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A Population-based Assessment of Depression and Anxiety in Patients with Brachial Plexus Injuries

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Abstract

Purpose—Reactive depression and anxiety are common after major life changes such as brachial plexus injuries (BPI). The purpose of this study was to evaluate the incidence and risk factors for coded depression and coded anxiety among BPI patients using a national database of commercial insurance claims.

Methods—We utilized the Truven MarketScan database from 2007–2013 to identify commercially-insured patients aged 18–64 who underwent BPI surgery. For comparison, a control group without BPI was frequency-matched 10:1 by age group, sex, number of provider visits, and length of insurance enrollment. Using ICD-9 diagnosis codes and pharmacy claims, we identified coded depression and coded anxiety in the 12 months prior and the 12 months following BPI surgery. Multivariable Cox regression models were used to determine risk factors for coded depression or coded anxiety, adjusting for known risk factors for depression or anxiety (e.g., alcohol, substance abuse).

Results—1,843 BPI patients and 18,430 controls were identified. Within the 12 months preceding surgery, coded depression and coded anxiety were present in 38% and 42%, respectively, of the BPI group; both were present in 25% and either were present in 54%. The rate of new-onset/postoperative coded depression among BPI patients was 142.1 per 1000 person-years (12%), and new-onset/postoperative coded anxiety 273.6 per 1000 person-years (20%). BPI patients were significantly more likely than controls to develop new-onset/postoperative coded depression (HR=1.3[1.1,1.5]) and new-onset/postoperative coded anxiety (HR=2.1[1.8,2.4]).

Conclusions—Patients undergoing BPI surgery have a high prevalence of coded depression and coded anxiety in the 12 months prior to surgery and are at higher risk for developing new-onset/postoperative coded depression and coded anxiety within 1 year after surgery. These findings can be used by BPI surgeons to inform perioperative counseling, guide emotional recovery from injury, and to facilitate coordinated or co-located care with mental health professionals.

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Level of evidence prognostic II (symptom prevalence study)

Keywords

anxiety; brachial plexus; depression; mental health; nerve injury

INTRODUCTION

Injury to the brachial plexus causes severe dysfunction and pain. Patients with brachial plexus injuries (BPI) might benefit from greater surgeon attention to the psychosocial aspects of recovery from major, life-changing injuries. Evidence that psychosocial factors are key determinants of patient-reported outcomes applies to the care of patients with BPI.[1–5] The emotional elements of brachial plexus injury are commonly mentioned by patients and family members.[6] Patient interviews have detailed the life-altering impact of this abrupt injury and the varied emotional responses which affect nearly every aspect of a patient's life.[2,7]

Single-center cohort studies have identified prevalence rates of depression in 20% to 45% of patients after orthopaedic trauma, nerve compression or nerve injury, and BPI.[5,8–13] However, generalizable rates of incident depression and anxiety in BPI patients remain unknown. The aims of our study were to estimate how frequently coded depression and anxiety are present at any point in the year prior to BPI surgery and the likelihood of developing new-onset coded depression and anxiety after BPI surgery. We utilized a national database of commercial insurance claims to compare patients who underwent BPI surgery to a frequency-matched control population. Data on the prevalence of coded depression and anxiety before and after surgery for BPI would provide a sense of the magnitude of psychosocial aspects of recovery from these severe injuries.

MATERIALS AND METHODS

Definition of population

We performed this study using administrative claims data from the Truven Health Analytics MarketScan® Commercial Claims and Encounters Database, which consists of private insurance medical and outpatient pharmacy claims for non-elderly individuals and their dependents who are employed, retired early, or on Consolidated Omnibus Budget Reconciliation Act (COBRA) plans. Following exemption from further review by our institutional review board, claims from 2007–2013 were examined from outpatient and hospital-based settings to identify patients aged 18–64 who underwent surgical intervention for BPI. Selection of patients with BPI surgery required: (1) a CPT-4 code specific for brachial plexus surgery (64861 or 64713), or (2) an ICD-9 diagnosis code specific for BPI (953.4) *plus* a CPT-4 code for non-specific nerve surgery (64708, 64856, 64857, 64859, 64872, 64874, 64876, 64892, 64893, 64897, 64898, 64901, 64902, 64905, 64907). Confirmation of surgical intervention was further verified by requiring all surgical patients to have at least one of the following: a CPT-4 code for anesthesia (00300-00474, 00600-00670, 01320-01860), an operating room revenue code (UB-04 0360, 0490), or a nerve surgery ICD-9-CM procedure code from a facility (ICD-9-CM 03.6, 04.49, 04.5, 04.6,

04.74, 04.76, 04.79) on a contemporaneous claim(s). To capture claims for depression and anxiety, we required continuous medical and prescription drug insurance coverage for 12 months prior to surgery and at least 1 month after surgery.

For comparison, a control group of adults aged 18–64 years without BPI was selected and frequency-matched 10:1 to the BPI group by age, sex, number of outpatient healthcare provider visits in the prior 12 months, and total length of insurance enrollment (ranging from 1–9 years). Control patients were required to have at least 13 months of continuous medical and prescription drug insurance enrollment to match the enrollment requirement for the BPI patients. To ensure control patients had no BPI or BPI surgical procedure within the selected enrollment period, patients were excluded if they had any of the CPT-4 or ICD-9-CM procedures codes used to define BPI or BPI surgery at any time. For the control group, a randomly selected reference date was identified resulting in at least 12 months of continuous enrollment preceding and at least 1 month of enrollment after the reference date, to provide comparable dates to the BPI group. Frequency-matching by age occurred through division into 9 categories (18–24, 25–29, 30–34, 35–39, 40–44, 45–49, 50–54, 55–59, 60–64). The number of healthcare provider visits included the combined number of outpatient office visits (defined by CPT-4 codes 99201 −99215) and Emergency Department treat-and-release visits during the 12-month period prior to the surgery date for BPI patients and the reference date for the control group. These were then categorized into six approximately equal groups (0–4, 5–6, 7–8, 9–11, 12–15, and 16 or more visits). We included the number of healthcare provider visits as a criterion for frequency-matching to adjust for the biases (specifically, informed presence bias) that may predispose individuals with more exposure to health care providers to receive a diagnosis of any concurrent condition.[14]

Primary outcome

Baseline coded depression and anxiety were established in both the BPI and control groups using a diagnosis code or a prescription for antidepressant and/or anxiolytic medication; for the BPI group, this baseline assessment encompasses the entire 12 months prior to BPI surgery, with coding of depression and anxiety occurring before or after the injury date (we are unable to distinguish before both surgery and injury versus before surgery but after injury).

Depression and anxiety diagnoses were identified using ICD-9-CM diagnosis codes (Supplement 1).[15] These diagnoses required one or more inpatient or outpatient claim coded for the condition in the year prior to surgery (BPI group) or the index/reference date (control group). Outpatient prescriptions for antidepressants (Supplement 2) and anxiolytics (Supplement 3) were identified in the year prior to surgery and within one year after surgery using the outpatient prescription drug file.[15]

Secondary outcome

For determination of postoperative (for the BPI group) or new-onset (for the control group) conditions, postoperative/new-onset coded depression was defined as either a new coded diagnosis of depression and/or a new prescription for antidepressant medication. If members in the BPI group had coded depression or coded anxiety in the year prior to surgery, or if

members of the control group had coded depression or coded anxiety in the year prior to their reference date, they were thought to already have depression or anxiety and excluded from analysis of the secondary outcome (postoperative/ new-onset coded depression or coded anxiety). Postoperative/new-onset coded anxiety was defined as either a new coded diagnosis of anxiety and/or a new prescription for anxiolytic medication.

Additional Variables

We identified comorbidities in the year prior to surgery requiring ≥1 inpatient claim or ≥2 outpatient claims spaced at least 30 days apart. In addition to the comorbidities included in the Elixhauser index,[16–18] we identified additional conditions that are known risk factors for depression or anxiety, including chronic pain (ICD-9-CM 338.21–338.4) and coronary artery disease (ICD-9-CM diagnosis codes 412–414.9, V45.81, and V45.82).[19,20]

Statistical Analysis

Demographic data in the BPI and control groups were compared using univariate descriptive statistics (t-tests for continuous variables and chi-square testing for categorical variables). Multivariate Cox proportional hazards models were performed with new-onset coded depression or new-onset coded anxiety as the dependent variables. Variables with $p<0.20$ in univariate analysis were entered into the multivariable Cox models. Patients were censored at the earliest of the following: loss of continuous insurance enrollment, death, event (new-onset coded depression or coded anxiety), or 365 days.

RESULTS

From 2007–2013, 1,843 BPI surgical patients and 18,430 controls were identified. The median age of patients was 45 years and 43% were males (Table 1). The geographic distribution of the BPI group differed from the controls with more BPI patients living in the North Central and West regions, and fewer in the Northeast and Southern regions of the United States.

Coded depression was present in 38% and coded anxiety was present in 42% of the BPI group in the 12 months prior to surgery; both pre-operative coded anxiety and coded depression were present in 25% in the 12 months prior to surgery. In the control group, baseline coded depression was present in 33% and baseline coded anxiety was present in 33% of the control group; both were present in 21%. Baseline coded depression and coded anxiety were significantly more common in the BPI group compared to the control group ($p<0.0001$ for both). Combined, 54% of the BPI group had coded depression and/or coded anxiety in the 12 months prior to surgery, compared to 46% for the control group.

Postoperative/new-onset coded depression and postoperative/new-onset coded anxiety were identified after excluding patients with baseline coded depression or anxiety (Table 2). The incidence rate of coded depression in BPI surgical patients was 142.1 per 1000 person-years (12%), and the incidence rate of coded anxiety was 273.6 per 1000 person-years (20%). In the control group, the incidence rate of coded depression was 102.2 per 1000 person-years (8%), and the incidence rate of coded anxiety was 127.2 per 1000 person-years (10%). In univariate analysis, there were significantly higher rates of new-onset/postoperative coded

depression (p=0.0003) and coded anxiety (p<0.0001) in the BPI group compared to the control patients.

A multivariable Cox proportional hazards model was used to analyze the association between new-onset/postoperative coded depression and BPI surgery, adjusting for sex, age, medical co-morbidities associated with depression, coded anxiety, alcohol abuse, drug abuse, and chronic pain. After adjusting for these variables, BPI surgery was significantly associated with new-onset coded depression compared to control patients (HR=1.3[1.1,1.5]) (Table 3). Significantly increased risk of developing new-onset/postoperative coded depression was associated with baseline coded anxiety (HR=2.6[2.3,2.9]), alcohol abuse (HR=2.2[1.4,3.5]), drug abuse (HR=2.3[1.6,3.4]), and chronic pain (HR=1.4[1.0–1.8]).

A similar multivariable Cox regression model was used to analyze the association between new-onset/postoperative coded anxiety and BPI surgery. BPI surgery was associated with significantly increased risk for new-onset/postoperative coded anxiety, (HR=2.1[1.8,2.4]), independent of other covariates (Table 4). Other independent risk factors for new- onset/ postoperative coded anxiety included baseline coded depression (HR=2.3[2.0,2.5]), metastatic cancer (HR=1.9[1.2,3.1]), drug abuse (HR=2.1[1.4,3.0]), and chronic pain (HR=1.4[1.1,1.8]).

DISCUSSION

Numerous psychological factors have been identified and linked to ultimate patient function and quality of life after musculoskeletal and neurologic trauma.[1–5,8,9,12,21–27] Prevalence rates of moderate to severe levels of depression have been reported in 20–26% of orthopaedic trauma patients, with clinically relevant depressive symptoms reported in as high as 45% of patients.[10,11] Furthermore, greater levels of disability and pain intensity in patients with depression have been identified in the postoperative period.[8,11,12,28] Our analysis of a national database of privately-insured patients demonstrates baseline coded depression in 38%, baseline coded anxiety in 42%, and both coded depression and coded anxiety in 25% of BPI surgical patients. These rates are substantially higher than those reported for the general population by the National Institute of Mental Health.[29,30] Coded depression, coded anxiety, or both were found in well over half of our surgically treated patients in the year prior to their surgery (54%), which is not surprising given the occurrence of a severe, life-changing condition such as BPI. One important limitation is that we cannot distinguish depression or anxiety that are present before the injury vs those that are coded in the time between injury and surgery. It should also be noted that the rates of coded depression and anxiety are relatively high in our control group – this is likely because our control group was frequency-matched based on the number of outpatient healthcare visits in the prior year. This was done in order to adjust for informed presence bias, in which individuals with more exposure to health care providers may be predisposed to receiving a diagnosis of any concurrent condition (ie: if you go to the doctor more frequently, you are more likely to receive additional diagnoses).[14] Because of this, our control group is unlikely to reflect the general population.

Our regression models indicate a relationship between coded depression and coded anxiety, with each condition acting as a risk factor for new-onset development of the other. While we are not able to further examine this relationship with claims data, the finding suggests that these two conditions have shared characteristics within the spectrum of mental health conditions. Because we utilized claims data from all clinicians (and not solely mental health professionals), coded depression and coded anxiety may not be clearly distinguished from each other in this study. With that limitation in mind, a larger theme should resonate: surgeons, hand therapists, and other clinicians working closely with BPI patients should be aware of the prevalence and risk factors of mental health conditions. Unfortunately, while we found very high levels of coded depression and coded anxiety in the year prior to BPI surgery, we were unable to determine whether that diagnosis was made before or after the patient sustained their injury, since we used BPI surgery as the reference point. To account for this high level of coded depression and anxiety in the year prior to BPI surgery, we removed patients with these diagnosis codes from further analysis. We identified an increased risk of developing new-onset/postoperative coded depression and new-onset/postoperative coded anxiety in BPI surgical patients compared to controls. However, this is likely attributable (at least in part) to the baseline characteristics of the two groups – unlike the control group, patients in the BPI group have sustained life-changing trauma severe enough to lead to surgery.

The methods utilized in this study design have inherent limitations. Our BPI surgical group demonstrated considerably distinct distributions of age (45 years) and sex (43% male) than those reported in other series (29 years, 89% male).[33] This may represent a selection bias from the use of a private insurer claims database. Thus, uninsured patients, government-insured patients, and those patients with claims covered by automotive insurance, who may represent a substantial portion of BPI patients, were not included in this study. A prior study using administrative data reported that 47% of BPI patients have private insurance[34]; our exclusion of BPI patients without private insurance limits the generalizability of our findings to all BPI patients. While it would be ideal to examine claims from an all-payer database, currently-available national datasets (such as those from Health Care Utilization Project [HCUP] and Agency for Healthcare Research and Quality) are limited in their length of follow-up (National Inpatient Sample tracks only individual hospitalizations), states/years available (HCUP statewide databases are not available for all states and all years), and data type available (pharmacy claims are not available in other datasets). Because of the difficulty in verifying the accuracy of a BPI diagnosis code in an administrative database without pairing it to a related surgery code, we only included patients who underwent BPI surgery (and not those BPI patients treated nonoperatively). This creates bias in our dataset, as patients with injuries severe enough to warrant surgical reconstruction are presumably more likely to be depressed or anxious before surgery. We accept the limitation that this creates, as our findings can only be generalized to privately-insured patients who undergo surgery for BPI. Additionally, inclusion in the study further required uninterrupted insurance coverage for at least one year prior to surgery/index date. This time of prolonged, stable insurance coverage *before surgery* was important for quantification of coded depression and anxiety in the year prior to surgery. Our exclusion of those patients with less than one year of baseline insurance coverage may lead to an underestimation of coded depression and anxiety. In the

time period *after surgery*, we required a minimum of one month of follow-up. Although this minimum requirement could conceivably have been extended to the 90-day "global window" of postoperative care without an appreciable difference, we did not extend it beyond this time period due to concerns for loss-to-follow-up and insurance instability. These concerns were rooted in the finding that during cohort assembly, 26% of the BPI patients had less than one year of follow-up after surgery. The decision to limit the required duration of follow-up may have also led to an underestimation of coded depression and anxiety. As patients may have lost their private insurance coverage, we could not capture their subsequent treatment due to lack of insurance (perhaps with loss of employment), or enrollment in Medicaid insurance. Without a national all-payer claims database, we are unable to track patients across different insurance plans. Lastly, our use of administrative claims data makes us reliant upon accurate coding of diagnoses, procedural codes, and pharmacy claims. Accuracy of diagnosis codes is limited, which is why we chose to pair the diagnosis codes to procedure codes to create our BPI surgical cohort. For pharmacy claims, anti-depressant medications that have "off-label" uses for neuropathic pain, (such as nortriptyline, amitriptyline, or duloxetine), may have resulted in a diagnosis of depression, for the purposes of this study. We based our methods for anti-depressants and anxiolytic pharmacy claims from a prior study using the same database[15] and note that we cannot discern off-label use of these medications. This may have led to an overestimation of coded depression and anxiety in our study.

The impact of depression, anxiety, and subsequent treatment on recovery after BPI is an area for future exploration, as both of these conditions can conceivably alter a patient's ability to endure a prolonged recovery process. In providing empirical data concerning the frequency and risk factors for both new-onset depression and anxiety, we hope that future investigation into the clinical impact of these conditions on BPI patients' coping strategies, engagement and expectations for treatment, and adherence to postoperative therapy, among other issues, can be undertaken.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline Patient Demographics

	BPI Surgery N=1,843	Control Sample N=18,430	*p*
Age, median (IQR)	45 (34–53)	45 (34–53)	>0.05
Male, n (%)	792 (43.0)	7,920 (43.0)	>0.05
Northeast, n (%)	212 (11.5)	2,960 (16.1)	<0.0001
North Central, n (%)	487 (26.4)	4,311 (23.4)	
South, n (%)	738 (40.0)	7,943 (43.1)	
West, n (%)	406 (22.0)	3,216 (17.4)	
Depression Diagnosis, n (%)	300 (16.3)	2,701 (14.7)	0.07
Anxiety Diagnosis, n (%)	220 (11.9)	2,529 (13.7)	0.03
Antidepressant, n (%)	648 (35.2)	5,656 (30.7)	<0.0001
Anxiolytic, n (%)	709 (38.5)	5,243 (28.5)	<0.0001
Alcohol Abuse, n (%)	28 (1.5)	239 (1.3)	0.42
Drug Abuse, n (%)	49 (2.7)	421 (2.3)	0.31
Depression or Antidepressant, n (%)	702 (38.1)	6,163 (33.4)	<0.0001
Anxiety or Anxiolytic, n (%)	765 (41.5)	6,142 (33.3)	<0.0001
Hypothyroidism, n (%)	125 (6.8)	1,117 (6.1)	0.22
Chronic Lung Disease, n (%)	127 (6.9)	1,285 (7.0)	0.90
Metastatic cancer, n (%)	30 (1.6)	181 (1.0)	0.009
Chronic pain, n (%)	206 (11.2)	699 (3.8)	<0.0001
Congestive Heart Failure, n (%)	<11 (NR)	185 (1.0)	0.0084
Paralysis, n (%)	30 (1.6)	66 (0.4)	<0.0001
Renal Failure, n (%)	<11 (NR)	271 (1.5)	0.0012
Liver Failure, n (%)	14 (0.8)	216 (1.2)	0.11
Coronary Artery Disease, n (%)	34 (1.8)	589 (3.2)	0.0014

In accordance with the data use agreement, absolute numbers below 11 cannot be reported.

Table 2

New-onset Depression and Anxiety in the BPI and Control Groups after Surgery or Index date

Condition	Group	n	Percent with incident condition	Person years of follow-up	Rate per 1000 person-years	p
Depression	BPI	1,141	11.7%	936	142.1	0.0003
	Control	12,267	8.0%	9,657	102.2	
Anxiety	BPI	1,078	20.4%	804	273.6	<0.0001
	Control	12,288	9.9%	9,572	127.2	

Table 3

Multivariate Cox Regression Model for New-Onset Depression after BPI Surgery or after Index Date (Controls)

DEPRESSION	Hazard Ratio	95% Hazard Ratio Confidence Limits		p-value
BPI Surgery	1.282	1.068	1.538	0.0076
Hypothyroidism	1.197	0.942	1.520	0.1412
Chronic Lung Disease	1.107	0.881	1.392	0.3832
Metastasis	1.369	0.867	2.161	0.1783
Pre-existing Anxiety	2.566	2.267	2.904	<.0001
Alcohol Abuse	2.179	1.354	3.508	0.0013
Drug Abuse	2.330	1.614	3.362	<0.0001
Chronic Pain	1.376	1.028	1.842	0.0319

Table 4

Multivariate Cox Regression Model for New-Onset Anxiety after BPI Surgery or after Index Date (Controls)

ANXIETY	Hazard Ratio	95% Hazard Ratio Confidence Limits		p-value
BPI Surgery	2.078	1.798	2.402	<0.0001
Hypothyroidism	1.120	0.903	1.388	0.3027
Chronic Lung Disease	1.083	0.881	1.331	0.4484
Metastasis	1.927	1.208	3.073	0.0059
Pre-existing Depression	2.268	2.030	2.534	<.0001
Alcohol Abuse	1.186	0.712	1.976	0.5130
Drug Abuse	2.074	1.443	2.980	<0.0001
Chronic Pain	1.388	1.070	1.800	0.0134