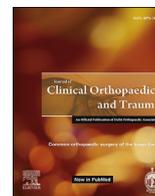




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Clinical characteristics associated with depression or anxiety among patients presenting for knee surgery

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ABSTRACT

Background: Preoperative depression and anxiety in patients undergoing surgery have been shown to be associated with increased postoperative complications, decreased functional improvement, and long-term dissatisfaction. The purpose of this prospective study was to measure the relationship between a diagnosis of depression or anxiety and Patient-Reported Outcomes Measurement Information System (PROMIS) domains, as well as to determine which preoperative factors are associated with depression or anxiety in patients undergoing knee surgery. We hypothesized that preoperative depression and/or anxiety would be associated with worse preoperative pain, function, and general health status.

Methods: Three-hundred and eighty-six patients undergoing knee surgery between 2015 and 2017 were administered health-related quality of life measures preoperatively, and their medical records were reviewed for relevant medical history. A propensity matched analysis was performed to determine clinical factors independently associated with preoperative depression and/or anxiety.

Results: The overall study population consisted of 216 males and 170 females, with a mean age of 39.4 ± 16.2 years. From this overall cohort, 43 (11.1%) patients had a positive preoperative diagnosis of depression and/or anxiety. After controlling for covariate imbalances, preoperative depression/anxiety was independently associated with PROMIS Anxiety ($p = 0.018$), PROMIS Depression ($p < 0.019$), and Tegner pre-injury ($p = 0.013$) scores. Regression analysis also determined that preoperative depression/anxiety was independently associated with arthroscopic anterior cruciate ligament reconstruction (ACLR) ($p = 0.004$), total knee arthroplasty (TKA) ($p = 0.019$), and uni-compartmental knee arthroplasty ($p < 0.05$).

Conclusion: The results support our hypothesis that preoperative depression/anxiety is associated with worse preoperative pain, function, and general health status. Furthermore, PROMIS Anxiety and Depression tools offer a reliable means of measuring psychological distress in the orthopaedic knee population. Similar to other studies, we also noted psychological comorbidity to be independently associated with ACLR and TKA.

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1. Introduction

The prevalence of knee surgeries in the United States has been steadily increasing each year, wherein it has increased from 0.13% in 1980 to 1.52% in 2010.¹ This trend is likely to continue as the

average life expectancy of the U.S. citizen continues to rise.² The elderly population is often at a higher risk of requiring knee surgery, due to an increased risk for knee arthritis as a result of mechanical and biochemical cartilage deterioration.³

As with any surgical procedure, postoperative dysfunction and complications do occur after orthopaedic knee surgeries. The rate of complications, including hemarthrosis, pulmonary embolism, and deep vein thrombosis, has been estimated to be 4.7% for arthroscopic knee operations between 2003 and 2009.⁴ Complications

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and dysfunction after surgery can result in higher financial burdens, slower recovery times, and lower quality of life.⁵ Essential in minimizing the risk of complications is identifying and minimizing preoperative factors associated with poor postoperative outcomes. Several such factors have been identified in the literature, which include age, body mass index (BMI), preexisting comorbidities such as diabetes and cardiac disease, and American Society of Anesthesiologists (ASA) classification.^{6,7}

Interestingly, psychological comorbidities, such as depression and anxiety, have been shown to be associated with increased postoperative complications, decreased functional improvement, lengthened rehabilitation, and long-term dissatisfaction.^{8–16} The prevalence of major depressive disorder, the most common of all mood disorders, has been estimated to be 29.9% of the general population in 2012.¹⁷ Thus, depression and anxiety may be common within orthopaedic surgery patients and negatively influence postoperative outcomes.

Recognition of preoperative risk factors, including depression and anxiety, may allow for intervention and optimization of postoperative outcomes. Patients with conditions requiring knee surgeries, in particular, could be at increased risk for psychological comorbidities due to fatigue, pain, and inability to carry out their usual activities due to lower extremity dysfunction.¹⁸ However, there is a lack of data regarding depression and anxiety assessment in patients undergoing knee surgery, and that which is reported is limited to patients undergoing knee arthroplasty.

The Patient-Reported Outcomes Measurement Information System (PROMIS) domains have been created by the National Institutes of Health (NIH) to provide an assessment of patient-reported outcomes that is cost effective, time effective, and generalizable over a wide variety of clinical patients.^{19,20} However, the data collected through PROMIS in orthopaedic patients is currently limited to foot, ankle, upper extremity, and spine injuries,^{20–23} with a lack of data regarding the use of PROMIS for patients undergoing knee surgery.

The primary objective of this study was to determine the potential demographic associations of preoperative depression and/or anxiety in patients undergoing a variety of knee surgeries. The secondary purpose was to determine whether preoperative depression/anxiety was a significant independent predictor of health-related quality of life (HRQOL) measures, including PROMIS, in patients undergoing knee surgery. Our first hypothesis was that preoperative depression/anxiety would be associated with worse demographic and clinical measures. Our second hypothesis was that preoperative depression/anxiety would be significantly and independently associated with worse HRQOL measures, including function, pain, and satisfaction.

2. Patients and methods

The investigation was observational cross-sectional study. A prospective orthopaedic database was used to evaluate patients preoperatively from June 2015 to June 2017 at a single institution.²⁴ All patients undergoing knee surgery at our institution were eligible for enrollment into an institutional review board-approved registry. All study data was collected within 7 days prior to surgery using the Research Electronic Data Capture (REDCap™) data collection system. Inclusion criteria were as follows: (1) patient undergoing orthopaedic surgery, (2) age more than 12 years, and (3) English speaking.

Demographic data, including a diagnosis of depression and/or anxiety, was self-reported by each respondent. Income level was assessed as approximate family income including wages, disability payment, retirement income, and welfare. This was done so as to account for very young patients who may have no income (i.e.

students) and the elderly that may be retired. Each patient's medical record was reviewed for relevant medical history, including their American Society of Anesthesiologists (ASA) score and current medications.²⁴

Patients enrolled in the registry were asked to complete an electronic baseline assessment of: (1) preoperative data, (2) six PROMIS (v1.2) computer adaptive testing tools (Domains: Physical Function, Pain Interference, Fatigue, Social Satisfaction, Anxiety, and Depression), (3) the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, (4) International Physical Activity Questionnaire (IPAQ), (5) Tegner activity measure (both prior to injury and preoperative), (6) Activity Rating Scale for the lower extremity (ARS), (7) Numeric Pain Scale (NPS, for the operative knee and body overall), and (8) pretreatment expectations (MODEMS, Musculoskeletal Outcomes Data Evaluation and Management System).

2.1. Statistical analysis

Descriptive statistics were used to analyze study variables (means, medians, standard deviations, and frequency). Demographic and clinical data were compared using the Wilcoxon rank sum test for continuous variables and the Pearson chi-squared test (or Fisher's exact test when more than 20% of cells had frequencies < 5) for categorical variables.

In addition, a propensity score matching analysis was implemented to reduce the effect of covariate bias and to better estimate the independent associations of preoperative depression and/or anxiety. Covariates that were previously reported to affect perioperative depression and anxiety, or that had a possible association with depression and/or anxiety in the current dataset were entered in the analysis. These covariates included: age, BMI, expectations overall, number of surgeries (ANY), gender, employment status, smoking status, preoperative opioid use, and ASA score.

The propensity score was the conditional probability for subjects who had depression/anxiety and those who did not as a function of predetermined covariates, added into a multiple logistic regression. Propensity scores derived from logistic regression models were determined. Using the calculated propensity scores, a 1-to-1 matched analysis was carried out by random selection of a patient who had depression/anxiety with one who did not using the closest calculated propensity score. The selected pair was suitable for matching if the propensity scores of the pair were within 0.6 standard deviation of all selected pairs. According to Cochran and Rubin, a caliper width of 0.6SD will remove almost 90% of the bias in observed confounders.²⁵ Those patients who did not have an acceptable range of propensity scores were excluded from analysis. Logistic regression models using propensity matched groups were used to identify independent association between each patient-reported outcome and preoperative depression/anxiety. A two-sided P value < 0.05 was considered statistically significant.

3. Results

From a total of 412 eligible patients between 2015 and 2017, medical record data regarding a preoperative diagnosis of depression and/or anxiety was available for 386 patients. The study population consisted of 216 males (56%) and 170 females (44%), with a mean age of 39.4 ± 16.2 years and mean BMI of 29.3 ± 5.7 kg/m². From this overall cohort, 43 (11.1%) patients had a positive preoperative diagnosis of depression and/or anxiety. The distribution of categorical variables of the patients studied, including demographic data, ASA score, drug use, and surgical history, is presented in Table 1. Bivariate analysis demonstrated that

Table 1
Categorical variables (n = 386).

	Depression and/or Anxiety				P value
	Yes		No		
	N	%	N	%	
	43	11.1%	343	88.9%	
Gender					
Male	10	23.3%	206	60.1%	<.0001
Female	33	76.7%	137	39.9%	
Ethnicity					
Hispanic or Latino	1	2.4%	18	5.4%	0.800
NOT Hispanic or Latino	41	97.6%	317	94.6%	
Race					
Black	12	27.9%	113	33.9%	0.706
White	27	62.8%	190	57.1%	
Other	4	9.3%	30	9.0%	
Education					
HS grad or above	42	97.7%	302	91.2%	0.284
Some HS or below	1	2.3%	29	8.8%	
Employment Status					
Employed for wages	21	48.8%	170	50.9%	0.026
Self-employed	2	4.7%	24	7.2%	
Out of work and looking for work	–	–	12	3.6%	
Out of work but not currently looking for work	–	–	6	1.8%	
Homemaker	2	4.7%	5	1.5%	
Student	2	4.7%	69	20.7%	
Military	–	–	1	0.3%	
Retired	7	16.3%	15	4.5%	
Unable to work	9	20.9%	27	8.1%	
Other	–	–	5	1.5%	
Income					
Less than \$10,000	5	14.3%	28	12.6%	0.835
\$10,000 - \$19,999	2	5.7%	12	5.4%	
\$20,000 - \$29,999	–	–	15	6.7%	
\$30,000 - \$39,999	2	5.7%	18	8.1%	
\$40,000 - \$49,999	1	2.9%	17	7.6%	
\$50,000 - \$59,999	3	8.6%	15	6.7%	
\$60,000 - \$69,999	3	8.6%	9	4.0%	
More than \$70,000	19	54.3%	109	48.9%	
Marital Status					
Single - never married	12	27.9%	168	50.1%	0.110
Married or domestic partnership	23	53.5%	135	40.3%	
Divorced, separated, or widowed	8	18.6%	32	9.6%	
Smoking Status					
Daily	6	14.0%	14	4.2%	0.049
Less than daily	3	7.0%	11	3.3%	
Quit smoking	11	25.6%	60	18.0%	
Never smoked	23	53.5%	249	74.6%	
Alcohol Consumption					
Never	16	39.0%	88	26.7%	0.814
Monthly or less	12	29.3%	94	28.5%	
2 to 4 times a month	6	14.6%	74	22.4%	
2 to 3 times a week	5	12.2%	51	15.5%	
4 or more times a week	2	4.9%	23	7.0%	
Recreational drug use					
No	38	90.5%	316	95.2%	0.592
Yes	4	9.5%	16	4.8%	
Preoperative Opioid Use					
No	28	65.1%	274	80.8%	0.009
Yes	15	34.9%	65	19.2%	
ASA score					
1	4	9.3%	156	45.7%	<.0001
2	33	76.7%	174	51.0%	
3	6	14.0%	11	3.2%	
Injury prior to surgery					
No	23	57.5%	118	35.3%	0.018
Yes	17	42.5%	216	64.7%	
Workers' compensation					
No	42	97.7%	331	96.5%	0.915
Yes	1	2.3%	12	3.5%	
Prior surgery on same knee					
No	22	52.4%	228	67.1%	0.192
Yes	20	47.6%	112	32.9%	

preoperative depression/anxiety was significantly associated with female gender ($p < 0.0001$), employment status ($p = 0.026$), smoking status ($p = 0.049$), preoperative opioid use ($p = 0.009$), ASA score ($p < 0.0001$), and the occurrence of an injury prior to surgery ($p = 0.018$).

The distribution of the continuous variables, including demographic data, preoperative expectations of surgical outcomes, and patient-reported outcome measures, are presented in Table 2. Bivariate analysis demonstrated multiple significant differences between those patients with a positive preoperative diagnosis of depression/anxiety and those without depression/anxiety. The average age of patients with preoperative depression/anxiety was 48.0 ± 14.4 years, while the average age of patients without depression or anxiety was 38.1 ± 16.1 years ($p = 0.0002$). Patients with preoperative depression/anxiety had a significantly worse mean Charlson Comorbidity Index (1.8 ± 1.7 vs. 0.8 ± 1.1 ; $p < 0.0001$) and significantly more prior surgeries of any type (4.3 ± 3.3 vs. 2.6 ± 3.2 ; $p < 0.0001$) than those patients without preoperative depression/anxiety. Patients with positive preoperative depression/anxiety had significantly worse scores across all PROMIS health domains, including Physical Function (37.8 ± 6.8 vs. 42.0 ± 8.1 ; $p = 0.0013$), Pain Interference (64.0 ± 6.5 vs. 59.8 ± 7.3 ; $p = 0.0005$), Fatigue (57.6 ± 10.1 vs. 51.7 ± 10.4 ; $p = 0.0006$), Social Satisfaction (39.6 ± 7.2 vs. 42.9 ± 9.4 ; $p = 0.015$), Anxiety (61.9 ± 7.6 vs. 54.4 ± 8.8 ; $p < 0.0001$), and Depression (54.7 ± 8.7 vs. 48.5 ± 9.0 ; $p < 0.0001$) (see Fig. 1). There were also significant differences in IKDC, IPAQ, Tegner pre-injury, ARS (lower extremity), and pain intensity (NPS, operative knee and overall body) scores between those patients with preoperative depression/anxiety and those without (Table 2).

After propensity matching to control for covariate imbalances, logistic regression analysis determined that PROMIS Anxiety ($p = 0.018$), PROMIS Depression ($p < 0.019$), and Tegner pre-injury ($p = 0.013$) scores were independently associated with a preoperative depression/anxiety. Logistic regression analysis also

determined that preoperative depression/anxiety was independently associated with arthroscopic anterior cruciate ligament (ACL) surgery (CPT 29888; $p = 0.004$), total knee arthroplasty (CPT 27447; $p = 0.019$), and uni-compartmental knee arthroplasty (CPT 27446; $p < 0.05$) (see Table 3).

4. Discussion

Knee surgery successfully restores physical function and relieves pain in millions of Americans each year. Despite the overwhelming success of many orthopaedic knee procedures, functional improvement varies widely. Poor functional measures have been correlated with poor emotional health, such as anxiety, depression, poor coping skills, and poor social support.^{26,27} This study identified several key associations of preoperative depression/anxiety in patients undergoing a variety of knee surgeries. Our primary hypothesis was supported as preoperative depression/anxiety was associated with multiple clinical factors including age, gender, employment, smoking, opioid use, worse comorbidities, and greater number of prior surgeries. Our secondary hypothesis was also supported as patients with preoperative depression/anxiety was associated with worse scores on all HRQOL measures. After adjusting for covariate imbalances, preoperative depression/anxiety demonstrated an independent association with PROMIS Depression, PROMIS Anxiety, Tegner pre-injury, ACL reconstruction, and knee arthroplasty.

Among the United States general population, the prevalence of depression is estimated between 3.4% and 29.9%,^{17,28,29} and the prevalence of anxiety is estimated between 9% and 33.7%.^{17,30} Comparatively, in our study the prevalence of depression and/or anxiety was 11.1%. Similar to the general U.S. population, our study identified preoperative depression/anxiety to be significantly associated with female gender, smoking, and opioid use.^{17,28,30–37} However, many of the commonly noted associations of depression/anxiety, such as race, BMI, and socioeconomic status, were not

Table 2
Continuous variables (n = 386).

	Depression and/or Anxiety						P value
	Yes			No			
	Mean	SD	Median	Mean	SD	Median	
Age (years)	48.0	14.4	49.2	38.1	16.1	36.5	0.0002
BMI (kg/m ²)	30.4	5.9	30.1	29.1	5.8	28.6	0.0879
Charlson Comorbidity Index	1.8	1.7	1.0	0.8	1.1	0.0	<.0001
Expectations Overall (MODEMS)	4.3	0.8	4.5	4.4	0.7	4.7	0.3359
1. Relief from symptoms	4.4	0.8	4.6	4.5	0.8	5.0	0.2510
2. Household or yard activities	4.4	0.8	5.0	4.5	0.9	5.0	0.2628
3. Sleep	4.3	1.1	5.0	4.3	1.0	5.0	0.9168
4. Job	4.4	0.9	5.0	4.5	0.9	5.0	0.1061
5. Exercise recreational	4.4	0.9	5.0	4.5	0.8	5.0	0.1449
6. Future disability	4.2	1.0	4.5	4.3	0.9	5.0	0.2341
Number of surgeries (ANY)	4.3	3.3	3.0	2.6	3.2	2.0	<.0001
Number of orthopaedic surgeries	1.5	1.8	1.0	1.3	1.7	1.0	0.2396
Number of knee surgeries	1.4	0.6	1.1	1.4	0.6	1.2	0.4960
PROMIS Physical Function	37.8	6.8	36.5	42.0	8.1	41.4	0.0013
PROMIS Pain Interference	64.0	6.5	64.2	59.8	7.3	59.7	0.0005
PROMIS Fatigue	57.6	10.1	58.7	51.7	10.4	50.6	0.0006
PROMIS Social Satisfaction	39.6	7.2	38.7	42.9	9.4	42.4	0.0150
PROMIS Anxiety	61.9	7.6	61.8	54.4	8.8	54.1	<.0001
PROMIS Depression	54.7	8.7	55.4	48.5	9.0	48.2	<.0001
IKDC	30.1	15.2	31.0	40.3	18.1	39.1	0.0008
IPAQ (MET/week)	2186.5	2422.5	1542.7	3603.8	3906.5	2772.0	0.0182
Tegner Pre-Injury	5.3	2.6	5.3	7.2	2.1	7.0	<.0001
Tegner Current (preoperative)	2.3	2.3	2.0	2.5	1.9	2.0	0.1667
ARS (Lower Extremity)	4.4	5.6	1.1	7.5	6.4	8.0	0.0034
NPS (Operative Knee)	6.0	2.7	6.8	4.7	2.9	5.0	0.0040
NPS (Overall body)	2.8	2.7	2.0	1.3	2.3	0.0	<.0001

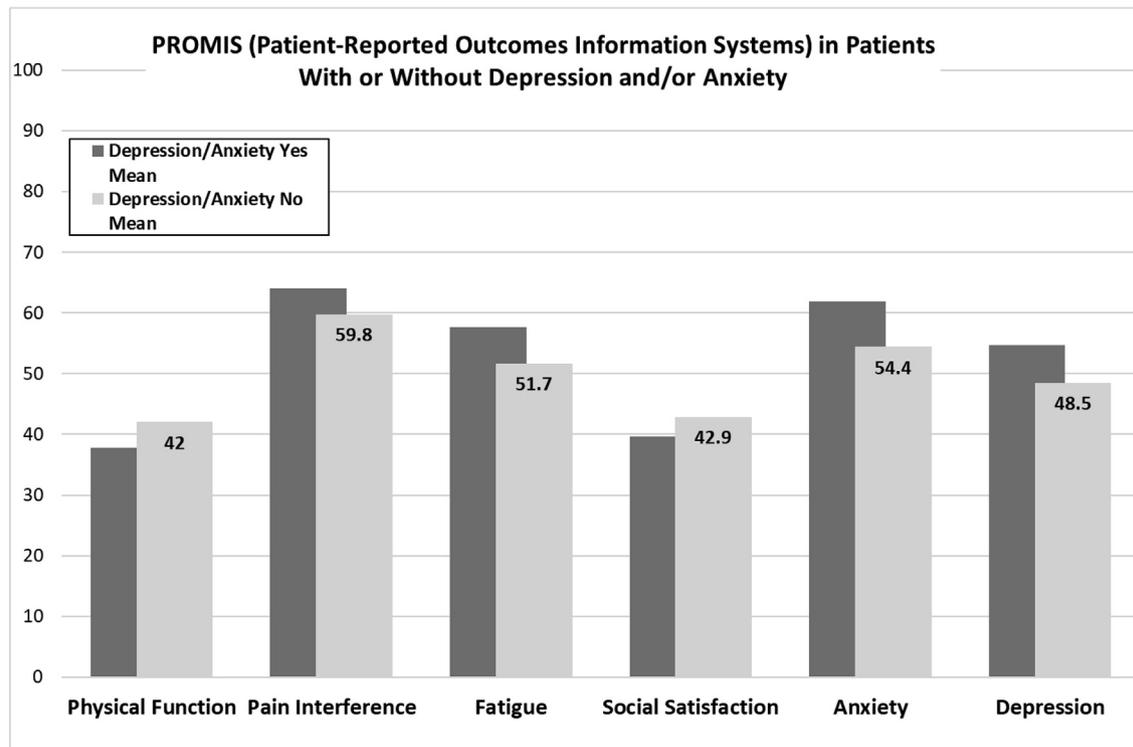


Fig. 1. PROMIS (Patient-Reported Outcomes Information Systems) in Patients with or without Depression and/or Anxiety.

Table 3
Top 10 most performed knee procedures.

CPT	Description	Count	P Value
29881	Arthroscopy, knee, surgical; with meniscectomy (medial OR lateral, including any meniscal shaving) including debridement/shaving of articular cartilage (chondroplasty), same or separate compartment(s), when performed	51	
29888	Arthroscopically aided anterior cruciate ligament repair/augmentation or reconstruction	86	0.0036
29876	Arthroscopy, knee, surgical; synovectomy, major, 2 or more compartments (eg, medial or lateral)	25	
29879	Arthroscopy, knee, surgical; abrasion arthroplasty (includes chondroplasty where necessary) or multiple drilling or microfracture	35	
29882	Arthroscopy, knee, surgical; with meniscus repair (medial OR lateral)	27	
20610	Arthrocentesis, aspiration and/or injection; major joint or bursa eg, shoulder, hip, knee joint, subacromial bursa)	2	
29877	Arthroscopy, knee, surgical; debridement/shaving of articular cartilage (chondroplasty)	10	
27447	Arthroplasty, knee, condyle and plateau; medial AND lateral compartments with or without patella resurfacing (total knee arthroplasty)	30	0.0192
29870	Arthroscopy, knee, diagnostic, with or without synovial biopsy (separate procedure)	32	
27446	Arthroplasty, knee, condyle and plateau; medial OR lateral compartment	19	0.0484

identified in our cohort of patients undergoing knee surgery.^{28,38,39}

Patient-reported outcomes (PROs) are increasingly being combined with electronic medical records throughout orthopaedic clinical practices. PROs are not only a research tool but are becoming a standard means of capturing patient-oriented indicators,²² and there has been growing interest in determining the capacity of PROs to predict which patients are the most suited to undergo specific orthopaedic treatments. Previous studies have identified multiple preoperative variables associated with worse outcomes after knee surgery, which include severity and chronicity of pain,^{40–42} psychological disease,^{26,43–46} and poor coping strategies.^{41,47} Psychological disease in orthopaedics has historically been elicited using the Mental Component Score of Short Form-36 or -12 general health questionnaires which measure a combination of anxiety, depression, and poor social support. Other psychological measures used include the Beck Depression Index⁴⁵ and the Hospital Anxiety and Depression (HAD) scale.⁴⁸ However, these measures are often limited by high respondent-burden, lack of precision, and inefficiency in comparison to normative data.

PROMIS is a high-throughput PRO measure that has proven to be valid and accurate in multiple orthopaedic patient populations.^{23,49–56} The growing body of literature supports the strength of PROMIS Physical Function as an orthopaedic PRO measurement,⁵⁴ but there is limited data regarding the use of PROMIS Depression and PROMIS Anxiety to measure psychological disease in the orthopaedic population,^{22,57} particularly in patients undergoing knee surgery. After adjusting for covariate imbalances by using propensity score matching analysis, preoperative depression and/or anxiety was found to be independently associated with PROMIS Depression and PROMIS Anxiety. This finding strengthens the argument for utilizing the PROMIS questionnaires for assessing psychological distress in the orthopaedic knee population. However, further studies in other orthopaedic surgical populations are needed before widespread use.

Preoperative depression and/or anxiety was also found to be independently associated with patients undergoing ACL reconstruction, uni-compartmental and total knee arthroplasty. A recent study by Chen et al.⁵⁸ demonstrated that preoperative PROMIS

Physical Function, Pain Interference, and Depression scores were highly predictive of outcome in the early postoperative period. The authors found that patients undergoing ACL reconstruction with a preoperative PROMIS Physical Function (PF) score of <42.5, Pain Interference (PI) score of >56.2, or Depression score of >44.8 were more likely to reach a minimal clinically important difference (MCID) at 20 weeks postoperatively. Comparatively, we found a significant difference in PROMIS PF, PI and Depression scores between patients with and without preoperative depression/anxiety. Though our patients demonstrated preoperative scores within the cutoff for MCID established in Chen et al.,⁵⁸ given that our study population consisted of patients undergoing a variety of knee surgeries, the true MCID in a heterogenous population might differ.

Given that the prevalence of documented depression in the total joint replacement literature ranges from 6.4% to 33%, psychological distress is a common medical comorbidity in this patient population.^{12,59} A recent study suggests that patients with preoperative depressive symptoms undergoing total joint arthroplasty have lower functional improvement and satisfaction compared to nondepressed patients postoperatively.¹² This study further reaffirms the association between mental health and joint arthroplasty by establishing an independent relationship between preoperative depression and/or anxiety and knee arthroplasty. Identifying and addressing psychological comorbidities in patients undergoing knee arthroplasty may improve knee pain and function and decrease postoperative risks of infection, anemia, psychosis, and pulmonary embolism.^{10,42,60}

There are several limitations in this study. Participants filled out a series of questionnaires, which might have affected the quality of collected data secondary to respondent-fatigue. As a study based on cross-sectional data, we cannot infer causality from our identified associations. Although we examined many demographic and clinical characteristics, there may be others that were outside our scope that could possibly act as confounders. While the risk of selection bias must be noted, a propensity matching analysis was used to mitigate the effect of possible covariates. Thus, this study is useful for hypothesis generation of potential associations that can be confirmed or refuted in more rigorous study designs. Contrary to most studies in the orthopaedic literature, we reported on a heterogeneous group of procedures, which could also be considered a strength of this study. We included all knee procedures performed at a single institution, and this may not be applicable to other patient populations of specific, isolated procedures. Furthermore, our study population is an urban population, which may not be applicable to other patient populations.

5. Conclusion

The results support our hypothesis that preoperative depression/anxiety is associated with worse preoperative pain, function, and general health status. Furthermore, PROMIS Anxiety and Depression tools offer a reliable means of measuring psychological distress in the orthopaedic knee population. Similar to other studies, we also noted psychological comorbidity to be independently associated with ACLR and TKA.

Conflicts of interest

Dr. Henn reports non-financial research support from Arthrex, Inc., outside the submitted work.

All other authors certify that they have NO affiliations with or involvement in any organization or entity with any financial interest (such as honoraria; educational grants; participation in speakers' bureaus; membership, employment, consultancies, stock ownership, or other equity interest; and expert testimony or

patent-licensing arrangements), or non-financial interest (such as personal or professional relationships, affiliations, knowledge or beliefs) in the subject matter or materials discussed in this manuscript.

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Approval

This study was approved by the Institutional Review Board (IRB) at the University of Maryland, Baltimore (HP-00062261).

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