



Comparison of proprioception between osteoarthritic and age-matched unaffected knees: a systematic review and meta-analysis

Sung-Sahn Lee¹ · Hyun-Jung Kim² · Donghee Ye³ · Dae-Hee Lee³

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Abstract

Purpose Theoretically, proprioceptive acuity could decrease in patients with knee osteoarthritis. However, there have been conflicting results in terms of proprioceptive deficit in osteoarthritic knees. The purpose of this systematic review and meta-analysis was to compare knee proprioception between osteoarthritic and healthy control knees.

Methods Studies comparing proprioception in osteoarthritic and healthy knees of age-matched control group using thresholds to detect passive motion (TTDPM) or joint position sense (JPS) tests were identified. JPS was assessed by measuring the reproduction of passive positioning (RPP) or active positioning (RAP) of the knees.

Results Seventeen studies were finally included in this meta-analysis. The pooled results of the analyses of the TTDPM for both 30° and 45° knee flexion showed that the mean angle of error was 0.83° greater (95% confidence interval: 0.44 to 1.23°; $p < 0.001$) in the osteoarthritic knees than in control knees. The pooled data of the RAP and RPP also showed that the mean angle of error was 1.89° greater in the osteoarthritic knees than in the control group. The mean difference in the angle of error between the osteoarthritic knees and control group was 1.06° greater in the JPS test than in the TTDPM ($p < 0.001$).

Conclusion The knee proprioceptive acuity of the patients with knee osteoarthritis was poorer than that of the patients with unaffected knees in the age-matched control group both in terms of the TTDPM and JPS; clinical relevance of these deficits needs to be clarified in further studies.

Level of evidence Meta-analysis, Level II.

Keywords Knee · Osteoarthritis · Proprioception · Threshold to detection of passive motion · Joint position sense

Sung-Sahn Lee and Hyun-Jung Kim contributed equally to the work.

✉ Dae-Hee Lee
eoak22@empal.com

Sung-Sahn Lee
sungsahnlee@gmail.com

Hyun-Jung Kim
moole02@naver.com

Donghee Ye
bananakicknow@gmail.com

¹ Department of Orthopaedic Surgery, Ilsan Paik Hospital, Inje University School of Medicine, Goyangsi, Gyeonggi-do, Korea

² Department of Preventive Medicine, Korea University College of Medicine, Seoul, Korea

³ Department of Orthopaedic Surgery, Samsung Medical Center, Sungkyunkwan University School of Medicine, 81 Irwon-ro, Gangnam-gu, Seoul 06351, Korea

Introduction

Knee joint osteoarthritis could destroy the joint articular cartilage and change the soft tissue structures around the knee joint, including the joint capsule [45], muscles, and tendons, where the mechanoreceptors are located [2, 16, 46]. Mechanoreceptors are well known for their involvement in knee joint proprioception, which encompasses the sense of joint position and sense of joint motion [39], because these senses are particularly derived from afferent neural inputs arising from the mechanoreceptor in the joints, muscles, tendon, and associated tissues. Theoretically, proprioceptive acuity could decrease in patients with knee osteoarthritis [40, 44, 51]. However, previous studies [22, 31, 37] have yielded conflicting results regarding whether a proprioceptive deficit occurs in osteoarthritic knees, with some studies finding a significant deficit, but others reported similar proprioception

in osteoarthritic knees compared with unaffected knees of an age-matched control group. In addition, the lack of a standardized method of measuring the proprioceptive acuity has made it difficult to conclude on the proprioceptive deficit of patients with osteoarthritic knees by pooling the data of previous studies. Further, it is difficult to compare the results obtained in various studies directly, although the threshold to detect passive motion (TTDPM) has been widely used as a measure of sense of joint movement, and reproduction of active joint repositioning (RAP) and reproduction of passive joint repositioning (RPP) have been frequently used to test joint position sense (JPS) [3, 11, 28, 30, 31, 37, 51].

Therefore, the purpose of this study was to determine whether the proprioceptive acuity is actually less in osteoarthritic knees compared with that in unaffected knees of the age-matched healthy control group. In addition, this study evaluated whether the proprioceptive deficit would vary on the basis of the method of proprioception measurement, such as the TTDPM measured between 30° and 45° knee flexion and the JPS test conducted between passive and active repositioning. It was hypothesized that the proprioception in patients with osteoarthritic knees would decrease compared with that in the patients with unaffected knees in the control group with a similar age, regardless of the method used to measure knee proprioception.

Materials and methods

Literature search

The study design was based on the Cochrane Review Methods. We conducted this study according to the guidelines of the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses, S1 PRISMA Checklist) statement. The study protocol was published online at the PROSPERO International Prospective Register of Systematic Reviews (<https://www.crd.york.ac.uk/PROSPERO>) under registration number CRD42018086249. Multiple comprehensive literature databases, including MEDLINE® (January 1, 1976–June 30, 2019), EMBASE® (January 1, 1976–June 30, 2019), and Cochrane Library (January 1, 1976–June 30, 2019), were searched for studies that compared the proprioception using the TTDPM and JPS test between patients with knee osteoarthritis and control groups without knee pain. There were no restrictions on the year of publication. The search terms used were the MeSH terms “knee”, “osteoarthritis”, and “proprioception”, and the individual corresponding free terms. Relevant articles and their bibliographies were searched manually following the initial electronic search.

Study selection

Two reviewers evaluated the titles and abstracts of the obtained articles and selected relevant articles for full review. If the abstract did not provide sufficient data to make a decision, the full text of the article was reviewed [20, 47]. Studies were included in the meta-analysis if (1) they dealt with patients with knee osteoarthritis; (2) they directly compared proprioception between osteoarthritic knees (diagnosed by American Rheumatism Association (ACR) criteria [1] for knee osteoarthritis) or knees with joint pain of Kellgren–Lawrence grade [26, 38] (K–L) grade 2 or higher and knees from a healthy age-matched control group (defined as healthy subjects with no history of pain in the knee joint and K–L grade 0 or 1); (3) they regarded comparisons of the TTDPM and/or JPS, and (4) the sample number, means and standard deviations were fully reported in their study.

JPS measurements are composed by two different methods—reproduction of passive positioning (RPP) and active repositioning (RAP). The RPP is measured using an electrogoniometer. The subject’s knee was placed at predetermined angle. The subject was ordered to remember that target position. The limb was passively moved to the predetermined angle. The subject was then instructed to stop the assessor when the limb returned to targeted position. On the other hand, in the RAP measurement, the knee joint was passively placed to predetermined angle by the examiner instead of by the electrogoniometer, and then the subject was ordered to reproduce predetermined angle actively. The JPS was quantified by angle difference between targeted and indicated by the subject. TTDPM is angle between starting position and halted position which the subject feels motion of their knee, measured digitally by electrogoniometer.

Data extraction

Two reviewers independently recorded data from each article using a predefined data extraction form. If there were discrepancies between the two reviewers, they were solved via a discussion. The variables extracted included the following: (1) mean and standard deviations of the TTDPM, reproduction angle error of the knee joint compared with that of the predetermined knee position in patients with osteoarthritic knees and control groups without radiographic knee osteoarthritis; (2) demographic data including age and sex and sample size of each osteoarthritis and control group; (3) knee joint angles and angular velocity when obtaining the TTDPM and predetermined target angle in the reproduction angle of the knee joint; (4) study type (e.g., prospective or retrospective comparison studies).

Assessment of methodological quality

Two reviewers independently assessed the methodological quality of each study using the Newcastle–Ottawa Assessment Scale [53], which is designed to appraise the quality of non-randomized studies. It consisted of three domains: selection, comparability, and outcome. For the selection (four numbered items) and outcome (three numbered items) domains, each assessed study could be given a maximum of one star for each numbered item. For the comparability (one numbered item) domain, a maximum of two stars could be given. A maximum of nine stars can be awarded. Studies with scores of ≥ 7 , 5–7, 3–5, and 0–2 were considered to have good, fair, poor-fair, and poor qualities, respectively. Any unresolved disagreements between the reviewers were resolved via a consensus.

Statistical analysis

Statistical analysis of the TTDPM and JPS measurements between the osteoarthritic knees and control knees was performed. To pool primary outcomes of included studies, random-effects meta-analyses were used by estimating the weighted mean differences and 95% confidence intervals (CIs) in the JPS and TTDPM between two groups. The I^2 statistic was calculated to present heterogeneity by estimating the proportion of between-study inconsistencies. All statistical analyses were performed using the RevMan version 5.2 and Stata/MP 13.0. The risks of bias (low, high, or unclear) were independently assessed by two investigators. Publication bias was also assessed using funnel plots and the Egger's test. To test for the potential bias effect of demographic data, meta-regression analyses were performed for evaluating the affection of different demographic data (age and sex) of including studies on the differences of TTDPM and JPS.

Results

Identification of studies

Figure 1 shows the details of the study identification, inclusion, and exclusion. The electronic search yielded 178 studies in the PubMed (MEDLINE), 327 in the EMBASE, and 61 in the Cochrane Library databases. Three additional publications were identified via manual searching. After removing 196 duplicates, 373 studies remained: of these, 340 were excluded upon reading the abstracts and full-text articles, and an additional 16 studies were excluded, since they did not have usable information which were only measured proprioception other than the TTDPM or JPS, or did not compare the proprioception of the age-matched control

group. After applying these criteria, 17 studies were finally included in this meta-analysis.

Study characteristics and patient populations

The 17 included studies evaluated 327 patients with knee osteoarthritis and 333 control subjects with unaffected knees who underwent proprioception measurement using the TTDPM or JPS test. All 17 included studies were prospective comparative studies. Seven studies measured the TTDPM, and 10 measured the JPS. Of the seven studies that measured the TTDPM, two measured the TTDPM at a knee flexion of 30°, and five measured the TTDPM at a knee flexion of 45°. Of the ten studies that measured the JPS, eight measured the reproduction of active positioning (RAP), and two measured the reproduction of passive positioning (RPP) (Table 1).

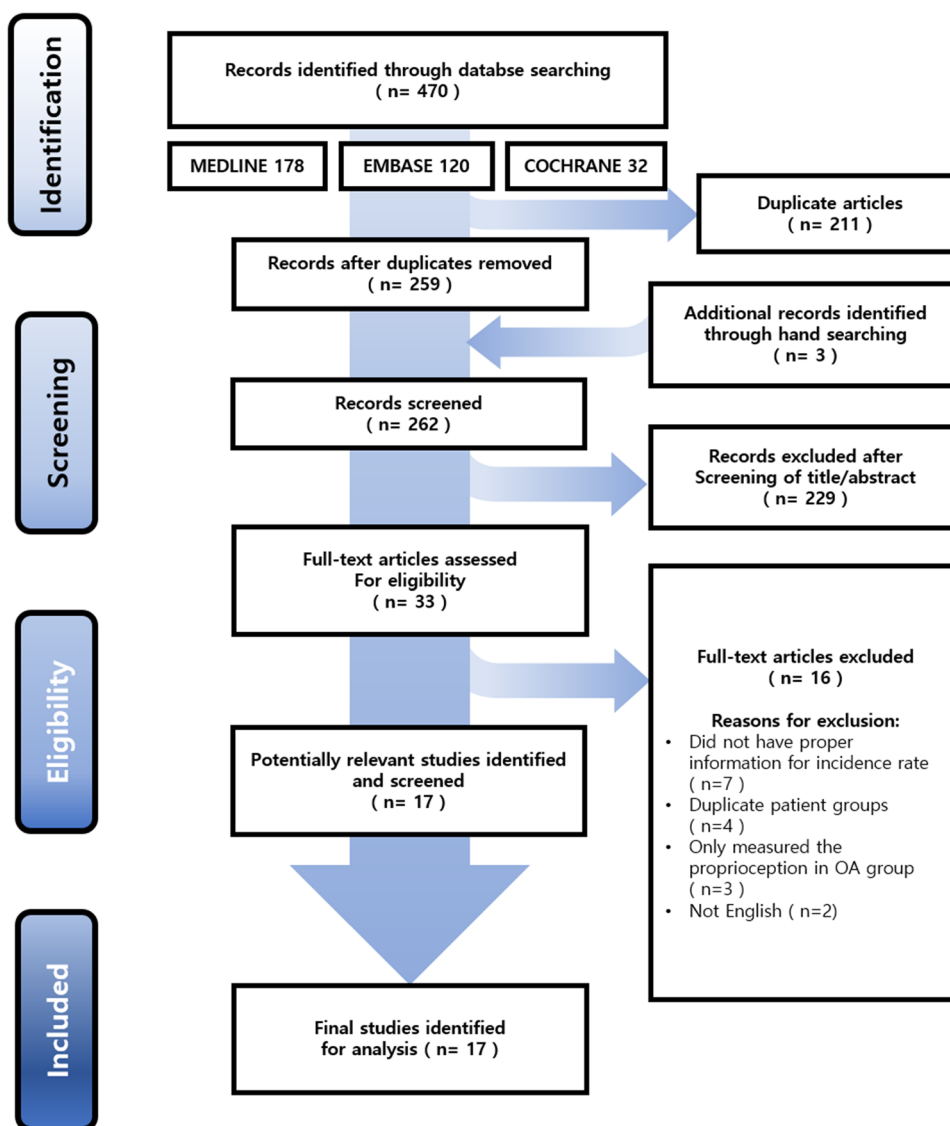
Quality appraisal and publication bias

Of the 17 studies, eight were found to be of a good quality, with five having eight stars and three having seven stars. The remaining nine studies were of a fair quality, with seven having six stars and two having five stars (Table 1). Publication bias was analyzed by assessing the JPS because it was the only parameter that was evaluated in more than ten studies. Except for two studies that were skewed to the right, the funnel plots showed that the weighted mean differences in the angle of error in the JPS between the osteoarthritic and unaffected knees were relatively symmetric, indicating a lack of publication bias (Fig. 2). The Egger's test also showed no significant publication biases in the angle of error in the JPS ($p = 0.561$).

TTDPM

Of the 17 studies, seven compared the TTDPM between the patients with knee osteoarthritis and unaffected control groups with a similar age. The analysis of the subjects who underwent the TTDPM test at 30° knee flexion showed that the mean angle of error was 0.83° greater (95% CI 0.36°–1.30°; $p < 0.001$) in the osteoarthritic knees than in control knees. Similar results were observed in the subjects who underwent the TTDPM test at 45° knee flexion, with the mean angle of error being 0.89° greater (95% CI 0.33°–1.44°; $p = 0.002$) in the osteoarthritic knees than in the control group. However, the pooled mean difference in the angle of error between the knees at 30° and 45° knee flexion was 0.06°, which was not statistically significant ($p = 0.878$). The pooled results of both TTDPM test at 30° and 45° knee flexion analyses also showed that the mean angle of error was 0.83° greater (95% CI 0.44°–1.23°; $p < 0.001$) in the osteoarthritic knees than in control knees (Fig. 3).

Fig. 1 Preferred reporting items for systematic reviews and meta-analyses flow diagram of the identification and selection of the studies included in this meta-analysis. OA osteoarthritis



JPS

Of the 17 studies, 10 compared the JPS between the osteoarthritic knees and unaffected knees of control group. The pooled data of the 306 osteoarthritic knees and 253 unaffected knees, which were examined by the reproduction of the targeted knee position tests showed that the pooled mean difference in the mean angle of error was 1.89° greater (95% CI 1.09° – 2.70° ; $p < 0.001$) in the osteoarthritic knees than in the unaffected knee of healthy control group. The analysis of the subjects who underwent RAP tests demonstrated that the pooled mean difference in the mean angle of error was 2.04° greater (95% CI 1.11° – 2.97° ; $p < 0.001$) in the osteoarthritic knees than in the unaffected knee of healthy control group, indicating that the osteoarthritic knees had a poor JPS than unaffected knee of healthy control group. Similarly, the analysis of the subjects who underwent RPP tests

showed that the mean angle of error was 1.54° greater (95% CI 0.82° – 2.26° ; $p < 0.001$) in the osteoarthritic knees than in the unaffected knees of healthy control group (Fig. 4). However, the mean difference in the angle of error of 0.5° between the RAP and RPP tests did not reach a statistical significance ($p = 0.408$).

TTDPM vs. JPS and meta-regression analyses

A comparison of the results of the TTDPM and JPS showed that the mean difference in the angle of error between the osteoarthritic knees and unaffected knees of healthy control group was 1.06° greater (95% CI 0.68° – 0.74° ; $p < 0.001$) in the JPS test than in the TTDPM test.

The results of the meta-regression analyses are reported in Table 2. The age and sex differences between the patients with knee osteoarthritis and control groups with unaffected

Table 1 Study characteristics

Study	Year	Study type	Sample size		Mean age		Sex		Mean BMI		Measured parameters	Quality score
			OA	Control	OA	Control	OA (M:F)	Control (M:F)	OA	Control		
Cammarata and Dhaheer [11]	2012	PCS	13	14	57.0	56.0	7:6	7:7	29.0	25.0	TTDPM (30°, extension, 1°/s)	7
Hewitt et al. [22]	2002	PCS	10	10	70.5	69.5	0:10	0:10	26.9	27.0	TTDPM (35°, extension, both 0.5°/s and 2.5°/s)	6
Koralewicz and Engh [30]	2000	PCS	117	40	67.9	68.3	66:51	34:6	29.4	26.9	TTDPM (45°, both extension & flexion, 0.5°/s)	7
Lund et al. [31]	2008	PCS	21	29	57.1	55.3	0:21	0:29	28.5	23.3	TTDPM (60°, extension, 1°/s), RAP	8
Pai et al. [36]	1997	PCS	30	29	68.2	71.3	8:22	12:17	28.6	24.9	TTDPM (45°, extension, 0.3°/s)	6
Pap et al. [37]	1998	PCS	25	20	63.9	61.7	10:15	9:11	NR	NR	TTDPM (45°, randomly extension or flexion, 0.34°/s)	6
Sharma et al. [40]	1997	PCS	28	29	65.5	71.0	13:15	13:16	28.9	26.3	TTDPM (45°, extension, 0.3°/s)	8
Baert et al. [3]	2013	PCS	45	20	64.0	62.9	0:45	0:20	27.8	25.2	RAP	6
Hall et al. [19]	2005	PCS	59	55	69.2	67.5	21:38	17:38	28.5	25.9	RAP	6
Hassan et al. [21]	2001	PCS	77	63	63.4	63.0	19:58	18:45	30.6	24.9	RAP	6
Hortobagyi et al. [23]	2004	PCS	20	20	57.5	56.8	5:15	5:15	29.3	28.3	RAP	8
Hurley et al. [24]	1997	PCS	69	25	60.7	65.6	26:43	7:18	29.4	27.5	RAP	5
Jerosch et al. [25]	1997	PCS	17	30	42.7	33.6	10:7	20:10	NR	NR	RAP	8
Marks et al. [33]	1993	PCS	10	10	56.6	48.2	0:10	0:10	30.1	24.4	RAP	6
Mohammadi et al. [34]	2008	PCS	30	30	46.4	45.5	0:30	0:30	27.1	26.9	RAP	8
Bayramoglu et al. [6]	2007	PCS	50	30	60.2	57.9	11:39	5:25	30.1	25.4	RPP	5
Garsden and Bullock-Saxton [17]	1999	PCS	20	20	62.8	60.8	10:10	10:10	NR	NR	RPP	7

All prospective comparison studies were the prospectively enrolled cross-sectional study

Quality score was based on Newcastle–Ottawa Assessment Scale

BMI body mass index, OA osteoarthritis, PCS prospective comparative studies, RAP reproduction of active positioning, TTDPM threshold to detect passive motion, RPP reproduction of passive positioning

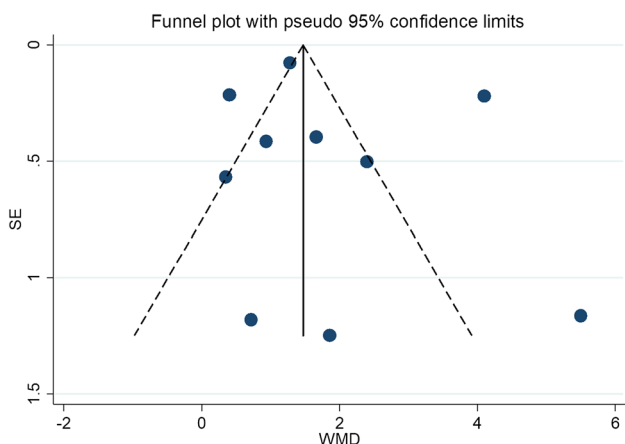


Fig. 2 Funnel plot showing the relatively symmetric mean differences in the mean angle of error in the joint position sense test between the osteoarthritic and unaffected knees. Eight of the ten included studies fell within or around the 95% confidence interval lines; the other two studies deviated to the right. *WMD* weighted mean difference

knees were not significantly associated with the differences in the mean angle of error both in the TTDPM and JPS tests. This finding indicated that the results of the current study were not biased by the differences in the demographic characteristics of the patients and control groups.

Discussion

The most important findings of this study were that proprioception was lower in the osteoarthritic knees than in the unaffected knees of the age-matched control group both in the TTDPM and JPS tests and that the mean angle of error was greater in the JPS test than in the TTDPM test.

Proprioception is the sense of movement and position of the body and it is achieved by peripheral sensory input including changes in muscle length and tension, joint angle, and stretch of skin. These sensory inputs are derived from a number of sources including muscle spindles in skeletal muscle, stretch-sensitive receptors in tendons (Golgi tendon organ), and motion-sensitive receptors in ligaments and

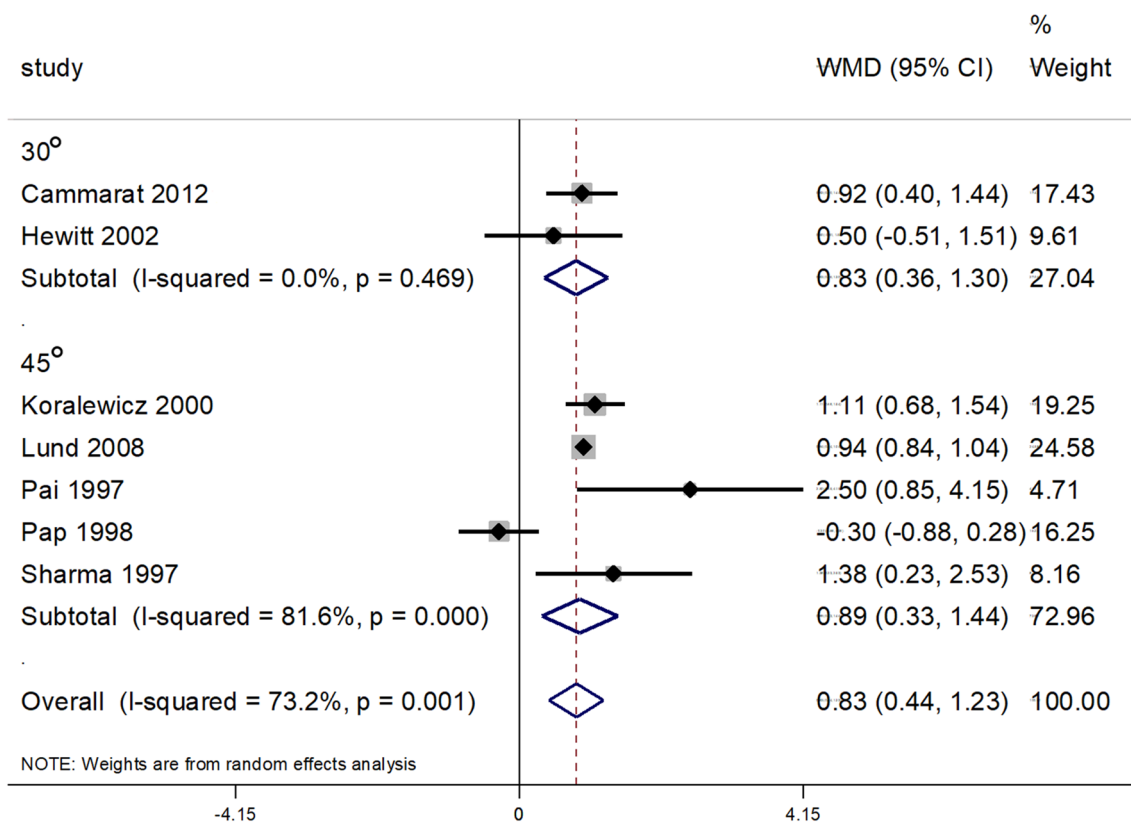


Fig. 3 Forest plot showing the mean differences of the threshold to detect passive motion (TTDPM) between the osteoarthritic and unaffected knees. The analysis of the TTDPM test at 30° and 45° knee flexion shows that the mean angles of error are significantly 0.83° and 0.89° greater in the osteoarthritic knees than in the unaffected knees. The pooled results of the TTDPM both in 30° and in 45° of knee flex-

ion also show a 0.83° greater mean angle of error in the osteoarthritic knees than in the unaffected knees. (The values to the right of point “0” mean the measure is worse in people with knee osteoarthritis than in age-matched controls.). *WMD* weighted mean difference, *CI* confidence interval

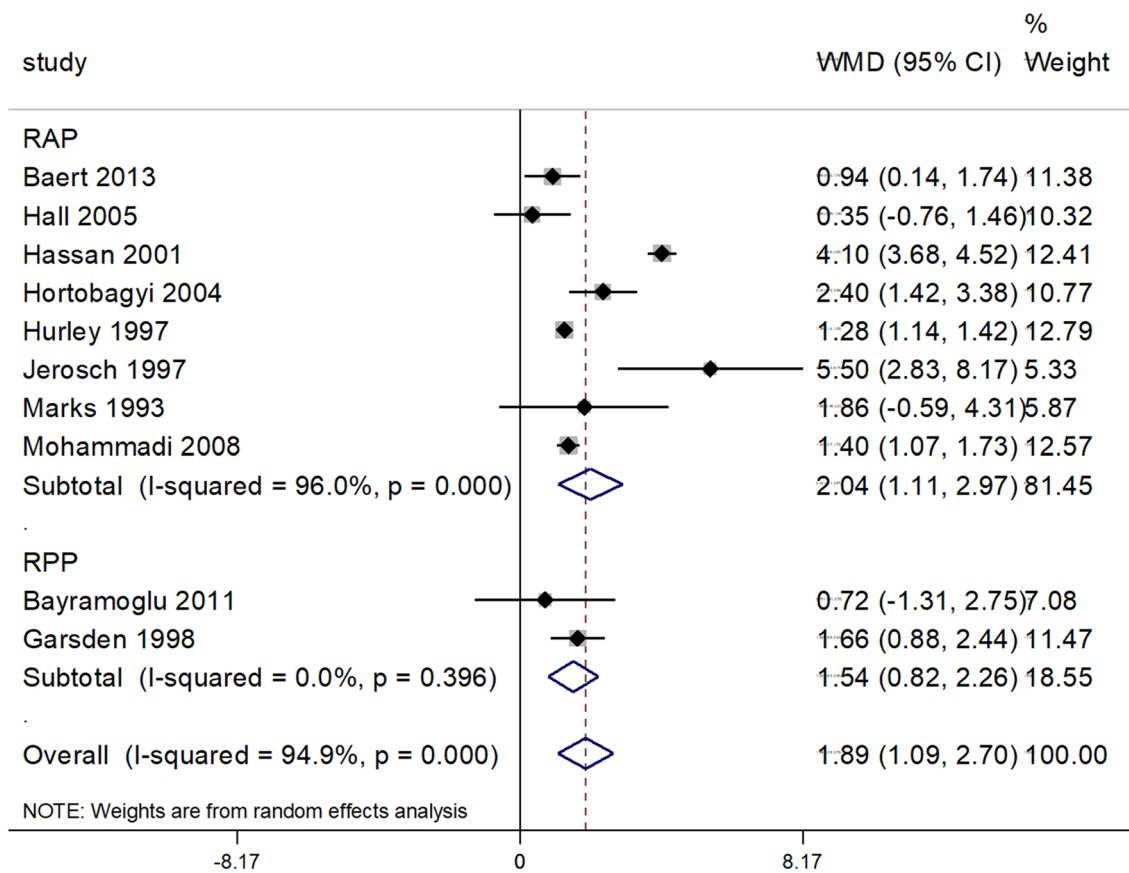


Fig. 4 Forest plot showing the mean differences in the joint position sense between the osteoarthritic and unaffected knees. The analysis of the reproduction of active (RAP) and passive (RPP) positioning of the targeted angle demonstrates that the mean angles of error are significantly 2.04° and 1.54° greater in the osteoarthritic knees than in the unaffected knees. The pooled data of the RAP and RPP also show

that the osteoarthritic knees had a 1.89° greater mean angle of error than the unaffected knees. (The values to the right of point “0” mean the measure is worse in people with knee osteoarthritis than in age-matched controls.). *WMD* weighted mean difference; *CI* confidence interval

Table 2 Meta-regression analysis comparing the associations of age and sex using the threshold to detect passive motion (TTDPM) and joint position sense (JPS) tests between the osteoarthritic knees and unaffected knees

Variable	Coefficient	Standard error	p value	95% confidence interval
TTDPM				
Age	-0.052	0.063	0.409	-0.174 to 0.071
Sex	-0.010	0.012	0.394	-0.034 to 0.013
JPS				
Age	-0.127	0.082	0.119	-0.287 to 0.033
Sex	-0.026	0.023	0.241	-0.071 to 0.018

joint capsules (Ruffini receptor and Pacinian corpuscle) [9]. In clinical studies, knee joint proprioception is measured by two different methods—joint movement (kinesthesia) is tested by TTDPM and joint position is tested by JPS [27]. The results of the current study showed decreased

proprioception not only in the joint movement sense but also in the joint position sense. It is possible that a reduction in proprioception in patients with knee osteoarthritis could be the result of a local effect of knee osteoarthritis or of the general development or progression of the osteoarthritis and muscle weakness [15, 28]. In terms of the local effect of knee osteoarthritis, the morphologic change in the knee joint resulting from knee osteoarthritis, including osteophyte, articular cartilage breakage, and increased joint effusion, could damage the mechanoreceptors in the articular cartilage and joint capsule. Beyond the intraarticular destruction, knee osteoarthritis could destroy or disturb the extraarticular soft tissues around the knee joint, therefore altering the function of the mechanoreceptors in the joint capsule, ligament, muscle, and tendinous portion surrounding the knee joint. Quadriceps muscle weakness or atrophy is well known for its correlation with progression of knee osteoarthritis. Previous studies showed a significant association between impaired motion sense and muscle weakness

and insisted that muscle weakness or atrophy might decrease muscle spindle sensitivity [24, 25, 52]. These widespread damages in the mechanoreceptors of the intraarticular and extraarticular structures are large enough to be detected by proprioception measurement tools, such as the TTDPM and JPS tests [41]. Conversely, decreased proprioception by osteoarthritis could induce the progression of osteoarthritis [40]. Disruption of the afferent component of protective neuromuscular reflexes due to impaired proprioception may lead to poor spatial and temporal coordination of position sense, decreased muscle activity, and poor coordination of the quadriceps and hamstring [28]. This situation could subsequently increase loads on the knee joint owing to poor load distributions, which resulted from an increased joint laxity by poor muscular control and activity, thus resulting in a greater exposure of the knee joint to wear and tear [31]. In addition, a recent study [31] showing systemic proprioceptive deficits of elbow as well as knee joints suggest that proprioceptive deficit of the knee joint could be a cause of osteoarthritis. Although the results of the current study could not clearly demonstrate such a causal relationship, we believe that impaired proprioception could be both a cause and a result of knee osteoarthritis, because either of these possibilities alone is insufficient to explain the presence of impaired proprioception in patients with knee osteoarthritis. Therefore, it is also probable that these two pathways may create the “self-perpetuating vicious cycle” of knee osteoarthritis progression.

Many studies had made an effort to prove which factors are the prognostic factors for the progression of knee osteoarthritis. Obesity, sex (female), varus malalignment, age, former knee injury, high serum levels of hyaluronic acid, and TNF- α are proven potential factors for the progression of knee arthritis [5, 14]. Low quadriceps muscle strength is also well-known factor which is associated with the progression of knee osteoarthritis; however, the causal relationship had not been clarified [4, 29, 48]. We think the decrement of proprioceptive function might be one of causal relationship between knee osteoarthritis and quadriceps strength. When the patients had advanced osteoarthritis with uncontrolled pain, total knee arthroplasty is considered as the gold standard [38]. It is still controversial that arthroplasty yields better proprioception; however, optimal collaboration between surgery and subsequent rehabilitation might guarantee the good outcomes in terms of patients' function [8, 12, 43].

In this study, the decrement of proprioception was greater in the JPS test (reproduction of angle) than in the joint motion sense (TTDPM) test. The difference in the decrement between the JPS and TTDPM tests could be explained in part by the fact that these two tests may measure different components of proprioception. Kinesthesia is the dynamic phase of proprioception and is, therefore, mainly regulated by rapid adapting mechanoreceptors (Pacinian corpuscles).

Joint position is the static phase of proprioception and is chiefly controlled by slow adapting mechanoreceptors, such as Golgi tendon organs or Ruffini receptors [35]. In addition, the TTDPM test maximally stimulates the articular mechanoreceptors with minimal stimulation of the muscle spindles, whereas the JPS test stimulates both receptors. The insensitivity to rapid adapting mechanoreceptors and lack of reflection for mechanoreceptors in the muscle spindles in the TTDPM test could underestimate the actual decrement in the proprioception in osteoarthritic knee joints. Another possible cause of the greater decrement in the JPS test than in the TTDPM test may be the higher degree of measurement error in the JPS test. While both the JPS and TTDPM tests require the participants' concentration abilities, only the JPS test is dependent on the participants' memory during the test. Therefore, the reliability of the JPS test decreases not only because of one or two lapses in concentration but also because of a memory bias during the test. This might also explain the greater reduction in the JPS test than in the TTDPM test in the osteoarthritic knees [31].

Previous studies using patient-reported questionnaires demonstrated that proprioceptive deficit of the knee joint was associated with functional disability in terms of walking speed [32, 36, 42]. One report [10] suggested that a greater than 5° reduction in proprioception may have clinically significant impacts on osteoarthritic knees, but presented no evidence to support this assertion. To date, no consensus has been reached on how much reduction of proprioception in the TTDPM and JPS tests is required to give rise to clinically relevant changes in the functional ability of patients with knee osteoarthritis. The results of our study, showing a 0.83° deficit on the TTDPM test and a 1.89° deficit on the JPS test, may be insufficient to cause observable changes in functional ability. However, the deficits observed in our study were considerably greater than the range of measurement error of previous studies (0.03°–0.25°), suggesting that they have clinical relevance [7]. Also, given that the proprioception test was conducted on a non-weight bearing condition and a relatively lower angular velocity of 0.2–2°/s, which could not reflect the daily living activities of patients, it is possible that with the limb moving at great velocities and subjected to high forces in daily living, these low values take on a greater clinical significance than what was first thought [10]. In addition, a previous study showed that the mean side-to-side differences in healthy subjects were only 0.1° on both TTDPM and JPS measurements [18], thus also indicating that the less than 2° differences observed in our study may be underestimations of the proprioceptive deficits of the osteoarthritic knees. Further, considering that the proprioceptive deficit of patients with anterior cruciate ligament tear was not good in a recent meta-analysis [27], as determined by both TTDPM (0.23°) and JPS (0.94°),

the proprioceptive deficit from 1° to 2° in the osteoarthritic knees in our study was relatively of a large magnitude, thus supporting the potential clinical relevance of these minimal proprioceptive deficits for the function of osteoarthritic knees. To prevent potential functional disability, early intervention, including muscle strengthening exercises, sensorimotor training or knee bandaging might be helpful to improve proprioceptive accuracy in patients with knee osteoarthritis [13, 25, 49, 50].

There were several limitations that should be considered in this meta-analysis. The heterogeneity of the demographic data among the included studies, such as age and sex distribution, could cause confounding effects on the results of this meta-analysis. However, the meta-regression analysis showed that age and sex were not significantly associated with the proprioceptive deficit in both the TTDPM and JPS tests in the osteoarthritic knees. In addition, we also could not exclude other potential confounders, such as habitual physical activity, concomitant medication, contralateral knee status [31], and prior medical or surgical conditions. These factors could have influenced the proprioception accuracy. Moreover, enrolled studies defined osteoarthritis using ACR criteria or K–L grade 2 or higher; therefore, it is hard to find the relationship between severity of osteoarthritis and decrement of proprioception. Another limitation was that the meta-analysis is based on a random effects analysis. In contrast to a fixed effects analysis, which can be used to estimate a common difference, a random effects analysis estimates an average difference, and the variability of this may have clinical implications. However, a random effects analysis was more adequate than a fixed effect model for pooling the data in this study because our results showed substantial heterogeneity ($I^2 > 50\%$). At last, the independent librarian who could supply more reliable data collection was not involved in the current study. It might be one of our limitations.

Conclusions

In conclusion, the knee proprioceptive acuity of patients with knee osteoarthritis was poorer than that of patients with unaffected knees in the age-matched control group both in terms of the TTDPM and JPS. Further evaluation is needed to determine the clinical relevance of these deficits.

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Compliance with ethical standards

Conflict of interest None of the authors have any conflicts of interest to disclose regarding this manuscript.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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