

Shockwave treatment for medial tibial stress syndrome in athletes; a prospective controlled study

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Accepted 3 February 2011
Published Online First
9 March 2011

ABSTRACT

Objective The purpose of this study was to describe the results of two treatment regimens for medial tibial stress syndrome (MTSS); a graded running programme and the same running programme with additional shockwave therapy (extracorporeal shockwave therapy; ESWT).

Design A prospective observational controlled trial.

Setting Two different sports medicine departments.

Participants 42 athletes with MTSS were included.

Intervention Patients from one hospital were treated with a graded running programme, while patients from the other hospital were treated with the same graded running programme and focused ESWT (five sessions in 9 weeks).

Main Outcome Measures Time to full recovery (the endpoint was being able to run 18 min consecutively without pain at a fixed intensity).

Results The time to full recovery was significantly faster in the ESWT group compared with the patients who only performed a graded running programme, respectively 59.7 ± 25.8 and 91.6 ± 43.0 days ($p=0.008$).

Conclusions This prospective observational study showed that MTSS patients may benefit from ESWT in addition to a graded running programme. ESWT as an additional treatment warrants further investigation in a prospective controlled trial with the addition of randomisation and double blinding.

Medial tibial stress syndrome (MTSS) is one of the most common complaints of the lower leg in the athletic population.¹ Incidences between 4% and 35% have been reported in both military and athletic studies.^{2–4} Different aetiological mechanisms have been proposed for MTSS. For years MTSS was thought to be caused by traction-induced periostitis.^{5–7} Another aetiological theory is that overloaded bone remodelling causes MTSS.^{8, 9} Recent studies showed that with overloaded remodelling the cortex appears osteopaenic on CT scans and that dual energy x-ray absorptiometry scans reveal decreased bone density.^{10, 11} When MTSS symptoms subside the bone density returns to normal values,¹² suggesting that MTSS is related to mechanical overloading of the bone.

In the treatment of MTSS a therapy in which bone cells are upregulated would possibly enhance bone density and thus decrease symptoms. Studies that tried to enhance the number of bone cells in the treatment of stress fractures and the non-union of fractures provided evidence for the plausibility of this theory.^{13, 14} In those studies extracorporeal shockwave therapy (ESWT) was used to stimulate the bone.

At the time of planning the study no studies had been published on the use of ESWT in MTSS. As some idea of effect size is necessary to perform an adequate power analysis for the proper planning of a randomised controlled trial it was decided to perform a prospective observational controlled study that could be simply realised in the local area. In two regional hospitals the treatment protocol used was different and this situation lent itself to performing this observational study. The effect on time to full recovery after ESWT and a graded running programme was compared with a group of MTSS patients who performed only a running programme. The aim of this study was to describe the results of two different treatment regimens on MTSS; one group was rehabilitated with a running programme, whereas the other group was rehabilitated with the same running programme in combination with ESWT.

METHODS

Subjects

Patients were included in two separate sports medicine departments of large general district hospitals by one sports medicine specialist. For inclusion in the study the Yates and White⁴ criteria from 2004 were used.

Pain history

The pain was induced by exercise and could last for hours or days after exercise. Pain was located on the posteromedial border of the tibia. There was no history of paraesthesia or other symptoms indicative of other causes of exercise-induced leg pain.

Location

The patients identified pain along the posteromedial border of the tibia. The site had to be spread over a minimum of 5 cm.

Palpation

Palpation of the posteromedial border of the tibia produced discomfort that was diffuse in nature and confined to the posteromedial border of the tibia.

Symptoms had to be present for at least 21 days for patients to be included.

Exclusion criteria

Patients were excluded if there was a past history of a tibial fracture and when ESWT had been used previously for MTSS symptoms.

Procedure

Patients were included in two different sports medicine clinics by the same investigator. In

one clinic, patients were advised to start ESWT in combination with a running programme. In the other clinic, as therapy, patients were advised to perform the same running programme.

At inclusion, various baseline parameters were measured: sex, weight, height, body mass index, kind of sport in which the patient is involved, centimetres of pain on palpation of the posteromedial border of the tibia, side of the symptoms and number of days with symptoms (see table 1). The study was performed in compliance with the Helsinki Declaration.¹⁵

Running test

Before starting treatment, all patients performed a running test. The test consisted of running on a treadmill at a fixed speed while wearing running shoes. Before the test, the patient was shown a visual analogue scale (VAS, 1–10). It was explained that a score of 4 on the analogue scale was associated with symptoms and pain that started to become annoying. With the onset of such leg symptoms by pointing at the 4 on the analogue scale, the running test would be stopped. The test started at 7.5 km/h for 2 min. After this initial phase of warming up, the distance was registered that could be run at 10 km/h until a 4 on the VAS scale was indicated by the patient. The distance ran at 7.5 km/h was subtracted from the total metres run and was called ‘metres run on a treadmill without pain’.

Treatment

The treatment consisted of focused ESWT in combination with a graded running programme or a running programme only (see table 2).

Running programme

All patients performed a graded running programme as part of the treatment.¹⁶ The programme consisted of six phases. In the first two phases the patient ran on a treadmill while in the following phases the patient ran outdoors. A starting point in the running programme was established using the results from the running test. If ‘metres run on a treadmill without pain’ was between 0 and 400 m, the patient was told to start the running programme in phase 1. If 401–800 m could be run, the patient started in phase 2. With 801–1200 m, the patient started in phase 3. If 1201–1600 m could be run, the patient started in phase 4. At 1600 m or more, patients started with phase 5. The running programme was not started if the patient experienced pain during walking. In that case, the patient was advised to avoid symptoms by reducing loading

of the leg. Only after two consecutive days without pain during walking, were they allowed to start the programme in the first phase. The programme was performed three times per week. Instructions were given not to run on consecutive days.

A new phase of the running programme could be commenced if the previous one could be finished without a pain score of 4 or higher on the 1–10 VAS pain scale. Also, if pain (4 or more on the VAS scale) was experienced immediately after the session of the running programme or 1 day after the session, the next phase was not commenced. In that case, the next running session started in the same phase with 2 min less to run. When phase 6 was finished, we advised patients gradually to start their own sport. They were instructed to practise sport and to adjust the intensity and duration to keep their pain score at 4 or lower on the 1–10 VAS pain scale.

ESWT and running programme

In addition to the running programme, one group of patients was treated with focused ESWT. All treatments were performed by one of the authors (SR) without local anaesthesia. A focused ESWT device (Duolith SD1; Storz Medical, Tägerwilten, Switzerland) was used in all patients. Five treatment sessions were scheduled in the weeks 1, 2, 3, 5 and 9 after inclusion. At the first session, 1000 shocks were administered with an energy flux density of 0.10 mJ/mm² with the patient supine and the knees flexed at 30°. The treatment frequency was 2.5 shocks per second. Before each treatment session, contact fluid was applied over the length of the posteromedial tibia. At the start of the first session, the part of the tibia that was painful on palpation was treated with the ESWT device and also highlighted with a waterproof marker. The zone that was highlighted with the marker was also treated in the consecutive sessions. At the second session (in the second week of treatment), 1500 shocks were applied with an energy flux density of 0.15 mJ/mm² and 2.5 shocks per second. The third session took place in the third week of treatment; 1500 shocks were applied with an energy flux of 0.20 mJ/mm² and 2.5 shocks per second. At the fourth session (in week 5 of the treatment), again 1500 shocks were applied with an energy flux density of 0.25 mJ/mm² and 2.5 shocks per second. The last session was in week 9 of the treatment. In this session, 1500 shocks were applied with an energy flux density of 0.30 mJ/mm² and 2.5 shocks per second.

The treatment was performed along the painful area on the posteromedial border of the tibia. No restrictions after the treatment sessions were given. The running programme started in the week of the first treatment with ESWT.

Table 1 Baseline values for the treatment groups

	Running programme (N=20)	Running programme + focused ESWT (N=22)	p Value
Sex (% male)	35	73	0.029
Weight (kg)	68.5 (SD 8.6)	74.2 (SD 10.1)	NS
Length (cm)	175.1 (SD 6.5)	178.5 (SD 10.3)	NS
Body mass index (kg/length in cm ²)	22.2 (SD 1.9)	23.2 (SD 2.2)	NS
Age (years)	22.7 (SD 7.2)	30.0 (SD 12.5)	0.027
Days with symptoms	189.3 (SD 339.8)	629.2 (SD 761.1)	0.022
Centimetres palpation pain on tibia	11.7 (SD 4.5)	11.3 (SD 6.4)	NS
Metres run on treadmill without pain	744.8 (SD 417.1)	1329.6 (SD 562.9)	0.001

ESWT, extracorporeal shockwave therapy; NS, not significantly different ($p > 0.05$).

Table 2 Running programme

Running phase	Surface	Minutes	Total (min)	Speed/intensity
1	Treadmill	2 2 2 2 2 2 2	16	2 = running at 10 km/h, 2 = walking at 6 km/h
2	Treadmill	2 2 2 2 2 2 2	16	2 = running at 12 km/h, 2 = walking at 6 km/h
3	Concrete	3 2 3 2 3 2 3 2	20	Intensity 1–2 (*) 3 = running, 2 = walking
4	Concrete	3 2 3 2 3 2 3 2	20	Intensity 2–3 (*) 3 = running, 2 = walking
5	Concrete	Continuous running	16	Intensity 1–2 (*)
6	Concrete	Continuous running	18	Intensity 2–3 (*)

*Intensity 1, running speed: light jogging; Intensity 2, running speed: jogging while able to speak; Intensity 3, running speed: jogging while speaking becomes difficult.

Outcome measure

The number of days from inclusion to completion of phase 6 of the running schedule (full recovery) was used as the primary outcome measure. When a patient did not fully recover according to the graded running programme, the Likert scale was used to assess the status of the patient.¹⁷ Scores varied on a scale from 1 to 6: 1, completely recovered; 2, much improved; 3, somewhat improved; 4, same; 5, worse; and 6, much worse.

Statistical analysis

After blinded, double, data entry, all analyses were carried out using SPSS version 17.0. To compare data between groups and explore for possible confounding factors, χ^2 analysis and analysis of variance (ANOVA) were used. Variables with a significant difference between treatment groups using univariate ANOVA or χ^2 analysis were considered as potential confounders. Their univariate relation with the outcome parameter, 'days to full recovery' was expressed by the (corrected) amount of variance explained using univariate ANOVA in the case of ordinal or nominal confounders, or by means of univariate regression analysis in the case of scale confounders.

All confounders were tested together in a multivariate ANOVA, with scale confounders as covariate and nominal or ordinal confounders as a random factor. All confounders were also tested in interacting with the treatment status. Statistical significance was set at $p \leq 0.05$.

RESULTS

In total, 42 athletes were included in the study. The athletes participated most frequently in recreational running (19.1%) and soccer (13.2%). Other sports that athletes practised were field hockey, tennis, basketball, athletics and dancing. The baseline characteristics of the athletes are shown in table 1.

One patient in the running programme group and two patients in the running programme with focused ESWT did not finish the last phase of the running programme due to persisting symptoms. The patient in the running programme group scored a 3 on the Likert scale (somewhat improved) on quitting the study. In the running programme with ESWT group two patients scored 4 on the Likert scale (same) on quitting the study. In total, 39 athletes finished the running programme.

Time to recovery

In the group of the running programme with ESWT the duration to full recovery was 59.7 (SD 25.8) days. In the group with the running programme only, the duration was 91.6 (SD 43.0) days. The means were significantly different between the

groups ($p=0.008$), with treatment explaining 17.5% of the total variance in the number of days to full recovery.

Multivariate risk factor analysis

Some baseline characteristics were different between the treatment groups: sex ($p=0.029$), age ($p=0.027$), days with symptoms ($p=0.022$) and metres run on a treadmill without pain ($p=0.001$).

Apart from sex ($p=0.039$), no confounder could explain a significant percentage of the variance (corrected R^2) in the number of days to full recovery: age, less than 1%; days with symptoms, less than 1%; metres run on a treadmill without pain, 3%. Women needed more days to complete phase 6 than men: 88.8 days (SD 38.4 days) versus 63.6 days (SD 35.1 days). With treatment used as fixed factor in a multivariate ANOVA on the number of days to full recovery, none of potential confounders mentioned above influenced the outcome parameter 'number of days to full recovery'. The use of ESWT was the only variable that explained the difference between the two groups.

DISCUSSION

This prospective observational controlled study described the time to full recovery for two different treatment protocols. The protocol in which ESWT was added to the running programme showed a significantly quicker recovery. This study is limited as it was observational and no randomisation or blinding was used. There are significant differences in the baseline characteristics between the groups, although on analysis these did not significantly affect the outcome. These results provide support for the hypothesis that the treatment of MTSS with a running programme combined with ESWT may be faster than treatment with a running programme alone.

The results of this study are in keeping with a recently published retrospective trial by Rompe *et al*,¹⁸ who studied the effect of ESWT on MTSS retrospectively. The authors compared this treatment with a control group that performed a home training programme. They found that the group receiving ESWT did recover faster, and more patients recovered than the control group. No studies were found that investigated ESWT for MTSS prospectively.

Other prospective studies on the treatment of MTSS could not find a significant difference comparing different treatment options. Three randomised controlled trials were performed in which the following interventions were investigated: ice massage with ice massage and aspirin, ice massage and fentanyl; ice massage and heel-cord stretching and a walking cast; active laser and placebo laser and a leg orthosis.^{2 19 20} It

should be noted that the studies mentioned had serious methodological shortcomings such as small numbers or the lack of blinding.

ESWT was only used for MTSS in one retrospective study by Rompe *et al.*¹⁸ The ESWT device used in that study was radial. One group was treated with ESWT, while the other group received a home exercise programme (calf stretches, heel raises and toe raises). As a primary outcome measure they used a six-point Likert to assess recovery (1, completely recovered; 6, much worse). They found that after 1, 4 and 15 months the group that was treated with ESWT had significantly better Likert scores ($p < 0.001$). Rompe *et al.*¹⁸ did not structurally report the time to return to sport. They stated that time to return to sport ranged from 6 weeks to 6 months. After 15 months, 85.1% of the athletes treated with ESWT had returned to their preinjury sport, while 46.8% of the athletes in the exercise group had returned to their preinjury sport.

This study did not measure time to return to sport, so a comparison with the study by Rompe *et al.*¹⁸ is difficult. The primary outcome measure in the current study was days to complete a running programme (termed full recovery). This was used to have an outcome measure that was the same for all athletes, regardless of the type of sport and level of sport. The time to full recovery in the running programme with ESWT group was 59.7 (SD 25.8) days. Rompe *et al.*¹⁸ reported that only 64% of their athletes with MTSS treated with ESWT were completely recovered or much improved after 4 months.

The difference in outcome may be explained by the differing outcome measures. In the present study the patients had to complete a running programme, whereas in the study by Rompe *et al.*¹⁸ the patients had to have made a full return to sport, which, for most athletes, would possibly involve more tibial loading than the running programme. The difference between the studies may also possibly be due to the fact that the present study used a focused ESWT instead of the radial ESWT used by Rompe *et al.*¹⁸ One study was found that compared radial and focused shockwave while treating bone.²¹ Differences in microcrack density and microcrack length were found. What these differences mean for clinical practice is not clear. The difference in outcome between our study and the study by Rompe *et al.*¹⁸ could also be explained by the fact that our study added a running programme to the ESWT. Waldorff *et al.*²² showed a significant decrease in microdamage in tibiae over time following weightbearing or intermittent weightbearing compared with limb suspension.

Finally, baseline characteristics for age and duration of symptoms were not the same between this study and the study by Rompe *et al.*¹⁸ This could also have influenced the outcome. However, Moen *et al.*²³ showed that days with symptoms (and metres run on a treadmill without pain) were not prognostic factors to predict time to full recovery.

Several recent studies investigated the impact and consequences of ESWT on cortical bone.^{13 14 24 - 27} Those studies showed an increase in osteoblast activity and an increase in bone matrix deposition *in vitro*.^{26 - 28} Promising clinical results of ESWT on bone healing were found in studies involving humans.^{13 14 24 25}

In this study, at baseline, several baseline characteristics were different between the groups, so these were considered possible confounding factors (age, days with symptoms and metres run without pain on a treadmill and sex). Univariate ANOVA with sex as a random showed only a weak relationship with days to full recovery. This could have possibly influenced the results in this study, because more men were present

What is already known on this topic

- ▶ A retrospective study was conducted before on the treatment of MTSS with shockwave.
- ▶ This study showed that shockwave was a good possible treatment option for MTSS.

What this study adds

- ▶ This study prospectively investigated the effect of shockwave on MTSS and showed promising results.
- ▶ This is the first prospective study on MTSS that was able to find a significant difference on primary outcome measures between two treatment groups.

in the running programme with ESWT group. However, after multivariate ANOVA and χ^2 analysis, no significant relationship was found between these parameters and days to full recovery.

This study has several limitations. First, although the study had a prospective design, it was not a randomised study. This explains the difference in baseline characteristics. With a randomised study the chance of unequal distributions of these characteristics would be lower. The prospective observational design of this study was chosen because of the limited availability of focused shockwave devices and the fact that the pre-existing protocols were well suited to this observational design to assess the possible effect size for future study planning. Also, the control group did not have contact with a physical therapist, whereas the patients in the treatment group did. This could have influenced the time to complete the running programme. The physical therapists who performed the ESWT were instructed to advise the patients as little as possible. However, the treatment in itself could have led to a placebo effect. In the future blinding would help eliminate this shortcoming.

Another limitation of the study is its relatively small number of participants. However, even with the limited numbers of participating athletes a significant difference between the two treatment groups was found. This allows for a good estimation of effect size of the treatment, which can now serve to perform a good power analysis for designing a randomised, blinded trial.

CONCLUSION

The time to full recovery in athletes with MTSS with a running programme and focused ESWT was significantly ($p = 0.008$) faster in the running programme and ESWT group (59.7 days (SD 25.8) and 91.6 days (SD 43.0), respectively). These results from this study provide a base for further research of the treatment of MTSS with ESWT combined with a running programme for the treatment for MTSS in a prospective, randomised, blinded study.

Acknowledgements The authors would like to thank Eric Bakker, from the Department of Clinical Epidemiology, Biostatistics and Bioinformatics, for his contributions to the article.

Competing interests None.

Patient consent Obtained.

Ethics approval This study was conducted with the approval of the Medical Ethical Committee South West Holland.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. **Clanton TO**, Solcher BW. Chronic leg pain in the athlete. *Clin Sports Med* 1994;**13**:743–59.
2. **Andrish JT**, Bergfeld JA, Walheim J. A prospective study on the management of shin splints. *J Bone Joint Surg Am* 1974;**56**:1697–700.
3. **Bennett JE**, Reinking MF, Pluemer B, *et al*. Factors contributing to the development of medial tibial stress syndrome in high school runners. *J Orthop Sports Phys Ther* 2001;**31**:504–10.
4. **Yates B**, White S. The incidence and risk factors in the development of medial tibial stress syndrome among naval recruits. *Am J Sports Med* 2004;**32**:772–80.
5. **Detmer DE**. Chronic shin splints. Classification and management of medial tibial stress syndrome. *Sports Med* 1986;**3**:436–46.
6. **Kortebein PM**, Kaufman KR, Basford JR, *et al*. Medial tibial stress syndrome. *Med Sci Sports Exerc* 2000;**32**:S27–33.
7. **Saxena A**, O'Brien T, Bunce D. Anatomic dissection of the tibialis posterior muscle and its correlation to medial tibial stress syndrome. *J Foot Surg* 1990;**29**:105–8.
8. **Beck BR**. Tibial stress injuries. An aetiological review for the purposes of guiding management. *Sports Med* 1998;**26**:265–79.
9. **Moen MH**, Tol JL, Weir A, *et al*. Medial tibial stress syndrome: a critical review. *Sports Med* 2009;**39**:523–46.
10. **Gaeta M**, Minutoli F, Vinci S, *et al*. High-resolution CT grading of tibial stress reactions in distance runners. *AJR Am J Roentgenol* 2006;**187**:789–93.
11. **Magnusson HI**, Westlin NE, Nyqvist F, *et al*. Abnormally decreased regional bone density in athletes with medial tibial stress syndrome. *Am J Sports Med* 2001;**29**:712–15.
12. **Magnusson HI**, Ahlberg HG, Karlsson C, *et al*. Low regional tibial bone density in athletes with medial tibial stress syndrome normalizes after recovery from symptoms. *Am J Sports Med* 2003;**31**:596–600.
13. **Taki M**, Iwata O, Shiono M, *et al*. Extracorporeal shock wave therapy for resistant stress fracture in athletes: a report of 5 cases. *Am J Sports Med* 2007;**35**:1188–92.
14. **Wang L**, Qin L, Lu HB, *et al*. Extracorporeal shock wave therapy in treatment of delayed bone-tendon healing. *Am J Sports Med* 2008;**36**:340–7.
15. World Medical Association Declaration of Helsinki 2008. 59th General Medical Assembly. Seoul: World Medical Association Declaration of Helsinki, 2008.
16. **Moen MH**, Bongers T, Bakker EW, *et al*. The additional value of a pneumatic leg brace in the treatment of recruits with medial tibial stress syndrome; a randomized study. *J R Army Med Corps* 2010;**156**:236–40.
17. **Likert R**. A technique for the measurement of attitudes. *Arch Psychol* 1934;**22**:1–55.
18. **Rompe JD**, Cacchio A, Furia JP, *et al*. Low-energy extracorporeal shock wave therapy as a treatment for medial tibial stress syndrome. *Am J Sports Med* 2010;**38**:125–32.
19. **Nissen LR**, Astvad K, Madsen L. [Low-energy laser therapy in medial tibial stress syndrome]. *Ugeskr Laeg* 1994;**156**:7329–31.
20. **Johnston E**, Flynn T, Bean M, *et al*. A randomized controlled trial of a leg orthosis versus traditional treatment for soldiers with shin splints: a pilot study. *Mil Med* 2006;**171**:40–4.
21. **Da Costa Gómez TM**, Radtke CL, Kalscheur VL, *et al*. Effect of focused and radial extracorporeal shock wave therapy on equine bone microdamage. *Vet Surg* 2004;**33**:49–55.
22. **Waldorff EI**, Christenson KB, Cooney LA, *et al*. Microdamage repair and remodeling requires mechanical loading. *J Bone Miner Res* 2010;**25**:734–45.
23. **Moen MH**, Bongers T, Bakker EW, *et al*. Risk factors and prognostic indicators for medial tibial stress syndrome. *Scand J Med Sci Sports* 2010; Jun 18. [Epub ahead of print].
24. **Elster EA**, Stojadinovic A, Forsberg J, *et al*. Extracorporeal shock wave therapy for nonunion of the tibia. *J Orthop Trauma* 2010;**24**:133–41.
25. **Furia JP**, Juliano PJ, Wade AM, *et al*. Shock wave therapy compared with intramedullary screw fixation for nonunion of proximal fifth metatarsal metaphyseal–diaphyseal fractures. *J Bone Joint Surg Am* 2010;**92**:846–54.
26. **Martini L**, Giavaresi G, Fini M, *et al*. Effect of extracorporeal shock wave therapy on osteoblastlike cells. *Clin Orthop Relat Res* 2003;**413**:269–80.
27. **Wang FS**, Wang CJ, Chen YJ, *et al*. Ras induction of superoxide activates ERK-dependent angiogenic transcription factor HIF-1alpha and VEGF-A expression in shock wave-stimulated osteoblasts. *J Biol Chem* 2004;**279**:10331–7.
28. **Tamma R**, dell'Endice S, Notarnicola A, *et al*. Extracorporeal shock waves stimulate osteoblast activities. *Ultrasound Med Biol* 2009;**35**:2093–100.



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Br J Sports Med 2012 46: 253-257 originally published online March 9, 2011

doi: 10.1136/bjasm.2010.081992

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