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Original research

Depression and Anxiety Screening Identifies Patients That may Benefit From Treatment Regardless of Existing Diagnoses

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ABSTRACT

Background: This study investigated the utility of depression and anxiety symptom screening in patients scheduled for total knee arthroplasty to examine differences in active symptoms according to patients' mental health diagnoses and associated prescription medications.

Material and methods: This cross-sectional study analyzed 594 patients scheduled for total knee arthroplasty at a tertiary practice between June 2018 and December 2018. Patients completed Patient-Reported Outcomes Measurements Information System (PROMIS) Depression and Anxiety Computerized Adaptive Tests in clinic quantifying active symptoms. Mental health diagnoses and associated medications were extracted from health records. Statistical analysis assessed between-group differences in mean PROMIS scores and the prevalence of heightened depressive and anxiety symptoms.

Results: Multivariable linear regression modeling demonstrated that being diagnosed with depression without medication (β 7.1; $P < .001$) and with medication (β 8.6; $P < .001$) were each associated with higher PROMIS Depression scores. Similar modeling demonstrated that patients diagnosed with anxiety and prescribed an anxiolytic (β 8.4; $P < .001$) were associated with higher PROMIS Anxiety scores than undiagnosed patients. Eighty-six (15%) patients experienced heightened anxiety and/or depressive symptoms. Heightened depressive symptoms were more prevalent among those diagnosed with depression (19% without medication, 24% with antidepressant vs 5% undiagnosed: $P < .001$). Heightened anxiety symptoms were most prevalent among those diagnosed with anxiety and on anxiolytic medication (25% vs 7% diagnosed with anxiety without medication, 8% undiagnosed: $P < .001$).

Conclusion: One in seven arthroplasty patients screened reported heightened depressive and/or anxiety symptoms. Despite the majority of arthroplasty patients on antidepressants and anxiolytics having symptoms controlled, these patients remain at increased risk of heightened active symptoms.

Introduction

A complex, bidirectional relationship exists between mental and physical health. Specifically, depression, anxiety, and coping abilities are all recognized to influence patients' pain experience. Because most orthopedic surgeries, including total joint arthroplasty (TJA), are elective procedures performed for pain relief, it is expected that comorbid depressive and anxiety symptoms are increasingly recognized as a risk factor for suboptimal surgical outcomes [1-11].

Among patients undergoing primary total knee arthroplasty (TKA), depression is also associated with greater pain, worse functional outcomes, more resource utilization, and higher risk for revision [1-10,12-23]. Although less well-studied in isolation, anxiety has been found to correlate with Oxford Knee Scores and Knee Society Scores following knee arthroplasty and is associated with requiring discharge to rehabilitation after lower extremity arthroplasty [24,25]. These prior studies have correlated a diagnosis of anxiety or depression to outcomes after TKA. However, there is a

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paucity of data regarding the utility of screening for active depression or anxiety symptoms and whether or not active symptoms better correlate with outcomes than a diagnosis of depression or anxiety.

Having a diagnosis of depression or anxiety does not in itself predict degrees of ongoing symptoms at presentation for orthopedic care. Patients with established diagnosis of depression and/or anxiety that is treated pharmacologically could potentially present to an orthopedic surgeon with average, or even below-average, levels of active depressive and/or anxiety symptoms. Therefore, the purpose of this study was to determine the utility of depression and anxiety symptom screening in patients who were scheduled for TKA to examine differences in active symptoms based on patients' history of mental health diagnoses and prescription medication use.

Material and methods

This cross-sectional study was approved by our institutional internal review board. Patients aged 21 to 90 years who underwent primary TKA at a single tertiary practice between June 1, 2018, and December 31, 2018, were identified via electronic medical records. As standard care in our practice, every patient at every visit completes self-administered Patient-Reported Outcomes Measurements Information System (PROMIS) Computerized Adaptive Tests, including Anxiety and Depression, in sequential order on a tablet computer (Apple iPad; Apple Inc., Cupertino, CA). Their PROMIS scores are automatically uploaded to their electronic health record upon completion. Six hundred eighty-eight patients met the initial inclusion criteria. Patients were excluded from analysis if they did not have a visit with a PROMIS Depression score (n = 94, 14% of total) prior to surgery. The final population of 594 patients analyzed were undergoing TKA for either osteoarthritis (n = 568, 96%), posttraumatic arthritis (n = 6, 1%), or other diagnoses (n = 20, 3%). Table 1 presents the demographics of the study population.

PROMIS is a set of validated health domain surveys scaled to a population mean of 50 and standard deviation of 10 [26]. Higher scores indicate more of each health domain such that a PROMIS Depression score of 60 indicates depressive symptoms one standard deviation greater than the US general population average. A minimal clinically important difference (MCID) of approximately 3.5 points on the PROMIS Depression measure has been proposed based on an analysis of randomized controlled trials including a cohort of patients with knee arthritis [27-29]. MCID estimates for PROMIS Anxiety have ranged from 2 to 6 points, with an estimated range of 2.3-3.4 points in patients with knee osteoarthritis [27,29-31]. Similar MCID values have been proposed on other PROMIS assessments in patients with musculoskeletal conditions [32-35]. Considering MCID values as a reasonable proxy for clinically relevant between-group differences, we set 4 points as our threshold for a clinically relevant difference in PROMIS Depression and Anxiety scores.

Table 1
Demographic data of patients scheduled for primary knee arthroplasty.

Variable (n = 594)	Mean ± SD or N (%)
Age (y)	64 ± 9
Female	332 (56)
Race	
White	523 (88)
Black	55 (9)
Other	16 (3)
BMI (kg/m^2)	32 ± 6
Knee diagnosis	
Osteoarthritis	568 (96)
Post-traumatic	6 (1)
Other	20 (3)
Menth health diagnosis	
None	417 (70)
Depression	87 (15)
Anxiety	39 (7)
Depression and anxiety	34 (6)
Depression and other	5 (1)
Other	12 (2)
PROMIS score	
Depression	47 ± 10
Anxiety (n = 587)	51 ± 10

The PROMIS Depression domain measures persistent negative mood, affect, and self-views in the last 7 days independent of any prior diagnoses of depression and/or anxiety [36,37].

Linkage tables crosslink PROMIS Depression scores to legacy measures [36]. A PROMIS Depression score of 59.9 corresponds to a Patient Health Questionnaire 9 score of 10, which has the optimal specificity and sensitivity for predicting a diagnosis of major depression [38,39]. Therefore, a PROMIS Depression score of ≥59.9 was the threshold for a patient experiencing heightened depressive symptoms.

The PROMIS Anxiety module captures the respondent's emotional distress caused by hyperarousal, fear, stress, and related somatic symptoms [36]. Patients were categorized as experiencing heightened anxiety symptoms based on a PROMIS Anxiety score threshold of 62. Scores of 62 or higher correspond with scores above 10 on the Generalized Anxiety Disorder 7 [39,40]. A score of 10 or higher on the Generalized Anxiety Disorder 7 represents the optimal sensitivity and specificity for detection of moderate anxiety considered sufficient to prompt formal anxiety evaluation for potential treatment [41].

Patients' history of diagnosed depression/anxiety and reported antidepressant and/or anxiolytic use was captured via manual review of their self-reported intake questionnaires in the electronic health record. On these questionnaires, patients reported their regularly used medications and the reason for the medication. Based on this information, we established 3 patient groups for both depression and anxiety: no prior diagnosis of depression/anxiety (undiagnosed), diagnosed depression/anxiety without medication, and diagnosed depression/anxiety with medication use.

Statistical analysis

Patient demographics were summarized using descriptive statistics. The percent of patients overall affected by heightened depressive and anxiety symptoms according to patient group was compared with chi-square testing. Between-group mean PROMIS Depression and Anxiety scores were compared using one-way analysis of variance and Fisher's least significant difference pairwise testing. Between-group differences were also assessed for clinical relevance (≥4 points). The percent of patients affected by heightened depressive and anxiety symptoms according to patient group was compared with chi-square testing. During this analysis, patients with other mental health diagnoses were removed to avoid bias (n = 51). Two multivariable linear regression models were constructed to identify predictors of PROMIS Depression and Anxiety scores (continuous variables). These forward stepwise models were used to determine whether patient groups remained significantly associated with PROMIS scores while accounting for demographic variables including age, sex, race, and body mass index (BMI). Appendix Table S1 presents demographics of patients according to depression group. An a priori sample size calculation was completed for our primary analysis, regarding the difference in PROMIS Depression/Anxiety scores between the 3 patient groups. This indicated the need for at least 66 patients overall to detect an effect size of 0.4 on PROMIS scores (a 4-point difference, standard deviation 10 points) with an alpha of 0.05 and power of 0.80.

Because we expected our patient groups to be of unequal size, we aimed to collect enough patients to have at least 22 patients in our smallest patient group.

Results

Among the 594 patients studied, 59 (9.9%, 95% confidence interval [CI] 7.7%-12.5%) reported currently heightened depressive symptoms. Sixty-nine (11.6%, 95% CI 9.2%-14.4%) of the patients reported heightened anxiety symptoms. In total, 86 (14.5%, 95% CI 11.0%-18.5%) experienced heightened anxiety and/or depression.

One hundred twenty-six (21%) patients had been diagnosed with depression. Ninety-nine (79%) of these patients reported antidepressant medication use. Mean PROMIS Depression scores were significantly different ($P < .001$) between the patient groups (undiagnosed: 45 ± 9, diagnosed depression without medication: 52 ± 9, diagnosed depression on medication: 54 ± 10) (Table 2). Pairwise comparisons indicated greater current depressive symptoms among patients with a history of diagnosed depression when not taking antidepressants (7 points greater than undiagnosed, 95% CI 4-11) and also when taking antidepressants (9 points greater than undiagnosed, 95% CI 7-11). These significant between-group differences in PROMIS Depression scores were deemed clinically relevant, as each "depression" group differed by at least 4 points from the undiagnosed group. Multivariable linear regression modeling demonstrated that being diagnosed with depression without medication (β 7.1 [3.6-10.5]; $P < .001$) and with medication (β 8.6 [6.7-10.6]; $P < .001$) were each associated with higher PROMIS Depression scores while accounting for patient age, sex, race, and BMI. Heightened depressive symptoms were detected in all groups but were more prevalent among those diagnosed with depression (19% with no medication, 24% with antidepressant medication) than among undiagnosed patients (5%) ($P < .001$).

Seventy-three (12%) patients had been diagnosed with an anxiety disorder. Fifty-nine (80%) of these patients reported anxiolytic medication use. Mean PROMIS Anxiety scores were significantly different ($P < .001$) between the patient groups (undiagnosed: 48 ± 10, diagnosed anxiety without medication: 51 ± 9, diagnosed anxiety on medication: 57 ± 10) (Table 3). Pair-wise comparisons indicated greater current anxiety symptoms among patients with a history of diagnosed anxiety when taking anxiolytics than among both undiagnosed patients (8 points greater than undiagnosed, 95% CI 6-11) and patients with diagnosed anxiety but not taking prescribed anxiolytic medication (6 points greater than undiagnosed, 95% CI 1-12). These differences exceeded the threshold for a clinically relevant difference of 4 points. Multivariable linear regression modeling demonstrated that being diagnosed with anxiety and concurrently taking anxiolytic medication (β 8.4 [5.8-11.0]; $P < .001$) was associated with higher PROMIS Anxiety scores while accounting for patient age, sex, race, and BMI. Heightened anxiety symptoms were detected in all groups but were most prevalent among those diagnosed with anxiety on medication (25% vs 7% diagnosed with anxiety not on medication, 8% undiagnosed, $P < .001$).

Table 2
Depressive symptomatology according to patient group.

Patient group (n)	PROMIS depression score, mean ± SD	Heightened depression symptoms, N (%)
No depression diagnosis (417)[a]	45 ± 9	21 (5)
Depression diagnosis without medication (27)	52 ± 9	5 (19)
Depression diagnosis with medication (99)	54 ± 10	24 (24)

[a] Fifty-one patients were excluded from the "no depression" group because they had a diagnosis of anxiety or other mental health condition.

Table 3
Anxiety symptomatology according to patient group.

Patient group (n)	PROMIS anxiety score, mean ± SD	Heightened anxiety symptoms, N (%)
No anxiety diagnosis (413)[a]	48 ± 10	31 (8)
Anxiety diagnosis without medication (14)	51 ± 9	1 (7)
Anxiety diagnosis with medication (61)	57 ± 10	15 (25)

[a] One hundred six patients were excluded from the "no anxiety" group because they had a diagnosis of depression or other mental health condition.

Discussion

Mental health diagnoses and their treatment are becoming an increasingly relevant area of research on patients undergoing TKA. Several previous studies have demonstrated that a diagnosis of depression or anxiety negatively impacts outcomes after TKA [42,43]. In their series of 280 patients, Kohring et al. found that patients without a diagnosis of depression had better PROMIS Physical Function scores than those with depression, but not on medication [42]. However, compared with other patients, patients taking antidepressants experienced similar improvement in PROMIS scores when examining change from the preoperative to postoperative PROMIS score. Conversely, Halawi et al. recently concluded that taking antidepressants for depression failed to mitigate the negative physical health impact of depression after TJA [43]. Both these studies documented a fairly substantial prevalence of comorbid depression among patients undergoing TJA, and both called for further investigation into this topic. Thus, the purpose of our study was to investigate the utility of screening for active mental health symptoms while also accounting for established mental health diagnoses and ongoing pharmacologic treatment.

The prevalence of depression and antidepressant use in both general and surgical populations is substantial and growing [44-52]. One in seven patients undergoing TKA at our institution report heightened depression or anxiety symptoms. This is lower than the 20% of nearly 15,000 patient visits to our orthopedic department in which patients reported heightened anxiety symptoms [53]. Studying patients offered TKA as opposed to all patients presenting with knee pain may have impacted our findings. One would expect surgeons to be selective when indicating patients for surgery such that patients offered an operation may have more knee pain but otherwise be healthier medically and mentally than all patients seeking care. Ottenhoff et al. demonstrated this in a study of thumb arthritis vignettes where surgeons tended to offer surgery in the setting of increased pain but were less likely to offer surgery when presented with a patient having increasing depressive symptoms [54].

A prior diagnosis of depression was associated with worse PROMIS Depression scores. This raises concerns that many patients diagnosed with depression are still experiencing relevant depressive symptoms. Antidepressants are generally understood to be efficacious for major depressive disorder, but the magnitude of their effect and the population for whom they are most beneficial remains unclear [55,56]. Our patients may have benefited from antidepressant use, but as a group, these patients still averaged greater current depressive symptoms than other patients. At the same time, our data also show that patients without diagnosed depression can present for orthopedic treatment while experiencing heightened depressive symptoms. Therefore, there is a

benefit of screening patients not just for prior diagnoses of depression or anxiety but also for active heightened symptoms of depression or anxiety. Notably, such assessments screen for depressive symptoms but not establish a clinical diagnosis of depression. This is a helpful distinction to explain to patients who are reluctant to answer survey questions about depressive symptoms when seeking orthopedic care.

Patients who presented with a diagnosis of anxiety and were prescribed anxiolytic medication were most likely to experience active anxiety symptoms. While we cannot determine how anxious these patients would have been without medication, this group continued to be more anxious than undiagnosed patients. Although less well studied than depression, it has been noted as a relevant comorbidity for patients undergoing TJA. Anxiety has been correlated with 12-week Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain scores in patients following total hip arthroplasty [57]. Anxiety is also inter-related with the experience of pain and coping [58,59]. Pain catastrophizing has been associated with lower physical function, greater pain, and poorer general health ratings after knee arthroplasty [60]. This suggests a role for supplemental treatment to improve anxiety in the perioperative time for TJA patients.

This study has several inherent limitations. In addition to being unable to examine before and after effects of antidepressant and anxiolytic medication, we did not design this study to determine the impact of such medication dosing, duration of treatment, or the delivery of any nonpharmacologic mental health treatment. We based our patient groups (diagnoses, medication use) on self-report intake questionnaires. Although patient omission and errors are possible, we felt the intake forms would best capture diagnoses and treatments from any provider even if outside of our health system. These forms have indications of “no medical problems” and “no medications used,” so we could distinguish negative histories from inadvertent omissions. If anything, omission of mental health diagnoses and medications would have artificially reduced the true prevalence of diagnosed depression and anxiety in our study population. Second, adherence to antidepressant medication is considered a major barrier to effective treatment of major depressive disorder in psychiatry, with estimates of adherence ranging from 80% to as low as 37% for some groups [61-64]. We attempted to minimize this bias by determining antidepressant use from patient self-report of medications taken, as opposed to physician-generated records. However, patient noncompliance with reported medications is still possible. Noncompliance would have biased our PROMIS scores toward underestimating the treatment effect of these medications. Third, all patients in this study presented for treatment of symptomatic knee pain. Such pain and/or impaired function could have been a psychological stressor because physical pain, anxiety, and depression can have bidirectional relationships [65]. Therefore, the depressive and anxiety symptoms measured by our PROMIS Computerized Adaptive Tests may reflect a combination of baseline depressive and anxiety symptoms, as well as depressive and anxiety symptoms produced by symptomatic knee pain. Similarly, PROMIS scores may be capturing transient or situational feelings due to specifically asking about experiences in the prior week. Lastly, while we identified that heightened depression and/or anxiety symptoms are present among both patients without those diagnoses as well as among those with those diagnoses being treated and untreated, further research is required to determine how the presence of these heightened anxiety or depression symptoms affect clinical outcomes after TKA.

Conclusions

In this study of patients preparing for TKA, mental health screening identified that nearly one in seven patients were experiencing heightened depressive and/or anxiety symptoms. Depression and anxiety screening detected heightened symptoms in patients with, and without, these diagnoses. Screening for active symptoms remains important in patients who are using prescribed antidepressants and/or anxiolytics because these patients were the group with the greatest magnitude of current symptoms. If a patient reports active depressive and/or anxiety symptoms, it may be reasonable for surgeons to facilitate further treatment (eg, return to, or discussion with, mental health provider or primary physician) prior to operating, as this may improve the ultimate functional outcome after TKA.

Conflicts of interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: A. Cheng is an associate editor for PM&R journal. C. P. Hannon is an AAHKS committee member. M. A. Adelani is in the editorial board of *Journal of Arthrolasty* and Diversity Advisory Board of American Associaion of Hip and Knee Surgeons. R. P. Calfee is an editor for the *Journal of Hand Surgery*.

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Appendix

Table S1
Demographic data according to depression group.

Variable	Mean ± SD or N (%)			
	Overall (n = 594)	No depression diagnosis (n = 417[a])	Depression diagnosis without medication (n = 27)	Depression diagnosis with medication (n = 99)
Age (y)	64 ± 9	65 ± 9	65 ± 7	62 ± 10
Female sex	56%	51%	59%	74%
BMI	32 ± 6	31 ± 6	31 ± 6	33 ± 6
White race	88%	87%	89%	89%

[a] Fifty-one patients were excluded from the “no depression” group because they had a diagnosis of anxiety or other mental health condition.