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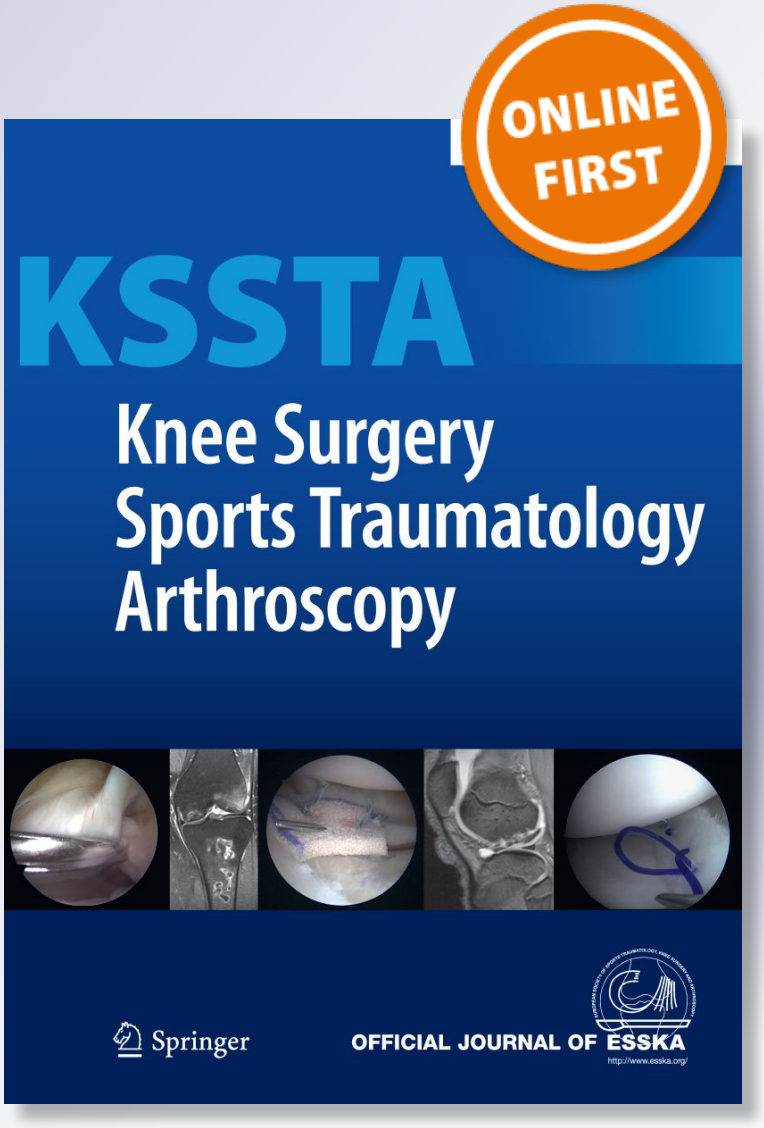

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Injection with autologous conditioned serum has better clinical results than eccentric training for chronic Achilles tendinopathy

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Abstract

Purpose Chronic Achilles tendinopathy is one of the most common causes of malfunction and pain, which can lead to a significant reduction of the quality of life. The hypothesis of this study argues that autologous conditioned serum (i.e. Orthokine) injections in chronic midportion Achilles tendinopathy have a better outcome than eccentric training.

Methods This study investigates, retrospectively, the effects of peritendinous autologous conditioned serum injections as compared to standard eccentric training in 50 patients with chronic Achilles tendinopathy between 2012 and 2015. Before injection or eccentric training and 6 weeks, 12 weeks and 6 months thereafter, the patients were assessed by means of the VISA-A-G score (Victorian Institute of Sport Assessment-Achilles questionnaire—German). An MRI was also performed before and 6 months after injection and eccentric training.

Results Both patient groups had statistically significant better VISA-A-G scores after injection or eccentric training compared to the baseline before injection (90 vs 40, respectively, $P<0.001$) or eccentric training (81 vs 47, respectively, $P<0.001$). Comparing the baseline corrected VISA-A-G scores, patients in the autologous-conditioned-serum-group had significantly higher changes in VISA-A-G scores than the eccentric-training-group after 12 weeks (40 vs 36, $P=0.018$) and 6 months (50 vs 34, $P=0.034$). Both patient groups had statistically significant ($P<0.001$) reduction of tendon thickness (autologous conditioned serum: 0.32; eccentric training: 0.24) and length of bursa (autologous conditioned serum: 0.24; eccentric training: 0.21) as well as significant ($P<0.001$) improvement of tendon quality in MRI (autologous conditioned serum: 14 vs 1; eccentric training: 14 vs 2). There were no statistical differences in MRI-findings between the two groups.

Conclusion Both therapies led to improvement of MRI-findings, including reduction of tendon thickness and tendon quality. Autologous-conditioned-serum-injections show greater clinical long-term benefit as compared to eccentric training and, therefore, offers a good alternative to eccentric training.

Level of evidence Therapeutic studies, Level III.

Keywords Achilles tendinopathy · Autologous conditioned serum · PRP · Injection · MRI · Achilles tendon · Tendinosis · Biologic healing enhancement · Imaging · Growth factors/healing enhancement

Introduction

Chronic painful mid-portion Achilles tendinopathy is a relatively common condition among recreational and elite athletes, but it is also seen in non-active individuals [1]. The incidence of Achilles tendinopathy in top level runners has been estimated between 7 and 9% [39]. Tendinopathy of mid-portion of Achilles tendon accounts for 55–65% of all injuries, and in approximately 20–25% of cases an insertional Achilles tendinopathy can be diagnosed [23]. Chronic painful mid-portion Achilles tendinopathy is most common between the age of 36 and 60 and very rare among individuals younger than 25 years [1]. The etiopathogenesis of Achilles tendinopathy is currently considered multifactorial and the interaction between intrinsic and extrinsic factors has been postulated [22]. Disturbances of the tendon structure lead to considerable loss of function in the lower extremities [27] and, in severe cases, it can interfere with activities of daily living [22].

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Eccentric muscle loading has become the dominant conservative intervention strategy for Achilles tendinopathy over the past decade [28]. Magnussen et al. showed in their review that the heavy load eccentric exercise programme has the most evidence of effectiveness in the treatment of chronic midportion Achilles tendinopathy [26].

Only 60% of athletic and non-athletic patients benefited from an eccentric training [24] and an additional therapy like injection therapy should be considered [24, 26]. Orthobiologics such as platelet-rich plasma (PRP), whole blood or autologous conditioned serum, hold promise as upcoming and novel treatment modalities [9]. Growth factors present in blood products and the potential of these growth factors to induce further release of such factors are thought to improve the healing process in chronic injuries and to accelerate repair in acute and chronic lesions [21]. Numerous studies have documented the beneficial effects of individual growth factors on tendon healing in animal models and although the effect of growth factors on tendon healing is impressive. It has become increasingly clear that tendon repair is not triggered by a single growth factor but requires the interplay of various such factors [27]. Some improvements have been achieved and are implemented in clinical practice using such biological "cocktails with growth factors" [31].

Kearney et al. concluded in their review that there is insufficient evidence to draw conclusions on the use, or to support the routine use, of injection therapies for treating Achilles tendinopathy [15]. A recent meta-analysis found no differences in treatment of chronic Achilles tendinopathy with eccentric training in combination with either PRP or saline [52]; another recent meta-analysis revealed that injection of autologous blood-derived products in patients with Achilles tendinopathy is not more effective than placebo [19]. These findings are still debated and, therefore, highlight a need for more research in the area of injection therapies for Achilles tendinopathy.

Autologous conditioned serum provides a convenient means of applying multiple, autologous growth factors [13]. Baltzer et al. reported in a study with 376 patients with knee joint osteoarthritis treated with autologous-conditioned-serum-injections that treatment with the autologous conditioned serum is safe [3]. A previous study showed its beneficial effect on the healing Achilles tendon in rats [27]. In a recent study Genç et al. confirmed these findings and stated that autologous conditioned serum may be favourable for the treatment of human Achilles tendon injuries and tendinopathies [12].

To our knowledge, the effect of autologous-conditioned-serum-injections in chronic midportion Achilles tendinopathy as compared to eccentric training has not yet been investigated. Therefore, this study evaluates autologous-conditioned-serum-injections vs eccentric training in patients with chronic midportion Achilles tendinopathy. The results should contribute to a better understanding of the role of autologous conditioned serum in treatment of chronic midportion Achilles tendinopathy and could offer a treatment that is not dependent on the compliance of the patient for physical therapy. The hypothesis of this study argues that autologous-conditioned-serum-injections in chronic midportion Achilles tendinopathy have a better outcome than eccentric training and that there is a correlation between clinical and MRT-findings.

This is the first comparative study investigating the effect of autologous-conditioned-serum-injections in chronic mid-portion Achilles tendinopathy and is the biggest study comparing the structural changes in MRI between injection-therapy and eccentric training in Achilles tendinopathy.

Materials and methods

Fifty consecutive patients (23 women, 27 men; mean age 54 ± 12 years; range 18–72 years) admitted to our hospital between 2012 and 2015 were enrolled in this study retrospectively. Before admission, all patients reduced their activities of daily living or suspended their sport activities due to their heel pain. Patients were included if they were ≥ 18 years, experienced persistent tenderness on palpation or distension in mid-portion of their Achilles tendon for at least 6 weeks. An MRI must also have been performed and was evaluated by the criteria of Weber et al. [51]. MRI is the gold standard in evaluation of tendon disorders [51].

Exclusion criteria were generalized inflammatory arthritis, including ankylosing spondylitis, rheumatoid arthritis or psoriatic arthritis, prior Achilles tendon tear, pregnancy, severe infection, known malignancy, bleeding disorder, nerve-related symptoms such as radiculopathy or osteoarthritis of the ankle, previous extracorporal shock wave therapy or injections or eccentric training during the 4 weeks prior to the study.

The patients either received a prescription of eccentric training with instruction and supervision by our physiotherapists or three sequential autologous-conditioned-serum-injections in 7-day intervals without eccentric training or prescription of physiotherapy. All patients were allowed to move their ankle but were advised to avoid sport activities for 4 weeks after injection. Non-steroidal anti-inflammatory drugs were not allowed for 6 months.

All patients who received a prescription of eccentric training were instructed by our physiotherapists to perform a training program recommended by Alfredson et al. [2]: The training program included eccentric training over a step—3×15 repetitions with straight and flexed knee performed 2 times/day, 7 days/week, for 3 months.

All patients who received an autologous-conditioned-serum-injection first had 60 ml of whole blood taken using a

special syringe with increased inner surface area (Orthokine, Orthogen, Düsseldorf, Germany). Medical grade glass beads in the special syringes increase the nonpyrogenic surface area. These glass spheres induce the dose-dependent production of IL-1Ra by white blood cells in whole blood incubated at 37 °C. After incubation, the blood-filled syringes were centrifuged, and the serum supernatant was filtered and aliquoted into four 2 ml portions. The aliquots were frozen at minus 20 °C. For injection, aliquots were thawed on ice, allowed to reach room temperature and 2 ml of autologous conditioned serum injected directly into the area of maximum pain as identified by the patient. All injections were performed by one of the authors.

Clinical evaluation

Before therapy or injection, after 6 weeks, 12 weeks and 6 months patients were examined in the outpatient clinic. Outcome was measured by the VISA-A (Victorian Institute of Sport Assessment-Achilles) questionnaire. The VISA-A-G questionnaire used in this study is the German version of the VISA-A questionnaire which was adapted and validated for use in German speaking populations [20]. The VISA-A questionnaire is a valid and reliable index of the clinical severity of Achilles tendinopathy and includes the three domains pain, functional status and activity [38]. Improvement on the VISA-A > 10 points is considered clinically significant [41].

Radiological evaluation

MRI was performed using a 1.5 T scanner (Siemens, Erlangen, Germany) before and 6 months after injection and eccentric training respectively. Axial (T2 TSE) and sagittal (T1-TSE and T1-TIRM) views were evaluated. All sequences were performed with a 16-cm field of view, 256×512 matrix and 3.5-mm slice thickness. Each time two of the three authors evaluated the MRI in consensus without knowing which kind of therapy had been done. No specific randomization was undertaken.

According to Weber et al. [51] anatomical quantitative measures (*A*) were performed in milimetres with measurement accuracy of one decimal: anterio-posterior diameter of the thickened tendon in sagittal T1-sequence 3 cm above the calcaneus (*A*4), length (cranial-caudal) of subachilleal bursa in sagittal STIR-sequence (*A*5), anterioposterior diameter in axial T1-sequence (*A*7) and mediolateral diameter in axial T1-sequence (*A*8) (Fig. 1). Because there was no axial T1-sequence or STIR-sequence, in this study axial T2-sequence and sagittal T1-sequence were used, respectively.

Using these parameters in the formula $R = -16.805 \times A4 - 8.429 \times A5 - 8.331 \times (\pi \times A7 \times A8/4) + 23.46$, it was possible to differentiate between healthy (i.e., asymptomatic) and pathological (i.e., symptomatic) changes in the Achilles tendon with a specificity of 91% and a sensitivity of 97% [51]. *R* above 0.5 means a tendon is normal and *R* under 0.5 is pathological.

Using just one of the parameters *A*4, *A*5 or the calculation of *F*, the elliptical tendon cross-section from maximum anteroposterior and mediolateral diameter ($\pi \times A7/2 \times A8/2$), a specificity of 82%, 62% and 80% and a sensitivity of 94%, 91% and 91% were achieved, respectively [51].

MRIs were also scored on a 0–3 severity scale created in dependence on the clinically relevant groups 1–4 of Weber et al. [51] modified from Schweitzer and Karasick [42]: 0, normal tendon signal, no peritendinous changes (this group was added by the authors); (1) only peritendinous changes (paratendonitis); (2) increase in the size of the Achilles tendon (hypoxic degeneration) with focal intratendinous changes; (3) visible morphological changes in the case of mucoid degeneration (e.g. signal amplification in T2 weighting); (4) ruptures (this group was removed from authors because this was an exclusion criterion in this study). In this study not only the T1-sequence was mostly used but also the axial T2-sequence for peritendinous changes and detecting the signal amplification.

Approval was obtained from the local medical ethics committee (University of Basel, Ethikkommission beider Basel, number 191/11) prior to the study.

Statistical analysis

Test of normality with Komolgorov–Smirnov was performed for every group for VISA-A-G score, *A*4, *A*5, *F* and age. All parameters were normal distributed. Paired sample two-tailed *t* test was used to analyse differences between pre- and posttherapeutic values. Independent sample two-tailed *t* tests were used to analyse differences between autologous-conditioned-serum-group and eccentric-training-group, also corrected for baseline, 6 week, 12 week and 6 month data as appropriate. Fisher's exact test was performed for gender, site of Achilles tendinopathy, *R* and change of *R*, MRI-severity-scale and the change of severity on the MRI-severity-scale. Significance levels were set at 0.05. Spearman's rho was calculated for the correlation between the change of the entire VISA-A-G scores and change of the entire MRI-values ($n = 50$, $\rho > 0.279$, p value < 0.05 and $\rho > 0.235$, p value < 0.1). Statistical analysis was done using Microsoft Excel (Microsoft Corporation, Redmond, WA, USA).

sample size calculation was performed a priori on the base of the primary outcome of VISA-A. A total of 18 patients were needed in each group to establish a clinically significant mean difference of 10 points (maximum score,

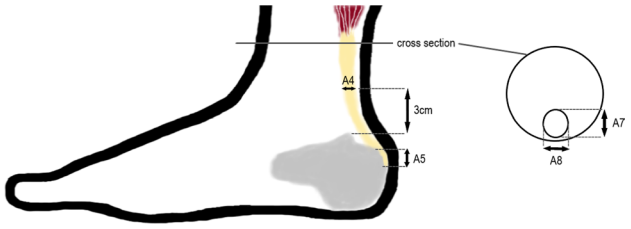

Fig. 1 Schematic representation of quantitative measures according to Weber et al. [51]

100 points) in the VISA-A score, with 80% power and an alpha level of 0.05.

Results

Twenty-five patients (mean age 55 ± 12 years) participated in the autologous-conditioned-serum-group and twenty-five patients (mean age 52 ± 13 years) in the eccentric-training-group (n.s.). There were 12 men and 13 women in the autologous-conditioned-serum-group and 15 men and 10 women in the eccentric-training-group (n.s.). Fifteen injections into the left and 10 into the right Achilles tendon were administered in the autologous-conditioned-serum-group. Sixteen patients with Achilles tendinopathy on the left side and 9 patients with Achilles tendinopathy on the right side were treated in the eccentric-training-group (n.s.). No infection was observed after injection in the autologous-conditioned-serum-group.

VISA-A-G scores

Both patient groups had statistically significant ($P < 0.001$) better VISA-A-G-scores after injection or eccentric training compared to the baseline before injection or eccentric training. This could also be found in the domains pain, functional status, activity except in the autologous-conditioned-serum-group for activity after 6 months. All VISA-A-G-scores were significantly ($P < 0.05$) better from time point to time point (prior to therapy to 6 weeks, 6–12 weeks and 12 weeks to 6 month) except for pain in both groups from 6 to 12 weeks.

Comparing both groups at all time points, patients in the autologous-conditioned-serum-group were significantly better after 6 months in VISA-A-G domain activity ($P = 0.034$) (Fig. 2).

There was significantly more improvement of the autologous-conditioned-serum-group compared to the eccentric-training-group 12 weeks vs baseline in VISA-A-G score ($P = 0.018$) and VISA-A-G-domain activity ($P = 0.018$) (Fig. 3).

There also was more significant improvement of the autologous-conditioned-serum-group compared to the eccentric-training-group 6 months vs baseline in VISA-A-G score ($P = 0.034$) and VISA-A-G-domain activity ($P = 0.014$) (Fig. 3).

Comparing 12 weeks vs 6 weeks there was more significant improvement in the autologous-conditioned-serum-group than in the eccentric-training-group in VISA-A-G score ($P = 0.019$) as well as in the domains pain ($P = 0.038$) and functional status ($P = 0.015$) (Fig. 3).

MRI

Both patient groups had statistically significant ($P < 0.001$) reduction of anatomical measures (*A*4, *A*5, *F*) and improvement of *R* after injection (14 vs 1 healthy tendons) or eccentric training (14 vs 2 healthy tendons) compared to the baseline before injection. This could also be found for MRI-severity-scale in the autologous-conditioned-serum-group (Before therapy: I: 1, II: 2, III: 22; after 6 month: 0:6, II: 7, III: 12; $P = 0.002$) and in the eccentric-training-group (Before therapy: II: 5, III: 20; after 6 month: 0:4, II: 7, III: 14; $P = 0.057$). Figure 4 illustrates a patient with very successful injection therapy as an example (Fig. 4).

There were no statistical differences in anatomical measures (*A*4, *A*5, *F*) or the change to the baseline between the two groups (n.s.) (Table 1).

There were no statistical differences in the change of *R* (autologous-conditioned-serum: 13 healthier and 12 equal vs eccentric training: 12 healthier and 13 equal) and in the change of MRI-severity-scale (autologous-conditioned-serum: 11 better, 14 equal vs eccentric training: 10 better, 11 equal, 4 worse) between the two groups (n.s.).

Correlations

There was a significant anticorrelation between the change of the anterio-posterior diameter of the thickened tendon 3 cm above the calcaneus (*A*4) and VISA-A-G score ($\rho = -0.279$, $p < 0.05$).

There were no significant correlations or anticorrelations between the change of cranial-caudal length of subachilleal bursa (*A*5), the change of elliptical tendon cross-section (*F*), the change of *R* or the MRI-groups and the VISA-A-G-scores (n.s.).

Discussion

The main finding of the present study indicates that both the autologous-conditioned-serum-injection and the eccentric training yield a positive clinical result in patients with Achilles tendinopathy in both the short- and long-term ranges.

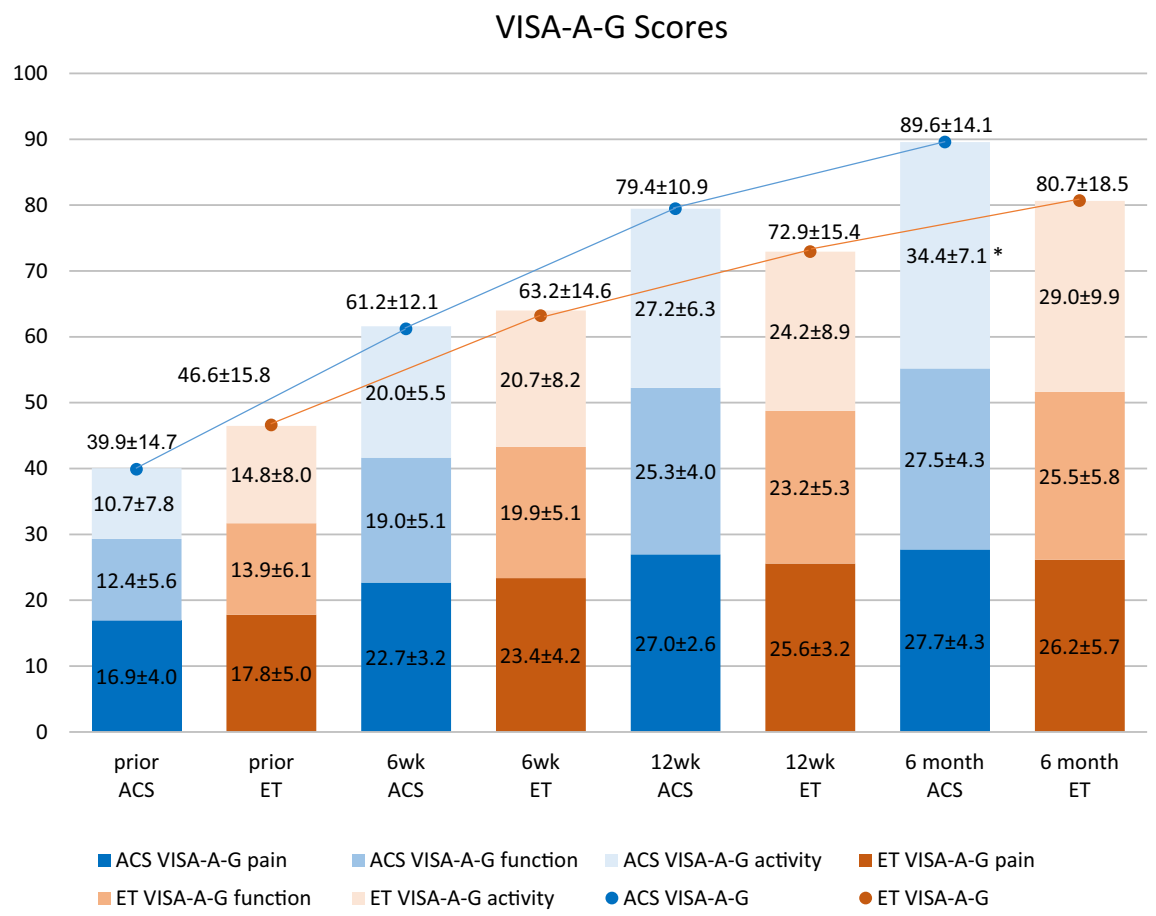

Fig. 2 VISA-A-G scores including domains: significant differences between the autologous-conditioned-serum-group (ACS) and eccentric-training-group (ET) are indicated with asterisks ($P < 0.05$)

There was a significant improvement in VISA-A-G score in both groups. Concomitant with the clinical improvement, there was a significant reduction in anterio-posterior diameter of the thickened tendon in sagittal T1-sequence 3 cm above the calcaneus (*A4*), length (cranial-caudal) of subachilleal bursa in sagittal STIR-sequence (*A5*), elliptical tendon cross-section from maximum anteroposterior and mediolateral diameter (*F*), improvement of tendon quality (*R*) and in MRI severity scale (modified from Schweitzer and Karasick [42]) as measured with MRI. Furthermore there is an anticorrelation between the baseline-corrected anterio-posterior diameter of the achilles tendon in sagittal T1-sequence 3 cm above the calcaneus (*A4*) and baseline-corrected VISA-A-G score.

The VISA-A-G-domain activity in the autologous-conditioned-serum-group was significantly greater than in the eccentric-training-group after 6 months. The change in VISA-A-G score and the domains pain and function from 6 to 12 weeks was significantly greater in the autologous-conditioned-serum-group. The baseline corrected VISA-A-G scores 12 weeks and 6 months after injection were also significantly greater than in the eccentric-training-group as well as the VISA-A-G-domain activity. The MRI-findings showed no significant differences between the two groups.

As hypothesized, peritendinous injection of autologous-conditioned-serum in Achilles tendinopathy has a better outcome compared to eccentric training as demonstrated by the 12 weeks' and 6 months' data analysis. However, this difference could not be seen in MRI, although there is an anticorrelation between VISA-A-G scores and MRI-findings.

In the current study, the patients had baseline VISA-A scores comparable with those previously reported in patients with Achilles tendinopathy [14, 47, 50]. Over the course of the 12-week intervention period, the VISA-A score improved more than 10 points in both groups on average. These are clinically meaningful improvements and, moreover, corroborate previous reports of the effect of loading regimens on tendinopathy [14, 40, 46, 47, 50].

In contrast to prior studies [2, 25] showing that most of the eccentric-training-patients resumed their previous activity levels at the end of the 12-week intervention period or were satisfied with their results [5] or returned to

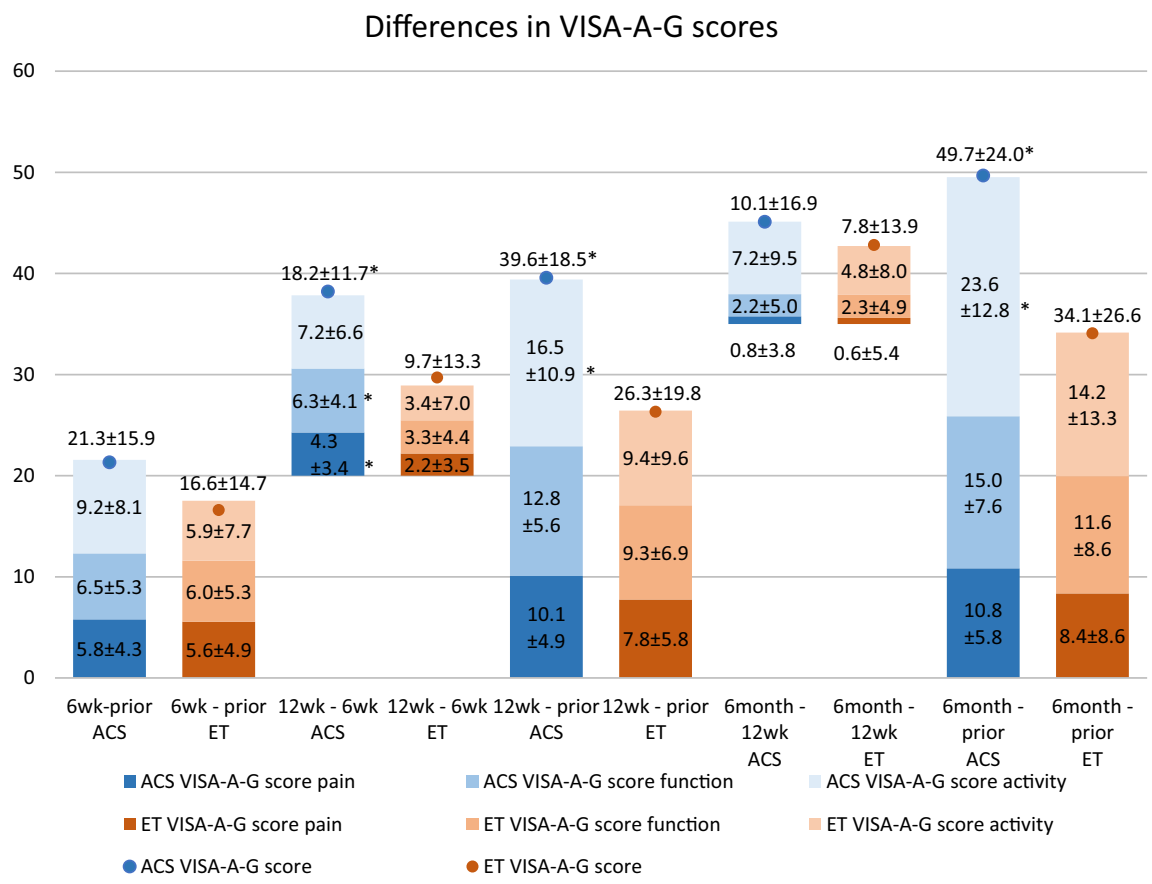

Fig. 3 Differences in VISA-A-G scores: Significant higher change in mean between the autologous-conditioned-serum-group (ACS) and eccentric-training-group (ET) is indicated with asterisks ($P < 0.05$)

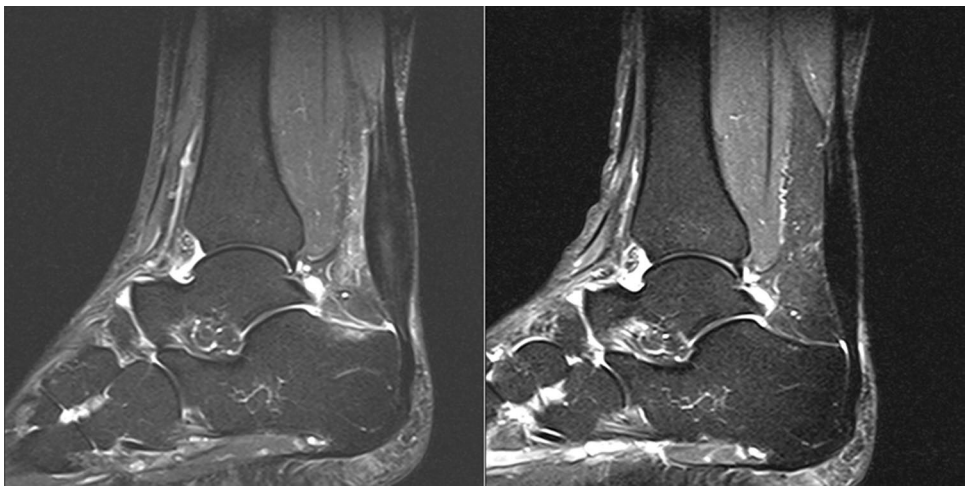

Fig. 4 MRI-example of a successful injection therapy before injection (left) and 6 months later (right)

their previous physical activities [45], this study achieved a VISA-A-G score of 80 or more. It is possible that not all of the patients in this study resumed their previous physical activity levels or were satisfied, although they had good clinical results. Other authors also had improvement in VISA-A scores, but many patients in other studies did not return to their previous activity level [40], were subjectively not good or excellent satisfied [50] nor had a VISA-A score of 80 or more [47]. Furthermore, the patients in this study achieved a VISA-A-G score of 80 or more after 6 months and not after 12 weeks as other authors reported above [5].

Table 1 Anatomical measures of Achilles tendon in MRI: autologous-conditioned-serum-group (ACS) versus eccentric-training-group (ET)

MRI—measure (mm)	Prior	6 months	6 months–prior
ACS—depth Achilles tendon sagittal (*A*4)	10.5 ± 3.4	7.3 ± 2.3	− 3.2 ± 2.0
ET—depth Achilles tendon sagittal (*A*4)	9.1 ± 3.4	6.8 ± 2.0	− 2.4 ± 2.4
ACS—length bursa (*A*5)	7.8 ± 0.7	5.4 ± 0.8	− 2.4 ± 0.9
ET—lenght bursa (*A*5)	7.5 ± 1.5	5.4 ± 1.5	− 2.1 ± 1.2
ACS—area Achilles tendon (*F*)	15.0 ± 6.8	9.3 ± 3.7	− 5.7 ± 3.8
ET—area Achilles tendon (*F*)	13.0 ± 5.4	8.2 ± 2.9	− 4.8 ± 4.2

The results of the current study suggest that autologous-conditioned-serum-injections and eccentric training improve symptoms and physical activity level in patients with mid-portion Achilles tendinopathy. Loading-based treatment in the form of eccentric training has become the principal non-surgical choice of treatment for Achilles tendinopathy [2] although there is no convincing evidence that it is the most effective exercise regimen [5]. In fact, a recent systematic review concluded that there is little clinical or mechanistic evidence that supports using the eccentric component alone and that well-conducted studies comparing different loading programs are largely lacking [28]. Nevertheless, it seems that loading itself yields positive clinical, structural and biochemical effects with respect to tendinopathy [16, 17, 25, 46].

To our knowledge there are no studies investigating autologous-conditioned-serum-injections in Achilles tendinopathy, but several studies investigate orthobiologics such as PRP or whole blood. A majority of studies show that there is insufficient evidence to support the use of PRP in the treatment of chronic Achilles tendinopathies [44]. In a Cochrane-review there is currently insufficient evidence to support the use of PRP for treating musculoskeletal soft tissue injuries [30], but in that review there was just one study [8] regarding Achilles tendinopathy and PRP. A recent study supports treatment with high-volume injection or PRP in combination with eccentric training [6]; another study found no benefit with injection of PRP in comparison to saline [18].

Bell and colleagues compared injection of wholeblood with eccentric exercises alone and found no additional benefit in the treatment of mid-portion Achilles tendinopathy [4], whereas Pearson et al. provide some evidence for small short-term symptomatic improvements with the addition of autologous blood injection to standard treatment for Achilles tendinopathy [35].

There is conflicting evidence as to whether a tendinopathic Achilles tendon normalizes anterio-posterior thickness after the eccentric-training-regimen [6, 7, 14, 18, 32, 36, 40, 48, 50]. In the present study, tendon anterio-posterior thickness was reduced in both groups with time, which is supported by prior reports [14, 18, 32, 48, 50].

Regarding the structural changes in MRI of the treated Achilles tendon there are several authors reporting as follows:

Monto et al. performed MRI in 18 of 30 patients treated with PRP-injections; the others were controlled by ultrasound [29]. Six months after treatment, 27 of 29 patients demonstrated interval healing of the treated injury zone as well as an improvement in the AOFAS score (American Orthopaedic Foot and Ankle Society). Owens and colleagues [34] retrospectively reviewed a small cohort of ten patients, all treated with intratendinous PRP injections and investigated MRI in six patients. Each tendon was assessed for percentage of tendinopathy and they found no changes. Another recent study compared 13 patients with Achilles tendon surgery and PRP to PRP alone and found improvement in the MRI scans as well as a correlation between the MRI scoring and the VISA-A score [33]. 20 Achilles tendons with chronic Achilles tendinosis before and 3 months after eccentric training were examined with a dynamic contrast-enhanced MRI and the authors found no change, no difference between the symptomatic and asymptomatic leg after treatment but more enhancement in the symptomatic leg before treatment and no correlation between MRI-findings and clinical performance [10]. The same research-group found, in 25 patients, a significant difference in mean intratendinous signal between symptomatic and contralateral asymptomatic tendons and a correlation between increased intratendinous signal in MRI and severity of pain and functional impairment [11]. Richards et al. examined ninepatients before and 1 year after treatment and found reduction in size, reduction of MRI-enhancement, morphological improvements and a correlation between VISA-A score and vascularity and anterio-posterior diameter as well [37]. 25 patients were examined by Shalabi et al. [43] and they concluded that eccentric training leads to less pain, better functional outcome, a decrease in tendon volume and intratendinous signal and found a correlation between pain and change of the intratendinous signal. Tsehaie et al. completed follow-up in 20 patients treated with eccentric training and found increased VISA-A score, decreased tendon volume and a correlation between VISA-A score and signal intensity in MRI [48]. Usuelli et al. investigated the difference in outcome between PRP and stromal

vascular fraction and reported clinical improvement in both groups but no correlation with MRI [49].

There are some limitations to this study: The injections were not controlled by ultrasound, the exact place of injection except being peritendinous and in the area of maximum pain could not be checked. In addition, it was not possible to definitely control whether the patients undertook their home exercises adequately or some extra gym training independently, even if they were supervised by the physiotherapists and asked not to do other exercises. The follow-up was only 6 months, so further functional recovery to 12 months or more could not be detected. Furthermore, the study was undertaken retrospectively and was not blinded or randomized. There was also no third control group where a saline injection would have been administered. MRI was performed using a 1.5 T scanner. In fact, there was a newer and better scanner available, which should be used in further studies to detect the MRI-changes more easily.

This study contributes new data to the discussion about orthobiologics and suggests autologous conditioned serum to be a good alternative to eccentric training in treatment of Achilles tendinopathy. This study could not find any evidence for specific changes in the MRI investigations.

Conclusion

This study suggests that injection with autologous conditioned serum for treatment of Achilles tendinopathy is favourable to the gold standard eccentric training with advantage of a clinical benefit 3 months after injection and with advantage of offering a treatment that is not dependent on the compliance of the patient for physical therapy. Therefore, autologous-conditioned-serum-injections should be further investigated in large randomized controlled trials with longer follow-up to provide clear evidence for their use in Achilles tendinopathy. The studies should have a third control group with injection of saline. Autologous conditioned serum vs saline could also be investigated to rule out the possible placebo effect of the injection itself. An investigation of the effect of autologous conditioned serum and eccentric training together, versus autologous conditioned serum and eccentric training alone would be of interest to find out if there would be a benefit to combine these two therapies. VISA-A score and MRI are good diagnostic tools for assessing the outcome in Achilles tendinopathy.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval Approval was obtained from the local medical ethics committee (University of Basel, Ethikkommission beider Basel, number 191/11) prior to the study.

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