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CURRENT CONCEPTS REVIEW

The Impact of Psychological Factors and Their Treatment on the Results of Total Knee Arthroplasty

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- There is a growing body of evidence implicating psychosocial factors, including anxiety, depression, kinesiophobia, central sensitization, and pain catastrophizing, as negative prognostic factors following total knee arthroplasty (TKA).
- Symptoms of anxiety and depression likely represent risk factors for negative outcomes in patients undergoing TKA. However, few studies have assessed the impact of preoperative interventions for these conditions on postoperative outcomes.
- The Tampa Scale of Kinesiophobia and the Central Sensitization Inventory have demonstrated value in the diagnosis of kinesiophobia and central sensitization. Higher preoperative indices of kinesiophobia and central sensitization predict worse patient-reported outcomes postoperatively.
- Although evidence is limited, cognitive-behavioral therapy for kinesiophobia and duloxetine for central sensitization may help to diminish the negative impact of these preoperative comorbidities. It is important to note, however, that outside the realm of TKA, cognitive-behavioral therapy has been recognized as a more effective treatment for central sensitization than medical treatment.
- Awareness of these issues will allow surgeons to better prepare patients regarding postoperative expectations in the setting of a comorbid psychosocial risk factor. Further research into the role of preoperative assessment and possible treatment of these conditions in patients undergoing TKA is warranted.

Many patients have reported persistent pain, functional limitations, and poor quality of life following total knee arthroplasty (TKA), with roughly 7.5% to 28.3% remaining dissatisfied according to postoperative surveys assessing satisfaction as a dichotomous variable or on a Likert scale¹⁻⁹. Greater symptom intensity and activity intolerance after technically adequate TKA are often ascribed to nuances in surgical technique and implant design. While the evidence has suggested that surgical technique and implant design have minimal influence, mounting evidence has suggested that inadequately addressed mental and social health factors merit greater attention¹⁰⁻¹³. In recent decades, there

has been increased awareness of the impact of mental health on physical well-being and pain in both lay society and the medical field, with pain being revealed to be the psychological output of a complex interaction among sensory, emotional, cognitive-evaluative, interpersonal, and cultural factors^{14,15}.

Given this perceptual shift, the International Association for the Study of Pain (IASP) defined pain as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.”¹⁶ Given the role of “emotional experience” and “potential tissue damage” in pain intensity, it is not surprising that poor mental

Disclosure: The **Disclosure of Potential Conflicts of Interest** forms are provided with the online version of the article (<http://links.lww.com/JBJS/G611>).

health has been identified as a negative prognostic factor¹⁷⁻³¹. Unaddressed psychosocial factors may impact outcomes by influencing perceived pain and perceived benefit. Alternatively, by influencing patients' ability to accommodate the symptoms associated with osteoarthritis (OA) pain, these patients may undergo TKA at an earlier time in the OA disease process. Because there is evidence that less severe OA at the time of TKA correlates with worse outcomes³²⁻³⁴, it is possible that mental health factors modulate outcomes by expediting the timing of TKA.

Given the impact of psychosocial factors, we believe there is a need for an increased understanding of these topics in arthroplasty. The purpose of this review was to define the most common relevant psychological factors and provide information regarding their epidemiology, diagnosis, impact, and treatment. Improved awareness may allow surgeons to modify patient selection criteria, to more accurately tailor expectations regarding outcomes and function in the setting of clinically important psychosocial factors, or to intervene on psychosocial barriers that hinder patients' ability to achieve optimal outcomes. Strategies that address OA from the biopsychosocial paradigm may reduce symptoms, whether a person chooses TKA or not.

Mental Health

Depression

Definition, Diagnosis, and Epidemiology

Depressive disorders all have the following characteristics in common: "the presence of sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect . . . function."³⁵ Despite occurring on a continuum of symptoms and feelings, depression is often described in the orthopaedic literature as a dichotomous variable based on a formal diagnosis of a mental disorder that involves depression or preoperative surveys identifying symptoms of depression. These differences in determining whether a research participant is categorized as depressed or nondepressed may contribute to variations in the described impact of depression on TKA outcomes in the literature.

Given the difficulty of truly defining depression, it is even more difficult to quantify the prevalence of this continuum of conditions. However, with respect to major depression, for example, the prevalence in the general population in the U.S. is roughly 6% to 7%, with a 1.5 to threefold higher prevalence in females and a threefold higher prevalence in individuals from 18 to 29 years old compared with those who are ≥60 years old^{35,36}. Given that TKA patients tend to be >60 years old, it is surprising that the prevalence of depression in patients undergoing TKA is roughly 20%, threefold to fourfold higher than expected³⁷.

Impact on Outcomes

Depression has a significant impact on postoperative pain, hospital length of stay (LOS), costs, patient-reported outcome measures (PROMs), complications, and readmissions after primary TKA. Pan et al. found that depression was associated with an increase in all assessments of pain, in addition to

multiple medical complications²⁶. Torres-Claramunt et al.³⁸ found that depression (defined categorically on the basis of the Geriatric Depression Scale Short Form) demonstrated higher average and maximum visual analog scale (VAS) pain scores in the first 3 days after primary TKA. Another study by Etcheson et al.³⁹ demonstrated that patients with a clinically documented diagnosis of depression consumed significantly more opioids postoperatively.

Depression is also a risk factor for increased LOS. Two large database studies found that LOS was up to 2 times greater for depressed patients^{40,41}. As a result, these patients also incur higher costs of care, including both day-of-surgery and 90-day episode-of-care costs^{40,42}.

Similarly, depressed patients and patients showing greater symptoms of depression have demonstrated correlations and associations with worse PROMs on preoperative and/or postoperative assessments, including both physical and mental health measures (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC], Short Form [SF]-12 and SF-36 physical component summary [PCS] and mental component summary [MCS], Knee Injury and Osteoarthritis Outcome Score [KOOS], Knee Society Score [KSS], Hospital Anxiety and Depression Scale [HADS], and Patient Health Questionnaire [PHQ])^{38,43-47}. Although the absolute PROM scores are lower for depressed than for nondepressed patients and for patients demonstrating greater symptoms of depression, they experience a similar magnitude of improvement in physical PROMs. Furthermore, while depressed patients do not achieve so-called normal scores, they experience a greater magnitude of improvement in mental health scores. In other words, while both sets of patients experience a similar benefit from TKA, patients with symptoms of depression are more likely to be dissatisfied with their final outcome. Despite substantial clinical improvement, depressed patients remain at up to a 6-times-higher risk for dissatisfaction after primary TKA than patients who are not depressed⁴⁷.

Several studies have also identified depression as a risk factor for objective complications after primary TKA, including mechanical failure and other implant-related complications^{24,40}, all-cause revisions⁴⁸, and medical complications^{26,41}. It is important to note, however, that there is no clear reason why psychosocial factors themselves would augment such risks. It is most likely that the comorbidities associated with these factors are the true drivers of the increased risk of medical complications. With respect to implant-related complications and revisions, it is possible that surgeons overinterpret or misinterpret examination and imaging findings in these patients because of their increased pain intensity and activity intolerance, which leads to an increased chance of reoperating on a patient who would have otherwise been treated more conservatively.

Treatments

A recent study has retrospectively assessed the impact of a history of treated versus untreated clinical depression on outcomes following total hip arthroplasty (THA) and TKA. In this single-center study, 280 patients were divided into 3 groups: patients with a coded diagnosis of major depression who received

medical treatment, patients with a coded diagnosis of depression who received no medical treatment, and patients with no coded diagnosis⁴⁹. The study demonstrated that patients treated with antidepressant or anxiolytic drugs and those who were not treated had similar gains in Patient-Reported Outcomes Measurement Information System (PROMIS) Physical Function scores. Additional high-quality studies are needed to determine if treatment of depression prior to TKA will improve outcomes.

Anxiety

Definition, Diagnosis, and Epidemiology

Patients with anxiety demonstrate “features of excessive fear and anxiety and related behavioral disturbances.”³⁵ Similar to depression, anxiety exists on a wide spectrum and, therefore, is difficult to define and quantify. However, with respect to generalized anxiety, for example, the 12-month prevalence of anxiety in the general population in the U.S. is roughly 2.9% to

6.3%, with a lifetime risk of 9.0%^{35,36}. Females have a twofold higher risk of experiencing anxiety, but unlike depression, it tends to peak in middle age. Similar to depression, however, the prevalence of preoperative anxiety in TKA patients, at roughly 20%³⁶, is far higher than expected.

Impact on Outcomes

Anxiety has a substantial impact on outcomes following TKA. Similar to their assessment of depression, Pan et al.²⁶ also identified anxiety as a risk factor for increased pain in all measures and multiple medical complications. Lindner et al.⁵⁰ demonstrated that patients with preoperative anxiety had worse WOMAC stiffness scores at 3 months postoperatively. However, preoperative anxiety was not found to have an impact on range of motion or functional outcome scores at 1 year after TKA, although anxiety did predict worse Oxford Knee Score (OKS) results at 1 year postoperatively⁵¹.

TABLE I Impact of CS on Outcomes as Assessed by PPTs*

Study	Level of Evidence	CS Diagnostic	Outcomes Assessed	End Point	Results
Wylde et al. ⁹³ (2017)	II	Forearm PPTs	• WOMAC pain	12 mo	• Forearm PPTs did not significantly predict postop. WOMAC pain
Leung et al. ⁹⁷ (2019)	II	Forearm PPTs and knee PPTs	• Satisfaction • WOMAC pain and function	6 mo 12 mo	• Forearm PPTs did not predict satisfaction or WOMAC scores at 6 or 12 mo • Knee PPTs did not predict satisfaction at 6 or 12 mo, or WOMAC scores at 6 mo • Knee PPTs did, however, predict WOMAC scores at 12 mo after adjusting for covariates (regression coefficient = 31.793; p = 0.012)
Kurién et al. ¹⁰² (2018)	II	PainDETECT, knee PPTs, and forearm PPTs	• VAS pain	6 mo	• PainDETECT (R = 0.397, p = 0.003) and knee PPTs (R = -0.262, p = 0.039) were correlated with postop. pain
Carlesso et al. ⁹⁸ (2019)	II	Forearm PPTs, knee PPTs, and TSP	• Development of persistent knee pain (i.e., pain on most of the previous 30 days at both the telephone screen and the clinic visit occurring on average 30 days apart, thus spanning a 2-mo period)	2 yr	• Patients with high response to PPTs and moderate response to TSPs were almost twice as likely as patients with normal thresholds for both to develop persistent pain (OR = 1.98; 95% CI, 1.07-3.68) • Results not differentiated between forearm and knee
Arendt-Nielsen et al. ¹⁰⁰ (2018)	II	Knee PPTs	• VAS pain	12 mo	• PPTs of the affected (p = 0.02) and contralateral (p = 0.04) extremity were a significant predictor of VAS pain at 12 mo
Rakel et al. ⁹⁹ (2012)	II	Knee PPTs	• NRS pain with movement and at rest	POD 0-2	• PPTs were a significant predictor of severe acute postoperative pain (OR = 0.66; 95% CI, 0.50-0.84; p = 0.003) with movement, but not at rest
Noiseux et al. ¹⁰¹ (2014)	II	Knee PPTs	• Pain at rest • Pain with range of motion	6 mo	• PPTs were not significant predictors of pain

*CS = central sensitization, PPTs = pressure pain thresholds, TSP = temporal summation of pain, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, OR = odds ratio, CI = confidence interval, VAS = visual analog scale, NRS = numerical rating scale, and POD = postoperative day.

TABLE II Impact of CS on Outcomes as Assessed by TSPs*

Study	Level of Evidence	CS Diagnostic	Outcomes Assessed	End Point	Results
Carlesso et al. ⁹⁸ (2019)	II	Knee PPTs, forearm PPTs, and TSP	• Development of persistent knee pain	2 yr	• Patients with high response to PPTs and moderate response to TSPs were almost twice as likely as patients with normal thresholds for both to develop persistent pain (OR = 1.98; 95% CI, 1.07-3.68)
Petersen et al. ⁸⁹ (2018)	II	TSP	• Chronic pain (<30% decrease from preop. VAS pain)	12 mo	• Low TSP associated with chronic pain ($p < 0.05$) • Low TSP correlated with chronic pain in Pearson correlation ($p = 0.010$) and linear regression ($p = 0.023$)
Petersen et al. ¹⁰³ (2015)	II	TSP	• VAS pain (low pain was VAS of <3, and high pain, VAS of ≥ 3)	2 and 12 mo	• Low TSP was associated with the high-pain group at 12 mo postop. ($p < 0.05$) • Low TSP correlated with raw VAS score at 12 mo ($R = 0.240$, $p = 0.037$)
Abrecht et al. ¹⁵⁶ (2019)	II	TSP	• VAS pain, • Opiate consumption	POD 0-2	• TSP predicted the presence of acute postop. pain ($p = 0.001$) and opiate consumption ($p = 0.011$)
Petersen et al. ⁸⁸ (2016)	II	TSP and CPM	• VAS pain	12 mo	• Low TSP thresholds alone did not predict postop. pain relief • Concomitant low TSP and CPM thresholds were associated with minimal pain relief ($p < 0.05$) compared with groups with normal measures
Rice et al. ¹⁰⁴ (2018)	II	TSP	• Moderate to severe PPT (WOMAC pain, 30/100)	6 mo and 12 mo	• TSP was not an independent predictor of persistent pain at 6 or 12 mo • However, TSP in conjunction with preop. pain anxiety, trait anxiety, and expected pain could predict 66% of patients with persistent pain at 6 mo but not 12 mo
Bossmann et al. ¹⁰⁵ (2017)	II	TSP	• Postop. pain	6 mo	• TSP not a significant predictor of pain

*CS = central sensitization, TSP = temporal summation of pain, PPT = pressure pain threshold, OR = odds ratio, CI = confidence interval, CPM = conditioned pain modulation, and VAS = visual analog scale.

Central Sensitization

Definition and Diagnosis

Central sensitization (CS) has been classified as “a behavioral learning factor” that is defined by “an increase in the intensity of a response when an identical stimulus is presented multiple times over an extended period of time.”⁵² This condition represents an aberrancy in evolutionarily protective pain-detection pathways that causes neurons in the central nervous system to achieve the signal threshold or to produce an augmented sensation of pain in response to previously non-noxious (allodynia) or subthreshold signals (hyperalgesia)⁵³⁻⁶³.

The methodology used to categorize patients as having or not having the characteristics of CS in orthopaedic studies is highly variable. The diagnosis is generally made using quantitative sensory testing (QST), including pressure pain thresholds (PPTs), temporal summation of pain (TSP), thermal hyperalgesia, and others⁶⁴⁻⁷⁰, or patient questionnaires, including the Central Sensitization Inventory (CSI)⁷¹⁻⁷³ and PainDETECT⁷⁴. While QST assesses pain associated with provocative stimuli, the CSI is a 25-item questionnaire that utilizes a 5-point Likert scale

(0 = never, 1 = rarely, 2 = sometimes, 3 = often, and 4 = always, yielding a maximum score of 100)⁷¹⁻⁷³. Scores of ≥ 40 indicate the presence of CS. Neuroimaging has also played a role in the detection of CS⁷⁵⁻⁸⁰. Roughly 20% to 40%⁸¹⁻⁸⁵ of patients undergoing primary TKA demonstrate some degree of CS.

Impact on Outcomes

CS has been correlated with postoperative pain intensity following interventions from abdominal surgery and thoracotomy to TKA⁸⁶⁻⁸⁸. Because CS is associated with allodynia and hyperalgesia, the augmented pain response in these patients seems intuitive. However, CS likely also impacts postoperative pain through a selection bias. As demonstrated by Petersen et al.⁸⁹ and others⁹⁰⁻⁹⁴, centrally sensitized patients tend to present with a significantly lower Kellgren-Lawrence grade of OA. Proponents of CS, therefore, have suggested that the underlying driver of pain may be neuropathologic rather than musculoskeletal, and addressing musculoskeletal defects fails to address a driver of heightened symptoms: underlying neuronal hypersensitivity⁸⁹⁻⁹⁴.

TABLE III Impact of CS on Outcomes as Assessed by Thermal and Electrical Hyperalgesia*

Study	Level of Evidence	CS Diagnostic	Outcomes Assessed	End Point	Results
Rakel et al. ⁹⁹ (2012)	II	TS	• NRS pain (resting and movement)	POD 0-2	• TS was a significant predictor of moderate and severe acute postop. pain (OR = 0.83, p = 0.007)
Lunn et al. ¹⁰⁶ (2013)	II	TS (short and long)	• Pain (walking)	POD 0-1, POD 1-7, and POD 14-30	• TS short (R = 0.25, p = 0.02) and long (R = 0.27, p = 0.01) correlated with pain on POD 1-7 • However, TS was not an independent predictor of pain in multivariate analyses
Martinez et al. ¹⁰⁷ (2007)	II	TS	• VAS pain (resting and movement) • Opiate use	POD 0-2, 1 mo, and 4 mo	• TS was not associated with differences in early or intermediate postop. pain • TS correlated with postop. opiate consumption (R = 0.63, p = 0.01)
Noiseux et al. ¹⁰¹ (2014)	II	TS	• Pain (resting and movement)	6 mo	• TS was not a significant predictor of pain
Lundblad et al. ¹⁰⁸ (2008)	II	ES	• VAS pain (resting and movement)	18 mo	• ES sensation ($\chi^2 = 4.00$, p = 0.045) and pain ($\chi^2 = 6.34$, p = 0.012) thresholds were significantly related to pain at rest at 18 mo postop. • ES pain threshold remained a significant predictor (OR = 9.19, p = 0.01) in a logistic regression analysis
Thomazeau et al. ¹⁰⁹ (2016)	II	ES	• NRS pain (resting and movement) • Opiate use	POD 0-4	• ES was not a significant predictor of postop. pain or opiate use

*CS = central sensitization, TS = thermal stimulation, NRS = numerical rating scale, OR = odds ratio, VAS = visual analog scale, POD = postoperative day, and ES = electrical stimulation.

Given the heterogeneity of the methods used to diagnose CS, there is contradictory literature regarding its influence on TKA. Studies using the CSI questionnaire have demonstrated stronger and more consistent relationships^{95,96}. Diagnoses using knee PPTs have shown stronger relationships of CS with PROMs than with forearm PPTs^{93,97-101}. Other diagnostic strategies have shown little or no correlation with PROMs.

QST and CSI

Assessments of the impact of CS diagnosed by PPTs on outcomes following TKA have shown mixed results. In general, forearm PPTs have not been consistent unique predictors of postoperative pain or WOMAC scores^{93,97,98,102}, while knee PPTs have⁹⁷⁻¹⁰² (Table I).

Studies assessing the predictive value of TSP on outcomes following TKA have often described a relationship between these 2 factors^{88,89,98,103}. The strength of this relationship, however, has generally been weaker than the relationship between knee PPTs and outcomes. Furthermore, TSP has often failed to serve as an independent predictor of pain. Rather, many studies have combined TSPs with PPTs, conditioned pain modulation (CPM), anxiety, or other factors (Table II)^{88,104,105}. Thermal hyperalgesia and electrical hyperalgesia have demonstrated no evidence of correlation with long-term pain^{99,101,106-109} (Table III).

Questionnaires used to detect preoperative CS have been more effective in predicting postoperative outcomes. While PainDETECT questionnaires have shown promise as prog-

nostic tools¹⁰², the CSI appears to be the most clinically useful prognostic instrument^{95,96} (Table IV).

Treatments

In a randomized controlled trial (RCT), Koh et al.⁸¹ found that duloxetine therapy significantly decreased pain and improved recovery quality in CS patients undergoing TKA. Duloxetine therapy was also associated with improved emotional function according to the affective subdimensions of the Brief Pain Inventory (BPI)-Interference assessment. Additionally, SF-36 MCS scores and HADS scores were significantly lower in the duloxetine therapy group at the 6- and 12-week end points. Furthermore, although Chappell et al.¹¹⁰ studied the impact of duloxetine in the general TKA population and not specifically in patients who were centrally sensitized, their RCT found improvement with respect to pain, Patient Global Impressions of Improvement, WOMAC physical functioning, BPI scores, SF-36 results, and EuroQol-5 Dimension (EQ-5D) scores.

In a double-blinded RCT, Luna et al.¹¹¹ assessed the effect of preoperative intra-articular methylprednisolone on pain after TKA in centrally sensitized patients. No significant differences were found in favor of the methylprednisolone group (Table V).

While the focus of the current review is to discuss the impact of CS specifically in the setting of TKA, given the differences between CS studied in TKA and other fields, it is important to discuss the findings associated with CS treatment

TABLE IV Impact of CS on Outcomes as Assessed by CSI and PainDETECT*

Study	Level of Evidence	CS Diagnostic	Outcomes Assessed	End Point	Results
Kurien et al. ¹⁰² (2018)	II	PainDETECT	• VAS pain	6 mo	<ul style="list-style-type: none"> • PainDETECT ($R = 0.397$, $p = 0.003$) and knee PPTs ($R = -0.262$, $p = 0.039$) were correlated with postop. pain • PainDETECT was the only independent predictor of postop. pain ($p = 0.006$)
Kim et al. ⁹⁶ (2018)	II	CSI	• NRS pain	POD 1-2, 1 mo, and 3 mo	<ul style="list-style-type: none"> • CSI was associated with higher acute postop. pain ($p = 0.001$), as well as pain at 1 mo ($p = 0.006$) and 3 mo ($p = 0.002$) • CSI was associated with the highest odds of having persistent pain at 3 mo (OR = 5.091, $p = 0.016$) • CSI was associated with increased postop. narcotic use ($p = 0.003$)
Kim et al. ⁹⁵ (2015)	II	CSI	• Wound complications (wound dehiscence, suture granuloma, prolonged wound oozing after POD 5, hematoma formation, or surgical site infection)	3 mo	<ul style="list-style-type: none"> • CS was associated with significant increases in hematoma formation ($p = 0.031$), drainage at 5 days postop. ($p = 0.016$), and wound dehiscence ($p = 0.001$) • CSI was associated with a 15.7-fold greater overall risk ($p < 0.001$) of postop. wound complications in a multivariate logistic regression

*CS = central sensitization, PPT = pressure pain threshold, CSI = Central Sensitization Inventory, VAS = visual analog scale, NRS = numerical rating scale, POD = postoperative day, and OR = odds ratio.

in other fields. While medical interventions have been the treatment of choice for CS in TKA, the study of CS in spinal pathology, migraines, abdominal pain, fibromyalgia, and other causes of musculoskeletal pain has documented limited effectiveness of medical interventions and better outcomes with cognitive-behavioral therapy (CBT)^{52,112-123}. Therefore, while the findings of Koh et al.⁸¹ are important to highlight, it is noteworthy that medical therapies, including duloxetine, have

demonstrated unsatisfactory outcomes in the general literature, and the use of multimodal treatment plans for CS is an important area of future research in TKA¹¹².

Kinesiophobia

Definition, Diagnosis, and Epidemiology

Kinesiophobia is an excessive and/or irrational fear of movement regarding concern for painful injury¹²⁴. The resultant

TABLE V Treatment Options for CS*

Study	Level of Evidence	Country	No. of Patients	Diagnostic Threshold	Intervention	Outcomes of Interest	Results
Koh et al. ⁸¹ (2019)	I	South Korea	80	Preop. CSI of ≥ 40	Duloxetine	• BPI	• Decreased pain at 2-12 weeks postop.
Luna et al. ¹¹¹ (2017)	I	Denmark	48	Pain with walking rated >5 on scale with max. of 10 and forearm PPT of <250 kPa	40 mg intra-articular MP injection	<ul style="list-style-type: none"> • NRS pain with walking 24 and 48 hr (% with moderate or severe pain) • AUC for pain, POD 1-14 (walking, rest, average, and worst) • AUC for opiate consumption, POD 1-14 • Raw score and change in PPT and TSP on POD 2 	<ul style="list-style-type: none"> • No difference in walking pain at 24 and 48 hr • No difference in pain for POD 1-14 • No difference in opiate consumption for POD 1-14 • No difference in PPT or TSP, with exception of a worse median change in TSP on POD 1 and POD 0 ($p = 0.03$) for the MP group

*CS = central sensitization, CSI = Central Sensitization Inventory, BPI = Brief Pain Inventory, PPT = pressure pain threshold, TSP = thermal stimulation of pain, NRS = numerical rating scale, AUC = area under the receiver operating characteristic curve, POD = postoperative day, and MP = methylprednisolone.

TABLE VI Impact of Kinesiophobia on Outcomes Following TKA*

Study	Level of Evidence	Kinesiophobia Diagnostic Instrument	Outcomes Assessed	End Point	Results
Brown et al. ¹⁴⁰ (2016)	I	TSK	<ul style="list-style-type: none"> Active range of motion Passive range of motion PT sessions Walking distance 	POD 1-4 and wk 2, 6, 12, and 26	<ul style="list-style-type: none"> Decreased active ($\beta = -0.47$, $p < 0.01$) and passive ($\beta = -0.66$, $p < 0.0005$) knee flexion
Doury-Panchout et al. ¹³⁴ (2015)	II	TSK	<ul style="list-style-type: none"> Pain Range of motion 6-min walk test LOS 	NR	<ul style="list-style-type: none"> Kinesiophobia associated with longer 6-min walk test, but not LOS, passive flexion, or pain
Kocic et al. ¹³⁵ (2015)	II	TSK	<ul style="list-style-type: none"> OKS (only at 6 mo) Pain Range of motion 	2 wk, 1 mo, and 6 mo	<ul style="list-style-type: none"> Decreased OKS at 6 mo (25.82 versus 34.48; $p = 0.0003$) Increased pain at 2 wk (6.09 versus 5.03; $p = 0.0123$), 1 mo (5.00 versus 3.12; $p < 0.0001$), and 6 mo (3.24 versus 1.81; $p = 0.0035$) Decreased flexion at 2 wk (47.35 versus 65.98; $p < 0.0001$), 1 mo (57.65 versus 88.20; $p < 0.0001$), and 6 mo (83.53 versus 105.33; $p < 0.0001$)
Helminen et al. ¹⁴¹ (2016)	II	TSK	<ul style="list-style-type: none"> WOMAC SF-36 RAND-36 Function Pain 	0, 3, and 12 mo	<ul style="list-style-type: none"> Decreased WOMAC function (-7.09; $p < 0.05$) Decreased RAND-36 function (8.69; $p < 0.05$) Decreased RAND-36 MCS (orthogonal) (3.50; $p < 0.05$) Decreased RAND-36 PCS (oblique) (4.05; $p < 0.01$) Decreased RAND-36 PCS (orthogonal) (3.89; $p < 0.01$)
Güney-Deniz et al. ¹³⁷ (2017)	II	TSK	<ul style="list-style-type: none"> Range of motion Pain 2-min walk test (2-MWT) Time on Up-and-Go test 	POD1-2	<ul style="list-style-type: none"> Decreased distance on 2-MWT ($p < 0.001$), ($R = -0.40$, $p = 0.003$)† Increased pain levels ($p = 0.003$), ($R = 0.80$, $p < 0.001$) Decreased knee flexion ($p = 0.025$), ($R = -0.47$, $p = 0.001$)
Vogel et al. ¹⁴² (2019)	II	TSK	<ul style="list-style-type: none"> WOMAC 	12 months	<ul style="list-style-type: none"> No association with pain ($p = 0.06$) or function ($p = 0.70$)
Filardo et al. ¹³⁸ (2016)	IV	TSK	<ul style="list-style-type: none"> SF-12 WOMAC Pain Function Range of motion 	POD 5, 1 mo, 6 mo, and 12 mo	<ul style="list-style-type: none"> POD 5 <ul style="list-style-type: none"> Pain ($p = 0.031$, $R = 0.225$) 6 mo <ul style="list-style-type: none"> SF-12 PH ($p < 0.001$, $R = -0.320$) WOMAC ($p = 0.005$, $R = 0.279$ and $p = 0.001$) 12 mo <ul style="list-style-type: none"> SF-12 PH ($p = 0.001$, $R = -0.334$) SF-12 MH ($p = 0.005$, $R = -0.277$) WOMAC ($p = 0.001$, $R = 0.317$) Perceived function ($p = 0.025$, $R = -0.223$) Pain ($p = 0.018$, $R = 0.234$)
Filardo et al. ¹³⁹ (2017)	IV	TSK	<ul style="list-style-type: none"> SF-12 WOMAC Function Pain Range of motion 	12 mo	<ul style="list-style-type: none"> Decreased WOMAC scores in univariate ($p = 0.005$, $p = 0.197$) and multivariate analyses ($p = 0.011$, partial $\eta^2 = 0.033$)

*TSK = Tampa Scale of Kinesiophobia, POD = postoperative day, PT = physical therapy, NR = not reported, LOS = length of stay, OKS = Oxford Knee Score, SF-12/36 = Short Form 12 and 36, WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index, MCS = mental component summary, PCS = physical component summary, PH = physical health, and MH = mental health. †First p value represents differences in 2-min walk test, pain, and knee flexion between patients with and without kinesiophobia, while the second represents correlations between level of kinesiophobia and scores on these respective assessments.

TABLE VII Treatment Options for Kinesiophobia*

Study	Level of Evidence	Country	No. of Patients	Intervention	Outcomes of Interest	Results
Monticone et al. ¹⁴³ (2013)	I	Italy	110	(1) Continued functional exercises twice/wk for 6 mo postop. (2) Home-exercise book that detailed cognitive-behavioral information geared toward education, management, and avoidance of kinesiophobia (3) Monthly calls from rehabilitation team to strengthen adherence and answer questions regarding rehabilitation and kinesiophobia	<ul style="list-style-type: none"> • TSK • KOOS • QOL • NRS pain • SF-36 	Intervention led to positive improvements in TSK ($p < 0.001$), KOOS ($p \leq 0.001$), QOL ($p = 0.001$), pain ($p < 0.001$), and SF-36 ($p < 0.001$)
Cai et al. ¹⁴⁴ (2018)	I	China	100	CBT	<ul style="list-style-type: none"> • TSK 	CBT led to greater decreases in postop. TSK scores ($\Delta = 8.08$ vs. 3.54 ; $p < 0.001$); results were significant for time effect, group effect, and group-by-time effect ($p < 0.001$)
Russo et al. ¹⁴⁵ (2017)	I	Italy	102	Videoin insight method	<ul style="list-style-type: none"> • SF-36 • STAI • BDI • TSK • KSS • VAS pain • WOMAC 	Videoin insight led to significant improvements in WOMAC (mean and SD, 79.9 ± 13.0 vs. 69.7 ± 9.5 ; $p < 0.005$), VAS (2.8 ± 1.6 vs. 4.0 ± 1.5 ; $p < 0.005$), KSS (87.8 ± 9.6 vs. 78.3 ± 8.2 ; $p < 0.005$), BDI (5.1 ± 4.8 vs. 9.4 ± 3.9 ; $p < 0.005$), STAI (30.8 ± 7.9 vs. 34.8 ± 7.8 ; $p < 0.005$), and TSK (24.4 ± 5.5 vs. 29.3 ± 4.8 ; $p < 0.005$)
Degirmenci et al. ¹³⁶ (2020)	I	Turkey	100	Anesthesia type: deep versus light	<ul style="list-style-type: none"> • Knee function • VAS pain • Range of motion • TSK 	TSK scores on POD 2 (mean, 40.5 vs. 46.9 ; $p = 0.005$) and POD5 (mean, 37.7 vs. 46.4 ; $p < 0.001$) demonstrated significant improvements in favor of the group that had received deep sedation.
<p>*TSK = Tampa Scale of Kinesiophobia, KOOS = Knee Injury and Osteoarthritis Outcome Score, QOL = quality of life, NRS = numerical rating scale, SF-36 = Short Form 36, CBT = cognitive behavioral therapy, SD = standard deviation, STAI = State-Trait Anxiety Inventory, BDI = Beck Depression Inventory, KSS = Knee Society Score, VAS = visual analog scale, and POD = postoperative day.</p>						

disuse of the affected joint can lead to decreases in strength and mobility, as well as concomitant depression and decline due to inactivity^{125,126}. If kinesiophobia follows trauma or surgery, such as after TKA, it can lead to disuse syndrome, which may hamper recovery by impeding normal tissue-healing¹²⁷⁻¹²⁹.

Kinesiophobia is formally diagnosed using the Tampa Scale of Kinesiophobia (TSK)^{130,131}. The TSK is a 17-item questionnaire with a 4-point scoring system (1 = strongly disagree, 2 = disagree, 3 = agree, and 4 = strongly agree, yielding a maximum score of 68). In the TKA literature, kinesiophobia has been studied as a dichotomous variable and a continuous variable, with studies defining it as a dichotomous variable using a score of ≥ 37 as the threshold to diagnose kinesiophobia¹³¹.

Although some studies have assessed kinesiophobia as a dichotomous variable despite the fact that it is a condition that exists on a continuum, studies have demonstrated that 58.2% of patients following orthopaedic trauma¹³², and between 20% and 40% of patients following TKA¹³³⁻¹³⁶, exhibit clinically important levels of kinesiophobia. The development of kinesiophobia is associated with an age of ≥ 76 years, lower education, poor coping mechanisms, increased pain, low self-efficacy, and limited social support¹³³.

Impact on Outcomes

Postoperative kinesiophobia is associated with decreased activity in studies assessing kinesiophobia both as a dichotomous and a

TABLE VIII Grades of Recommendation*

Recommendation	Impact on TKA Outcomes	Impact of Treatment
Depression	B	C
Anxiety	B	C
Central sensitization	B†	B
Kinesiophobia	A	A
Pain catastrophizing	C	C

*Two sets of recommendations show the grade of the evidence associating each psychosocial factor with worse outcomes after TKA, and the grade of the evidence associated with the impact of treatment of these psychosocial factors on subsequent outcomes. According to Wright¹⁵⁷, grade A indicates good evidence (Level-I studies with consistent findings) for or against recommending intervention; grade B, fair evidence (Level-II or III studies with consistent findings) for or against recommending intervention; grade C, poor-quality evidence (Level-IV or V studies with consistent findings) for or against recommending intervention; and grade I, insufficient or conflicting evidence not allowing a recommendation for or against intervention. †The impact of central sensitization on TKA outcomes is highly dependent on the method of diagnosis, with the Central Sensitization Inventory demonstrating the greatest prognostic value.

continuous variable^{136,137}. Furthermore, kinesiophobia has demonstrated associations with pain and decreased range of motion^{135,137-140}. As a result of increased pain levels, decreased activity, and decreased range of motion, kinesiophobia has demonstrated a strong association with decreased perceived function, as well as OKS, SF-12, RAND-36, and WOMAC scores^{135,138,139,141}. In opposition to these findings, Vogel et al.¹⁴² found no association between kinesiophobia and pain or function (Table VI).

Treatments

In an RCT, Monticone et al.¹⁴³ studied the combined impact of patient education and CBT on kinesiophobia and outcomes. Compared with kinesiophobia scores obtained on postoperative day (POD) 15, this intervention led to strong decreases in TSK scores at 6 months (mean difference [MD] = 12.2) and 12 months (MD = 15.4) ($p < 0.001$). The study demonstrated that such interventions may decrease postoperative TSK scores, as well as KOOS activities of daily living ($p < 0.001$), KOOS pain ($p < 0.001$), KOOS symptoms ($p < 0.001$), KOOS sport and recreation ($p = 0.001$), KOOS quality of life (QOL) ($p = 0.001$), pain ($p < 0.001$), and all domains of the SF-36 ($p < 0.001$).

In a double-blinded RCT, Cai et al.¹⁴⁴ assessed the impact of CBT on treating postoperative kinesiophobia. Patients were assessed on POD 1 and 2 for the presence of kinesiophobia and were then randomized to treatment with CBT or standard care. CBT consisted of 4 individually tailored 30-minute sessions with a physiotherapist and psychologist, and the patients demonstrated significantly better improvements in the TSK from preintervention to postintervention (a change of 8.08 versus 3.54; $p < 0.001$).

Russo et al.¹⁴⁵ assessed the impact of Videoin-sight, a program promoting self-confidence and psychological support, and found that as an adjunct to physical therapy, this addition led to improvements in WOMAC, VAS pain, KSS, Beck Depression Index, State-Trait Anxiety Inventory, and TSK ($p < 0.005$ for all). Degirmenci et al.¹³⁶ assessed the impact of regional anesthesia, light sedation, and deep sedation on the risk of kinesiophobia. Despite similar TSK scores preoperatively, TSK scores on POD 2 (40.5 versus 46.9; $p = 0.005$) and POD 5 (37.7 versus 46.4; $p < 0.001$) demonstrated significant improvements in favor of deep sedation (Table VII).

Pain Catastrophizing

Definition, Diagnosis, and Epidemiology

Pain catastrophizing (PC) is defined as “an exaggerated negative mental set brought to bear during actual or anticipated painful experience.”¹⁴⁶ Pain catastrophizing is generally diagnosed using the PC scale. The PC scale is a 13-item questionnaire that utilizes a 5-point Likert scale (0 = not at all, 1 = to a slight degree, 2 = to a moderate degree, 3 = to a great degree, and 4 = all of the time, yielding a maximum score of 52). Catastrophic thinking in response to nociception occurs on a continuum, but unfortunately it is often dichotomized in clinical studies^{147,148}.

Impact on Outcomes

Previous work has identified that patients who exhibit higher preoperative levels of PC have more pain after TKA at 3²¹ and 12 months²⁶. Masselin-Dubois et al.²¹ found that pain intensity scores at 3 months postoperatively were predicted by elevated preoperative PC scale scores. Sullivan et al.¹⁴⁹ demonstrated that the PC scale score was the sole unique predictor of postoperative pain severity ($\beta = 0.27$, $p < 0.05$) and physical function ($\beta = 0.34$, $p < 0.01$).

Treatments

Cai et al.¹⁴⁴ identified that CBT programs had significant group ($p < 0.001$), time ($p < 0.001$), and group-by-time interaction ($p < 0.001$) effects on PC and knee function at 6 months postoperatively.

Multiple studies by Riddle et al.¹⁵⁰⁻¹⁵² assessed the impact of pain coping CBT on outcomes and demonstrated mixed results. In a case-control study that utilized an 8-session CBT intervention for patients undergoing TKA, the treatment group demonstrated significant improvements in postoperative pain, knee function, and PC scores. In the RCT, however, no differences between treatment groups and controls were identified.

Discussion

Dissatisfaction remains a concerning issue following TKA, and a growing body of evidence has demonstrated that psychosocial factors may be a driver of suboptimal mental and physical outcomes. The current review demonstrates evidence that depression, anxiety, CS, kinesiophobia, and PC demonstrate a significant association with worse functional outcomes, PROMs, and satisfaction, as well as with an increased risk of pain and

complications following TKA. This evidence may support consideration of targeted screening of patients with pertinent psychosocial factors to assess whether the individuals fall within a region of the mental health spectrum that predisposes them to an adverse outcome. Awareness of the presence and impact of these psychosocial comorbidities will allow surgeons to more accurately moderate postoperative expectations regarding outcomes and function in the setting of known psychosocial factors, which may lead to improvements in postoperative outcomes.

Table VIII provides grades of recommendation for the impact of the various psychosocial factors on TKA outcomes and grading for how treating these psychosocial factors impacts outcomes. While data from the current review implicate depression and anxiety as important negative prognostic factors, there is limited evidence detailing the impact of treatment on outcomes following TKA. Furthermore, given the variability in the methods used to diagnose depression, it is unclear which method is the most predictive of negative outcomes. With respect to CS, there is evidence to suggest that the CSI has the greatest prognostic value. Based on the findings of Koh et al.⁸¹, the use of duloxetine (30 mg/day) in patients with CS beginning the day before surgery and continuing for 6 weeks postoperatively may be of benefit.

With respect to kinesiophobia, the TSK diagnostic tool has the greatest prognostic value. Based on the findings of Monticone et al.¹⁴³ and Cai et al.¹⁴⁴, patients may benefit from patient education and CBT. Similarly, based on findings by Riddle et al.¹⁵² and Cai et al.¹⁴⁴, the use of CBT may provide significant improvements with respect to pain and function. There is also evidence to suggest that CBT plays a role in diminishing the negative effects of pain catastrophizing. Outside the realm of TKA, cognitive behavioral therapy has been recognized as a more effective treatment for CS than medical treatment¹⁵³.

In this review, we found that certain psychosocial factors in the setting of TKA have a significant impact on outcomes. Given the prevalence of these various conditions in TKA patients, it is likely that patient dissatisfaction following TKA is partially attributable to these factors. Awareness of these factors will allow surgeons to counsel patients regarding postoperative expectations of outcomes and function in the setting of a comorbid psychosocial risk factor. Some, but not all, of the conditions discussed may be potentially addressable preoperatively in order to improve results after TKA. It is also important to note that other psychosocial factors, such as personality disorders, were not discussed in this review but are important^{154,155}. While the findings of this review are interesting and provocative, this was not a systematic review, and results reviewed may be biased by this methodology. Further research into the role of preoperative assessment and possible treatment of these conditions in patients undergoing TKA is warranted. ■

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