Anterior cervical discectomy and fusion case series

2022

Jang et al. analyzed 71 patients with 142 total spinal levels who underwent double-level ACDF (C4-5-6 and C5-6-7) with an allograft and plate at Seoul hospital between January 2012 and December 2018. Fusion grades were assessed using computed tomography and the Bridwell interbody fusion grading system at 1 year postoperatively. Radiological parameters were obtained from lateral cervical radiographs collected preoperatively and 1 month and 1 year after surgery.

There was no difference in fusion between the C4-5-6 and C5-6-7 ACDF procedures, but the fusion rate and Bridwell fusion grade at the caudal surgery level were lower than those at the cranial surgery level (93 vs. 79%, p < 0.001). The lower endplate of the caudal fusion level showed the most common pseudarthrosis (18 of 71 [25%]). There was no difference in radiological parameters and clinical outcomes between the fusion and pseudarthrosis groups.

In double-level ACDF procedures, the nonfusion rate was higher at the caudal fusion levels, especially at the lower endplates of the caudal fusion levels $^{1)}$.

A study aimed to evaluate the impact that these phenotypes have on preoperative, postoperative, and changes in Cervical spine alignment in patients undergoing anterior cervical discectomy and fusion (ACDF). Baker et al. performed a retrospective study of prospectively collected data of ACDF patients at a single institution. Preoperative magnetic resonance imagings (MRIs) were used to assess for the MC and EA. Patients were subdivided into four groups: MC-only, EA-only, the combined Modic-Endplate-Complex (MEC), and patients without either phenotype. Pre and postoperative MRIs were used to assess alignment parameters. Associations with imaging phenotypes and alignment parameters were assessed, and statistical significance was set at p < 0.5. A total of 512 patients were included, with 84 MC-only patients, 166 EA-only patients, and 71 patients with MEC. Preoperative MC (p = 0.031) and the MEC (p = 0.039) had significantly lower preoperative T1 slope compared to controls. Lower preoperative T1 slope was a risk factor for MC (p = 0.020) and MEC (p = 0.029) and presence of MC (Type II) and the MEC (Type III) was predictive of lower preoperative T1 slope. There were no differences in postoperative alignment measures or patient reported outcome measures. MC and endplate pathologies such as the MEC appear to be associated with worse Cervical spine alignment at baseline relative to patients without these phenotypes. Poor alignment may be an adaptive response to these degenerative findings or may be a risk factor for their development².

ACDF was performed monosegmentally under standardized conditions. X-rays were analyzed to determine the range of motion, fusion rates, and subsidence preoperatively and 3 and 12 months postoperatively. Clinical outcome measurements included neck disability index (NDI), visual analogue scale (VAS) for brachialgia and cervicalgia, and patient satisfaction.

Results: 18 patients were included in the study. The mean RoM decreased from $7.7^{\circ} \pm 2.6$

preoperatively to $1.7^{\circ} \pm 1.1^{\circ}$ after 3 months and $1.8^{\circ} \pm 1.2^{\circ}$ 12 months after surgery. The fusion rates were at 94.4% after 3 and 12 months. The mean subsidence was 0.9 mm \pm 0.5 mm 3 months postoperatively and 1.1 mm \pm 0.5 mm 12 months after surgery. The mean NDI improved significantly from preoperatively to 12 months postoperatively (34.6 \pm 6.2 and 3.4 \pm 4.1, respectively). The VASneck also showed a large improvement from 5.8 \pm 2.2 before and 1.3 \pm 1.4 12 months after surgery, as did the VAS-arm (6.4 \pm 1.5 and 0.9 \pm 1.6, respectively). Patient satisfaction was high throughout the follow-up period.

ACDF with a 3D printed titanium cage resulted in fast fusion without pathological subsidence. In comparison to other cage materials such as PEEK, the 3D printed titanium cage was noninferior in regard to its fusion rate and clinical results ³⁾

2021

Lee et al. from Yangsan retrospectively reviewed the medical records of 40 patients who underwent stand-alone single-level ACDF using a polyetheretherketone (PEEK) cage between January 2012 and December 2018. The study population comprised 19 male and 21 female patients aged 24-70 years. The minimum follow-up period was 1 year. Twenty-seven patients had preoperative bone mineral density (BMD) data on dual-energy X-ray absorptiometry. Clinical parameters included sex, age, body mass index, smoking history, and prior medical history. Radiologic parameters included the C2-7 cobb angle, segmental angle, sagittal vertical axis, disc height, and total intervertebral height (TIH) at the preoperative and postoperative periods. Cage decrement was defined as the reduction in TIH at the 6-month follow-up compared to preoperative TIH. To evaluate the bone quality, Hounsfield unit (HU) value was calculated in the axial and sagittal images of conventional computed tomography.

Lumbar BMD values and cervical HU values were significantly correlated (r=0.733, p<0.001). They divided the patients into two groups based on cage decrement, and 47.5% of the total patients were regarded as cage decrement. There were statistically significant differences in the parameters of measuring the HU value of the vertebra and intraoperative distraction between the two groups. Using these identified factors, we performed a receiver operating characteristic (ROC) curve analysis. Based on the ROC curve, the cut-off point was 530 at the HU value of the upper cortical and cancellous vertebrae (p=0.014; area under the curve [AUC], 0.727; sensitivity, 94.7%; specificity, 42.9%) and 22.41 at intraoperative distraction (p=0.017; AUC, 0.722; sensitivity, 85.7%; specificity, 57.9%). Using this value, they converted these parameters into a bifurcated variable and assessed the multinomial regression analysis to evaluate the risk factors for cage decrement in ACDF. Intraoperative distraction and HU value of the upper vertebral body were independent factors of postoperative subsidence.

Insufficient intraoperative distraction and low HU value showed a strong relationship with postoperative intervertebral height reduction following single stand-alone PEEK cage ACDF ⁴).

2020

The goal of a study of Hirvonen et al. was to asses the long-term outcomes of ACDF surgery among those members of the young adult population who have been operated on between the ages of 18 and 40 at the time of surgery who underwent the operation due to degenerative cervical disorders at Helsinki University Hospital between the years of 1990 and 2005 (476 patients).

Cervical reoperation rate, satisfaction with the surgery, employment status, Neck Disability Index (NDI) They sent questionnaires to all available patients at the end of the follow-up (median 17.5 years) to assess their current neck symptoms, general situations, and levels of satisfaction with the surgery. Furthermore, we compared the results for different types of ACDF surgeries (i.e., discectomy only versus synthetic cage or bone autograft implantation for fusion) in propensity-score-matched groups.

Of the 476 patients who were included in the study, surgery was performed in 72% of the cases due to intervertebral disc herniation and in 28% due to spondylotic changes. The total reoperation rate during the entire follow-up (median 17.5 years) was 24%, and 19.5% if early reoperations (<28 days from index surgery) were excluded. At 10 years post-surgery, the total reoperation rate was 16.8% and 12.8% with early reoperations excluded. The probability of surgery for adjacent level disease was 10.3% at 10 years and 16.8% for the duration of the entire follow-up, with the annual incidence rate of 1.1% for those with ASD requiring surgery. Statistically significant risk factors leading to the need for further cervical surgery included central spinal cord compression and smoking at the time of the index operation. After propensity score matching, there was no significant difference found between the outcomes of different types of surgery. A total of 443 patients were still able to be contacted 12-28 years after the surgery. Of the 281 patients responding to the questionnaires, 92% were still satisfied with the results. With respect to employment, 67% of patients were working, 7% were unemployed, and 7% were on disability due to cervical problems. The median NDI score was 12%, with 56% of patients having an NDI score lower than 15%; it has been suggested that this latter NDI score serves as a cut-off value for significant neck morbidity. The NDI scores were significantly higher among female patients, patients with spondylosis, and patients having undergone further cervical surgeries during the follow-up.

CONCLUSIONS: Long-term satisfaction with the surgery was very high, and the employment rate among patients resembled that of the general population in Finland. Thus, the long-term prognosis after having ACDF surgery at a younger age seems to be good, even though nearly half of the patients experienced some persistent neck symptoms later in life ⁵.

All patients who underwent ACDF from 2012 to 2015 in the National Surgical Quality Improvement Program were identified. Those who underwent concomitant posterior cervical spine surgery operations were excluded. Patients who were discharged to home were compared with those discharged to nonhome destinations (NHD) on the basis of demographics and outcomes. Multivariable models were created to assess whether NHD was an independent risk factor for postdischarge AEs and readmission.

NHD patients were significantly older (63.96 vs. 53.57 y; P<0.0001), more functionally dependent (13.87% vs. 1.09%; P<0.0001), more likely to have body mass index >40 (9.38% vs. 7.51%; P=0.004), and more likely to have ASA Class >2 (77.89% vs. 39.57%; P<0.0001). Patients who underwent NHD were significantly more likely to suffer severe AEs (14.44% vs. 0.93%; P<0.0001), minor AEs (7.22% vs. 0.24%; P<0.0001), and infectious complications (3.58% vs. 0.13%; P<0.0001) before discharge. When examining AEs after discharge, patients who underwent NHD were more likely to suffer severe AEs (6.37% vs. 1.34%; P<0.0001), minor AEs (4.09% vs. 0.74%; P<0.0001), death (1.25% vs. 0.07%; P<0.0001), and unplanned readmission (10.12% vs. 3.06%; P<0.0001). In adjusted analysis, NHD was found to independently predict severe AEs after discharge (odds ratio, 2.40; 95% confidence interval, 1.87-3.07; P<0.0001) and readmission (odds ratio, 1.77; 95% confidence interval, 1.46-2.14; P<0.0001).

NHD patients were significantly sicker than those discharged home. In addition, NHD is associated

with higher rates of postdischarge complications ⁶⁾.

2019

Wang et al. performed a retrospective review of patients who were treated with ACDF at their hospital between 2005 and 2017. Inclusion criteria were adult patients with either cervical PEEK cage or structural allograft, anterior plate fixation, and a minimum 2-year follow-up. Exclusion criteria were hybrid PEEK and allograft cases, additional posterior surgery, adjacent corpectomies, infection, tumor, stand-alone or integrated screw and cage devices, bone morphogenetic protein use, or lack of a minimum 2-year follow-up. Demographic variables, number of treated levels, interbody type (PEEK cage vs structural allograft), graft packing material, anterior cervical pseudarthrosis rates, revision surgery rates, subsidence, and cervical lordosis changes were collected. These data were analyzed by Pearson's chi-square test (or Fisher's exact test, according to the sample size and expected value) and Student t-test.

A total of 168 patients (264 levels total, mean follow-up time 39.5 ± 24.0 months) were analyzed. Sixty-one patients had PEEK, and 107 patients had structural allograft. Pseudarthrosis rates for 1-level fusions were 5.4% (PEEK) and 3.4% (allograft) (p > 0.05); 2-level fusions were 7.1% (PEEK) and 8.1% (allograft) (p > 0.05); and \geq 3-level fusions were 10% (PEEK) and 11.1% (allograft) (p > 0.05). There was no statistical difference in the subsidence magnitude between PEEK and allograft in 1-, 2-, and \geq 3-level ACDF (p > 0.05). Postoperative lordosis loss was not different between cohorts for 1- and 2-level surgeries.

In 1- and 2-level ACDF with plating involving the same number of fusion levels, there was no statistically significant difference in the pseudarthrosis rate, revision surgery rate, subsidence, and lordosis loss between PEEK cages and structural allograft ⁷⁾.

Kumar et al. from Louisville, performed a retrospective cohort analysis using the MarketScan Database of patients who underwent either Anterior cervical discectomy and fusion (ACDF) or Cervical Disc Arthroplasty (CDA) between 2007 and 2011 and had 5 years post-surgery follow-up. Outcomes related to healthcare utilization, cost, and reoperation were analyzed following propensity score matching (PSM).

Of 12,434 patients, 12,099 had ACDF and 335 had CDA procedure. The length of hospital stay and initial hospitalization cost was higher following ACDF compared to CDA. A higher number of CDA patients had early physical therapy compared to ACDF patients (CDA 30.15% vs ACDF 22.39%, p: 0.0176). 5 years post-surgery there was no significant difference in overall payments between ACDF and CDA patients. Reoperation rates were comparable at 5 years after the index procedure (CDA 8.06% vs ACDF 9.25%, p:0.5862). Patients who underwent ACDF exhibited a decreased usage of tramadol post-surgery (15.09% pre-surgery vs 9.55% post-surgery, p: <0.0001).

They found no difference in Healthcare utilization between ACDF and CDA procedures for degenerative disc disease (DDD) 5 years after surgery. Also, there was no difference in reoperation rates during the study period. ACDF resulted in a significant reduction in overall opioid use post-versus pre-procedure⁸⁾.

Since 2016, 35 of 50 USA states have passed opioid-limiting laws. The impact on postoperative opioid prescribing and secondary outcomes following ACDF remains unknown.

To evaluate the effect of opioid-limiting regulations on postoperative opioid prescriptions, emergency department (ED) visits, unplanned readmissions, and reoperations following elective anterior cervical discectomy and fusion (ACDF).

Retrospective review of prospectively-collected data PATIENT SAMPLE: 211 patients (101 pre-law, 110 post-law) undergoing primary elective 1-3 level ACDF during specified pre-law (December 1st, 2015 - June 30th, 2016) and post-law (June 1st, 2017 to December 31st, 2017) study periods were evaluated.

Demographic, medical, surgical, clinical and pharmacological data was collected from all patients. Total morphine milligram equivalents (MMEs) filled were compared at 30-day postoperative intervals, before and after stratification by preoperative opioid-tolerance. Thirty- and 90-day ED visit, readmission, and reoperation rates were calculated. Independent predictors of increased 30-day and chronic (>90 day) opioid utilization were evaluated.

Demographic, medical, and surgical factors were similar pre-law versus post-law (all p>0.05). Postlaw, ACDF patients received fewer opioids in their first postoperative prescription (26.65 vs. 62.08 pills, p<.001; 202.23 vs. 549.18 MMEs, p<.001) and in their first 30 postoperative days (cumulative 30-day MMEs 444.14 vs. 877.87, p<.001). Furthermore, post-law reductions in cumulative 30-day MMEs were seen among both opioid-naïve (363.54 vs. 632.20 MMEs, p<.001) and opioid-tolerant (730.08 vs. 1,122.90 MMEs, p=0.022) patient populations. Increased 30-day opioid utilization was associated with surgery in the pre-law period, preoperative opioid exposure, preoperative benzodiazepine exposure, and number of levels fused (all p<.05). Chronic (>90 day) opioid requirements were associated with preoperative opioid exposure (OR 4.42, p<.001) but not with pre/post-law status (p>0.05). Pre- and post-law patients were similar in terms of 30- or 90-day ED visits, unplanned readmissions, and reoperations (all p>0.05).

Implementation of mandatory opioid prescribing limits effectively decreased 30-day postoperative opioid utilization following ACDF without a rebound increase in prescription refills, ED visits, unplanned hospital readmissions, or reoperations for pain ⁹.

As the focus in spine surgery has shifted from radiographic to patient-centric outcomes, patient reported outcomes measures (PROMs) are becoming increasingly important. They are linked to patient satisfaction, and are used to assess healthcare expenditure, determine compensation and evaluate cost effectiveness. Thus, PROMs are important to various stakeholders, including patients, physicians, payers and healthcare institutions. Thus, it is vital to establish methods to interpret and evaluate these outcome measures.

To evaluate the correlation between Neck Disability Index (NDI), Patient Reported Outcome Measurement Information System Physical Function (PROMIS-PF) and Short Form-12 Physical Health Score (SF-12 PHS) in cervical spine surgery in order to determine the validity of PROMIS-PF in these patients.

Retrospective review of prospectively collected data PATIENT SAMPLE: Consecutive patients who underwent cervical surgery for degenerative spinal pathology with a minimum of 3 months follow-up OUTCOME MEASURES: Self-reported measures i.e. PROMs, including NDI, PROMIS-PF and SF-12 PHS METHODS: No funding was received for this study. The authors report no relevant conflict of interest. PROM collected pre-operatively and at each follow-up were analyzed using Pearson product-moment correlation.

Of the 121 patients included, 66 underwent ACDF, 42 cervical disc replacement, 13 posterior cervical decompression with or without fusion. A statistically significant improvement was achieved in all PROMs by 6 weeks and maintained at 1 year. Furthermore, the percentage of patients achieving an improvement greater than MCID was similar for NDI and PROMIS-PF, particularly at a follow-up of 3 months or more. A statistically significant negative correlation was seen between NDI and PROMIS-PF, which was moderate pre-operatively and in the early post-operative period (r = -0.565 to -0.600), and strong at 3 months or longer follow-up (r = -0.622 to -0.705). A statistically significant, negative correlation was also seen between SF-12 PHS and NDI, which was moderate pre-operatively and at 6 weeks (r = -0.5551 to -0.566); and strong at all other time-points (r = -0.678 to -0.749). There was a statistically significant positive correlation between SF-12 PHS and PROMIS-PF, which was strong to very-strong at all time-points (r = 0.644 to 0.822), except at 2 weeks (r = 0.570).

While NDI and SF-12 have been used for several years, PROMIS is a new outcome measure that is increasingly being implemented. The results of this study demonstrate the convergent and discriminant validity of PROMIS-PF, supported by the strong correlation between SF-12 PHS and PROMIS-PF at all time-points and the moderate correlation between NDI and PROMIS-PF pre-operatively and in the early post-operative period, respectively. Thus, while PROMIS-PF may not be a good surrogate for disease-specific outcome measures, it may extend value as a precise and efficient general health tool ¹⁰.

2018

One hundred-nine patients with one level cervical disc herniation, were randomized to one of the following treatments: Anterior cervical disc arthroplasty (ACDA), Anterior cervical discectomy and fusion (ACDF) with intervertebral cage, Anterior cervical discectomy (ACD) without fusion. Clinical and radiological outcome was measured by NDI, Visual Analogue Scale (VAS) neck pain, VAS arm pain, SF-36, EQ-5D, patients' self-reported perceived recovery, radiographic cervical curvature, and adjacent segment degeneration (ASD) parameters at baseline and until two years after surgery. BBraun Medical paid €298.837 to cover the costs for research nurses.

The NDI declined from 41 to 47 points at baseline to 19 ± 15 in the ACD group, 19 ± 18 in the ACDF group, and 20 ± 22 in the ACDA group after surgery (p=0.929). VAS arm and neck pain declined to half its baseline value and decreased below the critical value of 40 mm. Quality of life, measured by the EQ-5D, increased in all three groups. ASD parameters were comparable in all three groups as well. No statistical differences were demonstrated between the treatment groups.

The hypothesis that ACDA would lead to superior clinical outcome in comparison to ACDF or ACD could not be confirmed during a two-year follow-up time period. Single level ACD without implanting an intervertebral device may be a reasonable alternative to ACDF or ACDA ¹¹.

Lee et al., analyzed the data of 72 patients (ACDF, n=39; LP, n=33). Imbalance on Anterior cervical discectomy and fusion (ACDF) was associated with an increase in CA (balance: preoperative [PRE],

15.64° → follow-up [F/U], 15.74°, p=0.953; imbalance: PRE, -1.14° → F/U, 8.045°, p=0.008), whereas balance on LP was associated with a significant decrease in CA (balance: PRE, 16.26° → F/U, 11.59°, p=0.009; imbalance: PRE, $5.36^{\circ} \rightarrow F/U$, 2.38°, p=0.249). No significant difference was found in the RR and NDI changes in the ACDF group based on balance, but a significant difference was found in RR in the LP group (balance: 61.65%±19.88%, imbalance: 46.90%±15.71%, p=0.046).

They found a significant difference in postoperative alignment in cases of ACDF and LP according to preoperative cervical sagittal balance. The postoperative clinical results of the LP group were more affected by F/U alignment than by the degree of alignment change ¹².

Patients who had disc herniation, stenosis, and DDD and underwent ACDF with or without decompression were prospectively enrolled and followed for a minimum of 10 years with outcome assessment at various intervals. All 159 consecutive patients had autogenous tricortical iliac crest bone graft and plate instrumentation used. Outcomes included visual analog scale for neck and arm pain. pain drawing, Oswestry Disability Index, and self-assessment of procedure success. Preoperative adjacent-level disc degeneration, pseudarthrosis, and secondary operations were analyzed.

For all diagnostic groups, significant outcomes improvement was seen at all follow-up periods for all scales relative to preoperative scores. Outcomes were not related to age, gender, number of levels treated, and minimally to preexisting degeneration at the adjacent level. The use of narcotic pain medication decreased substantially. Neurological deficits almost all resolved. Patient self-reported success ranged from 85% to 95%. Over the long term, additional surgery for pseudarthrosis (10%) occurred in the early follow-up period, and for adjacent segment degeneration (21%), which occurred linearly during the >10-year follow-up period.

ACDF leads to significantly improved outcomes for all primary diagnoses and was sustained for >10 years' follow-up. Secondary surgeries were performed for pseudarthrosis repair and for symptomatic adjacent-level degeneration 13 .

Forty-five patients were prospectively enrolled with cervical degenerative disc disease who requiring ACDF with a PEEK cage. 23 patients were randomised to the study group (empty cages) and 22 patients were in the control group (cages filled with β -tricalcium phosphate). Both patient groups were fixed with a cervical locking plate. A CT scan was performed 12 months postoperatively and 24 months if not confirmed fused at 12 months to evaluate the status of fusion. Clinical status was evaluated using the Japanese Orthopaedic Association (JOA) score, the Oswestry Disability Index (ODI) and the Visual Analogue Scale (VAS).

46 levels (97.88%) in the study group and 44 levels (97.77%) in the control group were confirmed as fused at 24 months. There was no significant difference between the fusion rates observed in the study and control groups (p = 0.82). There was no significant difference in JOA, ODI, or VAS scores at 24 months follow-up. The results showed that the members of the non-fusion group tended to be older than the individuals in the fusion group at 12 months, but was not significant in statistics.

Similar fusion rates and clinical outcomes were achieved when using ACDF with PEEK cages and instrumentation, regardless of whether the cage was filled with bone substitute at 24 months follow-up. Fusion rates improved over time and are comparable between both groups ¹⁴⁾.

A retrospective review of a institutional database identified patients undergoing anterior cervical diskectomy and fusion between 2010 and 2013 with 2 years of clinical follow-up. Patients with substantial weakness, defined as preoperative grade ≤ 3 (on a scale from 0 to 5) in one or more upper extremity muscle groups, were identified. Regression analysis was used to determine risk factors associated with persistent postoperative weakness.

Of the 1,001 patients who were included, 54 (5.4%) demonstrated substantial weakness. By 2 years postoperatively, 47 of 54 patients (87%) demonstrated motor recovery. The duration of preoperative weakness was an independent predictor of recovery (median, 4 months of preoperative weakness among patients with recovery versus 10 months in patients with persistent weakness; P = 0.012).

Duration of preoperative motor weakness is an independent predictor of motor recovery after anterior cervical diskectomy and fusion in patients with substantial motor weakness ¹⁵.

2017

Alonso et al. performed a retrospective case-series of patients treated at a single tertiary care institution between March 2014 and March 2015. Inclusion criteria were age 18-100 years, one or two-level anterior cervical discectomy and fusion with a standalone cervical cage. Data collected included demographics, comorbidities, Charlson comorbidity score, primary diagnosis, and surgical characteristics. Descriptive statistics were performed for risk of readmission, implant failure, revision, and other complications.

They identified 211 patients who met the study criteria. Average surgical time was 107 ± 43 minutes with an estimated blood loss of 84.6 ± 32.4 cc's. There were 11 (5.2%) readmissions. There were 10 (4.74%) implant failures (five involving single-level surgery and five involving two-level surgery), with seven cases of pseudoarthrosis. Mechanisms of failure included a C5 body fracture, fusion in a kyphotic alignment following graft subsidence, and acute spondylolisthesis.

Revision surgery following standalone anterior cervical implants can be complex. Posterior cervical fusion remains a valuable approach to avoid possible vertebral body fracture and loss of fusion area associated with the removal of implants secured through the endplates of adjacent vertebral bodies¹⁶.

Fifty-nine patients were randomized to ACDF surgery with postoperative physiotherapy (30 patients) or to structured physiotherapy alone (29 patients). The physiotherapy program included general and specific exercises as well as pain coping strategies. Outcome measures included neck disability (Neck Disability Index [NDI]), neck and arm pain intensity (visual analog scale [VAS]), health state (EQ-5D questionnaire), and a patient global assessment. Patients were followed up for 5-8 years. RESULTS After 5-8 years, the NDI was reduced by a mean score% of 21 (95% CI 14-28) in the surgical group and 11% (95% CI 4%-18%) in the nonsurgical group (p = 0.03). Neck pain was reduced by a mean score of 39 mm (95% CI 26-53 mm) compared with 19 mm (95% CI 7-30 mm; p = 0.01), and arm pain was reduced by a mean score of 33 mm (95% CI 18-49 mm) compared with 19 mm (95% CI 0.13-0.45)

compared with 0.14 (95% CI 0.01-0.27; p = 0.12). Ninety-three percent of patients in the surgical group rated their symptoms as "better" or "much better" compared with 62% in the nonsurgical group (p = 0.005). Both treatment groups experienced significant improvement over baseline for all outcome measures. CONCLUSIONS In this prospective randomized study of 5- to 8-year outcomes of surgical versus nonsurgical treatment in patients with cervical radiculopathy, ACDF combined with physiotherapy reduced neck disability and neck pain more effectively than physiotherapy alone. Self-rating by patients as regards treatment outcome was also superior in the surgery group. No significant differences were seen between the 2 patient groups as regards arm pain and health outcome ¹⁷.

2016

Seventy-four cases of 1-level anterior cervical discectomy and fusion (ACDF1) and 2-level ACDF (ACDF2) (40 ACDF1 and 34 ACDF2 procedures) were retrospectively reviewed. Upright neutral lateral cervical spine radiography were assessed preoperatively and at 6 weeks and 1 year postoperatively. The measured radiographic parameters included focal lordosis, disc height, C2-7 lordosis, C1-7 lordosis, T1 slope, and C2-7 sagittal vertical axis. Correlation coefficients were calculated to determine the relationships between these radiographic measurements.

The mean values were as follows: preoperative focal lordosis was 0.574°, disc height was 4.48 mm, C2-7 lordosis was 9.66°, C1-7 lordosis was 42.5°, cervical sagittal vertebral axis (SVA) was 26.9 mm, and the T-1 slope was 33.2°. Cervical segmental lordosis significantly increased by 6.31° at 6 weeks and 6.45° at 1 year. C2-7 lordosis significantly improved by 1 year with a mean improvement of 3.46°. There was a significant positive correlation between the improvement in segmental lordosis and overall cervical lordosis. Overall cervical lordosis was significantly negatively correlated with cervical SVA. Improved segmental lordosis was not correlated with cervical SVA in ACDF1 patients but was significantly negatively correlated in ACDF2 patients. There was also a significant positive correlation between the T1 slope and cervical SVA.

In the study population, the improvement of focal lordosis was significantly correlated with an improvement in overall lordosis (C1-7 and C2-7), and overall lordosis as measured by the C2-7 Cobb angle was significantly negatively correlated with cervical SVA. Using lordotic cervical allografts, Gillis et al., successfully created and maintained significant improvement in cervical segmental lordosis at the 6-week and 1-year time points with values of 6.31° and 6.45°, respectively. ACDF is able to achieve statistically significant improvement in C2-7 cervical lordosis by the 1-year followup, with a mean improvement of 3.46°. Increasing the number of levels operated on resulted in improved cervical sagittal parameters. This establishes a baseline for further examination into the ability of multilevel ACDF to achieve cervical deformity correction through the intervertebral correction of cervical lordosis ¹⁸.

Seventy-four cases of 1-level ACDF (ACDF1) and 2-level ACDF (ACDF2) (40 ACDF1 and 34 ACDF2 procedures) were retrospectively reviewed. Upright neutral lateral radiographs were assessed preoperatively and at 6 weeks and 1 year postoperatively. The measured radiographic parameters included focal lordosis, disc height, C2-7 lordosis, C1-7 lordosis, T-1 slope, and C2-7 sagittal vertical axis. Correlation coefficients were calculated to determine the relationships between these radiographic measurements. RESULTS The mean values were as follows: preoperative focal lordosis was 0.574°, disc height was 4.48 mm, C2-7 lordosis was 9.66°, C1-7 lordosis was 42.5°, cervical sagittal vertebral axis (SVA) was 26.9 mm, and the T-1 slope was 33.2°. Cervical segmental lordosis

significantly increased by 6.31° at 6 weeks and 6.45° at 1 year. C2-7 lordosis significantly improved by 1 year with a mean improvement of 3.46°. There was a significant positive correlation between the improvement in segmental lordosis and overall cervical lordosis. Overall cervical lordosis was significantly negatively correlated with cervical SVA. Improved segmental lordosis was not correlated with cervical SVA in ACDF1 patients but was significantly negatively correlated in ACDF2 patients. There was also a significant positive correlation between the T-1 slope and cervical SVA. CONCLUSIONS In the study population, the improvement of focal lordosis was significantly correlated with an improvement in overall lordosis (C1-7 and C2-7), and overall lordosis as measured by the C2-7 Cobb angle was significantly negatively correlated with cervical SVA. Using lordotic cervical allografts, we successfully created and maintained significant improvement in cervical segmental lordosis at the 6-week and 1-year time points with values of 6.31° and 6.45°, respectively. ACDF is able to achieve statistically significant improvement in C2-7 cervical lordosis by the 1-year followup, with a mean improvement of 3.46°. Increasing the number of levels operated on resulted in improved cervical sagittal parameters. This establishes a baseline for further examination into the ability of multilevel ACDF to achieve cervical deformity correction through the intervertebral correction of lordosis ¹⁹.

A total of 1000 consecutive patients who underwent ACDF in an ambulatory surgery center (ASC) (outpatient ACDF) and 484 consecutive patients who underwent ACDF at Vanderbilt University Hospital Nashville, Tennessee (inpatient ACDF) from 2006 to 2013 were included in this retrospective study of patients' medical records. Data were collected on patient demographics, comorbidities, operative details, and perioperative and 90-day morbidity. Perioperative morbidity and hospital readmission were compared between the outpatient and inpatient ACDF groups.

Of the first 1000 outpatient ACDF cases performed in the authors' ASC, 629 (62.9%) were 1-level and 365 (36.5%) were 2-level ACDFs. Mean patient age was 49.5 ± 8.6 , and 484 (48.4%) were males. All patients were observed postoperatively at the ASC postanesthesia care unit (PACU) for 4 hours before being discharged home. Eight patients (0.8%) were transferred from the surgery center to the hospital postoperatively (for pain control [n = 3], chest pain and electrocardiogram changes [n = 2], intraoperative Cerebrospinal fluid fistula [n = 1], postoperative hematoma [n = 1], and profound postoperative weakness and surgical reexploration [n = 1]). No perioperative deaths occurred. The 30-day hospital readmission rate was 2.2%. All 90-day surgical morbidity was similar between outpatient and inpatient cohorts for both 1-level and 2-level ACDFs.

An analysis of 1000 consecutive patients who underwent ACDF in an outpatient setting demonstrates that surgical complications occur at a low rate (1%) and can be appropriately diagnosed and managed in a 4-hour ASC PACU window. Comparison with an inpatient ACDF surgery cohort demonstrated similar results, highlighting that ACDF can be safely performed in the outpatient ambulatory surgery setting without compromising surgical safety. In an effort to decrease costs of care, surgeons can safely perform 1- and 2-level ACDFs in an ASC environment²⁰.

Seventy-one patients who underwent 3-level ACDF and 26 patients who underwent 4-level ACDF were identified and followed for an average of 7.6 \pm 4.2 years. There was 1 case (3.9%) of deep wound infection in the 4-level group and 1 case in the 3-level group (1.4%; p = 0.454). Postoperatively, 31% of patients in the 4-level group complained of dysphagia, compared with 12.7% in the 3-level group (p = 0.038). The fusion rate was 84.6% after 4-level ACDF and 94.4% after 3-level ACDF (p = 0.122). At last follow-up, a significantly higher proportion of patients in the 4-level group continued to have axial

neck pain (53.8%) than in the 3-level group (31%; p = 0.039); the daily oral morphine equivalent dose was significantly higher in the 4-level group (143 ± 97 mg/day) than in the 3-level group (25 ± 10 mg/day; p = 0.030). Outcomes based on Odom's criteria were also different between cohorts (p = 0.044), with a significantly lower proportion of patients in the 4-level ACDF group experiencing an excellent/good outcome.

In this study, patients who underwent 4-level ACDF had significantly higher rates of dysphagia, postoperative neck pain, and postoperative narcotic usage when compared with patients who underwent 3-level ACDF. Pseudarthrosis and deep wound infection rates were also higher in the 4-level group, although this did not reach statistical significance. Additionally, a smaller proportion of patients achieved a good/excellent outcome in the 4-level group than in the 3-level group. These findings suggest a significant increase of perioperative morbidity and worsened outcomes for patients who undergo 4- versus 3-level ACDF ²¹⁾.

Fifty-four operated cervical disc hernia cases were retrospectively examined in 2 groups. Discectomy and osteophytectomy were carried out in Group A by using a high speed drill, while a curette was used for group B. Preoperative and postoperative computerized tomography and direct radiography were performed. Cervical disc height, cervical and segmental lordotic angles were calculated. The visual analogue scale and Odom's criteria were used in the assessment of pain and clinical healing. The fusion ratio of both groups was compared. The Mann-Whitney U test was used to compare data from the groups.

Satisfactory results were obtained in the groups where high-speed drill and curette were used. Independently from the surgical technique, pain scores were significantly reduced in both groups after surgery. No radiologically significant differences were identified between the two groups within the postoperative period ²²⁾.

Twenty-five cases with single level cervical disc herniation (CDH) who underwent microdiscectomy were included to this study. Reconstruction was performed using empty bladed cervical PEEK cages. Clinical (Visual analogue scale (VAS) and Odom's criteria) and radiological results (intervertebral disc and foraminal heights, mean cervical spine lordosis angle, and fusion rate) were reviewed one day and one year after surgery.

There were 18 males and 7 females, aged between 25 and 54 years (mean: 40.8). Mean neck and arm VAS scores reduced from 2.9 to 1.4, and from 7.2 to 1.8, respectively. Odom scores were found to be 1.6 and 1.4 at 1st day and one year postoperatively, respectively. Subsidence was seen in three cases (12%). There was no significant change in heights of neural foramina and intervertebral discs, and no change in cervical spine lordosis, when compared postoperative 1st day and one year radiographs. Fusion was detected in 92% of cases in one year.

Bladed cervical cages are safe with almost no risk of dislocation. Empty cages provide acceptable rates of fusion and subsidence ²³⁾.

In a retrospective cohort study, Haghnegahdar and Sedighi evaluated 68 patients who had undergone

ACDF for cervical disc herniation from March 2006 to March 2011. Outcome tools were as follows: (1) study-designed questionnaire that addressed residual and/or new complaints and subjective satisfaction with the operation; (2) recent (one week prior to the interview) postoperative VAS for neck and upper extremity radicular pain; (3) Japanese Orthopaedic Association Myelopathy Evaluation Questionnaire (JOACMEQ) (standard Persian version); and (4) follow-up cervical Magnetic Resonance Imaging (MRI) and lateral X-ray.

With mean follow-up time of 52.93 (months) \pm 31.89 SD (range: 13-131 months), we had success rates with regard to Δ VAS for neck and radicular pain of 88.2% and 89.7%, respectively. Except QOL functional score of JOAMEQ, 100% success rate for the other 4 functional scores of JOAMEQ was achieved.

ACDF is a successful surgical technique for the management of cervical disc herniation among Iranian population $^{24)}$.

2015

A total of 112 patients were enrolled and randomly assigned to receive saline or dexamethasone. Data gathered included demographics, functional status (including modified Japanese Orthopaedic Association myelopathy score, neck disability index, 12-Item Short-Form Health Survey score, and patient-reported visual analog scale score of axial and radiating pain), functional outcome swallowing scale score, interval postoperative imaging, fusion status, and complications/reoperations. Follow-up was performed at 1, 3, 6, 12, and 24 months, and CT was performed 6, 12, and 24 months after surgery for fusion assessment. RESULTS Baseline demographics were not significantly different between the 2 groups, indicating adequate randomization. In terms of patient-reported functional and pain-related outcomes, there were no differences in the steroid and placebo groups. However, the severity of dysphagia in the postoperative period up to 1 month proved to be significantly lower in the steroid group than in the placebo group (p = 0.027). Furthermore, airway difficulty and a need for intubation trended toward significance in the placebo group (p = 0.057). Last, fusion rates at 6 months proved to be significantly lower in the steroid group but lost significance at 12 months (p = 0.048 and 0.57, respectively).

Dexamethasone administered perioperatively significantly improved swallowing function and airway edema and shortened length of stay. It did not affect pain, functional outcomes, or long-term swallowing status. However, it significantly delayed fusion, but the long-term fusion rates remained unaffected. Clinical trial registration no.: NCT01065961 (clinicaltrials.gov)²⁵⁾.

2013

Retrospective analysis and investigation of long-term results for 41 consecutive patients who had undergone anterior cervical discectomy and fusion with an intervertebral cage for cervical disc hernia. The angle of lordosis, segmental height and range of motion were evaluated preoperatively and postoperatively at 1 month and 2 years. The clinical outcome was assessed by the visual analog scale and Odom's criteria.

The angle of lordosis increased by 2.62° and the range of motion angle increased by 5.14° after the operation. The segmental height did not change. The visual analog scale and Odom's criteria scores

decreased significantly after the operation.

Using a cage in anterior cervical discectomy prevents segmental collapse, so the segmental height and the angle of lordosis are preserved and newly-developed pain does not occur²⁶⁾.

Thirty-one patients who underwent anterior cervical fusion using a stand-alone polyetheretherketone (PEEK) cage packed with local autobone graft from July 2009 to december 2011 were enrolled in this study. Bone fusion was assessed by cervical plain radiographs and computed tomographic scan. Nonunion was evaluated according to the absence of bony bridge on computed tomographic scan. Subsidence was defined as a \geq 2 mm decrease of the interbody height at the final follow-up compared to that measured at the immediate postoperative period.

Subsidence was observed in 7 patients (22.6%). Of 7 patients with subsidence greater 2 mm, nonunion was developed in 3. Three patients with subsidence greater 2 mm were related with endplate damage during intraoperative endplate preparation. Solid bone fusion was achieved in 28 out of 31 patients (90.3%).

With proper patient selection and careful endplate preparation, anterior cervical discectomy and fusion (ACDF) using a stand-alone PEEK cage packed with local autobone graft could be a good alternative to the standard ACDF techniques with plating ²⁷⁾.

2012

A total of 25 consecutive patients suffering from degenerative cervical disc disease who underwent three-level anterior cervical discectomy and fusion (ACDF) including polyetheretherketone (PEEK) cages packed with allograft were followed up for at least two years. The fusion rate reached 72% (18/25), and asymptomatic pseudarthrosis was seen in 6 patients but without mobility on flexion-extension radiographs, and revision surgery was not needed. Cage subsidence occurred at one level (C67), but it was not progressive, and reoperation was not necessary. A significant increase (P < 0.001) in fused segment angle (FSA) and fused segment height (FSH) was observed postoperatively. Similarly, a significant clinical improvement (P < 0.001) was demonstrated postoperatively in terms of Japanese Orthopedic Association (JOA) score and visual analog scales (VASs) score. PEEK cages alone with allograft proved to be a safe and effective surgical option in the treatment of three-level degenerative cervical disc disease. Although the fusion rate was not high, this technique may offer improvement of symptomatology and maintenance of cervical spine's sagittal profile ²⁸⁾.

2010

258 patients who underwent ACDF for cervical disc degeneration (CDD). Fusion was attained with either tricortical AICG or PEEK cages without additional anterior plating, with treatment selected at surgeon's discretion. Radicular pain, neck-pain, headache and patient satisfaction with the treatment were scored using the visual analogue scale (VAS).

The median age was 47.5 (28.3-82.8) years, and 44% of patients were female. 59% had single-level ACDF, 40% had two level ACDF and 1% had three-level ACDF. Of the patients, 181 were fused with AICG and 77 with a PEEK-cage. After surgery, the patients showed a significant reduction in radicular pain (DeltaVAS = 3.05), neck pain (DeltaVAS = 2.30) and headache (DeltaVAS = 0.55). Six months

after surgery, 48% of patients had returned to work: however 24% were still receiving workers' compensation.Using univariate and multivariate analyses we found that high preoperative pain intensity was significantly associated with a decrease in pain intensity after surgery, for all three pain categories. There were no significant correlations between pain relief and the following patient characteristics: fusion method (AICG or PEEK-cage), sex, age, number of levels fused, disc level fused, previous neck surgery (except for neck pain), previous neck trauma, or preoperative symptom duration. Two hundred out of the 256 (78%) patients evaluated the surgical result as successful. Only 27/256 (11%) classified the surgical result as a failure. Patient satisfaction was significantly associated with pain relief after surgery.

ACDF is an effective treatment for radicular pain in selected patients with CDD after six months follow up. Because of similar clinical outcomes and lack of donor site morbidity when using PEEK, we now prefer fusion with PEEK cage to AICG. Lengthy symptom duration was not a negative prognostic marker in our patient population. The number of patients who returned to work 6 months after surgery was lower than expected ²⁹.

2009

Different types of surgical techniques are used for effective treatment of cervical disc prolapse. Techniques with fusion without stabilization have some disadvantages like collapse of the graft, extrusion of graft, nonunion and recurrence of symptoms.

Ali et al. carried out a prospective interventional study between March 2001 to November 2007 on 129 cases of cervical disc prolapse treated with anterior cervical discectomy, fusion & stabilization with plating at IBN SINA Hospital, Dhanmondi, Dhaka, Al-Manar Hospital, Lalmatia and Bangabandhu Sheikh Mujib Medical University, Shahbag, Dhaka. There were 106(82.17%) male and 23(17.82%) female patients. The commonest age group of the patients was 4th decade. The commonest level of disc prolapse was found in C5/6 level and in each case, diagnosis was made on the basis of clinical findings, plain X-ray and MRI of cervical spine. We performed anterior cervical discectomy, fusion and stabilization with plating in all cases. A per-operative marking film was taken in each case to identify proper level. Per-operative undue hemorrhage from donor site occurred in 1 case, 27 patients complained of dysphagia temporarily, 64 patients complained of donor site pain significantly which was relieved within 3-6 months of follow-up period. Donor site infection was found in 1 patient. The post operative follow-up period was 3 months to 6 years. The functional out come obtained excellent in 71.43%, good in 19.64%, fair in 8.93%, poor in 2.32% in this series ³⁰.

2007

Ninety-five patients with neck and radicular arm pain lasting for at least 6 months were randomly selected to receive ACDF with the CP or the CIFC. Questionnaires concerning pain and NDI were obtained from 83 patients (87%) at a mean follow-up time of 76 months (range 56-94 months). When evaluating clinical benefits regarding pain intensity 6 years after ACDF, according to different cut-off points and relative percentages, symptoms improved in 46-78% of patients. Improvement in NDI was seen in 18-20% of patients. Approximately 70% of the patients had persistent pain and disability at 6-year follow-up. There was no clinically important difference following CP versus CIFC. Thirty millimeter and 20% in pain intensity and NDI, respectively, are reasonable criteria to suggest a clinically relevant change after ACDF. Before patients undergo ACDF, they should be informed that they have an

approximate 50% probability of achieving pain relief and little probability of functional improvement. The findings demonstrate that there is poor evidence for difference between CIFC and CP 31 .

2005

Seventy-one patients who had anterior cervical discectomy and fusion with allograft and plating an average of 7.2 years prior responded to an invitation to return for a follow-up clinical and radiographic review.

At final review, symptom resolution remained greater than 82% and fusion occurred in 92.6% of the disc spaces operated on. No graft extrusion or migration occurred. Based on our strict criteria, the rates of collapse and subsidence were high, at 47.9% (34 patients) overall. However, in only 6 patients (8.5%) did segmental kyphosis result, none of whom required any revision surgery in the follow-up period. Implant complications occurred in 7 patients (9.9%), none of whom required revision surgeries. Adjacent level degeneration occurred in 52 patients (73.2%). Further cervical spine surgeries were required in 14 patients (19.7%), 2 for inadequate decompression, and 12 for adjacent level disease. Segmental and global cervical lordosis was restored and maintained by the surgery over the study period.

The use of allografts and plate fixation in combination for anterior cervical discectomy and fusion does not compromise the radiologic and clinical outcomes while providing the advantages of donor site morbidity elimination, restoration of cervical segmental lordosis, and not requiring postoperative immobilization ³²⁾.

All patients underwent a single-level ACDF at the authors' institution. Radiographs at early and final follow-up were examined, and three measurements were made: disc height, disc space angulation, and spinous process distance. These radiographic measurements were correlated with Visual Analog Scales (VASs) for neck and arm pain and Oswestry Disability Index (ODI).

RESULTS: There were significant changes in disc height (5.3 vs 7.0 mm) as well as disc space angulation (3.3 degrees vs 0.1 degrees). Reduction in neck pain VAS score (6.7 vs 3.2) and arm pain VAS score (5.1 vs 2.3) was significant. ODI scores were not statistically different, but improvement of 20.1% was observed. Correlations between radiographic parameters and clinical outcomes were moderate to low, and none was significant.

CONCLUSIONS: While restoration of Cervical spine alignment and disc height is important, clinical results are critical in analysis of outcomes following ACDF. We have shown that although clinical outcomes remain good, there does not appear to be any strong correlation with radiographic results. Emphasis on restoration of Cervical spine alignment appears justified, but its influence on clinical outcomes may be overstated ³³⁾.

2001

Long-term follow-up evaluation after surgery was performed in 249 patients (96 women and 153 men) with radicular signs only. The mean age was 46.0 +/- 8.7 years (range, 24-74 years), and the observation time ranged from 10-15 years (mean, 12.2 +/- 1.2 years). Clinical grading after surgery according to Odom's criteria was based on a questionnaire. The outcome was related to morphologic

findings, lumbar symptoms, physical stress, duration of symptoms, age, sex, and cervical level involved.

RESULTS: Complications related to surgery occurred in 13 (5.2%) patients, but only three (1.2%) had persistent problems. Of the 249 patients, 101 (40.6%) were without any symptoms (Odom I), 92 (36.9%) had a good outcome (Odom II), and 47 (18.9%) a fair outcome (Odom III). Only nine patients (3.6%) reported an unchanged or worse status than before surgery (Odom IV). Additional lumbar symptoms, high occupational physical stress, and discrepancy of preoperative findings were significantly correlated with a worse outcome. Short duration of symptoms and soft disc disease were favorable prognostic factors.

CONCLUSIONS: PMMA interbody fusion after ventral discectomy in cervical disc surgery is a safe and reliable method with few complications and an outcome comparable with other ventral procedures ³⁴⁾.

1995

Between 1983 and 1993, 153 patients underwent surgery for the treatment of cervical degenerative disc disease: in 139 cases the technique without fusion was applied. This retrospective study analyze clinical and radiological parameters in order to verify any possible prognostic factor. 108 patients with radiculopathy and 31 patients with myelopathy were followed up clinically for at least 12 months up to 10 years. An excellent or good long-term result was achieved in 90.9% of patients with radiculopathy and 58.1% of those with myelopathy. The age of the patients, the duration of symptoms before diagnosis and the pathogenesis of disc herniation did not represent significant parameters influencing the outcome of patients. The results of the present study show that anterior discectomy without fusion lead to good clinical long-term results, either in patients with pure radicular syndrome, or in cases with myelopathy. The presentation with pure radicular signs is the most important factor in predicting a good overall outcome ³⁵⁾.

1993

results of the Robinson method of anterior cervical discectomy and arthrodesis with use of autogenous iliac-crest bone graft, at one to four levels, in 122 patients who had cervical radiculopathy. A one-level procedure was done in sixty-two of the 122 patients; a two-level procedure, in forty-eight; a three-level procedure, in eleven; and a four-level procedure, in one. The average duration of clinical and roentgenographic follow-up was six years (range, two to fifteen years). The average age was fifty years (range, twenty-five to seventy-eight years). Preoperatively, 118 patients had pain in the arm, fifty-five had weakness of one or more motor roots, and seventy-seven had sensory loss. At the time of follow-up, eighty-one patients had no pain in the neck, twenty-six had mild pain in the neck, nine had moderate pain in the neck, four had mild radicular pain, and two had a combination of mild radicular pain and moderate pain in the neck. One hundred and eight patients had no functional impairment, and fourteen had a slight limitation of function during the activities of daily living. Nine of eleven patients who had symptoms related to a change at one level cephalad or caudad to the site of a previous arthrodesis had another operative procedure. Lateral roentgenograms of the cervical spine, made in flexion and extension, showed a pseudarthrosis at twenty-four of 195 operatively treated segments. Sixteen of the patients who had a pseudarthrosis were symptomatic, but only four had sufficient pain to warrant revision. The risk of pseudarthrosis was significantly greater after a multiple-level arthrodesis than after a single-level arthrodesis (p < p

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0.01). At the time of the most recent follow-up, fifty-three of the fifty-five patients who had had a motor deficit had had a complete recovery, and the two remaining patients had had a partial recovery. Seventy-one of the seventy-seven patients who had had a sensory loss had regained sensation. None of the patients had an increased neurological deficit postoperatively. Our results suggest that the Robinson anterior cervical discectomy and arthrodesis with an autogenous iliac-crest bone graft for cervical radiculopathy is a safe procedure that can relieve pain and lead to resolution of neurological deficits in a high percentage of patients ³⁶⁾.

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