Arch Orthop Trauma Surg
DOI 10.1007/s00402-011-1444-9

ORTHOPAEDIC OUTCOME ASSESSMENT

Extracorporeal shock wave therapy in early osteonecrosis of the femoral head: prospective clinical study with long-term follow-up

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Received: 6 March 2010

Abstract
Introduction Extracorporeal shock wave therapy (ESWT) may exert beneficial effects in avascular necrosis of femoral head (AVNFH).
Patients The current study evaluated the effectiveness of ESWT in reducing pain and in slowing down the progression of bone damage in 36 patients with unilateral AVNFH of stage Association Research Circulation Osseous (ARCO) I, II and III. At the beginning of the study, 10 hips were classified as stage I, 11 as stage II and 15 as stage III. Each treatment cycle included four sessions, with 2,400 impulses each administered at 0.50 mJ/mm^2, at 48–72 h intervals. Follow-up examinations were scheduled at 3, 6, 12 and then 24 months.
Method Clinical assessments included assessment of pain scores, Harris Hip Scores and Roles and Maudsley score. Plain radiographs and magnetic resonances of the hip were used to evaluate the size of the lesion, the extent of collapse of subchondral bone, and degenerative changes of the hip joint.
Results Patients from ARCO stage I group and stage II group achieved significantly better results than patients from ARCO stage III group at all follow-up time points ($p < 0.005$). During the follow-up period, 10 of the 15 stage III ARCO patients received an arthroplasty. ARCO stages I and II lesions were unchanged on radiographs and on magnetic resonance images.
Conclusion ESWT in ARCO stages I and II may help to prevent progression of the area of avascular necrosis and manage pain.

Keywords Shock wave therapy · Avascular necrosis of femoral head · ESWT · AVNFH · Conservative treatment

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Introduction

Avascular necrosis of femoral head (AVNFH) is caused by insufficient blood supply, and is histologically associated with death of osteocytes, followed by osteoclastic resorption of dead trabeculae and apposition of new bone tissue [1]. AVNFH affects more than 10,000 individuals in the USA each year, and is more common in males than females with a ratio 7–3, with the exception of cases associated with systemic lupus erythematosus [2, 3]. In a current model of AVNFH, an ischemic attack is followed by increased intraosseous pressure, probably from the edema in the bone marrow compartment, which is functionally closed, so that the venules and capillaries are constantly compressed. This leads to the establishment of a vicious circle similar to compartment syndrome of a limb.

Published online: 07 January 2012

Avascular necrosis of femoral head is assessed using plain anterior–posterior and lateral or "frog leg" radiographs. While radiographs have high specificity for advanced disease but a low sensitivity for early AVNFH, 99Tc bone scintigraphy is highly sensitive in the early stages of the disease, with the characteristic "cold to hot" appearance [4]. MRI remains the most important diagnostic aid, with a sensitivity of 99% and a specificity of 98% [5]. In T1-weighted sequences, there is a low signal line between healthy bone and ischemic bone, known as "band-like lesion", which corresponds to a zone of sclerosis and fibrosis. T2-weighted sequences show evidence of a second inner line of high signal (double line sign), indicative of hypervascularity resulting from the repair process [4].

The international classification system of the Association Research Circulation Osseous (ARCO) [6] was introduced in 1993, and has been proposed as a new classification system which includes the previous classifications [7].

Management options for AVNFH remain controversial. For the early stages of AVNFH, femoral head preserving procedures are recommended, including core decompression, vascularized or non-vascularized bone graft and osteotomy, while in advanced stages (ARCO III and IV) total hip arthroplasty is usually performed [8]. Conservative management modalities used in AVNFH include prostacyclin-analogue iloprost, enoxaparin treatment and alendronate [9–12]. The most used physical therapies are pulsed electromagnetic fields (PEMFs), which seem to be able to control inflammatory processes and facilitate the reparative processes of the bone, and extracorporeal shock wave therapy (ESWT), which can activate many cellular processes critical to neovascularization and tissue regeneration [8, 13–20].

This longitudinal study evaluated the effectiveness of high energy ESWT in reducing pain and in slowing down the progression of bone damage in patients with AVNFH of stage ARCO I, II and III.

Materials and methods

Between April 2003 and March 2009, we conducted this prospective, observational clinical study. The study protocol was approved by our Institutional Review Board. Recruitment of patients and data monitoring were performed in our university hospital (Sapienza University School of Medicine), by a physician not involved in the selection and treatment of the patients enrolled in the present investigation.

Inclusion criteria were stage I, II, or III AVNFH according to the ARCO international classification system. Exclusion criteria included skeletal immaturity, a IV ARCO stage lesion, current or previous infection, cardiovascular and neoplastic disease, an implanted pacemaker, blood coagulation disorders, use of anticoagulant drugs and pregnancy. All patients gave written informed consent to participate in the study.

Thirty-six patients (23 males and 13 females) met the inclusion criteria and were recruited for this study (Table 1).

Table 1 Baseline characteristics of patients

Characteristic	Stage I ARCO (n = 10)	Stage II ARCO (n = 11)	Stage III ARCO (n = 15)
Age, mean (SD), years	49.3 (11.9)	52.7 (14.6)	45.9 (14.1)
Sex, no. (%)			
Men	7 (70)	9 (81.8)	7 (46.7)
Women	3 (30)	2 (18.2)	8 (53.3)
Duration of symptoms, mean (SD), months	4.3 (2.4)	9.3 (4.6)	14.7 (5.9)
Affected hip, no. (%)			
Left	5 (5)	5 (45.5)	10 (66.7)
Right	5 (50)	6 (54.5)	5 (33.3)
Previous treatment, no. (%)			
Biphosphonate medications	1 (10)	5 (45.5)	8 (53.3)
Therapeutic exercises	1 (10)	7 (63.6)	12 (80)
Hyaluronic acid injections	–	1 (9.1)	3 (20)
Physical therapies			
PEMFs	1 (10)	4 (36.4)	10 (66.7)
Laser therapy	–	3 (27.3)	4 (26.7)
TECAR therapy	1 (10)	3 (27.3)	5 (33.3)
Iontophoresis	–	5 (45.5)	7 (46.7)

SD standard deviation, *PEMFs* pulsed electromagnetic fields

The diagnosis of AVNFH was confirmed with plain radiographs and magnetic resonance imaging (MRI). There were 18 patients without risk factors and therefore classified as idiopathic osteonecrosis, 2 patients with secondary congenital hip dysplasia, 4 patients with a history of acute traumatic events (2 with hip dislocation). In the remaining patients, identified risk factors were smoking and previous corticosteroid therapy. Patients were staged according to ARCO classification: at the beginning of the study 10 hips were classified as stage I, 11 as stage II and 15 as stage III.

Pre-treatment assessments consisted of a complete history and physical examination, MRI and radiographs of the affected hips. Other factors taken into account were objective activity restriction, mobility and ability to perform the activities of daily living.

Shock wave treatment

The shock weave treatment was applied using an electromagnetic shock wave generator (Modulith SLK, STORZ MEDICAL AG, Switzerland), with a penetration depth between 0 and 150 mm and a focus diameter of 4 mm. Shock waves were focused around (on the margins of) the necrotic bone of the femoral head under radiographic guidance. The treatment area was prepared with a coupling gel to minimize the loss of shock-wave energy at the interface between the head of the device and the skin.

All ESWT procedures were performed without general or regional anaesthesia. The administering physician was experienced in the use of extracorporeal shock-wave therapy in the treatment of various musculoskeletal disorders. Each treatment cycle included four sessions, with 2,400 impulses each administered at 0.50 mJ/mm^2, at 48–72 h intervals. After ESWT treatment, patients were instructed to walk on crutches and not to bear weight on the affected limb for 2 months. No other therapies were administered to any patient. Patients who did not respond to ESTW and those dissatisfied with the treatment results underwent total hip arthroplasty.

Outcome measures

Follow-up examinations were scheduled at 3, 6, 12 and then 24 months. Clinical assessments included assessment of pain scores, Harris Hip Scores and Roles and Maudsley score.

The intensity of pain was recorded on a visual analogue scale (VAS), ranging from 0 to 10, with 0 indicating no pain and 10 indicating severe pain.

The Harris Hip Score gives 91 points for assessment of pain and function and 9 points for range of motion and deformity [21].

The Roles and Maudsley score is a subjective 4-point patient assessment of pain and limitations of activity, and has been used extensively to assess outcome after ESWT [22]. On this scale, 1 point is defined as an "excellent" result with the patient having no symptoms. Two points is defined as a "good" result, with the patient significantly improved from the pre-treatment condition and satisfied with results. Three points is defined as a "fair" result with the patient somewhat improved from pre-treatment condition and partially satisfied with treatment outcome. Four points indicates a "poor" outcome with symptoms identical or worse than pre-treatment condition and with dissatisfaction with treatment results. In the present study, a hip converted to a total hip arthroplasty at any time during the study was also defined as "poor" outcome.

Antero-posterior and lateral radiographs were made before treatment, and at 3, 6, 12 and 24 months after treatment. Plain radiographs of the hip were used to evaluate the size of the lesion, the extent of collapse of subchondral bone and degenerative changes of the hip joint. MRI was performed before treatment, at 6 and 12 months after the end of treatment, and once a year thereafter, using axial, coronal, sagittal T1 and T2-weighted scans, STIR and T2 with fat saturation sequences. These images were used to measure the size of the lesion, assess the congruency of the femoral head, the presence of a crescent sign and/or degenerative changes of the hip joint, with the aim to stage patients' hips according to ARCO classification. Radiographic assessments and clinical examinations were performed, respectively, by two independent radiologists and two clinicians not involved in the treatment procedures. Every discrepant evaluation was discussed, and a decision was reached by consensus.

Statistical analysis

The aim of this study was to evaluate the clinical outcome and the diagnostic changes in each ARCO stage group and between the groups after focused ESWT at five time points (before treatment and at 3, 6, 12 and 24 months). The efficacy endpoints were prospectively defined as: reduction of the self-rated pain intensity scale (VAS), improvement of the Harris Hip Score, reduction of the Roles and Maudsley score and regression or stabilization of ARCO stage.

Descriptive statistics were applied for all ARCO stage groups. Continuous variables were summarized within ARCO groups using mean and standard deviation. The paired samples *t*-test was used for comparison of mean change of the VAS and the Harris Hip score between the pre-treatment and scheduled follow-up time points within each ARCO group. One-way analysis of variance was used to assess whether there were significant differences in the VAS and Harris Hip Score among the three groups at various follow-up periods. The Wilcoxon rank-sum test and the Mann–Whitney *U*-test were used respectively for comparing

changes of the Roles and Maudsley score within each group between pre-treatment and post-treatment assessments, and between groups at each evaluation time.

Data were analyzed using SPSS for Windows (version 16.0; SPSS, Chicago, III). p Values less than 0.05 were considered statistically significant.

Results

Of the 36 hips which underwent shock wave treatment, 3 failed and were converted to total hip arthroplasty within the 3-month follow-up because of persistence of pain at weight-bearing and functional limitations. In the following months, in another seven patients a total hip arthroplasty was necessary: one before the 12 month follow-up, four before the 24 month follow-up and two after 24 months. All the subjects who received an arthroplasty were at ARCO III stage. They were not followed up after conversion to a total hip arthroplasty. We, therefore, evaluated 33 hips at the first follow-up (3 months), 32 hips at the second follow-up (6 months), 28 hips at the third follow-up (12 months) and 26 hips at the last evaluation (24 months). The evolution of the population at all follow-up time points was summarized in Fig. 1.

Outcome measures (scores on the VAS, Harris Hip Score and Roles and Maudsley score) are shown in Tables 2 and 3.

At all follow-up periods, stage I ARCO patients showed significantly better results in VAS score (all $p < 0.001$) than before treatment. In ARCO stages II and III groups, significant reduction of the VAS was noted only at third and fourth follow-up time points after ESWT treatment (Table 2). Conversely, the Harris Hip Score showed statistically significant improvement at various follow-up time points from pre-treatment values for all treatment groups (all $p < 0.001$): ARCO stage I patients obtained satisfactory values (mean score > 75) from the first follow-up, while in the other two groups this mean score was obtained only from the second follow-up (6 months after treatment).

The VAS score in ARCO stage I group was significantly lower than in ARCO stage II group at 6 months ($p = 0.016$), whereas it was significantly better in ARCO stage I group than in ARCO stage III group at all follow-up time points (Table 2).

Association Research Circulation Osseous stage I patients showed significantly better results in Harris Hip Score than ARCO stage II group at second follow-up period ($p = 0.02$), and than ARCO stage III group at 3 and 6 months (respectively, $p = 0.009$ and $p = 0.007$).

No significant differences in the mean VAS and Harris Hip Score were observed between ARCO stages II and stage III groups at any follow-up period (all $p > 0.05$).

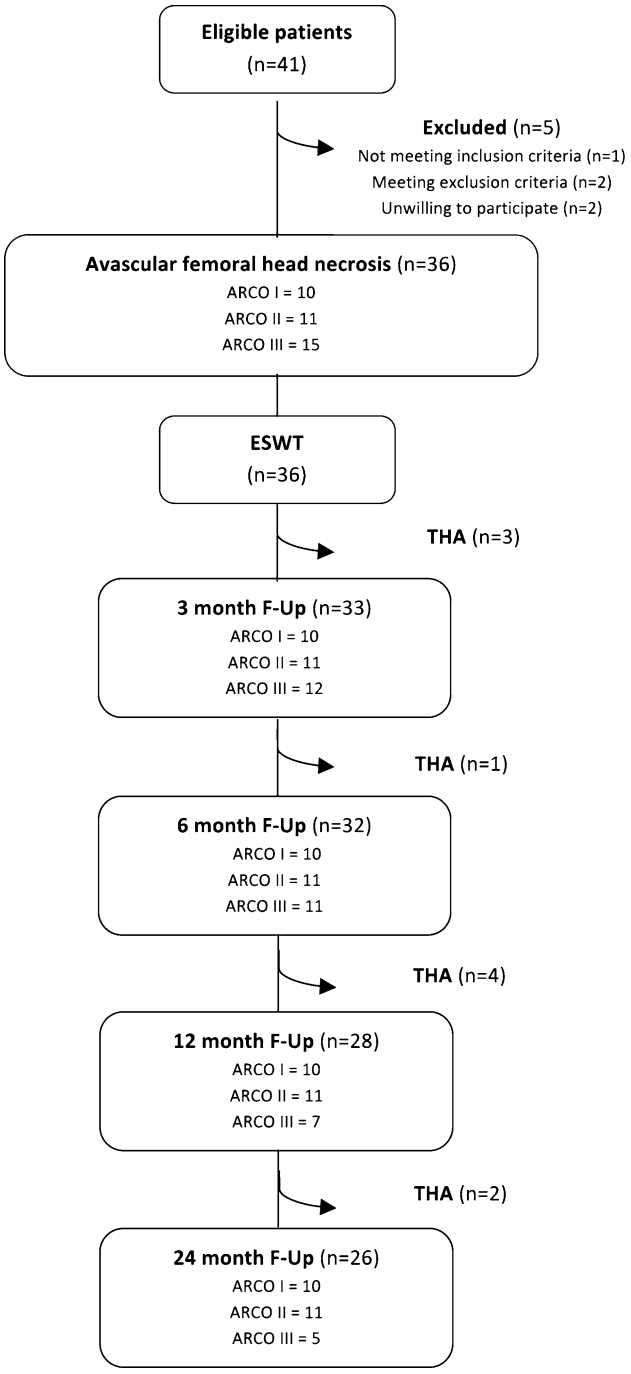

Fig. 1 Flow diagram of the study until the last follow-up from baseline

At pre-treatment evaluation, all patients rated the condition of the affected hip as "4" (poor) in the subjective four point Roles and Maudsley score. The 10 ARCO stage III patients submitted to total hip arthroplasty at various follow-up were defined as "4" (poor) outcome. No patient reported worsening of symptoms compared to pre-treatment (Table 3). The difference between the ARCO stage I

Table 2 Outcome assessment before and after treatment

	Baseline	3 months	6 months	12 months	24 months
Stage I ARCO					
Patients (no.)	10	10	10	10	10
VAS [0–10], mean (SD)	6.7 (1.2)	4.4 (2.5)	2.6 (0.9)	2.0 (0.8)	0.9 (0.9)
Difference versus baseline (*p* value)	–	*0.004*	*<0.001*	*<0.001*	*<0.001*
Difference versus stage II (*p* value)	0.976	0.418	*0.016*	0.314	0.118
Difference versus stage III (*p* value)	0.485	*0.014*	*0.043*	*0.038*	*0.033*
HHS [0–100], mean (SD)	42.5 (14.9)	83.1 (14.9)	89.8 (4.9)	88.9 (5.1)	89.6 (3.9)
Difference versus baseline (*p* value)	–	*<0.001*	*<0.001*	*<0.001*	*<0.001*
Difference versus stage II (*p* value)	0.494	0.055	*0.020*	0.066	0.056
Difference versus stage III (*p* value)	0.763	*0.009*	*0.007*	0.117	0.211
Stage II ARCO					
Patients (no.)	11	11	11	11	11
VAS [0–10], mean (SD)	6.7 (2.6)	5.4 (2.7)	4.7 (2.4)	2.9 (2.7)	2.5 (2.4)
Difference versus baseline (*p* value)	–	0.129	0.065	*0.003*	*0.002*
Difference versus stage III (*p* value)	0.609	0.107	0.912	0.429	0.920
HHS [0–100], mean (SD)	46.3 (22.1)	71.5 (11.1)	82.0 (8.4)	82.3 (9.6)	81.6 (10.6)
Difference versus baseline (*p* value)	–	*0.008*	*0.001*	*0.001*	*0.001*
Difference versus stage III (*p* value)	0.612	0.101	0.210	0.984	0.719
Stage III ARCO					
Patients (no.)	15	12	11	7	5
VAS [0–10], mean (SD)	7.2 (2.0)	7.1 (2.1)	4.9 (3.4)	4.0 (2.6)	2.6 (1.9)
Difference versus baseline (*p* value)	–	0.438	0.116	*0.015*	0.22
HHS [0–100], mean (SD)	42.2 (17.5)	59.7 (18.3)	75.3 (13.8)	82.1 (11.2)	83.8 (11.7)
Difference versus baseline (*p* value)	–	*0.015*	*0.020*	*0.008*	*0.025*

Italic indicates statistically significant values ($p < 0.05$)

no. number of the cases, *VAS* visual analogue scale, *SD* standard deviation, *HHS* Harris Hip Score

and stage II patients was significant at 6 months ($p = 0.004$). The difference in the success rate between the two groups was no longer significant. Patients from ARCO stage I group and stage II group achieved significantly better results than patients from ARCO stage III group at all follow-up time points. Overall, at 3 months follow-up, 6 of 10 patients (60%) in ARCO stage I group, 5 of 11 patients (45.5%) in stage II group and 3 of 15 patients (20%) in stage III group reported a 1 (excellent result) or 2 (good result) score on the Roles and Maudsley score; at 6 months follow-up, all the 10 patients (100%) in ARCO stage I group, 8 of 11 patients (72.7%) in stage II group and 4 of 15 patients (26.7%) in stage III group reported excellent or good results; at 12 and 24 months follow-up, all the 10 patients (100%) in stage I group, 9 of 11 patients (81.8%) in stage II group and 4 of 15 patients (26.7%) in stage III group reported excellent or good results.

At all follow-up time points, the lesions show no or only minimal changes on radiographs and on magnetic resonance images. Neither regression nor progression of lesions that had been graded before treatment as ARCO stage I and II were seen despite clinical improvement. However, in 10 of 15 ARCO stage III patients, there was clinical deterioration and the patients had a THA. In the rest of five patients, minimal radiographic or MRI changes were observed (Table 4).

Side effects

No clinically detectable neuromuscular, systemic or device-related adverse effects were observed. In all patients, only minor complications occurred after ESWT, such as transient soft tissue swelling or minor bruising. No other adverse effects were noted.

Discussion

Hips with AVNFH usually deteriorate, with collapse of the femoral head, leading ultimately to joint destruction and the need for arthroplasty. Ohzono et al. [23] reported the collapse of the femoral head in 94–100% of cases if the lesions are at the weight-bearing surface on the femoral head within 5 years.

Table 3 Roles and Maudsley score at various follow-up

	3 months				6 months				12 months				24 months			
Stage I ARCO																
Patients (no.)	10				10				10				10			
Roles and Maudsley score	E	G	F	P	E	G	F	P	E	G	F	P	E	G	F	P
No.	0	6	1	3	5	5	0	0	6	4	0	0	6	4	0	0
%	0	60	10	30	50	50	0	0	60	40	0	0	60	40	0	0
Difference versus stage II (p value)	1.000				*0.004*				0.086				0.086			
Difference versus stage III (p value)	*0.037*				*0.014*				*0.004*				*0.019*			
Stage II ARCO																
Patients (no.)	11				11				11				11			
Roles and Maudsley score, no.	E	G	F	P	E	G	F	P	E	G	F	P	E	G	F	P
No.	1	4	4	2	0	*8*	*3*	*0*	*3*	*6*	*0*	*2*	*3*	*6*	*0*	*2*
%	9.1	36.4	36.4	18.1	0	*72.7*	*27.3*	*0*	*27.3*	*54.5*	*0*	*18.2*	*27.3*	*54.5*	*0*	*18.2*
Difference versus stage III (p value)	*0.048*				*0.045*				*0.037*				*0.035*			
Stage III ARCO																
Patients (no.)	15				15				15				15			
Roles and Maudsley score, no.	E	G	F	P	E	G	F	P	E	G	F	P	E	G	F	P
No.	0	3	2	10	0	*4*	*0*	*11*	*0*	4	1	10	0	4	0	11
%	0	20	13.3	66.7	0	*26.7*	*0*	*73.3*	*0*	26.7	6.7	66.6	0	26.7	0	73.3

Italic indicates statistically significant values ($p < 0.05$)

E excellent, *G* good, *F* fair, *P* poor

Management of AVNFH remains controversial, and, if conservative measures fail, surgery is indicated. Non-surgical approaches to early AVNFH include protected weight-bearing and physical therapies, such as PEMFs or focused ESWT. PEMFs may limit local inflammation, preventing degeneration of the articular cartilage since they reduce the production of oxygen free radicals, limiting the catabolic effects of inflammatory cytokines on the articular cartilage by promoting the synthesis of proteoglycans, stimulate the reparative processes and may enhance the healing process by promoting neovascularization and the formation of new bone. These combined effects can be effective in pain control, for chondroprotection, and for optimization of the healing process [13, 14]. The exact mechanism through which ESWT operates remains unknown. In mice, ESWT regulate the expression of endothelial growth factor (VEGF) and BMP-2. The increase in the expression of VEGF and BMP-2 was evaluated by two different trials conducted in 2007 and 2008, respectively, using the same technique. These studies were performed on mice in which osteonecrosis had been induced after bilateral administration of methylprednisolone and lipopolysaccharide, and in which treatment with ESWT was performed 6 weeks after corticosteroid, at 2,000 pulses with a level of energy of 0.26 mJ/mm^2. Necrosis was induced bilaterally to use the left limb for treatment with shock waves and the right limb as control. Ma et al. [15] postulated that VEGF might be involved in the positive effects of shock wave therapy because VEGF is a specific mitogenic factor for vascular endothelial cells, which stimulates endothelial cells proliferation, promotes neovascularization and increases vascular permeability15. The increased expression of BMP-2 in femoral heads treated with ESWT was a key finding because the BMP-2 is a key mediator of bone development and repair for its capacity to mobilize osteoprogenitor cells, thereby promoting osteoblastic differentiation processes and resulting in bone formation [16]. Other effects of ESWT are: increase of the endothelial nitric oxide synthase, thereby promoting neovascularization, the increase of endorphins resulting in pain control and increase in other growth factors such as EGF, IGF 1 and PDGF. Finally, Wang et al. [24] demonstrated that local mechanical stimulation with shockwave may reflect the systemic effects of angiogenesis and osteogenesis and anti-inflammation in hips with AVNFH24. Recently, Hausdorf et al. [25] also showed that ESWT are able to propagate through the femoral head with a distance-related absorption and a pressure loss of about 50% within 10 mm of bone, and they stated that the shock wave energy used in clinical studies seems to be sufficient to produce biological responses in terms of vascular and bone growth.

The beneficial effects of ESWT in AVNFH has been confirmed by several recent clinical studies (Table 5). ESWT is effective in pain reduction, and in improving hip function and, consequently, the quality of life of patients with AVNFH, with better results in the early stages of the

Table 4 ARCO classification at various follow-up

	Baseline	3 months	6 months	12 months	24 months
Stage I ARCO					
Patients (no.)	10	10	10	10	10
Location, no. (%)					
Medial	5 (50)	5 (50)	5 (50)	5 (50)	5 (50)
Central	5 (50)	5 (50)	5 (50)	5 (50)	5 (50)
Lateral	–	–	–	–	–
Quantitation, no. (%)					
Area of involvement					
A: Minimal (<15%)	10 (100)	10 (100)	10 (100)	10 (100)	10 (100)
B: Moderate (15–30%)	–	–	–	–	–
C: Extensive (>30%)	–	–	–	–	–
Length of crescent					
A: <15%	10 (100)	10 (100)	10 (100)	10 (100)	10 (100)
B: 15–30%	–	–	–	–	–
C: >30%	–	–	–	–	–
Surface collapse and dome depression					
A: <15 and <2 mm	10 (100)	10 (100)	10 (100)	10 (100)	10 (100)
B: 15–30% and 2–4 mm	–	–	–	–	–
C: >30% and >4 mm	–	–	–	–	–
Stage II ARCO					
Patients (no.)	11	11	11	11	11
Location, no. (%)					
Medial	6 (54.5)	6 (54.5)	6 (54.5)	6 (54.5)	6 (54.5)
Central	2 (18.2)	2 (18.2)	2 (18.2)	2 (18.2)	2 (18.2)
Lateral	3 (27.3)	3 (27.3)	3 (27.3)	3 (27.3)	3 (27.3)
Quantitation, no. (%)					
Area of involvement					
A: Minimal (<15%)	2 (18.2)	2 (18.2)	2 (18.2)	2 (18.2)	2 (18.2)
B: Moderate (15–30%)	9 (81.8)	9 (81.8)	9 (81.8)	9 (81.8)	9 (81.8)
C: Extensive (>30%)	–	–	–	–	–
Length of crescent					
A: <15%	6 (54.5)	4 (36.7)	4 (36.7)	4 (36.7)	4 (36.7)
B: 15–30%	5 (45.5)	7 (63.3)	7 (63.3)	7 (63.3)	7 (63.3)
C: >30%	–	–	–	–	–
Surface collapse and dome depression					
A: <15% and <2 mm	10 (90.9)	10 (90.9)	10 (90.9)	10 (90.9)	10 (90.9)
B: 15–30% and 2–4 mm	1 (9.1)	1 (9.1)	1 (9.1)	1 (9.1)	1 (9.1)
C: >30% and >4 mm	–	–	–	–	–
Stage III ARCO					
Patients (no.)	15	12	11	7	5
Location, no. (%)					
Medial	1 (6.7)	1 (8.3)	1 (9)	1 (14.2)	–
Central	9 (60)	5 (41.7)	5 (45.5)	3 (42.9)	2 (40)
Lateral	5 (33.3)	6 (50)	5 (45.5)	3 (42.9)	3 (60)

Table 4 continued

	Baseline	3 months	6 months	12 months	24 months
Quantitation, no. (%)					
Area of involvement					
A: Minimal (<15%)	1 (6.7)	–	–	–	–
B: Moderate (15–30%)	5 (33.3)	6 (50)	5 (45.5)	3 (42.9)	3 (60)
C: Extensive (>30%)	9 (60)	6 (50)	6 (54.5)	4 (57.1)	2 (40)
Length of crescent					
A: <15%	2 (13.3)	1 (8.3)	1 (9.1)	1 (14.3)	–
B: 15–30%	7 (46.7)	5 (41.7)	4 (36.4)	2 (28.6)	3 (60)
C: >30%	6 (40)	6 (50)	6 (54.5)	4 (57.1)	2(40)
Surface collapse and dome depression					
A: <15% and <2 mm	2 (13.3)	1 (8.3)	1 (9.1)	1 (14.3)	–
B: 15–30% and 2–4 mm	8 (53.3)	5 (41.7)	4 (36.4)	2 (28.6)	3 (60)
C: >30% and >4 mm	5 (33.4)	6 (50)	6 (54.5)	4 (51.7)	2(40)

Table 5 Clinical researches on use of ESWT in the treatment of AVNFH

References	Study design	Number of hips	Treatments	Follow-up duration	Outcome
Ludwig et al. [18]	OLT	22	ESWT (4,000 impulses; EFD 0.62 mmJ/mm^2)	12 months	Patients with lower ARCO stages obtained better results
Russo et al. [19]	OLT	52	ESWT (3 × 4,000 impulses; EFD 0.26–0.95 mmJ/mm^2)	24 months	At 2 years follow-up the pain disappeared in 44/52 cases
Wang et al. [20]	RCT	57	ESWT (6,000 impulses; EFD 0.62 mmJ/mm^2) versus surgical procedure	24 months	ESWT appeared to be more effective than core decompression and non-vascularized fibular grafting
Wang et al. [21]	OLT	14	ESWT (6,000 impulses; EFD 0.62 mmJ/mm^2) plus THA versus THA alone	NP	ESWT group showed significantly more viable bone and less necrotic bone, higher cell concentration and more cell activities including phagocytosis
Wang et al. [22]	RCT	60	ESWT (6,000 impulses; EFD 0.62 mmJ/mm^2) plus alendronate (70 mg/week) versus ESWT alone (6,000 impulses; EFD 0.62 mmJ/mm^2)	24 months	ESWT and alendronate produced comparable result as compared with ESWT without alendronate in early AVNFH

ESWT extracorporeal shock wave therapy, *AVNFH* avascular femoral head necrosis, *EFD* energy flux density, *THA* total hip arthroplasty, *OLT* open-label trial, *RCT* randomized clinical trial, *NP* not presented

condition (ARCO stages I and II) [8, 18–20]. In the literature, some studies compared conservative and surgical management in AVNFH. One investigation showed that ESWT appeared to be more effective than core decompression and non-vascularized fibular grafting [19]. Finally, ESWT and alendronate may have synergistic effects through different mechanisms in early AVNFH [20].

Our results confirmed these findings. In fact, 10 of 15 ARCO stage III patients underwent total hip arthroplasty during the follow-up period because of persistence of hip pain and functional limitations. These subjects were considered as poor outcome on Roles and Maudsley score where, already at 6 months follow-up time, all patients in ARCO stage I group and 8 of 11 patients (72.7%) of subjects in stage II group reported excellent or good results. Conversely, during follow-up assessments, only 4 of 15 patients in stage III obtained good results and none of them reported excellent outcomes.

Furthermore, we observed a significant reduction of mean VAS score at short-, medium-- and long-term follow-up only in ARCO stage I patients**,** whereas the mean Harris Hip score showed statistically significant improvement at all follow-up time points from pre-treatment values for all treatment groups. Thus, the osteonecrosis progression appears to be the main factor in determining pain, but pain is not the only cause that affects hip functions in people with AVNFH. Finally, during the follow up period all hips with early AVNFH (ARCO I and II) treated with ESWT

alone appeared only minimal radiographic and MRI changes and overall a clinical improvement. Therefore, as the natural history of AVNFH is of progression, the beneficial effects of ESWT for the early stages, (ARCO I and II), is evident in the fact that the AVNFH area involved did not increase and the grade of it did not worsen. Furthermore, the patients had clinical improvement which was mostly obvious after the first 6 months of ESWT treatment.

We fully acknowledge the limitations in this study. For example, we have reported on a relatively small series of patients, and we lack a control group. However, in our setting, AVNFH is relatively uncommon, and it would have been difficult to mount a randomized controlled trial. Another limitation is that some patients were already treated on different methods previously and not with a very big gap before their ESWT beginning, as pointed out from Table 1. Finally, the comparison of results obtained in our study with other studies using ESWT is only partially possible, given the differences in the type of equipment used, treatment and evaluation protocols, inclusion criteria and number of patients treated.

Given the considerable impact of AVNFH on public health, multicenter studies should be conducted on the effectiveness of ESWT in the management of avascular necrosis, to collect larger numbers of patients treated in a homogeneous fashion and assessed with the same methodology.

Conclusion

High energy ESWT can be effective in the management of AVNFH ARCO stages I and II, but less so in the more advances stages of the condition. Early diagnosis and staging are, therefore, of extreme importance to obtain benefits from ESWT. Additionally, ESWT is non-invasive, has a low complication rate, does not require hospitalization and has a relatively low cost compared to other types of conservative and surgical approaches, with a relatively short time of application. Our results also confirm reports in the literature indicating that ESWT in ARCO stages I and II aims to slow down the worsening of the grade of the AVNFH in the avascular area and improve clinical features.

Further studies are needed with larger cohorts of patients using the homogenous classification system, and standardized treatment protocols to further assess the effectiveness of ESWT in the management of AVNFH.

The research was carried out in accordance with the ethical standards described by the Helsinki Declaration, and was approved by a local Ethical Committee.

Conflict of interest The authors declare that they have no conflict of interest.

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