Systematic Review and Meta-Analysis

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# Effectiveness of extracorporeal shock wave therapy in patients with tennis elbow

## A meta-analysis of randomized controlled trials

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**Abstract**

**Background:** The aim of the present study was to investigate the effectiveness of Extracorporeal Shock Wave (ECSW) in the treatment of lateral epicondylitis (LE) of humerus.

**Hypothesis:** ECSW therapy in people with LE effectively reduces the pain and gains functional rehabilitation.

**Materials/Methods:** Databases of PubMed, EMBASE, Web of Science and the Cochrane Library from inception to April 2020 was searched to identify all relevant RCTs comparing ECSW therapy with any other conservative treatment, including injection and local anesthetic versus placebo or control in patients aged 18 with LE. The primary outcome is the mean overall pain score at 12 weeks after treatment. Another secondary outcome mainly included Thomsen test, 50% pain reduction, grip strength and adverse effect at 12 weeks after treatment.

**Results:** Nine studies were included in the meta-analysis. Compared with the placebo group, ECSW cannot significantly reduce the pain score (mean deviation [MD]=-4.23, 95% confidence interval [CI]: -8.78 to 0.32, $P=.07$), but make more people acquire 50% pain reduction (MD=1.38, 95% CI: 1.09 to 1.75, $P=.008$). There was no significant difference between ECSW and control in decreasing the pain score of Thomsen test (MD=-3.22, 95% CI: -14.06 to 7.62, $P=.56$). ECSW was more effective in Grip strength as compared with control at 12 weeks-3 months (MD=3.52, 95% CI: 2.43 to 4.60, $P<.00001$)

**Conclusions:** Results suggested that ECSW cannot effectively reduce the mean overall pain, but it showed more people acquire 50% pain reduction and might be a better option for the treatment of LE. Because of study limitations, additional high level of evidence, more rigorously designed large-samples and high-quality randomized controlled trials are needed to guide clinical practice.

**Abbreviations:** CI = confidence interval, ECSW = extracorporeal shock wave, LE = lateral epicondylitis, MD = mean deviation.

**Keywords:** extracorporeal shock wave therapy, lateral epicondylitis, meta-analysis

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What is Known?

- Conservative treatment is the common therapy for LE, including physiotherapy, eccentric exercises, acupuncture, topical nitrates, epicondylar elbow straps, drug injections and so on, while operative treatment is optional for those patients with severe or persistent symptoms. As an alternative conservative treatment, ECSW is efficient. But the mechanism is still not completely clear.

What is New?

- Our meta-analysis included 9 RCTs suggested that ECSW cannot effectively reduce the mean overall pain, but it showed more people acquire 50% pain reduction and might be a better option for the treatment of LE.

## 1. Introduction

The "Tennis Elbow", known as lateral epicondylitis (LE), is tendinosis that defined as chronic traumatic inflammatory and degenerative diseases of the origin of the common extensor of the forearm.[1] It mainly cause elbow pain, with the occurrence from 1% to 3% of the population, typically occuring among those between 30 and 64 years of age without gender distribution.[2] It generally affects the dominant upper-limb which engages in repetitive and forceful activity.[3] LE was also characterized by pain of the lateral elbow, which was caused by symptomatic minor instability of the lateral elbow condition with the presence of lateral ligamentous patholaxity of the elbow and 1 or multiple intra-articular abnormalities including synovitis and lateral capitellar chondropathy.[4,5] A number of different treatments can be used in patients with varying degrees of pain. Conservative treatment are consist of physiotherapy, eccentric exercises, laser therapy, acupuncture, topical nitrates, epicondylar elbow straps, and drug therapy which include injections of corticosteroid, botulinum toxin, autologous blood and platelet-rich plasma. 90% of patients acquire a wide array of possibilities with a rate of improvement in conservative treatment. Operative treatment is optional for those patients with severe or persistent symptoms that cannot be alleviated by a well performed conservative treatment, which include open, percutaneous and arthroscopic approaches. It is estimated that about 4% to 11% of patients ultimately undergo surgery.[6]

The obvious underlying cause of most LE cannot be identified. Some activities with long-term repetitive use of the extensor muscles of the forearm (for example tennis, lifting weights, holding the pot, wring clothes, manual work) may increase the risk of the tendinitis.[7,8] Some significant risk factors have been identified, such as smoking and obesity.[3] In spite of all of these considerate factors, there is a lack of knowledge to reveal the great variability of symptoms among patients. Recent studies have been proposed peripheral nerve irritation and local altered pain response.[9] Neck-Shoulder pain is the most common symptoms in the population of lateral humerus epicondylitis, but it can be associated with changes of biomechanics in upper-limb.[10]

As an alternative conservative treatment, the mechanism of extracorporeal shock wave (ECSW) is still not completely clear. The operator directly applied a specific frequency sonic wave generator onto surface skin of the origin of the common extensor. And ECSW therapy produces energy which promotes tissue healing and stimulates nerve fibers to release analgesic substance and applies this energy to the interface of 2 materials with different acoustic impedance to possibly relief pain. A systematic review conducted by Schmitz C suggested that ECSW has been proven as an effective and safe noninvasive treatment option for tendon and other pathologies of the musculoskeletal system.[11] The National Institute for Clinical Excellence had updated its guidelines to reflect this and the US Food and Drug Administration had approved the treatment for plantar fasciitis and LE.[12,13] Although there is still a controversy in the management of LE.[13–17]

To investigate the effectiveness of ECSW used in LE, this meta-analysis was conducted, of which the results will offer evidence-based information for clinicians to choose appropriate treatment methods for LE.

## 2. Materials and methods

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[18] Due to all included analyses were based on the data extracted from previous published studies, this study did not require an ethics committee approval and informed consent.

### 2.1. Search strategy

The most frequently used medical electronic databases, such as PubMed, EMBASE, Web of Science and the Cochrane Library from inception to April 2020, were searched by 2 of authors to identify all relevant RCTs comparing ECSW therapy with any other treatment except conservative treatment, including injection and local anesthetic versus placebo or control in patients aged 18-year -old patients with LE. We also expanded the scope of the search and supplemented it by manually searching the reference lists of previously published random trials and repetitive articles.

We performed a comprehensive and systematic retrieval by using the following keywords: (tennis elbows OR LE OR lateral humeral epicondylitis) AND (ECSW OR shock wave OR radial shock wave therapy OR ECSW OR ECSW therapy OR extracorporeal high-intensity focused ultrasound therapy OR HIFU therapy OR high-intensity focused ultrasound therapy).

### 2.2. Inclusion and exclusion

The inclusion criteria for the study were randomized controlled trials with regard to LE.

(1) Older than 18 years;
(2) Unilateral single-site LE;
(3) Mean duration of pain lasting more than 3 months;
(4) Pain induced by the pain had to be induced at least 2 of the following tests: Palpation of the lateral epicondyle, Resisted wrist extension (Thomsen test), Resisted finger extension, Chair test.
(5) No any other treatment including local anesthesia was given within 1 month before the shock-wave therapy began or during the course of this treatment.
(6) Articles only with English languages that reported at least 1 of the outcomes mentioned in the following section.

We excluded case reports, editorials, letters to the editor, review articles, and animal studies.

### 2.3. Study selection

The titles and abstracts of all studies from the above databases were independently reviewed by 2 authors of us to exclude irrelevant studies and distinguish potentially relevant articles after making a literature search by each author independently. For potentially eligible studies, the full text was reviewed by 2 authors according to the inclusion criteria. We also scanned the reference lists of the included articles to find any other studies that met the inclusion criteria. Differences of opinion were resolved through discussion, and the third author made comments if necessary.

### 2.4. Data extraction and outcome of interest

The data on study characteristics (first author, year of publication, randomization method, study design, sample size, mean age, gender, mean duration of pain, injury site, intervention type, the time of following and outcomes). was extracted by 2 authors independently. Data on the following outcome measures were included: Mean overall pain, Thomsen test, Grip strength, 50% pain reduction, Adverse event. Other clinical outcomes were not contained in this meta-analysis, because of either insufficient data or variable outcomes in the different studies.

### 2.5. Quality assessment and statistical analysis

This study was conformed to all Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines and reported the required information accordingly (see Supplementary Checklist, http://links.lww.com/MD/E561). The methodological quality of the studies was independently evaluated by 2 of us according to the modified Jadad quality scale. The modified Jadad quality scale consists of 6 items designed to evaluate randomization, blinding method, withdrawals and dropouts, inclusion and exclusion criteria, adverse effects, and statistical analysis. Scores of 8 to 4 represent excellent to good quality, whereas scores of 3 to 0 denote low to poor quality. If there is any disagreement, it should be resolved by discussion and consultation with senior authors. All calculations and analyses were performed using Review Manager 5.39 (Cochrane Collaboration, Oxford, UK). The publication bias of the included studies was assessed by inspecting the asymmetry and the effect size distribution on the funnel plot and by the Egger regression test. We would not proceed to the analysis of publication bias if the study number was less than 10.[19–21] Continuous variables including mean overall pain, Thomsen test, Grip strength were assessed using the mean difference, and dichotomous variables such as 50% pain reduction were evaluated by odds ratios. A $P<.05$ was considered to be statistically significant, and 95% confidence intervals (CIs) were reported. Homogeneity between the studies was assessed with the Q statistic set at $P<.10$ and the $I^2$ statistic was used to quantify heterogeneity and was set at $I^2>$ 50%. Methods were applied with a random-effects model if there was significant heterogeneity between studies; otherwise, a fixed-effects model was used.

## 3. Results

In total, 332 studies were identified according to the search strategy described above and 218 studies remained after exclusion of the duplicates. After scanning the titles and abstracts of the remaining studies, 65 studies need to be evaluated carefully. Finally, the full text of 9 RCTs was evaluated for eligibility and was included in the present meta-analysis.[16,22–29]. The process of the search strategy is shown in Figure 1.

All included studies described randomization. 5 RCTs mentioned random sequence generation; randomization was generated by the computer in 3 studies, a study random numbers and (or) a sealed/unmarked envelope in 2 studies; 4 studies of all included studies did not describe the randomization method. 6 of all included studies used double-blinding and single-blinding in 2 studies, the only 1 study had not been blinded to the treatment. Only 2 studies of all included studies were directly evaluated the level evidence. One is Therapeutic Level I, the other is 1B. Th analysis of the publication bias of the included studies was not proceed in the meta-analysis. because 1 study included was not mentioned were or were not blinded to treatment and the study number included was only 9. The overall scores of methodological quality of all studies were relatively high, with a mean score of $7\pm1.11$. The detailed items of the modified Jadad quality scale and study characteristics for the included studies are listed in Tables 1 and 2.

A total of 715 patients was conducted from the included studies, 4 studies compared ECSW with placebo for LE. 2 studies compared ECSW with sham, 1 studies compared ECSW with US. 1 study compared ECSW with laser, the remaining 1 study compared different doses of ECSW. The details of the intervention, the time of follow up and outcomes are listed in Table 3.

### 3.1. Meta-analysis of clinical outcome

#### 3.1.1. Mean overall pain.

4 of all included studies reported the mean pain score with visual analog scale (1–100 mm). There was slightly high heterogeneity among these 3 RCTs ($df=3$, $I^2=60\%$, $\chi^2=7.48$, $P=.06$). A random-effects model was used. The pooled results showed that Compared with placebo, the pain score was not significantly reduced after ECSW (mean deviation [MD]=-4.23, 95% CI: -8.78 to 0.32, $P=.07$), although it was very close to the $P$ value of .05 Figure 2.

#### 3.1.2. 50% pain reduction.

4 RCTs mentioned the rate of 50% reduction in pain at 3 months. There was low heterogeneity among these 4 RCTs (df=3, $I^2=41\%$, $\chi^2=5.06$, $P=.17$). There was a significant difference between ECSW and control in the rate of 50% reduction in pain (MD=1.38, 95% CI:1.09 to 1.75, $P=.008$) Figure 3.

### 3.2. Thomsen test

3 RCTs analyzed the mean pain score for Thomsen test following up at 12 weeks -3 months. (df=2, I2=69%, $\chi^2=6.39$, $P=.04$). A random-effects model was used because of the slightly significant heterogeneity was slightly significant. There was no significant difference between ECSW and control in decreasing the pain score of Thomsen test (MD=-3.22, 95% CI: -14.06 to 7.62, $P=.56$) Figure 4.

### 3.3. Grip strength

OF the 9 included studies, 3 reported the effect on Grip strength. There was low heterogeneity among these 3 RCTs (df=2, I2= 0%, $\chi^2=0.67$, $P=.72$). The meta-analysis finds ECSW was more effective in Grip strength as compared with control at 12 weeks-3 months (MD=3.52, 95% CI: 2.43 to 4.60, $P<.00001$) Figure 5.

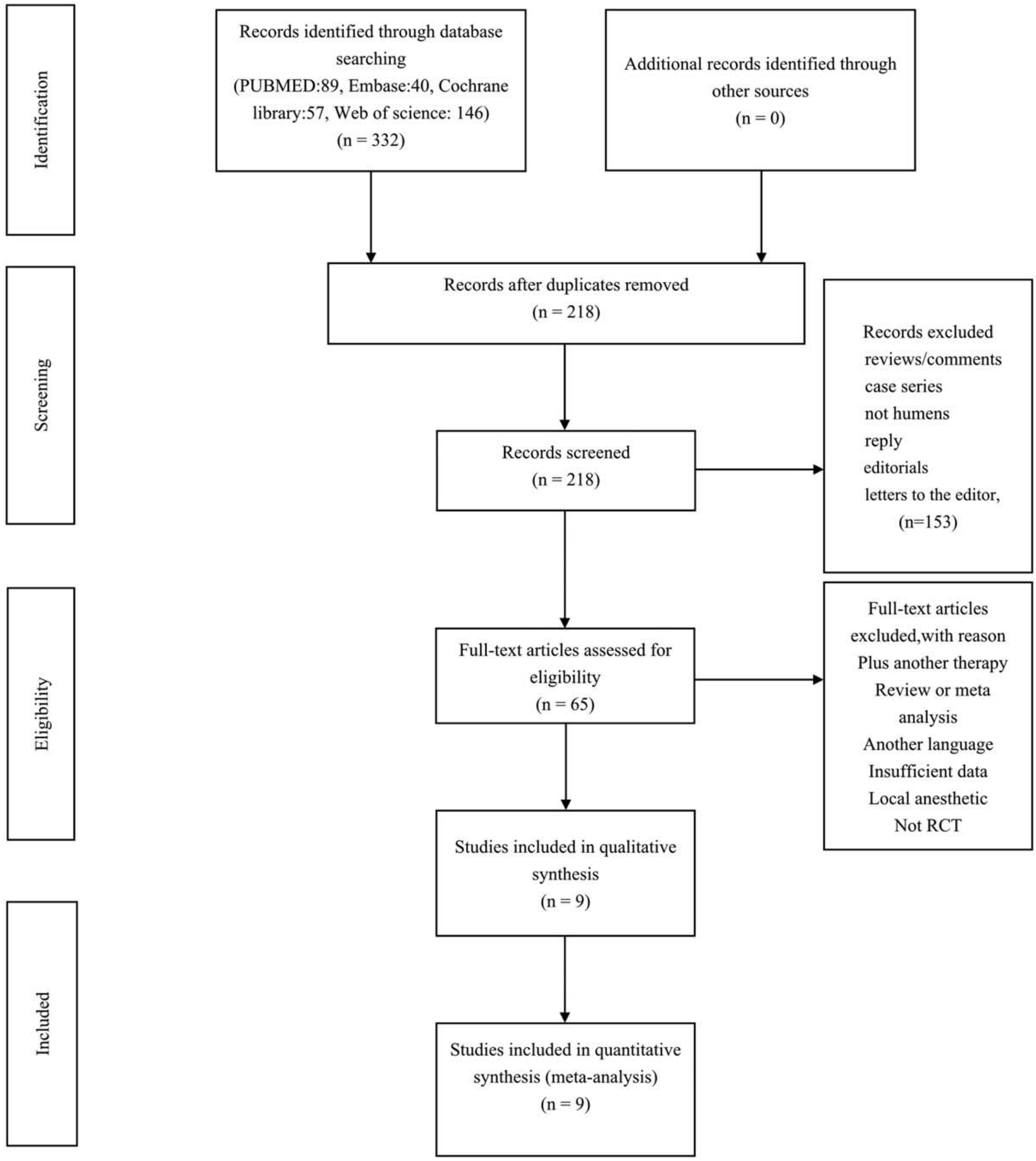


**Figure 1.** Flow diagram of studies identified, included, and excluded according to the format of Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

### *3.4. Adverse event*

Of all included studies, 4 trials reported some adverse events or complications. Pettrone FA reported 5 common adverse effects related to the ECSW: Pain, nausea, local reaction, sweating, dizziness, which are was transient. Staple M reported participants in the ECSW group reported increased pain, bruising or red spots, or a burning sensation in the arm following treatment. Vulpiani MC showed that all ECSW Group patients experienced pain at the limit of tolerability, but they ceased immediately after treatment. Collins ED reported some most common complications including localized swelling, bruising or petechia at the treatment site, as well as reactions to anesthetic agents during or shortly after treatment.

## 4. Discussion

The main findings of the study is to relieve pain, maintain movement, improve grip strength and endurance, and restore normal function. Several studies showed that ECSW is effective in the treatment of chronic persistent LE.[30–32] Mehra et al[33] think that the mobile lithotripter of the Electro Medical Systems is an effective way of treating tennis elbow and plantar fasciitis. Yang et al[34] study showed that ECSW using the Swiss DolorClast Master in addition to physical therapy had better and faster pain reduction, grip strength increase, and functional improvement in patients with LE than those who received physical therapy only. Lee et al[35] also consider that ECSW by using Dolarclast can improve as much as the local steroid injection group as a

**Table 1**

**Characteristics of included studies. The characteristics of included studies consists of first author, year of publication, randomization method, study design, sample size, mean age, gender, mean duration of pain, injury site.**

| studies/year | randomized method | study design | sample size | group | Number (female/male) | mean age, yr (range/SD) | mean duration of pain | site (left/right) |
|---|---|---|---|---|---|---|---|---|
| Pettrone et al,[17], 2005 | a unique study number | A randomized, multicenter, double-blind, | 114 | active group | 56 | 47 | 21 mo | 38/76 |
| | and a sealed envelope | controlled, parallel treatment protocol | | placebo group | 58 | | | |
| Speed et al[14], 2002 | NS | A double-blind placebo controlled trial | 75 | ESWT group | 40 (21/19) | 46.5 (26–70) | 15.9 (3–42) mo | NS |
| | | | | shame group | 35 (21/14) | 48.2 (31–65) | 12 (3–40) mo | NS |
| Staples et al[19], 2008 | computer-generated | A double-blind, randomized, placebo-controlled trial | 68 | ESWT group | 36 (14/19) | 49.8 (7.4) | 52.6 (64.3/10–300) wk | 8//25 |
| | | | | placebo group | 32 (12/18) | 49.1 (8.8) | 68.0 (98.8/6–520) wk | 10//20 |
| D'Vaz et al[18], 2006 | a table of random numbers | A double-blind randomized | 59 | active group | 29 (8//11) | 51 (45–57) | 8 (4–36) mo | 19//10 |
| | | controlled trial | | placebo group | 30 (17/13) | 50 (46–57) | 9 (3–48) mo | 24//1 |
| Vulpiani et al[23], 2015 | a computer-generated | A single-blinded, randomized, controlled study | 80 | ESWT group | 40 (11/29) | 49.7 (25–74/9.9) | 5.5 (1.5/4–8) mo | 11//29 |
| | | | | Cryo-US Group | 40 (16/24) | 53.4 (32–75/10.8) | 6 (1.5/4–8) mo | 11//29 |
| Capan et al[24], 2016 | a computer-generated | A double-blind, randomized, placebo-controlled trial | 56 | rESWT group | 28 (20/8) | 48.4 (33–66/9.0) | 7.9 (5.2) mo | 10//13 |
| | | | | sham reswt group | 28 (24/4) | 46.2 (33–57/7.4) | 7.7 (5.2) mo | 5//17 |
| Collins et al[21], 2011 | NS | A double-blind, randomized, controlled study | 183 | Active group | 93 (47/46) | 44 (22–66/7.61) | 684 d (1.9 yr) | NS |
| | | | | placebo group | 90 (49/41) | 46 (32–71/7.52) | 784 d (2.1 yr) | NS |
| Sabeti et al[20], 2008 | NS | A prospective, randomized, single blind pilot | 20 | ESWT group | 10 | 44.9 (10.4) | longer than 6 mo | NS |
| | | controlled study trial | | ESWT group | 10 | 48.0 (9.8) | | NS |
| Devrimse et al[22], 2014 | NS | NS | 60 | ESWT group | 30 (22/8) | 37.76 (8.52) | 14.16 (7.06/5–31) mo | 6//24 |
| | | | | laser group | 30 (20/10) | 40.30 (10.00) | 13.43 (7.46/4–33) mo | 8//22 |

Cryo-US = cryoultrasound, NS = not stated, rESWT = radial extracorporeal shock wave, SD = standard deviation.

treatment for medial and LE and it can be a useful treatment option in patients for whom local steroid injection is difficult.

Because most patients can well tolerate the treatment of ECSW. There was no need for local anesthesia for the levels of ECSW used in this study and most patients experienced comfort.[30–32] Surgery is optional for patients who unsuccessful to respond to conservative treatments. Patients with persistent pain and disability after a progress of well-performed conservative treatment needed to be clinically re-evaluated and, possibly, further operative treatment. Although surgery has a good outcome in most patients, the associated complications, such as infection, hematoma and nerve injury, temporary paresthesia.[36,37] And the not uncommon treatment failure have made the exploration of alternative treatment methods inevitable. ECSW is an alternative treatment for patients who do not benefit from conservative treatment and refuse surgical treatment.[38]

**Table 2**

**The modified Jadad quality of included studies. Jadad quality is a procedure to independently assess the methodological quality of a clinical trial included in this meta-analysis. The modified Jadad quality scale consists of 6 items designed to evaluate randomization, blinding method, withdrawals and dropouts, inclusion and exclusion criteria, adverse effects, and statistical analysis.**

| Scale item | Response option | Pettrone et al,[17] 2005 | Speed et al,[14] 2002 | Staples et al,[19] 2008 | D'Vaz et al,[18] 2006 | Vulpiani et al,[23] 2015 | Capan et al,[24] 2016 | Collins et al,[21] 2011 | Sabeti et al,[20] 2008 | Devrimse et al,[22] 2014 |
|---|---|---|---|---|---|---|---|---|---|---|
| 1. Was the study described as randomized? | Yes, appropriate (2) | ✓ | | ✓ | ✓ | ✓ | ✓ | | | |
| | Yes, unclear (1) | | ✓ | | | | | ✓ | ✓ | ✓ |
| | No, inappropriate (0) | | | | | | | | | |
| 2. Was the study described as blind? | Yes, appropriate (2) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | |
| | Yes, unclear (1) | | | | | | | | | |
| | No, inappropriate (0) | | | | | | | | | |
| 3. Was there a description of withdrawals and dropouts? | Yes, (1) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| | No, (0) | | | | | | | | | |
| 4. Was there a clear description of the inclusion or exclusion criteria? | Yes, (1) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| | No, (0) | | | | | | | | | |
| 5. Was the method used to assess adverse effects described? | Yes, (1) | ✓ | | ✓ | ✓ | ✓ | | ✓ | | ✓ |
| | No, (0) | | ✓ | | | | ✓ | | ✓ | |
| 6. Were the methods of statistical analysis described? | Yes, (1) | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| | No, (0) | | | | | | | | | |
| Total score | | 8 | 6 | 8 | 8 | 8 | 7 | 7 | 6 | 5 |

**Table 3**

**Characteristics of included studies. The characteristics of included studies consists of intervention type, the time of following and outcomes.**

| Studies/year | Group | Intervention | The time of follow up | Outcomes |
|---|---|---|---|---|
| Pettrone et al,[17]2005 | Active group | 2000 impulses at 0.06 mJ/mm$^2$, 1 treatment each wk for 3 wk | Follow-up before treatment and at 1, 4, 8 | 1. pain investigate<br>2. functional scale<br>3. activityimpression |
| | Placebo group | 2000 impulses at 0.06 mJ/mm$^2$ with sound-reflecting pad, 1 treatment each wk for 3 wk | 12 wk and at 6, 12 mo | 4. overall impression<br>5. grip strengththe<br>6. Device-Related Adverse Events |
| Speed et al,[14] 2002 | ESWT group | 1500 pulses at 0.18 mJ/mm2, received 3 ESWT at monthly intervals | Follow-up at baseline, 1, 2, 3 mo | 1. VAS<br>2. night pain |
| | Shame group | minimal energy pulses (0.04 mJ/mm2), received 3 ESWT at monthly intervals | 3.50% satisfaction | |
| Staples et al,[19] 2008 | ESWT group | 1062 mJ/mm2, 0.56 mJ/mm2 (SD 0.27, range (0.10–1.22), a total of 3 treatments given at weekly | Follow-up at baseline, at 6 wk, 3 mo, | 1. VAS<br>2. overall functional level of the upper limb<br>3. the presence or absence of discomfort in daily<br>4. upper extremity disability and syntom |
| | Placebo group | total dose received by the placebo group was 6.0 mJ/mm2 | and 6 mo after treatment. | 5. general quality of life<br>6. maximum pain -free grip strength<br>7. Adverse Events |
| D'Vaz et al,[18] 2006 | Active group | low intensity (30 mW/cm2), 1.5MHz ultrasound signal modulated by an ON/OFF square function, daily for 20 min over a 12-week period | Follow up at baseline and 6 and 12 wk | 1. VAS<br>2. the percentage change for the pain VAS and PREFQ outcome measures |
| | Placebo group | did not emit an ultrasound signal | | 3. difference in percentage reduction in grip strength<br>4. Compliance with the device |
| Vulpiani et, al[23] 2015 | ESWT group | 2400 pulses from 0.14 and 0.20 mJ/mm$^2$, 3 sessions with a time interval between sessions spanning between 48 and 72 h | Follow up before treatment and at 3, 6 | 1. VAS<br>2. achieved at least 50% satisfactory results |
| | Cryo-US Group | an ultrasound emission power rating of 1,8 Watt/cm$^2$, and a temperature of -2°C, a total of 12 sessions each in 3 wk (4 sessions per wk) | and 12 mo | 3. side effect |
| Capan et al,[24] 2016 | rESWT group | a total dose of 2000 pulses of 10 Hz frequency at a 1.8 bar of air pressure in each session. once weekly for 3 consecutive weeks a total of 3 sessions | Follow up before treatment and at 1 and | 1. VAS<br>2. Roles and Maudsley Score |
| | Sham reswt group | the same contact gel was applied to the same area; however, the contact of the applicator head with the skin covered by the gel was avoided. | 3 mo | 3. Patient-Rated Tennis Elbow Evaluation<br>4. Grip Strength |
| Collins et al,[21] 2011 | Active group | 1500 shocks delivered at a power setting of 18 KV by ESW | follow up at Baseline, 4, 8, 12wk | 1. status of "success"<br>2. VAS<br>3. Use of pain medications<br>4. SF-36 Health Survey Questionnaire |
| | Placebo group | a fluid-filled IV bag against the coupling membrane of the shock head to mimic the feel of the coupling membrane, the 1500 shocks were then delivered | and 6, 12 mo | 5. Resisted wrist extension (Thomsen test)<br>6. Resisted finger extension<br>7. complications |
| Sabeti et al,[20] 2008 | ESWT group | 1 000 impulses at each session, adapted to the patients pain tolerance (0.012 – 0.1mJ / mm$^2$), 3 times with an interval of 1 wk | follow up at 0, 6, 12 wk | 1. Tested Variables |
| | ESWT group | 2000 impulses at each session, adapted to the patients pain tolerance (0.012 – 0.1mJ / mm2), 3 times with an interval of 1 wk | | Dynamometer Chair Test Mid-fi nger Extension Test Pain under local pressure Thomsen Test Pain in activities of daily life and Pain during night) |
| Devrimse et al,[22] 2014 | ESWT group | 2000 shock waves, 3 times in 3 wk, a 1-wk interval | follow up before treatment and the 4th | 1. lateral epicondyle tenderness |
| | laser therapy | 10 sessions of lowdose-regimen laser therapy with 3.6 joule intensity, 500 Hz frequency, and 850 nm wavelength, 40 s in each session | and 12th wk | 2. HGS<br>3. VAS<br>4. SF-MPQ |

HGS = hand grip strength, PREFQ = the patient-related forearm evaluation questionnaire, SF-MPQ = the short-form McGill pain questionnaire, VAS = visual analog scale.

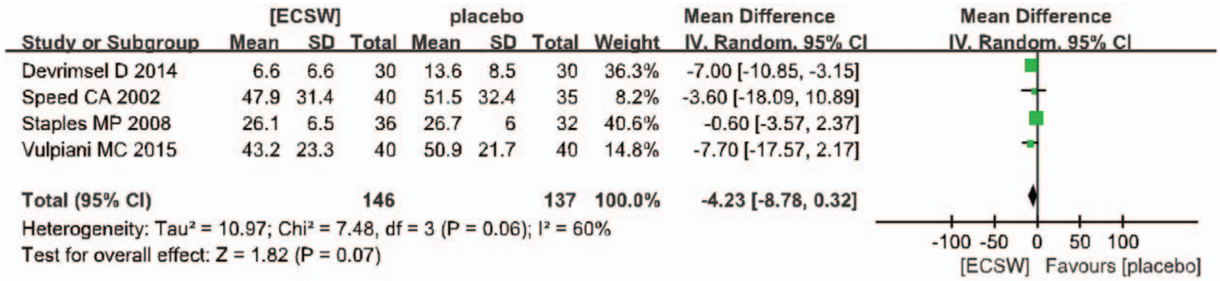


**Figure 2.** Forest plot and meta-analysis of mean overall pain. CI = confidence interval, IV = inverse variance methods, SD = standard deviation.

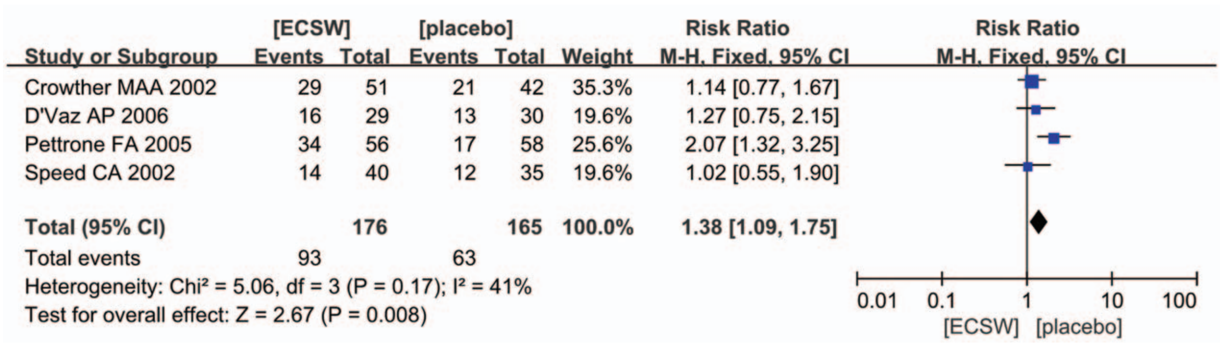


**Figure 3.** Forest plot and meta-analysis of 50% pain reduction. CI = confidence interval, IV = inverse variance methods, SD = standard deviation.

Although adverse events including (reddening of the skin, hematoma, pain, Nausea, sweating, dizziness, local ration and so on) can be caused by ECSW, no lasting adverse effects were found, and all of these events had resolved by the final follow-up evaluation.[22]

Vibration generated by Shock waves gives rise to the interaction of particles between tissues and blood, stimulating the circulation of blood. It has also been documented by other investigators that application of low-energy extracorporeal shockwave therapy leads to pain relief by direct stimulation of

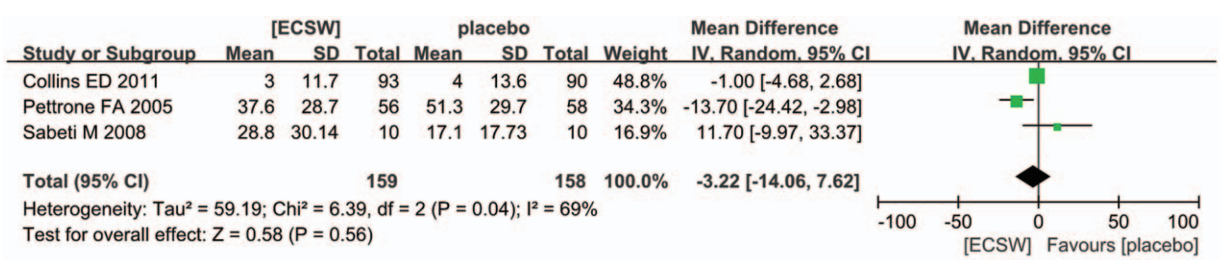


**Figure 4.** Forest plot and meta-analysis of Thomsen test. CI = confidence interval, IV = inverse variance methods, SD = standard deviation.

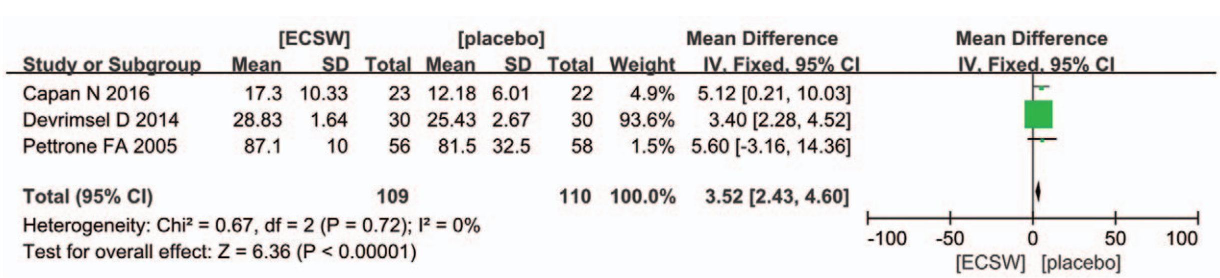


**Figure 5.** Forest plot and meta-analysis of Grip strength. CI = confidence interval, IV = inverse variance methods, SD = standard deviation.

the healing process, neovascularization, disintegration of calcium, and neural effect. ECSW also stimulates tissues to form new blood vessels and can increase the number of tissue growth factors.[39] These may involve alterations of the cell membrane permeability, preventing the development of potentials to transmit painful stimuli, direct suppressive effects on nociceptors, and hyperstimulation mechanism that blocks the gate control mechanism. Based on the above mechanism, we can suggest that ECSW provides a good and suitable environment for wound healing. ECSW may also inhibit pain impulse conduction, chemically alter pain receptor neurotransmission to prevent pain perception, and provide analgesia by physically change axons.[40]

The results of this meta-analysis suggest that ECSW treatment cannot significantly reduce the mean overall pain and pain in Thomsen test, comparing with place or control group; however, it can significantly more effective increase grip strength score. It showed statistically significant differences in the 50% pain reduction between ECSW group and placebo.

The most common presenting symptom of LE is a pain, which is the most frequently used outcome measure in clinical trials. therefore, the mean overall pain score is our primary. The present meta-analysis suggested that the mean overall pain was no significant difference between the 2 groups, although the result was almost near significant value. The results were consistent with several recent high quality, prospective, randomized trials of ECSW therapy, which did not find significant results.[13–17] Chung and Wiley recently evaluated ECSW therapy as a primary treatment of previously untreated LE of humerus in a double-blind, placebo-controlled trial.[17] Despite the improvement in pain scores within groups, there does not appear to be a meaningful difference between treating LE with ECSW therapy combined with sham ECSW with respect to resolving pain within an 8-week period of commencing treatment. Melikyan et al[41] evaluated the efficacy of extracorporeal shock-wave therapy for tennis elbow by using a single fractionated dosage in a randomized, double-blind study and showed that all patients improved significantly over time, regardless of treatment, but their study showed no evidence that extracorporeal shock-wave therapy for tennis elbow is better than placebo. There was slightly high heterogeneity among these 3 RCTs, the reason for this significant heterogeneity is difference protocol including focused waves, radial waves, lasting of treatment, frequency of treatment, a dose of treatment and different treatment methods in the control group.

Another secondary outcome mainly included Thomsen test, 50% pain reduction, grip strength, and adverse effect. The present meta-analysis results also suggested that there was a significant difference was present in the 50% pain reduction between the ECSW and placebo groups. Crowther et al[42] also reported a similarly result that after 3 months, 84% of patients in group 1 were considered to have had successful treatment compared with 60% in group 2, although he undertook a prospective, randomized study to compare the analgesic effect of injection of steroid and of extracorporeal shock-wave therapy (ECSW) for tennis elbow.

With the shoulder flexed to 60°, the elbow extended, the forearm pronated and the wrist extended about 30°, the pressure is applied to the dorsum of the second and third metacarpal bones in the direction of flexion and ulnar deviation to stress the extensor carpi radialis brevis and long, that is Thomsen test. Rompe et al[14] report a controlled, prospective study to investigate the effect of treatment by low-energy ECSWs on pain in tennis elbow and showed that there was significant relief of pain after 3, 6, 24 weeks between the 2 group. However, there was significant heterogeneity. the major factors that cause heterogeneity are diverse ECSW protocols and interval time of treatment.

In our meta-analysis, there were clinically significant differences between ECSW and placebo in Grip strength in our meta-analysis. Some studies also reported the same result.[14,25,43,44] Spacca et al[43] conducted a prospective randomized control single-blind study and found pain-free grip strength test scores has a significant difference comparing study group versus the control group. Two trials showed that there was no statistically significant difference between active and placebo groups, comparing ECSW with acupuncture therapy or low-dose ECSW therapy with local anesthesia in a randomized, double-blind, placebo-controlled trial.[45,46] From the above researches, there appears to be a clinically important difference in the treatment of LE with ECSW and a treatment for the treatment of LE.

### 4.1. Study limitations

The present meta-analysis has its own limitations. First, this meta-analysis included a relatively small sample size with 9 RCTs, a lack of sufficient data to draw powerful comparisons and analysis. Second, included RCTs adverse protocols for example, some used focused waves while others used radial waves; difference lasting of treatment, frequency of treatment, dose of treatment and different treatment methods in the control group; the strength and length of the waves and number of shocks delivered among the RCTs, which could potentially make the results controversy and cause the analysis of these outcomes. high statistical heterogeneity among all the included RCTs, although these included RCTs had relatively high methodological quality. Fourth, any subgroup analysis was performed due to no adequate outcome of the subgroup in these studies; this difference in definition probably increased the heterogeneity.

## 5. Conclusions

Results of the present study suggested that ECSW cannot effectively reduce the mean overall pain, but it showed that more people acquire 50% pain reduction. There appears to be a clinically important and significance difference in the treatment of LE with ECSW and might be better than others treatment such as injection and local anesthetic versus placebo for LE. Because of study limitations, additional high level of evidence, more rigorously designed large-samples and high-quality randomized controlled trials are needed to guide clinical practice.

## Author contributions

Donjie Zeng and Chenxiao Zheng designed, performed and analyzed the research and wrote the manuscript.
Donjie Zeng, Jiayi Chen and Sijing Liu advised on article inclusion and exclusion.
Jiayi Chen and Sijing Liu designed the Tables and fiures.
Chenxiao Zheng, Donjie Zeng, Jiayi Chen, Jianyi Li, Zhaohai Ruan and Wusheng Liang read and revised the manuscript.
All authors read and approved the final manuscript.

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