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Original Research

Development and Persistence of Suspected Neuropathic Pain After Total Knee Arthroplasty in Individuals With Osteoarthritis

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Abstract

Background: Despite the effectiveness of total knee arthroplasty (TKA) for osteoarthritis (OA), up to 20% will report knee pain 1 year after surgery. One possible reason is the development of neuropathic pain before or after TKA.
Objective: To longitudinally describe suspected neuropathic pain in patients pre- and post-TKA and to explore relations between pre-TKA suspected neuropathic pain and post-TKA outcomes.
Design: Prospective observational study.
Setting: Participants were recruited from orthopedic surgery clinics prior to inpatient elective primary TKA.
Participants: Convenience sample of 135 patients were assessed for eligibility; 99 were enrolled and 74 completed the 6-month follow-up.
Methods: Participants completed the Self—Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) and outcome measures at baseline (pre-TKA) and 1 and 6 months post-TKA by postal survey. Demographic variables included age, gender, and comorbidities. Descriptive statistics were calculated for the presence of suspected neuropathic pain at each assessment and course of outcomes for various suspected neuropathic pain trajectories. Further, *t*-tests were used to compare outcomes between those with and without suspected neuropathic pain at each assessment. Multiple linear regressions assessed the relationship between baseline suspected neuropathic pain and 6-month outcomes.
Main Outcome Measurements: Intermittent and Constant Osteoarthritis Pain (ICOAP), Pain Catastrophizing Scale (PCS), and the Patient Health Questionnaire (PHQ-9) for depression.
Results: Suspected neuropathic pain was present in 35.5% of pre-TKA patients, 39.0% at 1 month, and 23.6% at 6 months post-TKA. Those with suspected neuropathic pain had higher scores for ICOAP total pain ($P = .05$), pain catastrophizing ($P < .01$), and depression ($P < .01$) at each assessment. After adjusting for potential confounding, pre-TKA suspected neuropathic pain did not predict ICOAP total pain or PHQ-9 depression scores at 6 months.
Conclusions: Although 14% of individuals with knee OA had suspected neuropathic pain that persisted 6 months post-TKA and those with suspected neuropathic pain had higher levels of pain, catastrophizing, and depression, the clinical identification of neuropathic pain remains enigmatic. Preoperative suspected neuropathic pain, as measured by S-LANSS, may have limited prognostic value for post-TKA outcomes.
Level of Evidence: ■■■

Introduction

Despite the well-known benefits and safety of total knee arthroplasty (TKA) for osteoarthritis (OA), approximately 20% of patients undergoing TKA will experience debilitating chronic knee pain after surgery [1,2]. As the understanding of OA pathoanatomy has progressed from a cartilage disease to a whole joint disease, possible pain mechanisms have also become more complex. For instance, OA pain has been broadly separated into 3 types: nociceptive, inflammatory, and neuropathic [3]. Nociceptive and inflammatory OA pain is described as "pain that arises from actual or threatened damage to non-neural tissue and is due to the activation of nociceptors" [4]. Neuropathic pain is defined as pain caused by a lesion or disease of the peripheral or central

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somatosensory nervous system [4] and has been suggested to be a distinct mechanism for pain in knee OA [5,6].

Preclinical data support the hypothesis of neuropathic pain in OA. For example, animal OA studies have demonstrated altered sensory nerve morphology, the presence of ATF-3 in the spinal cord (a marker of nerve damage), and spontaneous firing of nociceptors, all of which are consistent with neuropathic pain [7-9]. In addition, recent work has identified a possible mechanism for which nerve damage may occur in OA. The presence of lysophosphatidic acid (LPA) in joint synovium has been found to correlate with myelin thickness and ATF-3 in OA animal models, and animals treated with an LPA antagonist display less myelin degeneration than those who are not treated [10]. In human OA, LPA is positively correlated with OA pain severity [10].

Although preclinical data support neuropathic pain as a distinct type of pain in OA, the clinical diagnosis of OA is enigmatic. The clinical diagnosis of neuropathic pain primarily involves the use of subjective screening instruments such as the S-LANSS, painDETECT, or the DN-4 [11-13]. A recent systematic review of OA in varied surgical and nonsurgical populations reported a 23% pooled prevalence of neuropathic pain in OA [14]. Specific to surgical populations, 5%-28% of patients with persistent post-TKA pain have symptoms of neuropathic pain at the 6-month, 3-4-year, and 1-3-year follow-up, respectively [1,2,15]. Taken together, these preclinical and behavioral data support neuropathic pain as a distinct type of pain in OA that is likely to involve pain mechanisms that differ from those associated with nociceptive and inflammatory-type pain. However, the clinical data are entirely cross-sectional, which limits the capacity to generate hypotheses about the extent the presence of neuropathic pain observed after TKA reflects pain recalcitrant to surgery, or neuropathic pain consequent to surgery, and whether the identification of neuropathic pain prior to surgery assists in predicting post-TKA outcomes. Thus, a clarification of the course of neuropathic pain in OA both before and after TKA is needed. The presence of neuropathic pain symptoms in individuals undergoing TKA also represents a potentially important prognostic factor that has scarcely been examined prospectively. The objectives of this prospective study were to (1) describe and compare the characteristics and course of pain pre-TKA, and then 1 and 6 months post-TKA in patients with and without suspected neuropathic pain, and (2) to determine the extent to which presurgical suspected neuropathic pain predicts postsurgical clinical outcomes at 6 months.

Methods

Participants and Procedures

Participants in this prospective observational study were recruited from the Alberta Hip and Knee Clinics, specializing in total knee and hip joint arthroplasty, in 2 Canadian cities within the same province. Participant recruitment occurred from April to December 2014 at the orthopedic surgeon consultation visit, after patients were triaged as candidates for surgery. Patients were eligible to participate if they were 18 years or older, elected for primary total knee arthroplasty for OA, were medically safe to undergo surgery, and could read and write English. Patients were excluded if they were undergoing a revision TKA, had a diagnosis of rheumatoid arthritis, or a history of neurologic conditions such as stroke, Parkinson disease, or multiple sclerosis. Eligibility criteria were determined via chart review.

After patients were triaged as eligible for primary TKA, consenting patients completed baseline questionnaires at the clinic visit. Participants then provided their mailing address to enable administration of follow-up questionnaires at 1 and 6 months postsurgery. Reminder letters were sent for follow-up questionnaires that were not returned within 10 and 21 days. Participants were considered lost to follow-up if there was no response after 2 reminder letters. The Health Research Ethics Boards at the Universities of Alberta and Calgary approved this study.

Measures

The Self-report Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS) was used to identify neuropathic pain. S-LANSS is a 7-item self-report questionnaire containing 5 symptom items and 2 clinical examination items, each with a weighted score. A recommended score of 12 or greater suggests pain of potentially neuropathic origin and has validity evidence for specific neuropathic pain conditions [11]. Based on the recommended assessment of neuropathic pain [16], the assessment tools available do not enable a definitive diagnosis of neuropathic pain (this would require a confirmatory test). Consistent with these assessment guidelines [16], patients scoring 12 or greater on the scale were defined as having *suspected* neuropathic pain. To assess suspected neuropathic pain trajectory, screening was carried out pre-TKA (baseline) and 1 and 6 months post-TKA. Participants with suspected neuropathic pain before and after both postsurgical follow-ups were described as having *persistent suspected neuropathic pain*, those with pre-TKA suspected neuropathic pain but no suspected neuropathic pain post-TKA were classified as having *resolved suspected neuropathic pain*, and those without suspected neuropathic pain pre-TKA who developed suspected neuropathic pain post-TKA were described as having *developed suspected neuropathic pain* (ie, neuropathic pain developed as a consequence of surgery, rather than OA).

To compare the characteristics and course of pain pre-TKA and 1 and 6 months post-TKA in patients with and without suspected neuropathic pain, the Intermittent and Constant Osteoarthritis Pain (ICOAP) measure