Review Over the Therapeutic Benefit of Extracorporeal Shockwave Therapy in Orthopaedic Patients

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Abstract

Shockwaves can be defined as transient pressure oscillations which propagate in three dimensions and offer an increased pressure in a very short period of time. Biological effects of shockwave therapy have been proven to stimulate the release of angiogenic growth factors, and contribute to the improvement of blood supply which leads to the repair of bone and soft tissue. The role of ESWT in the treatment of chronic calcifying tendinitis of the rotator cuff has been evaluated in many studies. ESWT has been gaining attention as an alternative option to surgical excision of calcification or when other conservative options have not proven efficient. The main purpose for using ESWT in heel spur is to increase the local blood supply by inducing neovascularisation. This action influences the inflammatory process and furthermore stimulates the local metabolism. Also, shockwaves have been proposed as a possible treatment in early phases of femoral head necrosis in adults. In case of patellar tendinopathy in vitro studies have shown biological effects, while clinical effects remain unclear. Data suggests that ESWT associated with other physical modalities achieve realiable clinical importance of pain reduction in lateral epycondylitis. However there is still a lack of standardisation and a consensus is needed regarding frequency and intensity.

Keywords: shockwave, rehabilitation, orthopaedics.

Rezumat

Undele de șoc pot fi definite drept oscilații de presiune tranzitorii ce se propagă tridimensional și oferă o presiune mărită într-o durată scurtă de timp. Principalele efecte biologice se referă la stimularea eliberării de factori angiogenici și influențarea influxului sanguin ce conduce la repararea țesutului osos și a țesuturilor moi periarticulare. Rolul ESWT în tratamentul proceselor de calciﬁcare dezvoltate la nivelul umărului a fost evaluat în numeroase studii. ESWT poate reprezenta o alternativă terapeutică la soluțiile chirurgicale sau atunci când alte opțiuni de tip conservator nu s-au dovedit a fi eficiente. Principalul motiv pentru utilizarea ESWT în patologia plantară este acela de a crește aportul sanguin local prin inducerea neovascularizației. Această acțiune afectează procesul inflamator și stimulează în același timp metabolismul local. De asemenea, tratamentul ESWT a fost propus în fazele incipiente ale necrozei aseptice de cap femural. În cazul tendinitei patelare, studiile in vitro au demonstrat efecte biologice, în timp ce efectele clinice rămân neclare. Datele din literatură sugerează că asocierea ESWT cu alte modificări fizice prezintă un impact clinic semnificativ în cazul epicondilitiei latere. Cu toate acestea, există încă o lipsă de standarizare și este necesar un consens privind frecvența și intensitatea.

Cuvinte cheie: ESWT, recuperare medicală, patologie ortopedică.
Shockwaves can be defined as transient pressure oscillations which propagate in three dimensions and offer an increased pressure in a very short period of time, typically in a matter of a few nanoseconds\(^\text{1,2}\). Their main characteristics are represented by positive (P\(\text{O}\)) and negative (P\(-\)) peak pressure, rise time (Tr) and impulsive width (Tw). The principles of shockwave application refer to the propagation of waves through tissue such as water, gas or inside solid state bodies, pressure pulses acting directly or indirectly regardless of the generating source\(^\text{3,4}\).

The first use of ESWT on the musculoskeletal system was made by Karpman et al. in an attempt to desintegrate the surrounding bone cement in patients scheduled for endoprosthesis replacement on the hip joint\(^\text{5}\). He was then followed by Valchanou et al. who applied shockwave therapy in pseudoarthrosis in the possibility of fragmenting the bone tissue\(^\text{6}\). It was further noticed an improvement in pain and functional levels from the application of ESWT for different chronic insertion enthesiopathies. Analgesic effect of ESWT was believed to be caused by overstimulation of the treated area which resulted in a reduction of signal transmission to the central nervous system. Although there weren't significant prospective studies, the number of ESWT applications had an extensive growth in the nineties decade, even surpassing the number of applications used in urology for lithotripsy\(^\text{7-9}\).

The main categories of shockwaves refer to focused shockwave therapy which involves single pressure pulses focused on a specific target and are generated in water inside the device, and radial shockwaves which are produced by acceleration of a projectile with the use of compressed air\(^\text{10,11}\). From a physical point of view the typical form of the shockwave is characterised by a very short ascent until the maximum pressure results from asymmetric attenuation when traveling through tissue\(^\text{12}\). Also, the biological effects of shockwave therapy tend to stimulate the release of angiogenic growth factors, and contribute to the improvement of blood supply which leads to the repair of bone and soft tissue\(^\text{13}\). Molecular effects of shockwaves have been observed in experimental models, especially regarding the release of substance P and prostaglandin E2 which can be responsible for the biological actions of ESWT. An indirect effect is the induction of cavitation, which is expressed as the appearance of gas filled bubbles in the presence of a negative pressure gradient\(^\text{14,15}\).

It has been observed that ESWT can lead to the development of histological changes in the applied area, the effects being partially dose dependent. Focal infiltration of the inflammation occurs at the skin level, and focal necrosis of the muscle fiber associated with inflammatory reaction has been observed, but with complete disappearance in time\(^\text{16,17}\). Also, osteoneogenesis has been observed depending on dose in case of high energy application, but with no effect in case of low energy application\(^\text{18-20}\). Due to these changes, induced by the physical and biological properties of shockwaves, the present review proposes the analysis of ESWT impact in different musculoskeletal disorders.

**BACKGROUND**

**MATERIAL AND METHODS**

A systematic review was conducted with the purpose of collecting potentially eligible publications, accessing the electronic databases available PubMed, Embase, and Cochrane library using the following terms: shock wave/shockwave, ESWT, plantar fasciitis, lateral epicondyritis, calcifying tendinitis, calcifying tendinitis, shoulder, avascular necrosis, tendinopathy, insertional. The searches were limited to articles in English. Additional studies were searched using the reference list of the chosen articles.

**RESULTS AND DISCUSSIONS**

The assessment of search results evidenced a significant amount of eligible studies, but also a variation in application methodology and number of sessions. The role of ESWT in treatment of chronic calcifying tendinitis of the rotator cuff has been evaluated in many studies\(^\text{21-27}\). Calcifying tendinitis is a frequent condition in orthopaedic and rehabilitation practice and represents a well documented cause for shoulder pain. It is characterised by the deposit of calcium hydroxyapatite crystals inside rotator cuff tendons\(^\text{28,29}\). ESWT has been gaining attention as an alternative option to surgical excision of calcification or when other conservative options have not proven efficient. Some studies have suggested the use of ESWT in athletes with refractory tendinitis as a preintervention therapy before arthroscopic surgery. Favorable results have also been observed for treatment of superior lateral brachial cutaneous nerve compression syndrome (SLBCN). Pan et al. observe an alleviation of pain intensity and an improvement of shoulder joint function in patients with SLBCN compared to the control group which received homone injection\(^\text{31}\). Kluter et al. analyses the associated effect of ESWT with electromagnetic transduction therapy (EMTT)
for rotator cuff tendinopathy on 86 patients and express a clinically relevant decrease of pain and higher Constant Murley scores compared to control group at baseline and follow-up period\textsuperscript{32}.

Plantar heel pain represents one of the most frequently met disorders of the foot region, well-documented in the literature, but without obtaining a uniform diagnosis, mostly because the background pathways are still unclear\textsuperscript{13,34}. Today, the term „painful heel” is used by many authors, as well as „heel spur”, although the condition is not always clearly evidenced by x rays. „Fasciitis plantaris” is a term that refers to an inflammatory status of the plantar fascia in the proximity of the calcaneal insertion\textsuperscript{35,36}. Main symptoms include pain, associated with decreased range of motion. A number of conservative treatments have been outlined, including physical therapy with low energy laser, ultrasound and iontophoresis associated with pharmacological treatment or steroid injections, but without clear evidence of their efficacy\textsuperscript{37-40}.

The main purpose for using ESWT is to increase the local blood supply by inducing neovascularisation. This action affects the inflammatory process and furthermore stimulates the local metabolism. In a meta-analysis on 9 studies and 935 patients on the use of shockwave therapy in chronic plantar fasciitis, the authors observed that ESWT groups had higher improvement rates than placebo groups (OR 2.58, 95% [CI] 1.97–3.39, \textit{p}< .001)\textsuperscript{41-43}. Another discussion regards the number of sessions that are needed for heel spur. Most protocols involve 4 to 5 sessions, but there are trials that evaluated the effect of a single session of ESWT in plantar fasciitis. Scheuer et al. performed an observational study on 284 patients (363 feet) that received ESWT and were required to complete a clinical questionnaire immediately after ESWT administration and after 19-77 weeks of follow-up. 76% of patients from the group that was treated with only 1 session expressed satisfying pain relief. Although the authors suggested that a single session of ESWT could offer similar outcomes as multiple sessions, further data is needed to establish the suitable number of treatment sessions as well as the adequate energy flux density that is required to increase the effectiveness of the treatment\textsuperscript{44}.

A systematic analysis by Roerdink et al. on the possible complications that can result from plantar application, reviewed 39 studies and 2697 heels and observed that no complications are to be expected until one year post treatment. However there isn’t any reliable data on long term complications, therefore some precautions are recommended. Also, in some cases transient pain after application, swelling and throbbing sensation were reported\textsuperscript{45}.

Shockwaves have been proposed as a possible treatment in early phases of femoral head necrosis in adults. From a morphopathological point of view, osteonecrotic lesions usually have similar patterns. Most frequently, it involves an underlying circulatory disorder, which is associated with bone cell destruction due to insufficient oxygen supply and malnutrition. Until now, no gold standard has been developed and treatment options are still in debate\textsuperscript{56-59}.

Conservative approaches include only measures that are designed to reduce the symptomatology without interrupting the progress of the disease. Shockwaves are documented to stimulate bone regeneration, and it has been suggested that it may also induce specific signals for growth and maturation of the mesenchymal progenitors of the bone marrow. At the same time, shockwaves produce increased concentrations of free radicals\textsuperscript{51-55}. A link has been detected between morphogenic proteins (BMP) and shockwave activity regarding bone regeneration. Literature data evidences that fact that ESWT can increase the expression of BMP in calus during fracture healing. However, precautions should be given, especially because in high doses it can create an imbalance in calcium homeostasis which can lead to tissue damage\textsuperscript{56-57}. In some case reports Durst et al. express the development of humeral head osteonecrosis, 3 years after the administration of high energy ESWT for calcific tendinitis, while Liu et al report a case of humeral head osteonecrosis in 3 month after receiving ESWT. Although these are isolated cases, it has been suggested that a diminished diameter of the anterior humeral circumflex artery in these two cases could explain for the development of complications\textsuperscript{58,59}.

In a systematic review by Zhang et al, with a total of 17 articles including 6 RCT, 2 cohorts, 9 open label trials and 2 case reports, the authors observed an improvement in motor function and pain relief in case of ESWT use for osteonecrosis of the femoral head. Although the imagistics evidenced a reduction of bone marrow edema, the evolution of bone necrosis could not be stopped after ESWT. Also, the association of other conservative treatments with shockwave therapy did not influence the final effect\textsuperscript{60}. However ESWT could offer some benefit in case of hip endoprosthesis decision, granting better bone conditions for the surgeon and a higher bone mass density.
Mackert et al. (2017) study the effect of low energy ESWT on metaphyseal fracture healing in osteoporotic rat models, and observe promising effects including an improvement of the biomechanical characteristics, enhanced callus quantity and quality and a modified expression of bone specific transcription factors. This could prove beneficial, especially because osteoporotic fractures present a severely diminished bone quality, which often requires surgical fixation. Nonetheless, diminished bone mass density contributes to prolonged healing periods and increases the risk of instability and complication rates. Therefore, ESWT could present as an alternative treatment option, with minimal side-effects compared to surgical or pharmacological modalities.

In case of epycondylitis humeri radialis or „tennis elbow”, there are numerous conservative options that are proposed as main therapeutic option, surgical interventions being indicated only in a small number of refractory cases. ESWT has been recommended as viable treatment option for these patients. However, a recent meta-analysis evidenced differences between the groups the received shockwave therapy and placebo group but not in a significant manner. On the other side, the group that received ESWT along with other physical modalities reached a reliable clinical significance of pain reduction.

ESWT role has been evaluated in sport pathologies such as patella syndrome and tibial anterior syndrome.

Patella syndrome or „jumper’s knee” represents a typical insertion tendinopathy, frequently caused by repetitive jumps. The syndrome is characterised by microruptures at the tendon to bone junction and is associated with fibrinoid necroses and mucoid degeneration. Van der Worp et al. (2012) perform a systematic review in order to identify randomized controlled trials that studied the effectiveness of ESWT for patellar tendinopathy. It was observed from the analysis that in vitro studies show biological effects, while clinical effects remain unclear. The conflicting data is however determined by multiple reasons. The first reason is the absence of a gold standard for the diagnosis of a tendinopathy. Secondly, shockwaves are more effective in some stages of evolution compared to other stages, and lastly the effectiveness is influenced by the methodological aspects which include the number of pulses, intensity and focal depth. In a systematic review by Haake et al. with the inclusion of 20 eligible studies, it was observed a variation of treatment sessions from 1 to 20 and also a disconcordance of the number of impulses that varied from 500 to 2500. Tibial anterior syndrome is often triggered by sudden load peaks and intensive running and consists of pain localised in the middel and lower third of the tibialis anterior, representing the third most common sports injury after achillodynia and stress fracture. By some authors, ESWT is proven more effective than traditional conservative treatments including nonsteroidal anti-inflammatory medication, standard physiotherapy program, kinesitherapy or, and the use of a knee strap.

Analysis of ESWT outcomes for painful stump neuroma has been documented in the literature. Jung et al. randomize thirty patients with stump neuroma at the distal end of an amputation site into two groups. One group benefited from ESWT at the area of the neuroma site which was identified using ultrasound guidance, and the second group benefited from transcutaneous electrical nerve stimulation and pharmacological treatment. Changes in McGill pain questionnaire were observed, but no significant changes in size or pressure threshold. However, the study demonstrated that the application of ESWT could reduce the side effects generated through injection therapies and surgical treatments.

Greater trochanteric pain syndrome (GTPS) represents a clinical condition which includes pain and tenderness around the greater trochanter area, which can radiate to the lateral side of the hip or thigh and is generally associated with trochanteric bursitis, but literature also suggests a degeneration process or a tearing of the gluteal tendons. Conservative treatment consists of medication, rest, physical therapy or corticosteroid injections. Surgical treatment with the lengthening of iliotibial band and fascia is considered only in refractory cases. Seo et al. investigate with the use of MRI the outcome of ESWT in GTPS patients and obtain succesful rates of pain reduction over long term follow up.

Other studies have tried to evaluate effectiveness of acupuncture compared to ESWT, resulting in favorable data for both treatments regarding pain relief. Also, the authors found no significant improvement of DASH score and maximum grip strength for both shockwave therapy and acupuncture. However the study had certain bias issues, including a relatively small sample of patients and also the fact that most enrolled patients reported to have applied massage therapy by themselves during the treatment period which could have lead to an underestimation of therapeutic effect in the stu-
died groups. The statement is correlated with a meta-
analysis by Biset et al.\textsuperscript{82} that reflected a positive effect
of manipulative massage on lateral epicondylitis\textsuperscript{83}.

Other indications of ESWT have been linked to
treatment of skin lesions, some authors finding an in
vitro bactericidal effect. Due to the fact that surface
defects were involved, modifications of the shockwa-
ve head had to be made, in order for it not to be fo-
cused but planar to the treated area. The authors used
low energy flow densities, with no anesthesia being
necessary due to defocusing and the low energy flux.
Encouraging results were obtained, with none of the
patients experiencing a worsening of the wound, and
a lessening of the infection was observed after the first
session\textsuperscript{84}. Sho et al. perform a prospective study regard-
ing effects of ESWT on burn patients with developed
scar pain which included 40 patients with complete
epithelization of open skin wounds that underwent
skin grafting. Shockwave therapy was applied around
the primary treatment site in accordance with the pa-
tients pain tolerance with an energy flux density of
0.05 to 0.15mJ/mm\textsuperscript{2} and a number of 100 impulses-
cm\textsuperscript{2}. Significant differences were reported regarding
pain threshold, and Roles and Maudsley scores com-
pared to sham group after 3 sessions, offering promi-
sing perspective over wound recovery\textsuperscript{85}.

Non orthopaedic indications refer to the benefit of
using ESWT as a treatment option for ischemic car-
diomyopathy. Different authors have studied in vitro
and in vivo effects based on the fact that shockwaves
can induce angiogenesis. Nishida et al.\textsuperscript{86} apply ESWT
on single donor human umbilical vein endothelial cells,
and observe a significant up-regulation of the mRNA
expression of vascular endothelial growth factor and its
receptors in vitro. Also, an increase of the regional myo-
cardial blood flow was detected, the results suggesting a
possible non-invasive therapeutic strategy for ischemic
heart disease. Vainer et al.\textsuperscript{87} evaluate the feasibility of
ESWT in 33 patients with end-stage coronary artery
disease with the application of 9 sessions of shockwave
with ECG and echocardiography guidance. The assess-
ment of patients included nitrate use, myocardial scin-
tigraphy, and MRI. The results evidenced at 4 month
follow-up a reduction of angina symptoms and nitra-
te use and an increase in exercise tolerance. Favorable
results were observed in the myocardial uptake within
the stress myocardial scintigraphy.

CONCLUSIONS

Shockwave therapy can be indicated as an alterna-
tive treatment to surgical modalities or when other
conservative methods have been proven insufficient.
Further in vitro and placebo controlled studies are nee-
ded to establish the role of shockwaves in avascular ne-
crosis of the femoral head. Low energy ESWT seems
to bring a significant improvement in pain levels and
shoulder function and can contribute to the resorbti-
on of calcium deposits. Action mechanisms of ESWT
need additional research, but accepted biological effects
include an ingrowth of neovascularization and a stimu-
lation of angiogenetic growth factors.

There is potential of posponing or replacing surgical
interventions in many orthopaedic disorders with the
use of ESWT, but there is still a lack of standardisation
and a consensus is needed regarding frequency and
intensity.

Abbreviations

ESWT Extracorporeal shockwave therapy
(PØ) Positive peak pressure
(P-) Negative peak pressure
(Tr) Rise time
(Tw) Impulse width
BMP Binding morphogenic proteins
GTPS Greater trochanteric pain syndrome
DASH The Disabilities of the Arm, Shoulder and
Hand Score
EMTT Electromagnetic transduction therapy
SLBCN Superior Lateral Brachial Cutaneous Nerve
Compression Syndrome

Compliance with ethics requirements:
The authors declare no conflict of interest regarding
this article.
The authors declare that all the procedures and experi-
ments of this study respect the ethical standards in the
Helsinki Declaration of 1975, as revised in 2008(5), as
well as the national law. Informed consent was obtai-
ned from all the patients included in the study.
References


