

REVIEW ARTICLES PREGLEDNI ČLANCI

PREDICTION OF TOTAL KNEE ARTHROPLASTY OUTCOME BASED ON PSYCHO-PHYSICAL TESTS

PREDIKCIJA ISHODA TOTALNE ARTROPLASTIKE KOLENA NA OSNOVU PSIHO-FIZIČKIH TESTOVA

Tijana ALEKSANDRIĆ^{1,2}, Larisa SUBIĆ^{1,2}, Dunja KOVAČEVIĆ^{1,2}, Viktor BRUSNJAI^{1,3}, Tijana SPASOJEVIĆ^{1,2} and Aleksandar KNEŽEVIĆ^{1,2}

ORCID NUMBER

Tijana Aleksandrić – 0009-0006-1049-064X

Larisa Subić – 0009-0001-3047-7681

Dunja Kovačević – 0009-0003-0587-3396

Viktor Brusnjai – 0009-0009-0337-8977

Tijana Spasojević – 0000-0002-4178-4740

Aleksandar Knežević – 0000-0002-9297-793X

University of Novi Sad, Faculty of Medicine Novi Sad¹

University Clinical Center of Vojvodina, Physical Medicine and Rehabilitation Clinic, Novi Sad²

Institute for Pulmonary Diseases of Vojvodina, Sremska Kamenica³

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Pregledni članak

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Abstract

Introduction. Osteoarthritis is the most prevalent joint disease worldwide, with knee osteoarthritis representing its most common form. Pain in knee osteoarthritis is known to have neuropathic components; however, the mechanisms leading to central sensitization remain incompletely understood. It is also unclear whether surgical pain relief achieved through total knee arthroplasty results in modulation of central sensitization and neuropathic pain. **Quantitative sensory testing in the prediction of postoperative pain after total knee arthroplasty.** Sensory profiling using quantitative sensory testing modalities – particularly temporal summation and conditioned pain modulation – has emerged as a valuable approach for identifying patients with osteoarthritis who are at risk of acute and chronic postsurgical pain. These modalities, when combined with other parameters, may facilitate individualized pain management strategies. Preoperative hyperalgesia and neuropathic pain features, detected through temporal summation testing and Pain-DETECT questionnaires, have demonstrated predictive value for the development of chronic postsurgical pain after total knee arthroplasty. Patients exhibiting centrally mediated pain mechanisms and established central sensitization tend to experience less postoperative pain relief following total knee arthroplasty. Female sex has been associated with higher magnitude of conditioned pain modulation and an increased prevalence of severe acute and chronic postsurgical pain, identifying it as a potential risk factor for pain chronification. **Conclusion.** Quantitative sensory testing modalities – particularly temporal summation, conditioned pain modulation, and pressure pain threshold – appear to be the most promising tools for predicting postoperative pain outcomes using quantitative sensory testing. Patients with evidence of central sensitization show reduced pain relief after total knee arthroplasty.

Key words: Osteoarthritis; Prognosis; Arthroplasty, Replacement, Knee; Treatment Outcome; Pain Measurement; Central Nervous System Sensitization; Pain, Postoperative

Sažetak

Uvod. Osteoarthritis predstavlja najčešću bolest zglobova, pri čemu je osteoarthritis kolena najzastupljeniji. Iako je poznato da bol kod osteoartritisa kolena delom jeste neuropatski bol, nejasno je koji mehanizam dovodi do centralne senzitivacije i da li će eliminacija bola hirurškom procedurom kao što je totalna artroplastika kolena dovesti do promena u vezi sa centralnom senzitivacijom i neuropatskim bolom. **Kvantitativno senzorno testiranje u predikciji postoperativnog bola nakon totalne artroplastike kolena.** Senzorno profilisanje pacijenata sa osteoartritisom korišćenjem kvantitativnog senzornog testiranja postalo je uobičajeno. Kvantitativni senzorni modaliteti, kao što su temporalna sumacija i uslovna modulacija bola, pokazali su se kao potencijalni prediktori akutnog i hroničnog posthirurškog bola i trebalo bi ih kombinovati sa drugim parametrima kako bi se postigla personalizovana terapija bola. Preoperativna hiperalgezija i neuropatski bol otkriveni tokom ispitivanja temporalne sumacije i pomoću upitnika *PainDETECT* imaju prediktivnu vrednost za razvoj hroničnog posthirurškog bola nakon totalne artroplastike kolena. Pacijenti sa centralno iniciranom senzitivacijom imaju nedovoljno smanjenje intenziteta bola nakon totalne artroplastike kolena. Ženski pol je povezan sa većim vrednostima uslovne modulacije bola i jačim akutnim i hroničnim posthirurškim bolom, izdvajajući se na taj način kao faktor rizika za hronifikaciju bola. **Zaključak.** Čini se da su modaliteti kvantitativnog senzornog testiranja kao što su temporalna sumacija bola, uslovna modulacija bola i prag bola na pritisak najperspektivniji modaliteti za pouzdano predviđanje postoperativnog bola uz pomoć kvantitativnog senzornog testiranja. Pacijenti kod kojih se detektuje prisustvo centralne senzitivacije imaju slabiju redukciju intenziteta bola nakon totalne artroplastike kolena.

Ključne reči: osteoarthritis; prognoza; totalna artroplastika kolena; ishod lečenja; merenje bola; senzitivacija centralnog nervnog sistema; postoperativni bol

✉ Corresponding author: Tijana Aleksandrić, E-mail: tijana.aleksandric@mf.uns.ac.rs

Abbreviations

OA	– osteoarthritis
KOA	– knee osteoarthritis
CS	– central sensitization
CNS	– central nervous system
NP	– neuropathic pain
CSI	– Central Sensitization Inventory
QST	– quantitative sensory testing
PDQ	– Pain Disability Questionnaire
CPSP	– chronic postsurgical pain
TKA	– total knee arthroplasty
THA	– total hip arthroplasty
TS	– temporal summation
CPM	– Conditioned Pain Modulation
PPT	– pressure pain threshold
WUR	– “wind up ratio”
APSP	– acute postsurgical pain

Introduction

Osteoarthritis (OA) is a degenerative joint disease that develops primarily as a result of progressive loss of articular cartilage. It is the most common joint disorder worldwide, with the knee being the most frequently affected joint. OA predominantly affects older individuals and occurs more often in women. According to its etiology, osteoarthritis is classified as primary osteoarthritis, which has no identifiable cause, and secondary osteoarthritis, which arises due to a known underlying factor such as previous trauma or surgery, congenital limb malformations, or other conditions. [1,2]. The clinical presentation of osteoarthritis of the knee (KOA) is characterized by the gradual onset of symptoms including pain during walking and at the initiation of movement after periods of rest (e.g., prolonged lying or sitting), accompanied by reduced range of motion in the affected joint [3]. Initial management is based on non-surgical approaches, including patient education, physical therapy, and pharmacological therapy [4]. These conservative measures do not halt the degenerative process itself but can substantially reduce pain and functional disability. When conservative treatment no longer provides adequate symptom relief, surgical intervention may be indicated [5].

As with many chronic pain conditions, pain mechanisms in patients with KOA are multifactorial, complex and not yet fully understood [6]. Numerous studies have demonstrated a poor correlation between radiographic severity and the intensity of pain or degree of disability in OA [7,8], highlighting the contribution of biopsychosocial mechanisms to pain perception in KOA [9].

Pain duration has been shown to correlate with perceived pain intensity [10]. Present nociceptive input from peripheral tissues, together with altered modulation by the central nervous system, can initiate central sensitization (CS) [11]. Central sensitization is defined as an amplification of neural signaling

from the periphery in the central nervous system (CNS), resulting in hypersensitivity [12,13]. The presence of CS may contribute to the development of a neuropathic pain (NP) component [14]. Although knee pain in KOA has been shown to include neuropathic pain (NP) [15,16], the precise mechanisms leading to CS remain unclear. Furthermore, it is not fully understood whether elimination of pain through surgical intervention, such as total knee replacement, results in reversal or modulation of CS and NP [17].

The Central Sensitization Inventory (CSI) and various quantitative sensory testing (QST) methods have been developed to assess clinical markers of CS [18,19]. Sensory profiling using quantitative sensory testing (QST), aimed at measuring and quantifying sensitization-related processes, has become increasingly common in clinical practice for patients with osteoarthritis. Recent studies have demonstrated that a substantial proportion of patients with KOA exhibit widespread hyperalgesia, enhanced temporal summation of pain, and impaired endogenous pain inhibition compared with healthy individuals. These alternations may influence pain transmission pathways and contribute to unfavorable long-term pain outcomes following arthroplasty [20].

Assessment of pain-related functional impairment is also essential for treatment planning and enhancing patients' quality of life [21]. Various instruments are available for this purpose, among which the Pain Disability Questionnaire (PDQ) has been shown to be a reliable and valid tool [22].

When conservative treatment fails to adequately reduce pain and improve function in patients with KOA, quality of life may be significantly compromised, and Total Knee Arthroplasty (TKA) may be indicated [23].

However, arthroplasty is associated with a considerable prevalence of chronic postsurgical pain (CPSP) [24], making identification of risk factors for its development clinically important. Several predictors have been proposed, including sociodemographic factors, pain mechanisms, psychological variables, and the presence of pain sensitization, yet the exact mechanisms underlying chronic pain remain incompletely understood [25]. Acute postoperative pain has also been recognized as a key predictor of CPSP and therefore represents a potential target for preventive strategies [26]. Current evidence supports the role of CS as a significant risk factor for persistent pain and patient dissatisfaction following TKA [12]. Although advances in pain management and surgical techniques have improved early postoperative recovery [27], the prevalence of CPSP remains high despite adequate early postoperative analgesia [28]. After TKA, reported rates of chronic pain range from 10%

to 34% and have remained largely unchanged for decades, often without a surgically identifiable cause [17].

The aim of the review was to analyze the available literature in order to determine the relevance of QST in predicting outcomes after TKA and to identify the most promising QST modalities for this purpose.

Quantitative Sensory Testing in the prediction of postoperative pain after total knee arthroplasty

QST modalities for reliable prediction of postoperative pain after TKA

According to current evidence, QST modalities such as temporal summation (TS) and conditioned pain modulation (CPM) appear to be the most promising tools for predicting postoperative pain [29]. Among various surgical populations, QST has demonstrated the strongest predictive value in patients undergoing orthopedic procedures [30]. In 2021, Brown et al. conducted a comprehensive literature review to assess the role of perioperative QST in predicting acute and chronic postoperative pain across different surgical disciplines. The authors analyzed studies employing a wide range of QST modalities to assess sensory perception, pain thresholds, and pain tolerance using standardized stimuli. These stimuli included pressure, vibration, thermal, and electrical inputs, which are commonly used to evaluate specific nerve fiber function, detect neuropathic pain, and identify neurological dysfunction. QST assessments typically measure sensory responses at the level of stimulus detection, pain threshold, and, when applicable, pain tolerance. Frequent used QST thermal tests include warm and cold detection thresholds, heat and cold pain thresholds, and pain intensity elicited by suprathreshold thermal stimuli. Mechanical testing is typically conducted with von Frey filaments, and pain thresholds are measured using blunt needles or pressure cuffs. Allodynia is assessed using soft materials such as cotton pads or brushes, while vibration perception is evaluated with tuning forks. Electrical QST modalities include electrical detection threshold, electrical pain threshold, and electrical pain tolerance. Pain intensity is typically quantified using the Numeric Pain Scale and the Visual Analogue Scale. The studies included in the review primarily focused on preoperative QST assessment across multiple surgical specialties. Although orthopedic surgery showed the strongest correlation between preoperative QST findings and postoperative pain outcomes, no single QST modality was identified as universally superior across all studies. Nevertheless, TS and CPM emerged as potential predictors of both acute and chronic postsurgical pain. Brown

et al. concluded that the QST method should be combined with other parameters, such as preoperative pain intensity, anxiety, and pain catastrophizing, to enable personalized pain management [29].

QST and PainDETECT questionnaire in the prediction of postoperative pain after TKA

A recent study by Vygotsky et al. (2024) evaluated the predictive value of the QST and the PainDETECT questionnaire for postoperative pain at 3, 6, and 12 months following total knee arthroplasty. The study included 77 patients with KOA and 41 healthy controls. QST assessments were performed preoperatively and repeated at 3 and 6 months postoperatively, followed by the PainDETECT questionnaire. The QST protocol comprised pressure pain threshold (PPT), pain tolerance threshold, conditioned pain modulation (CPM) and temporal summation (TS). Preoperatively, patients with OA exhibited pinprick hyperalgesia on the medial aspect of the affected knee and increased sensitivity to cuff pressure on the ipsilateral lower leg compared with healthy controls. Preoperative pinprick hyperalgesia and the presence of pain with a neuropathic component were significant predictors of both preoperative pain intensity and pain intensity one year after surgery. Additionally, lower cuff pressure pain thresholds and mechanical hyperalgesia induced by needle stimulation were associated with higher preoperative pain intensity in patients with KOA. Baseline hyperalgesia assessed by TS accounted for 25% of the variance in pain intensity at 12 months postoperatively, while preoperative NP scores explained 30% and 20% of the variance in postoperative pain at 6 and 12 months, respectively. Importantly, a reduction in hyperalgesia at 3 months after surgery compared with baseline was associated with lower pain intensity at 12 months following TKA. These findings suggest that preoperative hyperalgesia and NP, identified through TS and the PainDETECT questionnaire, have significant predictive value for the development of CPSP after TKA [31].

QST and central sensitization inventory in the prediction of postoperative pain after TKA

Another study published in 2024 investigated whether pain intensity over time differs among patients with KOA undergoing TKA based on distinct somatosensory profiles. The study included 223 patients (mean age 66 years) and evaluated the evolution of QST measures and the CSI preoperatively and one year after TKA. Participants were categorized into three groups according to changes of somatosensory functioning across seven variables: local PPT, widespread PPT, local heat allodynia, widespread heat allodynia, TS, CPM, and CSI. The normal group dem-

onstrated normal somatosensory function both before and after TKA. The recovered group exhibited impaired somatosensory function preoperatively but normalized findings postoperatively. The persistently impaired group showed abnormal somatosensory functioning both pre- and postoperatively. Comparisons of pain intensity preoperatively, postoperatively, and one year after TKA revealed significant group differences in four of seven variables: local PPT, local heat allodynia, TS, and CSI. Patients with persistently impaired somatosensory function experienced less improvement in pain (based on CSI and local heat allodynia) and higher pain scores one year after TKA (based on CSI, local PPT and heat allodynia, and TS) compared with patients who maintained normal somatosensory functioning. Moreover, this group also demonstrated worse pain scores at one year compared with the recovered group (based on CSI). These findings indicate that patients exhibiting centrally mediated sensitization in four out of seven examined variables are less likely to achieve meaningful pain relief and exhibit poorer pain scores following TKA [32].

QST and gender in the prediction of postoperative pain after TKA

When sociodemographic predictors are considered, female sex is frequently associated with a greater magnitude of the CPM [33] and with more severe APSP and CPSP [34], although conflicting findings have also been reported. Several studies based on somatosensory profiling indicate that women tend to exhibit greater pain sensitivity and enhanced endogenous pain facilitation [35]. Despite evidence suggesting that women generally report higher levels of anxiety [36,37], some studies have demonstrated that the association between anxiety and pain intensity is stronger in men [38]. These findings raise the question of whether the phase of the menstrual cycle should be considered when interpreting QST results. However, some investigations report no significant differences in selected QST parameters and emotional states across different menstrual cycle phases [39].

Only a limited number of studies have directly examined the role of gender in the relationship between QST parameters and postsurgical pain. In a study by Bossmann et al., impaired endogenous pain inhibition assessed by CPM was associated with more severe postsurgical pain in women, but not in men [40]. These findings highlight the need for a more detailed evaluation of gender-specific mechanisms underlying the relationship between QST outcomes and postoperative pain after TKA.

One of the few studies explicitly addressing gender as a modifying factor in arthroplasty outcomes was

conducted by Paredes et al. (2024). The authors investigated psychological and psychophysical variables associated with acute and chronic pain following TKA and total hip arthroplasty, and examined whether these relationships differed by sex. Assessments were performed 48 hours preoperatively and three months postoperatively, and included sociodemographic, pain-related, and psychological questionnaires, as well as QST. The study included 63 subjects (31 women, 32 men), of whom 34 (54%) underwent TKA and 29 (46%) underwent total hip arthroplasty (THA). Notably, most women underwent TKA, whereas most men underwent THA. Significant sex-related differences in QST parameters were observed at the hand, including mechanical stimulus detection thresholds, “wind up ratio” (WUR), and CPM. Women demonstrated lower mechanical sensitivity (higher mechanical stimulus detection threshold), greater pain facilitation (higher WUR) at both the hand and the affected joint, and reduced pain inhibition (higher CPM values) at the affected joint. No significant sex-based differences were observed in the analyzed variables 48 hours after surgery. However, at three months postoperatively, women reported significantly higher pain intensity than men. Acute postsurgical pain (APSP) at 48 hours was associated with impaired CPM, while CPSP at three months was associated with female sex, longer duration of preoperative pain, TKA, higher APSP intensity, and impaired CPM. In multivariate analysis, these clinical variables remained significant predictors of CPSP, with the exception of sex and CPM. Importantly, WUR was a significant predictor of APSP in men, whereas CPM was a significant predictor of CPSP in women. CPM of the affected joint emerged as the only QST measure demonstrating significant results at both time points: CPM assessed at the hand was related to acute pain, while CPM assessed at the affected joint was related to chronic pain. At both assessments, higher pain intensity was observed in patients with less efficient pain inhibition (higher CPM score). Patients with effective CPM at the hand experienced less pain at 48 hours, whereas those with effective CPM at the affected joint reported less pain at three months postoperatively. None of the psychological variables examined were significantly associated with pain intensity at either postoperative time point. In this trial, women reported higher pain intensity preoperatively and at three months postoperatively, supporting previous evidence that female sex is a risk factor for pain chronification [41]. It is important to note that most women in this study underwent TKA, whereas most men underwent THA. Since THA is associated with lower incidence of CPSP than TKA [42], and TKA is known to be associated with greater postoperative pain

and lower improvement rates [43], the observed sex-related differences in CPSP may be partially attributable to procedure-specific factors. Furthermore, women tend to undergo surgery at more advanced stages of osteoarthritis, often with a longer duration of preoperative pain, which may contribute to greater pain severity both before and after surgery [41].

Conclusion

Given the increasing prevalence of knee osteoarthritis, it is essential to identify reliable methods for predicting outcomes following operative treatment, particularly total knee arthroplasty, in order to optimize postoperative pain management. Quantitative sensory testing modalities – especially pressure pain threshold, temporal summation, and conditioned pain modulation

– have emerged as the most promising tools within quantitative sensory testing for predicting postoperative pain outcomes.

Evidence indicates that specific quantitative sensory testing parameters are associated with an increased risk of acute and chronic postsurgical pain, and that the associations may differ according to gender. This underscores the importance of recognizing that risk factors for pain chronification are not uniformly applicable to all patients, and that predictive models must be tailored to specific patient subgroups. The moderating role of gender may help explain the conflicting findings reported in the quantitative sensory testing literature. Future research should take into account the type of surgical procedure (total knee arthroplasty versus total hip arthroplasty) when assessing postoperative pain outcomes.

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