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Factors Associated With the Risk of Neuropathic Pain One Year After Total Knee Arthroplasty and the Protective Role of Local Infiltration Analgesia: A Registry-Based Prospective Cohort Study

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Objective. To identify predictors of reduced risk for neuropathic pain (NP) one year after total knee arthroplasty (TKA) among patients who did not report NP before surgery.

Methods. We included primary TKAs performed between January 1, 2014, and June 30, 2022. NP was defined as Douleur Neuropathique en 4 Questions scores ≥4 before and one year after TKA. We selected patients without NP before surgery and ran simple log-binomial regressions and a multiple log-binomial regression on the presence or absence of NP at one year after surgery. We included predictive variables associated with patient characteristics (sex, age at surgery, body mass index [BMI], smoking status, diabetes, medication, and short-form 12-question [SF-12] mental scores) and operative variables (patella resurfacing, type of anesthesia, glucocorticoids, and local infiltration analgesia [LIA]).

Results. A total of 889 patients were included for initial analysis, with 636 included in the log-binomial regression. The incidence of NP at one year among the latter was 8.6% (55 of 636). LIA had a strong protective effect with an adjusted risk ratio (RR) of 0.45 (95% confidence interval [CI] 0.26–0.77). LIA led to an NP risk reduction of 6.1% (95% CI 1.4–10.7; 12.2% of NP without infiltration and 6.1% with). The other protective factors identified were higher SF-12 mental scores (adjusted RR 0.97; 95% CI 0.95–1.00), older age (adjusted RR per decade 0.78; 95% CI 0.59–1.03), and BMI <35 (adjusted RR 0.60; 95% CI 0.33–1.09).

Conclusions. Our study identified factors associated with reduced risk of NP one year after TKA among patients without preoperative NP. The use of LIA was newly identified as being associated with a lower likelihood of NP after surgery.

INTRODUCTION

The number of total knee arthroplasty (TKA) surgeries is increasing worldwide, suggesting a great success of this intervention. Nevertheless, a substantial number of patients still complain about discomfort and/or chronic pain after TKA.[1,2] Although the exact causes remain unclear, chronic pain is widely recognized as a common and disabling complication after TKA,[3,4] with up to 15% to 25% of patients reporting persistent postsurgical pain.[1–8]

Chronic pain after surgery is defined as pain "persisting at least three months after surgery, that was not present before surgery, or that had different characteristics or increased intensity from preoperative pain."[9] There exists significant variability in the incidence of chronic pain following TKA, partly because of various assessment tools available to address pain such as the Western

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SIGNIFICANCE & INNOVATIONS

- Local infiltration analgesia (LIA) significantly lowered neuropathic pain risk, with a 6.1% absolute reduction (adjusted risk ratio of 0.45; $P = 0.003$).
- Other protective factors included higher short-form 12-question mental health scores, older age, and a body mass index below 35.
- Findings highlight LIA as a potential preventive measure for neuropathic pain after total knee arthroplasty.

Ontario and McMaster Universities Osteoarthritis Index (WOMAC), Oxford Knee Score pain scale, Knee Injury and Osteoarthritis Outcome Score, short-form McGill Pain questionnaire, Brief Pain Inventory, or Chronic Pain Grade.[10–16] Given the intricate and multidimensional nature of pain, it is advised to assess multiple aspects, including pain intensity, interference with daily activities, impact on physical functioning, temporal aspects, pain description, emotional effects, medication usage, and satisfaction with pain management and relief.[17]

Neuropathic pain (NP), a complex and enigmatic phenomenon, can contribute to chronic pain and discomfort after TKA.[18–21] NP results from a lesion or disease affecting the somatosensory nervous system. After TKA, even in the absence of demonstrable pathology in peripheral nerves, NP may arise due to intraoperative nerve injury. Clinical signs of NP may be observed before as well as after TKA, exhibiting sensory loss with paradoxical oversensitivity and an association with nerve injury, local inflammation, central sensitization, or dysfunction.[20,22,23] Clearly, NP and central sensitization in the setting of knee osteoarthritis (and TKA) are often confounded,[19,24] although central sensitization is an amplification of neural stimuli, resulting in pain hypersensitivity, in the absence of tissue (ie, nerve) damage,[25] whereas NP by definition is associated with tissue damage.[26]

Furthermore, NP, as well as chronic pain, can impact mental health, patient rehabilitation, sleep, mood, function, gait, and quality of life but also patient satisfaction after TKA.[27] Several tools and questionnaires are available to evaluate and diagnose NP, such as the self-report version of the Leeds Assessment of Neuropathic Symptoms and Signs pain scale (S-LANSS), the painDETECT questionnaire, and the Douleur Neuropathique en 4 Questions questionnaire (DN4—NP pain diagnostic questionnaire), by means of items related to pain quality (for instance, burning, electric shock, and touch-evoked allodynia) and for the painDETECT questionnaire items also related to intensity and frequency.[24,28,29]

In the literature, factors associated with NP after TKA are poorly described.[2,30] Indeed, most publications primarily focus on predictive factors for "chronic pain" after TKA, as reported in a recent meta-analysis.[31] Still, the presence of postoperative chronic pain is a strong predictor for NP,[32] and treating NP before surgery reduces postoperative chronic pain.[33] Phillips et al specifically measured NP after TKA with a mean follow-up of 46 months but were not able to find any predictive factors.[34] Razmjou et al reported associations with NP and perceived pain, physical dysfunction, and stiffness one year after TKA, without any associations with age, sex, or preoperative comorbidities such as diabetes.[18] In contrast, older age, sex, body mass index (BMI) ≥30 kg/m^2, high catastrophizing, depression, working status, radiologic osteoarthritis severity, symptom duration, presence of NP before surgery, and presence of comorbidities have been associated with NP more recently.[3,30,35,36] Given the lack of comprehensive understanding regarding the risk factors for developing NP after TKA, this study aimed at identifying factors (clinical and operative) associated with the risk for NP one year after TKA among patients who did not report NP before surgery.

MATERIALS AND METHODS

Study design and setting. This study used a registry-based cohort from a large tertiary hospital, the Geneva Arthroplasty Registry founded in 1996.[37] Data are collected prospectively. The completeness of the registry is 100%. All patients undergoing primary TKA between January 1, 2014, and June 30, 2022 (n = 1,887), with available NP-related baseline information who did not present NP before surgery (n = 1,188) and who did not refuse to participate, were eligible for the present study (n = 1,174; see Figure 1). Moreover, we excluded patients who died within the first year (n = 9), were lost to follow-up (n = 6), underwent a revision within the first year (n = 19), or did not respond to the NP questionnaire at one year (n = 251; final sample n = 889). The registry data collection and the present study were approved by the local ethics committee called Commission Cantonale d'Ethique de la Recherche sur l'être humain (CCER Geneva, Switzerland).

Outcomes. NP was the main outcome of interest, and it was assessed with a self-reported DN4 questionnaire 7 to 10 days before and one year after TKA.[29] This questionnaire encompasses 10 items related to pain's characteristics (burning, painful cold, and electric shocks), associated symptoms (tingling, pins and needles, numbness, and itching), hypoesthesia to touch and pinprick, and presence or increase of pain by brushing.[29] The DN4 questionnaire uses a binary response format, with "yes" or "no" as possible answers for each item, corresponding to subscores of 1 or 0, respectively. The global score is between 0 to 10, with each selected item increasing the score by one. The presence of NP was defined as a score of four or more, whereas the absence of NP was defined as a score of three or less. Secondary outcomes used in a sensitivity analysis were WOMAC in its reduced form,[38] and the patient's general health at one year was measured with a short-form 12-question (SF-12) survey.[39]

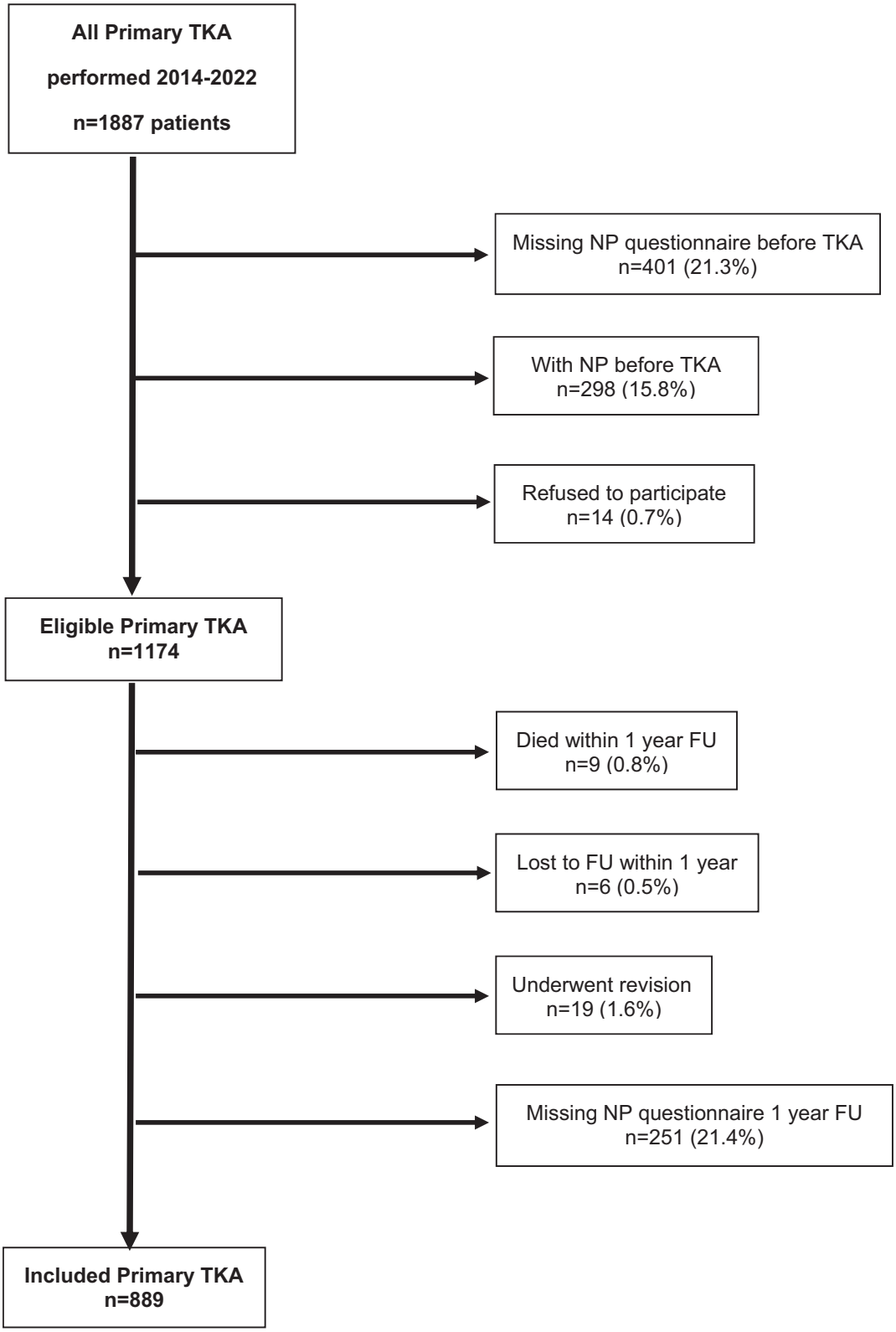

Figure 1. Flow chart of 889 primary patients with TKA included in this study in function of inclusion and exclusion criteria. FU, follow-up; NP, neuropathic pain; TKA, total knee arthroplasty.

Predictors. We included predictive variables associated with preoperative patient characteristics: sex, age at surgery, BMI (<35 or ≥35), smoking status (never or ever), diabetes (yes or no), medication (three variables: use of opioids, antidepressants, or anxiolytics), and SF-12 mental component scores. Moreover, we included predictors associated with operative

variables: patella resurfacing (yes or no), type of anesthesia (general or spinal), glucocorticoids (dexamethasone 8 mg intravenously, or if low body weight, 0.1 mg/kg of normal body weight; yes or no), and local infiltration analgesia (LIA; yes or no).

Other baseline characteristics. Presurgery pain, function, and general health were assessed via a questionnaire sent 7 to 10 days before surgery using WOMAC and SF-12. We also evaluated preoperative BMI as a continuous variable, physical status assessed by American Society of Anesthesiologists (ASA) score, and number of comorbidities (0 to >4).

Statistical analysis. We report patient characteristics as mean (±SD) for continuous variables and count (percentage) for categorical variables. We ran simple log-binomial regressions using each predictive variable and a multiple log-binomial regression including all variables on the presence or absence of NP at one year after surgery. Assumptions for the multiple regression were met: independence of errors (Durbin–Watson statistic = 2.03), no multicollinearity issue (variance inflation factor scores between 0.1 and 10), no outliers' issue (Cook's distances < 1), and satisfactory linearity of continuous predictive variables and log odds of the dependent variable.

We performed two sensitivity analyses. First, we ran a propensity score–matched analysis of the strongest association found (LIA and NP at one year). The matching was generated by a logistic regression, with sex, age at operation, BMI, ASA score, WOMAC pain and function, SF-12 physical and mental component scores, and smoking status at baseline used as predictors of LIA. We used one-to-one nearest neighbor matching without replacement and included a caliper of 0.1 SDs, which yielded adequate balance (standardized mean differences after matching < 0.1).[40] Then, we ran the multiple log-binomial regression including all variables on the presence or absence of NP at one year after surgery on the propensity score–matched patients. Second, we evaluated the impact of LIA on WOMAC pain at one year after TKA. Given that WOMAC scores were not normally distributed, we used nonparametric Brunner–Munzel tests to compare WOMAC pain at one year between patients with or without LIA.

Statistical significance was assessed at a two-sided 0.05 level for analyses on patient characteristics. Statistical significance was assessed at a two-sided 0.10 level for the regressions. All analyses were performed using R Statistical Software (version 4.2.2).[41]

Ethics. The registry data collection was approved by the local ethics committee (CCER Geneva, Switzerland). All the data used in this study is retrieved from the Geneva Arthroplasty Registry. Patient consent for data collection was obtained and protected in the registry.

RESULTS

Study population. Overall, 889 primary TKAs were included in the analysis. Patients consisted of more women (62%) than men (Table 1). The mean age was 71.5 years, and the mean BMI was 29.8 (kg/m^2).

Predictors of NP. Overall, 69 patients (7.8%) showed NP after surgery, whereas 820 (92.2%) patients did not. Of these, 636 patients had complete information on all factors and were included in the simple and multiple regression analyses (Table 2). The incidence of NP at one year among the latter was 8.6% (55 of 636). Both simple and multiple regression models revealed the same significant predictive variables ($P < 0.15$). Among them, LIA had the strongest effect, with an adjusted risk ratio of 0.45 (95% confidence interval [CI] 0.26–0.77). More specifically, LIA led to a NP risk reduction from 12.2% of NP without infiltration to 6.1% with infiltration (risk reduction 6.1%; 95% CI 1.4–10.7). This effect was observed irrespective of the type of anesthesia used, that is, general anesthesia (n = 532; risk reduction = 4.7%; 95% CI 0.2–9.5; 11.1% of NP without infiltration and 6.4% with infiltration) or spinal anesthesia (n = 104; risk reduction = 17.0%; 95% CI 0.6–33.5; 22.2% of NP without infiltration and 5.2% with infiltration).

We found a significant effect of the SF-12 mental scores with an adjusted risk ratio of 0.97 (95% CI 0.95–1.00), indicating that higher mental scores were associated with a lower incidence of NP. Moreover, we found a significant effect of age with an adjusted risk ratio of 0.78 (95% CI 0.59–1.03) per decade, indicating that NP risk was decreased in older patients. Finally, we found a significant effect of BMI with an adjusted risk ratio of 0.60 (95% CI 0.33–1.09), indicating that NP risk was decreased for patients with a BMI <35.

Sensitivity analyses. Propensity score matching allowed the match of 242 patients having received infiltration with 242 patients without infiltration, with standardized mean differences after matching of <0.1, indicating good balance regarding baseline covariates. The multiple regression on this dataset revealed LIA again as a significant predictor of NP at one year (adjusted risk ratio = 0.41; 95% CI 0.22–0.76) after matching patients for baseline covariates. Regarding the second analysis, patients with LIA tended to report better WOMAC pain scores at one year (mean 78.8; SD 19.6) than patients without LIA (mean 74.9; SD 22.7).

Table 1. Baseline characteristics of patients with eligible TKAs, included TKAs, TKAs included in regressions, and TKAs not included in regressions*

Characteristics	Eligible (n = 1,174)	Included (n = 889)	Included in regressions (n = 636)	Not included in regressions (n = 538)
Sex, n (%)				
Female	743 (63.3)	552 (62.1)	396 (62.3)	347 (64.5)
Male	431 (36.7)	337 (37.9)	240 (37.7)	191 (35.5)
Age at operation, mean (±SD)	71 (±9.5)	71.5 (±9.2)	71.2 (±9.4)	70.8 (±9.6)
BMI, mean (±SD)	30 (±5.6)	29.8 (±5.5)	29.9 (±5.5)	30 (±5.8)
ASA scores, n (%)				
1–2	860 (73.3)	664 (74.7)	471 (74.1)	389 (72.3)
3–4	314 (26.7)	225 (25.3)	165 (25.9)	149 (27.7)
WOMAC pain, mean (±SD)	38.7 (±16.8)	39.6 (±16.5)	39.1 (±16.4)	38.3 (±17.2)
WOMAC function, mean (±SD)	43.1 (±18.7)	44.4 (±18.6)	43.3 (±18.6)	42.8 (±18.8)
SF-12 physical component, mean (±SD)	33.4 (±7)	33.7 (±6.9)	33.4 (±6.8)	33.5 (±7.2)
SF-12 mental component, mean (±SD)	43.9 (±11.4)	44.7 (±11.5)	44.6 (±11.7)	43.1 (±11.1)
Smoking status, n (%)				
Current	167 (14.3)	119 (13.4)	88 (13.8)	79 (14.8)
Former	310 (26.5)	232 (26.2)	160 (25.2)	150 (28.1)
Never	693 (59.2)	536 (60.4)	388 (61.0)	305 (57.1)
Implant stability, n (%)				
Posterior stabilized	853 (72.7)	648 (72.9)	436 (68.6)	417 (77.7)
Medial pivot	307 (26.2)	232 (26.1)	192 (30.2)	115 (21.4)
Others	13 (1.1)	9 (1.0)	8 (1.3)	5 (0.9)
Number of comorbidities, n (%)				
0	59 (5.0)	48 (5.4)	36 (5.7)	23 (4.3)
1	152 (12.9)	121 (13.6)	80 (12.6)	72 (13.4)
2	281 (23.9)	217 (24.4)	153 (24.1)	128 (23.8)
3	288 (24.5)	222 (25.0)	164 (25.8)	124 (23.0)
≥4	394 (33.6)	281 (31.6)	203 (31.9)	191 (35.5)

*For eligible TKAs, 18 missing values on WOMAC pain, 43 on WOMAC function, 38 on SF-12 physical and mental component, 4 on smoking status, and 1 on implant stability. For included TKAs, 14 missing values on WOMAC pain, 30 on WOMAC function, 27 on SF-12 physical and mental component, and 2 on smoking status. For TKAs included in regressions, 6 missing values on WOMAC pain and 19 on WOMAC function. For TKAs excluded from regression, 12 missing values on WOMAC pain, 24 on WOMAC function, 38 on SF-12 physical and mental component, 4 on smoking status, and 1 on implant stability. ASA, American Society of Anesthesiologists; BMI, body mass index; SF-12, short-form 12 question; TKA, total knee arthroplasty; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2. Simple and multivariable log-binomial regression models for variables associated with neuropathic pain one year after surgery*

			Simple log-binomial regression		Multivariable log-binomial regression	
Characteristics	NP at one year (n = 55)	No NP at one year (n = 581)	Risk ratio (95% CI)	*P* value	Adjusted risk ratio (95% CI)	*P* value
Female, n (%)	31 (56.4)	365 (61.8)	0.78 (0.47–1.30)	0.345	0.74 (0.42–1.28)	0.279
Age at operation, mean (±SD)	68.9 (9.24)	71.4 (10.4)	0.78 (0.60–1.00)[a]	0.053[b]	0.78 (0.59–1.03)[a]	0.076[b]
BMI <35, n (%)	41 (74.5)	485 (83.5)	0.61 (0.35–1.08)	0.092[b]	0.60 (0.33–1.09)	0.095[b]
Never smoker, n (%)	31 (56.4)	357 (61.4)	0.83 (0.50–1.37)	0.460	0.88 (0.52–1.51)	0.649
Diabetes, n (%)	9 (16.4)	103 (17.7)	0.92 (0.46–1.82)	0.800	0.83 (0.41–1.66)	0.591
Opioids, n (%)	7 (12.7)	96 (16.5)	0.75 (0.35–1.62)	0.470	0.61 (0.28–1.32)	0.211
Antidepressant, n (%)	9 (16.4)	102 (17.6)	0.93 (0.47–1.83)	0.824	0.78 (0.38–1.62)	0.511
Anxiolytics, n (%)	7 (12.7)	53 (9.1)	1.40 (0.66–2.96)	0.377	1.60 (0.73–3.54)	0.243
SF-12 mental component, mean (±SD)	41.3 (11.6)	44.9 (11.6)	0.98 (0.95–1.00)	0.028[c]	0.97 (0.95–1.00)	0.034[c]
Patella resurfacing, n (%)	25 (45.5)	284 (48.9)	0.88 (0.53–1.46)	0.627	1.22 (0.71–2.09)	0.477
Type of anesthesia, n (%)						
General	45 (81.8)	487 (83.8)	(ref)	–	(ref)	–
Spinal	10 (18.2)	94 (16.2)	1.14 (0.59–2.18)	0.700	1.26 (0.65–2.46)	0.499
Glucocorticoids, n (%)	14 (25.5)	184 (31.7)	0.76 (0.42–1.35)	0.346	0.72 (0.38–1.33)	0.290
Local infiltration analgesia, n (%)	23 (41.8)	351 (60.4)	0.50 (0.30–0.84)	0.009[d]	0.45 (0.26–0.77)	0.003[d]

[a]Risk ratios for age per decade.
[b]$P < 0.15$.
[c]$P < 0.05$.
[d]$P < 0.01$.
*BMI, body mass index; CI, confidence interval; NP, neuropathic pain; SF-12, short-form 12 question.

DISCUSSION

Perioperative factors associated with reduction of NP one year after TKA among patients without preoperative NP were use of LIA, older age, BMI below 35, and higher SF-12 mental component scores. The main finding is the strong protective effect of LIA, evidenced by the lower incidence of NP in patients who received infiltration compared with those who did not, regardless of the type of anesthesia used.

During the last two decades, pain control in the immediate postoperative phase has gained more and more interest to improve recovery and limit hospital stay, with several strategies proposed, including the use of LIA.[42,43] LIA has already demonstrated its efficacy in pain control and the reduction of swelling and bleeding as well as in minimizing impairment in quadricep muscle strength, thereby facilitating earlier mobilization.[44–46] Wylde et al reported on a randomized controlled trial evaluating the effectiveness of LIA and standard care vs standard care only in reducing chronic pain 12 months after total hip arthroplasty (THA) and TKA.[47] Pain was measured with the WOMAC pain score as the primary outcome and painDETECT as one of the secondary outcomes. They observed a significant reduction of pain in the LIA group both on the WOMAC and painDETECT scores after THA. However, after TKA, no strong evidence for a protective effect of LIA was found. Additionally, LIA reduces the need for postoperative opioid use and its associated risks,[43,48] contributing to shorter hospital stays, lower overall public health costs,[46,49] and improved short-term well-being compared with other anesthesia methods. This approach may also facilitate faster knee recovery and rehabilitation.[50] In our practice, a mixture of ketorolac, ropivacaine, and (for the posterior part of the joint only) adrenaline diluted in saline solution is routinely used. Indeed, the combination of a local anesthetic with nonsteroidal anti-inflammatory drugs used in LIA has been proven to be effective in blocking both pain nerve conduction and pain sensitization, thus avoiding amplifying and sustaining pain intensity.[51] LIA is therefore a straightforward and efficient low-cost technique, offering lower complication rates and reduced systemic toxicity,[46] with a substantial impact on reducing NP, as demonstrated by the results of this study, which had not yet been reported.

The other predictive factors of reduced NP identified in the multivariable model were older age, BMI <35, and higher SF-12 mental component scores. Our findings are not fully in line with existing literature, particularly regarding the influence of age. Parvizi et al[52] reported that one in three younger patients continue to report pain and symptoms after TKA, and Scott et al[53] reported that one in four younger patients are less satisfied with surgical outcomes, often due to pain, residual symptoms, and high expectations. Tian et al, on the other hand, reported both older age (>80 years old) and a BMI >30 as risk factors for chronic pain after TKA, associated with pain at rest, possibly because of increased pressure at the subchondral bone level and weakness in the quadriceps muscles.[7] If a high BMI might explain the observed trends, the role of older age in developing chronic pain or protecting against NP needs further investigation. A potential explanation for this discrepancy could be found in the inclusion of all patients in the study of Tian et al, regardless of whether they experienced NP before surgery, whereas in our study, we excluded patients experiencing NP before surgery. Despite these aspects, one should be cautious to consider BMI alone as a factor precluding TKA for patients with knee osteoarthritis. Registry data show that patients with a high BMI tend to have smaller relative improvements compared with those with a lower BMI, but the differences between groups remain below the threshold considered clinically meaningful.[54,55]

The role of mental health appears to be more evident. Psychological factors such as mental health, anxiety, depression, and pain catastrophizing have been recognized as significant contributors to NP after TKA.[2] Patients with lower mental health scores before surgery are more likely to experience NP one year after TKA, highlighting the importance of identifying them to improve postoperative outcomes.[56] Interestingly, this study did not find associations with comorbidities such as smoking status or diabetes, contrary to findings by Tian et al, who identified smoking status as a protective factor.[7]

Our study has some limitations. First, we did not include parameters such as depression, anxiety, catastrophizing, or expected pain, which have been strongly associated with NP after TKA in another study.[57] Second, information on pain duration and central sensitization was lacking, which could have provided a more precise definition of NP. Third, we had a relatively high rate of missing data in some of the predictive variables. As a result, the sample size for the logistic regression was reduced by 28.5% because this analysis requires complete data for all variables. However, patient characteristics were similar among eligible TKAs, TKAs included in regressions, and TKAs not included in regressions, which suggests that the risk of bias is limited. Moreover, incidence of NP at one year was comparable between patients included overall and those with complete risk factor information. Last, there is no gold standard for evaluating NP with two other subjective tools such as S-LANSS or painDETECT. The DN4 questionnaire consists of several binary (yes or no) questions, whereas painDETECT offers multiple categorical response options (eg, never, hardly noticed, slightly, moderately, strongly, and very strongly), providing greater granularity in pain description, which may influence the final NP score. Bertram et al reported substantial differences in NP prevalence when using these two tools.[32] However, they also observed a consistency between DN4 and painDETECT (score ≥13) and found moderate statistical agreement, suggesting that both tools are appropriate and valid for screening NP in surgical populations. Despite the lack of a definitive standard, the DN4 questionnaire remains one of the most commonly used and accepted tools.[28,58]

Despite these limitations, this study represents the largest reported cohort of patients observed for NP after TKA up to one year. Focusing specifically on NP rather than chronic pain, it newly provides insights into significant predictors. The strength of this study also lies in the analysis of the protective effects of certain parameters one year after TKA in patients who did not have NP before surgery. This point is both a crucial aspect and an originality of this work.

Our study identified factors associated with a reduced risk of NP one year after TKA among patients without preoperative NP. The use of LIA was newly identified as being associated with a lower likelihood of developing NP postoperatively. This intervention, along with recent efforts on care pathways for early management of chronic pain after TKA,[59–61] should help improve mid- to long-term results after surgery. Given that LIA is a relatively simple, effective, and low-cost technique with a low complication rate and minimal systemic toxicity, its routine use may help reduce the incidence of NP following TKA.

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AUTHOR CONTRIBUTIONS

All authors contributed to at least one of the following manuscript preparation roles: conceptualization AND/OR methodology, software, investigation, formal analysis, data curation, visualization, and validation AND drafting or reviewing/editing the final draft. As corresponding author, Dr Bonnefoy-Mazure confirms that all authors have provided the final approval of the version to be published and takes responsibility for the affirmations regarding article submission (eg, not under consideration by another journal), the integrity of the data presented, and the statements regarding compliance with institutional review board/Declaration of Helsinki requirements.

REFERENCES

1. Beswick AD, Wylde V, Gooberman-Hill R, et al. What proportion of patients report long-term pain after total hip or knee replacement for osteoarthritis? A systematic review of prospective studies in unselected patients. BMJ Open 2012;2(1):e000435.
2. Rice DA, Kluger MT, McNair PJ, et al. Persistent postoperative pain after total knee arthroplasty: a prospective cohort study of potential risk factors. Br J Anaesth 2018;121(4):804–812.
3. Ashoorion V, Sadeghirad B, Wang L, et al. Predictors of persistent post-surgical pain following total knee arthroplasty: a systematic review and meta-analysis of observational studies. Pain Med 2023;24(4):369–381.
4. Kim DH, Pearson-Chauhan KM, McCarthy RJ, et al. Predictive factors for developing chronic pain after total knee arthroplasty. J Arthroplasty 2018;33(11):3372–3378.
5. Dembek DJ, Bicket MC. Advances in the management of persistent pain after total knee arthroplasty. Curr Opin Anaesthesiol 2023;36(5):560–564.
6. de Ladoucette A. Management of perioperative pain after TKA. Orthop Traumatol Surg Res 2023;109(1S):103443.
7. Tian M, Li Z, Chen X, et al. Prevalence and predictors of chronic pain with two-year follow-up after knee arthroplasty. J Pain Res 2022;15:1091–1105.
8. Wylde V, Hewlett S, Learmonth ID, et al. Persistent pain after joint replacement: prevalence, sensory qualities, and postoperative determinants. Pain 2011;152(3):566–572.
9. Werner MU, Kongsgaard UEI. I. Defining persistent post-surgical pain: is an update required? Br J Anaesth 2014;113(1):1–4.
10. Bellamy N, Buchanan WW, Goldsmith CH, et al. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. J Rheumatol 1988;15(12):1833–1840.
11. Dawson J, Fitzpatrick R, Murray D, et al. Questionnaire on the perceptions of patients about total knee replacement. J Bone Joint Surg Br 1998;80(1):63–69.
12. Roos EM, Roos HP, Lohmander LS, et al. Knee Injury and Osteoarthritis Outcome Score (KOOS)--development of a self-administered outcome measure. J Orthop Sports Phys Ther 1998;28(2):88–96.
13. Tan G, Jensen MP, Thornby JI, et al. Validation of the Brief Pain Inventory for chronic nonmalignant pain. J Pain 2004;5(2):133–137.
14. Pinedo-Villanueva R, Khalid S, Wylde V, et al. Identifying individuals with chronic pain after knee replacement: a population-cohort, cluster-analysis of Oxford knee scores in 128,145 patients from the English National Health Service. BMC Musculoskelet Disord 2018;19(1):354.
15. Melzack R. The short-form McGill Pain Questionnaire. Pain 1987;30(2):191–197.
16. Von Korff M, DeBar LL, Krebs EE, et al. Graded chronic pain scale revised: mild, bothersome, and high-impact chronic pain. Pain 2020;161(3):651–661.
17. Wylde V, Beswick A, Bruce J, et al. Chronic pain after total knee arthroplasty. EFORT Open Rev 2018;3(8):461–470.
18. Razmjou H, Boljanovic D, Wright S, et al. Association between neuropathic pain and reported disability after total knee arthroplasty. Physiother Can 2015;67(4):311–318.
19. Wluka AE, Yan MK, Lim KY, et al. Does preoperative neuropathic-like pain and central sensitisation affect the post-operative outcome of knee joint replacement for osteoarthritis? A systematic review and meta analysis. Osteoarthritis Cartilage 2020;28(11):1403–1411.
20. Güngör Demir U, Demir AN, Toraman NF. Neuropathic pain in knee osteoarthritis. Adv Rheumatol 2021;61(1):67.
21. Hasegawa M, Tone S, Naito Y, et al. Possible neuropathic pain in patients with osteoarthritis of the knee before and after total knee arthroplasty. J Pain Res 2021;14:3011–3015.
22. Gilron I, Watson CP, Cahill CM, et al. Neuropathic pain: a practical guide for the clinician. CMAJ 2006;175(3):265–275.
23. Finnerup NB, Kuner R, Jensen TS. Neuropathic pain: from mechanisms to treatment. Physiol Rev 2021;101(1):259–301.
24. Hochman JR, Davis AM, Elkayam J, et al. Neuropathic pain symptoms on the modified painDETECT correlate with signs of central sensitization in knee osteoarthritis. Osteoarthritis Cartilage 2013;21(9):1236–1242.
25. Clauw DJ, Hassett AL. The role of centralised pain in osteoarthritis. Clin Exp Rheumatol 2017;35(5):79–84.

26. Campbell JN, Meyer RA. Mechanisms of neuropathic pain. Neuron 2006;52(1):77–92.
27. Colovic D, Draschl A, Reinbacher P, et al. Evaluation of neuropathic pain after total knee arthroplasty: do yellow flags matter? J Clin Med 2023;12(24):7708.
28. Bennett MI, Smith BH, Torrance N, et al. The S-LANSS score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. J Pain 2005;6(3):149–158.
29. Bouhassira D, Attal N, Alchaar H, et al. Comparison of pain syndromes associated with nervous or somatic lesions and development of a new neuropathic pain diagnostic questionnaire (DN4). Pain 2005; 114(1–2):29–36.
30. Fernández-de-Las-Peñas C, Florencio LL, de-la-Llave-Rincón AI, et al. prognostic factors for postoperative chronic pain after knee or hip replacement in patients with knee or hip osteoarthritis: an umbrella review. J Clin Med 2023;12(20):6624.
31. Olsen U, Lindberg MF, Rose C, et al. Factors correlated with pain after total knee arthroplasty: a systematic review and meta-analysis. PLoS One 2023;18(3):e0283446.
32. Bertram W, Howells N, White SP, et al. Prevalence and patterns of neuropathic pain in people with chronic post-surgical pain after total knee arthroplasty. Bone Joint J 2024;106-B(6):582–588.
33. Buvanendran A, Kroin JS, Della Valle CJ, et al. Perioperative oral pregabalin reduces chronic pain after total knee arthroplasty: a prospective, randomized, controlled trial. Anesth Analg 2010;110(1):199–207.
34. Phillips JR, Hopwood B, Arthur C, et al. The natural history of pain and neuropathic pain after knee replacement: a prospective cohort study of the point prevalence of pain and neuropathic pain to a minimum three-year follow-up. Bone Joint J 2014;96-B(9):1227–1233.
35. Fernandes GS, Valdes AM, Walsh DA, et al. Neuropathic-like knee pain and associated risk factors: a cross-sectional study in a UK community sample. Arthritis Res Ther 2018;20(1):215.
36. Ghoshal A, Bhanvadia S, Singh S, et al. Factors associated with persistent postsurgical pain after total knee or hip joint replacement: a systematic review and meta-analysis. Pain Rep 2023;8(1):e1052.
37. Lübbeke A, Silman AJ, Barea C, et al. Mapping existing hip and knee replacement registries in Europe. Health Policy 2018;122(5):548–557.
38. Whitehouse SL, Lingard EA, Katz JN, et al. Development and testing of a reduced WOMAC function scale. J Bone Joint Surg Br 2003; 85(5):706–711.
39. Ware J Jr, Kosinski M, Keller SDA. A 12-item short-form health survey: construction of scales and preliminary tests of reliability and validity. Med Care 1996;34(3):220–233.
40. Austin PC. An introduction to propensity score methods for reducing the effects of confounding in observational studies. Multivariate Behav Res 2011;46(3):399–424.
41. R Development Core Team. A language and environment for statistical computing. R Foundation for Statistical Computing; 2021.
42. Turppo V, Sund R, Huopio J, et al. Pain medication purchases before and after total hip and knee arthroplasty: a register study of 329,743 arthroplasties. Acta Orthop 2022;93:534–541.
43. Tian Y, Tang S, Sun S, et al. Comparison between local infiltration analgesia with combined femoral and sciatic nerve block for pain management after total knee arthroplasty. J Orthop Surg Res 2020; 15(1):41.
44. Berninger MT, Friederichs J, Leidinger W, et al. Effect of local infiltration analgesia, peripheral nerve blocks, general and spinal anesthesia on early functional recovery and pain control in total knee arthroplasty. BMC Musculoskelet Disord 2018;19(1):232.
45. Karam JA, Schwenk ES, Parvizi J. An update on multimodal pain management after total joint arthroplasty. J Bone Joint Surg Am 2021;103(17):1652–1662.
46. Suthersan M, Pit S, Gordon L, et al. Local infiltration analgesia versus standard analgesia in total knee arthroplasty. J Orthop Surg (Hong Kong) 2015;23(2):198–201.
47. Wylde V, Lenguerrand E, Gooberman-Hill R, et al. Effect of local anaesthetic infiltration on chronic postsurgical pain after total hip and knee replacement: the APEX randomised controlled trials. Pain 2015;156(6):1161–1170.
48. Kurosaka K, Tsukada S, Seino D, et al. Local infiltration analgesia versus continuous femoral nerve block in pain relief after total knee arthroplasty: a randomized controlled trial. J Arthroplasty 2016;31(4): 913–917.
49. Sciberras SC, Vella AP, Vella B, et al. A randomized, controlled trial on the effect of anesthesia on chronic pain after total knee arthroplasty. Pain Manag 2022;12(6):711–723.
50. Reinbacher P, Schittek GA, Draschl A, et al. Local periarticular infiltration with dexmedetomidine results in superior patient well-being after total knee arthroplasty compared with peripheral nerve blocks: a randomized controlled clinical trial with a follow-up of two years. J Clin Med 2023;12(15):5088.
51. Kerr DR, Kohan L. Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. Acta Orthop 2008;79(2):174–183.
52. Parvizi J, Nunley RM, Berend KR, et al. High level of residual symptoms in young patients after total knee arthroplasty. Clin Orthop Relat Res 2014;472(1):133–137.
53. Scott CE, Oliver WM, MacDonald D, et al. Predicting dissatisfaction following total knee arthroplasty in patients under 55 years of age. Bone Joint J 2016;98-B(12):1625–1634.
54. Evans JT, Mouchti S, Blom AW, et al. Obesity and revision surgery, mortality, and patient-reported outcomes after primary knee replacement surgery in the National Joint Registry: a UK cohort study. PLoS Med 2021;18(7):e1003704.
55. McLaughlin J, Elsey J, Kipping R, et al. Access to hip and knee arthroplasty in England: commissioners' policies for body mass index and smoking status and implications for integrated care systems. BMC Health Serv Res 2023;23(1):77.
56. Springborg AH, Visby L, Kehlet H, et al. Psychological predictors of acute postoperative pain after total knee and hip arthroplasty: a systematic review. Acta Anaesthesiol Scand 2023;67(10):1322–1337.
57. Fitzsimmons M, Carr E, Woodhouse L, et al. Development and persistence of suspected neuropathic pain after total knee arthroplasty in individuals with osteoarthritis. PMR 2018;10(9):903–909.
58. Freynhagen R, Baron R, Gockel U, et al. painDETECT: a new screening questionnaire to identify neuropathic components in patients with back pain. Curr Med Res Opin 2006;22(10):1911–1920.
59. Bertram W, Wylde V, Howells N, et al. The STAR care pathway for patients with chronic pain after total knee replacement: four-year follow-up of a randomised controlled trial. BMC Musculoskelet Disord 2023;24(1):972.
60. Moore AJ, Wylde V, Bertram W, et al. Healthcare professionals' views on implementing the STAR care pathway for people with chronic pain after total knee replacement: a qualitative study. PLoS One 2023; 18(4):e0284406.
61. Wylde V, Bertram W, Sanderson E, et al; STAR trial group. The STAR care pathway for patients with pain at 3 months after total knee replacement: a multicentre, pragmatic, randomised, controlled trial. Lancet Rheumatol 2022;4(3):e188–e197.