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Original Article

Role of Gender in Improvement of Depressive Symptoms Among Patients Undergoing Cervical Spine Procedures

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Objective: There is a scarcity of research evaluating gender differences in depressive symptoms among patients undergoing cervical surgery. This study investigated gender differences with regard to depressive symptom severity, measured by Patient Health Questionnaire-9 (PHQ-9), in patients following anterior cervical discectomy and fusion (ACDF) or artificial disc replacement (ADR).
Methods: A prospectively maintained surgical registry was retrospectively reviewed for eligible spine surgeries. Depressive symptom severity was evaluated by PHQ-9 at both pre- and postoperative timepoints (e.g., 6 weeks, 12 weeks, 6 months, 1 year, and 2 years). A chi-square test and Student t-test evaluated differences between the gender for demographic and operative variables where appropriate. Differences between the gender subgroup mean PHQ-9 scores were assessed using a t-test pre- and postoperatively (e.g., 6 weeks, 12 weeks, 6 months, and 1 year) and a paired t-test was used to assess differences from preoperative scores at each postoperative time point.
Results: A total of 170 subjects underwent 125 ACDFs and 45 ADRs. Both pre- and postoperative timepoints demonstrated no significant differences between mean PHQ-9 scores by gender. Female patients demonstrated statistically significant improvement in PHQ-9 scores at 6 weeks, and 12 weeks, but not through 2 years. Male patients demonstrated statistically significant improvement in PHQ-9 scores at 6 weeks, 12 weeks, 6 months, 1 year, and 2 years.
Conclusion: Although there were no significant differences between mean PHQ-9 score between the genders, there was a difference in magnitude of improvement. Females had a significant improvement in depressive symptom severity over baseline at the 6- and 12-week timepoints only, whereas males had significant improvement through 2 years postoperatively.

Keywords: Anterior cervical discectomy and fusion, Artificial disc replacement, Depression, Gender, Patient Health Questionnaire-9

INTRODUCTION

Depression has become one of the most prevalent mental health disorders globally, affecting more than 264 million individuals worldwide.[1] While the implications of depression have significant impacts on mental health, investigators are finding its effects also extend to physical health. Prior studies looking at both the cervical and lumbar spine have demonstrated that worsened preoperative depression is significantly correlated with diminished improvement in a patient's postoperative quality of life as well as higher rates of adverse events.[2,3] The negative outcomes associated with the presence of depression have

made it imperative to accurately quantify and assess a patient's mental health status in the clinical setting, leading to the development of such tools as the 9-Item Patient Health Questionnaire (PHQ-9).

PHQ-9 is a validated Patient-Reported Outcome Measure (PROM) used to screen patients for depression across several disciplines, and is strongly correlated to other traditional PROMs in the cervical spine.[4] Unlike other mental health questionnaires, PHQ-9 is made up of 9 questions that were developed based on the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) diagnosis criteria for depressive disorders and provides an objective measure of the severity of depression.[5] This brevity, comparable sensitivity, and severity ranking make PHQ-9 a reliable tool to assess depression in a clinical setting as evidenced by past studies demonstrating poorer clinical outcomes in lumbar fusion patients with increased preoperative PHQ-9 scores.[6] Coupling this association with the fact that women experience major depressive disorder at almost twice the rate of men,[7] further investigations are warranted to elucidate the implications of potential gender differences in depressive symptoms for spine patients.

Earlier studies have provided insight into gender differences in depression severity among lumbar laminectomy patients and reported that women had lower tolerance for pain and worse mental health scores at the preoperative time point.[8] Conversely, investigators focusing on gender differences alone found no significant difference in pain, disability, and overall quality of life between men and women following lumbar procedures.[9] While earlier studies focused on gender differences in lower back pain studies, pathology of the cervical spine can also be associated with debilitating pain[10] and can be successfully treated with procedures such as anterior cervical discectomy and fusion (ACDF) or artificial disk replacement (ADR).

Although the current literature provides insight into the relationship between depression and cervical spine outcomes, there is a scarcity of comparative studies investigating gender differences among the cervical spine patient population. Studies that address this relationship are essential to inform providers and ameliorate preoperative counseling and postoperative care for patients at risk for depression and worse surgical outcomes. Therefore, the purpose of this study is to investigate gender differences with regard to depressive symptom severity, measured by PHQ-9, in patients following ACDF or ADR.

MATERIALS AND METHODS

1. Patient Population

Prior to the initiation of the current study, both written informed patient consent as well as Institutional Review Board approval of Rush University Medical Center (ORA 14051301) were granted. Use of a prospectively maintained surgical registry allowed for a retrospective query of eligible cervical spine procedures from March 2016 to May 2019. Patients were deemed eligible for this study if they underwent primary or revision, single or multilevel, ACDF, or ADR procedures. Patients lacking a completed preoperative PHQ-9 or who had a spinal diagnosis of infection, malignancy, or trauma were excluded from the study. All procedures were performed in either an ambulatory surgical center or inpatient hospital by a sole surgeon at a single academic institution.

2. Patient Characteristics

Differentiating the patient cohort was based on demographics, medical and spinal diagnoses, and both intraoperative and postoperative characteristics. Demographics included the collection of age, body mass index (BMI), smoking status at time of appointment, insurance collected, comorbidity burden as measured by ageless Charlson Comorbidity Index, and patient fitness as measured by American Society of Anesthesiologists physical status classification. Comorbid medical conditions and spinal diagnosis associated with the procedure were collected preoperatively. Operative characteristics were collected as type of procedure (ACDF or ADR), number of operative levels, total operative time (skin incision to skin closure), and intraoperative estimated blood loss (EBL). Postoperative information such as length of hospital stay and day of discharge were also collected.

3. Primary Outcome Measures

The primary outcome of interest for this study was depression severity. This was primarily measured using the PHQ-9, 12-Item Short Form mental composite score (SF-12 MCS), and 12-Item Veterans RAND mental composite score (VR-12 MCS). PHQ-9 is a 9-question survey modeled after the diagnostic criteria outlined by the DSM-IV. Use of this questionnaire allows for providers to objectify the severity of depressive symptoms and has been validated and deemed an accurate health questionnaire.[5,11] Questions are based on frequency of symptoms over the previous 2 weeks and are scored from 0–3. A total score of 0–4 indicates minimal to no depressive symptoms, 10–14 moderate, and 20–27 severe depression. All PHQ-9 data was

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administered prior to being evaluated by a clinician on a personal device or clinic-provided tablet using an online private portal. Questionnaires were completed at the preoperative timepoint and the 6-week, 12-week, 6-month, 1-year, and 2-year postoperative timepoint.

4. Secondary Outcome Measures

The secondary outcomes of interest were neck and arm pain, disability, and physical function. Both neck and arm pain were evaluated using the visual analogue scale (VAS) and disability was evaluated using the Neck Disability Index (NDI). Physical function was assessed using 2 separate outcome questionnaires: 12-Item Short Form physical composite score (SF-12 PCS) and Patient-Reported Outcome Measurement Information System physical function (PROMIS PF). All outcome questionnaires were administered prior to being evaluated by a clinician on a personal device or clinic-provided tablet using an online private portal. Questionnaires were completed at the preoperative timepoint and at the 6-week, 12-week, 6-month, 1-year, and 2 year postoperative timepoint.

5. Statistical Analysis

Prior to analysis, patients were separated based on either male or female gender. Differences in demographics, medical conditions, spinal diagnoses, intraoperative and postoperative characteristics were determined using chi-square analysis for categorical variables or a Student t-test for continuous variables. Differences in the primary outcome of interest were calculated as (postoperative values – preoperative values). Postoperative improvement from baseline values was evaluated using a paired Student t-test. Additionally, differences in patient-reported outcome values between genders were evaluated using an unpaired Student t-test. For all statistical analyses, a p-value of 0.050 was required for significance. All analysis was performed using StataMP 16.1 (StataCorp LP., College Station, TX, USA).

Table 1. Patient demographics by gender

Characteristic	Total (n = 170)	Male (n = 67)	Female (n = 103)	p-value†
Age (yr)	48.2 ± 10.5	47.85 ± 11.01	48.42 ± 10.18	0.731
Body mass index				0.223
Nonobese (< 30 kg/m^2)	102 (60.0)	44 (65.7)	58 (56.3)	
Obese (≥ 30 kg/m^2)	68 (40.0)	23 (34.3)	45 (43.7)	
Smoking status				0.451
Nonsmoker	151 (88.8)	58 (86.6)	93 (90.3)	
Smoker	19 (11.2)	9 (13.4)	10 (9.7)	
Insurance coverage				0.210
Private or WC	168 (99.4)	65 (98.5)	103 (100)	
Medicare/medicaid	1 (0.6)	1 (1.5)	0 (0)	
Ageless CCI	1.3 ± 1.4	1.21 ± 1.25	1.32 ± 1.55	0.639
Preoperative diagnoses				
Myocardial infarction	2 (1.2)	0 (0)	2 (1.9)	0.251
Diabetes	16 (9.4)	5 (7.5)	11 (10.7)	0.483
Hypertension	41 (24.1)	13 (19.4)	28 (27.2)	0.246
Neurologic disease	3 (1.8)	1 (1.5)	2 (1.9)	0.828
Malignancy	5 (2.9)	2 (3.0)	3 (2.9)	0.978
Spinal pathologies				
Degenerative spondylolisthesis	1 (0.9)	0 (0)	1 (1.4)	0.424
Degenerative disc disease	7 (4.1)	3 (4.5)	4 (3.9)	0.849
HNP	151 (88.8)	59 (88.1)	92 (89.3)	0.799

Values are presented as mean ± standard deviation or number (%).
WC, workers compensation; CCI, Charlson Comorbidity Index; HNP, herniated nucleus pulposus.
†p-value was calculated using Student t-test (continuous), chi-square (categorical), or Fisher exact test (categorical).

RESULTS

1. Patient Demographics

Our retrospective review of a prospective surgical registry identified 170 patients that met inclusion criteria with 103 being males and 67 females. Mean age of the cohort was 48.2 ± 10.5 years with only 40.0% of the population having a BMI ≥ 30 kg/m^2. Comparison of demographics demonstrated no significant differences between gender. Additionally, no significant difference in comorbidity burden was observed between groups. Hypertension was the major preoperative comorbidity for 19.4% of males and 27.2% of females. Majority of both males (88.1%) and females (89.3%) had a spinal diagnosis of herniated nucleus pulposus. These results are summarized in Table 1.

2. Perioperative Characteristics

ACDF was performed for 125 patients and ADR for 45 patients. Among all cervical procedures, 61.2% of patients underwent a single-level procedure. More specifically, 57.6% of ACDF patients and 71.1% of ADR patients underwent a single-level procedure. Mean operative time for ACDF was 56.9 minutes and ADR was 49.8 minutes. Average EBL was 29.4 ± 12.0 mL for ACDF patients and 28.4 ± 8.5 mL for ADR patients. No significant differences were demonstrated between gender for number of levels operated or operative time; however, EBL was significantly different between genders with females (30.89 ± 12.40 mL) demonstrating a larger mean value as compared to males (26.49 ± 8.57 mL) (p = 0.012) (Table 2) Postoperatively, mean length of hospital stay was 9.2 hours and with no significant differences between genders. Majority of all patients were discharged on postoperative day 0 and did not differ based on gender (Table 2).

3. Improvement in Depressive Symptoms

Females demonstrated a significant improvement in PHQ-9 scores from baseline preoperative values at the 6-week (p = 0.003) and 12-week (p < 0.001) postoperative timepoints. However, this improvement was not sustained at 6 months (p = 0.117), 1 year (p = 0.558), or 2 years (p = 0.8530) (Table 3). Females also demonstrated a significant improvement from baseline values for SF-12 MCS and VR-12 MCS at the 6-week (p = 0.020, p = 0.025), 12-week (p = 0.006, p < 0.003), and 6-month timepoint (p = 0.013, p = 0.002) (Table 3).

Males demonstrated a significant improvement in PHQ-9 scores from baseline preoperative values at 6 weeks (p < 0.001), 12 weeks (p < 0.001), 6 months (p = 0.001), 1 year (p = 0.011), and 2 years (p = 0.017) (Table 3). SF-12 MCS significantly improved from preoperative scores at the 6-week (p = 0.001), 12-week (p < 0.001), and 1-year timepoint (p = 0.002). VR-12 MCS significantly improved from baseline values from 6-week through the

Table 2. Operative characteristics by gender

Characteristic	Total (n = 170)	Male (n = 67)	Female (n = 103)	p-value†
Procedure				0.331
ACDF	125 (73.5)	52 (77.6)	73 (70.9)	
ADR	45 (26.5)	15 (22.4)	30 (29.1)	
No. of levels				0.479
1 Level	104 (61.2)	44 (65.7)	60 (58.3)	
2 Levels	52 (30.6)	18 (26.9)	34 (33.0)	
3 Levels	11 (6.5)	3 (4.5)	8 (7.8)	
4 Levels	3 (1.8)	2 (3.0)	1 (1.0)	
Operative time‡ (min)	58.7 ± 16.7	54.46 ± 19.50	61.41 ± 78.02	0.477
Estimated blood loss (mL)	29.1 ± 11.2	26.49 ± 8.57	30.89 ± 12.40	0.012*
Length of hospital stay (hr)	9.2 ± 29.6	14.32 ± 13.64	11.62 ± 11.35	0.173
Discharge day				0.328
POD 0	106 (68.8)	40 (64.5)	66 (71.7)	
POD 1	34 (22.1)	18 (29.0)	16 (17.4)	
POD 2	6 (3.9)	2 (3.2)	4 (4.4)	
POD 3	8 (5.2)	2 (3.2)	6 (6.5)	

Values are presented as mean ± standard deviation or number (%).
ACDF, anterior cervical discectomy and fusion; ADR, artificial disc replacement; POD, postoperative day.
*p < 0.05, statistically significant differences. †p-value was calculated using Student t-test (continuous), chi-square analysis (categorical), or Fisher exact test. ‡Operative time was measured from skin incision to skin closure.

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1-year timepoint (all $p < 0.05$) (Table 3). Comparison of PHQ-9, SF-12 MCS, and VR-12 MCS scores at all timepoints demonstrated no significant differences between genders (all $p > 0.05$) except at 6 months for SF-12 MCS ($p = 0.041$) (Table 3).

4. Improvement in Clinical Outcomes

The influence of gender on preoperative scores for VAS arm, NDI, SF-12 PCS, and PROMIS PF did not result in significant preoperative differences between groups ($p > 0.050$). However, VAS neck demonstrated significant differences between groups ($p = 0.022$). Postoperatively, mean scores did not significantly differ between genders from 6 weeks through 2 years (all $p > 0.05$). Male and female genders demonstrated similar significant improvements in VAS neck at the 6-week through 2-year timepoint (all $p < 0.05$). However, while females demonstrated a significant improvement in VAS arm scores at the 6-week through 2-year timepoint (all $p < 0.050$), males significantly improved at only the 6-week, 12-week, and 6-month timepoints (all $p < 0.001$). Improvement in NDI largely demonstrated a similar significant improvement for both genders (all $p < 0.05$) except for the 1-year timepoint for females ($p = 0.064$). Physical function significantly improved for females only at 12 weeks through 1 year ($p \leq 0.001$) for SF-12 PCS and from 6 weeks through 2 years for PROMIS PF (all $p < 0.050$). Both SF-12 PCS and PROMIS PF demonstrated significant improvements from 12 weeks through 2 years for males (all $p < 0.015$). A summary of improvement of secondary postoperative outcomes can be found in Table 4.

DISCUSSION

Clinical depression continues to be a growing health concern and spine surgeons have taken an increased interest as a growing number of studies link spinal pathologies with depressive symptoms.[12,13] While lumbar spine pain has been a central focus of depressive symptoms, cervical spine pathologies and associated pain have been deemed equally detrimental to a patient's health.[14] Given the increased risk of depression among females and their increased propensity for cervical disorders,[15,16] investigation into the effects of gender and depression on postoperative outcomes among spine patients remains important.

Table 3. Mental health outcomes by gender

Variable	Female	Δ	p-value†	Male	Δ	p-value†	p-value‡
PHQ-9							
Preoperative	7.67 ± 6.20	-	-	6.96 ± 5.92	-		0.454
6 Weeks	5.20 ± 5.55	-1.83 ± 0.59 (54)	0.003*	4.94 ± 5.73	-2.19 ± 0.62 (80)	< 0.001*	0.789
12 Weeks	4.86 ± 5.94	-2.72 ± 0.71 (43)	< 0.001*	4.37 ± 5.88	-3.28 ± 0.67 (65)	< 0.001*	0.673
6 Months	4.63 ± 6.89	-1.63 ± 1.01 (32)	0.117	4.96 ± 5.17	-3.07 ± 0.88 (55)	0.001*	0.796
1 Years	4.56 ± 5.96	-0.94 ± 1.57 (16)	0.558	4.16 ± 4.71	-3.88 ± 1.07 (32)	0.001*	0.798
2 Years	6.87 ± 8.23	0.33 ± 1.77 (15)	0.853	5.83 ± 6.10	-4.48 ± 1.73 (23)	0.017*	0.657
SF-12 MCS							
Preoperative	45.72 ± 13.00	-	-	47.52 ± 12.20	-	-	0.375
6 Weeks	50.98 ± 11.17	3.39 ± 9.81 (49)	0.020*	51.09 ± 10.85	4.68 ± 10.91 (70)	0.001*	0.96
12 Weeks	50.06 ± 11.50	4.75 ± 14.31 (37)	0.006*	51.46 ± 11.89	5.47 ± 10.80 (52)	< 0.001*	0.56
6 Months	54.56 ± 11.10	5.38 ± 10.19 (26)	0.013*	48.88 ± 11.09	3.46 ± 14.30 (41)	0.129	0.041*
1 Years	52.43 ± 9.89	2.92 ± 8.21 (15)	0.190	51.95 ± 11.90	8.42 ± 12.86 (29)	0.002*	0.889
2 Years	48.84 ± 10.69	0.17 ± 7.60 (12)	0.940	47.43 ± 10.11	4.87 ± 15.95 (20)	0.188	0.700
VR-12 MCS							
Preoperative	48.36 ± 13.26	-	-	50.30 ± 13.42	-	-	0.369
6 Weeks	53.06 ± 12.08	2.91 ± 8.79 (49)	0.025*	53.84 ± 10.89	4.26 ± 11.64 (70)	0.003*	0.707
12 Weeks	53.59 ± 11.77	5.47 ± 10.28 (37)	0.003*	53.98 ± 12.21	5.68 ± 10.30 (58)	< 0.001*	0.875
6 Months	57.28 ± 11.30	6.17 ± 9.27 (26)	0.002*	52.22 ± 11.31	4.73 ± 13.98 (41)	0.036*	0.072
1 Years	56.3 ± 9.98	5.05 ± 9.23 (15)	0.053	56.30 ± 10.24	10.11 ± 13.89 (29)	0.001*	0.968
2 Years	52.46 ± 11.19	1.21 ± 5.62 (12)	0.471	51.06 ± 10.62	7.06 ± 16.45 (20)	0.070	0.714

Values are presented as mean ± standard deviation (n).
PHQ-9, Patient Health Questionnaire-9; SF-12, Short Form 12-Item; VR-12, Veterans RAND 12-Item; MCS, mental component score.
*$p < 0.05$, statistically significant differences. †p-value was calculated using paired t-test (continuous) to compare each timepoint score to the preoperative value. ‡p-value was calculated using Student t-test (continuous) to compare mean scores.

Table 4. Physical health outcomes by gender

Variable	Female	Δ	p-value†	Male	Δ	p-value†	p-value‡
VAS arm							
Preoperative	6.41 ± 2.69	-	-	5.57 ± 2.77	-	-	0.063
6 Weeks	3.32 ± 4.31	-3.28 ± 4.68 (52)	< 0.001*	2.68 ± 2.80	-2.69 ± 3.57 (86)	< 0.001*	0.317
12 Weeks	3.63 ± 3.49	-2.87 ± 4.52 (49)	< 0.001*	2.85 ± 2.99	-2.60 ± 3.56 (75)	< 0.001*	0.183
6 Months	3.47 ± 3.54	-2.75 ± 4.12 (36)	< 0.001*	3.36 ± 3.10	-2.15 ± 3.83 (61)	< 0.001*	0.875
1 Years	3.44 ± 3.31	-3.01 ± 4.34 (12)	0.032*	4.44 ± 3.43	-1.12 ± 4.64 (25)	0.240	0.409
2 Years	5.13 ± 1.97	-2.10 ± 1.10 (7)	0.002*	4.07 ± 3.01	-2.22 ± 4.01 (10)	0.114	0.431
VAS neck							
Preoperative	6.78 ± 2.19	-		5.85 ± 2.69	-	-	0.022*
6 Weeks	3.90 ± 2.51	-2.62 ± 2.86 (52)	< 0.001*	2.99 ± 2.58	-2.65 ± 3.13 (88)	< 0.001*	0.041*
12 Weeks	3.31 ± 2.63	-3.37 ± 2.53 (51)	< 0.001*	2.71 ± 2.26	-2.85 ± 2.92 (77)	< 0.001*	0.171
6 Months	2.62 ± 2.61	-3.79 ± 3.01 (36)	< 0.001*	2.94 ± 2.3	-2.86 ± 3.08 (64)	< 0.001*	0.146
1 Years	3.37 ± 2.93	-2.88 ± 3.17 (12)	0.009*	4.01 ± 3.13	-1.52 ± 2.92 (25)	0.016*	0.559
2 Years	5.01 ± 2.39	-2.05 ± 1.55 (7)	0.013*	4.10 ± 3.42	-2.57 ± 3.34 (10)	0.037*	0.555
NDI							
Preoperative	41.7 ± 17.8	-	-	38.2 ± 20.4	-	-	0.259
6 Weeks	32.1 ± 19.7	-7.9 ± 19.2 (53)	0.004*	29.0 ± 19.2	-7.7 ± 17.2 (85)	< 0.001*	0.362
12 Weeks	29.3 ± 20.8	-14.6 ± 18.5 (50)	< 0.001*	24.7 ± 19.5	-12.5 ± 18.7 (75)	< 0.001*	0.199
6 Months	23.8 ± 19.6	-17.3 ± 19.9 (36)	< 0.001*	22.6 ± 17.9	-16.6 ± 19.6 (61)	< 0.001*	0.752
1 Years	28.5 ± 23.7	-15.2 ± 25.6 (12)	0.064	22.6 ± 18.7	-15.3 ± 20.0 (25)	< 0.001*	0.416
2 Years	33.7 ± 18.8	-16.0 ± 6.3 (7)	< 0.001*	31.8 ± 21.7	-14.6 ± 18.3 (10)	0.032*	0.853
SF-12 PCS							
Preoperative	34.6 ± 7.1	-	-	34.5 ± 9.4	-	-	0.952
6 Weeks	37.3 ± 9.6	2.4 ± 9.7 (49)	0.085	35.5 ± 8.6	0.9 ± 8.4 (70)	0.373	0.344
12 Weeks	40.5 ± 9.1	5.5 ± 8.6 (37)	< 0.001*	38.5 ± 10.3	2.6 ± 7.9 (58)	0.015*	0.327
6 Months	40.1 ± 10.1	6.5 ± 8.3 (26)	< 0.001*	39.6 ± 9.8	5.8 ± 8.9 (41)	< 0.001*	0.846
1 Years	43.4 ± 10.2	8.5 ± 8.4 (15)	0.001*	43.6 ± 10.4	6.9 ± 9.2 (30)	< 0.001*	0.472
2 Years	41.7 ± 9.9	3.9 ± 11.5 (12)	0.271	40.6 ± 11.1	8.8 ± 2.2 (20)	< 0.001*	0.787
PROMIS PF							
Preoperative	38.3 ± 6.4	-	-	40.1 ± 7.9	-	-	0.167
6 Weeks	42.7 ± 7.0	2.9 ± 6.4 (38)	0.007*	42.7 ± 8.7	1.9 ± 8.1 (50)	0.111	0.969
12 Weeks	45.8 ± 8.2	6.6 ± 7.5 (31)	< 0.001*	44.6 ± 10.1	4.5 ± 8.5 (45)	< 0.001*	0.586
6 Months	45.7 ± 8.1	7.0 ± 6.9 (24)	< 0.001*	38.7 ± 6.9	6.3 ± 8.3 (36)	< 0.001*	0.921
1 Years	45.0 ± 8.3	6.5 ± 7.3 (14)	0.005*	47.1 ± 6.6	8.2 ± 7.5 (28)	< 0.001*	0.346
2 Years	45.5 ± 9.5	5.0 ± 8.8 (15)	0.045*	46.1 ± 9.2	8.8 ± 11.7 (24)	0.001*	0.858

Values are presented as mean ± standard deviation (n).
VAS, visual analogue scale; NDI, Neck Disability Index; SF-12 PCS, Short Form 12-Item physical component score; PROMIS PF, Patient-Reported Outcome Measurement Information System physical function.
*$p < 0.05$, statistically significant differences. †p-value was calculated using paired t-test (continuous) to compare each timepoint score to the preoperative value. ‡p-value was calculated using Student t-test (continuous) to compare mean scores.

Our study was able to determine that while PHQ-9, SF-12 MCS, and VR-12 MCS scores did not differ between genders, improvement in depressive symptoms for females was restricted to the acute timepoint and was not sustained longitudinally.

While there is an abundance of studies relating the presence of depressive symptoms in the lumbar spine population, few

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studies have established this relationship in the cervical spine. Some investigators have demonstrated that among patients undergoing ADR, those with lower PHQ-9 scores reported less pain and disability.[17] Others have implicated depression as a contributor to reduced Euro-QoL-5D (EQ-5D) and lower rates of achievement of the patient-centered outcome metric, minimum clinically important difference (MCID), following posterior cervical fusion,[18] which is in contrast to Alvin et al.'s and others study in patients undergoing ACDF.[11,19] Although an MCID provides a relative threshold for what patients perceive as a meaningful change in their symptoms, and EQ-5D assesses overall quality of life, there may be limited evidence that supports the favorable physical and mental health outcomes following an anterior cervical procedure.

To strengthen the assertion that ACDF and ADR can improve a patient's quality of life, there is evidence that both procedures may also improve mental health. Our study observed a significant improvement in depressive symptoms following cervical procedures for the male gender. This improvement was not restricted to the immediate postoperative timepoint and extended up to the 2-year follow-up time period, suggesting the lasting effects of the procedure. Though ACDF or ADR should be implicated in the observed improvement of depressive symptoms among our male cohort, other factors should also be considered. Firstly, males report their depressive symptoms at about half the rate of females.[20] Secondly, investigators have reported that males typically report a lower preoperative and postoperative depressive score and thus may not be at increased risk for persistent depression.[15] While these aspects may act as "protective" factors for depression in males, the same cannot be said for females. Lastly, the impact of improvement of other postoperative clinical outcome measures (pain, disability, physical function) on postoperative depression should also be considered. Previous studies have established that depressed patients undergoing lumbar decompression reported significantly worse pain, disability, and physical function.[21] This suggests a distinct relationship between both mental and physical health, which is supported by the observation that our study's male cohort demonstrated similar improvements in PHQ-9 and VAS, NDI, SF-12 PCS, and PROMIS PF. Interestingly, the current study's female cohort was unable to demonstrate this same observation.

Our study demonstrated that the female cohort significantly improved PHQ-9 scores at both the 6- and 12-week timepoints, but these improvements were not sustained through the 2-year follow-up. Unsurprisingly, SF-12 MCS and VR-12 MCS demonstrated similar improvements, as previous studies have established their strong correlation with PHQ-9.[22] It can be inferred by these results that a recurrence in depressive symptoms may have occurred or alternatively, a large variability in the reported PHQ-9, SF-12 MCS, or VR-12 MCS values exists. Given that our analysis did not reveal a large skewness, what should be considered instead is the possibility of the association of the female gender with a lack of postoperative depression improvement or return of depressive symptoms. In one study, female patients undergoing treatment for degenerative cervical myelopathy were reportedly associated with a higher proportion of psychiatric disorders, and were not able to achieve a clinically important change for SF-36 MCS.[16] Additionally, Kanaan et al.[23] established the female gender as a negative predictive factor for postoperative improvement of EQ-5D and health-related quality of life measures among lumbar spine patients. While some outcome measures are not as specific to depression as PHQ-9, our results in conjunction with past studies suggest that females, while demonstrating an initial improvement, may have a recurrence of symptoms in the long term. Interestingly, analysis for new-onset depression and anxiety following spinal fusion surgery identified the female gender (OR, 1.25–1.67), among other factors, as a significant risk factor.[22] However, further investigations in our cohort are warranted to determine whether female patients experienced a resurgence of depressive symptoms.

Comparison in the current study of postoperative mental health outcome scores by gender demonstrated a nonstatistically significant difference. Few studies have established this relationship through direct comparison of mental health outcome measures and there is an even greater scarcity in the literature when considering the cervical spine population. Individuals who underwent procedures for lumbar spine pathologies were reported to differ based on gender with respect to pain, disability, and mental health scores, as measured by SF-8 MCS.[8] Although Kobayashi et al.[8] established a significant preoperative difference between genders, it was not maintained throughout the entire postoperative period. A similar result was demonstrated in our study with the exception that genders did not differ in their preoperative PHQ-9, SF-12 MCS, or VR-12 MCS score. It is possible that similar preoperative values but dissimilar postoperative improvement could be affected by any treatments a patient received, by way of antidepressants or cognitive behavioral therapy. For instance, previous studies have suggested that use of antidepressants or treatment for anxiety allowed patients to achieve similar improvements in pain, disability, and

mental health as compared to nondepressed controls.[24-26] Collectively, these results suggest that the impact gender plays on postoperative improvement may not be large enough to detect and instead may interact with other covariates. However, this is beyond the scope of the current study and could be addressed in future comparative studies.

There are several limitations associated with this study. Mental health questionnaire scores were collected at both preoperative and postoperative timepoints; however, the accuracy of these questionnaires may be influenced by response and recall bias. Additionally, the use of a depressive symptom health questionnaire would be further strengthened by confirmation of clinical depression by a medical professional. Similarly, confirmation of treatment modality for depressive symptoms, whether pharmaceutical or behavioral, would help strengthen the interpretation of this study's results; however, this information was unavailable for the study cohort. Analysis of our results also included postoperative follow-ups to the 2-year timepoint. As with any longitudinal study, the impact of the result is largely dependent on the proportion of patients who follow up through all timepoints. Lastly, patients underwent treatment at a single institution, performed by a single surgeon. This will limit our ability to generalize our results and it may be possible to increase the strength of this study by using multiple centers.

CONCLUSION

Improvement from preoperative baseline depressive symptoms by the 1-year timepoint was observed for males after treatment of cervical spine pathologies. Females demonstrated significant improvements in depression up to the 6-month postoperative timepoint, but these were not sustained through the 2-year timepoint. Comparison of depression scores largely did not significantly differ by gender from the preoperative to the 2-year postoperative timepoint. These results provide evidence that although females may be associated with higher incidence of depression, genders did not differ in postoperative depression scores at the short term but females may be at risk of recurrent depressive symptoms in the long term.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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