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Diagnostic accuracy of examination tests for lateral elbow tendinopathy (LET) – A systematic review

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ABSTRACT

Background: Reviews on the diagnostic performance of the examination tests for lateral elbow tendinopathy (LET) based on updated context-specific tools and guidelines are missing.

Purpose: To review the diagnostic accuracy of examination tests used in LET.

Design: Systematic review following PRISMA-DTA guidelines.

Methods: We searched MEDLINE, PubMed, CINAHL, EMBASE, PEDro, ScienceDirect, and Cochrane Library databases. The QUADAS-2 checklist was used to assess the methodological quality of the eligible studies. We included diagnostic studies reporting the accuracy of physical examination tests or imaging modalities used in patients with LET.

Results: Twenty-four studies with 1370 participants were identified reporting the diagnostic performance of Ultrasound Imaging (USI) (18 studies), physical examination tests (2 studies) and Magnetic Resonance Imaging (MRI) (4 studies). Most studies (97%) were assessed with "unclear" or "high risk" of bias. Sonoelastography showed the highest sensitivity (75- 100%) and specificity (85- 96%). Grayscale with or without Doppler USI presented poor to excellent values (sensitivity: 53%-100%, specificity: 42%-90%). MRI performed better in the diagnosis of tendon thickening and enthesopathy (sensitivity and specificity: 81%-100%). The Cozen's test reported high sensitivity (91%) while a grip strength difference of 5%-10% between elbow flexion and extension showed high sensitivity (78%-83%) and specificity (80%-90%).

Conclusions: Cozen's test and grip strength measurement present high accuracy in the diagnosis of LET but are poorly investigated. USI and MRI provide variable diagnostic accuracy depending on the entities reported and should be recommended with caution when differential diagnosis is necessary. Substantial heterogeneity was found in inclusion criteria, operator/ examiner, mode of application, type of equipment and reference standards across the studies.

Systematic review registration: PROSPERO ID CRD42020160402

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Introduction

Lateral elbow tendinopathy (LET) or "tennis elbow" is the most common cause of pain in the elbow due to tendinopathy of the common extensor tendon at the lateral epicondyle.[1] Patients with LET present a complex clinical presentation, with increased disability and productivity loss.[2] Presenting equally in men and women, 1%-3% of the population will experience LET at the age range of 35-50 years.[3,4] The clinical diagnosis of LET is based on the presence of pain in the lateral aspect of the elbow radiating to the forearm, tenderness of the lateral epicondyle, and positive response to gross provocation tests, namely the Cozen's, Mills, or Maudsley's

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tests.[5-7] Even though these tests are commonly applied both in clinical practice and research, the reports for their diagnostic validity are sparse.[8]

Diagnostic ultrasound imaging (USI) is proposed as an accurate and cost-effective method for examining the common extensor tendon (CET) of the elbow, with several advantages over magnetic resonance imaging (MRI).[6] A high reliability for diagnosing tendon abnormalities such as tears, focal degenerative lesions and calcification has been shown.[9,10] More recently, the use of Doppler imaging and USI elastography has been argued to improve the validity of USI in tendinopathy, allowing the assessment of neovascularity and tissue stiffness, respectively.[11,12]

Previous systematic reviews[8,13,14] advocated the diagnostic performance of examination tests used in LET, reporting moderate validity for USI and high diagnostic performance of one physical examination test (grip strength test). Often, systematic reviews of diagnostic accuracy studies present suboptimal reporting, critical flaws in design or conduct, and substantial heterogeneity of results.[15] Aiming to improve quality, context-specific tools and guidelines have been published such as the Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) tool for assessing the risk of bias and applicability,[16] and the Preferred Reporting Items for Systematic reviews and Meta-analyses for Diagnostic Test Accuracy studies (PRISMA-DTA) statement for reporting,[17] Previous systematic reviews in diagnostic imaging of LET[13,18] did not adhere to these published guidelines and were based on quality assessment tools instead of a comprehensive assessment risk of bias. Evaluating the risk of bias as compared to other quality appraisal tools has been found to generate critical differences in assessment findings, which in turn affects inferences about the credibility of reviews' findings.[19]

Traditionally, physical examination test and diagnostic imaging are used interchangeably or in conjunction for the clinical diagnosis of LET in the absence of a "gold diagnostic standard." Most clinical tests are based on provocation of symptoms, while imaging aims to identify degenerative tissue changes or abnormalities. However, the relationship between structural tissue disorganization and symptoms is limited as tendinopathy symptoms are independent of the presence and the extent of pathology within the tendon.[20] This review aimed to evaluate the diagnostic accuracy of physical examination tests and imaging for patients with LET, and inform clinical practice based on published guidelines, rigorous risk of bias assessment criteria, and a transparent approach for the quality of evidence.

Methods

Protocol and guidelines

We adhered to the PRISMA-DTA guidelines[21] in search strategy and reporting of this prospectively registered diagnostic review (PROSPERO registration CRD42020160402).

Information sources and search strategy

We systematically searched from inception to March 11, 2020 the following databases: MEDLINE, PubMed, CINAHL, EMBASE, PEDro, ScienceDirect, and Cochrane Library. Gray literature was searched via OpenGrey and WHO online collection, as well as the following clinical trial registries: Clinical Trials. gov, Australian New Zealand Clinical Trials registry and Cochrane CENTRAL Register. The complementary use of MeSH terms, subject headings, and free-text searching was implemented (Supplementary Material 1).[17,22]

Additionally, we screened reference lists and citation tracking results, and conducted discussions with colleagues for serendipitous discoveries to retrieve additional articles.[21]

Study selection

Search results were imported into EndNote V.X7 and following removal of duplicates, a two-stage screening process was implemented to select relevant studies. Initially, each title and/or abstract was independently evaluated by two reviewers (SK and MM). Subsequently, the full text of potentially eligible studies was retrieved and evaluated against the criteria for eligibility by the same independent reviewers. A third reviewer (VK) was consulted if consensus was not reached.[23] Rejected studies were categorized into clearly irrelevant studies, and studies that did not meet one or more eligibility criteria.

Eligibility criteria

We included prospective and retrospective observational studies which (1) reported on a cohort of adult patients with LET of both sexes, (2) reported on the diagnostic accuracy of physical examination tests, medical imaging, or questionnaires for the diagnosis of LET, (3) included any physical examination test used as a reference standard (ie, palpation, other clinical examination diagnostic tests or a combination of reference standard tests performed by a physician or expert clinician) as there is no known gold standard for the diagnosis of LET, (4) reported a 2 $\times$ 2 contingency table or results in sufficient detail to allow reconstruction of 2 $\times$ 2 contingency tables. We set no limit for duration of symptoms and patient sample size, and no language restrictions; however, we excluded animal and cadaveric studies and LET caused by a fracture or systemic disease (ie, rheumatoid arthritis).

Data extraction

Data for each eligible study was extracted in duplicate and independently by two reviewers (SK and MM) and discrepancies were resolved by discussion with a third reviewer (VK). Pilot testing of 30% of the included studies was performed and the reviewers assessed, practiced, and extracted the available data.[17,22] The retrieved data included study design, sample size, demographics, severity and duration of symptoms, index test, examiner profession, reference standard, assessment details, and findings including sensitivity, specificity, true positive, true negative, false positive, and false negative values.

Quality assessment

All included studies were assessed by the two independent reviewers (SK and MM) for methodological quality using the four domains of QUADAS-2 checklist: 'patient selection', 'index test', 'reference standard', and 'flow and timing'[16]. These domains were assessed for the risk of bias, and the first three were also assessed for applicability. Each item was scored "low," "high," or "unclear" for risk of bias and applicability. Studies rated as "low" on all domains received an overall judgement of "low" risk of bias and "low" concerns of applicability. If a study was rated "high" or "unclear" on at least one domain, then overall judgement was "at risk of bias" or concerns regarding "applicability." All disagreements were resolved by discussion with a third reviewer (VK).

Diagnostic accuracy measures, data synthesis and analysis

The extracted data was recorded in diagnostic 2 $\times$ 2 contingency tables and were used to calculate sensitivity, specificity, like-

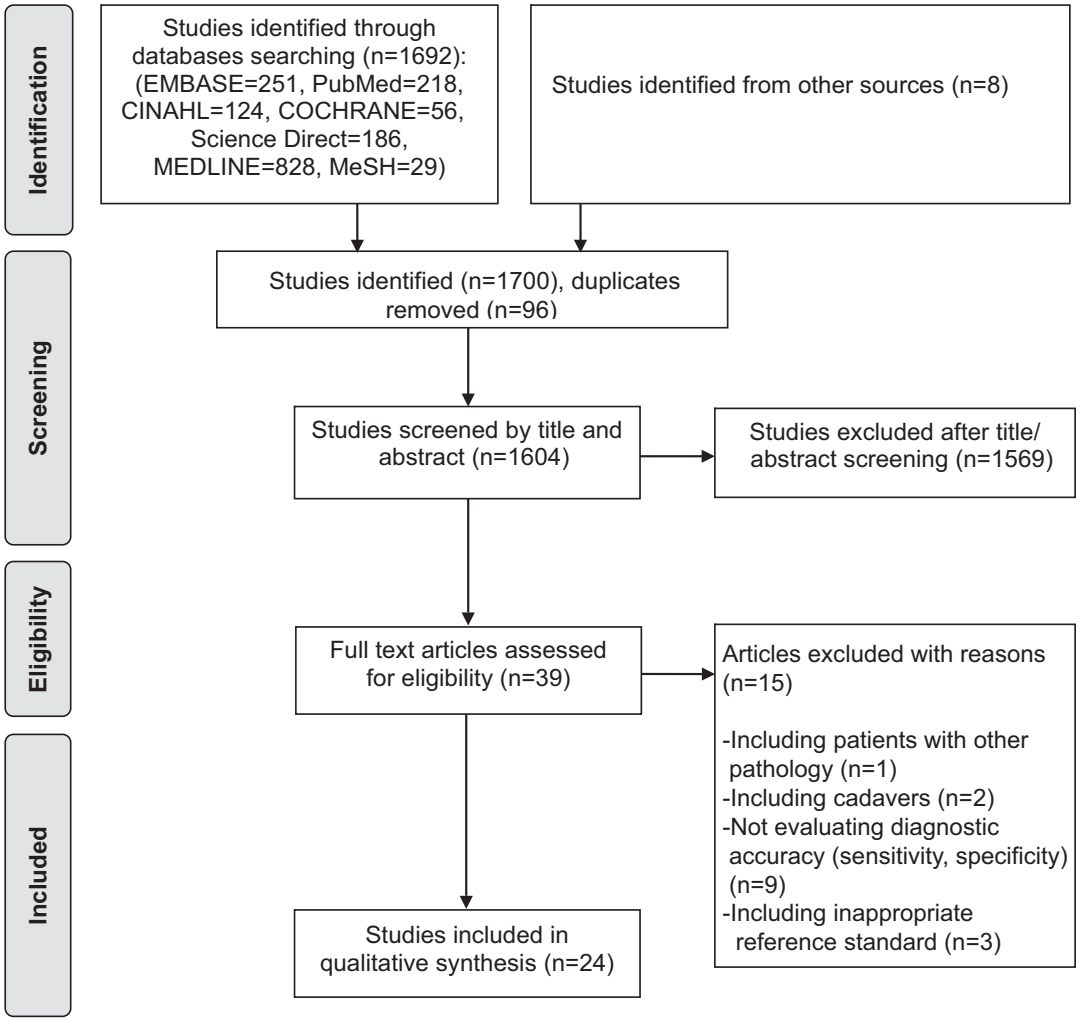

Fig. 1. Study selection flow chart, Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy studies.

lihood ratios (LRs) and their respective 95% confidence intervals (CI) for the diagnosis of LET. Positive LR (LR+) indicating post-test probability of disease presence >10 and negative LR (LR−) indicating post-test probability of disease absence <0.1, were defined as large.[24]

Studies were subgrouped according to the index test implemented (physical examination test or imaging modality). Subsequently, data from included studies were assessed for heterogeneity in a two-stage procedure. Initially, we screened and categorized studies according to the criteria in determining a positive test or abnormality (ie, the same pain provocation test, hypoechogenicity, tendon thickening, tear, calcification, enthesopathy, cortical irregularities, neovascularity, elastographic changes or combinations). For the studies reporting tendon thickening, the test was considered positive when >10% difference was found between affected an unaffected side.[12,14,25] Then, we assessed subgroup heterogeneity using inclusion criteria, mode and type of equipment (ie, frequency of transducer), qualification of the examiner (operator or reader), sample demographics (ie, duration of symptoms, age) and reference standard used. Since evidence for substantial heterogeneity was demonstrated we followed a narrative synthesis approach.

Results

Study selection and characteristics

The search strategy identified 1604 publications. Following full text assessment, 15 studies were excluded with reasons (Supplementary Material MA 2) and 24 studies met the eligibility criteria (Fig. 1).

Study characteristics are presented in Supplementary Material 3, and a summary of diagnostic accuracy results in Supplementary Material 4. All included studies were published in English and were carried out in 13 countries, with the most common being South Korea (4 studies) followed by Turkey, USA and Australia (3 trials each). The total number of participants was 1370 (2086 elbows), the sample size ranged from 8 to 224 participants (8-408 elbows) with a mean age 44.3 years.

Reference standard

All eligible studies included a type of physical examination as a reference standard for the diagnosis of LET,[11,12,14,26-46] with nine of them (37%) using local tenderness during palpation of the com-

mon extensor origin and pain with resisted wrist extension test (Cozen's test).[28,30,33,34,39-41,43,44] Additive to these two tests, three studies used pain during gripping,[11,12,31] two studies used the Mill's test (pain with the elbow extended and the wrist flexed and pronated)[38,46] and one study used the resisted supination test.[45] Three studies used local tenderness during palpation of lateral epicondyle and a cluster of three tests (Cozen's, Mill's and Maudsley test-pain with resisted middle finger extension).[26,32,35] Two studies described only the presence of pain over the lateral epicondyle[14,29] and 2 studies did not include the details of the clinical diagnosis.[27,37]

Index test

The majority of included studies (75%) evaluated the diagnostic accuracy of sonography including different modalities separately or in combination, such as grayscale ultrasound (17 studies),[11,12,14,27-34,36,37,39-41,43] doppler ultrasound (11 studies)[11,12,14,27,30,31,33,34,36,41,43] and elastography (5 studies).[11,31,33,34,44] Four studies evaluated the diagnostic accuracy of MRI[38,42,45,46] and two studies assessed a variety of pain provocation tests such as grip strength, Cozen's, Maudsley and Mill's test.[26,35]

Risk of bias and applicability concerns within studies

The risk of bias and applicability concerns for each individual domain is presented in Fig. 2. Eighteen studies (75%) were rated as "high," 5 (21%) as "unclear" in one or more items of the risk of bias domain, and only one study was rated as "low risk of bias." In terms of the applicability domain, most of the eligible studies (54%) were rated with "low," one third of them with "unclear" and the minority (12%) with "high concerns".

Patient selection was rated as "high" risk of bias in 66% of the eligible studies, due to a case-control design or inappropriate exclusions criteria. We rated the risk of bias of the index test as "unclear" in 42% and as "high" in 21% of the studies due to no information or lack of blinding from the results of the reference standard. In 2 studies,[26,29] the reference standard was considered questionable to correctly classify the target condition while, in three studies[27,30,44] a clear description was lacking. We rated 54% of the studies with "unclear" risk of bias due to no information for the interval between the index test and reference standard. The applicability concern was "unclear" in 25% of the studies due to the lack of description of sample demographic characteristics and settings. The conduction and interpretation of the index test and reference standard was rated with 'low concern' in 96% and 83% of the studies, respectively.

Test diagnostic accuracy

Sonography

Eighteen studies assessed the diagnostic accuracy of sonography.[11,12,14,27-34,36,37,39-41,43,44] The US probe frequencies ranged between 4 and 18MHz. Hypoechogenicity, described as a loss of the normal fibrillar pattern, was the most common entity reported by eleven studies.[12,14,27,30,33,34,36,37,39,40,43] Sensitivity and specificity ranged from 35 to 100% (Table 1).

Tendon thickening was reported by 6 studies.[12,14,27,36,37,41] Substantial heterogeneity was evident in the diagnostic criteria used for the measurement of tendon thickening among the eligible studies, such as the anteroposterior maximal thickness of the CET perpendicularly to the flatform surface,[12,14,37] or the deepest point of the capitellum, or the mid-point of the radiocapitellar joint.[41] Two studies did not describe their measurement method or the cut off points used.[27,36] The sensitivity ranged from 13% to 100% and specificity from 52% to 100% (Table 1).

Tear detection, defined as an anechoic area with no fibers intact in the CET, was reported by nine studies.[14,27,30-34,36,41] The results showed low sensitivity (3%-64%) and excellent specificity (99%-100%) (Table 1).

Tendon calcification was evaluated in nine studies[14,30,32-34,36,37,40,41] showing low sensitivity (5%-42%) compared to specificity (83% to 100%) (Table 2). Five studies[12,14,30,37,41] evaluated cortical irregularities, showing a sensitivity ranging from 18% to 63% and a specificity from 63 to 100% (Table 2). Enthesopathy was reported in five studies[27,29,32,39,40] and considered positive if the proximal part of the tendon was enlarged with alterations in echogenicity. The reported sensitivity and specificity ranged from 8 to 65% and 85 to 86%, respectively (Table 2).

Grayscale US including all entities showed a sensitivity between 53% and 98% and a specificity between 42% and 90%[12,28,30,32,36,37,40,41,43] (Table 3). When neovascularity assessment was added in the diagnostic accuracy reports sensitivity ranged from 54% to 100% and specificity from 47 to 90% (Table 3).[11,12,30,31,36,41]

Tissue elasticity through color-coded mapping was evaluated using transient, strain or shear wave elastography in five studies.[11,31,33,34,44] Both sensitivity and specificity were reported very high, ranging from 75 to 100% and 85 to 96%, respectively (Table 3).

MRI

The validity of MRI in LET was evaluated in four studies[38,42,45,46] with a variety of diagnostic entities. Sensitivity and specificity for tendon thickening were high (83% and 94%, respectively), while oedema showed an excellent sensitivity (100%), but fair specificity 65%.[38] The diagnostic accuracy of focal changes varied between 69% and 96% for sensitivity and 61 to 83% for specificity. The diagnostic accuracy of MRI for enthesopathy was reported high (81%-100%),[46] while the results for tear detection presented low for sensitivity (57%) and high for specificity (92%-100%) (Table 4).[38,46]

Physical examination tests

The diagnostic performance of physical examination tests was assessed in 2 studies.[26,35] The Cozen's test showed the highest sensitivity (91%, 95% CI: 81-96) followed by the Mill's (76%, 95% CI: 63-85), static MGS (66%, 95% CI: 53-76) and Maudsley test (70%, 95%CI: 57-80). Dorf et al., (2007), reported an excellent sensitivity (78%, 80% and 83%) and specificity (80%, 85% and 90%) with a decrease in grip strength of 5%, 8%, and 10% in elbow extended compared with elbow flexed position, respectively (Online Supplementary File 4).

Discussion

Main findings

Twenty-four studies with 1370 participants were analysed to evaluate the diagnostic accuracy of medical imaging and physical examination tests in LET. USI was the most prevalent index test presenting diverse and variable diagnostic accuracy with a wide spectrum of abnormal musculoskeletal findings reported. Sonoelastography presented consistently high sensitivity and specificity values compared to B-mode USI. Grayscale and power doppler

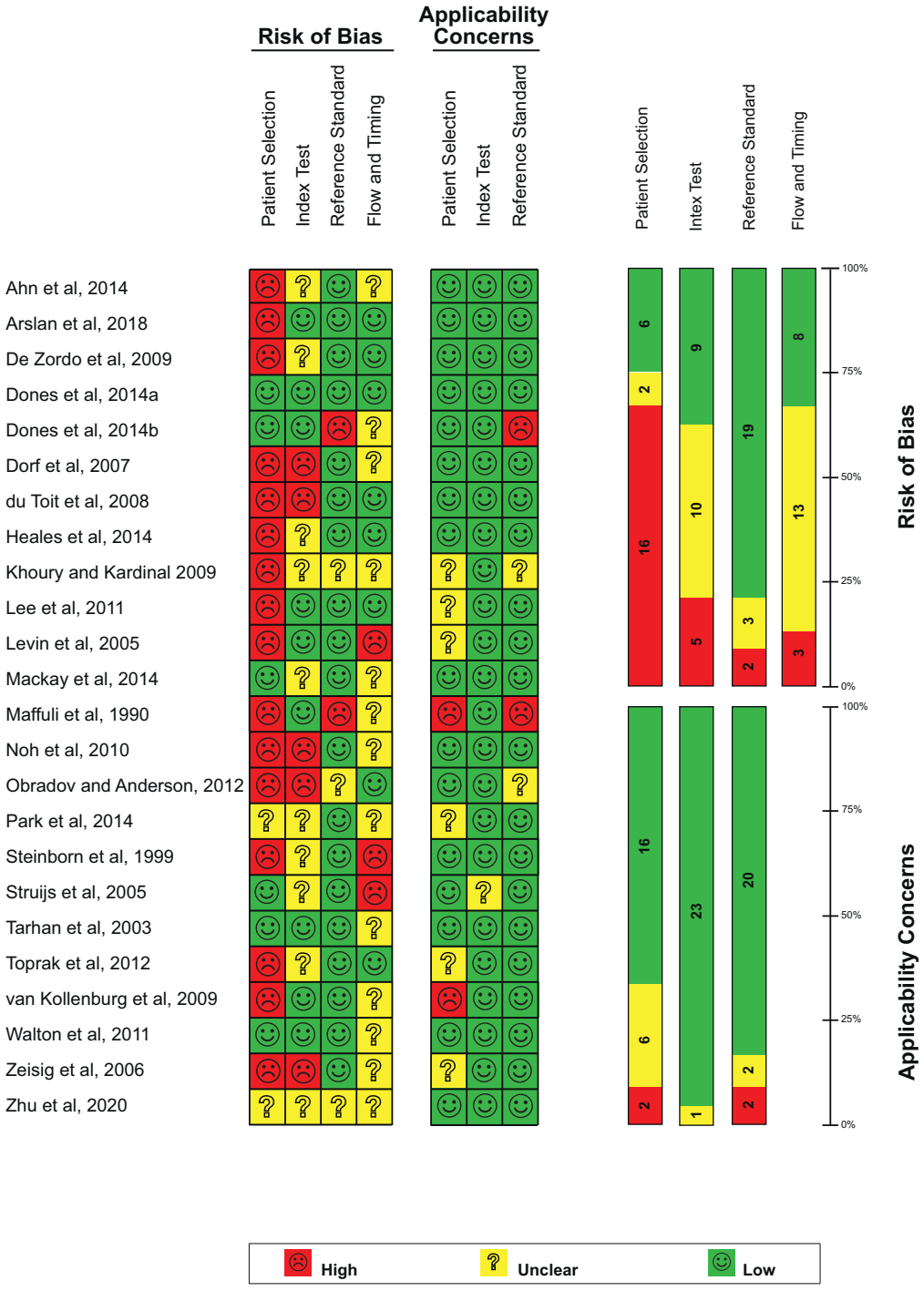

Fig. 2. Risk of bias and applicability concerns of the included studies with review authors' judgements about each domain presented as percentages across included studies.

USI assessing a cluster of entities provided fair to excellent values for sensitivity and specificity. Diagnostic accuracy of tissue abnormalities by using USI ranged from very low to high sensitivity, but showed consistently high specificity. MRI presented also variable results depending on the tissue abnormality identified. MRI had higher accuracy ranges in tendon thickening and enthesopathy compared to focal changes and oedema detection.

Finally, physical examination tests' diagnostic accuracy was under-researched. The available evidence suggests that Cozen's test is highly sensitive, while a decrease of 5%-10% in grip strength between elbow extension and flexion is highly sensitive and specific in the diagnosis of LET.

Comparison with previous reviews

To our knowledge, three systematic reviews have evaluated the diagnostic performance of USI[13,18] and physical examination tests in LET.[8] Differences in the number of studies which met the eligibility criteria and data synthesis methods limit a meaningful comparison with our review. In terms of diagnostic performance of

Table 1
Diagnostic accuracy of hypoechogenicity, tendon thickening, and tear detection by using ultrasound imaging as an index test in LET

Study (year)	Entity	SN% (95%CI)	SP% (95%CI)	PPV% (95%CI)	NPV% (95%CI)	LR+	LR-
Ahn et al., 2014	Hypo-echogenicity	89.7 (81.8-94.9)	96.6 (90.5-99.3)	96.7 (90.5-98.9)	89.6 (82.7-93.9)	26.61 (8.73-81.1)	0.11 (0.06-0.19)
Arslan et al., 2018	Hypo-echogenicity	92 (80.8-97.8)	94 (83.4-98.7)	93.9 (83.6-97.9)	92.2 (82.1-96.8)	15.33 (5.1-46.07)	0.09 (0.03-0.22)
Dones et al., 2014 †	Hypo-echogenicity	67 (46-82)	38 (21-60)	55 (38-72)	50 (18-72)	1.08 (0.7-1.67)	0.88 (0.4-1.92)
Dones et al., 2014 ∓	Hypo-echogenicity	81 (64-91)	64 (45-80)	74 (57-85)	73 (52-87)	2.2 (1.3-3.88)	0.3 (0.14-0.66)
du Toit et al., 2008	Hypo-echogenicity	53 (30- 70)	89 (80- 100)	74 (50- 90)	77 (60-90)	4.96	0.53
Heals et al., 2014	Hypo-echogenicity	53 (36-70)	60 (42-75)	47 (30-65))	46 (27-66)	1.33 (0.77-2.31)	0.78 (0.48-1.26)
Khoury & Cardinal, 2009	Hypo-echogenicity	100 (63-100)	N/A	N/A	N/A	N/A	N/A
Lee et al., 2011	Hypo-echogenicity	35 (22-50)	94 (85-98)	82 (62-93)	64 (59-69)	5.56 (2.01-15.4)	0.69 (0.56-0.85)
Noh et al., 2010	Hypo-echogenicity	59.3 (38.8-77.6)	85.2 (66.3-95.8)	80 (60.6-91.2)	67.6 (56.4-77.2)	4.00 (1.54-10.4)	0.48 (0.3-0.77)
Obradov & Anderson 2012	Hypo-echogenicity	86 (73-93)	100 (72-100)	100	59 (36-78)	-	0.14
Struijs et al., 2005	Hypo-echogenicity	67 (53-79)	80.7 (68.1-89.9)	77 (66- 85.8)	71 (62-78)	3.45 (1.97-6.1)	0.41 (0.28-0.61)
Zeisig et al., 2006	Hypo-echogenicity	100 (84.5-100)	100 (84.5-100)	100	100	-	0.00
Dones et al., 2014 †	Thickening	13 (4-31)	100 (85-100)	100 (44-100)	50 (36-64)	-	0.88 (0.75-1.02)
Dones et al., 2014 ∓	Thickening	13 (5-29)	96 (80-100)	80 (38-96)	47 (34-61)	3.27 (0.38-27.1)	0.91 (0.78-1.06)
du Toit et al., 2008	Thickening	72 (50-90)	52 (30-80)	59 (40-90)	67 (40-90)	1.53	0.53
Heals et al., 2014	Thickening	70 (52-83)	67 (49-81)	68 (49-83)	69 (49-84)	2.10 (1.20-3.67)	0.45 (0.25-0.82
Khoury & Cardinal, 2009	Thickening	100 (63-100)	N/A	N/A	N/A	N/A	N/A
Lee et al., 2011	Thickening	86 (74-94)	83 (71-91)	80 (70-87)	88 (79-94)	4.94 (2.86-8.55)	0.17 (0.08-0.33)
Toprak et al., 2014	Thickening	38 (32-44.2)	85 (78-90.1)	80 (72-85)	47 (44-50)	2.53 (1.69-3.78)	0.73 (0.65-0.82)
Ahn et al., 2014	Tear	8 (3.5-15.3)	99 (93.9-100)	88.9 (50.5-98.4)	49.1 (47.6-50.7)	7.19 (0.92-56.4)	0.93 (0.87-0.99)
Arslan et al., 2018	Tear	8 (2.2- 19.23)	100 (92.9- 100)	100	52.1 (50- 54.1)	-	0.92 (0.85- 1.00)
Dones et al., 2014 †	Tear	4 (1-20)	100 (85-100)	100 (21-100)	48 (34-62)	-	0.96 (0.88-1.04)
Dones et al., 2014 ∓	Tear	3 (1-16)	100 (87-100)	100 (21-100)	45 (33-58)	-	0.97 (0.91-1.03)
Heals et al., 2014	Tear	43 (27-61)	100 (89-100)	100 (72-100)	64 (48-77)	-	0.57 (0.41-0.78)
Khoury and Cardinal, 2009	Tear	38 (9-76)	N/A	N/A	N/A	N/A	N/A
Obradov & Anderson 2012	Tear	14 (8-27)	100 (72-100)	100 (63-100)	19 (11-32)	-	0.86
Park et al., 2014	Tear	46	N/A	N/A	N/A	N/A	N/A
Tahran et al., 2003	Tear	35 (29-41.3)	100 (98-100)	100	50 (48-52.1)	-	0.65 (0.59-0.71)
Toprak et al., 2012	Tear	9.6	N/A	N/A	N/A	N/A	N/A

† Refer to study results in acute patients with LET (<6weeks).
∓ Refer to study results in chronic patients with LET (<6weeks).
Abbreviations: LET = lateral elbow tendinopathy; CI = confidence intervals; SN = sensitivity; SP = specificity; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NA = nonapplicable.
Note: (-), infinity; (NA) when it was unfeasible to calculate values

Table 2
Diagnostic accuracy of calcification, cortical irregularities and enthesopathy by using ultrasound imaging as an index test in LET

Study (year)	Entity	SN% (95%CI)	SP% (95%CI)	PPV% (95%CI)	NPV% (95%CI)	LR+	LR-
Ahn et al., 2014	calcification	32 (22.8-42.2)	99 (93.9-99.9)	96.9 (81.2-99.5)	57.1 (53.7-60.5)	28.44 (3.96-204.05)	0.69 (0.60-0.79)
Arslan et al., 2018	calcification	16 (7.2-29.1)	92 (80.8-97.8)	66.7 (39.1-86.1)	52.3 (48.6-55.9)	2.00 (0.64-6.22)	0.91 (0.79-1.06)
Dones et al., 2014 †	calcification	42 (24-61)	90 (71-97)	83 (55-95)	58 (41-73)	4.38 (1.08-17.7)	0.65 (0.45-0.93)
Dones et al., 2014 ∓	calcification	39 (24-56)	92 (75-98)	86 (60-96)	55 (40-69)	4.84 (1.19-19.6)	0.67 (0.50-0.90)
Heals et al., 2014	calcification	7 (2-21)	83 (66-93)	29 (5-70)	47 (34-61)	0.40 (0.08-1.90)	1.12 (0.93-1.35)
Obradov & Anderson 2012	calcification	33 (21-47)	100 (72-100)	100 (80-100)	23 (13-34)	-	0.67
Lee et al., 2011	calcification	6 (1.2-16.3)	95 (87-99)	50 (17-83)	56 (54-58)	1.24 (0.26-5.86)	0.99 (0.90-1.08)
Struijs et al., 2005	calcification	5 (1.1-14.6)	100 (93.7-100)	100	51 (49.8-52.9)	-	0.95 (0.89-1.01)
Tahran et al., 2003	calcification	10	N/A	N/A	N/A	N/A	N/A
Toprak et al., 2012	calcification	31 (25.3- 37.2)	99 (95- 100)	97 (90- 99)	48 (46-50)	24.84 (6.19- 99.69)	0.70 (0.64- 0.76)
Dones et al., 2014 †	Cortical irregularities	30 (15-50)	81 (60-92)	64 (35-85)	50 (34-66)	1.53 (0.52-4.51)	0.88 (0.63-1.22)
Dones et al., 2014 ∓	Cortical irregularities	23 (11-40)	76 (57-89)	54 (29-77)	44 (30-49)	0.94 (0.36-2.44)	1.02 (0.76-1.36)
duToit et al., 2008	Cortical irregularities	63 (40-80)	63 (50-80)	49 (30-60)	75 (60-90)	1.67 (0.90-2.07)	0.60 (0.41-1.16)
Obradov & Anderson, 2012	Cortical irregularities	18 (10-11)	100 (72-100)	100 (69-100)	20 (11-33)	-	0.82
Lee et al., 2011	Cortical irregularities	18 (8-30)	95 (87-99)	75 (46-91)	59 (55-62)	3.71 (1.06-12.98)	0.86 (0.75-0.99)
Toprak et al., 2012	Cortical irregularities	55 (48.4-61.1)	91 (86-95)	90.7 (85-94)	57 (53-60)	6.27 (3.75-10.47)	0.49 (0.43-0.57)
Koury & Cardinal, 2009	Enthesopathy	63 (24-91)	N/A	N/A	N/A	N/A	N/A
Maffuli et al., 1990	Enthesopathy	12	N/A	N/A	N/A	N/A	N/A
Noh et al., 2010	Enthesopathy	55 (35.3-74.5)	85 (66.3-95.8)	78.95 (58.8-90.8)	65.7 (55-75)	3.75 (1.43-9.85)	0.52 (0.33-0.82)
Struijs et al., 2005	Enthesopathy	65 (51-77.1)	86 (74-93.7)	82.2 (70-90)	71 (63-78)	4.62 (2.37-9.04)	0.41 (0.28-0.59)
Tahran et al., 2003	Enthesopathy	8	N/A	N/A	N/A	N/A	N/A

† Refer to study results in acute patients with LET (<6weeks).
∓ Refer to study results in chronic patients with LET (<6weeks).
Abbreviations: LET = lateral elbow tendinopathy; USI = ultrasound imaging; SN = sensitivity; SP = specificity; PPV = positive predictive value; NPV = negative predictive value; LR+ = positive likelihood ratio; LR- = negative likelihood ratio; NA = nonapplicable.
Note: (-), infinity; (NA) when it was unfeasible to calculate values.

USI, both previous reviews[13,18] presented pooled diagnostic validity estimates, with contradictory values for sensitivity and specificity. Latham and Smith,[13] suggested variable USI diagnostic accuracy with higher sensitivity than specificity values by pooling ten studies (range 64%-100% and 36%-100%, respectively), while Dones et al.,[18] reported higher specificity than sensitivity values by pooling four clinically and methodologically homogeneous studies (range 82% to 100% and 26% to 64%, respectively). With regards to diagnostic performance of physical examination tests in LET, one systematic review[8] included only one study[35] and re-

Table 3
Diagnostic accuracy of Grayscale entities, Grayscale entities with or without neovascularity and elastography changes by using ultrasound imaging as an index test in LET

Study (year)	Entity	SN% (95%CI)	SP% (95%CI)	PPV% (95%CI)	NPV% (95%CI)	LR+	LR-
du Toit et al., 2008	Grayscale	81 (60-90)	63 (50- 80)	55 (40- 70)	85 (70- 90)	2.17	0.30
Heals et al., 2014	Grayscale	87 (70-95)	50 (33-67)	63 (47-77)	79 (54-93)	1.73 (1.18-2.55)	0.27 (0.10-0.71)
Lee et al., 2011;	Grayscale	76 (63-87)	76 (64-86)	74 (63-82)	80 (71-87)	3.44 (2.12-5.60)	0.30 (0.18-0.50)
Levin et al., 2005¶	Grayscale	81 (71-89)	46 (36-56)	54 (49-59)	76 (65-84)	1.50 (1.21-1.86)	0.41 (0.24-0.69)
Levin et al., 2005¥	Grayscale	75 (63-84)	42 (32-52)	50 (44.7-55.3)	68 (57-77)	1.28 (1.03-1.59)	0.61 (0.39-0.96)
Obradov & Anderson 2012	Grayscale	98 (89-100)	90 (59-98)	98 (89-100)	43 (59-98)	9.80	0.02
Struijs et al., 2005	Grayscale	75 (62-86)	80 (68-89)	80 (69-87)	77 (67-84)	3.91 (2.25-6.78)	0.30 (0.19-0.49)
Tahran et al., 2003	Grayscale	53	N/A	N/A	N/A	N/A	N/A
Toprak et al., 2014	Grayscale	54 (48-60)	88 (82-93)	88 (82-92)	55 (52-59)	4.55 (2.94- 7.05)	0.52 (0.45-0.60)
De Zordo et al., 2009	Grayscale &/or NV	95 (82.2-99.3)	89 (75.4-96.2)	87.8 (75.9-94.3)	95.1 (83.4-98.7)	8.34 (3.64-19.09)	0.06 (0.02-0.23)
du Toit et al., 2008	Grayscale &/or NV	97 (80100)	61 (50- 70)	58 (40-70)	97 (90-100)	2.47	0.05
Heals et al., 2014	Grayscale &/or NV	90 (74-97)	47 (30-64)	63 (47-77)	82 (56-95)	1.69 (1.18-2.4)	0.21 (0.07-0.67)
Obradov & Anderson 2012	Grayscale &/or NV	100 (93-100)	90 (59-98)	98 (90- 100)	100 (69- 100)	10.00	0.00
Park et al., 2014	Grayscale &/or NV	89 (71-98)	90 (73-98)	89.3 (74-96)	89.7 (75-96)	8.63 (2.93-25.39)	0.12 (0.04-0.35)
Toprak et al., 2014	Grayscale &/or NV	54 (48-60)	88 (82-93)	88 (82-92)	55 (52-59)	4.55 (2.94-7.05)	0.52 (0.45-0.60)
Ahn et al., 2014	Elastography	75 (65.5-83.5)	85 (76.3-92)	84.9 (77.0-90.4)	76 (68.9-81.9)	5.15 (3.08-8.62)	0.29 (0.20-0.41)
Arslan et al., 2018	Elastography	78 (64-88.5)	92 (80.8-97.8)	90.7 (79-96.2)	80.7 (71.1-87.6)	9.75 (3.77-25.25)	0.24 (0.14-0.41)
De Zordo et al., 2009	Elastography	100 (90.7-100)	88.6 (75.4-96.2)	88.4 (76.9-94.5)	100	8.80 (3.86-20.09)	0.00
Park et al., 2014	Elastography	96.4 (81.6-99.9)	96.4 (81- 99.9)	96.4 (80- 99.5)	96.4 (80- 99.5)	27.00 (3.93-185.27)	0.04 (0.01-0.25)
Zhu et al., 2020	Elastography	93 (84.3-98.2)	93 (84.3-98.2)	93.5 (84.9-97.4)	93.5 (84.9-97.4)	14.5 (5.61-37.5)	0.07 (0.03-0.18)

¶ Refer to study results in 1st reading of USI.
¥ Refer to study results in 2nd reading of USI.
Abbreviations: LET = lateral elbow tendinopathy; USI = ultrasound imaging; NV, neovascularity; SN = sensitivity; SP = specificity; PPV = positive predictive value; NPV = negative predictive value; LR+ + positive likelihood ratio; LR- = negative likelihood ratio; NA = nonapplicable.
Note: (-), infinity; (NA) when it was unfeasible to calculate values.

Table 4
Diagnostic accuracy of MRI and physical examination tests as index tests in LET

Study (year)	Index Test (Entity)	SN% (95%CI)	SP% (95%CI)	PPV% (95%CI)	NPV% (95%CI)	LR+	LR-
Mackay et al., 2014	MRI (Oedema)	100 (85.2-100)	64.7 (38.3-85.8)	79.3 (66.8-87.9)	100	2.83 (1.49-5.39)	0
	MRI (Tendon thickening)	82.61 (61.2-95)	94.1 (71.3-99.8)	95 (73.8-99.2)	80 (62-90.7)	14.04 (2.08-94.9)	0.18 (0.08-0.45)
	MRI (Tear)	56.5 (34.5-76.8)	100 (80.5-100)	100	63 (51.6- 73)	-	0.43 (0.27-0.69)
Steinborn et al., 1999 ρ	MRI Signal intensity changes	95.6 (78.0-99.9)	61.1 (35.7-82.7)	75.8 (63.6-84.9)	91.6 (60.9-98.7)	2.46 (1.37-4.42)	0.07 (0.01-0.5)
Steinborn et al., 1999 Ъ	MRI Signal intensity changes	69.6 (47.1-86.8)	83.3 (58.6-96.4)	84.2 (64.7-93.9)	68,2 (52.8-80.4)	4.17 (1.43-12.14)	0.37 (0.19-0.7)
Van Kollenburg et al., 2009	MRI Enthesopathy	100 (85.7-100)	81.2 (67.4-91)	72.7 (59.7-82.8)	100	5.33 (2.96-9.6)	0
	MRI Tear	58.3 (36.6-77.9)	91.7 (80-97.7)	77.8 (56.3-90.5)	81.5 (73.1-87.7)	7.00 (2.58-18.98)	0.45 (0.28-0.74)
Walton et al., 2011	MRI Tendinosis	86	N/A	N/A	N/A	N/A	N/A

ρ Refers to study results using T1-weighted spin-echo sequences in axial and coronal slice orientation.
Ъ Refers to study results using T2-weighted spin-echo sequences in axial and coronal slice orientation.
Abbreviations: LET = lateral elbow tendinopathy, SN = sensitivity; SP = specificity; PPV = positive, predictive value; NPV = negative predictive value; LR+ + positive likelihood ratio; LR- = negative likelihood ratio; LE = lateral epicondyle; NA = nonapplicable; MRI = magnetic resonance imaging.
Note: (-), infinity; (NA) when it was unfeasible to calculate values.

ported similar results with the present review for grip strength test.

In contrast to the previous systematic reviews, we included a significant number of studies evaluating the use of sonoelastography, suggesting consistently better diagnostic accuracy than Grayscale Power Doppler US showing a LR+: 5.15-0.29 and LR-: 0-27. Our results are in agreement with recent systematic reviews for the use of shear wave, transient, or strain elastography in different tendinopathies compared to other USI applications in common extensor origin and other tendinopathies as well.[47] Although sonoelastography seems a more promising diagnostic tool, its use as a gold standard diagnosis is not yet established. Compression is a key element during its application where too heavy or too gentle compression may influence accuracy due to changes in tissue elasticity.[48] Hence, the inter- or intrareliability of sonoelastography in healthy and unhealthy individuals remains contradictory.[47-49]

Consistent evidence suggests that both sensitivity and specificity are overestimated in diagnostic accuracy studies with a case-control design.[16,50] Our findings showed that almost half (48%) of the eligible studies included a control group, similarly with both previous reviews.[13,18] Based on calculations from individual studies, the specificity of USI, irrespective the abnormal musculoskeletal finding, was greater than the sensitivity; however, this finding should be interpreted with caution. Most of the studies evaluating the diagnostic accuracy of imaging used as a reference standard the clinical examination, and its validity as the gold standard has yet to be ascertained.

Variability in the participants' characteristics or the type of measurements, and in the study design or the methodology implemented, led to clinical or methodological heterogeneity, respectively.[51] In diagnostic accuracy studies, the variability of diagnostic test performance when applied to different patient subgroups or asymptomatic controls in different settings introduces the risk of spectrum bias.[52] Hence, the interpretation of the findings of a systematic review on test performance can be largely affected. We identified several sources of variability among studies that may have potentially affected tests' performance and the external validity of pooled results (Supplementary Material 5). Four eligible studies[27,35,41,53] did not report patient characteristics, while a broad spectrum of inclusion criteria was implemented among studies. On top of the differences in inclusion criteria, the clinical heterogeneity of recruited populations was evident by the broad range of symptom duration (1 day up to 5 years), the wide age span (24.3-52.6 years), and the diverse occupational background

of the eligible patients (ie, tennis players, manual workers). Evidence from other tendinopathies suggests that age, occupation, or most importantly the stage of tendinopathy influences significantly test performance[10,54] and the data indicate that the condition of included patients covered a broad spectrum of the continuum of tendinopathy.[55]

From a different perspective, USI and interpretation in tendon pathology is highly dependent on operator's skills and experience, mode of application, and equipment characteristics.[9,56,57] In our review increased heterogeneity in imaging equipment was evident, with most studies including frequency transducers ≤14MHz,[28,30-34,37,41,43,44] 2 studies using frequencies between 7 and 7.5 MHz,[29,40] and some including transducers ≥15MHz.[11,12,14,27,36] Transducer frequency reported is considered appropriate for tendon pathology (7-15 MHz)[57] while the use of higher frequencies provides improved resolution in superficial structures.[56] However, using higher frequencies (>15 MHz) may limit penetration depth which requires accurate adjustments during the placement of the transducer and the settings used.[56] Similarly, intra- and interobserver reliability of USI has been strongly related to readers background and experience.[58,59] We identified four different professional backgrounds of readers and operators with varied experience among the eligible studies. Therefore, results from studies including operators and readers with inappropriate background or experience should be interpreted with caution.

Clinical implications and considerations

Based on our findings we suggest that the use of the Cozen's test during physical examination can be a good tool to rule-out LET while the grip strength difference between elbow flexion and extension presents good diagnostic values for ruling-in or ruling-out the condition; however, the available evidence is coming only from 2 studies[26,35] with high risk of bias and should be interpreted with caution. The use of USI provides variable sensitivity and specificity in the diagnosis of LET and only Sonoelastography presents a good ability to predict the pretest probability of having LET. The use of MRI presents a high accuracy for the diagnosis of specific criteria such as tendon thickening, tear or enthesopathy. Nevertheless, the diagnostic accuracy of clinical tests should be considered for their ability to replace other examination tests (with greater burden, invasiveness and cost), or to be additive to other tests enhancing diagnosis which will guide treatment decisions.[60] It seems that the use of USI or MRI in LET is not satisfying any of the latter criteria. The diagnostic relationship of individual imaging findings was variable and the LRs showed a very small effect on post-test probability apart from sonoelastography and MRI for tendon thickening. However, their low diagnostic value in guiding treatment decisions in patients with LET[5] along with the increased cost of medical imaging limit their use in clinical practice. Additionally, evidence suggests that a significant proportion of asymptomatic individuals presents structural tendon abnormalities in the upper[61-63] and the lower limb.[64-69] In agreement with previous reports, it seems that medical imaging in LET could be more beneficial when differential diagnosis is required according to patient presentation (ie, when massive tears are suspected, joint chondral changes mimicking tendon pain etc.).[9,18]

In LET, similar to lower limb tendinopathies, there is a lack of homogenous diagnostic criteria or a valid clinical gold standard. The physical examination tests routinely used for LET diagnosis are easily performed in the clinical setting compared to medical imaging; however, when pain provocation tests are exclusively used in clinical diagnosis allow a significant room for criticism due to their poor clinical relevance to condition severity, prognosis and treatment decisions.[70] According to a recent tendinopathy consensus a range of core outcome measures including physical, psychosocial, and overall quality of life impact are considered valuable in guiding research and clinical practice.[71] Possibly, the addition of impairment measures such as pain-free grip test and the Patient-Rated Tennis Elbow Evaluation seem essential to increase the diagnostic validity of standard clinical testing and imaging in this patient population.[5]

Limitations and future research

We aimed to perform a meta-analysis, but this was not feasible due to the substantial heterogeneity of eligible studies. We acknowledge that an appropriate gold standard reference test for tendinopathy is lacking. Possibly, a consensus within the research and clinical fields with regards to the most appropriate diagnostic test or cluster of tests for LET is essential. Similar to other tendinopathies[72,73] future research should evaluate the validity of a cluster of physical examination tests in patients with LET including homogenous patient groups and appropriate gold standard reference test.

The role of imaging or individual physical examination tests in patients with LET may be somewhat narrowed in the clinical setting due to their poor correlation with clinical presentation or treatment success.[5,55] Based on the large variability found on the diagnostic performance of the examination tests in patients with LET, we suggest further research investigations on their validity according to the continuum of tendon pathology.

The development of new imaging techniques such as USI tissue characterization or sonoelastography which include more quantifiable parameters have been shown to enhance diagnostic accuracy essential for differential diagnosis[9] and should be further investigated for their predictive value in the development of symptoms or monitoring the efficacy of treatments in patients with LET. More comprehensive investigations are needed to answer whether tendons remain stable or change over time[74] and if these changes are related to the extent of tissue pathology and the patients' clinical outcomes.

Conclusions

The use of USI and MRI in the diagnosis of LET provides variable diagnostic accuracy values depending on the tissue abnormalities reported. The generalizability of the findings is limited due to the substantial heterogeneity found in inclusion criteria, operator skills, experience, mode of application, and equipment characteristics. Based on limited evidence, the Cozen's test and a decrease in grip strength between elbow flexion and extension present high sensitivity values. The additive use of certain imaging findings should be cautiously considered in clinical practice within the context of individual patient presentation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.jht.2021.02.002.

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Quiz: # 917

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1. The study design is
   a. RCTs
   b. systematic review
   c. prospective cohort
   d. case series
2. Diagnostic performance of _____ was investigated
   a. MRI
   b. USI
   c. physical examination
   d. all of the above
3. LET is seen
   a. more frequently in the UK than in the US
   b. in women more frequently than in men
   c. in men as frequently as in women
   d. in men more frequently than in women
4. Both _____ and _____ were calculated for each Dx tool
   a. ease of use and cost
   b. specificity and sensitivity
   c. selectivity and specificity
   d. reliability and validity
5. Cozen's Test and grip strength were highly inaccurate tools in diagnosing LET
   a. not true
   b. true

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