Sonographically Guided Intratendinous Injection of Hyperosmolar Dextrose to Treat Chronic Tendinosis of the Achilles Tendon: A Pilot Study

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OBJECTIVE. Chronic tendinosis of the Achilles tendon is a common overuse injury that is difficult to manage. We report on a new injection treatment for this condition.

SUBJECTS AND METHODS. Thirty-six consecutive patients (25 men, 11 women; mean age, 52.6 years) with symptoms for more than 3 months (mean, 28.6 months) underwent sonography-guided intratendinous injection of 25% hyperosmolar dextrose every 6 weeks until symptoms resolved or no improvement was shown. At baseline and before each injection, clinical assessment was performed using a visual analogue scale (VAS) for pain at rest (VAS1), pain during normal daily activity (VAS2), and pain during or after sporting or other physical activity (VAS3). Sonographic parameters including tendon thickness, echogenicity, and neovascularity were also recorded. Posttreatment clinical follow-up was performed via telephone interview.

RESULTS. Thirty-three tendons in 32 patients were successfully treated. The mean number of treatment sessions was 4.0 (range, 2–11). There was a mean percentage reduction for VAS1 of 88.2% ($p < 0.0001$), for VAS2 of 84.0% ($p < 0.0001$), and for VAS3 of 78.1% ($p < 0.0001$). The mean tendon thickness decreased from 11.7 to 11.1 mm ($p < 0.007$). The number of tendons with anechoic clefts or foci was reduced by 78%. Echogenicity improved in six tendons (18%) but was unchanged in 27 tendons (82%). Neovascularity was unchanged in 11 tendons (33%) but decreased in 18 tendons (55%); no neovascularity was present before or after treatment in the four remaining tendons. Follow-up telephone interviews of the 30 available patients a mean of 12 months after treatment revealed that 20 patients were still asymptomatic, nine patients had only mild symptoms, and one patient had moderate symptoms.

CONCLUSION. Intratendinous injections of hyperosmolar dextrose yielded a good clinical response—that is, a significant reduction in pain at rest and during tendon-loading activities—in patients with chronic tendinosis of the Achilles tendon.

Keywords: Achilles tendon, ankle, interventional radiology, musculoskeletal imaging, sonography, sports medicine, tendinosis

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Chronic tendinosis of the Achilles tendon is a common overuse injury that is seen not only in athletes but also in the general population [1]. This condition is painful and a cause of considerable distress and disability. Previous research has shown that histologically tendinosis is a noninflammatory process resulting from a failed wound-healing cascade with evidence of disordered, haphazard healing; intratendinous collagen degeneration; fiber disorientation and thinning; hypercellularity; scattered vascular ingrowth; and increased interfibrillar glycosaminoglycans [2, 3]. Studies have also shown that these areas of collagen degeneration correspond to the hypoechoic areas seen on sonography [4].

Hyperosmolar dextrose has been used for years by medical practitioners as part of prolotherapy regimens for the treatment of chronic musculoskeletal pain with varying degrees of success reported in the literature [5]. Prolotherapy is a technique in which a small volume of an irritant solution (proliferant) is injected at multiple sites around a ligament or tendon insertion [6]. This solution is purported to initiate a local inflammatory response at the site of injection, which induces fibroblast proliferation and subsequent collagen synthesis resulting in a tighter and stronger ligament or tendon [7]. We report on a modification of this therapeutic injection technique for the treatment of chronic Achilles tendinosis. Instead of injecting a proliferant around the tendon insertion and performing the procedure blindly, we performed intratendinous injections of hyperosmolar dextrose under sonographic guidance, targeting the abnormal anechoic and hypoechoic areas in the tendon, to induce an inflammatory reaction and initiate a wound-healing cascade and subsequent collagen synthesis.

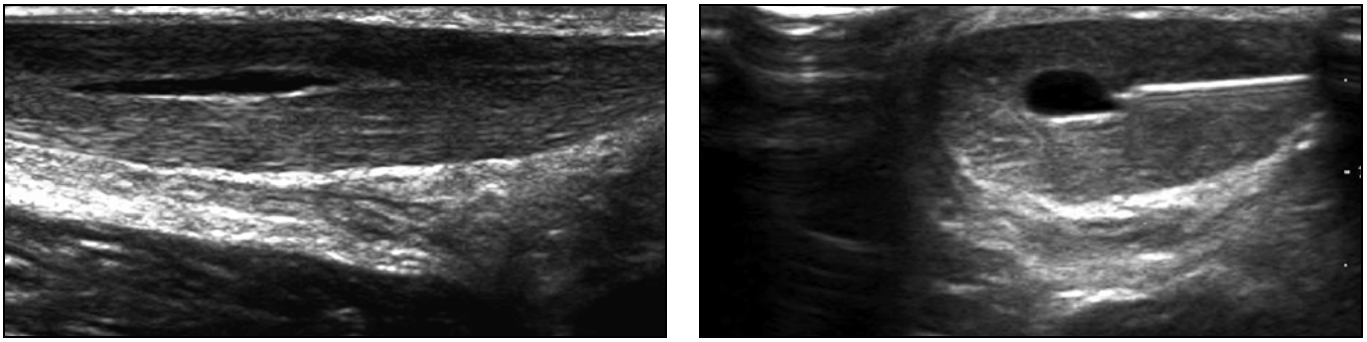

Fig. 1—58-year-old woman with midportion Achilles tendinosis.
A, Longitudinal sonographic image obtained using 5-12–MHz linear array transducer shows large anechoic cleft in midportion of Achilles tendon.
B, Transverse sonographic image of same anechoic cleft after insertion of 27-gauge needle shows tip of needle is located at edge of cleft.

Subjects and Methods

Thirty-six consecutive patients, 25 men and 11 women (mean age, 52.6 years; range, 23–82 years), with chronic tendinosis of the Achilles tendon—that is, those with symptoms for more than 3 months (mean, 28.6 months; range, 3–120 months)—participated in this prospective study. In all the patients in the study group, multiple previous conservative treatments had failed. Some of the treatments included physiotherapy ($n = 19$), acupuncture ($n = 5$), shock-wave therapy ($n = 2$), sonography ($n = 8$), intramuscular stimulation ($n = 3$), steroid injections ($n = 4$), orthotics ($n = 4$), massage ($n = 3$) water running ($n = 1$), and laser treatment ($n = 1$). In 22 patients, there was minimal improvement after completion of a heel-drop program, which is the current standard conservative treatment for Achilles tendinosis. Exclusion criteria included patients with acute tendinitis or symptoms associated with acute trauma. Patients who had surgery or interventional procedures within the preceding 3 months were also excluded. All patients were fully informed about the study and provided written consent. The study was approved by the local institutional ethics review board.

Sonography Examinations

The sonography examinations and injection procedures were performed by a radiologist with extensive experience in musculoskeletal sonography. The Achilles tendon was examined with the patient in a prone position with both feet hanging over the end of an examination table. The sonography examinations were performed on a unit (HDL 5000, Philips Medical Systems) using both a 5-12–MHz and a 7-15–MHz linear array high-resolution transducer. The tendon in its entirety was examined in the longitudinal and transverse planes. Care was taken to image the tendon parallel with the fibers in the longitudinal plane and perpendicular to the fibers in the transverse plane to avoid artifact such as anisotropy. Color flow Doppler imaging was used to diagnose neovascularity. Tendon thickness, the presence of anechoic clefts or foci, echogenicity, neovascularity, the presence of intratendinous calcification, and the presence of cortical irregularity at the tendon insertion were all recorded for each tendon at baseline and before each injection procedure.

Tendon thickness was recorded as the maximum anteroposterior diameter (in millimeters) of the tendon measured on the transverse images. A distinction was made between anechoic clefts or foci (intrasubstance tears) and abnormal hypoechoic areas (collagen degeneration). A grading system for tendon echogenicity was devised as follows: grade 0 represented normal fibrillar echotexture; grade I, mild focal inhomogeneous echotexture; grade II, moderate focal inhomogeneous echotexture; and grade III, severe diffuse inhomogeneous echotexture. A grading system for neovascularity was also devised as follows: grade 0 represented no neovascularity (no detectable vessels); grade I, mild neovascularity (one or two vessels identified extending into the tendon); grade II, moderate neovascularity (three or four vessels identified extending into the tendon); and grade III, severe neovascularity (more than four vessels identified extending into the tendon). If the sonographic changes of tendinosis were seen in the midportion of the tendon, the patient was diagnosed as having midportion tendinosis; however, if the sonographic changes were seen in only the distal portion of the tendon, the patient was diagnosed as having insertional tendinosis. The study population was therefore divided into subjects with midportion tendinosis and those with insertional tendinosis. The final sonographic evaluations were performed 6 weeks after treatment.

Hyperosmolar Dextrose Injection

A 3-mL syringe was filled with 1 mL of 2% lignocaine (20 mg/mL) and 1 mL of 50% dextrose (25 g/50 mL) (dextrose monohydrate, 500 mg), giving a 25% dextrose solution. Care was taken to expel all air from the syringe and needle before the injection. Each injection procedure was performed under aseptic conditions using a 27-gauge needle. Abnormal hypoechoic areas and anechoic clefts or foci (Fig. 1) in the thickened portion of the tendon were targeted under sonographic guidance using the 7-15–MHz hockey-stick linear array transducer. The volume of solution injected varied slightly from tendon to tendon and depended on the degree of resistance during the injection and on spread of the solution within the tendon. In general, less than 0.5 mL was injected at any one site. One, two, or three sites were injected during a treatment session. The tendon was reimaged after the injection procedure to assess for spread of the dextrose solution (Fig. 2) and to identify any intrasubstance or partial tears that may have become more conspicuous after the injection.

Patients were instructed to refrain from any heavy tendon-loading activity during the first 2 weeks after the procedure. They were also cautioned against taking aspirin or other antiinflammatory agents to relieve any discomfort. Acetaminophen-based analgesia was allowed.

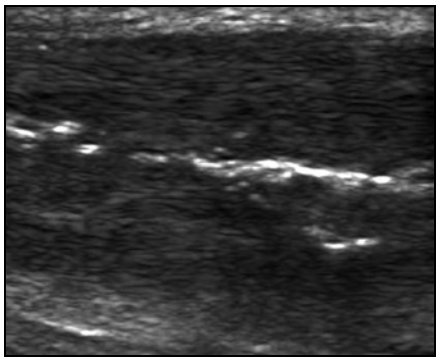

Fig. 2—Sonographic image obtained after injection in 82-year-old man with midportion Achilles tendinosis shows hyperechoic dextrose solution dispersing within abnormal tendon.

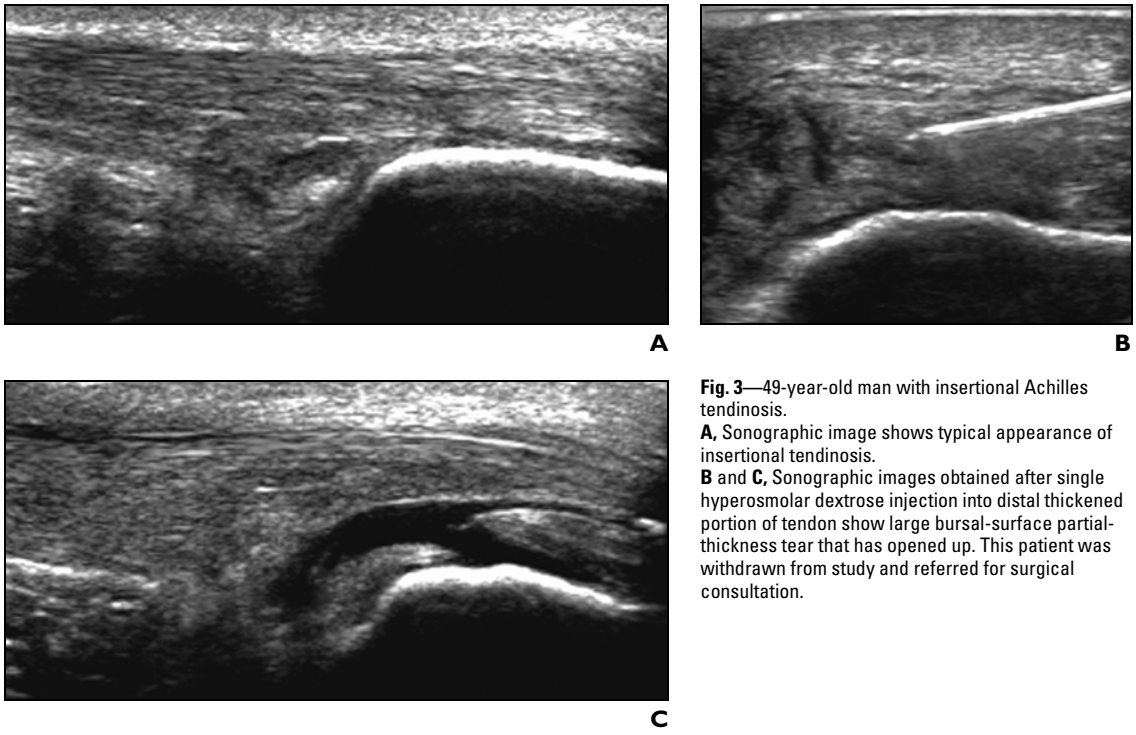

Fig. 3—49-year-old man with insertional Achilles tendinosis.
A, Sonographic image shows typical appearance of insertional tendinosis.
B and **C,** Sonographic images obtained after single hyperosmolar dextrose injection into distal thickened portion of tendon show large bursal-surface partial-thickness tear that has opened up. This patient was withdrawn from study and referred for surgical consultation.

Each patient was asked to return for repeat sonography and injection approximately every 6 weeks depending on scheduling. This continued until either the patient's symptoms resolved or no improvement was evident, at which time the treatment was discontinued. In general, if there was no improvement after four injection procedures, the treatment was discontinued.

Data Collection

At the initial consultations, all patients were asked to complete a questionnaire regarding their condition including participation in sporting activity, length of symptomatic period, previous and current treatments, and level of disability.

Visual analogue scale (VAS) scores were recorded for assessment of tendon pain. This scale is a 100-mm-long line marked with anchors at each end. One anchor was labeled "No pain" and corresponded to 0, whereas the second anchor was labeled "Severe pain" and corresponded to 100. Patients were asked to mark with an X on the line the point that corresponded to their level of tendon pain. They were asked to complete a VAS for tendon pain at rest, tendon pain during normal daily activity, and tendon pain during or after sporting or other physical activity. VAS scores were recorded at baseline and before each injection. Final VAS scores were recorded 6 weeks after treatment.

A telephone interview with each study group participant was performed a mean of 12 months (range, 4.5–28 months) after the last treatment to assess the medium- to long-term efficacy of dextrose injection therapy.

Data Analysis

Descriptive and mean comparisons of the study data were analyzed using statistical software (JMP version 4.0.0 [2000], SAS Institute). A paired samples Student's t test compared the change in scores before and after treatment for VAS1, VAS2, and VAS3 and for tendon thickness, which was recorded in millimeters. Data for comparisons were divided as follows: subjects with midportion Achilles tendinosis, those with insertional Achilles tendinosis, and both groups combined (i.e., all Achilles tendinosis subjects). A second paired Student's t test was performed using the location of tendinosis as an additional level for comparison of VAS scores before and after treatment. Statistical significance relating in the clinical context for this study was set at a p value of 0.10.

Results

After receiving multiple injections, three patients with insertional tendinosis showed only minimal response to the injection therapy and the treatment was therefore discontinued. A fourth patient was referred for surgical consultation after the initial intratendinous injection revealed a large tear in the distal insertional fibers of the Achilles tendon. This large irregular bursal surface partial-thickness tear became apparent on sonography only after injection of the dextrose solution (Fig. 3).

Thirty-three tendons in 32 patients were successfully treated. The location of the tendinosis was midportion in 23 tendons and insertional in 10 tendons. The mean number of treatment sessions for the study group was 4.0 (range, 2–11). The mean volume of solution injected into the tendon during each treatment session was 1.35 mL.

VAS Scores

Table 1 illustrates the mean VAS scores before and after treatment for tendon pain at rest (VAS1), tendon pain during normal daily activity (VAS2), and tendon pain during or after sporting or other physical activity (VAS3) for the study population. There was a significant improvement in the VAS scores for the study group (midportion and insertional), with a mean percentage reduction in pain for VAS1 of 88.2% ($p < 0.0001$), for VAS2 of 84.0% ($p < 0.0001$), and for VAS3 of 78.1% ($p < 0.0001$). There was no significant difference between the midportion and insertional groups for VAS1 or VAS2; however, there was a significant difference between groups for VAS3 ($p = 0.06$).

TABLE 1: Visual Analog Scale (VAS) Scores for Study Group Before and After Dextrose Injection Therapy for Treatment of Chronic Achilles Tendinosis

	Mean VAS Score						Mean % Change in VAS Score[a]		
	Before Therapy			After Therapy					
Score	Midportion	Insertional	Combined	Midportion	Insertional	Combined	Midportion	Insertional	Combined
VAS1	41.7	30.3	38.2	4.7	4.1	4.5	88.7	86.5	88.2
VAS2	55.5	45.3	52.4	7.8	9.6	8.4	85.9	78.8	84.0
VAS3	73.9	66.4	71.6	12.4	23.4	15.7	83.2	64.7	78.1

Note—Combined = both groups combined (all subjects), VAS1 = pain at rest, VAS2 = pain during normal daily activity, VAS3 = pain during or after sporting or other physical activity.

[a] $p < 0.001$.

Sonographic Evaluation

Table 2 outlines the results of sonographic evaluations before and after treatment for the study population. The mean tendon thickness decreased from 11.7 mm before treatment to 11.1 mm after treatment ($p = 0.007$). Anechoic clefts or foci were seen in 18 tendons (55%) before treatment; however, only four of these tendons had evidence of clefts or foci after treatment. In 27 tendons (82%), echogenicity was unchanged after treatment. Six tendons (18%) were downgraded from grade II to grade I. There was no neovascularity present in four tendons (12%) before or after treatment. In 11 tendons (33%), neovascularity was unchanged after treatment. In 18 tendons (55%) there was decreased neovascularity after treatment: Six tendons decreased from grade III to grade I, three tendons decreased from grade III to grade II, and nine tendons decreased from grade II to grade I. Insertional cortical irregularity was seen in six tendons (18%) before and after treatment. Insertional intratendinous calcifications were seen in seven tendons (21%) before treatment. These calcifications were unchanged after treatment.

Follow-Up Telephone Interview

Thirty of the 32 patients were successfully contacted by telephone a mean of 12 months after treatment (Table 3). Twenty of the 32 patients were still asymptomatic, with 19 patients giving a satisfaction level of 95–100%. Nine patients described only mild symptoms and had a satisfaction level of 70–90%. One patient had moderate symptoms and described only 50% satisfaction level.

Discussion

Banks [8] proposed that hyperosmolar dextrose induces an inflammatory reaction at the site of injection by dehydrating cells (osmotic proliferant) causing localized tissue trauma. Local tissue damage causes an influx of inflammatory cells and initiates the wound-healing process. Granulocytes, which are attracted to the injection site by cellular debris and chemotactic agents, begin to chemically débride the injection site and during the process secrete humoral factors that attract macrophages. The macrophages phagocytize cellular debris and secrete polypeptide growth factors that attract and activate fibroblasts. The fibroblasts infiltrate the injection site and begin new collagen synthesis. This new collagen undergoes contraction due to a process of cross linking and dehydration of the newly formed fibers, resulting in stronger and tighter connective tissue at the injection site. In a human biopsy study by Klein et al. [9], a 60% increase in collagen fibril diameter measured at 3 months was shown with high statistical significance ($p < 0.001$) after 6 weekly proliferant injections into the lumbar and sacroiliac ligaments in three patients with lower back pain.

In most of the previously published research on prolotherapy, investigators report its efficacy in treating ligament instability. Several studies have looked at its role in musculoskeletal lower back pain and osteoarthritis, particularly of the knee [10–13]. Very few published studies have reported on its role in treating chronic tendinosis. Topol et al. [14] injected 24 elite rugby and soccer players who had chronic groin pain. Those investigators performed monthly injections of 12.5% dextrose and 0.5% lidocaine into the thigh adductor origins, suprapubic abdominal insertions, and symphysis pubis. At final data collection a mean of 17 months after treatment, 20 of the 24 patients had no pain and 22 of 24 patients were unrestricted with sports activity. In our study, the dextrose injections were intratendinous as opposed to injections around the tendon insertion, and the injections were performed under sonographic guidance so that the hypoechoic and anechoic areas could be precisely targeted. To our knowledge, there is no mention in the published prolotherapy literature of sonographic guidance being used in the injection procedure.

In our study, we make a distinction between hypoechoic areas and anechoic clefts or foci. We believe both are part of the spectrum of tendon degeneration with anechoic clefts or foci representing intrasubstance microtears and hypoechoic areas representing abnormal areas of collagen degeneration [4, 15, 16]. In 18 tendons (55%), there were small anechoic clefts or foci present on the pretreatment sonography examination. In one patient with insertional tendinosis, a large partial-thickness tear became apparent only after the initial injection of the dextrose solution (Fig. 3). This preinjection sonographically occult tear was so large that the patient was withdrawn from the study and referred for surgical consultation due to fear of tendon rupture. This observation emphasizes the fact that intrasubstance and partial-thickness tears in chronic tendinosis may be sonographically occult. In 27 tendons (82%), the hypoechoic areas in the thickened portion of the tendon were unchanged after treatment. We expected that more tendons would have shown improvement or resolution of the abnormal hypoechoic areas. There was no evidence of echogenic scar tissue formation on the final sonography examination. This may be related to the fact that a longer period of time than the treatment period is required for the tendon to remodel itself.

Ohberg and Alfredson [17] proposed in their study that neovascularity is associated with chronic tendon pain; however, whether its presence indicates an unfavorable outcome is still unclear. Zanetti et al. [18] proposed that tendon inhomogeneity seems to be more relevant to outcome than neovascularity. In our study, injections were not targeted at the neovessels but rather at the hypoechoic and anechoic areas in the tendon. Despite this, 18 tendons (55%) had decreased neovascularity after treatment. We postulate that neovascularity may represent an attempt by the body to reverse the intratendinous changes of tendinosis by improving the blood supply to the areas of collagen degeneration.

TABLE 2: Sonographic Evaluation of Study Group Before and After Dextrose Injection Therapy for Treatment of Chronic Achilles Tendinosis

Characteristics of Tendons on Sonography	Before Treatment	After Treatment
Mean tendon thickness (mm)	11.7	11.1
Anechoic clefts or foci present	18	4
Echogenicity[a]		
Grade 0	0	0
Grade I	15	21
Grade II	17	11
Grade III	1	1
Neovascularity[b]		
Grade 0	4	4
Grade I	10	25
Grade II	10	4
Grade III	9	0
Cortical irregularity at tendon insertion present	6	6
Intratendinous calcifications present	7	7

Note—All data except mean tendon thickness are the number of tendons.

[a]Grade 0 = normal fibrillar echotexture, grade I = mild focal inhomogeneous echotexture, grade II = moderate focal inhomogeneous echotexture, grade III = severe diffuse inhomogeneous echotexture.

[b]Grade 0 = no neovascularity (no detectable vessels), grade I = mild neovascularity (one or two vessels identified extending into the tendon), grade II = moderate neovascularity (three or four vessels identified extending into the tendon), grade III = severe neovascularity (more than four vessels identified extending into the tendon).

TABLE 3: Results of Telephone Interview Performed a Mean of 12 Months After Last Dextrose Injection Therapy

No. of Patients	Symptoms				Satisfaction Level (%)
	None	Mild	Moderate	Severe	
19	19				95–100
7	1	6			80–90
2		2			70
2		1	1		50
Total: 30	20	9	1		

Note—The remaining two patients could not be contacted for an interview.

The results of our study show a significant reduction in tendon pain at rest and during tendon-loading activities. Unfortunately, we cannot fully explain the exact cause for the reduction in tendon pain. We do not believe that the reduction in tendon pain can be attributed totally to a reduction in neovascularity because 11 tendons (33%) in this study had unchanged neovascularity after treatment despite these patients having a significant reduction in tendon pain. The results and observations in our study are similar to those recently reported by Connell et al. [19]. In contrast to our study, they performed autologous blood injections under sonographic guidance on 35 patients for the treatment of refractory lateral epicondylitis. They hypothesized that fibroblast growth factor, which is carried in blood, acts as a humoral mediator and induces the wound-healing cascade when injected into an abnormal tendon. The end result of fibroblast proliferation and initiation of the wound-healing cascade is common to both treatments.

There were three unsuccessful outcomes in our study. All three patients had insertional tendinosis with evidence of cortical irregularity at the insertion of the tendon and intratendinous calcification. It is our experience that some patients with insertional tendinosis are more difficult to treat and have less favorable outcomes than patients with midportion tendinosis. This is emphasized by less marked reduction in tendon pain for VAS3 in the insertional group when compared with the midportion group (65.1% vs 82.7%, respectively) ($p = 0.06$).

We realize there are certain limitations to our study. First, there was no control group and the patients were not blinded to what they perceived was a new treatment. The mean symptomatic period of our study population was 28.6 months, which is consistent with long-standing refractory Achilles tendinosis. The results of our follow-up telephone interview performed a mean of 12 months after treatment showed that 20 patients were still asymptomatic, nine patients had only mild symptoms, and only one patient had moderate symptoms (Table 3). There was a satisfaction level of 80–100% in 26 of the 30 patients contacted.

Despite the absence of a control group, the results of this pilot study are very promising and indicate satisfactory medium- to long-term efficacy of the dextrose injection therapy. We recognize that further clinical studies comparing hyperosmolar dextrose injections with other therapies and with no therapy are required.

There were no adverse effects or complications of the dextrose injection therapy identified in this study. Hyperosmolar dextrose has an excellent safety profile and is cost-effective.

In conclusion, sonography-guided intratendinous injections of hyperosmolar dextrose showed good clinical response in patients with long-standing refractory Achilles tendinosis with significant reduction in tendon pain at rest and during tendon-loading activities.

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