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# High-energy focused extracorporeal shock wave therapy for bone marrow edema syndrome of the hip

## A retrospective study

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**Abstract**

The objective of this retrospective study was to evaluate the efficacy of high-energy focused extracorporeal shock wave therapy (HF-ESWT) on painful bone marrow edema syndrome (BMES) of the hip and shorten the natural course of disease.

Thirty-four consecutive patients with BMES of the hip were treated with HF-ESWT in our department between August 2017and July 2018. The progression and treatment results of BMES were evaluated by imaging examination and clinical outcomes. The clinical outcomes include hip pain and function which were measured using the visual analog scale (VAS) and Harris hip score (HHS), respectively, and the VAS and HHS of all patients were calculated and evaluated before treatment (s0), at 1 month (s1), 3 months (s2), 6 months (s3)post-treatment. Imaging examination including Pelvic radiographs and frog views and double hip magnetic resonance imaging (MRI) were also obtained and scheduled before treatment, at 1, 3, 6, and the final follow-up post-treatment to exclude avascular necrosis and other pathology.

All patients successfully completed the treatment and follow-up. Compared with pretherapy, the pain was alleviated to varying degrees and the HHS was significantly improved, and the VAS was significantly reduced at S1–2 (1- and 3-months post-treatment) after therapeutic intervention ($P < .05$). The mean improvements were strongly statistically significant between S0 and S1 and between S1 andS2 ($P < .0001$) and less significant between S2 and S3 ($P < .01$). The mean improvement between 6 months (S3) and final follow-up (more than 12 months) was not statistically significant. The MRI findings demonstrated that the diffuse BMES in the femoral head and neck disappeared completely.

HF-ESWT is a safe, effective, reliable, and noninvasive treatment in patients with painful BMES of the hip, and it can accelerate the recovery of BMES of the hip, shorten the treatment time and course of disease, improve hip joint function and the quality of life of patients.

**Abbreviations:** BMES = bone marrow edema syndrome, ESWT = extracorporeal shock wave therapy, HF-ESWT = high-energy focused extracorporeal shock wave therapy, HHS = Harris hip score, MRI = magnetic resonance imaging, ONFH = osteonecrosis of the femoral head, SD = standard deviations, VAS = visual analog scale.

**Keywords:** bone marrow edema syndrome, extracorporeal shock wave therapy, hip

## 1. Introduction

The bone marrow edema syndrome (BMES), which is also referred to as "transient osteoporosis", "transitory demineralization" and "migratory osteolysis", is a kind of self- limiting disease with unclear etiology, which mainly occurs in the main weight-bearing joints of lower limbs including hip, knee, foot, and ankle, among which the hip joint is more common.[1–4] The natural time course for improvement of clinical symptoms and normalization in MRI lasts from 3 to 18 months.[5] And that

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*All ICMJE Conflict of Interest Forms for authors are on file with the publication and can be viewed on request. Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained. This work was performed at Medical Center of Hip, Luoyang Orthopedic-Traumatological Hospital, Luoyang, China.*

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BMES of the hip is normally spontaneously self-limiting within 4 to 24 months.[6] In general, at present, there are many treatments for BMES of the hip, which can be divided into surgical treatment (Core decompression) and non-surgical treatment. And there is controversy regarding whether treatment should be conservative or invasive, so, there is no gold standard for the treatment of BMES of the hip.

Traditionally conservative treatments usually consists of avoiding load on the hips, physical therapy, analgesics as well as the use of nonsteroidal anti-inflammatory drugs, bisphosphonates, and vasoactive prostacyclin analog drugs like iloprost, and blood-activating and stasis-removing drugs, which can improve local hemodynamic characteristics.[7–11] Unfortunately, given that the cause of the disease is not well understood, these traditional treatments sometimes do not effectively relieve pain and shorten recovery time, what is worse is that some patients have gradually worsened and even developed avascular necrosis of the femoral head. Marrow core decompression is a common surgical method at present, which reduces pain through relief of intraosseous pressure, and it has been shown to provide symptom relief within 4 weeks.[12,13] But at the same time, there are some common complications,[13,14] and for many Chinese, it is still an unacceptable treatment. Therefore, it is necessary to have a new effective and safe non-invasive therapy between surgery and non-surgery.

Extracorporeal shock wave therapy (ESWT) has proved to be effective in treating musculoskeletal disorders due to its angiogenic, analgesic and anti-inflammatory effects.[15] More specifically, clinical trials also highlight their effectiveness in treating the early stages of osteonecrosis of the femoral head (ONFH), reducing the bone edema and pain and improving the function of the hip.[16–18] Moreover, recent studies have shown the highlighted the efficacy of using ESWT in the treatment of nonunion of fractures.[19,20]

Given these considerations, we hypothesized that high-energy focused extracorporeal shock wave therapy (HF-ESWT) could accelerate the resolution of the bone edema, shorten the natural course of this disease and result in rapid pain relief and functional improvement of the affected hip with BME and observe its possible complications.

## 2. Patients and methods

From August 2017 and July 2018, 34 patients suffered with BMES of the hip joint were recruited to participate in this study. Written informed consent was obtained from each patient, and the study was approved by the institutional review board (20190081). The patients included 23 men (67.65%) and 11 women (32.35%). The average age was 39.4 years (range, 19–56 years), Table 1. The inclusion criterion for the study was the presence of acute hip pain associated with a bone marrow lesion and typical MR imaging findings: bone marrow edema and joint effusion without necrosis (a hypointense area on T1-weighted sequences and a hyperintense area on T2-weighted sequences). Exclusion criteria were BMES with any MRI finding of avascular necrosis, defined as a crescent area in the subchondral bone (low-intensity signal subchondral area on T1-weighted sequences); Hip dysplasia with bone marrow edema, advanced osteoarthritis of the hip (Ahlback's grade 3 or 4); systemic conditions such as rheumatoid arthritis, autoimmune diseases, or tumors; patients who had contraindicate for ESWT were also excluded.

**Table 1**

**Patient characteristics.**

| Characteristic | n(34) |
|---|---|
| Males (n %) | 23 (67.65%) |
| Females (n %) | 11 (32.35%) |
| Age (years) Mean ± SD | 39.4 ± 2.4 |
| BMI(Kg/m$^2$) Mean ± SD | 24.3 ± 3.2 |
| Preoperative VAS Mean ± SD | 6.14 ± 1.25 |
| Preoperative HHS Mean ± SD | 72.25 ± 5.23 |
| TC Mean ± SD | 5.25 ± 0.69 |
| TG Mean ± SD | 2.13 ± 0.52 |
| HDL-C Mean ± SD | 0.92 ± 0.26 |
| LDL-C Mean ± SD | 3.17 ± 0.46 |

BMI = Body Mass Index, HDL-C = high-density lipoprotein cholesterol, HHS = Harris hip score, LDL-C = low-density lipoprotein cholesterol, TC = total cholesterol, TG = triglyceride, VAS = Visual Analog scale.

Patients underwent HF-ESWT using a shock wave (SW) electromagnetic source (Dornier Compact DeltaII, Dornier MedTech GmbH, Wessling, Germany) fitted with an C-arm perspective machine device which can achieve precise localization, real-time monitoring of the impact site and recording the impact energy value in the treatment process as shown in Figures 1 and 2 and followed a protocol: On the first day of hospitalization, the patient -related examination was completed, and the patients were screened. The SW treatment was started on the second day. It was performed every 3 days for a total of 3 treatments. At each treatment session, 4 to 5 treatment points were selected and each treatment point was impacted 500 shocks, and total 2500 to 4000 shots were applied with a flux energy density of 0.50 mJ/mm$^2$. One treatment course was 10 days for a total of 2 treatments. The treatment interval is 20 to 30 days, for a total of 8 weeks. Patients were instructed to avoid weight bearing with the use of 2 crutches until partial or full weight bearing was tolerated and did not cause worsening of the pain. Laboratory tests suggest that patients with hyperlipidemia should be given symptomatic treatment with oral A-lipid- lowering drugs. The patients were followed and examined and evaluated by the same physician. Pain was calculated through the Visual Analog Scale (VAS) in millimeters, ranging from 0 to 100 mm and measuring subjective pain and discomfort felt by the patient, 0 mm being pain-free and 100 mm being unbearable pain. Clinical functional assessment was made by the Harris Hip Scores (HHS). VAS and HHS of all patients were calculated and evaluated before treatment (s0), at 1 months (s1), 3 months (s2), 6 months (s3) post-treatment. Imaging examination including Pelvic radiographs and frog views and double hip MRI were also obtained and scheduled before treatment, at 1, 3, 6, and the final follow-up (more than 12 months) post-treatment to exclude avascular necrosis and other pathology. An experienced radiologist calculated the area of edema on one slide with the most obvious edema on both the sagittal and coronal planes, in mm$^2$ on fat-suppressed fast spin echo T2W sequences using the PACS software (Kodak version 11.0, MA) to verify whether the edema lesion showed unchanged, reduced or regressed completely.

### 2.1. Statistical analysis

The clinical data of patients were analyzed by SPSS 19.0 software (Chicago, IL). The mean and standard deviations (SD) were calculated for the HHS and VAS values at each of the four time points (S0 through to S3). The area of BME on MR images were

**Figure 1.** High-energy focused extracorporeal shock wave therapy equipment used in the current study (Dornier Compact Deltall, Dornier MedTech GmbH, Wessling, Germany).

also calculated with means and SD. Student *T* Test was used to calculate differences between values and a probability (*P*) value $<.05$ was considered to be of statistical significance.

## 3. Results

All patients successfully completed the treatment and follow-up and 5 patients developed subcutaneous congestion points after treatment, but all disappeared completely within 1 week, and there were no other side effects. Compared with pretherapy (S0), the pain was alleviated to varying degrees and the HHS was significantly improved, and the VAS was significantly reduced at S1–2 (1- and 3-months post-treatment) after therapeutic intervention ($P<.05$). In the VAS and HHS score during the peri-treatment time, the mean improvement between S0 and S1, S2, S3, and between S1 and S2 had significant statistical significance ($P<.05$), and the HHS of S1 and S3 also had significant statistical significance ($P<.05$), while the mean VAS and HHS improvement between S2 and S3 had no significant statistical significance (Fig. 3).

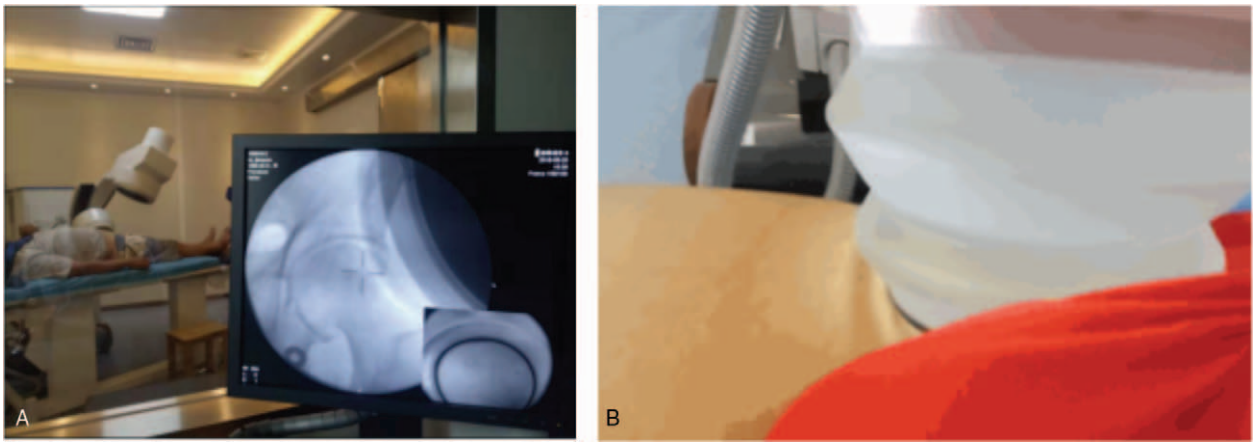


**Figure 2.** Extracorporeal shock wave photograph with A. Precise localization, B. Real-time monitoring of the impact site.

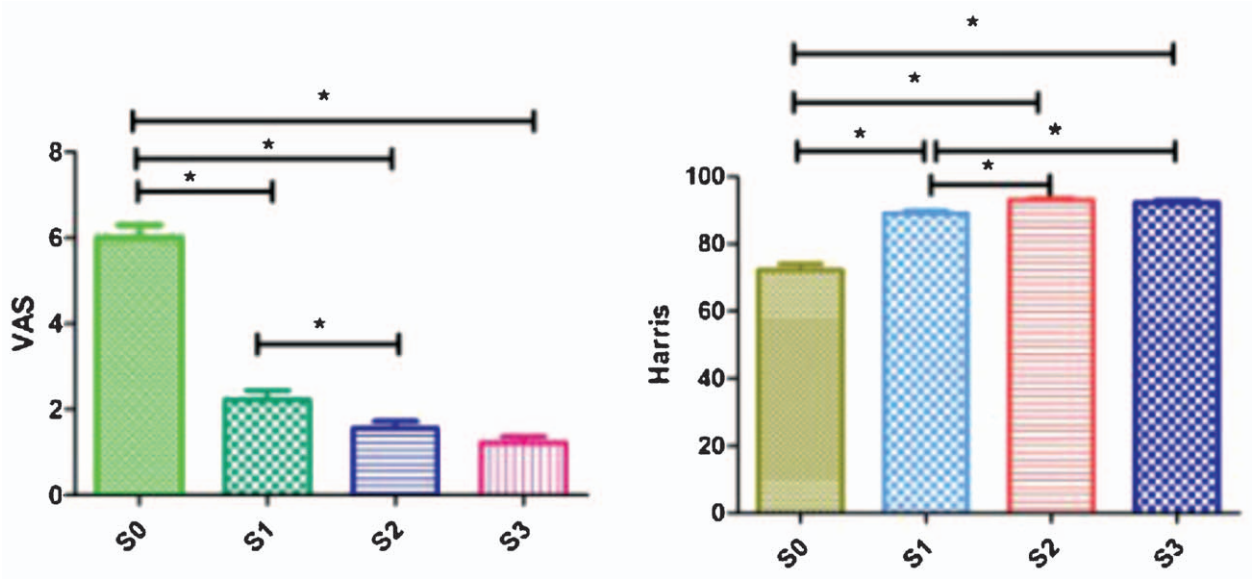


**Figure 3.** The peri-treatment time.

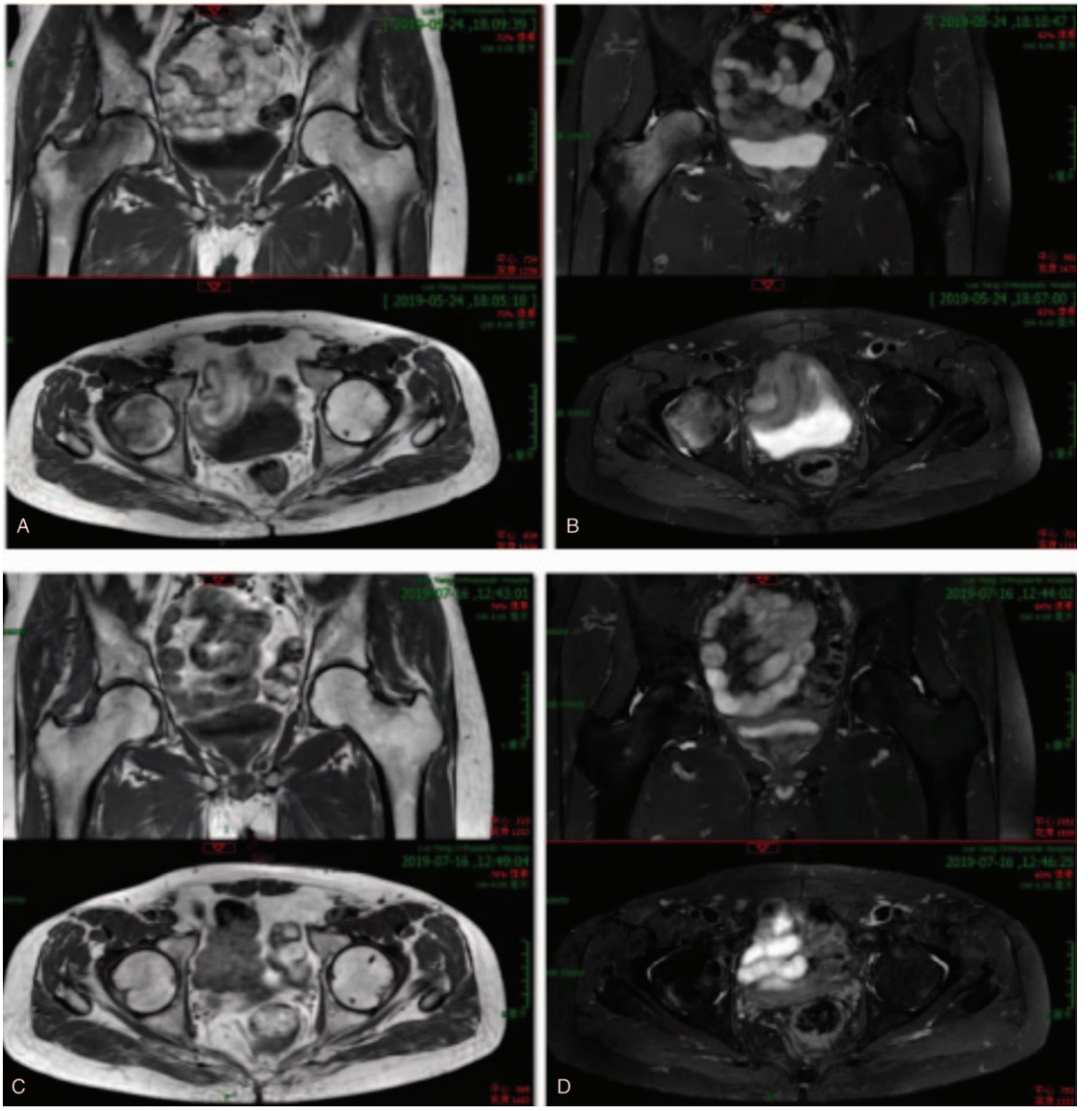


**Figure 4.** The pretherapy MRI (A,B) showing a large BME within the right hip. The MRI of 1.5 months posttreatment (C,D) showing reduction in the diffuse hyperintense signal of the femoral head and neck disappeared basically, and only a small amount of fluid remained in the hip joint cavity.

BMES in femoral head and neck of patients was typical after one course of treatment. The MRI findings demonstrated that the diffuse BME in the femoral head and neck disappeared basically.

BMES of the right hip was diagnosed by MRI in a 34-year-old, male, who had been treated with oral non-steroidal anti-inflammatory drugs and bisphosphonates for 3 weeks, and the pain has not improved significantly and underwent three treatments in our hospital. After 15 days, the symptoms of hip pain basically disappeared, the function of hip joint returned to normal. After 1.5 months, the results of MRI showed that the edema of femoral head and neck was basically eliminated (Fig. 4). The VAS score dropped from 7 points preoperatively to 1 point and the HHS score increased from 61 points preoperatively to 94 points post-treatment.

## 4. Discussion

BMES is a rare condition of unclear etiology that is characterized by hip pain, limited osteopenia on plain radiography, and characteristic MRI findings. At present, the etiology and pathogenesis of bone marrow edema are still under study, and scholars have put forward a variety of theories. Among the many doctrines, the ischemic injury theory has received more support, but its specific mechanism remains unclear. Berger reported on the familial occurrence of transient BMES of the hip in three female family members, suggests that a genetically determined elevation of lipoprotein (a) may be an important predisposing factor in these patients.[21] Kim et al suggested that the decrease of local blood flow during the transformation of red bone marrow into yellow bone marrow might be the cause of BMES.[22]

Yumano reported that An angiographic examination of BMES patients showed no circulatory obstruction and vasodilation.[23] He thus speculated that vasodilation was a reflective expansion after transient ischemia and suggested that BMES is a reversible process of ischemic hypoxemia. Koo et al also performed angiographic examination, which also showed vasodilation.[24] Radionuclide scanning showed an increase in nuclide uptake, indicating an increase in blood flow or an increase in capillary permeability. They believe that early ischemic arterial contracture, perfusion reduction, vasodilation in the next few weeks, reactive hyperemia, increased perfusion, interstitial edema, and considered edema associated with ischemia and that BMES is a secondary response to ischemia.

In general, at present, there are many treatments for BMES of the hip, which can be divided into surgical treatment and non-surgical treatment. In view of the fact that the etiology and pathogenesis of BMES are not fully understood, the results lead to the lack of gold standards in the treatment of this condition, and the best treatment is still under investigation. The goal of treatment is to reduce pain, improve function, avoid fractures, and further development of femoral head necrosis. There have been many studies on non-surgical treatment which consists of avoiding load on the hips, physical therapy, analgesics as well as the use of nonsteroidal anti-inflammatory drugs, bisphosphonates, and vasoactive prostacyclin analog drugs like iloprost, in the treatment of BMES. Some of the results indicate that the clinical effect is effective and the outcomes are encouraging. However, some patients have not been effectively relieved after conservative treatment, what is worse is that some patients have gradually worsened and even developed avascular necrosis of the femoral head, becoming protracted and intractable. The use of core decompression for the treatment of BMES is still controversial. Core decompression has been reported to alter the natural course of the disease and to immediately relieve pain, significantly shortening the time to recovery compared with conservative treatment.[7,25] However, despite the positive results achieved by this approach, some authors believe that it is too invasive for self-limited diseases with variable clinical processes.[2,3] For Chinese patients, if there are other non-invasive options at the initial stage of treatment, that is, drug therapy, then most patients will definitely not choose surgical treatment. Moreover, there are certain risks and postoperative complications including wound infection, hematoma formation, reflex sympathetic dystrophy, and bone tunnel drilling related fractures, therefore, it is necessary to carry out a new, effective and safe non-invasive treatment between surgery and non-surgery.

Since the application of SW in medicine, its good clinical efficacy in musculoskeletal diseases has been gradually recognized. Furthermore, the application of ESWT for the management of musculoskeletal diseases and pathologies has been reported with a large acceptance in the medical literature. These observations reflect the potential benefits of ESWT. SW has been shown to promote neovascularization and tissue regeneration, reducing inflammatory processes and improving bone reparative processes.[26] SW also stimulate osteoblasts and periosteal cells and induce the osteogenic differentiation of mesenchymal stem cells.[27] Furthermore, SW significantly increase the production of osteocalcin, C-terminal procollagen type I (bone matrix deposition marker) and of several growth factors.[28] A noticeable increase in vascular endothelial growth factor (VEGF), transforming growth factor (TGF-Beta1), bone morphogenetic protein (BMP-2), von Willebrand factor (vWF) and alkaline phosphatase (ALP) was found in peripheral blood of patients treated with SW for non-unions and ONFH.[29] In addition, some clinical studies have reported the application of ESW in treatment of femoral head necrosis, where ESWT significantly can effectively relieve pain, improve the function of the hip, reduces the extension of both necrotic area and BME surrounding the ischemic lesion, especially resulting in considerable improvement in early stage ONFH.[17,18]

Our study demonstrated a significant improvement of the clinical outcomes include hip pain and function, and MRI edema area, showing great reduction. Furthermore, the mean VAS and the clinical improvement in HHS showed a dramatic improvement from pre-treatment values at all follow-up time-points, especially at S1 (1 month) and S2 (3 months) post-treatment ($P < .05$). We observed a quick positive response to the therapy in our study. A patient who underwent 3 treatments, and the symptoms of hip pain basically disappeared, the function of hip joint returned to normal. The results of magnetic resonance examination showed that the edema of femoral head and neck was basically eliminated. The remarkable curative effect and rapid recovery rate were greatly inspiring and exciting. In view of our encouraging research results, we believe that ESWT could be a non-invasive, non-pharmacological treatment for a rapid and safe and reasonable technique of BME symptoms. Our results are similar to those of recent studies on SW therapy for BME of hip.[14,15]

While achieving satisfactory clinical efficacy, we also acknowledge that there are some limitations in this study. Firstly, the limited number of patients included in the study and lack of control group and need to continue to observe more cases. Secondly, the mechanism of SW treatment of BMES has not been studied clearly, so the treatment standard for SW treatment of BMES has not yet been perfected, so, we only introduced our treatment experience and treatment program. Third, theoretically, all the patients with hip pain should be scanned by ultrasound because some tendon/muscle pathology may mimic BMES, and high resolution ultrasound (US) has emerged as a useful tool in the evaluation of nerve shape and size and muscle quantity and quality.[30,31] Unfortunately, in present study, we lack of ultrasound data of hip joint before treatment, which leads to the lack of relevant data to clearly analyze the pathological changes of tendon and nerve around hip joint. Furthermore, multicenter randomized controlled study with standardized protocols, large sample sizes and long-term follow-up are needed in further studies.

## 5. Conclusions

HF-ESWT can achieve precise localization, real-time monitoring of the impact site and recording the impact energy value in the treatment process, and ultimately achieve the purpose of accurate and efficient treatment. It is a valid, reliable, safe, effective, and noninvasive treatment in patients with painful BMES of the hip with low complication rate and a relatively low cost, and it can accelerate the recovery of BMES of the hip, shorten the treatment time, improve hip joint function and the quality of life of patients.

## Author contributions

**Data curation:** Leilei Zhang,Yuzhi Cui.
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**Project administration:** Xiantao Chen.

**Software:** Dawei Liang.
**Supervision:** Youwen Liu.
**Writing – original draft:** Leilei Zhang.

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