

- 1 **Diagnostic accuracy of ultrasound and magnetic resonance imaging in**
- 2 **detecting Stener lesions of the thumb: Systematic review and meta-analysis**

ABSTRACT

This study aimed to assess diagnostic test accuracy of ultrasound and magnetic resonance imaging (MRI) in diagnosing thumb Stener lesions. MEDLINE, PubMed, Embase and Cochrane CENTRAL were searched for studies using ultrasound or MRI to detect Stener lesions following suspected thumb ulnar collateral ligament injuries. The reference standard was surgical exploration or clinical joint stability. Risk of bias was assessed using the QUADAS-2 tool. A random-effects bivariate meta-analysis was used to estimate pooled sensitivity and specificity. Forest plots were generated. Nine ultrasound ($n = 315$) and six MRI ($n = 107$) studies were included in meta-analysis (all high risk of bias). Pooled sensitivity and specificity for ultrasound was 95% (95% confidence interval 76-99) and 94% (88-97), and for MRI was 93% (69-99) and 98% (70-100). Both ultrasound and MRI demonstrate high diagnostic accuracy in detecting Stener lesions. Ultrasound is an appropriate first-line imaging modality.

Level of Evidence: II

INTRODUCTION

A Stener lesion is a full-thickness tear of the UCL, where the ligament is displaced proximal and superficial to the adductor pollicis aponeurosis (Stener, 1962). Of full-thickness tears of the distal UCL, 64-87% have been reported to result in a Stener lesion (Mahajan and Rhemrev, 2013). Surgical intervention for Stener lesions is advocated as the interposed aponeurosis prevents healing of the dislocated ligament. As such, early and correct diagnosis of Stener lesions is therefore vital to ensure appropriate management and prevent long-term sequelae of chronic pain, instability, or osteoarthritis (Christensen et al., 2016).

Clinical assessment of thumb ligamentous injuries in the acute phase can be difficult due to excessive pain, swelling and muscle spasm. Imaging modalities such as ultrasound (US) and magnetic resonance imaging (MRI) are frequently used to help identify a Stener lesion and select patients for surgery (Figure 1). Whilst previous studies have investigated the role of US and MRI (Beutel et al., 2019; Papandrea and Fowler, 2008), there is no clear consensus on which imaging modality to utilise in clinical practice. The aim of this study was to perform a systematic review and meta-analysis to assess the diagnostic test accuracy of US and MRI in diagnosing Stener lesions of the thumb UCL.

METHODS

This systematic review and diagnostic test accuracy meta-analysis conferred to the Preferred Reporting Items for Systematic reviews and Meta-Analysis (PRISMA) statement (Moher et al., 2009) and the Synthesising Evidence from Diagnostic Accuracy Tests (SEDATe) guidelines (Sotiriadis et al., 2016). The index test was US or MRI in patients with suspected UCL injuries of the thumb. The reference standard for this review was either surgical

exploration, or joint stability of the thumb metacarpophalangeal joint during clinical examination by a surgeon at follow-up, in a joint which was unstable at presentation.

Literature search

The literature search was conducted in MEDLINE, PubMed, Embase and Cochrane CENTRAL electronic databases from inception until 23rd April 2019. The following keyword search strategy was used: [“skier’s thumb” *or* “gamekeeper’s thumb” *or* “Stener” *or* “ulnar collateral ligament”] *and* “ultrasound” *or* “ultrasonography”, *or* “magnetic resonance imaging” *or* “MRI”. Database records were imported to Rayyan’s QCRI systematic review tool for study screening and selection (Ouzzani et al., 2016).

Eligibility criteria

Inclusion criteria was as follows: (a) original studies which evaluated the diagnostic accuracy of US or MRI for assessing thumb UCL injuries, (b) the reference standard for studies was surgical exploration, in addition to clinical follow-up of joint stability (c) the absolute number of true-positive (TP), false-positive (FP), false-negative (FN), true-negative (TN) were reported, derivable or communicated by authors within two months upon request. Non-English language, scientific abstract, and cadaver studies were excluded.

Data extraction and risk of bias

Identified studies were scrutinised in terms of publication authors, study institution, recruitment period, and publication date to prevent inclusion of duplicate data. Data was extracted on study design, total number of patients, number of patients who underwent surgery or clinical follow-up, patient demographics, time interval between injury/imaging/surgery/clinical follow-up, US technique, MRI protocol, and diagnostic test

accuracy data. Risk of bias was assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool (Whiting et al., 2011).

Statistical analysis

Diagnostic test accuracy data (TP, FP, FN, TN) was imputed into a 2 x 2 diagnostic matrix. A random-effects meta-analysis, using a generalised linear mixed model, was performed to calculate pooled sensitivity and specificity (Chu and Cole, 2006). Forest plots were generated. Study heterogeneity was assessed by visual inspection of the forest plots. The presence of threshold effect, when studies use different cut-offs to define a TP or TN result, was investigated by a Spearman's rank correlation between sensitivity and sensitivity; a significant negative correlation suggests threshold effect (Zamora et al., 2006). Publication bias was not assessed because Deek's asymmetry test is not recommended when there are less than ten studies per meta-analysis (Deeks et al., 2005; The Cochrane Collaboration, 2011). Statistical analysis was performed using Stata version 14.2 (StataCorp, 2015) and Review Manager (RevMan) version 5.3 (The Cochrane collaboration, 2014).

RESULTS

Study selection

There were 929 titles identified from the search, of which 394 were duplicates. After title and abstract screening, 26 articles proceeded to full text screening. Eligibility criteria was met by eleven articles assessing US, five articles assessing MRI, and one article assessing both. (Figure 2). From the eligible sixteen studies, fifteen studies (nine US and six MRI studies) proceeded to meta-analysis. Specific considerations in study selection for meta-analysis are outlined below.

The studies by Kohut and O'Callaghan (1993) and O'Callaghan et al (1994) shared the same study location (Kohut and O'Callaghan, 1993; O'Callaghan et al., 1994). The former, smaller study was excluded from US meta-analysis. Similarly, the study by Hergan et al (1995) of both US and MRI patients was excluded from US meta-analysis, as it shared the same study location as the larger US study by Hergan and Mittler (1995) (Hergan and Mittler, 1995; Hergan et al., 1995). The study, however, is included in MRI meta-analysis.

In the study by Lohman et al (2001) there were four patients with equivocal Stener lesion findings on either imaging or surgical exploration (Lohman et al., 2001). To permit inclusion in the 2×2 diagnostic matrix, unclear cases were re-classified as positive findings. These cases are likely to reflect high-grade injuries necessitating surgical repair, as with a Stener lesion.

In the study by Harper et al (1996), fourteen patients who underwent MRI arthrography were not included in meta-analysis, as this technique was not a consideration of this review (Harper et al., 1996).

Study characteristics

Nine single-centre studies assessed US (Hergan and Mittler, 1995; Hoglund et al., 1995; Melville et al., 2013; Murphey et al., 1997; Noszian et al., 1995; O'Callaghan et al., 1994; Schnur et al., 2002; Shinohara et al., 2007; Susic et al., 1999) (Table 1). All, but two studies (Melville et al., 2013; Schnur et al., 2002) were prospective. The number of patients included in each study ranged from 14 to 69. The most frequently used US probe was a 7.5MHz linear array transducer. Six studies recorded the time interval from injury to US, with a range between four hours to 203 days (Hergan and Mittler, 1995; Hoglund et al., 1995; Melville et

al., 2013; Noszian et al., 1995; O'Callaghan et al., 1994; Susic et al., 1999). Two studies recorded the time from US (or injury) to surgery, with a range of 1 to 405 days (Hoglund et al., 1995; Melville et al., 2013). In five studies, clinical follow-up ranged from 17 days to 5 years (Hoglund et al., 1995; Murphey et al., 1997; Noszian et al., 1995; O'Callaghan et al., 1994; Schnur et al., 2002; Susic et al., 1999).

Six single-centre studies assessed MRI (Harper et al., 1996; Hergan et al., 1995; Hinke et al., 1994; Lohman et al., 2001; Milner et al., 2015; Romano et al., 2003) (Table 2). All but one (Milner et al., 2015) were prospective. The number of patients undergoing MRI ranged from 5 to 43. Three studies recorded the time interval to MRI and this ranged from three days to two years (Harper et al., 1996; Hinke et al., 1994; Romano et al., 2003). One study recorded the time interval from MRI to surgery and this was between 10 weeks and over one year (Lohman et al., 2001). Magnetic strength ranged between 0.5-1.5 Tesla. Four of six studies reported using a radiofrequency surface coil (Harper et al., 1996; Hinke et al., 1994; Lohman et al., 2001; Romano et al., 2003).

Risk of bias

All fifteen studies included in meta-analysis were found to have a high risk of bias (Figure 3). The 'Patient Selection' domain was of high risk of bias in all studies. All but two studies (Schnur et al., 2002; Susic et al., 1999) did not state whether a consecutive or random sample of patients was recruited. Susic et al (1999) and Schnur et al (2002) recruited random samples of patients, but did not record any study exclusion criteria (Schnur et al., 2002; Susic et al., 1999). O'Callaghan et al (1994), Hoglund et al (1995) and Nozian et al (1995) all included participants under the age of 18 years old (Hoglund et al., 1995; Noszian et al., 1995; O'Callaghan et al., 1994). The 'Reference Standard' domain was of high risk of bias in

all studies except Susic et al (1999), primarily because it was unclear whether the person undertaking surgical repair or follow-up physical examination was blinded to the imaging findings (Susic et al., 1999). Additionally, only five studies reported blinding of the imaging operator to clinical findings (Hergan and Mittler, 1995; Hoglund et al., 1995; Noszian et al., 1995; Lohman et al., 2001; Romano et al., 2003). The 'Flow and Timing' domain was found to be of high risk of bias in all studies. The time interval to the reference standard was either unclear or considered to be prolonged.

The overall clinical applicability concerns to the review question were low in all studies but four (Harper et al., 1996; Lohman et al., 2001; Noszian et al., 1995; Susic et al., 1999) (Figure 3). The 'Patient Selection' domain was of high concern in the study by Noszian et al (1995) as some patients were identified as developing a full-thickness tear secondary to stress radiography whilst in the studies by Harper et al (1996) and Lohman et al (2001) the injuries were conspicuously chronic (Harper et al., 1996; Lohman et al., 2001; Noszian et al., 1995). The 'Index Test' domain was of high concern in the studies by Lohman et al (2001) and Harper et al (1996) as consensus was used to determine the imaging result (Harper et al., 1996; Lohman et al., 2001). The 'Reference Standard' domain was of high concern in the study by Susic et al (1999), as one patient with a possible dislocated ligament refused surgery (Susic et al., 1999).

Meta-analysis of US

Nine studies ($n = 315$) assessed the diagnostic test accuracy of US. The pooled sensitivity was 95% (95% confidence interval 76-99%), and pooled specificity was 94% (88-97%) (Figure 4). Visual inspection of the forest plot showed evidence of large inter-study

variability in sensitivity, with relatively homogenous specificity. There was no evidence of threshold effect to explain underlying heterogeneity (Spearman's $R = 0.20$, $P = 0.60$).

Meta-analysis of MRI

Six studies ($n = 107$) assessed the diagnostic test accuracy of MRI. The pooled sensitivity was 93% (69 to 99%) and pooled specificity was 98% (70 to 100%) (Figure 4). There was no evidence of threshold effect to explain underlying heterogeneity (Spearman's $R = 0.89$, $P = 0.015$).

DISCUSSION

This systematic review and meta-analysis demonstrates that both US and MRI have high diagnostic accuracy for the detection of Stener lesions, although the current evidence stems from sparse heterogenous studies with evidently high risk of bias.

US demonstrated high sensitivity (95%) and specificity (94%) for the diagnosis of a Stener lesion. The study by Susic et al (1999) showed an exceptionally low sensitivity of 40% (Susic et al., 1999). The utilised imaging technique was not reported in this study and consideration should be given to the operator-dependant nature of US. The aforementioned Susic et al (1999) study and the Shinohara et al (2007) study reported the lowest specificities of 78% and 71% respectively (Shinohara et al., 2007; Susic et al., 1999). The latter study illustrates important Stener lesion mimics, such as a ruptured aponeurosis or dorsal capsule, that may falsely depict a Stener lesion on US (Shinohara et al., 2007). Nevertheless, the high diagnostic yield of US along with its advantageous low cost, accessibility, and dynamic imaging capabilities confirm this is an excellent first-line imaging modality for assessing the position of the UCL in suspected Stener lesions.

MRI also demonstrated high diagnostic accuracy, with a pooled sensitivity of 93% and specificity of 98% despite uncertainty in summary estimates. In particular, sensitivity was 100% in three studies (Harper et al., 1996; Hergan and Mittler, 1995; Milner et al., 2015) and specificity was 100% in four of six studies (Harper et al., 1996; Hergan and Mittler, 1995; Milner et al., 2015; Romano et al., 2003). In the earliest study by Hinke et al (1994) the diagnostic test accuracy was lower than that of other studies (Hinke et al., 1994). In this study, the first three cases were misdiagnosed on MRI but were correctly diagnosed retrospectively following surgical correlation, suggesting a learning curve in MRI interpretation (Hinke et al., 1994). Similarly, the study by Lohman et al (2001) of predominately chronic UCL injuries reported lower sensitivity and specificity than other MRI studies (Lohman et al., 2001). Excessive scarring and the absence of high signal oedema, often seen with an acute ligamentous injury, can make it difficult to reliably interpret the position of the chronically injured UCL, likely accounting for their low accuracy. Unfortunately, the paucity of reportable data and the wide time interval between injury and imaging reported in the studies of this review made it impossible to distinguish acute and chronic UCL injuries. Future research is required to assess the diagnostic accuracy of US and MRI in identifying acute and chronic Stener lesions respectively.

The superior contrast resolution and three-dimensional capabilities of MRI should allow excellent assessment of intricate features UCL injuries. Two MRI studies in this review frequently encountered full-thickness tears of the UCL with a 3mm or greater separation of the torn ends, despite the ligament remaining below the aponeurosis (Milner et al., 2015; Romano et al., 2003). Termed the ‘quasi-Stener’ by Milner et al (2015) the study demonstrated that 90% of these injuries fail conservative management and require surgical

repair (Milner et al., 2015). Interestingly, a recent systematic review from our institution has shown limited evidence and consensus on the treatment of full-thickness UCL injuries (Mikhail et al., 2018). Further research is required to determine if specific imaging features on MRI could play a role in therapeutic stratification, beyond the position of the torn UCL relative to the aponeurosis.

The studies in this review are hindered by significant drawbacks. The sparse number of patients, non-consecutive recruitment, and retrospective nature of some studies implicate spectrum bias. Blinding was largely unclear and suboptimal. Studies frequently failed to report time interval between injury, imaging, and the reference standard which has clear implications for diagnostic accuracy. A proportion of studies are arguably outdated by technological advances in imaging, raising wider clinical applicability concerns. Modern US examination advocates the use of high frequency 12-15MHz transducers, often in conjunction with a small footprint (hockey stick) probe to improve resolution (Singh et al., 2016). High magnetic strength MRI scanners, such as 3 Tesla, are becoming more widely available and allow for improved signal-to-noise ratio, thinner slice acquisition, and shorter examination time compared to lower strength scanners (Malone et al., 2016). There are several important limitations relating to the review and meta-analysis. The reference standard for this meta-analysis was surgery (the ‘gold standard’) or resolution of joint instability at clinical follow-up. However, joint instability does not necessarily imply an underlying Stener lesion and vice versa. Because not all patients with UCL injuries can be reasonably expected to undergo surgery, the resolution of acute symptoms and absence of joint instability at follow-up was considered reasonable means to exclude a Stener lesion. Due to study heterogeneity, a random-effects model was used. Therefore, it is likely that the large uncertainty obtained in summary estimates, particularly for MRI, could be explained by sampling variation rather

240 than heterogeneity. The high uncertainty in summary estimates of sensitivity compared to
241 specificity for US supports this notion, with far fewer patients with the target condition (TP)
242 than without (TN).

243

244 In conclusion, both US and MRI demonstrate high diagnostic accuracy for the diagnosis of
245 Stener lesions of the thumb UCL. US is a reliable first line imaging modality, although
246 institutions are best suited to utilise their choice of imaging based on local availability and
247 radiological expertise. The results of this meta-analysis are limited by sparse data and high
248 bias, and require confirmation through future robust multi-centre studies analysing US and
249 MRI accuracy.

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TABLE AND FIGURE LEGENDS

Table 1: Characteristics of studies investigating the diagnostic accuracy of ultrasound in diagnosing Stener lesions compared to surgery or clinical follow up of joint stability

Table 2: Characteristics of studies investigating the diagnostic accuracy of magnetic resonance imaging (MRI) in diagnosing Stener lesions compared to surgery or clinical follow up of joint stability

Figure 1: Stener lesion of the thumb ulnar collateral ligament (A) Illustration of the ruptured ulnar collateral ligament (arrow) dislocated superficial and proximal to the adductor aponeurosis (arrowhead) (B) Coronal short tau inversion recovery (STIR) magnetic resonance imaging (MRI) of the thumb with a Stener lesion (C) Longitudinal axis ultrasound at the level of the first metacarpophalangeal joint with a Stener lesion. MC = Metacarpus; PP = Proximal Phalanx

Figure 2: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram for identification and screening of studies using ultrasound or magnetic resonance imaging (MRI) for the detection of Stener Lesions. Nine ultrasound and six MRI studies were included in the diagnostic meta-analysis.

Figure 3. The quality of ultrasound ($n = 9$) and MRI ($n = 6$) studies included in meta-analysis as assessed using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool; Risk of bias is indicated as high (red) or low (green).

Figure 4. Forest plots of sensitivity and specificity for individual ultrasound studies ($n = 9$) and magnetic resonance imaging (MRI) studies ($n = 6$) in detecting Stener lesions. The reference standard is surgical exploration or joint stability on clinical follow-up.

SUPPLEMENTARY MATERIAL (not for online publication)

Supplementary material 1: PRISMA 2009 checklist

Supplementary material 2: Data (xlsx file)

Supplementary material 3: Data (csv file)

Supplementary material 4: Data analysing and coding (STATA file)