ACCURACY OF THE LEVER SIGN TO DIAGNOSE ANTERIOR CRUCIATE LIGAMENT TEAR: A SYSTEMATIC REVIEW WITH META-ANALYSIS

Michael P. Reiman, PT, DPT, SCS, ATC, FAAOMPT, CSCS^{1,2}

Carly K. Reiman³

Simon Décary, PT, PhD⁴

ABSTRACT

Background: The Lever sign has gained recent notoriety for its purported anterior cruciate ligament (ACL) diagnostics and simplicity of performance.

Purpose: The purpose of this systematic review with meta-analysis is to summarize the diagnostic accuracy of the Lever sign for use during assessment of the knee for an ACL tear in subjects with suspected acute and chronic knee injury.

Study Design: Systematic review with meta-analysis

Methods: A computer-assisted literature search of MEDLINE, CINAHL, and EMBASE databases using keywords related to diagnostic accuracy of the knee joint. The *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guidelines were used for the search and reporting phases of the study. Quality assessment of bias and applicability was conducted using the Quality of Diagnostic Accuracy Studies (QUADAS). Mixed effects models were used to summarize accuracy.

Results: Eight articles, with only two demonstrating high quality, were included. Six of the articles were included in a meta-analysis. Diagnostic values, utilizing arthroscopy as a gold standard, were: pooled SN 0.55 (95% CI 0.22 to 0.84), pooled SP 0.89 (95% CI 0.44 to 0.99), positive likelihood ratio (+LR) 9.2 (95% CI 0.70 to 46.1), negative likelihood ratio (-LR) 0.58 (95% CI 0.18 to 1.28). Post-test probability with a positive finding (57% sampling prevalence) reached 92% (95% CI 83 to 97%). Post-test probability with a negative finding (57% sampling prevalence) reached 43% (95% CI 39 to 47%).

Conclusions: Based on limited evidence of heterogeneous methodological quality, the Lever sign can moderately change post-test probability to rule in an ACL tear. These results should be interpreted cautiously due to a limited number of studies, with small sample sizes and study quality affecting test accuracy. Future investigation should be expanded to include additional high-quality studies examining diverse clinical contexts, as they become available, to enable a more comprehensive clinical examination of this test.

Key words: anterior cruciate ligament, diagnostic accuracy, Lever Sign, knee, sensitivity, specificity

Level of evidence: 3a

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CORRESPONDING AUTHOR

Michael P. Reiman, PT, DPT, SCS, ATC,
FAAOMPT, CSCS

Duke University School of Medicine
Department of Orthopedic Surgery
Doctor of Physical Therapy Division
DUMC 104002

Durham, NC 27710

Phone: (919) 668-3014; Fax: (919) 684-1846

E-mail: reiman.michael@gmail.com

¹ Duke University Medical Center, Department of Orthopedic Surgery, Durham, NC, USA

² Duke University Orthopaedic Fellowship, Duke University Medical Center, Durham, NC, USA

³ Department of Biological Sciences, North Carolina State University, Raleigh, NC, USA

⁴ Université Laval, Faculty of Medicine, Québec, Canada.

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INTRODUCTION

A tear of the anterior cruciate ligament (ACL) is a significant knee injury which can leave patients with sustained complaints of instability in daily and sporting activities as well as increasing their risk of knee osteoarthritis later in life.^{1,2} Current best practices for the management of symptoms in young adults propose early rehabilitation or surgery.³ Thus, there is a need for an accurate initial diagnosis based on history and physical examination, although this may be difficult to achieve.⁴

Diagnostic accuracy of physical examination tests for ACL tear has been extensively studied.⁵ The three most studied tests, the Lachman, the pivot shift and the anterior drawer test have shown overall adequate accuracy for clinical use.⁵⁻⁸ However, these tests also yielded lower accuracy when utilized acutely post injury compared to a chronic tear,⁸ when the knee has a combined lesion to the meniscus instead of an isolated ACL tear, and when the tear is partial compared to complete.⁵⁻⁸ Moreover, inter-rater reliability of these tests may be lower when executed by non-expert clinicians because of technical difficulties and interpretation of the outcomes.^{9,10}

In response to these limitations, Lelli et al. proposed a new physical examination test to diagnose ACL tear called the Lever sign.¹¹ This test requires the evaluator to place his or her fist under the calf muscle to create a “fulcrum” extending the knee while applying a moderate downward force to the distal part of the femur.¹¹ In an intact knee, the ACL completes a lever mechanism, making the heel rise in response to the force applied to the femur.¹¹ In an ACL-deficient knee, the heel does not rise indicating a positive Lever sign.¹¹ In their initial study, the authors demonstrated a perfect sensitivity and specificity in a sample of acute and chronic patients with both partial and complete ACL tears.¹¹

Several years following its introduction, this test is rapidly gaining the interest of clinicians due to its simplicity. Yet, none of the recent systematic reviews examining accuracy for ACL clinical tests have included this test to verify if subsequent studies supported the initial claims.^{5,8} Therefore, the purpose of this systematic review with meta-analysis is to summarize the diagnostic accuracy of the Lever

sign for use during assessment of the knee for an ACL tear ACL tear in subjects with suspected acute and chronic knee injury.

METHODS

Registration

The study was registered with the International Prospective Register of Systematic Reviews (PROSPERO#CRD42018084954) on January 15, 2018. PROSPERO is a database of prospectively registered systematic reviews for health and social topics. The study was registered after the pilot search and prior to updated data search and extraction.

Data Sources

The *Preferred Reporting Items for Systematic Reviews and Meta-Analyses* (PRISMA) guidelines were utilized during the search and reporting phase of this review. The PRISMA statement includes a 27-item checklist that is designed to be used as a basis for reporting systematic reviews of randomized trials,¹² but the checklist can also be applied to multiple forms of research methodologies.¹³

A computer-assisted literature search of MEDLINE, CINAHL, and EMBASE databases was performed from inception of each respective database to December 23, 2017, and updated on April 2, 2018. The goal was to optimize the sensitivity of the search strategy,^{14,15} increasing the likelihood that all appropriate studies were identified. The search strategy was developed in collaboration with a medical information specialist and used controlled vocabulary and key words related to diagnostic accuracy of the lever test relative to ACL tear. Screening filters were initially used during assessment of title, abstract and full text documents. The search was further limited to humans and English or French-only publications. The search strategy for MEDLINE is provided in Appendix 1.

Selection criteria

Articles were eligible if they met all of the following criteria: 1) it included participants with suspected ACL tear/injury, 2) it included the Lever sign test to diagnose ACL tear/injury, 3) it utilized an acceptable reference standard, 4) it reported diagnostic values in sufficient detail to allow reconstruction of

contingency tables, and 5) it was written in English or French.

An article was excluded if: 1) the pathology assessed was associated with a condition not located at the knee joint, 2) the study did not evaluate the Lever sign test, 3) the study did not provide sufficient detail to calculate diagnostic accuracy, 4) the clinical tests were performed on cadavers, 5) the study reported on specialized instrumentation, questionnaires or performance measures, or 6) the study was performed on infants/toddlers.

Study selection

Two reviewers (MPR, CKR) independently performed the search. Because computerized search results for diagnostic accuracy data frequently omit many relevant articles,¹⁶ the reference lists of all selected publications were checked to retrieve relevant publications that were not identified in the computerized search. Unpublished literature was also hand searched and included publications, posters, abstracts, or conference proceedings. To identify relevant articles, titles and abstracts of all identified citations were independently screened. Full-text articles were retrieved if the abstract provided insufficient information to establish eligibility or if the article passed the first eligibility screening.

All criteria were independently applied by two reviewers (MPR, CKR) to the full text of the articles that passed the first eligibility screening. Disagreements among the reviewers were discussed and resolved by consensus. Articles to be included (for meta-analysis) were determined by using clinical and statistical judgment of study heterogeneity. Clinical judgment criteria involved assessment of similarity of populations, assessment context (e.g., test performed *a priori*), reference standard (e.g. MRI or arthroscopy), and method in which specific tests were applied.¹⁷ In addition, after approval using clinical judgment, studies were statistically pooled for meta-analysis when ≥ 2 studies examined the Lever sign test and diagnosis with the same reference standard.

Risk of Bias/Quality Assessment

The Quality Assessment of Diagnostic Accuracy Studies tool (QUADAS), the original tool for quality

assessment in diagnostic accuracy studies, was used to analyze the quality of the study. QUADAS consists of 14 items with each having a “yes”/“no”/“unclear” answer options. A “yes” score indicated sufficient information, with bias considered unlikely. A “no” score indicated sufficient information, but with potential bias from inadequate design or conduct. An “unclear” score indicated that insufficient information was provided in the article or the methodology was unclear. The total score is formed by the count of all of the criteria scored “yes”, valued as “1” whereas, “no” and “unclear” scores carried a zero score value. If a “yes” score was present for all 14 items, the maximum attainable unweighted score is 14/14. The methodological quality and risk of bias of each of the studies was independently assessed by two reviewers (MPR, SD). Disagreements among the reviewers were discussed and resolved with consensus. Inter-rater reliability was calculated with weighted Kappa.

Qualitatively, studies that exhibit higher QUADAS values are associated with less risk of design bias than those of lower values. Studies were stratified as “high quality/low risk of bias” if the QUADAS score was $\geq 10/14$, and “low quality/high risk of bias” if the study score $< 10/14$. This dichotomizing stratification level was chosen since it has been utilized successfully previously and no other strategy is advocated to discriminate low and high bias diagnostic accuracy studies.¹⁸⁻²³

Data extraction and analysis

One reviewer (MPR) independently-extracted information and data regarding study population, setting, examiner, duration of symptoms, mechanism of injury, test performance, diagnostic reference-standard, and number of true positives, false positives, false negatives, and true negatives for calculation of sensitivity (SN), specificity (SP), positive likelihood ratios (+LR), and negative likelihood ratios (-LR) when not provided. Extracted data was verified by the other study authors (CKR, SD).

It has been suggested that post-test probability can be altered to a minimal degree with +LRs of 1 to 2 or -LRs of 0.5 to 1, to a small degree with +LRs of 2 to 5 or -LRs of 0.2 to 0.5, to a moderate degree with +LRs of 5 to 10 and -LRs of 0.1 to 0.2) and to a large

and almost conclusive degree with +LRs greater than 10 and -LRs less than 0.1.²⁴ Pretest probability is defined as the probability of the target pathology before a diagnostic test result is known. It represents the probability that a specific patient, with a specific past history, presenting to a specific clinical setting, with a specific symptom complex, has a specific pathology.²⁴

STATISTICAL METHODS

Meta-Analysis

Der-Simionian and Laird²⁵ mixed effects models, which incorporate both between and within study heterogeneity, were used to produce summary estimates of SN, SP, LR+, LR-, PPV, and NPV. An I-squared value of >50% and Cochrane's-Q p-value of <0.10 were the criteria to indicate significant between-study heterogeneity, of SN and SP and likelihood ratios respectfully. Publication bias was not formally tested due to low power of the tests with limited included studies.²⁶ All analyses were conducted in R version 3.4.2 (package: mada, <http://cran.r-project.org/>).

RESULTS

Selection of Studies

The systematic searches of MEDLINE, CINAHL, and EMBASE, as well as hand search, netted 305 abstracts after duplicates were removed. Abstract and full text review reduced the acceptable papers to eight^{11,27-33} (Figure 1 and Table 1). Abstract screening inter-rater agreement was $\kappa=0.80$ (95% CI: 0.60 to 0.94) and full text agreement was $\kappa=0.92$ (95% CI: 0.85 to 0.99); both indicating almost perfect agreement. The search strategy utilized for MEDLINE is listed in Appendix I. Excluded studies are listed in Appendix II.

This review included 977 subjects across the eight studies (Tables 1 & 2).^{11,27-33} The sample size of the studies ranged from 33²⁷ to 400 subjects (Table 1).³¹ All studies were prospective in study design (Table 1). Sources of support and conflicts of interest reporting is detailed in Appendix III.

Quality Scores

Inter-rater agreement was $\kappa=0.62$ (95% CI: 0.48 to 0.78), indicating substantial agreement. Table 1

provides the overall risk of bias score, with two studies^{29,31} demonstrating low risk of bias. Details of each the individual study quality scores are presented in Appendix IV.

Study Characteristics

Detail on subject sex, mean age, duration of symptoms, and mechanism of injury are listed in Table 1. The clinicians performing the examination and the setting in which the examination was performed are listed in Table 2. The reference standards utilized, as well as the professional training of the clinicians performing the Lever sign are also listed in Table 2.

META-ANALYSIS

Six studies^{11,29-33} qualified for meta-analysis (Tables 1-3). Three studies (n = 234 subjects) utilized arthroscopy as a gold standard in surgical candidates,^{30,32,33} while three studies (n = 539 subjects) utilized MRI as a reference standard.^{11,29,31}

Figures 2 through 4 illustrate pre- to post-test probability changes utilizing the Lever sign with arthroscopy and MRI reference standards, respectively. Diagnostic accuracy and probability shifts were calculated utilizing MRI as a reference standard with high quality/low risk of bias studies^{29,31} only (Figure 2) and with all studies^{11,29,31} (one additional study was low quality/high risk of bias). Pre- to post-test probability for positive and negative findings on the Lever sign are presented in Table 3. As shown in this table, the adding of one high risk of bias study¹¹ substantially change the estimates.

RESULTS OF INDIVIDUAL DIAGNOSTIC STUDIES

One study²⁹ utilized arthroscopy as a gold standard, but did not qualify for meta-analysis as the subjects were examined under anesthesia, unlike the other two studies.^{17,20} The prevalence of ACL tear in this study with this gold standard was 54%. Post-test probability with a positive finding was 86%, while a post-test probability with a negative finding was 16%.

Three studies^{11,27,28} examining those with ACL tear/injury reported only SN (Table 4). Two studies^{27,28} utilized arthroscopy as a reference standard, and both examined the Lever sign pre- and post-anesthesia.

Figure 1. Flow diagram for study.

Chong et al.²⁷ found a SN range of 0.82 (physician assistant examiner) to 0.88 (orthopaedic surgeon examiner) pre- and 0.97 (orthopaedic surgeon) to 1.0 (physician assistant) post-anesthesia in a group of 33 subjects with ACL tear of at least 72 hours prior to examination. Deveci et al.³² demonstrated a SN of 0.94 pre- and 0.98 post-anesthesia in a group of 117 subjects with ACL tear of a mean of 8.7 (4 to 25 weeks) from onset of injury.

One of the studies³⁰ utilized a separate reference standard, therefore not qualifying for meta-analysis. Besides arthroscopy as a gold standard, Mulligan et al.³⁰ also utilized a clinical test cluster as a reference standard in 41 subjects, demonstrating diagnostic

values of: SN 0.44 (95% CI 0.17 to 0.74), SP 0.75 (95% CI 0.67 to 0.83), +LR 1.78 (95% CI 0.69 to 4.58), -LR 0.74 (95% CI 0.40 to 1.37). The prevalence of ACL tear in this study with clinical test cluster reference standard was 22%. Post-test probability with a positive finding was 33%, while a post-test probability with a negative finding was 17%.

DISCUSSION

The aim of this systematic review with meta-analysis was to summarize the diagnostic accuracy of the Lever sign when used to diagnose an ACL tear. Based on limited evidence of heterogeneous methodological quality, the Lever sign can moderately

Table 1. Demographics and risk of bias in included studies.

Study	Level of Evidence	Study Design	Risk of Bias (QUADAS)	Subjects; Gender; Mean Age; Duration of Symptoms	Mechanism of Injury
Chong et al. (2017) ²⁷	III	Cohort study	High	33 patients diagnosed with ACL injury at least 72 hours prior to examination Females (n=12) Mean age: 30.6 ± 17.0 (15–60) years (females) 30.9 ± 14.3 (11–62) years (males) Injury onset: knee injury was not sustained within 72 hours prior to data collection	NR
Deveci et al. (2015) ²⁸	IV	Cohort study	High	117 patients diagnosed with ACL tear based on symptoms, physical exam and (+) 1.5T MRI Females (n=21) Mean age: 25.8 ± 5.9 (17–45) years Injury onset: 8.7 (4–25) weeks	NR
Jarbo et al. (2017) ²⁹	II	Cohort study (diagnosis)	Low	102 patients with acute (≤4 weeks) symptomatic knees Females (n=44) Mean age: 23 years Injury onset: within 4 weeks of their injury or the onset of symptoms	NR
Lichtenberg et al. (2018) ³³	II	Cohort study (diagnosis)	High	94 patients with trauma to the knee. Patients with locking knee complaints or previous ACL were excluded. Females (n=37) Mean age: 34 ± 15 years Injury onset: ranging from acute (< 3 weeks) to chronic (> 12 weeks)	Trauma to the knee
Lelli et al. (2014) ¹¹	IV	Cohort study	High	400 patients Group A (acute injury, (+) MRI for complete ACL rupture); 29 females; 27 years Group B (chronic injury, (+) MRI for complete ACL rupture); 35 females; 26 years Group C (acute injury with (+) MRI for partial ACL rupture); 24 females; 26.8 years Group D (chronic injury with (+) MRI for partial ACL rupture); 31 females; 25.9 years Mean age: 26.4±14.9 years Injury Onset: <ul style="list-style-type: none">acute phase: 20 days from injury,chronic phase: more than 20 days from injury (range 20 days–4 years)	NR
Massey et al. (2017) ³¹	II	Cohort study	Low	91 patients subjects after a knee injury with subjective swelling, or an objective effusion 30 females Mean age: 28±11 years Injury onset: NR	Noncontact or contact knee injury
Mulligan et al. (2017) ³⁰	III	Cohort study	High	60 patients with complaint of knee pain (<7/10) 22 females Mean age: 42±13.4 (18–65) years Injury onset: 55±80 (1–304) days	NR
Thapa et al. (2015) ³²	II	Cohort study	High	80 patients with complaints of knee symptoms of giving way/locking/pain 30 females Mean age: 32.12 (21–42) years Injury onset: NR	Sports activities (62.8%)

NR, not reported; QUADAS, Quality Assessment of Diagnostic Accuracy Studies scores; studies were stratified as “high quality/low risk of bias” if the QUADAS score was ≥10/14, and “low quality/high risk of bias” if the study score < 10/14.

change post-test probability to rule in or rule out an ACL tear based upon studies with lower risk of bias. Interpretation of the methodological quality of the primary diagnostic studies is presented, as well as comparisons to the findings of previous meta-analyses of other ACL tests.

Methodological quality of the primary diagnostic studies and impact on accuracy

Eight primary diagnostic studies, including the original article by Lelli et al., have investigated this test. Only two studies were considered to have a low risk of bias.^{29,31} Out of the five other studies^{11,27,28,30,32}, three

Table 2. Characteristics of included studies.					
Study	Subjects (n)	Reference Standard	Examiners	Examination Setting	Examiner Reliability
Chong et al. (2017) ²⁷	33	Arthroscopy	Experienced sports medicine orthopaedic surgeon & Experienced orthopaedic physician assistant	Both under anaesthesia and without anaesthesia during arthroscopy	<i>Inter-rater</i> Pre-anaesthesia 0.30 κ; 82% agreement Post-anaesthesia NA κ; 97% agreement <i>Intra-rater</i> 0.05 κ; 85% agreement (OS); NA κ; 67% agreement (PA)
Deveci et al. (2015) ²⁸	117	Arthroscopy	Two orthopedic surgeons	Both under anaesthesia and without anaesthesia during arthroscopy	0.89 to 0.96 ICC (inter-rater)
Jarbo et al. (2017) ²⁹	102	MRI RS (n=48) Surgical GS (n=54)	Randomly assigned undergraduate student, medical student, orthopaedic resident, or orthopaedic fellow	Initial clinic visit (for nonsurgical patients) or under anesthesia in the operating room (for surgical patients)	NR
Lichtenberg et al. (2018) ³³	94	Arthroscopy	Orthopedic surgeon and physiotherapist	University medical center outpatient clinic	<i>Inter-rater</i> 0.82 κ; (OS and PT)
Lelli et al. (2014) ¹¹	400	MRI	Single clinician	Surgical clinic	NR
Massey et al. (2017) ³¹	91	1.5 T MRI	2 board-certified orthopaedic surgeons	Surgical clinic, with patient awake	NR
Mulligan et al. (2017) ³⁰	60	RS (n=41) Clinical test cluster	Licensed physical	Hospital clinical setting	NR
		GS (n=19) Surgery	Therapist with 36 years of sports physical therapy experience		
Thapa et al. (2015) ³²	80	Arthroscopy	NR	Sports clinic in department of orthopedics	NR
MRI=magnetic resonance imaging, RS=reference standard, GS=gold standard, NR=not reported, n=number, T=Tesla, κ=kappa, OS=orthopaedic surgeon, PA=physician assistant, PT=physiotherapist, ICC=intraclass correlation					

Table 3. Pooled diagnostic properties for the diagnosis of Lever sign for ACL tear/injury.							
	# studies (sample size)	SN (95% CI)	SP (95% CI)	+LR (95% CI)	-LR (95% CI)	Post-Test Change for (+) Result	Post-Test Change for (-) Result
Surgery	3 ^{30,32,33} (n=234)	0.55 (0.22, 0.84)	0.89 (0.44, 0.99)	9.2 (0.70, 46.1)	0.58 (0.18, 1.28)	Pretest=57% Posttest=92%	Pretest=57% Posttest=43%
MRI (High quality studies only)	2 ^{29,31} (n=139)	0.77 (0.55, 0.90)	0.91 (0.55, 0.99)	13.1 (1.9, 52.4)	0.28 (0.14, 0.46)	Pretest=54% Posttest=94%	Pretest=54% Posttest=25%
MRI (all studies)	3 ^{11,29,31} (n=539)	0.95 (0.34, 1.0)	0.97 (0.58, 1.0)	128 (0.97, 832.0)	0.18 (0.00, 1.0)	Pretest=70% Posttest=100%	Pretest=70% Posttest=30%
DerSimonian-Laird mixed-effects models used throughout. SN=sensitivity, SP=specificity, +LR=positive likelihood ratio, -LR=negative likelihood ratio, (+)=positive, (-)=negative, PPV=positive predictive value, NPV=negative predictive value, CI=confidence interval, MRI=magnetic resonance imaging, n=number							

low-quality studies^{11,27,28} included 644 out of the 977 patients (66%) in this systematic review.

An important bias in these three studies is the assessment of the Lever sign on cohorts including only

ACL-deficient knees prior to obtaining arthroscopic surgery.^{11,27,28} Accordingly with QUADAS methodological assessment, this bias precludes investigators from adequate blinding when the index test was executed, which likely overestimated accuracy.³⁴ More

Figure 2. Pre- to post-test probability shifts for Lever sign with arthroscopy gold standard (pooled analysis). Blue line represents positive and red line represents negative probability shifts.

so, because of the absence of non ACL-deficient cases in these cohorts, only SN could be calculated. Thus, these studies only informed on the capacity of the Lever sign to assist in “ruling out” the presence of injury when the test is negative.³⁵ Lastly, Lelli et al. measured SP of the Lever sign by evaluating the test on the healthy knees of the patients as a control.¹¹ This represents a case-control bias which can also overestimate accuracy.^{34,36}

This meta-analysis demonstrates the impact of low-quality studies on analysis of accuracy. The pooled estimates for positive and negative LR using MRI as a reference standard was 13.1 and 0.28 when considering only the two high-quality studies.^{29,31} When adding one low-quality study¹¹ to the meta-analysis, pooled estimate for +LR increased approximately

10-fold to 128.0 and negative LR to 0.18. The addition of 400 true positives and true negatives without added false positive and false negative findings because of possible biases yielded wide 95% CI and unprecise estimates to guide clinical decision-making.

Clear utilization of blinding for test interpretation was reported in only one study²⁹ in this review. Test interpretation with knowledge of index test findings is a significant bias in diagnostic accuracy studies. A meta-review³⁷ and one review³⁸ have reported that overall accuracy was higher in the presence of diagnostic review bias (person interpreting the reference standard was aware of the index test results).

These biases were also found in recent diagnostic studies investigating other ACL tests.⁸ Researchers are urged to follow Equator Network guidelines (<http://www.equator-network.org>) and QUADAS,³⁹ in future study designs to advance our understanding of these diagnostic tests.

Comparison of the accuracy of Lever sign to other ACL tests

The accuracy estimates from this meta-analysis must be compared with meta-analyses of other ACL tests⁵ to inform regarding clinical utilization of these tests. The studies in this review report a SN of 55% to 95% (depending on the gold standard), yielding negative LR of 0.18 to 0.58. This induces a small to moderate change in negative post-test probability of 14% to 40% to rule out an ACL tear when the test is negative. A SP of 88% to 97% was also reported in the included studies, yielding a positive LR of 9.2 to 128. This induces a moderate change in positive post-test probability of 30 to 35% to rule in an ACL tear when the test is positive. Because of the limited number of patients included in this meta-analysis, estimates from this review demonstrate wide 95% CI and should be interpreted cautiously. From the two high-quality studies, one found SN of 63% and SP of 90%,²⁹ while the other found SN of 83% and SP of 80%.³¹

The most comprehensive meta-analysis summarizing the accuracy of other ACL tests included 28 primary studies and demonstrated the following statistics.⁶ For the Lachman test, SN and negative LR was 85% and 0.2, while SP and positive LR was 94% and 10.2. For the Pivot shift test, SN and negative LR was 24% and 0.90, while SP and positive LR

Table 4. Summary of independent articles reporting on the diagnostic accuracy of Lever sign for ACL tear/injury.

Authors	Subjects (n)	SN/SP (95% CI)	+LR/-LR	PPV/NPV	Reference Standard	Post-Test Probability
Chong et al. (2017) ²⁷	33	OS 0.88 SN (NR) (pre-anesthesia); 0.97 (NR) (post-anesthesia) PA 0.82 SN (NR) (pre-anesthesia); 1.0 SN (NR) (post-anesthesia)	NA	NA	Arthroscopy	NA
Deveci et al. (2015) ²⁸	117	0.94 (NR) (pre-anesthesia) 0.98 SN (NR) (post-anesthesia)	NA	NA	Arthroscopy	NA
Jarbo et al. (2017) ²⁹	54	0.86 (0.68 to 0.96)/0.85 (0.64 to 0.96)	5.4/0.16	0.86/0.84	Arthroscopy	86% with (+) test 16% with (-) test (54% pre-test prevalence)
Mulligan et al. (2017) ³⁰	41	44 (14 to 78)/75 (57 to 89)	1.8/0.74	0.33/0.83	Clinical test cluster	33% with (+) test 17% with (-) test (22% pre-test prevalence)

SN=sensitivity, SP=specificity, +LR=positive likelihood ratio, -LR=negative likelihood ratio, (+)=positive, (-)=negative, PPV=positive predictive value, NPV=negative predictive value, CI=confidence interval, n=number, NR=not reported, OS=orthopedic surgeon, PA=physician assistant, NA=not applicable

was 98% and 8.5. For the anterior drawer test, SN and negative LR was 55% and 0.50, while SP and positive LR was 92% and 7.3. When comparing estimates and 95% CI from meta-analyses, the Lever sign may demonstrate diagnostic accuracy comparable to other ACL tests. This conclusion mirrors one high-quality study³¹ in this review which directly compared all ACL tests in one cohort and found no significant difference between the estimates. Video performance of the Lachman test and Lever sign are demonstrated in Figure 5, available online.

Future direction

The results from this first meta-analysis regarding diagnostic accuracy of the Lever sign show potential for its use in clinical practice. Given the available scarce evidence and low to moderate study quality, further investigation is required to match the level of understanding of the other common tests used to examine those with suspected ACL tear.⁵ Other high-quality diagnostic studies are required to better understand the accuracy of this test in diverse clinical contexts and in various patient profiles. Notably, it remains to be demonstrated that this test can

replace other ACL tests for contexts such as acute presentation or for partial ACL tears. Also, while the test was developed as a simplified alternative to other more technically challenging tests or for evaluators with small hands compared to a patient's muscle size, only three studies have shown inter-rater reliability to be "fair" or "high".^{27,28,33} Previous evidence examining ACL diagnostic tests indicates that reliability can be lowered when the evaluator is inexperienced.¹⁰ In most studies on the Lever test, there were only experienced clinicians. Future studies should assess if this test can be valid and reliable when used by clinicians with a diversity of clinical experience, with an emphasis on primary care clinicians. It is likely that the required training for this test, as well as describing optimal condition for execution (eg. cushioning of the examination table, amount of force applied), must be standardized.

Limitations

Due to heterogeneity of studies and variable reference standards only five of the seven studies qualified for meta-analysis with two different reference standards (MRI and arthroscopy). Despite moderate shifts in

Figure 3. Pre- to post-test probability shifts for Lever sign with MRI reference standard (only low risk of bias studies in pooled analysis). Blue line represents positive and red line represents negative probability shifts.

positive and negative post-test probability using the Lever sign compared to both reference standards, caution is warranted due to study quality. Other limitations of this study include: limiting the search strategy to only those articles written in English or French, lack of comparison of subject inclusion and exclusion across the studies and primary studies performed in settings of high pre-test probability. Lastly, only one author extracted the data points, but both of the other authors verified all data points.

CONCLUSION

This meta-analysis summarizes the diagnostic accuracy of the Lever sign when used to diagnose ACL tear. Based on limited evidence of heterogeneous methodological quality, the Lever sign can moderately change post-test probability to rule in or rule

Figure 4. Pre- to post-test probability shifts for Lever sign with MRI reference standard (low and high risk of bias studies included in pooled analysis). Blue line represents positive and red line represents negative probability shifts.

out an ACL tear in studies with lower risk of bias. These results should be interpreted cautiously due to the limited number of studies in this review, and the likelihood that small sample sizes and study quality may have affected test accuracy. The Lever sign is simple to use and could complement a complete physical examination, specifically in contexts where the traditional tests may be difficult to execute. The evidence for the Lever sign remains scarce and warrants additional investigation to guide clinical utility.

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APPENDIX I. MEDLINE SEARCH STRATEGY

("Clinical Examination" OR "Clinical Exam"[tiab] OR Physical Examination OR "Physical Exam"[tiab] OR "Orthopedic Examination"[tiab] OR "Orthopedic Exam"[tiab] OR "musculo-skeletal examination"[tiab] OR "musculo-skeletal examination"[tiab] OR "musculoskeletal exam"[tiab] OR "musculo-skeletal exam"[tiab] OR "Clinical evaluation"[tiab] OR "Physical evaluation"[tiab] OR "musculoskeletal evaluation"[tiab] OR "musculo-skeletal evaluation"[tiab] OR "Clinical inspection"[tiab] OR "Physical inspection"[tiab] OR "musculoskeletal inspection"[tiab] OR "musculo-skeletal inspection"[tiab] OR "Sensitivity" [tiab] OR "Specificity" [tiab] OR "Accuracy" [tiab]) AND ("knee"[MeSH Terms] OR "knee joint"[MeSH Terms] OR Knee[tiab] OR knees[tiab] OR "tibiofemoral joint"[tiab] OR "Anterior Cruciate Ligament Injuries"[MeSH Terms] OR ("Anterior Cruciate Ligament"[MeSH Terms] OR "Anterior Cruciate Ligament"[tiab] OR ACL[tiab]) AND (Injury[tiab] OR injuries[tiab] OR "injuries"[Subheading] OR tear[tiab] OR tears[tiab] OR "lacerations"[MeSH Terms] OR "lacerations"[tiab] OR "laceration"[tiab] OR "rupture"[MeSH Terms] OR "rupture"[tiab] OR "ruptures"[tiab])) AND (randomized controlled trial[pt] OR controlled clinical trial[pt] OR randomized[tiab] OR randomised[tiab] OR randomization[tiab] OR randomisation[tiab] OR placebo[tiab] OR drug therapy[sh] OR randomly[tiab] OR trial[tiab] OR groups[tiab] OR Clinical trial[pt] OR "clinical trial"[tiab] OR "clinical trials"[tiab] OR "evaluation studies"[Publication Type] OR "evaluation studies as topic"[MeSH Terms] OR "evaluation study"[tiab] OR evaluation studies[tiab] OR "intervention studies"[MeSH Terms] OR "intervention study"[tiab] OR "intervention studies"[tiab] OR "case-control studies"[MeSH Terms] OR "case-control"[tiab] OR "cohort studies"[MeSH Terms] OR cohort[tiab] OR "longitudinal studies"[MeSH Terms] OR "longitudinal"[tiab] OR longitudinally[tiab] OR "prospective"[tiab] OR prospectively[tiab] OR "retrospective studies"[MeSH Terms] OR "retrospective"[tiab] OR "follow up"[tiab] OR "comparative study"[Publication Type] OR "comparative study"[tiab] OR "Cross sectional studies"[mesh] OR "cross sectional"[tiab]) NOT (Editorial[ptyp] OR Letter[ptyp] OR Case Reports[ptyp] OR Comment[ptyp]) NOT (animals[mh] NOT humans[mh])

Appendix II. Excluded Studies (Abstract & full text review)		
Study	Title	Reason Excluded
Antinolfi P, et al. (2017) ¹	Relationship between Clinical, MRI, and Arthroscopic Findings: A Guide to Correct Diagnosis of Meniscal Tears	Lever test not utilized in study
Chong et al. (2017) ²	Evaluating Different Clinical Diagnosis of Anterior Cruciate Ligament Ruptures In Providers with Different Training Backgrounds.	Reliability study; diagnostic accuracy not reported
Cinque ME, et al. (2017) ³	The Heel Height Test: A Novel Tool for the Detection of Combined Anterior Cruciate Ligament and Fibular Collateral Ligament Tears.	Lever test not utilized in study
Kilinc BE, et al. (2016) ⁴	Evaluation of the accuracy of Lachman and Anterior Drawer Tests with KT1000 in the follow-up of anterior cruciate ligament surgery.	Lever test not utilized in study
Orlando Júnior N, et al. (2015) ⁵	Diagnosis of knee injuries: comparison of the physical examination and magnetic resonance imaging with the findings from arthroscopy.	Lever test not utilized in study
Mouton C, et al. (2016) ⁶	Combined anterior and rotational knee laxity measurements improve the diagnosis of anterior cruciate ligament injuries.	Not diagnostic accuracy study.
Geraets SE, et al (2015) ⁷	Diagnostic value of medical history and physical examination of anterior cruciate ligament injury: comparison between primary care physician and orthopaedic surgeon.	Lever test not utilized in study
Srisuwanporn P, et al. (2016) ⁸	Accuracy of a New Stress Radiographic Device in Diagnosing Anterior Cruciate Ligament Tear.	Not physical examination diagnostic accuracy study
Speziali A, et al. (2016) ⁹	Diagnostic value of the clinical investigation in acute meniscal tears combined with anterior cruciate ligament injury using arthroscopic findings as golden standard.	Lever test not utilized in study

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Appendix III. Potential Sources of Support (if reported in study, statements are in quotations)	
Study	Potential Sources of Support (if reported in study)
Chong et al. (2017) ²⁷	“Conflict of Interest Statement: This study did not receive any funding support for this research. The participants and authors of this study did not receive any payments or other personal benefit, or commitments or agreements that were related in any way to the subject of the research that was conducted. No benefits of any form have been received directly or indirectly to the subject of this article. The authors report no actual or potential conflict of interest in relation to this article.”
Deveci et al. (2015) ²⁸	“Competing interests The authors declare that they have no competing interests.”
Jarbo et al. (2017) ²⁹	“The authors declared that they have no conflicts of interest in the authorship and publication of this contribution.”
Lelli et al. (2014) ¹¹	No acknowledgement or reporting of sources of support or conflict of interest in manuscript
Lichtenberg et al. (2018) ³³	The authors declared that they have no conflicts of interest in the authorship and publication of this contribution. Ethical approval for this study was obtained from VU University Medical Center Amsterdam (MTC/2015.327).
Massey et al. (2017) ³¹	“The authors report the following potential conflicts of interest or sources of funding: J.D.H. receives support from NIA Magellan and Slack. He is a member of editorial board of Arthroscopy and Frontiers in Surgery, and a committee member of AOSSM Self-Assessment and AAOS OAFP Workgroup. P.C.M. receives support from NIA Magellan, Genzyme, Slack, DePuy, A Johnson & Johnson Company, Arthrex, and Zimmer. He is a member of editorial board of Journal of Knee Surgery and Orthobullets.com.”
Mulligan et al. (2017) ³⁰	“We declare that we have no conflicts of interest in the authorship or publication of this contribution.
Thapa et al. (2015) ³²	“Conflict of interests: None declared.”

Appendix IV. QUADAS Values for Accepted Studies.															
Article	1	2	3	4	5	6	7	8	9	10	11	12	13	14	Total
Chong et al. (2017) ²⁷	N	N	Y	Y	Y	Y	U	Y	Y	U	U	U	N	N	6
Deveci et al. (2015) ²⁸	U	U	Y	Y	Y	Y	U	Y	Y	U	N	N	N	N	6
Jarbo et al. (2017) ²⁹	Y	Y	Y	U	Y	Y	Y	Y	Y	Y	Y	Y	N	N	11
Lichtenberg et al. (2018) ³³	Y	Y	Y	U	U	Y	N	Y	Y	Y	U	Y	N	N	8
Lelli et al. (2014) ¹¹	U	U	Y	U	Y	Y	Y	Y	N	U	U	U	N	N	5
Massey et al. (2017) ³¹	Y	Y	Y	U	Y	Y	N	Y	Y	Y	N	Y	Y	Y	11
Mulligan et al. (2017) ³⁰	Y	Y	U	U	Y	N	Y	Y	Y	Y	U	Y	U	Y	9
Thapa et al. (2015) ³²	Y	Y	Y	U	Y	Y	N	Y	Y	Y	N	Y	N	N	9
Abbreviations: Y, yes; N, No; U, Unknown; QUADAS, Quality Assessment of Diagnostic Accuracy Studies scores; studies were stratified as “high quality/low risk of bias if the QUADAS score was $\geq 10/14$, and “low quality/high risk of bias of the study score $< 10/14$.															