to 33.3)	60.4 (57.5 to 63.3)	60 (26 to 102)	29.1 (25.0 to 33.3)	24 (0 to 78)	13.4 (5.7 to 21.2)	<0.001	
EQ-5D	0.30 (0.21 to 0.39)	0.2 (-0.2 to 0.7)	0.53 (0.41 to 0.65)	0.7 (-0.2 to 1.0)	0.73 (0.66 to 0.79)	0.46 (0.40 to 0.52)	0.6 (-0.2 to 0.8)	0.73 (0.66 to 0.79)	0.8 (-0.2 to 1.0)	-0.16 (-0.29 to -0.03)	0.014	
VAS neck	59.2 (51.7 to 66.8)	68 (4 to 90)	40.0 (31.2 to 48.7)	40 (0 to 89)	26.1 (20.8 to 31.4)	56.9 (51.9 to 62.0)	60 (0 to 100)	26.1 (20.8 to 31.4)	18 (0 to 95)	13.3 (3.7 to 22.9)	0.007	
VAS arm	58.2 (50.7 to 65.7)	60 (0 to 97)	28.8 (19.9 to 37.7)	23 (0 to 88)	21.6 (16.7 to 26.5)	56.2 (51.1 to 61.2)	60 (0 to 100)	21.6 (16.7 to 26.5)	14 (0 to 100)	7.0 (-2.3 to 16.4)	0.14	

ANCOVA = analysis of covariance.

synapses in the cortex as chronic pain and therefore can contribute to potentiation of the pain experience.^{20,34}

Our study has several strengths. First, we had a long-term follow-up period of 5 years. Second, the follow-up rate after 5 years was 88%, and we used multiple imputation to perform an ITT analysis for the primary outcome. Third, patients and surgeons were blinded to results from the PROMs both before surgery and at the follow-up visits; thus, they were not influenced during decision making or reporting on the patients' health status.

Our study also has some limitations that merit discussion. First, we did not use the HADS at the follow-up visits after surgery. Hence, we do not know what happened with the high HADS scores (i.e., if they remained high in the patients who had them or if they normalized after surgery). Second, the patients had no diagnosis of depression and were not asked about their use of antidepressants. A more thorough investigation about the patients' psychiatric history and medication would have been useful. Third, the HADS was designed as a screening instrument, not a diagnostic tool. Because of the comorbidity of anxiety and depression, uncertainty regarding the ability of these scales to discriminate between the 2 symptoms has been discussed.²⁷ A fourth limitation is that this was a post hoc study of an RCT, and so the results do not have the same strength as those based on the RCT's primary outcome variable.

Conclusions

We found the HADS score, but not allocated treatment, to be a useful instrument for finding patients with a lower level of improvement after surgical treatment for cervical radiculopathy. Recognizing these patients who are likely to improve less is important so that extra attention and better treatment strategies can be considered to prevent secondary long-term complications. More research on the effects of interventions and specialized care to achieve better results in these patients is needed.

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Conception and design: MacDowall, Skeppholm, Olerud. Acquisition of data: MacDowall. Analysis and interpretation of data: MacDowall. Drafting the article: MacDowall. Critically revising the article: Skeppholm, Robinson, Olerud. Reviewed submitted version of manuscript: MacDowall, Olerud. Approved the final version of the manuscript on behalf of all authors: MacDowall. Statistical analysis: Lindhagen. Study supervision: Skeppholm, Robinson, Olerud.

Supplemental Information

Previous Presentations

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