



Review

Current concepts of shockwave therapy in stress fractures

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HIGHLIGHTS

- Extracorporeal shockwave treatments (ESWT) stimulate bone turnover and neovascularization in delayed unions and avascular necrosis.
- ESWT is a safe and effective non-invasive outpatient procedure.
- Medium and high energy focused ESWT has shown excellent results in treating stress fractures, with faster return to competition and athletic activity.

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ABSTRACT

Stress fractures are common painful conditions in athletes, usually associated to biomechanical overloads. Low risk stress fractures usually respond well to conservative treatments, but up to one third of the athletes may not respond, and evolve into high-risk stress fractures. Surgical stabilization may be the final treatment, but it is a highly invasive procedure with known complications. Shockwave treatments (ESWT), based upon the stimulation of bone turnover, osteoblast stimulation and neovascularization by mechanotransduction, have been successfully used to treat delayed unions and avascular necrosis. Since 1999 it has also been proposed in the treatment of stress fractures with excellent results and no complications. We have used focused shockwave treatments in professional athletes and military personnel with a high rate of recovery, return to competition and pain control. We present the current concepts of shockwave treatments for stress fractures, and recommend it as the primary standard of care in low risk patients with poor response to conventional treatments.

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1. Introduction

Bone is a very specialized dynamic organ that forms the primary structural element of the human body. It is the solid base of the muscle-joint-bone complex and has the unique characteristic, as an engineering material, of changing form, geometry and physical properties according to mechanical demands. This process has been referred to as mechanical homeostasis, a complex biological response to physical loads that rule not only fracture healing but also bone geometry and even the evolution of species.

Bone remodeling is an essential biological process as old as the bone itself [47]. The fossil records show that the skeletons of the earliest weight bearing vertebrates contained osteonal structures

and other evidence of coordinated bone resorption and formation. This process has been essential for a healthy functional skeleton for millions of years. Probably the genes that enable bone remodeling have been continued to be selected because they confer important survival advantages.

The function of bone remodeling has been debated for centuries. The vision of the anatomists and histologist of the 19th century was that the Osteon structure is a nearly perfect mechanical and biological complex and it definitely serves a mechanical function. When the discovery that calcium serum levels must be regulated to prevent muscle tetany the story changed, and the metabolic significance of calcium brought the concept of bone remodeling as a metabolic process. Both visions are correct, meaning the importance of the process of bone remodeling nowadays. But the system is not perfect, because it fails in certain conditions. Microdamage is a biological form of fatigue, creep or other accumulative mechanical processes by which the microstructure of a loaded material is

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permanently altered.

Stress fractures are similar to fatigue failures in engineering materials in a sense that are due to a relatively large number of repetitions, which if applied once, do not cause failure. Microdamage ranges from microcracks to diffuse damage, cross-hatching and finally microfractures, depending on the amount of energy, the accumulative fatigue stress, and the mechanical resistance of bone as a material.

The importance of bone remodeling must be emphasized, because microdamage is increased by fatigue loading at physiological strains. Such damage is a normal consequence of skeletal function, thus, microdamage can only be removed from bone by means of resorption and replacement of bone tissue through remodeling [68]. This process is done by the activation of Bone Multicellular units, both randomly to control calcium homeostasis, and targeted to control specific microdamage areas [14,65,66].

This means that if we inhibit the remodeling process we could increase the risk for microdamage. On the other side, if repetitive cyclic loading of bone is excessive, then Fatigue overuse on bone that accumulates more stress than BMU activation will cause microdamage.

The way we study bone as a material is applying known loads to specific areas and recording the mechanical behavior of the material. The elasticity modulus is determined, as well as the yield point and the ultimate failure point. To study fracture risk we simply go beyond the failure point and that way we can determine variations between specimens. For Stress fractures we need to repetitively load the bone with energies lower than the yield point. This energy applied once has no significance, but the accumulative loads will fracture the bone in certain areas.

If we compare the amount of stress needed to fracture a bone, it is clear that a great amount of stress is required to start a bone fracture and very little to finish the job. However, deformation is almost the same, which means that the material becomes more plastic after the initial failure point. The energy required to initiate the fracture is represented in the stress–strain graph by the areas under the curve.

These has been deeply studied by Keaveny and Hayes [45,46], and stress fractures are in the range of the pre yield or linear region, with small amounts of energy loaded in cycles that cause microfractures as a response of misbalanced bone remodeling.

Bone is especially weak under transverse and tensional loads. This means that insertional, or traction forces applied in cycles to bone could result in higher fracture risk. Also tensional areas of normal bone loaded repetitively could represent a higher fracture risk.

Taylor [82] proved how the medial tibia is one of the most vulnerable areas in the skeleton, as a result of the tibial shaft curves, the asymmetric mechanical loads in normal gait and exercise, and it's poor vascularity. He proposed a mathematical model that gives a guide for prediction of stress fractures under certain exercise conditions, time and age.

Repetitive cyclic loading of bones is the most relevant etiologic factor in the genesis of stress fractures. The fine balance between Bone Microdamage & Remodeling marks the outcome of bone failure under repetitive loading conditions [18]. The three possible scenarios for bone failure under fatigue loading are: normal bone & abnormal loading – normal loading & abnormal bone and abnormal loading on abnormal bone. The most common bones affected are tibia, metatarsals, fibula, navicular, pelvis and femur [10,59].

2. Diagnosis and classification

The first cases of stress fractures were described by Breithaupt in

Prussian Soldiers with leg pain in the war of 1850 [28]. The global incidence ranges from 1% to 20% depending on the physical activities of the patients [28]. They usually appear as a progressive localized bone pain after physical activity or sports [43]. Symptoms usually disappear with rest and have short recovery periods. The etiology of stress fractures is a biomechanical misbalance of loads that result in a progressive breakage of the gait kinetic chain [63]. This is very relevant in athletes and military personnel that repetitively overload under-trained skeletons and cause unbalanced bone remodeling resulting in bone failure [43]. Clinical diagnosis is relatively easy with physical examination that shows pain at a pin pressure point that may or not be associated to swelling. There is pain when eccentric loads are applied to the muscles inserted on the affected bone, and specific tests have been described for stress fractures such as the hyperextension, the fulcrum or the hop tests [95].

Stress fractures are classified upon the risk of a complete bone failure, as low, medium or high risk [13,16,64]. Frederickson [29,30] described an image-based classification using both X rays and MRI, associating recovery time with four stages of bone damage. It is especially valuable to determine prognosis. Low risk stress fractures usually respond to conservative treatments, while high risk fractures usually require surgical procedures in order to prevent a complete fracture. Up to one third of low risk stress fractures may not respond to conventional treatments and continue with pain during exercise [30,50,77]. They may evolve into high-risk stress fractures if load conditions and bone turnover is not balanced. It is a primary goal of the sports medicine and orthopedic specialists to prevent the progression of a low risk stress fracture.

Diagnostic images are mandatory in order to determine staging [64]. The first reports of a radiological classification of stress fractures was done by Savoca [76] in 1971, and he correlated clinical symptoms with early metaphyseal sclerosis, periosteal reaction or partial fractures. Magnetic resonance images are the best tool to determine bone marrow edema, periosteal reaction and soft tissue damages in all stages of stress fractures [22]. Bone scans are very sensitive to determine increased bone turnover areas in early stages, but it is not very specific as many other situations may mark as false positive, and is an invasive procedure with potential risks [52,71]. (Fig 1). However, in early stages it is the most specific and sensitive test available, as radiographic findings only appear after three weeks of the initial microfracture [27,79].

3. Treatment

Treatment of stress fractures is based on a mechanical and a

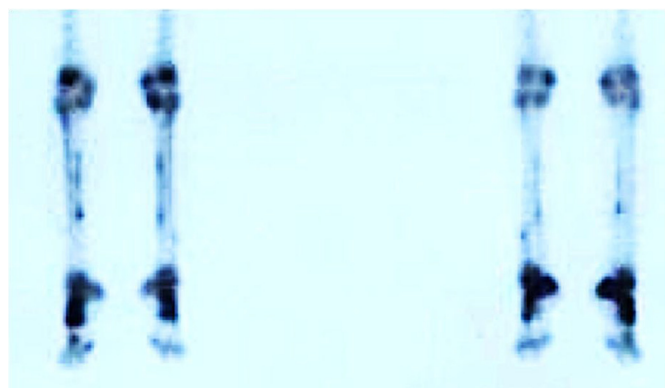


Fig. 1. Bone scans of tibial stress fractures in a high performance athlete. This is the most specific and sensitive test for stress fracture diagnosis. X Rays do not show early changes. Bone scans may remain positive after the patient has recovered from treatments and is painful.

biological approach [72]. Load control on the mechanical side is the basic treatment, in order to allow the biological bone turnover to recover the stressed area. In patients with localized bone pain and a history of mechanical stress, a diagnosis with x rays, bone scans and MRI will confirm the diagnosis. All accepted treatment protocols include as a gold standard a progressive retraining and physical therapy that goes from total rest to sprint running and specific agility drills. This requires a program of load controls and rest that allows the biological process to beat the mechanical overloads. Patients are directed onto risk factor control, both intrinsic and extrinsic. There is a higher risk in Caucasians, as well as in women with nutritional menstrual disorders. (Stress fracture risks are more related to inadequate training and exercise programs [31,44,54].

This is a long process that may take as much as 3–6 months. This is usually too long for a professional athlete, so most of non-surgical treatments are focused on reducing the recovery time. The most common form of treatment with physical therapy is a two-stage protocol [36,53]. The first stage is based on rest and pain control, while the second is focused on muscle balance and strength, balance, proprioception, flexibility and progressive sports specific retraining [40,48,53].

The use of electromagnetic fields and low energy pulsed ultrasound was promising two decades ago, but failed in improving stress fracture healing in time. Most of the studies are focused on the treatment of delayed unions [9,15,19,73].

In many cases stress fractures fail to heal [21]. In these cases, surgical procedures have been indicated in order to stabilize the fracture and reduce the risk of an unstable complete fracture [84]. In some patients the choice of a surgical procedure has been the first option, especially in high performance athletes that require assurance of recovery and are under pressure of professional teams. The truth is that no low-risk stress fracture should progress into a high-risk complete fracture, and our focus as specialists is to prevent this progression. This also means stress fractures should not evolve into a point of requiring a surgical stabilization. Surgery is not a simple procedure, and usually requires an invasive protocol with internal fixation, grafting and a long recovery time, with known and well reported complications [21,96,97,99]. There are more reports on surgery and their complications than studies that support improving the healing process and the bone turnover on stress fractures.

4. Shockwave treatments and stress fractures

Extracorporeal Shockwave Treatment (ESWT) is a relatively new approach in the treatment of stress fractures [32]. It has been widely used in orthopedics and sports medicine [55,78,86], initially in Europe in the late 80's as a musculoskeletal application of high energy focalized ultrasound shockwaves, based upon the principles that were used clinically in urology for the implosion of kidney stones [69].

Physics studies have revealed that the differences in acoustic resistance of materials exposed to high energy sound waves may create failures. This was studied initially in aviation engineering, and applied in medicine to obtain biological responses in different areas. The physical properties of acoustic shockwaves are widely known and can be readily validated, as well as the characterization of the shockwave itself, being a high-energy ultrasound single pulse [33]. The main difference between a sound wave and a shockwave is speed: a regular sound wave travels slower than the speed of sound, whereas a shockwave travels faster than the speed of sound, creating an energy front that can be controlled in magnitude and direction. The effects of shockwaves on biologic tissues come from both a direct impact and a cavitation process [5].

The biological effects of shockwave application have been studied deeply in the past 20 years. Rompe, Wang, D'Agostino, Caccio and Schaden [20,25,74,75,77,86,88,91,92], have published basic and clinical studies that prove that shockwaves increase the endogenous production of Growth Factors, NO's and free radicals that result in an increased healing process [3,24,93,94]. Specifically in bone, there is a clear effect in neovascularization, periosteal stimulation, and osteo-induction [57,58,80]. This final outcome is useful in the treatment of delayed unions, avascular necrosis and stress fractures.

There is a global consensus about the influence of mechano-transduction in bone turnover, with clinical use in bone delayed unions [38,42,77,83,87,98]. Using high-energy shockwaves, there is a clear stimulation of vascularity, as well as osteoblast differentiation from mesenchymal stem cells and inactive cells [2,23,60–62]. There is also a clear effect on periosteal cells that contribute to cell migration and the development of callus in healing impaired bone [8,17,35,67]. The clinical use in delayed bone fracture healing [11,12,70,85], and in avascular necrosis [4,26,37,56,89,90] has grown both experimentally and in clinical use in the past decade.

Until now, there are no blinded randomized control trials that can prove with level-one evidence the benefits of ESWT and recommend it as the first choice of treatment. In Austria, shockwave therapy is the first treatment of choice of delayed bone unions, but still it's use in stress fractures requires more evidence. However it's use is biologically logical, has no complications and the case reports have been encouraging [32].

Hotzinger [41] reported the first case of stress fractures treated with ESWT at the ISMST meeting in London in 1999. He studied the role of MRI in the diagnosis of multiple stress fractures of the tibia, and treated a case with high-energy shockwaves with good results. After this first case report, we were the first group to run a clinical study on ESWT and stress fractures [49–51]. We performed an Experimental, Randomized, Single Blinded, Self Controlled Clinical Study with twenty six 18 year old navy cadets with identical bilateral tibial stress fractures in 2001 [39,51]. They were all symptomatic for more than three months and responding poorly to conventional treatment. We evaluated a visual analog pain scale in four conditions: rest, sports, after sports and pressure. We followed them for a year, and kept the Physical therapy protocol, and evaluated also x rays, bone scans and nutritional conditions.

In the most symptomatic tibia we applied 2000 focused shockwaves in two sessions one week apart, at medium–high range energy of 0.1–0.27 mJ/mm². The treated tibias had less pain in all clinical situations, earlier than the control tibias. Both treated and control tibias were pain free after 12 months, but pain was significantly lower in shockwave treated tibias in periods as short as three weeks, both during physical activity, rest, after sports and pressure testing. We did not find major changes in bone scans, and X rays were significantly similar. We concluded that ESWT significantly reduced pain and recovery time in high performance athletes with tibial stress fractures [49,50].

There are several case reports and series with encouraging results of ESWT in stress fractures. Audain [6,7] and Gordon [34] have reported several cases of high performance athletes with good results in pain control and return to competition. Abello and Leal [1] also reported a good outcome in treating a foot navicular bone stress fracture in an Olympic gymnast. Taki [81] studied five athletes with stress fractures that did not respond to conventional treatments in 2007. He used a very high energy of 0.29–0.40 mJ/mm², 2000–4000 shots in one session, and was able to significantly reduce the recovery time to 3–6 months. These results are similar to our findings. Moretti [65,66] reported in 2009 the results of treating 10 high performance athletes with stress fractures of tibias or metatarsals, with 3–4 sessions of mid energy ESWT. Their

protocol used 4000 shockwaves of 0.09–0.17 mJ/mm². They obtained a 100% healing rate at 8 weeks post treatment, and all patients returned to competition levels.

All protocols reported have used focused mid and high-energy shockwave devices. (Fig 2). The use of radial or pressure waves have been very successful in treating tendinopathies, but they do not have evidence in the current literature for the treatment of stress fractures. Applying shockwaves on a painful bone usually require sedation or anesthesia, and the best results are obtained with high-energy shockwave generators. Most authors have used the same devices and protocols approved for bone healing in the treatment of delayed unions. The general consensus and the best results have been obtained using one or two sessions of minimum 2000 shockwaves of 0.2 mJ/mm² with a focused device over the fracture site.

5. Conclusion

Stress fractures are common causes of pain in athletes with overuse syndromes. Low risk and early stages are usually responsive to physical therapy, medication and load control. High-risk stress fractures may not respond to conservative treatments and may even require surgical stabilization. Stopping the progression to a high risk fracture is part of the treatment protocols of this medical condition. Shockwave treatments have proven success with a high rate of efficacy and safety, as an extracorporeal non-invasive procedure with minimal complications.

Mechanical stimulation by extracorporeal shockwaves has proven to stimulate proliferation, migration and activation of osteoblasts [60,61]. We know that high energy focused ultrasound

induces nitric oxide liberation in bone cells [3] and stimulates osteogenesis through core binding factors [100].

There is a direct effect of mechanotransduction in bone gene expression, and neovascularization that have been used in delayed unions, avascular necrosis and osteochondritis dissecans. The use of this technology for stress fractures is simple and biologically logical. More controlled studies are required, but the present literature of case series and expert reports, based upon a serious solid basic science background, marks a research path with high efficiency and safety, and certainly with a clear future in the treatment of stress fractures in sports medicine.

Conflict of interest

The authors do not have any conflict of interests for the publication of the paper *Current Concepts of Shockwave Therapy in Stress Fractures*.

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Author contribution

Prof Dr Carlos Leal MD is the principal author. Cristina D'Agostino, Santiago Gomez-Garcia and Arnold Fernandez participated as collaborators and coauthors.

Guarantor

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Fig. 2. The treatment is done placing the ESWT unit over the stress fracture area. The use of membrane applicators with focused energy has the better results. The treatment area is marked previously under X-rays.

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