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SPORTS IMAGING (J LINKLATER, SECTION EDITOR)

The Use of Ultrasound-Guided Injections for Tendinopathies

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Abstract

Purpose of Review The purpose of the study was to review the efficacy and safety of common ultrasound-guided injections for tendinopathy conditions. Corticosteroid injections have historically been the most common injection used for tendinopathy; however, there are an increasing number of injections including platelet-rich plasma, hyaluronan, polidocanol, botulinum toxin, and high volume saline injections.

Recent Findings There is growing evidence that while corticosteroid injections for tendinopathies usually have short-term efficacy, they may result in medium-term harm, particularly for tennis elbow (lateral epicondylitis). Corticosteroid injections appear to have more clinical utility for tenosynovitis conditions. There is insufficient evidence regarding other injection options to make a broad recommendation in favour, although individual trials for certain tendons illustrate benefits for some of the non-corticosteroid options.

Summary When considering the use of ultrasound-guided corticosteroid injections for tendinopathies, the risk of possible medium-term harm must be weighed up against any short-term efficacy. Other injection-based therapies may be appropriate in certain clinical situations; however, the evidence and clinical circumstances must be considered for the particular tendon and patient. Load-based rehabilitation remains the cornerstone of tendinopathy management.

Keywords Tendinopathy · Tenosynovitis · Ultrasound-guided · Injection · Corticosteroid · Platelet-rich-plasma

Introduction

Injections for tendinopathies (and related conditions) have been common practice in musculoskeletal medicine for the past 60 years, ever since injectable corticosteroid preparations become readily available [1]. Injections have the attraction of being "minimally invasive" management with relatively low risk of complications compared to surgical interventions. In the last 20 years, ultrasound guidance has also been regularly used, in theory to improve the accuracy of injection location. However, the evidence-base both for the efficacy of injections is not always consistent with common practice and even to a standard set of guidelines. For example, the most recent Australian edition of Therapeutic Guidelines: Rheumatology [2] recommends cortisone injections for almost every common tendinopathy (for example, rotator cuff tendinopathy, tennis elbow, De Quervain's tenosynovitis), whereas the evidence for efficacy is not nearly as prescriptive. This narrative review aims to summarise the best evidence with respect to ultrasound-guided injections for the most common tendinopathy conditions, for both corticosteroid injections (CSIs) and other commonly used injection options.

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Cortisone Injections for Tennis Elbow (Lateral Epicondyle Pain)

The evidence-base regarding cortisone injections for tennis elbow has become very clear over the last 10 years based on high-quality Randomised Controlled Trials (RCTs), and for this reason it is an ideal introductory condition to summarise. The value in reviewing the tennis elbow literature relates to understanding potential effects of cortisone injection on tendons in the real world, although the value of ultrasound guidance is less appreciated as the superficial common extensor origin can be easily injected using an unguided technique. It is noteworthy that in 2002 [3], the best quality systematic review correctly (based on the evidence at the time) or incorrectly (based on current evidence) recommended that cortisone injections were probably effective for tennis elbow. With the benefit of hindsight, it is clear that an incorrect conclusion was made based on studies prior to the mid-2000s being observational or having only a short follow-up period ($\leq$ 3 months). From 2002 to 2016, there have been seven randomised controlled trials (RCTs) all consistently showing that cortisone injections *improve* tennis elbow outcomes against control comparators in the first 6 weeks but from a time period from 3 months to at least 6 months, cortisone injections actually demonstrate net *harm* against control comparators [4–10] (albeit that CSI improves against baseline parameters, just *less* so than controls). Studies which have included both physiotherapy and placebo arms have dispelled the myth that the early improvement that cortisone injection provides allows physiotherapy to be more effective later, showing the medium-term harm of cortisone is independent of physiotherapy [5–7].

Non-cortisone Injections for Tennis Elbow

There are multiple non-cortisone injection options for tennis elbow, many of which have a low degree of evidence which suggests that they are more effective than either CSI or placebo injection. It must be noted that CSI outcome at 3–6 months is harmful, so that placebo injection *is superior to* CSI with this duration of follow-up.

Platelet-rich plasma (PRP) is an autologous injection technique where blood is withdrawn from the patient's own vein, then spun down, and the serum component of the blood (with high platelet concentration) injected as the active agent. It is important to note that different PRP preparations vary in the dose/concentration of platelets and leukocytes, which may impact the efficacy of the treatment. A recent meta-analysis found leukocyte-rich PRP was associated with better outcomes than other preparations across all tendinopathies, of which tennis elbow was well represented [11].

Reviews of PRP specific to tennis elbow remain inconclusive. One systematic review [12] of PRP for tennis elbow which concluded that it was ineffective has been rebutted by the lead author of one of the placebo-controlled RCT studies [13] excluded for being low-quality as this author argued that the Pedro ratings for this study were incorrect [14]. Other reviews have found PRP to be effective [15, 16]. The true efficacy of PRP for tennis elbow remains in doubt although the improvements of PRP in direct comparison to CSI [17, 18] add further weight to the argument that CSI is harmful for tennis elbow. Future studies may hopefully resolve whether PRP improves outcomes over placebo [19]. Autologous blood injections—somewhat similar to PRP—have also been used with success compared to placebo [15, 16].

A single RCT has shown good efficacy of hyaluronan gel injection for treating tennis elbow compared to placebo [20]. It is noteworthy that the results of the placebo group in this study did not show much improvement which raises the suspicion of non-blinding/expectation bias, as generally placebo groups improve in tennis elbow studies. Other lower-quality studies have supported this form of injection [10, 21, 22]. It should be noted that hyaluronan is most commonly used in musculoskeletal medicine for osteoarthritis (particularly knee osteoarthritis) and the dose for a tennis elbow injection should be lower ($\leq$ 2.5 ml) than the typical dose for a knee joint injection.

There have been only been low-quality studies showing effectiveness of polidocanol (a sclerosing agent) for tennis elbow [9]. The correct technique for injecting sclerosing agents is under ultrasound guidance using Colour Doppler to reveal the location of excessive neovessels, where present. This choice of injection therefore does warrant ultrasound guidance, compared to cortisone or PRP injections which can be done unguided, with the caveat that there are no high-quality placebo-controlled trials to support this management.

There are fewer studies (compared to shoulder injections) regarding the value of guided versus unguided technique for tennis elbow injection. In theory, a guided technique (Fig. 1) can ensure peritendinous versus intratendinous injection, but the common extensor origin tendon is so small that almost all of any injection (even if volume as small as 1 ml) would automatically be injected around rather than into the tendon. The justification for ultrasound guidance for tennis elbow injection may instead be to avoid inadvertent injection into the radial collateral ligament deep to the tendon.

Botulinum toxin injection (e.g. 60 units Dysport) into the finger extensor muscles distal to lateral epicondyle appears to be somewhat effective at relieving pain in tennis

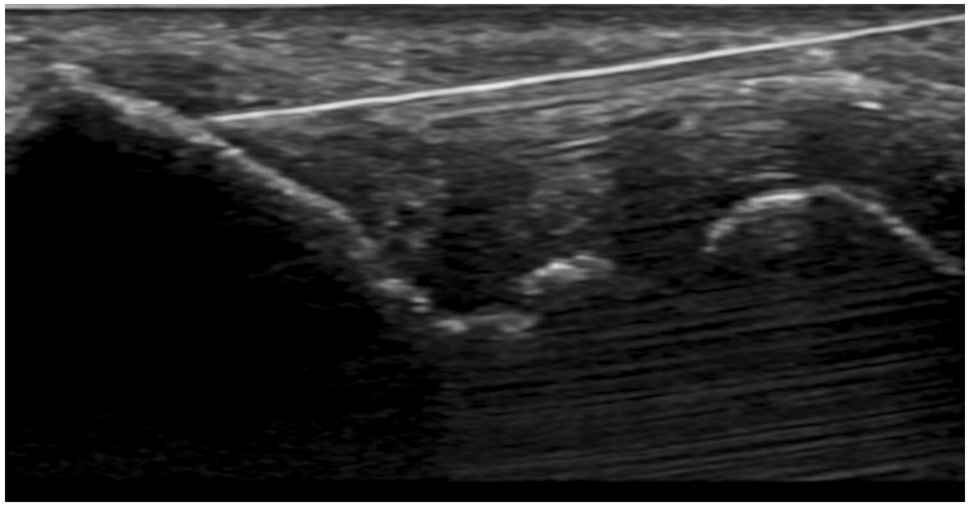

Fig. 1 Injection of common extensor origin at elbow under ultrasound guidance

elbow [23], but sometimes at a cost of function in that 3rd or 4th finger extension can be weak or even absent for months after the injection. Although it can be injected around the tendon [16], it is more logical to inject Botulinum toxin to the proximal extensor muscles as it is a muscle inhibitor. Given the role of these injections is to reduce muscle strength, the best-case scenario is a loss of function (power) being traded against reduced pain for a few months.

Percutaneous tenotomy (also referred to as tendon fenestration) has some favourable evidence to suggest an improvement in pain and function for tennis elbow [24], usually under ultrasound guidance. However, inconsistencies in technique, no RCTs and high risk of bias limit this finding and further research is required.

Recommendations for Injection Treatment in Tennis Elbow

There is good evidence that load-based rehabilitation is the gold standard for tennis elbow treatment [25]. Therefore, any form of injection therapy should only be considered after the patient has failed to progress with a reasonable period of good quality rehabilitation. Based on the strong evidence of delayed harm, it is now a reasonable position to assert that CSI should almost never be used in tennis elbow. It is also reasonable to discuss possible exceptions, with the caveat that these rare exceptions should not be used as an excuse not to change existing practice with respect to CSI for tennis elbow. The RCT studies which show delayed harm also show short-term benefit for approximately 1 month. The major possible exception would be where a patient's upcoming month is patently far more important to them than any other month on the medium-term horizon (e.g. an athlete about to compete in the Olympics or a PhD student writing up a thesis before going on leave). Intractable pain could be considered another possible exception, but only if the need to reduce pain in the very short-term can be justified over the likelihood that it may be worsened in the medium-term. If a patient considered a "rare exception" requested a repeat injection 2 months after the first, it would indicate that there was inadequate understanding of the justification for the exception. It is very hard to ever envisage a scenario where a repeated CSIs could now be justified for tennis elbow and there is some recent evidence that this increases the risk of requiring surgery [26, 27•]. On the topic of surgery, while a recent RCT suggests that whilst surgery is effective for tennis elbow, it is no more effective than placebo surgery [28] and therefore the associated unloading and gradual reloading over many months which is the standard postsurgical protocol, is perhaps the effective treatment.

With respect to other ultrasound-guided procedures, it is reasonable to conclude that there is not strong evidence for any specific alternative, although the most common alternatives (PRP, autologous blood and hyaluronan) are almost certainly preferable to CSI.

Sadly it appears that high-quality RCTs have not changed practice with respect to use of CSI for tennis elbow according to recent studies of British specialists [29], US upper limb surgeons [30] or Australian GPs [31•].

Cortisone Injections for Shoulder (Rotator Cuff) Tendinopathy

CSI for shoulder tendinopathy (generally affecting rotator cuff tendons although occasionally others, and therefore usually administered into the subacromial space) has good evidence for some short-term efficacy [32••, 33•], but also good evidence that there is no long-term benefit of treatment compared to placebo [32••]. The most pertinent question which future studies should address is whether there is long-term harm associated with subacromial CSI. It is quite likely that shoulder pain has heterogenous causes which clinical examination may not be able to readily differentiate, and that the various diagnoses may have different long-term prognoses with the use of CSI. An alternative explanation may be that future requirements for shoulder loading can differentiate patients who may suffer harm from repeat subacromial CSI. Studies of both symptomatic and asymptomatic subjects [34, 35] find high rates of abnormalities and even full thickness rotator cuff tears in the asymptomatic elderly [36]. The fear of exacerbating a rotator cuff tear (Fig. 2) with a CSI in a low-demand elderly patient may therefore be low. However, in a middle-aged manual worker, a full thickness rotator cuff tear may require surgical repair and possibly even be career ending, so the risk of exacerbating a rotator cuff tear with a CSI may be significant.

There have been studies of other injection options for rotator cuff tendon pain, although no other option has strong evidence of efficacy. A recent RCT (with low power) found no difference between US-guided glucose prolotherapy injections and US-guided CSI for rotator cuff tendinopathy [37]. Another RCT assessing hyaluronan and physical therapy vs physical therapy alone (no placebo) [38] for supraspinatus tendinopathy found that those receiving hyaluronan returned to pre-injury activity earlier; however, there were no differences in pain scores between groups.

Utility of Ultrasound-Guided Technique for Subacromial Injections

A Cochrane review in 2012 found that whilst there was evidence that ultrasound guidance improved the accuracy of a subacromial injection (Fig. 3), this did not necessarily translate to improved clinical outcomes [39]. This review suggested that ultrasound guidance may be avoided for "cost" reasons, if there was no strong evidence of clinical improvement compared to an unguided injection. The use of an ultrasound-guided technique has been recently questioned by the Australian Rheumatology Association [40]. A weakness of this argument is that it is not based on unguided injections being superior, just the perceived lack of clear advantage of more accurate injections, as measured by clinical outcomes. This argument itself becomes weaker as the cost of ultrasound decreases, and as it becomes a more routine part of point-of-care practice. Other reviews of ultrasound-guided injections for shoulder tendinopathy have concluded the opposite finding that ultrasound-guided injections to the subacromial space have superior efficacy to unguided injections [41•, 42, 43].

Regardless of the potential role of ultrasound for guided injections, ultrasound does have utility in diagnosis of shoulder pain. The additional information available from ultrasound examination above and beyond clinical assessment may be critical in determining whether or not to proceed with CSI in the first place. In the event that different degrees of rotator cuff pathology correlate with long-term outcome from CSI, then ultrasound can be fully justified as part of patient selection. A recent study has in fact

Fig. 2 A small supraspinatus tear, such as that visualised, might be a relative contraindication for corticosteroid injection in shoulder pain

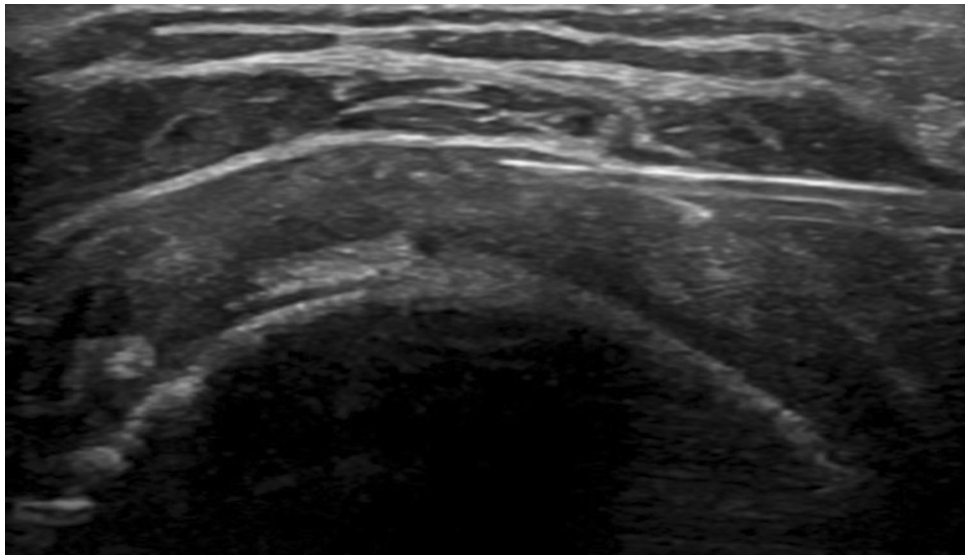

Fig. 3 Injection of subacromial bursa above supraspinatus tendon under ultrasound guidance

shown that for US-guided CSI to the subacromial space, the presence of a rotator cuff tear was significantly associated with a worse longer-term (12 months) outcome [44••] although a second recent study did not make this finding [45]. The findings of the first study [44••] suggest that ultrasound can be used to help decide which patients to offer CSI to (i.e. CSI may be more appropriate in those with significant shoulder pain but without rotator cuff tear).

A retrospective study on a cohort who underwent surgical rotator cuff repair found that those who received a CSI within 6 months prior to their surgery were more likely to have to have a repeat operation within the next 3 years [46•]. However, correlation does not necessarily imply causation as patients who fail to respond to a cortisone injection might be also unresponsive to a rotator cuff repair.

Ultrasound (and also X-ray) may also assist with the diagnosis of calcific rotator cuff tendinopathy, which increases in prevalence with age. CSI is particularly indicated for calcific rotator cuff tendinopathy [47], as is shock wave treatment (which itself can be done with ultrasound guidance), which further adds weight to the routine use of ultrasound when managing shoulder pain in middle-aged and elderly patients.

Cortisone Injections for De Quervain's Tenosynovitis (TSV) and Other Upper Limb Conditions

The literature for De Quervain's TSV is more similar to rotator cuff tendinopathy than tennis elbow in that there is good evidence of short-term improvement with CSI [48–50, 51•] without high-quality evidence of long-term benefit having been demonstrated. While this is the case, there is a caveat that future studies may possibly show long-term harm as has been demonstrated by superior quality studies of tennis elbow. However, it is also possible that being a tenosynovitis, De Quervain's may simply be more suitable for CSI than a tendinopathy.

There is some low-quality evidence that ultrasound guidance using CSI injected into different compartments provides greater relief than unguided CSI for De Quervain's TSV [52•, 53].

There have been few studies on intersection syndrome [54] which is a related entity that appears to behave in a similar fashion to De Quervain's TSV. There is an argument that because intersection syndrome and De Quervain's TSV occur in different locations that ultrasound guidance can assist in injecting the "correct" location by revealing the pathology. The evidence for efficacy of CSI for treating the less common tendinopathies in the upper limb, such as intersection syndrome and medial epicondyle pain, is of low level because of the relative lack of RCTs [55].

Trigger finger is a stenosing tenosynovitis usually effecting the A1 pulley, which appears to have good response to CSI with no substantial evidence of harm [56].

Cortisone Injections for Hip Tendinopathies and Utility of Ultrasound Guidance

CSI is also routinely used for trochanteric pain, previously thought to be mainly caused by "trochanteric bursitis", an entity which does exist but not commonly, which is now considered to be primarily an insertional gluteal tendinopathy (Fig. 4). As with the rotator cuff tendons, full thickness tears of gluteus minimus and medius can occur and may not be that uncommon in the elderly both symptomatic and even possibly asymptomatic individuals. There is now emerging evidence that both high-quality exercise programs [57••] and PRP [58•] are superior to CSI for insertional gluteal tendinopathy, although CSI may be more effective than no treatment in the short-term [57••].

Around the hip region, there is special utility of CSI when combined with local anaesthetic (LA), or even LA itself without CSI, for diagnostic utility. Different structures can be injected and the response in terms of pain relief can be compared to ascertain the most likely source of pain in the common scenario where imaging such as MRI scan has demonstrated multiple pathologies. The most important of these scenarios relates to the differential diagnosis of hip osteoarthritis. A patient with severe anterior and lateral hip region pain with both moderate hip osteoarthritis and an insertional gluteal pathology demonstrated on imaging clearly needs the primary source of pain proven, especially if surgery such as hip replacement is being contemplated.

The groin, hip and buttock region contains a huge number of tendon insertions, all of which can give rise to pain on occasion and for which ultrasound-guided procedures can assist greatly in diagnosis. The insertions (origins) of sartorius and tensor fascia lata at ASIS, rectus femoris at AIIS, adductor longus at pubis and the iliopsoas tendon at the level of femoral neck are all potential culprits causing pain in this region, even though these diagnoses are less common than, say, adductor-related pain [59].

The hamstring origin at the ischial tuberosity is another common cause of pain and maybe the most common cause of direct pain on sitting. It is yet another tendon with equivocal evidence regarding injection management. CSI may be harmful in the medium-term with respect to tendinopathy or partial rupture of the hamstring origin; yet it is recognised that secondary sciatic nerve irritation is commonly associated with hamstring origin pathology and CSI may be helpful at relieving adhesions affecting the sciatic nerve. The evidence-base regarding hamstring origin CSI is limited to case series of good rates of improvement in the very short-term and low-moderate rates of improvement in the medium-term [60, 61]. The evidence-base for PRP injections in proximal hamstring tendinopathy is similar with case series reports only and no published high-quality RCTs [62].

Cortisone Injections for Plantar Fasciitis and Utility of Ultrasound Guidance

At the risk of becoming repetitive, there is moderate evidence for some short-term relief up to 1 month of CSI in plantar fasciitis, but no evidence for any long-term benefit [63–65]. There is currently insufficient evidence to compare the effectiveness of CSI compared to most other treatment modalities including oral NSAIDs, physiotherapy, and shockwave [64••].

The risk of infection, plantar fascia rupture and fat pad degeneration associated with CSI have all been reported and should be considered when deciding on the clinical utility of CSI for plantar fasciitis. Ultrasound guidance for injections may be preferable to avoid direct injection into the fat pad which may occur using an unguided injection.

Plantar fascia injection can be extremely painful and of all the ultrasound-guided injections to the limbs, it is the one where a preceding local anaesthetic block (to the median calcaneal branches of the tibial nerve in this instance) is preferable to a mix of CSI and local anaesthetic

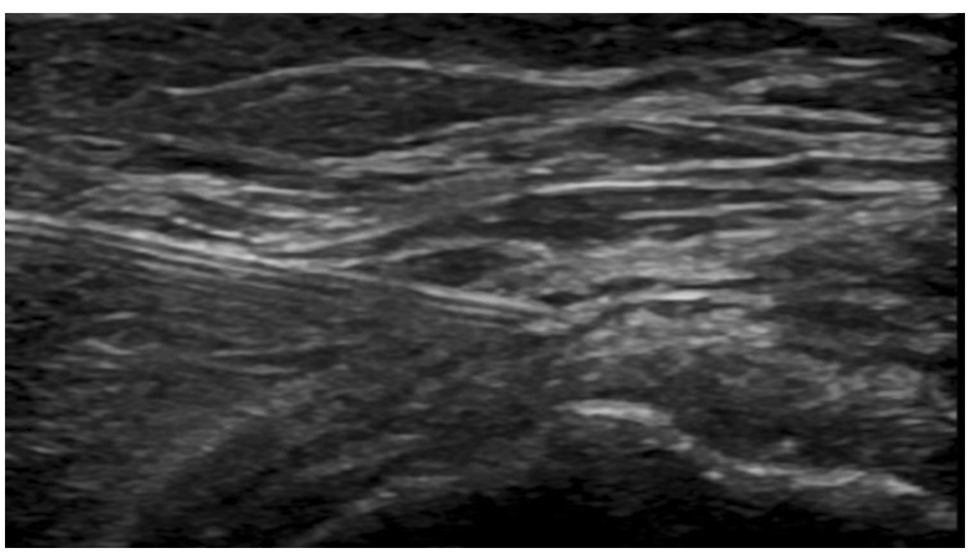

Fig. 4 Injection of superficial trochanteric bursa over gluteus medius tendon under ultrasound guidance

in a single injection (the technique most commonly used for other locations where a single injection is less painful).

Platelet-Rich Plasma Injections for Plantar Fasciitis

There are now 9 RCTs comparing PRP injections to CSI for plantar fasciitis [66••]. These show no improvement between injection types at 4–12 weeks, but superior results for PRP over CSI at 24 weeks for pain (although no difference in functional measures) [66••]. These results are consistent with other body locations where the effect of CSI is greatest in the first 2 months but with PRP injection generally being superior to CSI after this time period. This begs the question of whether such results are due to genuinely improved results when using PRP after many months or whether the discrepancy reflects harm of CSI after 3 months.

Cortisone Injections for Achilles and Patellar Tendinopathies

The evidence-base for the use of CSI in Achilles and patella tendinopathies comes with the usual disclaimer about the lack of high-quality placebo-controlled studies with adequate follow-up (6 months or longer) [67•]. However, the theoretical risk of harm with respect to these tendons is much higher and hence the benefit of any doubt almost certainly should not be given to CSI. Although it is a somewhat uncommon complication, rupture of Achilles and patella tendons is a particularly devastating outcome and Achilles rupture has been linked with both CSI and oral cortisone use for some time [68–75]. However, in a similar caveat to warning of possible lack of benefit of CSI, it is worth noting that the reports of Achilles rupture after CSI are also case series and therefore this complication is not necessarily proven as causative.

A recent article has implicated CSI as being associated with greater risk of progression to surgery in calcific Achilles tendinopathy [76•].

There is low-quality evidence that Achilles tendinopathy in association with seronegative spondyloarthropathy responds better to CSI [77], demonstrated in Fig. 5.

Ultrasound-Guided Polidocanol Injections for Achilles and Patellar Tendinopathies

Neovascularisation of the Achilles (in mid substance and insertion) and patella tendon (at origin) is a very common finding associated with painful tendinopathy (Fig. 6). It has been claimed to also be an association with inflammatory disease as well. There is less evidence regarding the cause of the neovascularisation (whether primarily load related or inflammatory related) and also whether the vessels are a healthy part of repair of damaged tendon or in fact represent abnormal healing and are a marker of localised nociception potentially leading to persistent pain perception [78, 79]. If one belongs to the school of thought that the vessels represent abnormality rather than utility, then there is a strong rationale to use any treatment which would decrease vascularity like a sclerosing agent. Despite these theoretical reasons, there is still only low-quality evidence in favour of use of polidocanol injections for Achilles [80] and patellar [81] tendinopathies.

There has been one recent case report of an Achilles tendon rupture shortly after polidocanol treatment [82].

Hyaluronan has also been used for treatment of Achilles and patella tendinopathy [83–85], however there are no RCTs available to date for further guide to its use.

High-Volume Ultrasound-Guided Injections for Achilles Tendinopathies

A recently popular version of the Achilles tendon CSI (given the warnings associated with this) is the “high-volume” injection which contains mainly saline but a small dose of corticosteroid. There is some evidence of pain relief in the short-term but again a lack of high-quality RCT data with long follow-up [86•, 87–90]. If—and it is a significant if—high-volume injection is effective for Achilles tendon in the longer-term, it is very important to try to determine whether it is due to the saline component or the corticosteroid component, as the addition of the latter possibly exposes the patient to the increase risks of late harm and rupture.

Ultrasound-Guided Cortisone Injections for “Unusual” Tendinopathies

Compared to other areas of medicine where the unusual or atypical may be associated with a worse prognosis, an “atypical” tendon presenting with pain usually has a much better prognosis than a common tendinopathy. The “common” tendinopathies (e.g. Achilles) are common because they occur in tendons under a high degree of load in almost everyone which can be challenging to return to their previous premorbid ability to handle such load. Tendons under a lesser degree of load therefore have a more benign prognosis (e.g. a tendinopathy of tensor fascia lata tendon at the hip). For this reason, the immediate pain-relieving benefit of CSI to an “atypical” tendon may come

Fig. 5 injection of Achilles tendon under ultrasound guidance

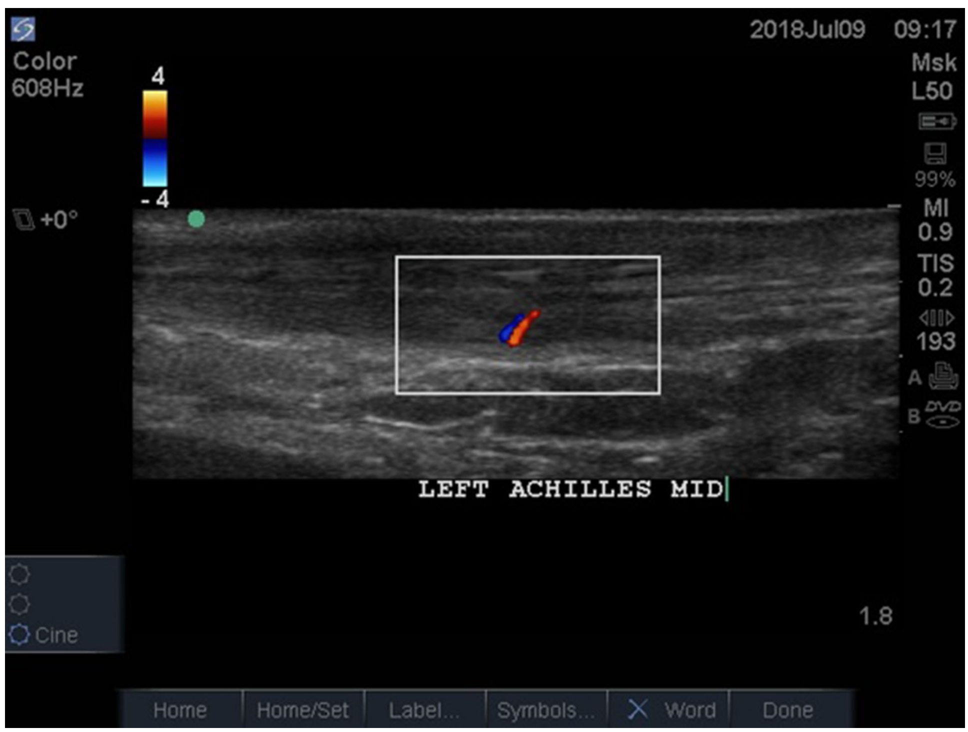

Fig. 6 Colour Doppler may allow detection of in substance vessels within the Achilles tendon body, pathology which may be amenable to ultrasound-guided sclerosing agent treatment

with a much lower risk of future recurrence or harm, compared to the more common tendons.

Other Novel Injection Options

There are many other injection options available other than CSI and PRP. A relatively commonly used injection is glucose prolotherapy. This may alternatively be used with the thought that it is a generic inert substance that may achieve improvement from the non-specific effects of any injection (without the harms of drugs), or that it is a disease-modifying agent. If the latter was actually correct it would need RCTs comparing glucose prolotherapy to saline. A common, but unproven, regime of glucose prolotherapy in clinical practice is to inject multiple times over many weeks, in a similar fashion to non-invasive treatments. Sometimes this is referred to as “wet acupuncture”.

Acupuncture or dry needling for soft tissue conditions, including tendinopathy, is controversial itself as it is hard to conduct a non-biased RCT that can adequately exclude placebo effect. A systematic review on prolotherapy for tendinopathy showed safety but was inconclusive with respect to efficacy [91].

There was some low-quality evidence in favour of aprotinin (an inhibitor of matrix metalloproteinases, which break down tendon) injections prior to 2010 [92–94], although this drug was withdrawn from the market worldwide at this time due to inferiority to a similar drug, tranexamic acid (TXA). To date there have been no studies of TXA for treatment of tendinopathy in humans, although animal studies suggest that TXA reduces vascularity in rat tendon which may negatively affect tendon healing [95].

Conclusion

Ultrasound is now cheap, non-radiating, able to be used to assess tendon structure and able to guide injection into the desired region, usually directly around a painful tendon. The limitation of ultrasound-guided injection in tendinopathy is chiefly a lack of clarity regarding the efficacy of most injection agents. There is widespread evidence, over many tendon locations, of improvement after CSI in the first month after injection, but equally and of concern there is some evidence of harm associated with CSI in the medium-term (3–6 months) for some tendon locations, particularly tennis elbow. PRP injections appear to have greater efficacy than CSI in some tendinopathies in the medium-term (typically 6 months), but it is not well established how much of this superiority equates to harm of CSI versus benefit of PRP. Injections (and the results of ultrasound) should not be used as an alternative to good load-based rehabilitation, which is the mainstay of tendon management. Occasionally, ultrasound can be useful at finding tendon ruptures which may preclude injection therapy or indicate surgery, but the common finding of partial tendon degeneration should not suggest any modification of load-based rehabilitation as the primary treatment.

Compliance with Ethical Guidelines

Conflict of interest John W. Orchard, Richard Saw, and Lorenzo Masci each declare no potential conflicts of interest.

Human and Animal Rights and Informed Consent None of the images illustrated in this study were obtained from live patients where consent would have been required (either cadaver models or self-images of the authors were used for all Figures).

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- • Of importance
- •• Of major importance

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