Synovitis after Total Knee Arthroplasty: Possible Cause of Residual Postoperative Pain (Preliminary Study)

Natsuki Sugimura (jm-snatsuki@kochi-u.ac.jp)  
Kochi University

Koji Aso  
Kochi University

Masashi Izumi  
Kochi University

Masahiko Ikeuchi  
Kochi University

Research article

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Abstract

Purpose: The cause of residual pain after total knee arthroplasty (TKA) was unknown. Little attention has been given to postoperative synovitis as a cause of unexplained residual pain after TKA. Here we preliminarily investigated the relationship between synovitis after TKA and pain with ultrasonography.

Methods: This study was conducted using convenient outpatient samples followed for TKA. Synovitis was assessed with ultrasonography. We originally made synovitis scores, which are a summation of the synovitis grade in the entire knee. Pain assessments including rest, moving pain visual analog scale (VAS) and WOMAC score and its subscale were evaluated. Correlations between synovitis scores or the maximum grade and pain assessments were analyzed. Pressure pain thresholds (PPTs) on synovitis were evaluated.

Results: 46 knees in 37 patients (34 female, 3 male) were evaluated. Synovitis scores correlated with rest and moving VAS (r = 0.439; 0.355, p = 0.002, 0.016). PPTs on positive synovitis significantly decreased compared with grade zero (average PPTs (SD) on grade zero, one, two = 484(21), 255(13), 268(20) kPa; p < 0.001).

Conclusion: Synovitis after TKA was associated with residual unexplained pain. Ultrasonography and synovitis scores should be available to evaluate synovitis after TKA.

Background

Total knee arthroplasty (TKA) is one of the most common and successful orthopaedic surgeries performed throughout the world. The number of TKA has been increasing exponentially and will continue to grow along with the aging population. Most patients with severely damaged knees can benefit greatly in their quality of life following TKA. Although good pain relief can be achieved with TKA, a significant proportion of patients experience residual pain that is the leading cause of dissatisfaction after TKA. A systematic review of recent studies showed that 10–34% of patients complain of residual pain [1].

Common etiologies of residual pain include implant malpositioning, aseptic loosening of prosthesis, instability, and infection. Although most of these etiologies can be diagnosed with radiological images and laboratory analysis, up to 13% of patients with residual pain have unexplained pain [2] [5]. It has been well established that synovitis causes joint pain in various joint diseases including osteoarthritis and rheumatoid arthritis. Unlike rheumatoid arthritis, synovitis associated with osteoarthritis is considered secondary to cartilage wear. Therefore, it is likely that preoperative synovitis subsides after TKA. However, there are a few reports describing postoperative synovitis in painful TKA such as patella clunk syndrome [3, 17] and recurrent hemarthrosis [13, 14]. Synovitis was incidentally observed when they treated the etiologies of painful TKA. Thus far, little attention has been given to postoperative synovitis as a cause of unexplained residual pain after TKA. We hypothesized that postoperative synovitis could be a common finding after TKA, and could be associated with residual pain in patients where painful TKA etiology is...
absent. Herein, we preliminarily examined replaced joints using ultrasonography and investigated the relationship between ultrasound synovitis and residual pain in patients who underwent TKA.

**Materials And Methods**

**Study design and Patient Selection**

This exploratory study was conducted on convenient samples of patients to obtain the available primary data of synovitis after TKA. The patients were recruited in the outpatient clinic of our department between September 2017 and October 2019. Patients were informed of this study, and consented to participate. The inclusion criteria were 1) diagnosed with osteoarthritis preoperatively and 2) at follow-up more than one year later. The exclusion criteria were 1) diagnosed with rheumatoid arthritis preoperatively and 2) displaying no obvious painful TKA etiologies such as infection, malalignment, instability, aseptic loosening of component, patella clunk syndrome, hemarthrosis etc.

All procedures used in this research were approved by the Ethical Review Board of Hata Prefectural Hospital (IRB number 31–280).

**Clinical evaluation**

Demographic data were collected, including age, gender, and the period post-surgery. The symptoms were evaluated by questioning the patient (WOMAC score) and a rest and moving pain visual analog scale (VAS). The WOMAC score is a concise questionnaire about the clinical symptoms and physical limitations for postoperative evaluation of the knee. The WOMAC score comprises three subscales, including pain (five items, 0–20 points), joint stiffness (two items, 0–8 points) and physical function (17 items, 0–68 points) —and has a minimum score of 0 (best score) and a maximum score of 96 (worst score). The WOMAC form was translated and adapted to our cultural settings. Pain was evaluated with a 100 mm VAS where 0 indicates no pain, whereas 100 indicates intractable pain.

**Ultrasonographic Evaluation of Synovitis**

To have images of the synovitis, we adopted power Doppler ultrasonography (PDUS) rather than gray scale or magnetic resonance imaging, because of its higher concordance with pathological synovial change than gray scale or magnetic resonance imaging [18]. All ultrasonographic evaluations were conducted by a single experienced orthopaedic doctor (N.S. with 12 years’ experience in musculoskeletal imaging). Knee joints were examined by patellofemoral transverse, lateral longitudinal and medial longitudinal scanning at the neutral supine position using a 18 MHz electronic linear transducer (HI VISION Preirus, Hitachi Tokyo, Japan). The findings of synovitis in PDUS were assessed with the standard settings according to recommendations [9, 15]. Pulse repetition frequency was 800 Hz, Doppler frequency 7.5 MHz and Doppler gain to avoid random noise was used. PD signal, which represents vascularity in the synovial tissue, also grading from 0 to 3 as follows; grade 0: normal (undetectable power Doppler vessel signals in ultrasonographic synovial thickening area), grade 1: mild (intrasynovial
power Doppler flow signal distribution was detectable over < 25%), grade 2: moderate (< 50%), grade 3: marked (> 50%). Positive PD signal at quadriicipital and or patellar entheses were excluded.

Since the knee joint is spacious, to evaluate severity of synovitis of the knee joint we originally devised a scoring system for synovitis of the knee with ultrasonography. Firstly synovitis knee mapping was developed to evaluate localization of synovitis. There are 15 areas with grid lines in this knee synovitis mapping; 1 supra-medial, 2 infra-medial, 3 supra, 4 supra-lateral, and 5 infra-lateral patellofemoral joint, 6 supra-patellar porch, 7 antero-medial, 8 postero-medial, 9 antero-lateral, and 10 postero-lateral tibial plateau, 11 antero-medial, 12 postero-medial, 13 antero-lateral, 14 postero-lateral femoral condyle, and 15 posterior patellar tendon (Fig. 1). The synovitis grade of each area was recorded. The synovitis score was calculated as a summation of all synovitis grades.

**Inter-observer reliability**

For inter-observer reliability, another orthopaedic doctor (K.A. with 13 years’ experience in musculoskeletal imaging) independently assessed ultrasonographic examinations in 60 areas of four patients.

**Pressure Pain Threshold**

To investigate the direct relationship between synovitis and local pain, we evaluated pressure pain thresholds (PPTs). A handheld pressure algometer (Somedic, Hörby, Sweden) mounted with a 1-cm² probe (covered by a disposable latex sheath) was used to record the PPT on a mark where the synovitis was observed with ultrasonography. An interval of at least 20 seconds was kept between each PPT assessment. The PPT was defined to the subject as “the time point at which the pressure sensation changed into pain.” Pressure was increased gradually at a rate of 30 kPa/s until the pain threshold was reached and the subject pressed a button.

**Radiographical Evaluation**

The standing anteroposterior radiographs of the lower extremities, lateral radiographs, and skyline patellar radiographs were taken of the outpatients. The orientation of the components and sagittal alignment were measured according to the method of Ewald [6] as α° (coronal femoral angle, optimum, 96), β° (coronal tibial angle, optimum, 90). Varus and valgus stress radiography in extension with maximum manual force was performed by a single orthopaedic doctor (NS). All alignment data were measured using PACS digital radiographic software (Synapse5, Fujifilm, Tokyo, Japan). Knee with a malalignment of over 5 degrees were excluded.

**Statistical analysis**
Descriptive statistics were used for all variables with distributions assessed. All data are expressed as the mean ± standard deviation (SD). For assessment of relationships between synovitis and pain, association between maximum synovitis grade or synovitis score and rest or moving pain VAS or WOMAC score were determined using Spearman's rank correlation coefficient.

One-way analysis of variance (ANOVA) was performed on PPTs using the synovitis grade. The Tukey-Kramer (TK) tests were used for post hoc comparisons incorporating corrections for the multiple comparisons when ANOVA showed significant factors or interactions. The difference was considered to be statistically significant at the P < 0.05 level. Inter-observer reliability was assessed using intraclass correlation coefficient (ICC) for synovitis scores, and kappa statistics for frequency of each ultrasonographic finding. The degree of agreement based on the ICC and kappa values was interpreted using the following criteria: 0–0.20 poor, 0.21–0.40 fair, 0.41–0.60 moderate, 0.61–0.80 good, and 0.81–1.00 excellent[11].

All analysis was performed using JMP 10.0 software (SAS Institute Inc. Cary, NC, USA).

**Results**

**Demographic data**

Conventional 49 knees in 40 Japanese patients (46 female, 3 male) were evaluated. Three patients with a malalignment of over five degrees were excluded and 46 knees in 37 patients (34 female, 3 male) were included in this study. All patients underwent TKA for knee osteoarthritis. Demographic data is shown in Table 1.

**Incidence and Location**

Synovitis was observed in 89% of patients. Maximum synovitis grade one and two was observed in 46% and 43%, respectively. Grade three was not observed. Mean synovitis score was 4.3 ± 4.2.

The prevalence rate of synovitis in synovial mapping is shown in Fig. 2. Among patients with synovitis, the highest prevalence (41%) of synovitis was observed at antero-lateral tibial plateau (area 11), followed by supura-lateral patelo-femoral area (area 4) (35%), infra-lateral patelo-femoral area (area 5) (33%), antero-lateral femoral area (area 13) (33%), postero-lateral femoral area (area 14) (31%).

The ICC value between observers was 0.821 for grade of synovitis. Based on the ICC value, the inter-observer reliability was considered to be excellent.

**Relationship between pain and synovitis**

Synovitis scores correlated with rest and moving VAS (r = 0.439; 0.355, p = 0.002, 0.016) (Fig. 3). Maximum synovitis grades did not correlate with any pain evaluation.
The ANOVA of PPTs demonstrated a significant group factor indicating that PPTs significantly decreased in positive synovitis grades compared with grade zero (Fig. 4; average PPTs (SD) on grade zero, one, two = 484(21), 255(13), 268(20) kPa; ANOVA: p < 0.001; TK: p < 0.001). There was no significant difference between grade one and two (p = 0.862).

Discussion

The notable results in this study were that there was a correlation between rest and moving pain VAS with a decrease in synovitis scores and PPTs on synovitis area. These results indicate synovitis after TKA exists consistently with pain. This is the first report about association between residual pain and synovitis after TKA. In osteoarthritis, synovitis and bone marrow lesions are the primary pathologic lesions that have been consistently associated with pain [7, 8, 19]. Generally the cause of residual pain after TKA is considered to be neural sensitization [10, 16]. In addition, synovitis is more strongly associated with pain sensitization than bone marrow lesion [12]. Thus synovitis after TKA is said to be another important cause of residual pain in terms of not only the direct inflammatory pain but also sensitization. Although postoperative residual pain including sensitization after TKA is multifactorial, patients with residual pain after TKA should be examined with ultrasonography to detect synovitis in addition to undergoing a physical examination and conventional radiography.

We originally devised synovitis mapping of the knee and synovitis scores because the knee is spacious compared with small joints which are generally associated with rheumatoid arthritis for which the synovitis grade was developed [15]. Synovitis scores correlated with pain, although the maximum synovitis grade did not. This result suggests the efficacy of the synovitis score for evaluation of entire knee inflammation. In a magnetic resonance imaging study on osteoarthritis patients, larger bone marrow lesions are associated with greater knee pain [4]. This study suggested the efficacy of a summation of each grade across the entire knee joint to evaluate entire knee pain.

There are some limitations to this study. First, because we used convenient samples, this study does not qualify, strictly speaking, as a cross-sectional study. Therefore it is supposed that mean moving pain VAS of our samples was over twenty, in addition prevalence rate of synovitis was as high as 89%. This study is considered preliminary, and a rigorous cross-sectional study will be necessary to reveal the epidemiology of synovitis after TKA. Secondly, although the observation methods of synovitis are generally not only ultrasonography, but contrast-enhanced magnetic resonance imaging, single photon emission computed tomography, or historical examination. Takase et. al. simultaneously assessed ultrasonography and magnetic resonance imaging in comparison with histopathological changes in the knee joints of long-lasting arthritis patients [18]. Because positive power Doppler ultrasonography findings were closely associated with all pathological comportments of synovitis including inflammatory cell infiltrates, synovial lining layer thickness and vascularity, they concluded both imaging techniques are useful for the visualization of synovitis. Thirdly, there was a lack of significant information on the possible causes of synovitis: for example, existence of preoperative synovitis, synovectomy in primary surgery, changes in synovitis activity over the course of time, soft tissue balance, or implant design. To
investigate the causes of synovitis after TKA, researchers will need to conduct a longitudinal study that includes these items. To investigate the pathology of synovitis after TKA, arthroscopic synovectomy may be useful if severe synovitis is observed in ultrasonography [3].

Conclusions

Synovitis after TKA was associated with residual pain. Ultrasonography and synovitis scores should be available to evaluate synovitis after TKA.

Abbreviations

Total knee arthroplasty: TKA, visual analog scale: VAS, power doppler ultrasonography: PDUS, pressure pain thresholds: PPTs

Declarations

Ethics approval and consent to participate
All procedures used in this research were approved by the Ethical Review Board of Hata Prefectural Hospital (IRB number 31-280). All patients was informed about this study by N.S. and consented to participate in this study.
Consent for publication
Not applicable.
Availability of data and materials
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.
Competing interests
The authors have no conflicts of interest to declare.
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Authors’ contributions
N.S designed the experiments. N.S. and M.I. wrote manuscript. N.S. and A.K. performed experiment. N.S., K.A., M.I., and M.I. analyzed and interpreted results. M.I. directed the study.

Acknowledgements
Not applicable.

References


Table

Due to technical limitations, Table 1 is only available for download from the Supplementary Files section.

Figures

Figure 1

Fifteen areas with grid lines in the knee synovitis mapping; 1 supra-medial, 2 infra-medial, 3 supra, 4 supra-lateral, and 5 infra-lateral patellofemoral joint, 6 supra-patellar porch, 7 antero-medial, 8 postero-medial, 9 antero-lateral, and 10 postero-lateral tibial plateau, 11 antero-medial, 12 postero-medial, 13 antero-lateral, and 14 postero-lateral femoral condyle, and 15 posterior patellar tendon.
Figure 2

Synovitis mapping. Figures represent percentage of synovitis recognized.
Figure 3

Correlation between synovitis and pain. Synovitis scores correlated with rest pain VAS and moving pain VAS. r: coefficient of correlation.
Pressure pain thresholds (PPTs) on synovitis. PPTs significantly decreased on grade one and two synovitis (*: p<0.01)

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- Table1.JPG