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Review Article

The Efficacy of High Volume Image Guided Injections in Chronic Patellar Tendinopathy: a Systematic Review -

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ABSTRACT

Introduction: Patellar Tendinopathy (PT) is an overuse condition most often seen in elite athletes enrolled in jumping sports. Presently, the pathological model of tendinopathies envolves inflammation mediated responses in which neovascularization plays an import role. High Volume Image Guided Injection (HVIGI) has been considered as a treatment option for chronic patellar tendinopathy, consisting of the high volume of fluid injection targetting the area of neovascularization at the interface between the tendon and the Hoffa fat pad.

Objective: The main goal of this paper was to review the effectiveness of high-volume image-guided injections in the management of patellar tendinopathy.

Material and Methods: A systematic review addressing the clinical question according to the PICO model was performed in May 5 2018, using the most relevant electronic databases. We included studies about HVIGI in the adult population with at least 5 patients which had full text available in the English language. Excluded were papers consisting of systematic reviews or meta-analysis, case reports, congress posters or abstracts.

Results: We found 4 suitable papers matching our criteria. These studies had several limitations in design and execution, all of them with a low level of evidence, nevertheless, all showed evidence of neovascularization disruption, pain relief and statistically significant improvement in function measured by the VISA-P scores and also very low complication rate.

Conclusion: Despite all these studies have shown benefits in the utilization of HVIGI in the management of chronic recalcitrant patellar tendinopathy, the available literature is scarce with only limited studies of suboptimal quality of evidence. High-quality randomized control trials are needed.

Keywords: High volume image guided injection; Tendinopathy; Patellar tendon; Chronic patellar tendinopathy; Injection; Ultrasound

INTRODUCTION

Patellar Tendinopathy (PT) is an overuse condition most often seen in elite athletes enrolled in jumping sports such as basketball and volleyball [1], nevertheless, this condition can also affect non-elite athletes or people who do not enroll in sports activities [2,3].

The pathological model of tendinopathies has evolved, and if in the past it had been postulated that painful overuse tendinopathies were non-inflammatory processes, presently it is most accepted that tendinopathy is a clinical and painful condition developing in a continuum process, where abnormal load being regarded as its primary cause and optimal load management valued as the primary treatment [4,5]. This active process of on-going tendon degeneration has many aspects of inflammation-mediated responses occurring in different stages and with the progressive development of neovascularization [4-6]. Nevertheless, while some authors regard neovascularization to be associated with both pain and nerve ingrowth [7], others refute this idea [8].

The clinical presentation of PT is generally a gradual increase in anterior knee pain which can prevent normal activity, being essentially a clinical diagnosis [9], which severity can be assessed by the validated VISA-P scale [10]. Ultrasound (US) evaluation of PT can depict structural changes such as decreased tendon echogenicity, intratendinous calcifications or cystic changes and neovascularization proliferation [3], the latter can be seen and graded with US Doppler [4].

Treatment options for PT

Various treatments have been suggested for PT, such as Eccentric Loading Exercise (EL), which is used in PT and other tendinopathies [5], regarding PT, eccentric squat exercises are considered the primary line of treatment, however the outcomes are rather poor with only 55% of patients achieving a return to good or excellent status in a long period of time [11]. A recent Randomized Control Trial (RCT) demonstrated that Heavy Slow Resistance Exercise (HSR) is an alternative to EL, showing similar results for HSR and EL in terms of pain and function [12].

Extracorporeal Shockwave Therapy (ESWT) role still has to be more clearly established, it has been reported to have good results in PT, specifically in a trial when comparing to control, with statistically significant differences in VISA-P scores at 2-3 year follow up [13], however a RCT with 62 participants demonstrated no effect of ESWT in the treatment of PT in competing jumping athletes [14].

It has been previously suggested that there is no difference between injection and control groups when using Platelet-Rich Plasma Injections (PRP) [11], nevertheless, some trials have demonstrated beneficial effects of PRP in the treatment of PT [15], and a recent study comparing PRP injection with or without High Volume Image Guided Injection (HVIGI) showed good results, especially when both techniques were combined, however, more solid evidence is still needed [15]. Similarly, there is controversial and mixed evidence on sclerosing injections [11] and no supportive solid evidence for the utilization of steroid injections, autologous blood and dry needling [11].

Importantly, if these treatment options still fail to respond, as unfortunately can succeed, the next step in management is still guided with uncertainty, as the surgical option in spite of demonstrating VISA-P score improvement similar to conservative treatment, requiring longer period of rehabilitation, with success rates in the order of 50% [11,16].

Recently, some studies showed promising results in the utilization of HVIGI in the treatment of PT [9,15,17,18] and a currently ongoing double-blind randomized controlled trial has the potential to further establish its role [5]. The current evidence on this treatment option is the target of our review.

What is high volume image guided injection

HVIGI consist of high volume injections of fluid targeted at the area of neovascularization in the interface between the tendon and the Hoffa's fat pad, generally containing anesthetics and normal saline with or without other components such as corticosteroids or apronitin [5,9,15,17,18]. Besides its utilization in PT it has been proposed as a treatment option for other tendinopathies such as non-insertional Achilles tendinopathy [19].

It has been hypothesized that the pain model in tendinopathy involves mechanisms such as angiogenesis and associated neoneuralisation [9], concordantly, it has been proposed that HVIGI could lead to disruption of neovessels and nerves, and the breakage of adhesions, due to the high amount of saline solution [9,15,17,18], whether this is achieved by its mechanical actions or combined neurotoxic and vasoconstriction effects by an initial anesthetic bolus, is still discussed [20]. Nevertheless, the utilization of HVIGI has to be followed by a standardized rehabilitation program to achieve optimal recovery and return to activity [9].

MATERIAL AND METHODS

Objective

To investigate if HVIGI is an effective treatment for chronic patellar tendinopathy. The clinical question according to P.I.C.O. model is showed in table 1.

A research addressing the clinical question was performed guided by the Bhandari review criteria [21].

The main goal was to review the effectiveness of high-volume image-guided injections in the management of patellar tendinopathy. Accordingly, the outcomes measured were fundamentally paining scores such as Visual Analogue Score (VAS) and functional evaluation through a score such as Victorian Institute of Sports Assessment for Achilles tendon (VISA-P) and the existence of complications.

Research information data

The search for his review was performed during 5 May 2018 and the articles used were found using the electronic databases of Embase, Medline, and PubMed and The Ovid search engine.

Additionally the Cochrane Control Trials register was searched to find possible unpublished studies and one ongoing trial was found, titled "Study protocol: a double blind randomised control trial of high volume image guided injections in Achilles and patellar tendinopathy in a young active population", which is still in progress.

A cross-reference search was also undertaken in the reviewed papers to identify any additional relevant articles.

Keywords: The keywords used in the research were: Patellar tendinopathy, high-volume image-guided injection, high-volume ultrasound-guided injection, hydrodissection (with also possible misspelling and similar terms being covered). The terms were used under mesh headings and Boolean operators "AND" and "OR" were used in combination. The summary of the research results is seen in table 2.

Exclusion and inclusion criteria: The reviewed original studies included had:

- The inclusion of HVIGI
- At least 5 patients included

Table 1: Clinical question - P.I.C.O. model.

Population	Technique	Comparison	Outcomes
Adults with chronic recalcitrant patellar tendinopathy	HVIGI	Other minimally invasive techniques and conservative treatment (physiotherapy)	Primary Functional: Visa-P Score Secondary: Pain: VAS Score US findings including neovascularization Complications

Table 2: Research results.

Keywords	Results
High-volume image-guided injection	39
High-volume ultrasound guided injection	16
Hydro dissection	415
Patellar tendinopathy	769
(1 OR 2 OR 3) and 4	5

- Adult population
- English language
- Full text available

Also excluded were papers which were:

- Systematic reviews or meta-analysis
- Case reports
- Congress posters or abstracts

RESULTS

Selected articles

After running researches, eliminating duplicates and applying the above-stated exclusion criteria, 4 suitable articles were identified. The double-blind randomized controlled trial (still in progress) by Barker et al. [5] was not taken into consideration in this review.

Of these selected articles, 3 papers consisted of single-center case series studies with no control population (Level IV evidence). The study by Abate et al. [15] compared the effects of HVIGI with or without Platelet Rich Plasma (PRP) injection using 3 different groups (Level III evidence).

Comparison

There were no control groups in the first 3 papers and, therefore, there was no comparison. Abate et al. [15] only compared the effects of HVIGI with or without Platelet Rich Plasma (PRP).

Population

In all the 4 studies the population came from a single center, which does not sample the general adult population. The study by Morton et al. from the total 20 patients included, only 8 patients were recruited prospectively.

Additionally, in all the studies, the included patients had been previously diagnosed with chronic recalcitrant patellar tendinopathy before receiving the injection and showed neo-vascularization at power Doppler ultrasound.

Procedure protocol

In all 4 studies, the procedures were undertaken under ultrasound guidance and sterile technique using a 21G needle. The Crisp et al. Study [17] procedure protocol consisted of an injection containing 10 ml 0.5% Bupivacaine, 25 mg Hydrocortisone and between 12 and 40 ml normosaline, given at the interface between the patellar tendon and Hoffa's body.

The protocol in the study by Maffulli et al. [18] comprised of an injection of a mixture of 10 mL of 0.5% bupivacaine hydrochloride, 62500 international units of aprotinin, and 40 mL of normal saline

solution aimed at the interface between the tendon and Hoffa's fat pad adjacent to the area of neovascularization.

The protocol of the Morton et al. [9] study was an injection of 10 ml 0.5% Bupivacaine, 25 mg Hydrocortisone and 30 mL normal saline, also targetting the interface between the tendon and Hoffa's fat pad and the area of neovascularization

Finally, in the study from Abate et al. [15], all the 3 groups protocols included an initial peritendinous anaesthesia consisting of 10 mL of mepivacaine 2%.

In the first group, HVIGI standalone, after anaesthesia, 30 mL of normal saline was administered and the procedure repeated after 2 weeks. In the second group, PRP standalone, after anaesthesia a 21G needle was inserted into the degenerated tendon and small autologous pure PRP depots were left at the site of the most damaged areas and adjacent regions (peppering technique), for a total amount of 4-5 mL. Lastly, in the third group, HVIGI in combination with PRP, both administrations were performed concomitally, delivering the anaesthesia, thereafter 30 mL of saline solution (at the interface between the tendon/paratenon and the fat pad), and finally, PRP, moving the needle into the degenerated tendon. As previously, the procedure was repeated after 2 weeks.

Outcome assesment

VAS is a valid, reliable and user-friendly tool which seems to assess more accurately the patients experience. The results are quantitively registered which allows direct comparison. Occasionally, it may raise comprehension difficulties among its users and require further explanation and assistance by the physician [22].

The VISA-P provides a subjective functional evaluation of the patellar tendon, and consists of a number of questions which evaluate both pain and function in daily and sport activities. Its results can range from 0 to 100, where 100 means any or scarce functional limitations [10].

In the study by Crisp, et al. 2 weeks after the procedure Pain and Functional VAS scores were measured, with a mean improvement 2 weeks after injection of 58 mm on function VAS ($p = 0.018$) and pain VAS of 56 mm ($p = 0.018$). At a mean follow up of 9 months, an improvement of 22 points on the VISA-P questionnaire was established $p = 0.028$). In addition to the short term significant improvement of both pain VAS, function VAS and VISA-P scores, the neovascularization disappeared immediatly after the procedure in all patients.

In the study by Morton et al, functional assesment of VISA-P Scores were obtained with an improvement from 45 to 64 ($p < 0.01$) for all subjects, with the prospective group improving 16.4 over 12 weeks ($P < 0.01$) and the retrospective group 19.9 at 9 months ($P < 0.01$). However, the VAS pain score was not evaluated in this study. In this study, there was a significant improvement in both VISA-P of prospective and retrospective recruited subjects and following the injection, there was a resolution of the neovascularisation in all.

In the Maffuli et al. study the VISA-P scores showed improvement by 29.3 at 15 months follow up ($P = 0.003$), and additionally the VAS pain score improved by 63 at 15 months ($P = 0.01$). The neovascularization disappeared in all patients immediately after the injection and on the last follow-up, the mean VISA-P score, pain VAS, and function VAS were all significantly improved compared with baseline.

In the comparative trial of Abate et al. in the HVIGI standalone group the VISA-P scores improved by 12.9 at 3 months ($p = 0,0001$) and 10.6 at 6 months ($p = 0.002$) compared to the baseline. Also in this group, the VAS pain scores at rest and with activities slightly improved from the baseline.

Table 3: Results summary of the reviewed studies.

Authors	Study design	Intervention	Population	Function VISA-P Scores	Pain VAS Scores
Crisp et al. [17]	Case series single center retrospective study	10ml 0.5% Bupivacaine 25mg Hydrocortisone 40ml N Saline	N = 9	+ 22 9m P = 0.018	Pain + 56 2w P = 0.018 Function + 58 2w P = 0.018
Morton et al. [9]	Case series single center retrospective study	10 ml 0.5% Bupivacaine 25mg hydrocortisone 30ml N saline	N = 20 (12 + 8)	PR + 16,4 9m P = 0.01 RP + 19.9 9m P = 0.01	No VAS Score
Maffuli et al. [18]	Case series single center retrospective study	10ml 0.5% Bupivacaine 62500 IU Aprotinin 40ml N saline	N = 44	19 (P < 0.01)	+ 63 15m P = 0.003
Abate et al. [15]	Retrospective observational trial – 3 cohorts	10 mL of mepivacaine 2% + Group I 30 mL N saline Group II PRP 4-5 mL Group III 30 mL N saline + 4-5 mL PRP	N = 54 Group I N = 18 (HVIGI) Group II N = 18 (PRP) Group III N = 18 (GVIGI + PRP)	Group I + 12.9 3M (p = 0,0001) +10.6 6M (p = 0.002)	Group I + 8 3m P = 0.00001 + 9 6m P + 0.003

Table 4: Strengths and weaknesses.

Authors	Outcome Measures	Strenghts	Weaknesses	Conclusion
Crisp et al. [17]	Primary: VISA-P Secondary: Pain VAS Functional VAS Neovascularization after procedure	Use of VISA-P Use of both functional and pain VAS Standardized management recommendation	Retrospective VISA-P and VAS not validated for retrospective answer Recall bias Selection bias Very small number of patients No randomisation No control group Short follow up (9m) Use of corticosteroid No compliance of management evaluated	High volume injections disrupt the neovascularisation in patellar tendinopathy and are helpful in the management of this condition
Morton et al. [9]	Primary: VISA-P Secondary: Neovascularization after procedure	Use of validated VISA-P scores Standardized management recommendation	Restrospective Selection bias Recall biasv No randomisation No control group Realtive small number of patients Short follow up No VISA scores used Use of corticosteroid No compliance of management evaluated	High volume image-guided injections should be considered as a treatment in recalcitrant chronic patellar tendinopathy
Maffuli et al. [18]	Primary: VISA-P Secondary: Pain VAS Neovascularization after procedure	Use of validated VISA-P and VAS scores Approval of local ethics committee Single radiologist—board certified performed the injections Independent assessor examined the patients at follow-up Longer follow up Standardised management with the guidance of a chartered physiotherapist	Retrospective Selection bias No control group No randomization Use of apronitin Relative small number of patients. No compliance of management evaluated	HVIGI improves in the short-term symptoms and function of the knee in cases of chronic recalcitrant patellar tendinopathy.
Abate et al. [15]	Primary: VISA-P Secondary: Pain VAS at rest and with activities US features + Neovascularization	Comparable clinical and demographical cohorts Grading of US damage and neovascularization at baseline Use of validated VISA-P and VAS scores Standardised management Compared 3 groups	Retrospective trial No blinding process Relatively small number of patients Relative short follow up No control with conservative management or sham fluid injection No compliance of management evaluated	The contemporaneous administration of PRP and HVIGI, grants a greater improvement for patellar tendinopathy

The scores of ultrasound lesions and of neovascularisation were also evaluated at 6 months and a decrease in the degree of neovascularization was similar for all groups. The grading of US lesions did not show important differences at all follow-up periods. Additionally, this study concluded that despite the HVIGI and PRP standalone groups had demonstrated good results, it was the association of both procedures (HVIGI + PRP) which granted the best outcomes.

No complications derived from these procedures were mentioned however in the stufy of Maffuli et al. HVIGI was ineffective in 3 patients which ultimately underwent surgical exploration. In table 3 we present a summary of their results.

Strenghts and weaknesses

There are obvious limitations in the interpretation of these studies due to their design, retrospective nature and ultimately their low quality of evidence. Nevertheless, these could be used as the pillars in the construction of further high-quality randomised controlled trials. A summary of the main strenghts and weaknesses of these studies can be seen in table 4.

DISCUSSION

When comparing all of theses studies, we observed consistency in the results of the primary outcome, with concordance in the evaluation of the VISA-P scores and similar end results, so the general conclusion that HVIGI disrupts the neovascularisation and improves the VISA-P scores, being a potential valuable tool in the management of this condition can be drawn.

Unfortunately, besides the weaknesses inherent to all the studies designs, there are additional limitations in their comparison, especifically when evaluating secondary outcomes, such as pain, due to the absence or non uniform utilization of VAS scores. There is also a considerable variation in follow up and the inclusion of corticosteroid or apronitin in the injections, which leads to interpretation difficulties in the results. Even a small amount of corticosteroids could become a confounding factor to assess if the therapeutic effect lies solely on high volume saline injections. Importantly, there are concerns with possible complications related to apronitin injections, which were addressed and are no longer used by the respective authors.

While the results of these studies regarding are encouraging when it comes to neovascularization disruption this may not be the sole cause of the symptoms in patellar tendinopathy, otherwise all patients should have reffered no pain immediately after treatment. Also, the compliance to the rehabilitation programmes were not assessed, which can be important and potentially affect the outcomes.

Nevertheless these papers have shown promising results and a future research with valid high quality and good level of evidence studies could have the sufficient impact to establish the benefits of HVIGI in the treatment of chronic patellar tendinopathy, especially when compared to other conservative treatments, such as eccentric exercise. The existence of sub-group analysis would also determine additional features that could predict positive treatments. Currently, there is an ongoing study with a double blind and randomised control design with the potential to better determine the efficacy of HVIGI in patellar and also Achilles tendinopathy.

CONCLUSION

It is possible to conclude from our review that HVIGI could be considered as one of the many treatment options in the short- to medium-term management of chronic recalcitrant patellar tendinopathy, providing benefits in terms of neovascularization disruption, improvement in function and pain and also having a very low complication rate. However, the current available literature on this topic is scarce and with limitation such as suboptimal quality of evidence, their design and execution. Therefore, more evidence from good-quality randomised controlled trials is required to better evaluate the efficacy of this treatment option.

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