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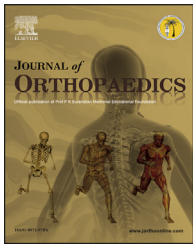

Original Article

Predictive role of scintigraphy (BS) in bone union induction using extracorporeal shock wave treatment (ESWT)

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ABSTRACT

Aims: Pseudoarthrosis and delayed bone union are the main complications in the healing process of long bones fractures. The surgical intervention is currently the treatment of choice, but there is a number of non-operative interventions are being developed, such as extracorporeal shock wave therapy (ESWT). There is a range of issues related to the proper qualification, monitoring, and outcome assessment measures. Bone scintigraphy (BS) exclusively allows the assessment of the bone turnover dynamics in non-invasive, semi quantitative method.

Methods: The study group comprised of 31 subjects with bone healing complications. The study population was divided in two subgroups as related to the treatment outcome assessed 24 weeks after ESWT procedure. Group I ($n = 19$) included the cases with no complete bone union. Group II ($n = 12$) covered the subjects with complete bone union. BS was performed right before ESWT and 2 weeks after the procedure.

Results: Increase of agent uptake after ESWT procedure was noted in both groups which proves that ESWT increases bone metabolism dynamics in most patients. Significantly higher uptake increase was noted in patients with complete bone union. In patients with unsuccessful treatment the agent uptake before ESWT was much higher.

Two weeks after ESWT procedure BS reveals an increase in bone metabolism in the area of complicated fracture proving positive reaction of bony tissue on mechanical waves.

Conclusion: Scintigraphy may facilitate qualification patients with bone union disorders for further mode of treatment. One can suppose that positive bone reaction is achievable only in bone where the metabolism is lowered.

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1. Introduction

Pseudoarthrosis and delayed bone union are the main complications in the healing process of long bones fractures.[1] As surgical intervention is currently the treatment of choice in the ones it has several limitations and may not lead to the successful outcome. Thus, a number of non-operative methods are being developed, such as electrical, electromagnetic, and ultrasound stimulation of the fracture site.[2]

The general idea behind fractured bone stimulation treatment approach with extracorporeal shock wave treatment (ESWT) is to produce shock wave supposed to result in: callous formation, neovascularization and increased expression of angiogenic growth factors inducing differentiation as well as proliferation of cultured osteoblasts along with the regulation of genes involved in osteoblast proliferation and differentiation processes.[3–6]

However, ESWT still has a range of issues related to the proper qualification, monitoring, and outcome assessment measures that require systematic appraisal along with guideline formation.[2] Bone scintigraphy (BS) exclusively allows the assessment and visualization of the bone turnover in non-invasive method. It enables both the evaluation of metabolic processes rate in the bone tissue as well as the diagnostic differentiation in the imaging of pathological processes that may affect healing process. BS is characterized by high sensitivity. However, its specificity is low.[7] It mainly results from the limitation of that method being quantitative evaluation measure with no standardized procedure. That issue arises with the majority of the studies and requires study-specific, semi-quantitative assessment of hyperactive focuses as compared to the normal bone uptake of the tracer.

The aim of this study was to evaluate the metabolic changes in bone fracture healing with BS in chronological course of the medical intervention before and after ESWT. The secondary study outcome was to assess of usefulness of BS in predicting the procedure's efficacy in the treatment of bone union complications (pseudoarthrosis and delayed bone union) in scope of guidance for the practical method implementation.

2. Patients and methods

The study group comprised of 31 subjects, 11 women aged 31–68 (mean 51, ±3) and 20 men aged 21–72 (mean 45, ±4) with long bone union complications. Twenty-two patients were diagnosed with pseudoarthrosis, 9 with delayed bone union. The patients characteristics is demonstrated in Table 1.

Before ESWT procedure all patients were inefficiently treated using conventional operative and non-operative methods. During the procedure 26 patients had bony fragments stabilized with metal uniting material.

The inclusion criteria to the study were patients' informed consent, pseudoarthrosis and delayed long bone union with unsuccessful treatment with conventional operative or non-operative methods. Patients were also qualified on the basis of clinical examination and CT images. The exclusion criteria were osteitis in the location close to the place of the treatment, neoplasm, pregnancy, breastfeeding, coagulopathy, osteomyelitis, neuropathy, peripheral vascular disease.

The study population was divided in two subgroups as related to the treatment outcome assessed 24 weeks after ESWT procedure. Group I ($n = 19$) included the cases with no complete bone union. Group II ($n = 12$) covered the subjects with complete bone union.

Thirty-one patients were treated with extracorporeal shock wave therapy (ESWT) at a single referral trauma center in an attempt to determine the feasibility and factors associated with the use of ESWT in the treatment for long-bone nonunion. In Table 2 the fractured bones are listed.

ESWT was performed with electrohydraulic lithotripter Econolith 2000 (Medispec, USA) set on the delivery of 3000 impulses at 20–21 kV with post-treatment immobilization of the bone. The probe focused the treatment waves on the area of 8 × 50 mm, where it triggered pressure impulse of 300 bars during 1 ms. The impulse frequency was 60–120/min.

BS was performed right before ESWT and 2 weeks after the procedure. Scintigraphy was performed using Multispect (Siemens, DE) gamma camera, in supine position after intravenous administration of 600–800MBq of $^{99}Tc^{m}$-MDP. AP and PA bone scans of affected region were obtained 3 h p.i.

Scintigraphic tests analysis was based on semi-quantitative assessment. In order to categorize data obtained a semiquantitative scale of degree of accumulation of the radiopharmaceutic in fractured area was created: 0) no accumulation – 0 points, 1) poor accumulation, but higher than in healthy, homonymous bone – 1 point, 2) intensive accumulation, but not dominative – 2 points, 3) intensive accumulation, dominative, but comparable with accumulation in another hyperactive anatomic structure – 3 points, 4) intensive, dominative accumulation – 4 points. The average evaluation measurements from three independent observers were calculated using the scale described above.

Twenty-four weeks after the procedure patients were subjected to clinical and radiological evaluation in order to perform follow-up observation.

The study used descriptive and quantitative statistic methods. Compatibility analysis among three independent

Table 1 – Groups of patients.

Group (treatment)	n	Time since injury (weeks)	Sex		Mean age	Type of complication	
			F	M		Pseudoarthrosis	Delayed bone union
Group I (unsuccessful)	19	109.89	6	13	47.2	14	5
Group II (successful)	12	71.33	5	7	47.9	8	4

Table 2 – Fractured bones.

Bone	Radius	Ulna	Femur	Tibia	Humerus	Metatarsal
$n = 31$	5	5	4	8	8	1

observers was performed, using kappa statistics (Cohen's test). Comparing distribution of semi-quantitative features was conducted using Mann–Whitney *U* test. The significance level was set at $p < 0.05$.

3. Results

Interobserver agreement on the basis of Kappa statistics was from 0.77 to 1.00, which proved satisfactory quality of chosen criteria.

The basal agent uptake in group I was higher on average of 0.74 pts. As related to the uptake in group II and the difference was found to be statistically significant ($p = 0.036$). The increase in uptake after ESWT procedure was noted in both groups. The uptake ratio between the group II and I was 1.6 on control BS evaluation. In group II the increase in bone metabolism dynamics after ESWT procedure was statistically significant ($p = 0.028$) as related to baseline. After ESWT procedure eleven subjects in group I revealed increase in the metabolic bone activity on average of 1.5 pts. In the remaining 8 patients the accumulation rate was similar or lower. After ESWT procedure 8 subjects in group II revealed increase in the metabolic bone activity on average of 2.45 pts. In the remaining 4 patients the accumulation rate was similar before and after the procedure. The results are presented in Table 3.

The common trend indicates the lower the activity of radiopharmaceutical agent accumulation in area of complicated fracture in test performed before ESWT the better outcome as the union induction.

4. Discussion

Predictive value of DS in the assessment on bone union seems to play crucial role in the clinical assessment.[8] According to Günlap et al[9] bone scintigraphy is particularly useful tool in the assessment of risk and incidence of complications related to the healing process where lack of bone union is of prime interest.

The substantial research and diagnostic problem in BS is the variability of assessment measures used by different teams. For example, Günlap et al performed a scintigraphic examination in patients with diagnosed lack of bone union after using ESWT. The results of scintigraphy were subjected to qualitative assessment. Günlap et al proposed some manualised quantification criteria enabling systematic methodological approach. Patients are to be allocated into one of three groups, on the basis of patterns of radioligand uptake:

- group 1 – homogenic increase of the agent accumulation in area of non-union. The most frequently observed pattern
- group 2 – including two subgroups:
  - subgroup 2a – increase of the agent uptake is observed at the bony ends adjacent to the fracture with deficiency of uptake in the fissure
  - subgroup 2b – generalized decrease of the agent uptake at the bony ends adjacent to the fracture
- group 3 – includes subjects with uptake pattern inconsistent with group 1 and 2 criteria or with no defined location of the fracture based on scintigraphic result

In first group 87.5% of bone union were obtained. In the third group 42.8% experienced bone union. However, in the second group no union was observed. In our study the similar results were observed in group I, presenting significantly higher agent uptake before treatment.

Smith et al[10] assessed bone metabolism with scintigraphic tests at 6, 12 and 24 weeks after fracture. He applied quantitative scale with the major consideration on the agent uptake. The authors classified fractures on the basis of radioligand concentration around fracture as follows:

- radioligand around the fracture,
- radioligand in homonymous bone in the area equivalent to the fracture,
- radioligand in the area above/below the fracture,
- radioligand in homonymous bone in the area equivalent to the one above/below the fracture.

Smith et al proved that the degree of agent uptake in fracture area is of predictive value of bone union or complications indicating the risk of incidence of non-union after 6 months from injury. The highest predictive value is associated with the test performed two weeks after the injury when biggest differences in the average values of uptake in fractured areas (between the groups with union and non-union) are observed. On the other hand, according to Oni et al[11] the highest predictive value has a scintigraphic examination performed 6 weeks from the injury. In our work we performed BS at the moment of declared bone union complication, i.e. much later – 4 months to 5 years post fracture, in order to evaluate its prognostic role in ESWT of non-unions.

Barros et al[12] in their report on scintigraphic tests in 40 subjects with conservative treatment of tibia fracture concluded that the decrease in bone turnover intensity may be regarded as soft predictor of poor fracture healing. Thus, it seems important proving lack of active bone metabolic turnover in the fracture area that may be associated with the risk of bone non-union. In the group II of this study the similar observation was made. Lower activity in the fracture area related to complete union.

Table 3 – Average results according to semi-quantitative scale for scintigraphic procedures, considering dividing patients in two groups ($p < 0.05$).

Time of study		Before ESWT	After ESWT
Group I ($n = 19$)	Mean	2.43	3.13
	SD	0.9	0.82
Group II ($n = 12$)	Mean	1.69	3.24
	SD	0.87	0.68

On the other hand, O'Reilly et al[13] in the study on a population of 22 patients with delayed long-bone fracture found no statistically significant differences among scintigrams resulting in the proper and uncomplicated healing process regardless BS data. In our work in group I a variety of uptake values was also observed. The study demonstrates that there is the significant difference in the agent uptake between the group with no complete bone union (group I) and group with complete bone union (group II) in BS tests performed before ESWT procedure. The trend indicates the higher the uptake in the fractured area the higher risk of incomplete bone union in the outcome point. It may be hypothesized that in patients with complete bone union there is the decrease in metabolic activity during the healing process that was, so far, considered as unfavorable prognostic factor. It turns out, these patients when exposed to ESWT procedure increased the rate of accumulation of $^{99}Tc^{m}$-MDP dramatically eventually leading to the complete union induction.

The increase in the uptake observed in the group with no complete bone union did not reach statistically significant level. It is important to notice that in these patients agent accumulation was initially high and that some further activation of bone metabolism rate might be limited.

The decrease of radiopharmaceutical agent uptake after ESWT procedure was infrequently observed only in group with no complete bone union (group I). The increase of agent uptake was observed in both groups, however it was definitely higher in the group with the complete bone union. The high agent uptake in the fracture area observed in tests performed before ESWT procedure seems to predict non-union at the end of the treatment. On the contrary, low metabolic bone dynamics may be a predicting factor for the positive treatment outcome in the complicated bone union treatment with ESWT intervention.

To conclude, BS reveals an increase in bone metabolism in the area of complicated fracture two weeks after ESWT procedure proving a metabolic reaction of bony tissue on this kind of treatment. That observation also applied to chronic conditions. Scintigraphy may facilitate qualification patients with bone union disorders for further mode of treatment.

Conflicts of interest

All authors have none to declare.

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