Impact of Depression Severity on Patient-Reported Outcome Measures Following Multilevel Anterior Cervical Discectomy and Fusion

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ABSTRACT

Background: Few studies have investigated the effects of preoperative depression and multilevel procedures on patient-reported outcomes (PROs) following anterior cervical discectomy and fusion (ACDF). This study aims to determine the impact of preoperative depression on PROs in single vs multilevel ACDF procedures.

Methods: Eligible primary single or multilevel ACDF procedures were retrospectively reviewed from 2015 to 2020 using a surgical database. PROs included visual analog scale (VAS), Neck Disability Index (NDI), 12-Item Short Form Physical Composite Summary and Mental Composite Summary (SF-12 PCS and MCS), and Patient-Reported Outcomes Measurement Information System physical function (PROMIS PF). PROs were collected preoperatively and at 6 weeks, 12 weeks, 6 months, and 1 year postoperatively. Patients were stratified into 3 groups based on Patient Health Questionnaire-9 (PHQ-9) score. Differences in PROs were assessed based on preoperative depression severity or both preoperative depression severity and number of operative levels.

Results: Our patient cohort included 42 individuals with minimal preoperative depressive symptoms, 32 having mild and 27 having moderate to severe. Baseline PRO values were significantly different between groups (all $P < 0.01$). Improvement significantly differed between groups at 6 weeks for VAS arm, NDI, and SF-12 MCS (all $P < 0.05$), and at 12 weeks for VAS neck, NDI, SF-12 PCS and MCS, and PROMIS PF (all $P < 0.05$). SF-12 PCS and MCS at 6 months and VAS arm and SF-12 MCS at 1 year demonstrated significant intergroup differences (all $P < 0.05$). VAS arm at 1 year ($P = 0.029$), NDI at 12 weeks ($P = 0.034$), PROMIS PF at 6 weeks ($P = 0.038$), and SF-MCS at all postoperative time points were impacted by both preoperative depression severity and number of levels fused.

Conclusion: Depression severity impacted recovery of pain, disability, and physical function preoperatively and at intermittent postoperative time points. Both severity and multilevel procedures impacted pain and mental health at intermittent postoperative time points. In addition to depression, multilevel ACDF procedures are an additional factor that must be considered in expected improvement of postoperative outcomes.

Level of Evidence: 4.

Clinical Relevance: Multilevel ACDF procedures and preoperative depression severity both impact postoperative pain, disability, and physical function.

INTRODUCTION

Depression is one of the most common mental disorders globally, with more than 250 million suffering from the disease, and it is considered one of the leading causes of disability worldwide.¹ With how commonplace this disorder is becoming, it is increasingly important for clinicians to consider a patient’s mental health as a contributing factor toward their overall health. One method to keep track of a patient’s overall mental well-being is through the use of patient-reported outcome measures (PROMs), which gauge their perception of various aspects of their health status.

One such PROM to assess depression is the Patient Health Questionnaire-9 (PHQ-9). This questionnaire is a reliable and accurate screening tool for major depressive disorder and is based on criteria outlined in the Diagnostic and Statistical Manual of Mental Disorders (DSM-5).² Although a self-reported questionnaire, PHQ-9 has been established as a useful diagnostic tool for clinicians and has been validated in both lumbar and cervical spine patient populations.³⁻⁵ Its application has been especially useful among cervical radiculopathy patients presenting with pain and disability; both of which are proven risk factors for depression.⁶⁻⁷ Anterior cervical discectomy and fusion
(ACDF) is a proven treatment for a radiculopathy and has demonstrated favorable outcomes and high satisfaction ratings. However, when considering the impact of depression on postoperative improvements, current studies indicate less favorable outcomes.

ACDF patients preoperatively diagnosed with depression are at an increased risk of adverse outcomes, increased opioid consumption, and increased healthcare expenses compared to those without depression. While an overwhelming majority of studies outline a strong association between preoperative depression and worse overall outcomes in pain and disability following single-level ACDF procedures, few report on the effects of depression on multilevel procedures. Such procedures have been demonstrated to have higher instances of complications, increased rates of revisions, and worse postoperative outcomes with the increasing number of operative levels. Coupled with the negative effects of depression on postoperative outcomes, it is possible that depressed individuals undergoing multilevel procedures may be at even greater risk for poorer outcomes and ultimately lower health-related quality of life. Currently, there is a dearth of information surrounding depression and its effects on outcomes in multilevel ACDF procedures, and no study to date has focused on depression severity and its impact on these specific procedures. Therefore, the study aims to focus on the impact that multilevel procedures have on outcomes among individuals with varying levels of depression to help clinicians better counsel patients preoperatively. We hypothesize that patients will demonstrate worse pain, disability, and mental health following a multilevel ACDF as compared to single-level procedures.

METHODS

Patient Population

In accordance with our institution’s ethical guidelines, Institutional Review Board approval (ORA 14051301) and patient-informed consent were obtained for this study. A retrospective review of a surgical database was performed to identify eligible cervical spine procedures from March 2015 to January 2020. All procedures were performed by a single attending physician at a single institution. Inclusion criteria were defined as adult patients who underwent a primary, elective, single, or multilevel ACDF for degenerative spinal pathology. Exclusion criteria were defined as patients undergoing a primary or revision procedure for treatment of an infection, malignancy, or trauma. Initial screening of the surgical registry identified 305 eligible patients. After inclusion and exclusion criteria were applied the final study cohort consisted of 101 patients.

Data Collection

Information pertaining to patients’ age, sex, body mass index, smoker status, ethnicity, and diabetic status were collected as the part of their demographics. Physical classification and comorbidity burden were also recorded as American Society of Anesthesiologists classification and Charlson Comorbidity Index, respectively. Spinal pathologies were recorded along with perioperative characteristics, which included operative duration (skin incision to skin closure), estimated blood loss, length of postoperative stay, and day of discharge. The primary outcomes of interest were PROMs for pain, disability, physical function, and mental health.

Neck and arm pain were evaluated using the visual analog scale (VAS) whereas disability was assessed using the Neck Disability Index (NDI). Physical function was evaluated using 2 separate PROMs, either 12-Item Short Form Health Survey Physical Component Score (SF-12 PCS) or Patient-Reported Outcome Measurement Information System physical function (PROMIS PF). Lastly, mental health was evaluated using both the PHQ-9 as well as the 12-Item Short Form Mental Composite Score (SF-12 MCS). All PROMs were collected at the preoperative time point and subsequently at the 6-week, 12-week, 6-month, and 1-y postoperative time points.

Statistical Analysis

All statistical analysis was performed using StataIC 16.1 (StataCorp, College Station, TX, USA). Prior to analysis, patients were categorized into 3 groups based on preoperative PHQ-9: minimal (<5), mild (5–9), and moderate to severe (>9). Descriptive statistics were performed for demographic and perioperative characteristics as well as for all PROMs. Univariate analysis was performed to evaluate significant differences, in demographics and perioperative characteristics, between depression groups using either a chi-square test for categorical variables or a two-tailed t test for continuous variables. The impact of preoperative depression severity on PROM values was evaluated using a simple linear regression. In order to determine the impact of multilevel procedures in addition to severity of preoperative depression on postoperative PROMs scores, a multiple linear regression was performed. All statistical analysis required a $P \leq 0.050$ for significance.
RESULTS

Of the 101 patients included in this study, 42 were categorized as having minimal depressive symptoms, 32 having mild symptoms, and 27 having moderate to severe. The study cohort had a mean age of 48.1 years with 60% being men and 59% nonobese (BMI < 30 kg/m²). Tests for independence of demographics between groups demonstrated no significant differences except for ethnicity ($P = 0.028$) (Table 1). Majority of patients had a spinal pathology of myeloradiculopathy (88.1%), and a higher proportion of procedures were treated at the single level (58.4%). Mean operative time was 54.3 min with an average estimated blood loss of 29.8 mL. No significant perioperative differences were observed between depression groups (all $P > 0.100$) (Table 2).

Primary Outcomes

Regression analysis revealed that preoperative scores for VAS neck, VAS arm, NDI, SF-12 PCS,
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PROMIS PF, and SF-12 MCS worsened based on preoperative depression severity (all \( P < 0.010 \)). VAS neck demonstrated significantly different postoperative scores based on preoperative depression severity at the 12-week timepoint only (\( P = 0.012 \)). VAS arm demonstrated significant differences between groups at the 6-week (\( P = 0.031 \)) and 1-year (\( P = 0.031 \)) postoperative time points. NDI scores were significantly worse with the increasing severity of preoperative depression at the 6-week (\( P = 0.019 \)) and 6-month (\( P = 0.038 \)) timepoint only. Similarly, PROMIS PF demonstrated worse postoperative scores with more severe preoperative depressive symptoms at the 12-week timepoint only (\( P = 0.046 \)). Mental health demonstrated significant differences between all groups at all postoperative timepoints (all \( P < 0.01 \)). A summary of postoperative PROM scores as a function of worsening preoperative depression is found in Table 3.

Impact of Multilevel Procedures

The collective impact of multilevel ACDF procedures and preoperative depression severity demonstrated significant effects on postoperative scores for VAS arm, NDI, PROMIS PF, and SF-12 MCS (all \( P < 0.05 \)). More specifically, although no difference in scores due to the added effect of a multilevel procedure was demonstrated for VAS neck, VAS arm demonstrated a significant difference between groups at the 12-week timepoint only (\( P = 0.046 \)).

Table 3. Postoperative improvement by depression severity and number of levels fused.

| PROM          | Minimal | Mild          | Moderate/Severe | \( P \) value* | \( P \) value† |
|---------------|---------|---------------|-----------------|---------------|---------------|
|               | Mean ± SD (n) | Mean ± SD (n) | Mean ± SD (n)   |               |               |
| VAS neck      |         |               |                 |               |               |
| Preoperative  | 4.7 ± 2.4 (40) | 6.5 ± 2.1 (30) | 7.4 ± 2.3 (27)  | <0.001        |               |
| 6 wk          | 3.0 ± 2.6 (38) | 3.4 ± 2.4 (30) | 3.6 ± 2.7 (24)  | 0.292         | 0.789         |
| 12 wk         | 1.9 ± 2.3 (32) | 3.3 ± 2.2 (24) | 3.6 ± 2.5 (21)  | 0.012         | 0.172         |
| 6 mo          | 2.1 ± 2.5 (28) | 3.1 ± 2.2 (22) | 2.9 ± 2.8 (19)  | 0.251         | 0.629         |
| 1 y           | 2.4 ± 2.3 (15) | 3.0 ± 2.9 (9)  | 4.4 ± 3.5 (7)   | 0.143         | 0.554         |
| VAS arm       |         |               |                 |               |               |
| Preoperative  | 5.0 ± 2.6 (40) | 6.6 ± 2.2 (30) | 6.9 ± 2.6 (27)  | 0.002         |               |
| 6 wk          | 2.0 ± 2.3 (38) | 3.2 ± 2.8 (30) | 3.8 ± 5.2 (24)  | 0.031         | 0.326         |
| 12 wk         | 3.3 ± 3.7 (32) | 2.3 ± 2.4 (24) | 3.5 ± 3.4 (21)  | 0.824         | 0.231         |
| 6 mo          | 2.9 ± 3.7 (28) | 3.1 ± 2.4 (22) | 3.3 ± 3.4 (17)  | 0.693         | 0.991         |
| 1 y           | 3.0 ± 3.0 (15) | 3.0 ± 3.3 (9)  | 7.0 ± 3.8 (7)   | 0.031         | 0.029         |
| NDI           |         |               |                 |               |               |
| Preoperative  | 25.7 ± 16.5 (40) | 41.4 ± 17.0 (30) | 50.5 ± 15.8 (27) | <0.001        |               |
| 6 wk          | 23.5 ± 18.8 (38) | 35.1 ± 17.7 (30) | 35.4 ± 20.1 (24) | 0.009         | 0.074         |
| 12 wk         | 17.7 ± 17.2 (32) | 29.9 ± 18.1 (24) | 35.5 ± 24.5 (21) | 0.001         | 0.034         |
| 6 mo          | 17.7 ± 20.4 (28) | 24.0 ± 14.5 (22) | 22.2 ± 23.3 (17) | 0.388         | 0.755         |
| 1 y           | 16.5 ± 16.3 (15) | 20.8 ± 22.8 (9) | 20.2 ± 20.7 (7) | 0.621         | 0.969         |
| SF-12 PCS     |         |               |                 |               |               |
| Preoperative  | 39.0 ± 9.1 (41) | 34.7 ± 7.4 (32) | 31.8 ± 6.7 (27)  | <0.001        |               |
| 6 wk          | 36.9 ± 9.3 (34) | 33.1 ± 5.3 (28) | 33.3 ± 6.8 (23)  | 0.062         | 0.172         |
| 12 wk         | 41.2 ± 10.1 (26) | 39.1 ± 7.3 (21) | 35.0 ± 8.4 (17)  | 0.019         | 0.216         |
| 6 mo          | 43.6 ± 10.8 (24) | 40.6 ± 9.1 (20) | 36.6 ± 10.3 (12) | 0.038         | 0.417         |
| 1 y           | 46.4 ± 8.0 (17) | 47.6 ± 7.7 (9)  | 41.2 ± 15.7 (8)  | 0.254         | 0.524         |
| SF-12 MCS     |         |               |                 |               |               |
| Preoperative  | 55.2 ± 10.4 (41) | 45.6 ± 8.6 (32) | 33.4 ± 11.5 (27) | <0.001        |               |
| 6 wk          | 55.3 ± 9.5 (34) | 49.0 ± 11.3 (28) | 43.4 ± 12.4 (23) | <0.001        | 0.003         |
| 12 wk         | 57.4 ± 8.5 (26) | 50.6 ± 9.1 (21) | 39.6 ± 13.7 (17) | <0.001        | <0.001        |
| 6 mo          | 57.8 ± 7.8 (24) | 45.1 ± 10.5 (20) | 42.7 ± 14.1 (12) | <0.001        | 0.001         |
| 1 y           | 57.0 ± 8.9 (17) | 53.8 ± 5.9 (9)  | 43.9 ± 16.3 (8)  | 0.006         | 0.025         |
| PROMIS PF     |         |               |                 |               |               |
| Preoperative  | 42.9 ± 7.6 (42) | 37.4 ± 6.2 (32) | 35.4 ± 4.9 (27)  | <0.001        |               |
| 6 wk          | 43.2 ± 7.1 (33) | 38.0 ± 7.6 (23) | 41.0 ± 6.1 (17)  | 0.147         | 0.038         |
| 12 wk         | 47.8 ± 12.2 (20) | 44.6 ± 4.7 (20) | 40.9 ± 9.5 (12)  | 0.046         | 0.372         |
| 6 mo          | 49.3 ± 8.0 (23) | 42.5 ± 9.4 (14) | 44.5 ± 8.4 (10)  | 0.070         | 0.145         |
| 1 y           | 49.3 ± 6.1 (16) | 48.0 ± 8.3 (13) | 45.3 ± 6.1 (9)   | 0.180         | 0.347         |

Abbreviations: NDI, Neck Disability Index; PROM, patient-reported outcome measure; PROMIS PF, Patient-Reported Outcome Measurement Information System physical function; SF-12 MCS, 2-Item Short Form Mental Composite Summary; SF-12 PCS, 12-Item Short Form Physical Composite Summary; VAS, visual analog scale.

*\( P \) values calculated using linear regression to assess outcomes between Patient Health Questionnaire-9 severity groups.

†\( P \) values calculated using multiple linear regression to assess the impact of both preoperative Patient Health Questionnaire-9 severity and multilevel procedures on postoperative outcomes.

Boldface indicates significance.
1-year timepoint \((P = 0.029)\). NDI also demonstrated significant differences between groups at the 12-week timepoint \((P = 0.034)\) only. Physical function outcomes did not significantly differ as a result of worsening preoperative depression and performing a multilevel procedure at any timepoint except at 6 weeks for PROMIS PF \((P = 0.038)\). Performing a multilevel procedure demonstrated significant additive effects on SF-12 MCS for all postoperative timepoints \((all \ P < 0.050)\). A summary of the added effect of a multilevel procedure with preoperative depression on PROM scores can be found in Table 3.

**DISCUSSION**

As the number of mental health studies among spine patients continues to grow, surgeons are becoming more attuned to its impact on postoperative outcomes and a patient’s well-being. Although the direct mechanism is still unclear, some studies have suggested that poorer recovery may be a result of decreased motivation or potential dissatisfaction with their overall medical treatment.\(^{15,16}\) However, among patients undergoing ACDF, a consensus has yet to be reach regarding depression’s impact on outcomes and studies have largely been limited to either analysis at the single level or a mixed single or multilevel cohort.\(^{10,11,17,18}\) The current study aimed to provide some clarity on this matter and demonstrated that while preoperative depression still remains a significant risk factor for worse postoperative outcomes, undergoing a multilevel procedure should also be considered a risk factor that exacerbates the negative effects of poorer preoperative mental health.

Among the different timepoints we assessed in the current study, the analysis of preoperative scores demonstrated that baseline pain, disability, and mental and physical health were consistently worse among moderate-to-severe depression groups. Previous studies have established a similar relationship whereby depression, as measured by SF-12 MCS or PHQ-9, was also associated with worse preoperative VAS neck, VAS arm, and NDI.\(^{12,18–20}\) Additionally, Blozik et al\(^{21}\) postulated that both depression and anxiety act as determinants of neck pain. Interestingly, few studies have established a similar relationship between preoperative depression severity and physical function using SF-12 PCS\(^{12,20}\) or the Nurick Score,\(^{10}\) and even fewer, if any, using PROMIS PF. While our preoperative findings support results from the current literature, this difference between depression severity groups was not maintained through the 1-year timepoint.

Even though baseline arm pain, neck pain, and disability demonstrated differences based on preoperative depression severity, postoperatively, this result did not persist through the 1-year timepoint except for VAS arm. Similar results were also reported by Jenkins et al,\(^{20}\) where the authors demonstrated that differences in preoperative VAS arm and neck, and NDI were not observed at the 1-year timepoint. However, other investigators have reported dissimilar results, with depression severity associated with worse postoperative VAS arm and NDI but not VAS neck.\(^{12,18}\) The conflicting results and overall lack of consensus between our study and others may be attributed to a difference in assessment of preoperative depression severity. While our study not only grouped and matched patients into 3 different categories, instead of 2 (depressed vs nondepressed), we also did so using preoperative PHQ-9 rather than SF-12 MCS. Regardless of the psychometric used, collectively our results and others’ suggest that patients with increasing depression severity may have an initial delay in improved pain and disability but should be assured that a significantly improved outcome could be attained by 1-year follow-up.

Preoperative depression severity may also be detrimental to the improvement of physical function. While depression’s negative effects on physical function may not be intuitive, a large prospective cohort study \((n = 4757)\) among general medical practices reported significant associations between lower baseline physical function and depression.\(^{22}\) Additionally, the same authors also determined that while the improvement in physical health between nondepressed and depressed individuals did not differ, mean physical function scores at their respective 2-year follow-up were significantly different. The current study evaluated physical function using 2 separate metrics, SF-12 PCS and PROMIS PF, and demonstrated that while preoperative scores may differ between groups, this was not maintained at the 1-year timepoint. A number of other investigators also reported that, within their respective ACDF cohorts, preoperative depression severity was not a significant predictor of physical function.\(^{12,18–20}\) However, it should be noted that Phan et al\(^{10}\) reported that increased levels of depression were associated with higher Nurick scores, which serve as a classification system for ambulatory function. These collective results raise the question of whether the underlying reason for depressive symptoms are in fact a “de novo” mental illness or a result of the underlying spinal pathology. In an attempt to address this line of thought, Mangan et al investigated the impact of comorbid depression and/or anxiety on improvements of pain,
disability, and physical function and demonstrated that no significant associations existed. Therefore, the results presented in the current study along with those of others suggest that patients undergoing ACDF should expect to achieve a significant improvement in physical function, but may require an extended length of time to reach an appreciable difference.

When considering the potential added risk of a multilevel procedure, the current literature establishes that both single and multilevel ACDF procedures demonstrate significant improvements in postoperative outcomes. However, a number of studies have suggested that multilevel procedures may be associated with long-term adverse events. In an effort to evaluate this possibility, we assessed the interaction or collective effect of both preoperative depression and multilevel procedures, which is the main strength of the current study. Few studies have assessed the individual contribution by a number of operative levels and even fewer assessed the collective effect of operative levels and depression severity. Alvin et al observed that worse outcomes were attributed to preoperative depression, as evaluated by PHQ-9, but the investigators were unable to establish multilevel procedures as a risk factor. However, the authors of the study assessed the quality of outcomes based on the EuroQol-5D quality of life measure at the 1-year timepoint instead of evaluating more specific metrics individually. Conversely, the current study was able to account for both the number of levels fused among preoperative PHQ-9 matched patients and determined that VAS arm, SF-12 MCS, PROMIS PF, and NDI were affected at intermittent timepoints. This suggests that while it may be prudent for surgeons to consider the impact of both multilevel procedures and degree of depression on a patient’s potential outcomes, their combined effect may not be detrimental to postoperative outcomes outside of arm pain and mental health.

The findings of the current study may suggest differences in postoperative recovery with respect to preoperative depressive symptoms following either a single or multilevel ACDF procedure. When considering a cervical fusion procedure, surgeons should be mindful to counsel patients with worse depressive symptoms that following surgery, pain, disability, and physical function will significantly improve but to a limited extent. Both providers and patients should be confident that the addition of another operative level may not be detrimental to the course of postoperative improvement except for mental health outcomes. Therefore, patients presenting with worse depressive symptoms should be advised to seek treatment by a mental health professional prior to or following both single and multilevel ACDF procedures.

**Limitations**

This study had a number of limitations that could be addressed in future studies. Patients included in our cohort underwent procedures at a single institution by a sole surgeon, which limits the ability to generalize our results to a much broader population. It is possible that a multicenter study with multiple physicians may provide ample power and allow for a more generalizable result in future studies. Additionally, assessment of all preoperative and postoperative outcomes was conducted through patient-reported health questionnaires. This carries potential recall and responder biases and could affect the results of our study. Moreover, our preoperative assessment of depression was not validated by a mental health professional and instead was based on a validated questionnaire for depression screening. Future studies that confirm a diagnosis of depression and/or anxiety may strengthen the results. Lastly, our patient cohort and available data were not conducive to confirming whether treatment of depressive symptoms was sought out prior to or following surgery. Use of therapy, whether cognitive or pharmacologic, could have an impact on reported PROMs and ultimately the combined impact of both depression and multilevel procedures.

**CONCLUSION**

Patients with more severe preoperative depressive symptoms demonstrated significantly different baseline values for pain, disability, physical function, and mental health. While patients demonstrated improvements in the postoperative period, disability, arm and neck pain, physical function, and mental health all were intermittently affected by the severity of their respective preoperative depressive symptoms. However, these negative effects on neck pain, disability, and physical function did not persist to the 1-year timepoint. When considering the added effect of a multilevel procedure with severity of preoperative depression, the added numbers of operative levels were not significant contributors to worsened outcomes except for mental health and arm pain. This may suggest that while preoperative depression may significantly impact the course of a patient’s postoperative improvement, spine surgeons should be aware of the limited but significant added effect of multilevel procedures.
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