



Efficiency of knee ultrasound for diagnosing anterior cruciate ligament and posterior cruciate ligament injuries: a systematic review and meta-analysis

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Abstract

Objective To evaluate the diagnostic performance of knee ultrasound for anterior cruciate ligament (ACL) and posterior cruciate ligament (PCL) injuries.

Materials and methods PubMed and EMBASE databases were searched for diagnostic accuracy studies that used ultrasound for diagnosing ACL and PCL injuries. Bivariate and hierarchical summary receiver operating characteristic modeling was used to evaluate diagnostic performance. Subgroup analysis was performed by assessing studies conducted using the ultrasound technique (functional ultrasound versus conventional ultrasound) for diagnosing ACL injury. We performed meta-regression analyses for a potential source of heterogeneity.

Results Eleven (938 ultrasound/878 patients) and six articles (281 ultrasound/237 patients) were included for ACL and PCL injuries respectively. The summary sensitivity, summary specificity, and area under the hierarchical summary receiver operating characteristic for ACL and PCL injuries were 0.88 (95% confidence interval [CI], 0.81–0.93) and 0.99 (95% CI, 0.49–1.00), 0.96 (95% CI, 0.91–0.98) and 0.99 (95% CI, 0.73–1.00), and 0.97 (95% CI, 0.96–0.98) and 1.00 (95% CI, 0.99–1.00) respectively. In subgroup analysis, there was no significant difference between sensitivity ($p = 0.63$) and specificity ($p = 0.72$) of functional and conventional ultrasound. Among the various potential covariates, patient enrollment, patient position, and ultrasound performer were associated with heterogeneity in terms of sensitivity, and proportion of the ACL injury was associated with heterogeneity in terms of specificity.

Conclusion Knee ultrasound demonstrates high diagnostic performance for ACL and PCL injuries, particularly when performed by experienced musculoskeletal radiologists. Future prospective studies to compare the cost- and time-effectiveness between ultrasound and magnetic resonance imaging and to determine the optimal ultrasound parameters are warranted.

Keywords Anterior cruciate ligament · Posterior cruciate ligament · Knee ultrasound · Meta-analysis · Data accuracy

Introduction

Knee injuries commonly occur during daily sports activities and are common presenting concerns in the emergency department [1]. Among various knee injuries, anterior cruciate

ligament (ACL) and posterior cruciate ligament (PCL) injuries are important owing to their biomechanical function [1]. Failure to recognize acute disruption of the ACL is associated with a higher risk of subsequent damage to the menisci, particularly the medial meniscus, and the articular cartilage [2]. Similarly, although conservative treatment is recommended for isolated PCL injuries, in combined ACL–PCL injuries, failure to recognize acute disruption of the PCL may lead to inappropriate treatment and a poor prognosis [3]. Thus, early and accurate diagnosis of ACL and PCL tears are important [2, 3].

For the diagnosis of ACL and PCL tears, initial diagnosis of ligament injury is usually made by thorough assessment of patients' medical history and physical examination tests. However, these tests demonstrate relatively low sensitivity

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and high variability [4, 5]. Although magnetic resonance imaging (MRI) is the gold standard for the evaluation of ligament injuries in the knee, routinely performing MRI as an initial method is not cost-effective and not readily available in the emergency setting [1].

Musculoskeletal ultrasound is increasingly recognized for its diagnostic value in the emergency setting because of its accuracy and real-time imaging capability [6]. With this background, knee ultrasound imaging could be an option with higher priority owing to its lack of radiation exposure, and cost- and time-effectiveness. However, ultrasound has some disadvantages related to the subjective nature of the modality (operator-dependent modality), such as failure of detection, long learning curve, and limited reproducibility [7]. Previous ultrasound evaluation studies regarding ACL and PCL injuries have shown varied results. Therefore, we believe that the performance of knee ultrasound in the diagnosis of ACL and PCL injuries needs further exploration, and high-level evidence needs to be presented via quantitative synthesis of data from existing studies. Additionally, the pooling of results will be interesting because published studies have used different methodologies (functional ultrasound and conventional ultrasound).

This systematic review and meta-analysis was aimed at evaluating the diagnostic performance of knee ultrasound for diagnosing ACL and PCL injuries. In addition, we performed a subgroup analysis to evaluate the diagnostic performance of knee ultrasound according to the ultrasound technique (functional versus conventional).

Materials and methods

This meta-analysis followed the revised guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses of Diagnostic Accuracy Studies (PRISMA-DTA) statement [8].

Data sources

The PubMed and EMBASE databases were searched for studies published or e-published up to 1 February 2019 that used ultrasound for the diagnosis of ACL and PCL injuries. Search terms that were related to “ACL”, “PCL”, and “ultrasound” were combined with “sensitivity,” “specificity,” or “receiver operating characteristic” as follows: (“anterior cruciate ligament”) OR (“ACL”) OR (“posterior cruciate ligament”) OR (“PCL”) AND (“ultrasound”) OR (“ultrasonography”) OR (“sonogram”) OR (“sonography”)) AND (“diagnosis”) OR (“accuracy”) OR (“sensitivity”) OR (“specificity”) OR (“receiver operating characteristic”) OR (“ROC curve”).

The bibliographies of the articles identified were also screened to identify additional relevant studies. Two investigators screened the titles and abstracts for potential eligibility, and disagreements were resolved through discussion.

Study selection

The inclusion criteria were studies that included the following:

1. Patients with acute knee injury or chronic instability or both
2. Knee ultrasound as the index test (diagnostic performance study with knee ultrasound as the test examination)
3. Use of surgical finding or MRI with or without clinical follow-up as the reference standard for confirmation of the ACL and PCL injuries
4. Original research article as the publication type in the English language

The exclusion criteria were as follows:

1. Case report or case series
2. Review articles, guidelines, consensus statements, letters, editorials, and conference abstracts
3. Studies not pertaining to the field of interest
4. Studies not performed on humans
5. Studies with insufficient data for a 2×2 table

Data extraction and quality assessment

Two investigators independently extracted data regarding patient and study characteristics. The same investigators evaluated methodological quality using the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool [9]. Inconsistencies between the reviewers were resolved through discussion.

A standardized form was used to extract data regarding:

1. Patient characteristics (number of total patients, proportion of the ligament tears, mean age, age range, and sex)
2. Study characteristics (study location, publication year, study design, reference standard, and blinding to the reference standard)
3. Ultrasound characteristics (probe, technical parameters, and ultrasound performer)

Study outcomes were also extracted to create 2×2 tables (i.e., true-positive, true-negative, false-positive, and false-negative results). The 2×2 tables were calculated using the Bayesian method if only sensitivity and specificity were presented for an eligible study. If two or more reviewers independently

assessed the diagnostic accuracy, the result with the highest accuracy was extracted.

Data synthesis and analysis of diagnostic performance

Patient demographic characteristics and extracted covariates were summarized using standard descriptive statistics. Continuous variables were expressed as means and 95% confidence intervals (CIs), whereas categorical variables were expressed as frequencies or percentages unless stated otherwise.

We used a bivariate random-effects model for analyzing and pooling the diagnostic performance (sensitivity and specificity) measurements across studies. To derive summary estimates of diagnostic performance, we plotted estimates of the observed sensitivities and specificities for each test in forest plots and hierarchical summary ROC (HSROC) curves derived from individual study results [10–12]. These results were plotted using HSROC curves with 95% confidence and prediction regions.

Heterogeneity was determined using Cochran's Q test ($p < 0.05$ indicated the presence of heterogeneity) and the I^2 test (0–40%, heterogeneity may not be present; 30%–60%, moderate heterogeneity; 50%–90%, substantial heterogeneity; and 75%–100%, considerable heterogeneity) [13]. Sensitivity and specificity are commonly inversely correlated and influenced by the threshold (cut-off) value [10–12]. In addition, Spearman's correlation coefficient between the sensitivity and false-positive rate was calculated to determine any threshold effect; a coefficient of >0.6 was considered to indicate a considerable threshold effect [14]. We omitted Deeks' funnel plot [15] of individual studies to check for publication bias according to the PRISMA-DTA.

Subgroup analysis

We performed a subgroup analysis for the detailed evaluation of the diagnostic performance of knee ultrasound in the diagnosis of an ACL tear. We extracted the eligible studies in which ultrasound was classified as functional ultrasound or conventional ultrasound for subgroup analysis. In the functional ultrasound method, the ultrasound was performed with certain force to the proximal tibia using the manual method or an arthrometer; studies that used functional ultrasound generally evaluated the translation of the proximal tibia. In the conventional ultrasound method, the ultrasound was performed without any force; studies with conventional ultrasound evaluated the morphology (continuity, echogenicity, thickness) or change of the adjacent structure (such as posterior capsular bulging) of the ACL.

Meta-regression analysis

Meta-regression analyses using several covariates were performed to explore the potential causes of heterogeneity:

1. Locale (Germany versus countries other than Germany)
2. Patient enrollment (consecutive versus nonconsecutive)
3. Patient characteristics (only acute injury versus include chronic instability/injury)
4. Total patients (≥ 60 vs < 60)
5. Proportion of ACL tear ($\geq 50\%$ vs $< 50\%$)
6. Mean age (≥ 30 vs < 30)
7. Ultrasound position (prone versus supine)
8. Ultrasound performer (musculoskeletal radiologists versus others)
9. Reference standard (surgical finding [operation or arthroscopy] versus include nonsurgical finding [MRI or clinical follow-up])

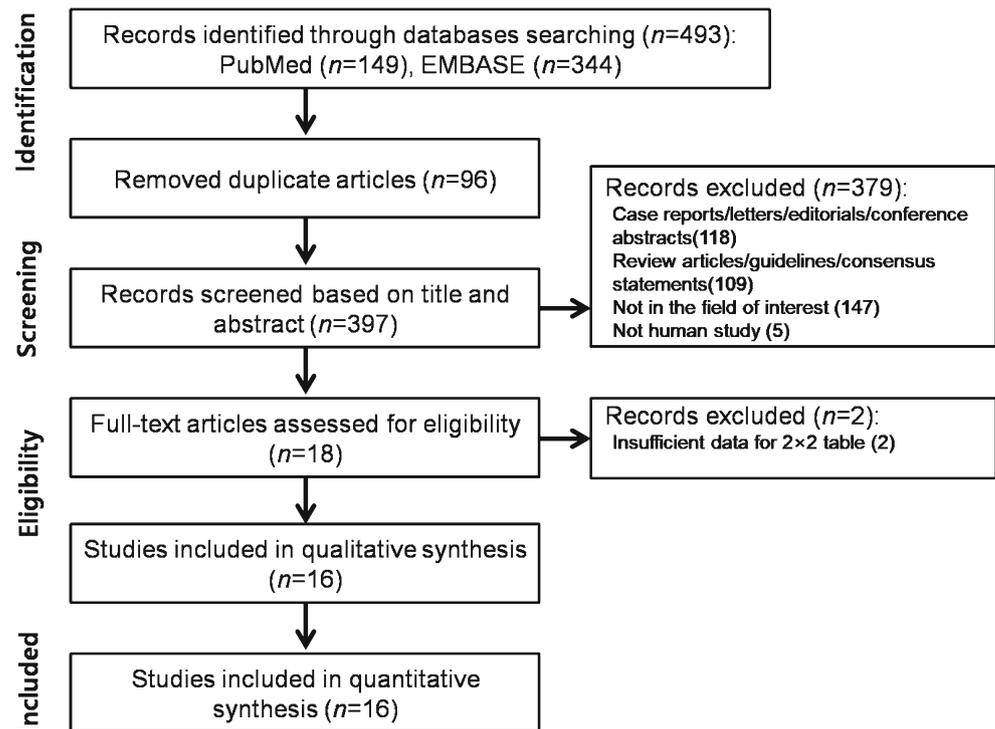
All statistical analyses were performed by one author (S.J.Y.) who has 4 years' experience performing systematic reviews and meta-analyses. The statistical analyses were performed using the "midas" and "metandi" modules in Stata software (version 10.0; StataCorp LP, College Station, TX, USA) and the "mada" package in R software (version 3.4.1; R Foundation for Statistical Computing, Vienna, Austria). Results were considered statistically significant at a p value < 0.05 .

Results

Literature search

Figure 1 shows a flow diagram summarizing the literature search. During the initial search, 493 studies were identified. After excluding 96 duplicates, we reviewed 397 titles and abstracts and then excluded 379 studies for the following reasons: case reports/letters/editorials/conference abstracts ($n = 118$), review articles/guidelines/consensus statements ($n = 109$), not in the field of interest ($n = 147$), and not a human study ($n = 5$). After reviewing the full text of 18 eligible articles, we excluded two studies that had insufficient data to build 2×2 tables ($n = 2$) [16, 17]. Ultimately, 16 original research articles [18–33] were included in the meta-analysis. Among them, 11 studies [19–22, 24–29, 31] including 878 patients (938 knee ultrasound examinations) were selected for ACL injury, and 6 studies [18, 23, 30–33] including 237 patients (281 knee ultrasound examinations) were selected for PCL injury. One study [31] simultaneously evaluated the diagnostic performance of the knee ultrasound for ACL and PCL injuries.

Fig. 1 Study selection process for the meta-analysis



Characteristics of the studies and included patients

The patient characteristics are summarized in Table 1. The sample sizes of the studies included regarding the diagnosis of ACL and PCL injuries ranged from 37 to 193 and 19 to 63 respectively. The study and ultrasound characteristics are summarized in Table 2. All studies were prospective and single-centered, with blinding to the reference standard. In 11 studies [18–20, 22, 24–29, 32] consecutive enrollment was performed and in 5 studies [21, 23, 30, 31, 33] case–control (nonconsecutive) enrollment was performed. For the diagnosis of ACL injury, the ultrasound technique (functional or conventional) and patient position (supine or prone) were mixed. For the diagnosis of PCL injury, all studies [18, 23, 30–33] performed conventional ultrasound with patients in prone position.

Quality assessment

Overall, none of the studies was considered to be seriously flawed according to the QUADAS-2 tool. All the studies satisfied ≥ 4 of the 7 items.

The risk of bias regarding the patient selection domain was considered high in 5 studies [21, 23, 30, 31, 33] because in this study case–control enrollment was performed. Regarding the index test, all studies were considered to have a low risk of bias. Regarding the reference standard domain, 5 studies [18, 22, 28, 29, 32] were considered to have a high risk of bias because these used two or more methods for the reference

standard. Regarding the flow and timing domain, 11 studies [18, 19, 21–23, 25, 27, 28, 30, 31, 33] had an unclear risk of bias because the mean interval between ultrasound and the reference standard was not reported. All studies exhibited low applicability to our research question in the patient selection, index test, and reference standard domains.

Diagnostic performance of ultrasound for diagnosing ACL injuries

The 11 studies [19–22, 24–29, 31] had sensitivity values that ranged from 0.58 to 1.00 and specificity values that ranged from 0.80 to 1.00. The pooled sensitivity and specificity values were 0.88 (95% CI: 0.81–0.93) and 0.96 (95% CI: 0.91–0.98) respectively. The Q test revealed significant heterogeneity ($Q = 18.330$, $p < 0.001$), with considerable and substantial heterogeneity detected for sensitivity ($I^2 = 83.41\%$) and specificity ($I^2 = 74.85\%$) respectively. A threshold effect was observed in the coupled forest plot of sensitivity and specificity (Fig. 2) and in the correlation between sensitivity and the false-positive rate (0.267, 95% CI: -0.397 to 0.767). The area under the HSROC curve was 0.97 (95% CI, 0.96–0.98; Fig. 3).

Diagnostic performance of ultrasound for diagnosing PCL injuries

Six studies [18, 23, 30–33] had sensitivity ranging from 0.83 to 1.00 and specificity ranging from 0.86 to 1.00. The pooled

Table 1 The demographic characteristics of the patients included

References	Patient characteristics	Number of patients	Number of examinations	ACL/PCL injury, %	Mean age, years	Age range, years	Male, %	Mean time interval between injury to ultrasound (symptom duration)
Studies with ACL evaluation								
Friedl and Glaser [19]	Acute knee injury	84	84	45.2	32	NR	65.5	NR
Fuchs and Chylarecki [20]	Acute knee injury	193	193	68.9	34	13–63	64.2	7 days
Gebhard et al. [21]	Acute knee injury	60	120	100.0	26.5	17–32	NA	NR
Grzelak et al. [22]	Acute knee injury	83	83	44.6	30	16–50	62.7	42 days
Khan et al. [24]	Acute knee injury	60	60	53.3	35	20–60	100.0	Within 7 days
Kumar et al. [25]	Knee instability and/or locking of knee joint	130	130	85.4	28.3	14–52	93.8	NR
Mautner et al. [26]	Acute knee injury	69	69	76.8	26.5	16–50	49.3	13 days
Palm et al. [27]	Acute knee injury	41	41	80.5	35.5	16–	NA	Within 1 weeks
Paszniak et al. [28]	Acute knee injury	37	37	86.5	27	16–46	56.8	Within 10 weeks
Skovgaard Larsen and Rasmussen [29]	Acute knee injury	62	62	25.8	29.2	11–62	66.1	9 days
Suzuki et al. [31]	Acute or chronic knee injury	59	59	15.3	NR	NR	NA	NR
Studies with PCL evaluation								
Cho et al. [18]	Acute knee injury	28	28	53.6	42	18–65	64.3	NR
Hsu et al. [23]	Acute knee injury	19	30	57.9	25.8	NR	68.4	NR
Sorrentino et al. [30]	Acute or chronic knee injury	33	33	39.4	24.6	19–36	60.6	NR
Suzuki et al. [31]	Acute or chronic knee injury	59	59	8.5	NR	NR	NA	NR
Wang et al. [32]	Acute knee injury	35	35	34.3	29.2	17–55	NA	154 days
Wang et al. [33]	Acute or chronic knee injury	63	96	49.2	37	18–	54.0	NR

ACL anterior cruciate ligament, PCL posterior cruciate ligament, NR not reported, NA not available

Table 2 Study and ultrasound characteristics

Reference	Year	Locale	Study period	Reference standard	Ultrasound position	Ultrasound model (vendor)	Frequency (MHz)	Ultrasound performer	Other lesions or ancillary findings
Studies with ACL evaluation									
Friedl and Glaser [19]	1991	Germany	April 1987	Operation	Supine with 20° flexion	Pickler LSC 7000 (Hitachi)	5	Surgeon	MCL injury, meniscal tear
Fuchs and Chylarecki [20]	2002	Germany	NR	Arthroscopy	Prone with 20–30° flexion	NR	NR	OS	NR
Gebhard et al. [21]	1999	Germany	NR	Arthroscopy	Prone with 20–30° flexion	Sonoline SL 2 (Siemens)	5	OS	NR
Grzelak et al. [22]	2015	Poland	2008–2012	Operation or clinical follow-up	Supine with 70–80° flexion	GE Vivid 7 (GE)	6–14	OS	NR
Khan et al. [24]	2006	Saudi Arabia	July 1997 to March 1999	Operation	Supine with 90° flexion	Acuson 128 (Siemens)	7.5	MSK radiologist	Meniscal tear
Kumar et al. [25]	2018	India	May 2014 to August 2016	MRI	Prone with 20° flexion	m-Turbo (Sonosite)	6–13	MSK radiologist	NR
Mautner et al. [26]	2018	USA	NR	MRI	Prone with knee extension	S8 12 L RS (GE)	4–12	Physiatrist	Hematoma at the intercondylar notch, posterior capsule protrusion, wave-like PCL
Palm et al. [27]	2009	Germany	NR	Arthroscopy	Prone with 20° flexion	Sonoline Versa plus (Siemens)	7.5	OS	MCL injury, meniscal tear
Paszniak et al. [28]	1995	Australia	NR	MRI and arthroscopy	Prone position	Acoustic Imaging 5200 machine (Dornier), (Phoenix)	7.5, 5.0	MSK radiologist	Hematoma at the intercondylar notch
Skovgaard Larsen and Rasmussen [29]	2000	Denmark	May 1996–July 1997	Arthroscopy or clinical follow-up	Prone with knee extension	Acuson 128/XP-10 (Siemens)	7.0, 5.0	MSK radiologist	Hematoma at the intercondylar notch
Suzuki et al. [31]	1991	Japan	NR	Operation or arthroscopy	Supine with maximal flexion	SDU-500 (Shimazu)	7.5, 5.0	OS	NR
Studies with PCL evaluation									
Cho et al. [18]	2001	South Korea	NR	Surgery or MRI	Prone with knee extension	HDI or HDI-3000 (Philips)	5–10	MSK radiologist	NR
Hsu et al. [23]	2005	Taiwan	NR	Arthroscopy	Prone with knee extension	LOGIQ 700MR (GE)	5–10	Physiatrist	NR
Sorrentino et al. [30]	2009	Italy	NR, 15 months	MRI	Prone with knee extension	HDI 5000 (Philips)	7–12	MSK radiologist	NR
Suzuki et al. [31]	1991	Japan	NR	Operation or arthroscopy	Prone with knee extension	SDU-500 (Shimazu)	7.5, 5.0	OS	NR
Wang et al. [32]	2009	Taiwan	2003–2005	MRI with/without arthroscopy	Prone with knee extension	HDI 5000 (Philips)	7–14	Physiatrist	NR
Wang et al. [33]	2017	Taiwan	2013–2014	MRI	Prone with knee extension	Acuson S2000 (Siemens)	4–9	Physiatrist	NR

MCL medial collateral ligament, MRI magnetic resonance imaging, MSK musculoskeletal, OS orthopedic surgeon

sensitivity and specificity values were 0.99 (95% CI: 0.49–1.00) and 0.99 (95% CI: 0.73–1.00) respectively. The Q test revealed significant heterogeneity ($Q = 8.690$, $p = 0.006$), with considerable heterogeneity detected for sensitivity ($I^2 = 90.74\%$) and specificity ($I^2 = 95.85\%$). A threshold effect was observed in the coupled forest plot of sensitivity and specificity (Fig. 4) and in the correlation between sensitivity and the false-positive rate (0.279, 95% CI: -0.414 to 0.792). The area under the HSROC curve was 1.00 (95% CI: 0.99–1.00; Fig. 5).

Subgroup analysis according to ultrasound techniques for diagnosing ACL injuries

For the diagnosis of ACL injury, 5 studies [19, 21, 22, 25, 27] used functional ultrasound and 6 [20, 24, 26, 28, 29, 31] used conventional ultrasound. In terms of functional ultrasound, the pooled sensitivity and specificity were 0.88 (95% CI, 0.80–

0.97) and 0.96 (95% CI, 0.92–1.00) respectively. In terms of conventional ultrasound, the pooled sensitivity and specificity were 0.89 (95% CI, 0.81–0.97) and 0.96 (95% CI, 0.92–1.00) respectively. There was no significant difference in sensitivity ($p = 0.63$) and specificity ($p = 0.72$) between the two ultrasound techniques.

Meta-regression analysis results

The results of the meta-regression analyses with regard to ACL injury are summarized in Table 3. We did not perform meta-regression analysis with regard to PCL injury owing to the small number of studies. The significant sources of heterogeneity in terms of sensitivity were patient enrollment ($p = 0.03$), patient position ($p < 0.01$), and ultrasound performer ($p = 0.03$), with higher sensitivity reported in studies with case–control enrollment, patients in prone position, and musculoskeletal radiologists as ultrasound performers than in

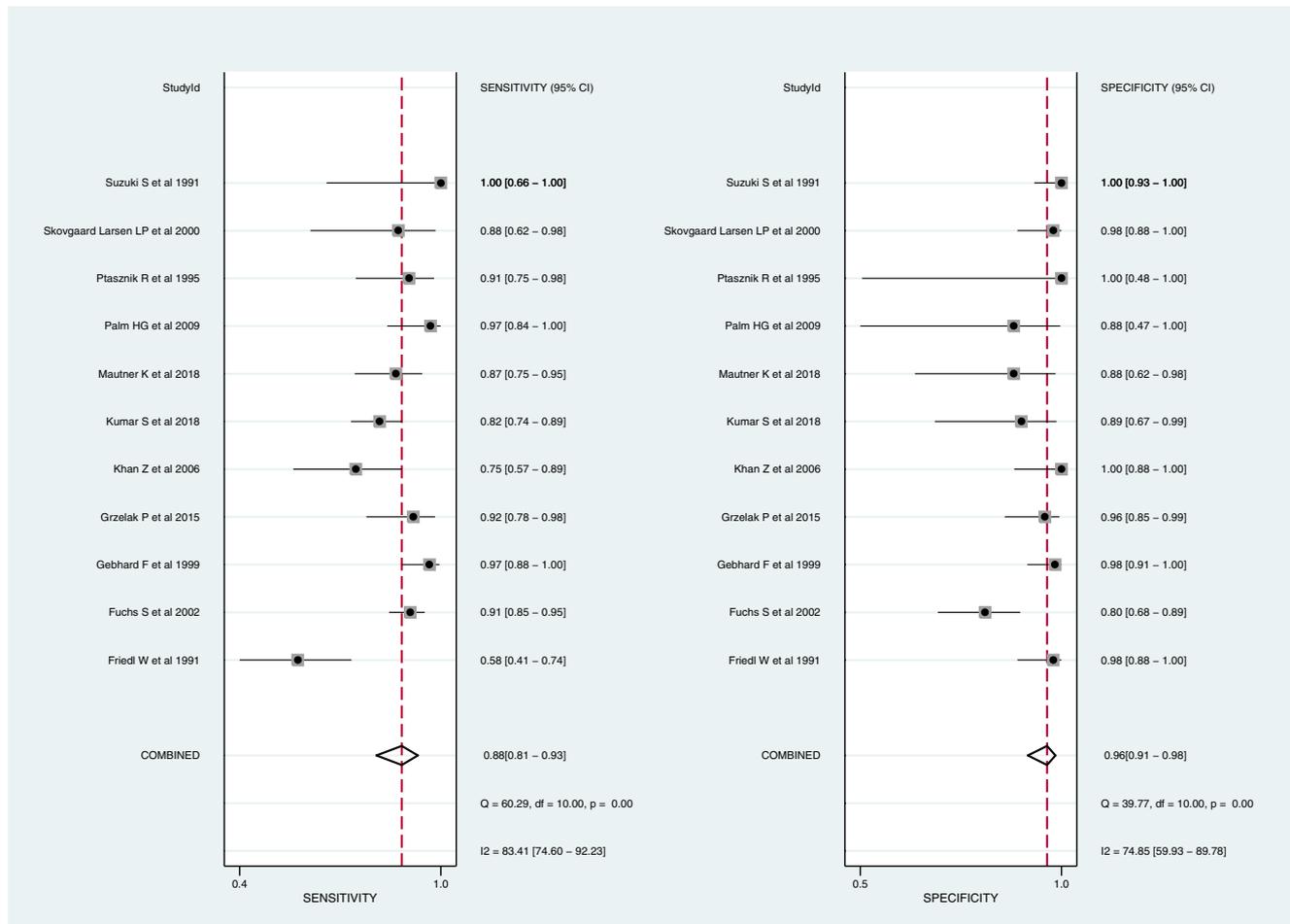


Fig. 2 Coupled forest plots for the summary sensitivity and specificity of knee ultrasound for anterior cruciate ligament injury. Dots in squares represent sensitivity and specificity. Horizontal lines represent the 95% confidence interval (CI) for each study included. The combined estimate

(Combined) is based on the random-effects model and is indicated with diamonds. Corresponding heterogeneities (I^2) with 95% CIs are provided at the bottom right-hand corner: $I^2 = 100\% \times (Q - df)/Q$, where Q is Cochran's heterogeneity statistics and df indicates the degrees of freedom

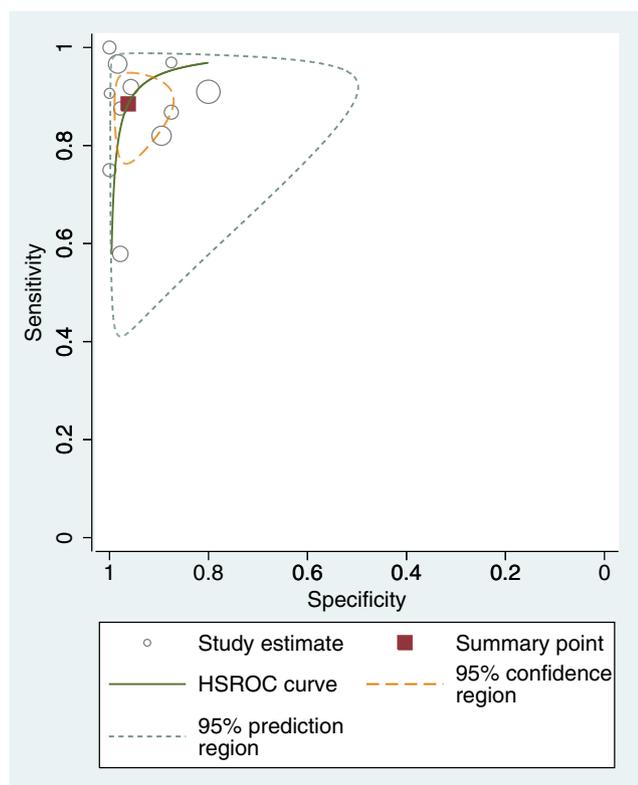


Fig. 3 Hierarchical summary receiver operating characteristic (HSROC) curve for using knee ultrasound for anterior cruciate ligament injury. The summary point (red box) indicates that the summary sensitivity was 0.88 and the summary specificity was 0.96. The 95% confidence region represents the 95% CIs of summary sensitivity and specificity, and the 95% prediction region represents the 95% CIs of sensitivity and specificity for each study included. The study estimates indicate the sensitivity and specificity estimated using the data from each study. The size of the marker is scaled according to the total number of patients in each study

those with consecutive enrollment, patients in supine position, and individuals other than musculoskeletal radiologists as ultrasound performers. The significant source of heterogeneity in terms of specificity was the proportion of ACL injuries ($p = 0.02$), with higher specificity reported in studies with a relatively low proportion of ACL injuries (<50%) than in those with a relatively high proportion of ACL injuries ($\geq 50\%$).

Discussion

The present meta-analysis revealed that knee ultrasound was an excellent tool for the diagnosis of ACL (sensitivity: 88%, specificity: 96%) and PCL injuries (sensitivity: 99%, specificity: 99%). Considering these findings, knee ultrasound is a useful imaging modality for the diagnosis of ACL and PCL injuries. In subgroup analysis, there was no significant difference in the sensitivity and specificity between functional and conventional knee ultrasound for the diagnosis of ACL injury.

Traditionally, acute knee trauma patients with suspected ACL and PCL injuries are initially evaluated by thorough physical examination [4, 5] and stress radiographs [34]. Regarding physical examinations, the anterior drawer test, Lachman test, and pivot shift test are used for the diagnosis of ACL injuries. However, the sensitivity (anterior drawer test, 38–62%; Lachman test, 69–87%; pivot shift test, 10–61%) and specificity (anterior drawer test, 25–92%; Lachman test, 81–100%; pivot shift test, 81–99%) of these physical examinations vary widely [5]. Furthermore, previous studies demonstrate that only <20% of patients with ACL injuries are being diagnosed correctly, using medical history and physical examination tests, at the time of initial presentation [2, 35].

With regard to PCL injuries, the posterior drawer test, posterior sag sign test, and quadriceps active test are being used as physical examinations. Similar to the tests for ACL, these physical examinations for PCL injuries also show variable sensitivity (posterior drawer test, 51–90%; quadriceps active test, 54–98%) or relatively low sensitivity (posterior sag sign, 79%) [4]. Alternatively, stress radiography can be performed for the diagnosis of ACL and PCL injuries. According to a recent meta-analysis [34], for the diagnosis of ACL, stress radiography showed variable or low sensitivity (43–100%) and variable specificity (76–100%). For the diagnosis of PCL, stress radiography also showed a wide range of sensitivity (88–100%) and specificity (77–100%). No standardization for a stress radiographic technique or the magnitude of force applied during stress radiography has been established for assessing anterior and posterior knee stability [34]. Furthermore, the value of physical examination and stress radiographs in the acute phase is debatable because it is difficult to perform exact physical examination and stress radiography because of the severe pain, refractory muscle spasm, and edema of the surrounding soft tissue [1, 36].

To overcome this limitation in performing physical examination and stress radiography, knee ultrasound may be useful. In addition, knee ultrasound has some clinical implications: a real-time comparison between the traumatic and nontraumatic contralateral knees [36] could be performed, and a dynamic test using ultrasound (functional ultrasound) could be performed [19, 21, 22, 25, 27].

A recent review article [37] reported that the femoral attachment site of the ACL was not easily visualized, and only partial visualization was possible. It is possible that the ability to visualize might vary depending on the extent of fat present in the patient's knee; thus, we predict that the ACL could be fully and easily visualized in patients with a low proportion of fat.

Our meta-regression analysis revealed that patient position and ultrasound performer were sources of heterogeneity. In particular, the pooled sensitivity was higher in studies conducted with patients in prone position and by musculoskeletal radiologists than in studies conducted with patients in supine

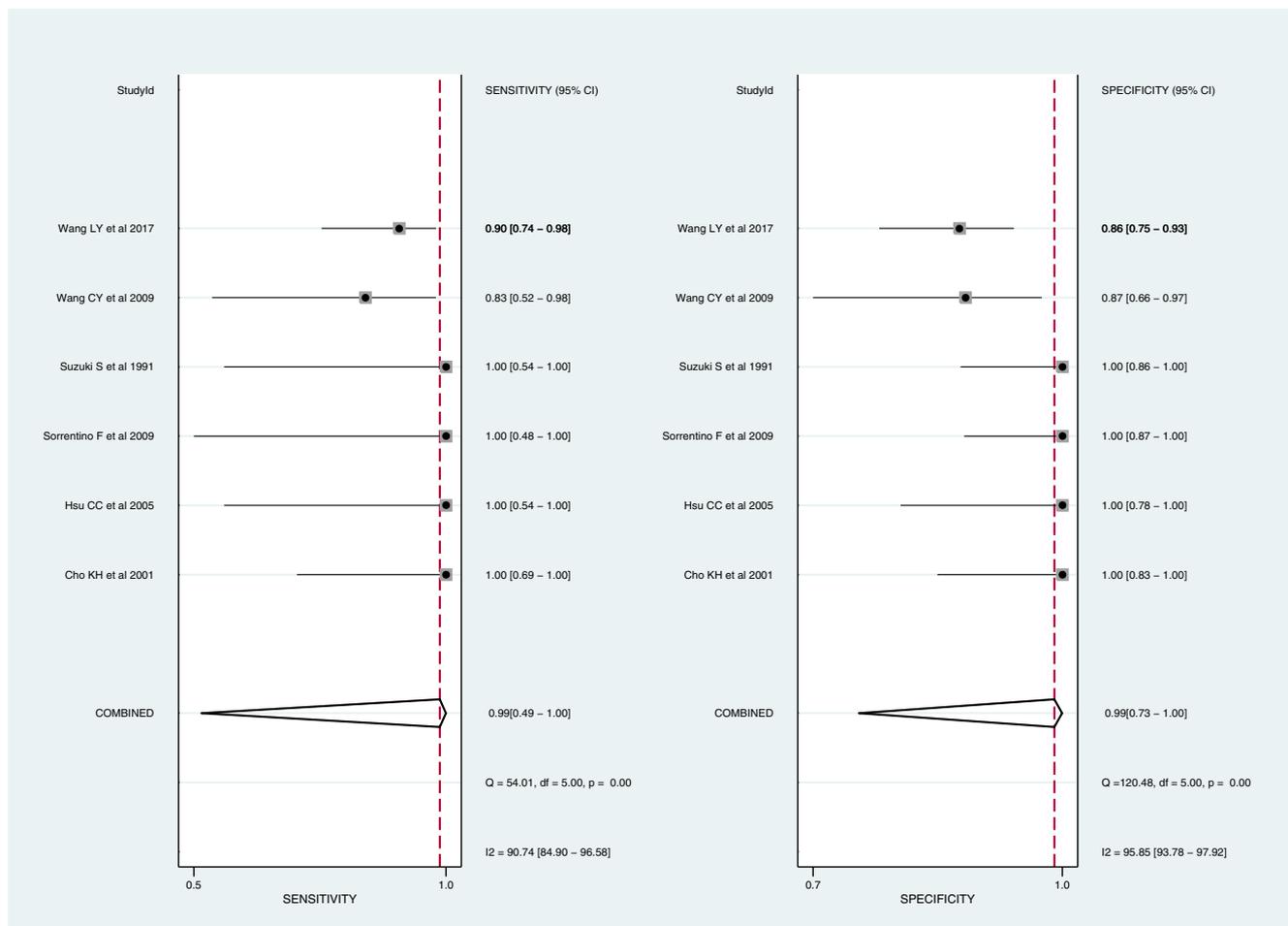


Fig. 4 Coupled forest plots for the summary sensitivity and specificity of knee ultrasound for posterior cruciate ligament injury

position and by specialists other than musculoskeletal radiologists. Thus, we recommend that musculoskeletal radiologists perform the initial ultrasound with patients in prone position for diagnosing ACL and PCL injuries. If clinical physicians, including emergency physicians, perform knee ultrasound, we speculate that focused musculoskeletal ultrasound training might be required because musculoskeletal ultrasound can show different diagnostic performance according to the operator's proficiency [38].

One previous meta-analysis [39] has evaluated the diagnostic performance of knee ultrasound for ACL injury; however, this study had several limitations. First, the authors did not use a hierarchical model (e.g., the bivariate and HSROC models), which are recommended statistical tools for meta-analysis evaluating diagnostic accuracy [10, 11]. Second, they did not perform a thorough analysis of the potential sources of heterogeneity, as they did not distinguish between sensitivity and specificity for the effects of covariates, which precluded any recommendations regarding methods of increasing the diagnostic performance of knee ultrasound. Third, they only included a limited number of studies, which is probably

associated with missing or restricted search terms. Finally, the technique of 2×2 table evaluation when two or more reviewers independently assessed their diagnostic accuracy remains unclear. In our meta-analysis, the result with the highest accuracy was extracted.

Our meta-analysis only examined studies in which the diagnostic performance of knee ultrasound was based on conclusive cases, as the eligible studies did not include cases with equivocal or inconclusive findings. In practice, a lot of symptomatic patients have equivocal or inconclusive outcomes from ultrasound investigation. Moreover, almost all studies using knee ultrasound emphasized its diagnostic performance alone and did not compare it with other modalities. At last, availability (costs, number, and time of sequences) and necessity of MRI to plan the operation via an orthopedic surgeon should not be overlooked. Thus, a prospective cost and time-effectiveness study that includes equivocal and inconclusive cases and other methodologies (e.g., comparison with MRI) is warranted to confirm the usefulness of knee ultrasound as an initial diagnostic tool in routine clinical practice.

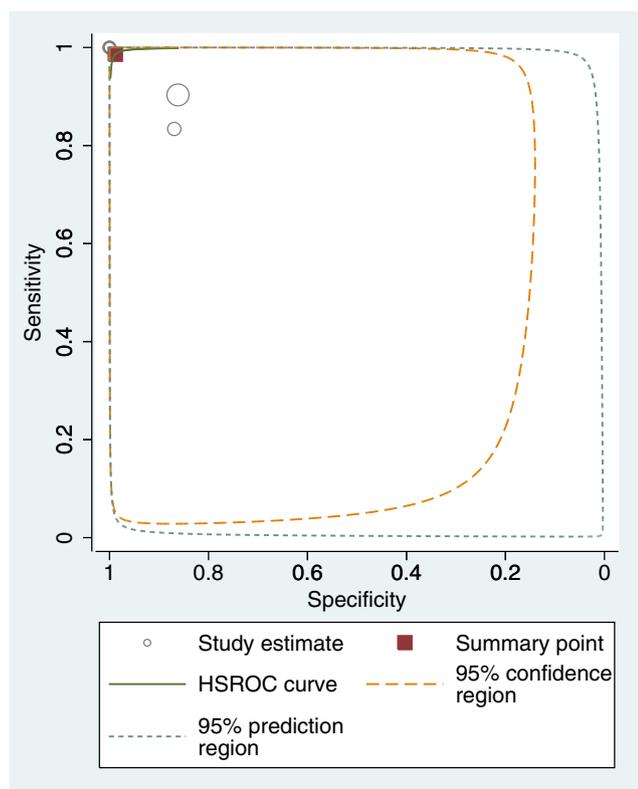


Fig. 5 HSROC curve for the use of knee ultrasound for posterior cruciate ligament injury. The summary point (red box) indicates that the summary sensitivity was 0.99 and the summary specificity was 0.99

Our study has several limitations. The first limitation is the relatively small number of studies included. Nevertheless, we were able to draw several important conclusions regarding the diagnostic performance of knee ultrasound and related factors, which we believe provides a useful overview because we used broad search terms and only included easily accessible studies (published in English and available in the PubMed and EMBASE databases). The second limitation is that all the studies included revealed positive results, and this could be attributed to publication bias (there is a possibility that unpublished studies showing negative or equivocal results exist). Although we omitted Deeks' funnel plots according to the PRISMA-DTA guidelines, we observed a low probability of publication bias (overall, $p = 0.10$ – 0.71), which suggests that this factor did not undermine our results. The third limitation is the methodological differences among the studies included, and the extensive meta-regression analysis revealed that these variables were also significant sources of heterogeneity. In meta-regression analysis, patient enrollment and proportion of ACL injuries affected the pooled sensitivity and pooled specificity respectively. Additionally, ultrasound technical parameters may affect the pooled estimates; however, it could not be assessed in the meta-regression analysis because not all studies reported the values for gain, dynamic range, and mechanical index. Further prospective studies with larger sample sizes with consecutive enrollment and a high proportion of ACL and PCL injuries are needed to determine the optimal parameters for knee ultrasound.

Table 3 Meta-regression analyses for potential sources of heterogeneity in terms of ACL injury

Covariate	Number of studies	Sensitivity (95% CI)	<i>p</i> value	Specificity (95% CI)	<i>p</i> value
Locale			0.13		0.63
Germany	4	0.88 (0.78–0.97)		0.96 (0.90–1.00)	
Countries other than Germany	7	0.89 (0.81–0.96)		0.97 (0.93–1.00)	
Patient enrollment			0.03		0.26
Consecutive	9	0.85 (0.78–0.91)		0.94 (0.89–0.99)	
Nonconsecutive	2	0.97 (0.92–1.00)		0.99 (0.98–1.00)	
Patient characteristics			0.57		0.36
Only acute injury	9	0.89 (0.82–0.95)		0.96 (0.92–1.00)	
Include chronic instability/injury	2	0.88 (0.72–1.00)		0.97 (0.92–1.00)	
Number of patients			0.12		0.92
≥ 60	8	0.87 (0.79–0.93)		0.96 (0.92–1.00)	
< 60	3	0.91 (0.89–1.00)		0.99 (0.95–1.00)	
Proportion of ACL injury			0.50		0.02
≥ 50%	7	0.90 (0.84–0.96)		0.93 (0.87–0.99)	
< 50%	4	0.85 (0.72–0.98)		0.98 (0.96–1.00)	
Mean age			0.23		0.26
≥ 30	5	0.87 (0.76–0.95)		0.94 (0.89–1.00)	
< 30	5	0.89 (0.82–0.97)		0.96 (0.92–1.00)	
Ultrasound position			< 0.01		0.21
Prone	7	0.91 (0.86–0.96)		0.93 (0.87–0.99)	
Supine	4	0.81 (0.68–0.94)		0.99 (0.97–1.00)	
Ultrasound performer			0.03		0.52
MSK radiologist	4	0.91 (0.84–0.97)		0.95 (0.91–1.00)	
Others	7	0.84 (0.73–0.96)		0.98 (0.94–1.00)	
Reference standard			0.13		0.42
Surgical finding	6	0.89 (0.81–0.97)		0.97 (0.93–1.00)	
Include nonsurgical finding	5	0.88 (0.80–0.97)		0.95 (0.90–1.00)	

Italics indicate statistical significance ($p < 0.05$)

CI confidence interval

In conclusion, knee ultrasound demonstrates high diagnostic performance in the diagnosis of ACL and PCL injuries, particularly when performed by experienced musculoskeletal radiologists.

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Compliance with ethical standards

Ethical approval Institutional review board approval was not required because this study was a systematic review and meta-analysis.

Informed consent Written informed consent was not required.

Conflicts of interest All authors declare that they have no conflicts of interest.

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