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Volume 2 • Issue 1 • 2018

Review Article

Medical Research and Clinical Case Reports

ISSN: 2578-3416

The Applications of Ultrasound Imaging in Tendinopathy

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Received: June 06, 2018; **Published:** June 15, 2018

Abstract

Tendinopathy is a debilitating tendon disease which affects millions of Americans and costs billions of healthcare dollars every year. The current treatments of tendinopathy are often ineffective and alternative treatment options are sought after. The use of ultrasound has become popular amongst physicians in recent years as it represents a readily available, cost-effective imaging modality to improve characterization of tendon diseases. Further, ultrasound can be used to increase procedure accuracies, enabling improved safety and accuracy of technically challenging procedures for tendons. In this review, we will introduce the applications of ultrasound in the diagnosis and treatment of tendinopathy. We will also highlights advances in ultrasound-related procedures as basic science research tool, applications in the treatments of tendinopathy with animal models including high-frequency ultrasound imaging, ultrasound-guided injection and surgery, as well as ultrasound guided drug delivery and microdialysis.

Keywords: *Tendinopathy; Ultrasound-guided injection; Animal tendon; High frequency ultrasound*

Abbreviations: Ultrasound: US; Musculoskeletal ultrasound: MSK-US; Nonsteroidal anti-inflammatory drugs: NSAIDS; Mmatrix metalloproteinases: MMPs; Glycosaminoglycans: GAG; Percutaneous ultrasonic tenotomy: PUT

Volume 2 Issue 1 June 2018

Introduction

Tendons are connective tissues consisted of collagen, elastin, proteoglycans, and cells. Tendons are constantly subjected to mechanical loading by transmitting muscular forces to bone [1] and respond to mechanical forces by changing the metabolism as well as their structural and mechanical properties. Damaged tendon, caused by repetitive mechanical loading, lead to significant disability, pain, healthcare cost, and lost productivity [2]. Studies suggest that 16% of the general population suffers from shoulder pain caused by rotator cuff diseases [3] and 11% of runners suffer from Achilles tendinopathy [4,5]. Aging is known to adversely affect the human body and lead to degenerative changes in tissues and aging tendons are frequently ruptured and re-ruptured [6].

Tendon tissue is poorly vascularized and predominantly utilize anaerobic energy systems, which results in poor healing potential after acute or overuse injury [7,8]. The healing process of injured tendon is slow and results in scar tissue formation. Current therapeutic options for addressing tendon disorders are often ineffective, and the ideal treatment for tendon disorders remains unclear and there is an urgent need to find an effective and lasting treatment for tendon injury. In recent years, musculoskeletal ultrasound (MSK-US) imaging has gained increasing popularity among physicians by offering readily available, cost-effective means to diagnose and treat tendinopathy. In this brief review, we will introduce the applications of MSK-US in the clinical setting to assist in the diagnosis of tendinopathy, monitor the efficacy of treatments and assess the risk of developing symptoms. We will also discuss the recent advances in MSK-US procedures with high-frequency imaging as well as MSK-US guided percutaneous ultrasonic tenotomy (PUT). Additionally, as an application of US in tendinopathy research using animal models, we will suggest a new technique for measurement of substance for animal tendinopathy model with MSK-US guided microdialysis.

Applications of ultrasound in tendinopathy diagnosis

In the clinical setting, MSK-US allows improved characterization of diseased tendon tissues [9]. Painful tendons have structural abnormalities seen on MSK-US, which are typically localized tendon thickening with hypoechoic areas and altered vascularity [10-12]. Degenerative change is one of the characterizations of tendinopathy identified by the presence of the angio-fibroblastic hyperplasia on MSK-US [13]. Neovascularization (47-100%), increased the thickness of the tendon (100%) with disorganized tendon structure (100%), formed calcific plaques (29-52%) and hypoechoic region (74-100%) are seen in the tendons with Achilles tendinopathy [14-18]. Additional MSK-US findings for tendinopathy are described as the follows.

Neovascularization

Findings at each stage of tendinopathy can be correlated with pain. A positive correlation between neovascularization and subjective pain measurement has been reported by several authors [18,15,19]. The increased blood flow in injured tendons with focal hypoechoic lesions can be detected by a Color Doppler, as well as a Power Doppler, where as normal tendons have no blood flow detectible within them [18]. In chronic Achilles tendinopathy, increased vascularity (neovascularization) has been demonstrated to be closely related to chronic tendon pain [20]. The association with neovascularization inside and outside the tendon with chronic pain but not in the healthy tendons has been reported by Alfredson [19,20]

Increased tendon thickness

Increased tendon thickness is classified as a non-tear abnormality and may be associated with edema and the swelling of the tendon, which are relatively common symptoms of tendinopathy among middle aged recreational athletes [21-23]. Following clinical pain in the Achilles tendon, the tendon undergoes structural changes that are detected by MSK-US imaging. Tendon thickening is one of the most common MSK-US findings for the tendinopathy. The morphological characteristics of Achilles tendinosis can be viewed with MSK-US including an area with a high concentration of glycosaminoglycans and disorganized fiber pattern and arrangement in the tendon, however the amount of inflammatory cell infiltrates is the same as the acute phased [24]. The alignment of the collagen fibers in healthy tendon is well organized, while the disorganized fibrillary pattern was found in the tendons with tendinopathy.

Hypoechoic region (A hole-like lesion)

In comparison with MRI, MSK-US and surgical findings concluded that if the diameter of the hypoechoic region is more than 10 mm, it will be suggested a partial tear more than in pure tendinosis [25]. The hypoechoic region is considered with loss of the fibrillar structure in chronic tendinopathy [26]. Hypoechoic areas on MSK-US and the areas with increased signal intensity on MRI correspond to the areas of altered collagen fiber structure and increased interfibrillar ground substance (hydrophilic glycosaminoglycans) [27,28]. Percutaneous ultrasonic tenotomy (PUT) is a novel surgical technique with a minimally invasion for specific tendinopathy state which is recalcitrant tendinopathy with hypoechoic region [29]. This machine is needed with MSK-US visually guidance that is being highly sensitive for hypoechoic lesions and MSK-US has proven to be a useful tool for localizing and targeting ablation of the pathologic tissue for properly suctioning scared tissue out [29,30].

There however, are some questions remaining. One diagnostic MSK-US tendinopathy study showed that 68% of symptomatic human Achilles tendinopathy was found with hypoechoic region [18] while 11% of asymptomatic tendon was also found [31]. There was no significant difference of improvement after conservative treatment between chronic Achilles enlarged tendon and the tendon containing a hypoechoic area, regardless of size with chronic Achilles tendinopathy [31]. One reported that hypoechoic area on ultrasonography did not correlate with an improved clinical outcome [32].

Calcification

Calcific tendinopathy is thought to be caused by poor oxygen supply within a tendon. Calcific tendinopathy has four stages: pre-calcific, calcific, resorptive, and post-calcific even though the MSK-US, as well as MRI, cannot distinguish those four stages by its visualization [33,34]. The stage of calcification is usually related to the consistency of the deposit: soft during the pre-calcific stage, hard during the calcific stage, and fluid during the early resorptive phase. Rotator cuff calcific tendinopathy, a common disease in daily clinic situation occurs in up to 7.5% of asymptomatic adults and up to 20% of painful shoulders, is frequently seen in women in their 40s and 50s [35-37]. It is believed that calcific tendinopathy is one of the reasons of highly disabling shoulder pain. The clinical studies have demonstrated that women aged between 30 and 60 years with subacromial pain syndrome and a calcific deposit of >1.5 cm in length have the highest chance of suffering from symptomatic calcific tendinopathy of the rotator cuff [38]. The results showed that 7.8% of the asymptomatic patients were false positive as diagnosed by MRI calcific tendinopathy [38]. US-guided percutaneous irrigation of calcific tendinopathy is widely accepted as the primary treatment and effective for a deposit calcification [33,39]. The hard calcification possibly will have to be removed out by surgical procedure and PUT with US guidance as well [40].

Applications of ultrasound in tendinopathy treatment

Clinical studies have shown macroscopic changes in the tendons with tendinopathy including tendon thickening, loss of mechanical properties, and pain [41]. Recent studies demonstrated that degenerative changes have been occurred in the tendons with tendinopathy including disruption of collagen fibers, non-collagenous matrix such as matrix metalloproteinases (MMPs), glycosaminoglycans (GAG), fatty areolar tissue, calcification as well as neovascularization [24,31, 42-46]. The net results of tendinopathy are tendon degeneration, weakness, tearing, and pain [47]. Although oral nonsteroidal anti-inflammatory medications (NSAIDs) have been used extensively for decades to treat pain associated with tendon overuse, the evidence suggests that NSAIDs are effective in relieving the pain associated with tendinopathy only in short term and many studies showed no improvement with NSAIDs [48-50].

Percutaneous ultrasonic tenotomy

It is well known that long-term NSAID use increases the risk of gastrointestinal, cardiovascular, and renal complications associated with these medications. Thus, physical therapy has been commonly used for the treatment of tendinopathy. In recent years, a new physical therapy modality used in the tendinopathy treatment is therapeutic ultrasound [47]. MSK-US has been used in advanced tendinopathy to remove the calcified scared tissue [51]. It is believed that calcification in the tendon can be a risk factor for leading the tendon tears even partial tear and rupture. Therefore, PUT via a Tenex™ device (TenexHealth, Lake Forest, CA) has been established as a mostly new minimum invasive surgery for chronic particular case of tendinopathy and has been approved by FDA in the United States of American in 2011. The clinical results have shown that PUT can be used with a tiny skin incision and break the scared tissue for suctioning out [13, 14,18].

Ultrasound-guided injection or procedures

US-guided injection and procedures can place the needle tip on the exact target area of the tendons. The US-guided tendinopathy injection technique is taking the place of the primary tool instead of traditional blinded injection [52]. The US imaging shows the exact location of nerve, vessels, and target soft tissue since ultrasound wave is penetrating subjects. Using a grey scale, color Doppler and power Doppler can also recognize vascular flow condition. These findings can be easy to understand the status of tendon, ligament, muscle, periosteum and bone surface. US-guided injection is more accurate than blinded injection even when it is done by the rookie physicians, with no X-ray exposure, cost-effective and repetitive use.

US-guided injection technique has been used for the treatment of tendinopathy by delivering corticosteroid, hyaluronic acid, platelet-rich plasma (PRP) into the tendons to treat tendinopathy [53-56]. Sclerosing polidocanol injections can target the neovascularization area and result in pain relief during Achilles tendon loading activity [19,53]. Scraping is the relatively new pain killer method to chronic tendinopathy by using an 18 G needle to cut out the neovascularization and the sensory pain nerves paralleling with the expanding vessels branches [57].

Applications of ultrasound in tendinopathy research using animal models

It is well known that animals and people get many of the same illnesses. Certain types of animals can stand in for humans with particular diseases. Medical research with animals is always required for conducting the clinical studies with humans. Tendinopathy is a prevalent tendon disorder that affects millions of Americans and costs billions of health care dollars every year. Current clinical treatments for tendinopathy are largely palliative because the precise cellular and molecular mechanisms of the disorder are not defined. Intensive and excessive mechanical loading is considered to be a major factor responsible for acute and chronic tendon injuries. Additionally, aging is also known to induce the degenerative changes of the tendons [58]. Many studies focus on tendinopathy using animals [59-62], only several recent studies, however, revealed the potential of MSK-US usage in animal studies due to the size of the animal tendons and ultrasound sensitivity.

Ultrasound frequencies

In clinical settings, the US frequencies in diagnostic radiology range are from 2 MHz to approximately 15 MHz. For deep abdomen, obstetric and gynaecological imaging, the US frequency is 2.5 MHz. For general abdomen, obstetric and gynaecological imaging, the US frequency is 3.5 MHz. For vascular, breast, pelvic imaging, ultrasound frequency is 5.0 MHz. For breast, thyroid, the US frequency is 7.5 MHz. For superficial masses and structures, the US frequency is 10 MHz. For musculoskeletal imaging, the US frequency is 15.0 MHz. It is known that high frequencies are used for the superficial body structures and low frequencies are used for those that are deeper. The animal tendons are much smaller than human tendons, the US frequency used for animal tendons should be much higher than that used for human. Some new MSK-US applications have been developed [63-65]. Currently, the highest US frequency can be 70 MHz (Vevo 3100, FUJIFILM SonoSite, Toronto, Canada).

Animal models

Currently, a high-frequency MSK-US has been used for many animal studies. MSK-US-guided needle positioning near the sciatic nerve has been used to elicit compound muscle action potentials of the rats [59]. The efficacy of intra-tendinous injection of PRP in treating tendinosis was also studied by MSK-US guided injection using a rat model [60]. The structure and organization of the animals were also investigated by high frequency MSK-US [60].

Several MSK-US guided injection studies have been done by rabbit models. The earliest publication was in 1999, Kuo., *et al*. successfully used a 5 MHz circular transducer to visualize Achilles tendons of New Zealand white rabbits [62]. In 2012 Gehmert group assessed rabbits Achilles tendon injury model by a 6-15 MHz matrix linear probe [63]. A novel study for treating tendinosis was performed by Kamineni group in 2015, they created a chronic Achilles tendinosis model by injecting collagenase into rabbit Achilles tendon and Tenex procedure with MSK-US visualization [64]. MSK-US imaging can be used to determine tendon thickening and softening developed during the early process of Achilles tendinopathy in a rabbit model [62]. Moreover, the US-guided injection with 6-13 MHz liner probe was also used for a porcine phantom model [66]. The results indicated that for the small animal tendon study, at least 40 MHz high frequency MSK-US and probe are required.

The US-guided microdialysis as a new technique for measuring real-time drug distribution has been development recently [67]. The local concentrations of glutamate and prostaglandin E2 (PGE2) have been determined in human tendons using MSK-US-guided microdialysis [68]. The US-guided microdialysis technique is also used to determine the glutamate in human patellar tendons [69]. The studies have demonstrated that US-guided microdialysis is a useful approach for pharmacokinetics of the drugs [70]. The results have shown that it is possible to use intra-tendinous microdialysis to investigate the mechanisms of tendinopathy and the metabolism of some drugs used for tedinopathy treatment.

Conclusion

Tendon injuries and tendinopathy are very common, especially in athletes and older populations. The complete restoration of injured tendons is a great challenge in orthopedic research due to the regenerative capability of tendons is very poor and the treatments are mostly ineffective. The published results have shown that MSK-US imaging can be used to find the changes of tendinopathic tendons and remove the degenerative tissues from the tendinopathic tendon. The efficacy of US in treating tendinopathy or promoting tendon healing has been documented by previous studies. The high frequency MSK-US imaging has been successfully used for animal tendinopathy studies. The US-guided injection and procedures, as well as US-guided drug delivery and microdialysis have brought the new approaches for clinical tendinopathy treatments.

Conflict of interest

The authors have declared that no any conflict of interest exists.

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