Association between Neuropathic Pain and Reported Disability after Total Knee Arthroplasty

Helen Razmjou, MSc, PhD, PT;^{*,†} Dragana Boljanovic, BSc, MSc;^{*,‡}
 Stewart Wright, MD, FRCSC;^{†,§} John Murnaghan, MD, MSc, FRCSC;^{†,§}
 Richard Holtby, MB, BS, FRCSC^{†,§}

ABSTRACT

Purpose: To determine whether reporting neuropathic pain (NP) at an average of 5 years after total knee arthroplasty (TKA) was related to patient age, sex, preoperative comorbidity, arthritis self-efficacy, or disability before surgery and at 1 year after surgery. The estimate of NP prevalence and cross-sectional group differences were explored at 5 years after surgery. **Methods:** A subsample of participants in a formal research study was contacted via mail approximately 5 years after undergoing surgery and were sent four questionnaires: the Western Ontario and McMaster Universities Osteoarthritis Index, the Patient Health Questionnaire, the Self-Administered Leeds Assessment of Neuropathic Signs and Symptoms (S-LANSS), and a satisfaction questionnaire. NP was defined as an S-LANSS score of 12 or more. **Results:** Of 89 patients who met the inclusion criteria, data for 63 (71%) patients (47 women; mean age 67 [SD 8] y) were used for analysis. Of these 63, 9 (14%) were identified as having NP. None had a report of failure of prosthesis or other surgical complications according to most recent medical records. There was no relationship between preoperative patient characteristics and development of NP. However, the NP group on average had a higher report of stiffness ($p = 0.020$), physical dysfunction ($p = 0.019$), and pain ($p = 0.050$) at 1 year after surgery. Cross-sectional comparisons showed higher levels of pain ($p = 0.001$), stiffness ($p = 0.008$), physical dysfunction ($p = 0.003$), and depression ($p = 0.005$) and lower satisfaction ($p = 0.018$) at the time of the survey than the patients without NP. **Conclusion:** The estimated prevalence of NP was 14%. Patients with NP reported higher levels of disability as early as 1 year after surgery. They remained more disabled, with a higher level of depression and less satisfaction, at an average of 5 years after surgery.

Key Words: arthroplasty, knee; mobility limitation; neuropathic pain.

RÉSUMÉ

Objet : Déterminer si la déclaration de douleurs neuropathiques cinq ans en moyenne après une arthroplastie totale du genou (ATG) est liée à l'âge, au sexe ou à la comorbidité préopératoire, l'auto-efficacité concernant l'arthrite ou l'invalidité du patient avant la chirurgie et un an après celle-ci. L'estimation de la prévalence de douleurs neuropathiques et les différences transversales entre les groupes ont été examinées cinq ans après l'opération. **Méthodes :** Un sous-échantillon de participants à une étude officielle ont été joints par courriel environ cinq ans après avoir subi leur opération, et quatre questionnaires leur ont été envoyés: le Western Ontario et McMaster sur l'arthrose (WOMAC), le Questionnaire sur la santé du patient (QSP-9), l'auto-évaluation de Leeds des signes et des symptômes neuropathiques (A-ELSSN) et un questionnaire sur la satisfaction. Les douleurs neuropathiques étaient définies comme étant un résultat de ≥ 12 à l'A-ELSSN. **Résultats :** Parmi les 89 patients qui répondaient aux critères d'inclusion, les données de 63 (71 %) d'entre eux (47 femmes; âge moyen de 67 ans [ET 8]) ont été utilisées aux fins d'analyse. Parmi ces 63 personnes, 9 (14 %) avaient déclaré souffrir de douleurs neuropathiques. D'après la plupart des récents dossiers médicaux, personne n'avait signalé une défaillance de la prothèse ou d'autres complications chirurgicales. Il n'y avait aucun lien entre les caractéristiques préopératoires des patients et le développement de douleurs neuropathiques. Toutefois, le groupe souffrant de douleurs neuropathiques avait en moyenne signalé dans une proportion plus forte des raideurs ($p = 0,020$), une dysfonction physique ($p = 0,019$) et des douleurs ($p = 0,050$) un an après la chirurgie. Au moment de l'enquête, les comparaisons transversales ont fait état de degrés élevés de douleurs ($p = 0,001$), de raideurs ($p = 0,008$), de dysfonction physique ($p = 0,003$) et de dépression ($p = 0,005$), ainsi que d'un degré inférieur de satisfaction ($p = 0,018$) par rapport aux patients ne souffrant pas de douleurs neuropathiques. **Conclusion :** La prévalence estimée de douleurs neuropathiques était de 14 %. Les patients souffrant de douleurs neuropathiques ont signalé des niveaux supérieurs d'invalidité dès la première année suivant la chirurgie. Leur invalidité s'était accrue; ils souffraient davantage de dépression et étaient moins satisfaits, cinq ans en moyenne après la chirurgie.

From the: *Department of Rehabilitation and †Department of Orthopedic Surgery, Holland Orthopaedic and Arthritic Centre, Sunnybrook Health Sciences Centre; ‡Department of Physical Therapy and §Division of Orthopaedic Surgery, Department of Surgery, University of Toronto, Toronto.

Correspondence to: Helen Razmjou, Holland Orthopaedic and Arthritic Centre, 43 Wellesley St. East, Toronto, ON M1Y 1H1; helen.razmjou@sunnybrook.ca.

Contributors: Helen Razmjou conceived the idea, designed the study, supervised data extraction and entry, performed data analysis, and drafted the manuscript. Dragana Boljanovic assisted with study design and data collection. Stewart Wright, John Murnaghan, and Richard Holtby performed the surgical procedures. All authors critically revised the article and approved the final draft.

Competing Interests: None declared.

A modified version of this study was presented as an abstract at the eighth combined meeting of the Orthopaedic Research Societies in Venice, Italy, October 2013.

Acknowledgements: The authors thank Kamelia Rostami for her contribution to this study.

Physiotherapy Canada 2015; 67(4):311–318; doi:10.3138/ptc.2014-46

Total knee arthroplasty (TKA) is an effective means of relieving pain and improving function for people with osteoarthritis (OA)^{1–4} and remains one of the most common elective procedures in North America and Europe.⁵ However, some people continue to suffer from ongoing chronic postoperative pain.^{6,7} A systematic review of the prevalence of persistent pain published in 2012 found that between 10% and 34% of people report significant chronic pain after TKA.⁸ It has been reported^{9–12} that a subset of patients with chronic postoperative pain present with clinical signs of neuropathic pain (NP). NP has different characteristics than other types of pain.^{9–12} NP may or may not involve actual damage to the nervous system; it is frequently experienced as being similar to burning or electric shock and is commonly characterized by allodynia (pain caused by a minor stimulus such as light touch). Nociceptive pain, however, is caused by irritation or injury to nociceptors, which respond to actual tissue damage by transmitting pain signals to the brain. Nociceptive pain is usually well localized and constant and often has an aching or throbbing quality. Nociceptive pain typically resolves once the inflammation or tissue damage is healed, whereas NP may persist for months or years after the apparent healing of any damaged tissues.

The pain associated with OA appears to be a combination of nociceptive¹³ and neuropathic pain.^{14–17} Both Haroutiunian and colleagues¹⁸ and Wylde and colleagues¹⁹ have noted that approximately 6% of patients present with symptoms characteristic of NP after TKA. Some authors have reported a higher prevalence (21% at 1 mo and 13% at 3 and 6 mo after TKA surgery).¹⁷

Postoperative pain may affect both physical and mental components of quality of life (QOL)²⁰ and influence physical function and self-rated recovery.²¹ Because NP symptoms are a significant contributor to increased disability, poorer QOL, and greater use of health care services,^{22,23} patient characteristics, predisposing factors, and time frame between surgery and NP development warrant further research.

The primary purpose of our study, therefore, was to determine whether a person's likelihood of reporting NP at an average of 5 years after TKA was related to age, sex, preoperative comorbidity, arthritis self-efficacy, or disability before surgery and at 1 year after surgery. Secondary purposes were to estimate the prevalence of NP and to explore cross-sectional group differences 5 years after surgery.

We hypothesized that patients experiencing NP at 5-year follow-up might show distinct characteristics before surgery and at 1 year after surgery and that the NP group would have higher levels of disability and depression and lower satisfaction with surgery at 5-year follow-up.

METHODS

Our study population consisted of people who had undergone a primary unilateral TKA in the past and had

participated in a formal study. For this study, we chose a subsample of patients with complete preoperative demographic and disability data whose surgeries had been performed by one of three surgeons. The study protocol was approved by the Human Ethics Research Board of the Sunnybrook Health Sciences Centre.

A total of 89 people met the inclusion criteria. We began by sending a letter describing the nature of the study to all candidates by postal mail; a second letter enclosing the four questionnaires (see below) was mailed approximately 10 days later. Patients who did not respond received a reminder approximately 2 months after the initial mailing.

The second letter included four questionnaires: the Self-Administered Leeds Assessment of Neuropathic Symptoms and Signs Pain Scale (S-LANSS),²⁴ the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC),²⁵ the Patient Health Questionnaire (PHQ-9),²⁶ and a satisfaction survey. We reviewed the medical records of participants who met the criteria for NP to rule out any prosthetic failure or other medical condition that might have contributed to chronic NP. In addition, to distinguish between subjective and objective stiffness, we obtained the actual knee range of motion (ROM) documented by the attending physical therapist at 1-year follow-up for these participants.

Dependent variable

The S-LANSS was used to identify NP at the time of the survey (an average of 5 y after TKA surgery). The S-LANSS, a seven-item questionnaire that returns scores ranging from 0 to 24,^{27,28} shows a diagram of the human body (anterior and posterior) on which respondents are asked to identify the exact location of pain. The time frame is limited to the past week. Previous studies have suggested that scores of 12 or more indicate NP.^{28,29} This measure has been shown to be valid and reliable for identifying NP.²⁴

Independent variables

Independent variables (predictors of NP at 5 y) were patient demographics (sex, age); presence of comorbidity before surgery; preoperative level of self-efficacy;³⁰ and disability, as measured by the WOMAC,²⁵ both before and 1 year after surgery. This information was available from previously collected data.

Presence of comorbidity was documented as yes or no in eight areas (heart or lung conditions, hypertension, diabetes, low back pain, thyroid conditions, and history of stroke or cancer).

Self-efficacy was measured using the Function subscale of the Arthritis Self-Efficacy Scale,³⁰ which consists of nine items asking respondents about their ability to execute certain functions. Each item is scored on a scale ranging from 10 to 100 on which higher scores correspond to greater self-efficacy. This measure has been validated in people with OA.^{31,32}

Disability was measured using the WOMAC, a self-report measure commonly used with people with hip and knee OA that consists of 24 items in three domains: pain (5 items), stiffness (2 items), and physical function (17 items).²⁵ The answers are equally weighted and reported as sums; higher numbers indicate greater levels of symptom or disability. Sub-scale scores can take the following range of values: function, 0–68; pain, 0–20; and stiffness, 0–8.²⁵ WOMAC has been used for more than 2 decades and is reported to have acceptable measurement properties in people with OA of the knee.^{33–36}

Cross-sectional comparisons

We used the PHQ-9 to identify depressive and other mental disorders commonly encountered in primary care and among people with OA.²⁶ The PHQ-9 is a self-administered nine-item questionnaire with scores varying from 0 to 27, representing different levels of depressive moods or behaviours. It has been shown to be valid for people with musculoskeletal complaints and OA of the knee joint.^{37–41}

In addition, we asked all participants, “How satisfied are you with the results of your surgery?” Participants rated their satisfaction level on a 6-point Likert-type scale: *very satisfied*, *somewhat satisfied*, *a little bit satisfied*, *a little bit dissatisfied*, *somewhat dissatisfied*, and *very dissatisfied*.

Statistical analysis

We calculated descriptive statistics for sex, age, and time between surgery and survey. For the primary purpose, we used univariate logistic regressions to examine the relationship between NP development at an average of 5 years after TKA and individual predictors (age, sex [male or female], and preoperative and 1-year postoperative WOMAC domains [pain, stiffness, physical function, arthritis self-efficacy score, and comorbidity; yes–no]). We calculated an estimate of prevalence (a secondary purpose of our study) as the number of NP cases divided by the total number of participants, calculating both point and interval estimates (95% CI) of the prevalence of NP. Because our study was limited to a small sample of TKA patients available for surveying, our binominal sample-size calculation for estimating prevalence was based on a formula suggested by Daniel:⁴²

$$n = \frac{Z^2 P(1 - P)}{d^2}$$

where Z is the Z statistic for a level of confidence (1.96 for 95% CI), P is the expected prevalence, and d is precision.

Reported prevalence of NP after TKA varies from 6%¹⁹ to 28%,⁴³ depending on the time frame and population being studied. With a moderate precision of 10% (width of CI = $2d$), the sample size would vary from 22 to 62. We therefore felt that a sample of at least 62 patients would be required.

For our third purpose, we examined cross-sectional group differences at 5 years after surgery using Wilcoxon two-sample tests for non-normally distributed continuous data and Fisher's exact test for categorical data. Our statistical analyses used SAS version 9.1.3 (SAS Institute, Cary, NC). Statistical results are reported using two-tailed p values, with significance set at $p < 0.05$.

RESULTS

We sent introductory letters to 89 patients, of whom 3 had died and 6 were lost to follow-up because of change of address. Of the remaining 80 candidates, 3 declined and 12 did not respond after a second reminder. Thus, 65 patients participated in the study (a 73% response rate). After reviewing the pain questionnaires, we excluded 2 patients with discogenic referred pain. Data for 63 patients (47 women [75%] and 16 men [25%]; mean age 67 [SD 8] years, range 43–80 years) were used for analysis (see Figure 1). Mean time elapsed between surgery and final data collection was 5 (SD 0.35) years.

Estimated prevalence and predictors of neuropathic pain

On the basis of their S-LANSS scores, nine participants were identified as having neuropathic pain (NP group), for an estimated prevalence of 14% (95% CI, 1.93–16.07). Mean S-LANSS scores were 16.44 (SD 3) for the NP group and 1.1 (SD 3) for the non-NP group. Electronic and paper chart review (including most recent radiographs and follow-up reports) for participants with NP found no indications of prosthesis failure or other surgical complications.

We found no relationship among age, sex, preoperative comorbidity, or disability and development of NP ($p > 0.05$), but the NP group did report higher levels of pain, stiffness, and physical dysfunction 1 year after surgery than the non-NP group (see Table 1).

Cross-sectional group differences

Cross-sectional comparisons at the time of the survey showed statistically significant between-groups differences on the PHQ-9 and all three domains of the WOMAC; the NP group reported more pain, stiffness, physical dysfunction, and depression. Moreover, although 91% of participants without NP said they were very satisfied with their surgery, only 56% of participants with NP did so. (No one in either group reported being very dissatisfied.) Table 2 shows postoperative scores for all outcome measures and distribution of satisfaction categories.

DISCUSSION

Etiology of neuropathic pain

Postoperative persistent NP has become a subject of interest in the past decade. Unfortunately, the exact nature of this problem remains unclear. Mechanisms for increased acute pain leading to NP may involve either peripheral or central sensitization. In the early stages of healing after TKA surgery, surgery-related inflammation

Figure 1 Diagram of recruitment.

or damage to tissues is expected to produce nociceptive pain; the question of why some patients develop persistent NP has not yet been clearly answered. Lavand'homme and colleagues⁴⁴ were able to establish an association between severity of pain during the initial stages of recovery (days 3–8) and the existence of NP-like symptoms at 3 months after surgery, which may indicate that severe symptoms in the acute phase of recovery can predispose the nervous system to perceiving NP later on.

Local nerve damage after surgery is a hypothesis that has not been clearly tested because of the complexity of detecting such subtle damage to the knee joint after surgery. It has been speculated that the infrapatellar branch of the saphenous nerve, which innervates the skin below the patella and the anterior inferior knee capsule,⁴⁵ may be injured during TKA.¹⁴ Intra-operative nerve damage

to peroneal and tibial nerves may also occur during TKA.^{46,47} Jacob and colleagues⁴⁸ found that increased tourniquet time and bilateral TKA procedures contributed to development of nerve injury; they suggested that the use of peripheral nerve block may impede complete neurological recovery. Valdes and colleagues¹⁴ found a higher rate of NP among people with a history of previous knee surgery (arthroscopic repair, meniscectomy, or joint replacement). In our study, review of routine post-surgical radiological findings and clinical examination documented by the clinicians, including ROM, showed no evidence of prosthesis failure or other surgical complications. However, a lack of evident surgically induced damage does not necessarily rule out subtle dysfunction of the sensory nerves, and more objective tools such as electroneuromyography are required to document this potential cause of NP.

Prevalence of neuropathic pain

In our study, the prevalence of NP symptoms was 14% in people who had undergone a primary TKA an average of 5 years earlier. Our findings indicate that NP is a problem that can exist without any obvious clinical or radiological evidence of failure. A small study by Pinto and colleagues⁴⁹ reported a 49% prevalence rate of NP (19 of 39) in the early phase of recovery at 4–6 months after TKA, based on scores on a shortened version of the Neuropathic Pain Questionnaire. In a study similar to ours, Boljanovic-Susic,⁴³ who surveyed 67 of 148 patients with chronic pain after total joint arthroplasty (including 42 patients with TKA), reported a 28.4% prevalence of NP, based on S-LANSS at a maximum of 3.5 years after surgery. The higher rate of NP in this study is due to using patients with chronic pain, compared with our study, which surveyed all patients after TKA. Laveand'homme and colleagues⁴⁴ reported a prevalence of 11% at 3 months after TKA, and Philips and colleagues⁵⁰ reported a prevalence of 14% (possible and likely NP) at 46-month follow-up. Harden and colleagues¹⁷ reported a prevalence of 13% at 3 and 6 months after surgery; Haroutianian and colleagues¹⁸ and Wylde and colleagues¹⁹ reported lower prevalences (5.7% at 6–96 mo after surgery and 6% at 3–4 y after surgery, respectively). Differences in assessment tools, post-surgical time frames, and samples studied may explain the slight discrepancies among these studies.

Characteristics of patients with neuropathic pain

In our study, age and sex did not predict the development of NP. These findings are consistent with those of two studies^{19,44} and a master's thesis⁴³ that found no relationship between sex and age and NP symptoms. Valdes and colleagues¹⁴ found that among people with OA of the knee, patients with NP were slightly younger (61 vs. 65 y); however, a sample with varying degrees of OA should be expected to show more variability in age than a sample restricted to those who have undergone TKA. Similar to sex and age, preoperative comorbidity,

Table 1 Univariate Logistic Regressions: Relationship between Neuropathic Pain (Dependent Variable) and Predictors

Independent variable	Estimate	R^2_1	OR (95% CI)	Wald χ^2 value	<i>p</i> -value
Age	−0.05	0.02	0.95 (0.88–1.03)	1.36	0.241
Sex		0.03	0.36 (0.083–1.54)	1.90	0.168
Female	−0.51				
Male	0.00				
Arthritis self-efficacy	0.003	0.02	1.00 (0.99–1.00)	1.24	0.264
Comorbidity	1.00	0.03	2.72 (0.65–11.4)	1.86	0.172
Preop WOMAC					
Pain	0.09	0.01	1.09 (0.88–1.35)	0.67	0.413
Stiffness	0.26	0.02	1.30 (0.08–2.07)	1.18	0.278
Physical function	0.03	0.02	1.03 (0.97–1.10)	1.17	0.279
1-year WOMAC					
Pain	0.25	0.08	1.29 (0.99–1.66)	3.82	0.050
Stiffness	0.11	0.12	1.93 (1.12–3.36)	5.51	0.020
Physical function	0.10	0.12	1.11 (1.02–1.21)	5.37	0.019

OR = odds ratio point estimate; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index.

Table 2 Cross-Sectional Group Differences at an Average of 5 Years

Variable	No NP (S-LANSS < 12; <i>n</i> = 54)	NP (S-LANSS ≥ 12; <i>n</i> = 9)	<i>p</i> -value (between-groups differences)*
WOMAC (final), mean (SD)			
Pain	1.50 (2)	5.33 (3)	0.001
Stiffness	1 (1)	4.33 (6)	0.008
Physical function	6.94 (8)	19.33 (12)	0.003
Final PHQ-9	2 (4)	7 (6)	0.005
Postoperative satisfaction, no. (%)			0.018‡
Very satisfied	49 (91)	5 (55)	
Somewhat satisfied	3 (5)	3 (33)	
A bit satisfied	2 (4)	0	
Somewhat dissatisfied	0	1 (11)	
A bit dissatisfied	0	0	
Very dissatisfied	0	0	

Note: Wilcoxon two-sample tests were used for continuous data and Fisher's exact test was used for categorical data.

*Unless otherwise indicated.

‡Very satisfied was compared with all other categories

NP = neuropathic pain; S-LANSS = Self-Administered Leeds Assessment of Neuropathic Signs and Symptoms; WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index; PHQ-9 = Patient Health Questionnaire–9.

including diabetes, was not associated with NP in our sample.

Higher level of disability before surgery does not appear to be related to NP development later on. A study by Philips and colleagues,⁵⁰ who prospectively examined patients for an average of 3 years after surgery, suggested that preoperative scanning might not be useful for detecting future NP development. Similarly, in our study patients with NP did not have higher scores on the WOMAC sub-scales before surgery.

Lower self-efficacy also did not predict the development of neuropathic pain. Wylde and colleagues,⁵¹ in their study of 251 TKA patients at 1 year after surgery, found that self-efficacy significantly predicted functional ability but not pain; van den Akker-Scheek and colleagues⁵² found that self-efficacy had a positive influence

on walking speed after TKA but did not influence perceived function. A recent systematic review of the impact of self-efficacy in people undergoing joint replacement found no conclusive evidence that self-efficacy influences functional recovery outcomes.⁵³

At the time of our survey, the NP group reported higher levels of depression and lower levels of overall satisfaction with surgery. Other studies have found that major depression, anxiety, and higher disability are significantly and independently associated with persistent pain after TKA.^{19,43,54,55}

At 1 year and at approximately 5 years after surgery, the NP group in our study reported higher levels of pain, stiffness, and physical dysfunction as measured by domains of the WOMAC. The higher report of stiffness did not correlate with the actual knee ROM measured

by the attending physical therapist at 1-year follow-up, which highlights the subjective nature of these symptoms. Our results are consistent with those of two cross-sectional studies^{14,19} using WOMAC scores. In Valdes and colleagues' study,¹⁴ patients with NP had higher WOMAC sub-scale scores cross-sectionally, which is expected. Wylde and colleagues,¹⁹ who used the pain sub-score of the WOMAC, reported persistent pain in 44% of patients after TKA. Our longitudinal study found an association between perceived pain, physical dysfunction, and stiffness and NP as early as 1 year after surgery. We hypothesize that apart from pain and difficulty functioning, tightness and stiffness may in fact be a component of a more complex abnormal NP-type pain.

Satisfaction with surgery has been explored in one previous study,⁵⁰ which reported that among dissatisfied patients, more than 80% had high levels of pain and 45% had possible NP. None of our participants reported dissatisfaction, but the NP group was less likely to be very satisfied with surgery.

LIMITATIONS

Our study has several limitations. First, we used data from patients of surgeons specializing in total knee reconstruction in an academic centre, which may limit the applicability of our results. Second, our study was based on self-report tools; including objective sensory assessment can be expected to improve accuracy in diagnosing NP. Third, cohort studies are problematic with respect to power analysis when the condition of interest is rare; our study had a small sample size, and our results should be viewed with caution. Future research should use a case-control or prospective study design, with larger samples and more frequent post-surgical follow-ups, to better represent prevalence and detect the more accurate timing of NP development and its predisposing factors.

CONCLUSIONS

The prevalence of NP was estimated at 14% in our sample at 5 years after TKA. Participants with NP reported higher levels of pain, stiffness, and physical dysfunction as early as 1 year after surgery that continued up to an average of 5 years after surgery. NP was also associated with higher levels of pain, disability, and depression 5 years after surgery. By identifying factors that distinguish patients with NP early in the process of recovery, clinicians may be able to better manage this disabling condition in the long term.

KEY MESSAGES

What is already known on this topic

The previous literature has identified the existence of neuropathic pain (NP) after total knee arthroplasty (TKA). Prevalence of severe persistent NP is relatively

low; because of the dramatic increase in joint-replacement surgeries over the past 2 decades, however, this number translates to a considerable number of people with ongoing severe symptoms.

What this study adds

Our study confirms the existence of NP after TKA. People with symptoms of NP at 5 years after surgery show distinct differences in pain, stiffness, and physical function as early as 1 year after surgery, which may indicate a need for early intervention. These high-risk patients may be identifiable early in the postoperative period and could benefit from preventive strategies.

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