

## CURRENT CONCEPTS REVIEW

# The Role of Extracorporeal Shockwave Treatment in Musculoskeletal Disorders

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- ▶ Increasing evidence suggests that extracorporeal shockwave treatment (ESWT) is safe and effective for treating several musculoskeletal disorders.
- ▶ Two types of technical principles are usually included in ESWT: focused ESWT (F-ESWT) and radial pressure waves (RPW). These 2 technologies differ with respect to their generation devices, physical characteristics, and mechanism of action but share several indications.
- ▶ Strong evidence supports the use of ESWT in calcifying tendinopathy of the shoulder and plantar fasciitis.
- ▶ The best evidence for the use of ESWT was obtained with low to medium energy levels for tendon disorders as well as with a high energy level for tendon calcification and bone pathologies in a comprehensive rehabilitation framework.

Shockwave therapy was originally developed to disintegrate urinary stones 4 decades ago<sup>1</sup>. Since then, there has been remarkable progress regarding the knowledge of its biological and therapeutic effects. Its mechanism of action is based on acoustic mechanical waves that act at the molecular, cellular, and tissue levels to generate a biological response<sup>2</sup>.

Increasing evidence suggests that extracorporeal shockwave treatment (ESWT) is safe and effective for treating several musculoskeletal disorders<sup>3-5</sup>. The purpose of this article was to provide current evidence on the physical and biological principles, mechanism of action, clinical indications, and controversies of ESWT.

## Physical Principles and Wave Generation

Two types of technical principles are included in ESWT—focused ESWT (F-ESWT) and radial pressure waves (RPW), which are often referred to in the literature as radial shockwaves. These 2 technologies differ in their generation devices, physical

characteristics, and mechanism of action, but they share several indications.

As shown in Figure 1, the following 3 shockwave-generation principles are used for F-ESWT<sup>6,7</sup>:

1. Electrohydraulic sources (Fig. 1-A) produce a plasma bubble by high-voltage discharge between 2 electrodes in water at the focus closest to a paraellipsoidal reflector. The plasma expansion generates a shock front, which is reflected off the reflector and focused on a second focus at the target tissue.

2. Electromagnetic sources (Fig. 1-B) with flat or cylindrical coils are also used. In the first system, a high-voltage pulse is sent through a coil, which is opposite a metallic membrane. The coil produces a magnetic field, resulting in a sudden deflection of the membrane and generating pressure waves in a fluid. The waves are focused by a lens and steepen into a shockwave near the focus. The second electromagnetic generation source consists of a cylindrical coil and metallic membrane that is arranged inside a fluid-filled parabolic reflector. The

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membrane is accelerated away from the coil by a magnetic field. An acoustic pulse emerges radially, and it is concentrated onto the focus of the system after reflection off the reflector.

3. Piezoelectric sources (Fig. 1-C) produce shockwaves by a high-voltage discharge across a pattern of piezoelectric elements mounted on the inner surface of a spherical backing that is placed inside a fluid-filled cavity. Each element expands, generating a pressure pulse that propagates toward the center, or focal region, of the arrangement. Superposition of all pressure pulses and nonlinear effects produce a shockwave at focal region.

In RPW generators (Fig. 1-D), compressed air accelerates a projectile inside a cylindrical guiding tube. When the projectile hits an applicator at the end of the tube, a pressure wave is produced and radially expands into the target tissue. These devices do not emit shockwaves<sup>8</sup> because the rise times of the pressure pulses are too long and the pressure outputs are too low (Fig. 2). Nevertheless, RPW may induce acoustic cavitation<sup>9</sup>.

The modes of action and the effects of RPW on living tissue may differ from those of focused shockwaves because

bioeffects are related to the pressure waveform. F-ESWT and RPW may complement each other. While RPW is suitable for treating large areas, focused shockwaves can be concentrated deep inside the body.

### Mechanism of Action

Despite the clinical success of the treatment, the mechanism of action of ESWT remains unknown. In 1997, Haupt proposed the following 4 possible mechanisms of reaction phases of ESWT on tissue<sup>10</sup>.

1. Physical phase: This phase indicates that the shockwave causes a positive pressure to generate absorption, reflection, refraction, and transmission of energy to tissues and cells<sup>11</sup>. Additional studies demonstrated that ESWT produces a tensile force by the negative pressure to induce the physical effects, such as cavitation, increasing the permeability of cell membranes and ionization of biological molecules. Meanwhile, many signal transduction pathways are activated, including the mechanotransduction signaling

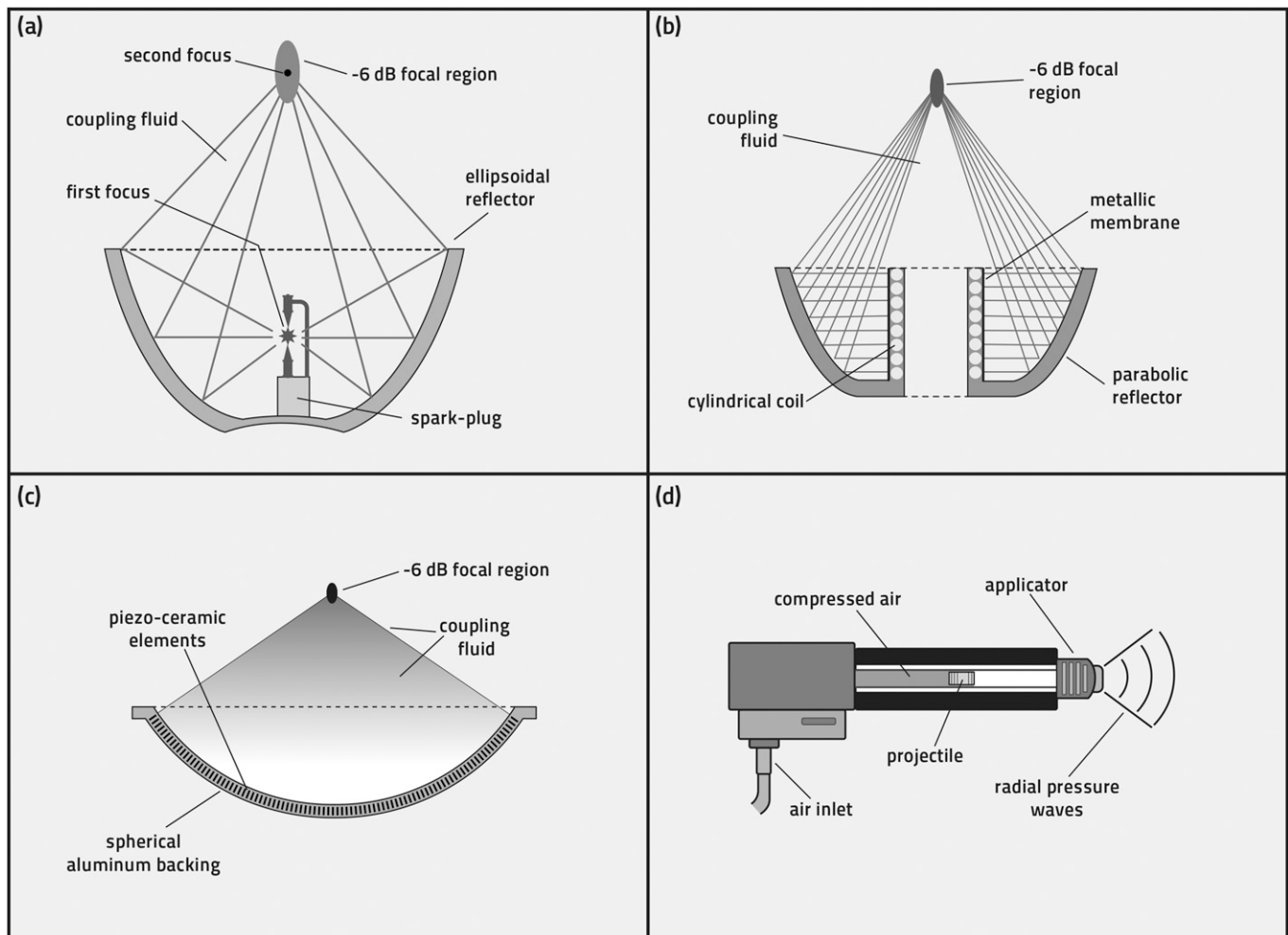


Fig. 1  
Figs. 1-A through 1-D Illustrations of an electrohydraulic (Fig. 1-A), an electromagnetic (Fig. 1-B), and a piezoelectric shockwave source (Fig. 1-C) and a radial pressure wave source (Fig. 1-D). The -6 dB region is defined as the volume within which the positive pressure is at least 50% of its maximum.

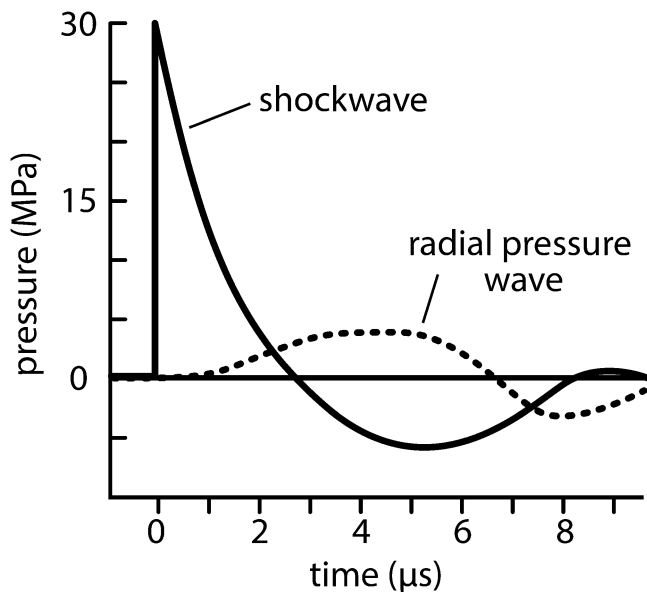


Fig. 2  
Illustration showing the difference in pressure waveform between a shockwave and a radial pressure wave as used in medical applications.

pathway, the extracellular signal-regulated kinase (ERK) signaling pathway, focal adhesion kinase (FAK) signaling pathway, and Toll-like receptor 3 (TLR3) signaling pathway, to regulate gene expressions<sup>2,5,12-14</sup>.

2. Physicochemical phase: ESWT stimulates cells to release biomolecules, such as adenosine triphosphate (ATP), to activate cell signal pathways<sup>15,16</sup>.

3. Chemical phase: In this phase, shockwaves alter the functions of ion channels in the cell membrane and the calcium mobilization in cells<sup>17,18</sup>.

4. Biological phase: Previous studies have shown that ESWT modulates angiogenesis (vWF [von Willebrand factor], vascular endothelial growth factor [VEGF], endothelial nitric oxide synthase [eNOS], and proliferating cell nuclear antigen [PCNA]), anti-inflammatory effects (soluble intercellular adhesion molecule 1 [sICAM] and soluble vascular cell adhesion molecule 1 [sVCAM]), wound-healing (Wnt3, Wnt5a, and beta-catenin), and bone-healing (bone morphogenetic protein [BMP]-2, osteocalcin, alkaline phosphatase, dickkopf-related protein 1 [DKK-1], and insulin-like growth factor [IGF]-1)<sup>18-22</sup>.

The effects of ESWT are summarized in Table I, with new functional proteins induced by ESWT promoting a chondroprotective effect, neovascularization, anti-inflammation, anti-apoptosis, and tissue and nerve regeneration<sup>2,12-14,16,19,22-52</sup>. Furthermore, ESWT stimulates a shift in the macrophage phenotype from M1 to M2 and increases T-cell proliferation in the effect of immunomodulation<sup>27,28</sup>. ESWT activates the TLR3 signaling pathway to modulate inflammation by controlling the expression of interleukin (IL)-6 and IL-10 as well as improves the treatment of ischemic muscle<sup>12,13</sup>.

TABLE I Overview of Effects and Functional Proteins After ESWT\*

	Upregulation Factors	Downregulation Factors
Chondroprotective effect <sup>2,14,16,29-40</sup>	BMP-2, 3, 4, 7; IGF-1; TGF $\beta$ -1; VEGF; Wnt3; RUNX2; osteocalcin; alkaline phosphatase; osteopontin; FAK; ERK1/2; c-Fos; c-Jun; p38 MAPK; P2X7 receptor; SOX9; PDGF; b-FGF; FGF-2; Ras; substance P; prostaglandin E(2); Hsp70	DKK1, Wnt5a, calcitonin gene-related peptide, miR-138
Neovascularization <sup>25,43-45</sup>	VEGF, Flt1, Flt2, CD31, vWF, FGF, PIGF, KDR, PCNA	
Anti-inflammation <sup>12,13,22,25,46</sup>	TGF $\beta$ -1, TLR3, eNOS, nNOS, IL-10, IL-6, IL-8, cyclophilin B, cyclophilin A, EGF-like domains 2, IFN- $\beta$ 1	sICAM, sVCAM, iNOS, IL-18, TNF $\alpha$ , NF-kB
Anti-apoptosis <sup>25,47</sup>	Bcl2, heme oxygenase (HO)-1, NAD(P)H quinone oxidoreductase-1	Bax, cleaved caspase 3, cleaved PARP, $\gamma$ -H2AX, NOX1, NOX2, TUNEL activity
Tissue and nerve regeneration <sup>35,48-52</sup>	COL1A1, COL2A1, MMP2, MMP9, glycosaminoglycan, collagen type III, S100b, p75, c-Jun, GFAP, activating transcription factor 3 (ATF3), growth-associated phosphoprotein (GAP-43)	MMP-1, MMP-13, myelin marker PO

\*BMP = bone morphogenetic protein, IGF = insulin-like growth factor, TGF = transforming growth factor, VEGF = vascular endothelial growth factor, RUNX2 = runt-related transcription factor 2, FAK = focal adhesion kinase, ERK = extracellular signal-regulated kinase, MAPK = mitogen-activated protein kinase, PDGF = platelet-derived growth factor, FGF = fibroblast growth factor, Hsp = heat-shock protein, DKK = dickkopf-related protein, miR = microRNA, Flt = FMS-like tyrosine kinase, vWF = von Willebrand factor, PIGF = phosphatidylinositol-glycan biosynthesis class-F protein, KDR = kinase insert domain receptor, PCNA = proliferating cell nuclear antigen, TLR = Toll-like receptor, NOS = nitric oxide synthase, eNOS = endothelial NOS, nNOS = neuronal NOS, IL = interleukin, EGF = epidermal growth factor, IFN = interferon, sICAM = soluble intercellular adhesion molecule, sVCAM = soluble vascular cell adhesion molecule, iNOS = inducible NOS, TNF $\alpha$  = tumor necrosis factor alpha, NF-kB = nuclear factor kappa B, Bcl = B-cell lymphoma, NAD = nicotinamide adenine dinucleotide, PARP = poly(ADP-ribose) polymerase, H2AX = H2A histone family member X, TUNEL = terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling, COL1A1 = collagen type-1 alpha 1, COL2A1 = collagen type-2 alpha 1, MMP = matrix metalloproteinase, and GFAP = glial fibrillary acidic protein.

Finally, it appears that ESWT participates in mechano-transduction, producing biological responses through mechanical stimulation on tissues<sup>2,4,7,26</sup>.

### Clinical Indications

ESWT is indicated in chronic tendinopathies in which conventional conservative treatment is considered unsatisfactory after a prolonged and comprehensive management or as an

alternative to surgery in patients with nonunion. ESWT is a noninvasive alternative in select cases when the indication for surgical treatment arises.

The International Society for Medical Shockwave Treatment (ISMST) has developed a list of approved clinical indications that are based on the strength of the supporting evidence<sup>53</sup>. The recommendations for ESWT indications and contraindications are summarized in Table II and Table III, respectively.

**TABLE II Grades of Recommendations According to Clinical Indications for ESWT**

Pathology	Technology	Studies*				Grade of Recommendation†
		Positive		Negative		
		RCTs	Reviews, Systematic Reviews, and Meta-Analyses	RCTs	Reviews, Systematic Reviews, and Meta-Analyses	
Calcifying tendinopathy of the shoulder	Focused	Gerdesmeyer et al. <sup>58</sup> , Cosentino et al. <sup>59</sup> , Hsu et al. <sup>60</sup> , and Rompe et al. <sup>69</sup>	Moya et al. <sup>55</sup> , Ioppolo et al. <sup>61</sup> , Bannuru et al. <sup>62</sup> , Huisstede et al. <sup>63</sup> , Louwerens et al. <sup>64</sup> , Speed <sup>65</sup> , and Verstraelen et al. <sup>66</sup>	Albert et al. <sup>56</sup> and Kim et al. <sup>67</sup>		A
Calcifying tendinopathy of the shoulder	Radial	Cacchio et al. <sup>57</sup>			Moya et al. <sup>55</sup> , Bannuru et al. <sup>62</sup> , Huisstede et al. <sup>63</sup> , Speed <sup>65</sup> , and Verstraelen et al. <sup>66</sup>	I
Noncalcifying tendinopathy of the shoulder	Focused or radial			Speed et al. <sup>71</sup> and Engbretsen et al. <sup>72</sup>	Moya et al. <sup>55</sup> , Bannuru et al. <sup>62</sup> , Huisstede et al. <sup>63</sup> , and Speed <sup>65</sup>	C
Lateral epicondylopathy of the elbow	Focused or radial	Pettrone and McCall <sup>85</sup> , Lee et al. <sup>86</sup> , and Radwan et al. <sup>87</sup>	Thiele et al. <sup>80</sup> and Rompe and Maffulli <sup>84</sup>	Speed et al. <sup>79</sup>	Sims et al. <sup>81</sup> , Buchbinder et al. <sup>82</sup> , and Dingemanse et al. <sup>83</sup>	B
Greater trochanter pain syndrome	Radial	Rompe et al. <sup>88</sup> and Furia et al. <sup>89</sup>	Mani-Babu et al. <sup>90</sup>			B
Patellar tendinopathy	Focused or radial	Wang et al. <sup>96</sup> , Furia et al. <sup>97</sup> , and Peers et al. <sup>99</sup>	Mani-Babu <sup>90</sup> , Leal et al. <sup>91</sup> , Larsson et al. <sup>94</sup> , and Everhart et al. <sup>98</sup>	Zwerver et al. <sup>101</sup> and Thijs et al. <sup>102</sup>		B
Achilles tendinopathy	Focused or radial	Rasmussen et al. <sup>110</sup> , Furia <sup>111</sup> , Furia <sup>112</sup> , Rompe et al. <sup>113</sup> , and Rompe et al. <sup>114</sup>	Mani-Babu et al. <sup>90</sup> , Gerdesmeyer et al. <sup>108</sup> , Al-Abbad and Simon <sup>115</sup> , Kearney and Costa <sup>116</sup> , and Roche and Calder <sup>117</sup>	Costa et al. <sup>109</sup>	Scott et al. <sup>105</sup>	B
Plantar fasciitis	Focused or radial	Chuckpaiwong et al. <sup>121</sup> , Wang et al. <sup>122</sup> , Gerdesmeyer et al. <sup>123</sup> , Ibrahim et al. <sup>124</sup> , Gollwitzer et al. <sup>125</sup> , Ogden et al. <sup>126</sup> , Rompe et al. <sup>127</sup> , Aqil et al. <sup>128</sup> , Saxena et al. <sup>133</sup> , Weil et al. <sup>134</sup> , Thomas et al. <sup>135</sup> , and Wang et al. <sup>136</sup>	Dizon et al. <sup>130</sup> , Othman and Ragab <sup>131</sup> , Radwan et al. <sup>132</sup> , and Chen et al. <sup>137</sup>	Buchbinder et al. <sup>119</sup> and Haake et al. <sup>120</sup>		A
Bone nonunion	Focused	Notarnicola et al. <sup>155</sup> , Schaden et al. <sup>157</sup> , and Lyon et al. <sup>158</sup>	Furia et al. <sup>154</sup> , Kuo et al. <sup>156</sup> , and Thiele et al. <sup>160</sup>			B

\*RCT = randomized controlled trial. †According to Wright<sup>164</sup>, grade A indicates good evidence (Level-I studies with consistent findings) for or against recommending intervention; grade B, fair evidence (Level-II or III studies with consistent findings) for or against recommending intervention; grade C, poor-quality evidence (Level-IV or V studies with consistent findings) for or against recommending intervention; and grade I, there is insufficient or conflicting evidence not allowing a recommendation for or against intervention.

TABLE III ESWT Contraindications

ESWT Contraindications*	
High-Energy Focused Shockwaves	Low-Energy Focused and Radial Shockwaves
1. Lung tissue in the treatment area	1. Malignant tumor in the treatment area
2. Malignant tumor in the area	2. Fetus in the treatment area
3. Epiphyseal plate in the area	
4. Brain or spine in the area	
5. Severe coagulopathy	
6. Fetus in the treatment area	
*According to the International Society for Medical Shockwave Treatment <sup>53</sup> .	

After ESWT, a comprehensive post-treatment schedule, individualized for each pathology and each patient's clinical status, should be given to the patient including avoidance of the use of the anatomic structure, a specific exercise program, and instructions to avoid overload.

### Shoulder Tendinopathies

#### Calcifying Tendinopathy of the Shoulder (CTS)

ESWT has emerged as an alternative therapy prior to invasive procedures when conservative treatment has failed as described for Gärtner type-I or II rotator cuff calcifications<sup>54,55</sup> (Fig. 3).

The rate of successful reabsorption reported by different authors has a very wide range<sup>56-66</sup>.

Gerdesmeyer et al.<sup>58</sup>, in a multicenter randomized controlled trial (RCT) that included 144 patients, reported significantly better results in patients treated with F-ESWT, both low and high energy, compared with placebo, resulting in improvement with respect to pain, shoulder function, and calcium resorption in 86% in the high-energy group at 1 year compared with 37% in the low-energy group and 25% in the placebo ESWT group. Cosentino et al.<sup>59</sup>, in a single-blind trial using F-ESWT, reported a significant increase in shoulder function, a decrease in pain compared with placebo, and calcium resorption of 71% by using F-ESWT, at 6 months. Hsu et al.<sup>60</sup>, in an RCT, achieved good or excellent results in 87.9% of patients treated with high-energy F-ESWT.

Cacchio et al.<sup>57</sup> obtained a surprisingly high rate of reabsorption using RPW (86.6% complete and 13.4% partial resorption) at the 6-month follow-up; however, most studies have considered that high-energy F-ESWT is more likely to result in better radiographic and clinical outcomes<sup>55,56,58-66</sup>.

Several systematic reviews and meta-analyses have demonstrated that high-energy F-ESWT is a safe, effective treatment for CTS<sup>61-66</sup>.

Kim et al.<sup>67</sup> compared RPW with ultrasound-guided needling and reported that the latter treatment method was more effective in functional restoration and pain relief in the short term. However, Moya et al.<sup>68</sup> pointed out numerous methodological flaws in that study. There was missing information about the ESWT device used (focused or radial), methodological

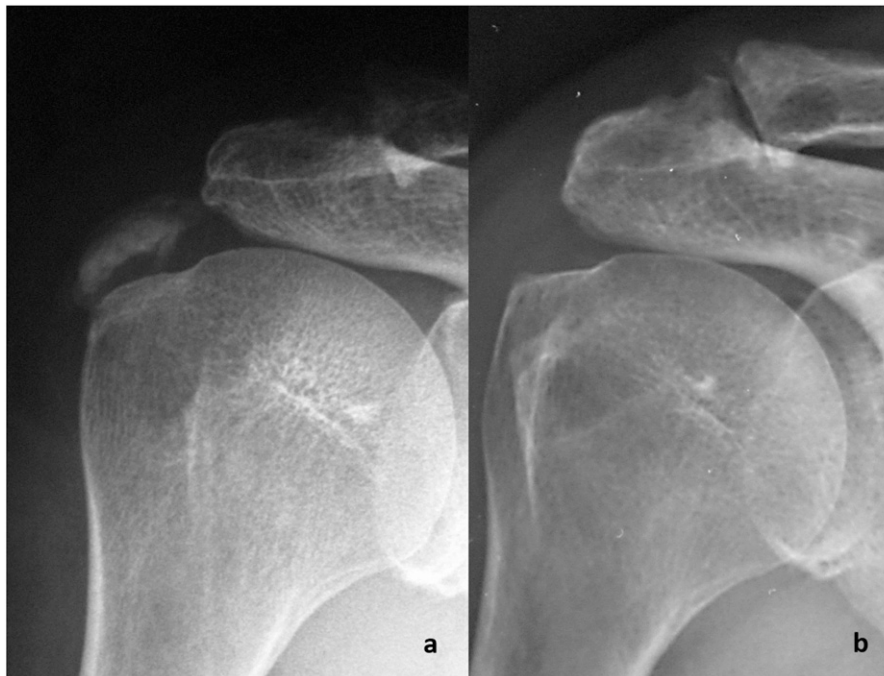


Fig. 3

Anteroposterior radiographs of a right shoulder with a Gärtner type-II calcification of the supraspinatus before focused shockwave treatment (Fig. 3-A) and at 3 months after treatment (Fig. 3-B), showing that the calcification has disappeared.

explanations were short and imprecise, the point of maximum tenderness was treated instead of focusing on topographic anatomy or locating calcium deposits with fluoroscopy or ultrasound, and the ESWT treatment protocol was nonstandard<sup>68</sup>.

Rompe et al.<sup>69</sup> and Rebutzi et al.<sup>70</sup> compared F-ESWT with open and arthroscopic surgery in CTS, respectively. They concluded that the results are comparable and that high-energy F-ESWT should be the first choice when conservative treatment has failed, because of its noninvasiveness.

In summary, given its efficacy in pain reduction<sup>55,56,58-65,69,70</sup> and functional outcomes<sup>55,58,61-66,69,70</sup>, resorption rate<sup>55,58-61,63,64,66,69</sup>, safety<sup>55,59,60,64</sup>, noninvasiveness<sup>55,69,70</sup>, reduced recovery time<sup>55</sup>, and cost-effectiveness<sup>55</sup>, we consider that high-energy F-ESWT is the treatment of choice in CTS when conservative treatment has failed.

### Noncalcifying Tendinopathy of the Shoulder

Unlike CTS, the treatment of noncalcified tendinopathies with shockwaves is controversial<sup>71</sup>. Both favorable and poorly performing studies in many cases present inadequate inclusion criteria (wide age ranges, heterogeneous populations, and insufficient diagnostic evaluations). It is inadmissible to consider “subacromial pain”<sup>72</sup> or “non-specific shoulder pain”<sup>73</sup> as a diagnosis of shoulder disease if all possible differential diagnoses have not been ruled out. This confusion is reflected in the results of the meta-analyses and systematic reviews<sup>62,63,65</sup>.

Huisstede et al.<sup>63</sup> found no strong evidence to support the efficacy of ESWT to treat noncalcific rotator cuff tendinosis beyond the applied energy level. Speed<sup>65</sup> did not support low-dose or high-dose F-ESWT.

We are unable to recommend the use of ESWT in noncalcific tendinopathy of the shoulder because of the lack of compelling evidence.

### Lateral Epicondylitis of the Elbow

There are many therapeutic options for treating lateral epicondylitis. The existing evidence does not clearly support the efficacy of any of the available treatment methods for this clinical condition<sup>74-79</sup>. ESWT is not the exception<sup>79</sup>, although it was approved by the U.S. Food and Drug Administration (FDA) for treating this disease in 2002<sup>80</sup>.

Several systematic reviews and meta-analyses have shown conflicting evidence<sup>81-83</sup>. It is difficult to interpret the data because of the variety of study designs and the use of different shockwave devices<sup>84</sup>.

Pettrone and McCall<sup>85</sup> reported a significant improvement with respect to pain and function in the active treatment group at 6 and 12 months compared with the placebo group in a study with Level-I evidence.

In a review study by Thiele et al.<sup>80</sup>, the authors stated that several clinical trials have achieved very good results with the use of ESWT for lateral epicondylitis of the elbow. That review only included Level-I studies using focused ESWT and RPW, and the authors concluded that lateral epicondylitis is a primary indication for ESWT.

Lee et al.<sup>86</sup> found similar outcomes when comparing steroid injections with ESWT in lateral and medial epi-

condylitis. Radwan et al.<sup>87</sup> found no significant differences between F-ESWT and percutaneous tenotomy.

Although the strength of the supporting evidence is not strong, no method to treat lateral epicondylitis is backed by studies with a high level of evidence. As the benefits largely exceed any potential harm, we recommend the use of radial or focused ESWT technologies when conventional rehabilitation treatment has failed.

### Greater Trochanteric Pain Syndrome

There is no agreement about the optimal management for greater trochanteric pain syndrome<sup>88</sup>. Numerous conservative treatments (nonsteroidal anti-inflammatory drugs, physiotherapy, and corticosteroid injections) have been recommended<sup>88</sup>.

Two studies provided Level-II and III evidence for RPW effectiveness in 74% of patients at 15 months<sup>88</sup> and 78.8% at 12 months<sup>89</sup>, respectively.

Rompe et al.<sup>88</sup> compared RPW with 2 other treatment methods, steroid injection and home training exercise, in a quasi-RCT. Although RPW was inferior to steroid injection at 1 month, RPW demonstrated better outcomes at 4 months compared with steroid injection and home exercise training, and it matched home training at 15 months<sup>88</sup>. Furia et al.<sup>89</sup> compared RPW and nonoperative therapy in patients with greater trochanteric pain syndrome. The RPW group had significant improvement with respect to pain, function, and Roles and Maudsley scales than the standard treatment group at 12 months<sup>89</sup>.

Although the available evidence on ESWT in greater trochanteric pain syndrome is limited, RPW appears more effective than a home exercise program and local corticosteroid injection after short-term and mid-term follow-up (up to 15 months) of greater trochanteric pain syndrome<sup>88-90</sup>.

### Patellar Tendinopathy

Patellar tendinopathy treatment represents a challenge<sup>91</sup>. There is no evidence-based protocol for the appropriate management of patellar tendinopathy<sup>90,92-95</sup>. Eccentric training appears to be the first-line treatment<sup>92-95</sup>.

New therapies, such as prolotherapy, dry-needling, platelet-rich plasma (PRP), cell therapy, or hyaluronic acid, may offer alternatives to standard treatments<sup>93,94</sup>.

Promising results have been shown with ESWT<sup>90,91,96-100</sup>. Wang et al.<sup>96</sup> compared F-ESWT and conservative treatment in an RCT and obtained good or excellent results in 90% of the ESWT group at the 2 to 3-year follow-up evaluation compared with 50% in the conservative treatment group. Furia et al.<sup>97</sup> compared RPW and standard treatment in a retrospective study at 1 year and reported satisfactory results in 75.8% of patients receiving a single session of low-energy radial pressure waves compared with 17.2% in other nonoperative therapies.

By contrast, in an RCT, Zwerver et al.<sup>101</sup> compared real and placebo piezoelectric ESWT in athletes and did not find significant differences between the groups in terms of pain and function at 22 weeks. Another recent RCT on 52 athletes diagnosed with patellar tendinopathy evaluated the effect of ESWT or

sham ESWT in addition to an eccentric training program and did not find differences at 6 months of follow-up<sup>102</sup>.

However, these studies describing poor results with the use of ESWT included certain features and methodological errors such as: no complementary studies were performed to rule out calcification or partial rupture with a different prognosis<sup>101,102</sup>; applying ESWT with a piezoelectric device<sup>101,102</sup>; adapting the ESWT intensity to patient tolerance instead of a specific therapeutic energy level<sup>101</sup>; high energy levels<sup>101</sup>; allowing for training and competition during and after ESWT treatment instead of removing the patient from sports<sup>101,102</sup>; and ESWT as a solitary treatment not combined with exercise<sup>101</sup>.

Peers et al.<sup>99</sup> retrospectively compared F-ESWT with surgery in 28 patients at an average of 24 months and showed excellent or good results according to the Roles and Maudsley score in 66% of the ESWT group, which was comparable with 58% in the surgery group. The authors concluded that F-ESWT in chronic patellar tendinopathy is an alternative to surgery, without resulting in incapacity, when conservative treatment fails<sup>99</sup>.

Review of the literature shows that ESWT is safe and effective in the treatment of patellar tendinopathy<sup>90,91,98</sup>. Current evidence supports the use of F-ESWT and RPW for patellar tendinopathy with moderate or low-intensity protocols, especially in patients attempting to avoid an invasive intervention.

### Achilles Tendinopathy

Achilles tendinopathy affects active athletes as well as the sedentary population<sup>103</sup>. According to its anatomical location, it is

classified into 2 categories, insertional and noninsertional or midportion tendinopathy.

Conservative treatment includes pain medication, heel lifts, eccentric exercises, physiotherapy, steroid and platelet-rich plasma injections, low-level laser therapy, and radiofrequency, among others<sup>104-109</sup>. Different shockwave sources and protocols have been used. A Level-I study with 48 patients compared piezoelectric F-ESWT and placebo ESWT and found better results for the ESWT group<sup>110</sup>. Furia reported good results for insertional<sup>111</sup> and noninsertional<sup>112</sup> Achilles tendinopathies with RPW.

In an RCT, Rompe et al.<sup>113</sup> demonstrated that RPW is more effective than eccentric loading exercises for insertional Achilles tendinopathy at the 15-month follow-up evaluation. Furthermore, there is demonstrated superior efficacy of combining eccentric loading and ESWT compared with eccentric loading alone in those patients<sup>114</sup>.

Gerdesmeyer et al.<sup>108</sup> highlighted the efficacy of both F-ESWT and RPW in chronic Achilles tendinopathy. On the other hand<sup>109</sup>, Costa et al. found no significant differences between the F-ESWT and control groups in terms of pain, function, and quality of life for 49 patients with Achilles tendinopathy at 3 months in a Level-I RCT<sup>109</sup>. Those authors concluded that there was no support for the use of ESWT in Achilles tendinopathy. ESWT was performed once a month for 3 months, instead of at weekly intervals as per the standard recommendations<sup>4,5</sup>. Two elderly patients had an Achilles rupture after ESWT, but, surprisingly, no complementary explorations were performed before treatment to rule out previous partial ruptures.

**TABLE IV ESWT Success Rate in the Treatment of Delayed Fracture-Healing and Nonunions**

Study	No. of Patients	Material	Success Rate
Valchanou and Michailov <sup>142</sup> (1991)	82	Nonunions*	84%
Rompe et al. <sup>144</sup> (2001)	43	Tibial and femoral diaphyseal and metaphyseal nonunions	72%
Wang et al. <sup>145</sup> (2001)	72	Nonunions (41 femora, 19 tibiae, 7 humeri, 1 radius, 3 cubiti, and 1 metatarsal)	80%
Schaden et al. <sup>146</sup> (2001)	115	72 shaft fractures in long bones and 43 fractures in cancellous bones	75.7%
Bara and Snyder <sup>148</sup> (2007)	81	42 delayed unions and 39 nonunions (49 tibiae, 13 femora, 10 radial and ulnar bones, and 5 humeri)	83%
Xu et al. <sup>149</sup> (2009)	69	Nonunions (22 femora, 28 tibiae, 13 humeri, 5 radii, and 1 ulna)	75.4%
Cacchio et al. <sup>152</sup> (2009)	126	Long-bone nonunions	71%
Elster et al. <sup>150</sup> (2010)	192	Tibia	80.2%
Furia et al. <sup>154</sup> (2010)	23	Nonunion of proximal fifth metatarsal metaphyseal-diaphyseal fractures	87%
Notarnicola et al. <sup>155</sup> (2010)	58	Carpal scaphoid nonunions	75.9%
Zelle et al. <sup>151</sup> (2010)	924	Systematic review of 10 case series and 1 RCT including delayed union and nonunion	76%
Kuo et al. <sup>156</sup> (2015)	22	Atrophic nonunions of the femoral shaft	63.6%

\*Patient history, concomitant treatment, and follow-up were not specified.

Three systematic reviews<sup>90,115,116</sup> and 1 review<sup>117</sup> showed satisfactory evidence of the effectiveness of low-energy ESWT in insertional and noninsertional chronic Achilles tendinopathy after failure of conservative treatment and before considering surgery, especially in combination with eccentric loading.

#### *Plantar Fasciitis*

Plantar fasciitis is a degenerative musculoskeletal disorder<sup>118</sup>. In 2002, Buchbinder et al.<sup>119</sup> found no evidence to support the use of ESWT in plantar fasciitis. In 2003, another RCT considered electromagnetic ESWT to be ineffective in this field<sup>120</sup>.

Since then, several studies with a high level of evidence have supported both focused<sup>121,122</sup> and radial<sup>123,124</sup> technologies for this disorder. Gollwitzer et al.<sup>125</sup>, in a study of the treatment of recalcitrant plantar fasciitis with an electromagnetic device, reported pain reduction in 69.2% of the patients in the ESWT group compared with 34.5% in the control group. Ogden et al.<sup>126</sup>, in an RCT, concluded that electrohydraulic F-ESWT is effective and safe and that the clinical improvement lasts beyond 1 year. In a Level-I study, Wang et al.<sup>122</sup> compared F-ESWT with conservative treatment modalities. The shockwave group had excellent or good results in 82.7% of the patients compared with 55% in the control group at a follow-up

of between 60 and 72 months; also, the shockwave group had a much lower recurrence rate.

Gerdesmeyer et al.<sup>123</sup>, in an RCT, reported an overall success rate of 61% with RPW compared with 42.2% in the placebo group at 12 weeks.

Recently, a multicenter study<sup>127</sup> showed that the combination of a plantar fascia-specific stretching program with low-energy RPW achieves better results than RPW alone. Three meta-analyses<sup>128-130</sup> found that ESWT is effective for treating chronic plantar fasciitis. Aqil et al.<sup>128</sup> recommended the use of shockwave treatment in plantar fasciitis on the basis of its efficacy and safety.

Several studies have compared F-ESWT with surgery<sup>131-134</sup>, supporting the use of shockwave treatment because of its effectiveness<sup>128,132,134</sup> and because patients can quickly resume full activities<sup>131</sup> and athletes have a chance to continue sports activities<sup>133</sup>.

Since 2010, the American College of Foot and Ankle Surgeons has recommended ESWT as a treatment of choice for plantar fasciitis with or without a plantar spur when nonoperative treatment has failed<sup>135</sup>.

#### *Bone Disorders*

Haupt<sup>10</sup>, in 1997, recognized the dynamic interaction between ESWT and bone. It was initially hypothesized that shockwaves

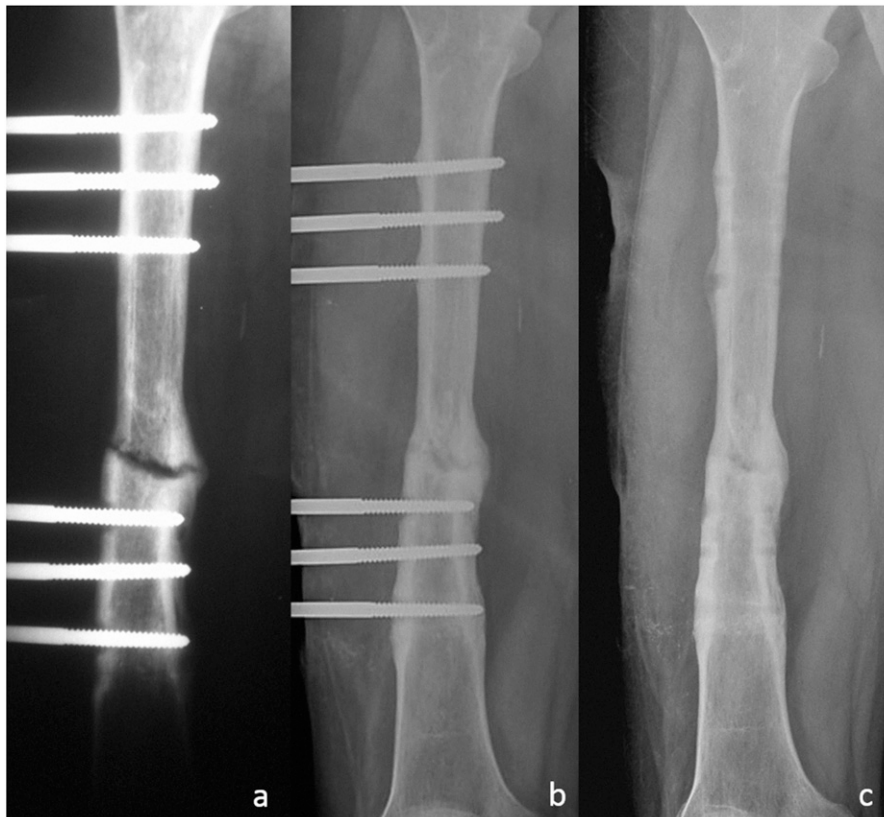


Fig. 4

**Figs. 4-A, 4-B, and 4-C** Anteroposterior radiographs of the right femur of a 37-year-old man who had sustained a femoral fracture in a motorcycle accident; the fracture was initially treated with an intramedullary nail, but it was revised 14 months later because of nonunion and an external fixator was applied. **Fig. 4-A** At 6 months after the second surgery, there were no signs of bone-healing. **Fig. 4-B** At 4 months after F-ESWT, a successful union of the fracture was evident. **Fig. 4-C** The final result after external fixator removal demonstrated complete healing.



created microlesions in treated bone. This appreciation completely changed when Wang et al.<sup>19,20</sup> demonstrated that shockwaves generate upregulation and expression of various pro-angiogenic and pro-osteogenic growth factors, stimulating bone-healing. Basic research has shown that because of mechanical forces delivered by shockwaves to the cells and to the extracellular matrix, messengers are liberated and activate different genes and groups of genes in the cell nucleus<sup>50,136-140</sup>. This phenomenon of biological conversion from a mechanical stimulus into electrochemical activity is called “mechanotransduction.”<sup>141</sup>

The use of ESWT for nonhealing fractures was first reported, to our knowledge, in 1991 by Valchanou and Michailov<sup>142</sup>. Since then, several observations and trials have supported the efficacy of ESWT for nonunion and delayed fracture-healing<sup>143-157</sup> (Table IV).

Cacchio et al.<sup>152</sup>, in a Level-I RCT, compared different ESWT high-energy levels (0.4 mJ/mm<sup>2</sup> [Group 1] and 0.7 mJ/mm<sup>2</sup> [Group 2]) and surgery (Group 3) for the treatment of hypertrophic long-bone nonunions and obtained success rates of 70%, 71%, and 73%, respectively, at 6 months. No adverse effects occurred in the ESWT groups compared with a 7% rate of complications in the surgical group.

Similar results were reported by Furia et al.<sup>154</sup>, who observed that high-energy F-ESWT was as effective as intramedullary screw fixation in the treatment of nonunion of a fracture of the fifth metatarsal; however, screw fixation was more often associated with complications that frequently resulted in additional surgery.

Notarnicola et al.<sup>155</sup> found that the results of ESWT were comparable with those of surgical stabilization and bone graft for the treatment of carpal scaphoid pseudarthrosis.

Kuo et al.<sup>156</sup> reported that the success rate of ESWT was 63.6% in the treatment of atrophic nonunions of the femoral shaft and could be as high as 100% if applied within 12 months after the initial treatment. Poor results were associated with instability, a gap at the nonunion site of >5 mm, and atrophic nonunion.

As some Level-I and II evidence has demonstrated that the efficacy of ESWT is comparable with that of surgery for the treatment of nonunions<sup>152,154,155</sup>, and ESWT is practically free of adverse effects and more economic, it may progressively be considered as the first choice in the treatment of stable nonunions with a gap of <5 mm in long bones (Fig. 4). For bone treatment, the basic principles of acute fracture management should be implemented after F-ESWT (immobilization, casting, and weight-bearing restrictions).

ESWT seems to be an effective option in adult osteochondritis dissecans<sup>158-160</sup>, but further studies are required to determine long-term results.

### Economic and Administrative Considerations

We acknowledge that it is currently difficult to obtain reimbursement for ESWT in the United States. We hope that heightened awareness as to the efficacy of ESWT, as well as recognition of how ESWT can be a cost-saving measure, will lead to changes in reimbursement coverage.

Shockwave treatment is indicated when standard conservative treatment has failed, so its cost should be compared

with the cost of surgery. Dubs<sup>161</sup> compared the efficacy and costs of ESWT with the usual treatments for CTS. In addition to demonstrating that ESWT was more efficacious, it also allowed for an average savings of US\$2,000 per patient in comparison with alternative therapies.

Haake et al.<sup>162</sup> showed that the cost of treatment for CTS was between €2,700 and €4,300 per patient for ESWT compared with €13,400 to €23,450 for surgery and concluded that the cost of surgery was 5 to 7 times higher than ESWT. Ramón et al.<sup>163</sup> reported, in absolute numbers, a savings of approximately €2,000 per patient for ESWT compared with surgery for the treatment of calcifying tendinopathy of the shoulder.

### Overview

ESWT is considered to be an alternative to surgery for several chronic tendinopathies and nonunions because of its efficacy, safety, and noninvasiveness. The best evidence supporting the use of ESWT was obtained with low to medium levels of energy for tendon disorders as well as with a high energy level for tendon calcification and bone pathologies in a comprehensive rehabilitation framework.

Because of the variability in the treatment protocols, the methodological quality of many ESWT studies is limited. Further research from well-designed, high-quality studies is required to standardize the treatment parameters and demonstrate the optimal ESWT approach for health-care decision-making.

With adequate patient selection, appropriate indications, homogeneous ESWT therapeutic protocols, and proper application, ESWT could make a paramount contribution to noninvasive treatment of certain musculoskeletal disorders. ■

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