# Effect of combined treatment with focused mechano-acoustic vibration and pharmacological therapy on bone mineral density and muscle strength in post-menopausal women

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**Summary**

***Introduction.*** **Osteoporosis is a systemic disease of the skeleton characterized by a reduction in bone mass and alterations in microarchitecture accompanied by increase in fracture risk, with a relevant decline in quality of life and important social, economic, and health implications, representing one of the most common causes of disability and a major financial item of health cost in many Countries. The best therapy for osteoporosis is prevention, consisting in measures to avoid or slow the onset of the disease. Treatment includes measures aimed at osteoporotic individuals, with or without previous fractures and a high risk of a first or additional fracture.**
***Method.*** **We enrolled thirty post-menopausal osteoporotic women, allocated in the first group underwent a 6-month personalized drug therapy and focused mechano-acoustic vibration (2 sessions per week, each lasting 15 minutes); women allocated in the second group underwent only 6-month personalized drug therapy. Patients were evaluated performing dual-energy X-ray absorptiometry (DXA) and isokinetic machine evaluation, and administration of Tinetti scale and ECOS-16 questionnaire.**
***Result.*** **Show improvement of bone mineral density (BMD) and T-score at the lumbar spine and femoral neck, handgrip strength and isokinetic strength of the knee estensors, balance and gait, and quality of life.**
***Conclusion.*** **Hence, the combined treatment with focused mechano-acoustic vibration and pharmacological therapy has a beneficial effect on BMD and T-score as well as on the muscle strength and quality of life of osteoporotic subjects.**

*KEY WORDS: osteoporosis; post-menopausal women; focused vibration; bone mineral density; T- score; muscle strength.*

## Introduction

Osteoporosis is a systemic disease of the skeleton characterised by a reduction in bone mass and alterations in microarchitecture, accompanied by increase in fracture risk (1, 2).
In the United States, more than 20 millions of people are affected by osteoporosis, which causes about 1,5 millions of fractures every year (3), representing thus a socially relevant disease. Its incidence increases with age up to interest a major part of the over 80-year-old population. General prevalence varies from 5% in 50-year-old women up to 50% in 85-year old women, while among men is 2.4 and 20%, respectively (4). In Italy, according to the epidemiological study ESOPO (Epidemiological Study On the Prevalence of Osteoporosis), the prevalence of osteoporosis is 22.8 and 42.3% in women aged between 40 and 79-year old and 14.5 and 34.3% in men aged between 60 and 79-year-old, respectively. It has been observed a significant association between osteoporosis and history of fractures in both sexes (5). It has been estimated that today about 3.5 millions of women and 1 million of men are affected by osteoporosis in Italy. As it is estimated that in the next 20 years the Italian population over 65-year-old will experience a 25% increase, it is expected a proportional increase of incidence of osteoporosis. Furthermore, it is necessary underline that the real prevalence is underestimated, since the disease is often clinically silent until the onset of the most important complication, that is fracture.
Fracture produces a relevant decline in quality of life, with important social, economic, and health implications, as it represents one of the most common causes of disability and a major financial item of health cost in many Countries. The social impact of osteoporosis is so relevant that the lifetime risk of femoral fracture is higher than the risk of breast or endometrial cancer (15 *versus* 10 and 2.6%, respectively) for a

50-year-old Caucasian woman (6). Moreover, irrespective of the involved skeletal segment, a fracture increases of 50-100% the probability that an additional fracture occurs (7). It has been estimated that in American population 40% of 50-year-old women and 13% of 50-year-old men during lifetime will experience at least a frailty fracture. The most important consequences of osteoporotic fracture are mortality, morbidity, and relevant financial and social costs. In Italy, data about management of over 65-year-old patients with hip fracture indicates that the total cost relative to the year 2002 was more than one billion euro, and the main costs are the rehabilitation and social costs, which overall represent 50% of the total (8). According to epidemiological data, with the progressive ageing of the population, the prevalence and incidence of osteoporosis and resulting fractures are going to increase considerably, with significant implications from an economic and health point of view.
The best therapy for osteoporosis is prevention, consisting in measures to avoid or slow the onset of the disease. Everyone should be recommended the adoption of an appropriate lifestyle, including regular physical activity, adequate exposure to sunlight and nutrition including calcium-rich foods (9); in case of vitamin D deficiency and insufficient dietary intake of calcium, their supplementation is necessary. *A fortiori*, an adequate intake of calcium and vitamin D is the unavoidable premise for any specific pharmacological treatment; in fact, the lack of calcium and/or vitamin D is the most common cause of lack of response to drug therapy. To maintain the functionality of the musculoskeletal system and reduce the risk of fracture and its complications, it is advisable to ensure a protein intake (10). Lastly, tobacco addiction and alcohol abuse have to be discouraged. Especially in the elderly are useful advices to reduce the risk of falling.
Treatment includes measures aimed at osteoporotic individuals, with or without previous fractures and a high risk of a first or additional fracture. Non-pharmacological measures for prevention and treatment are comparable. Among them, the vibration therapy has emerged over the last decades as a promising non-invasive treatment for osteoporosis. In fact – through a mechanism not yet univocally clarified – high-frequency vibratory stimulation is able to significantly stimulate osteogenesis in animal models (11-14), and studies in human indicate that it improves bone mineral density (BMD), muscle strength and proprioception, particularly in people with osteoporosis or those with motor impairment from neuromuscular diseases of various etiologies (15-30).
The aim of this study is to evaluate the effect of combined treatment with focused mechano- acoustic vibration and pharmacological therapy on BMD and muscle strength in post-menopausal women.

## Materials and methods

*Study sample:* Our study was performed in agreement with the Helsinki Declaration (1983). Thirty osteoporotic women came to the University Centre of Physical and Rehabilitation Medicine (CUMFeR) of "Gabriele d'Annunzio" University of Chieti-Pescara, Italy. We enrolled only post-menopausal subjects aged 50-75 years (mean 67.8 years) affected by clinically defined primary osteoporosis (T-score <-2.5 at a dual-energy X-ray absorptiometry [DXA] performed within 2 years prior to the enrollment) and with body mass index between 20-25 kg/m$^2$. Subjects were excluded if had a history of irregular menstrual cycles, smoking, alcohol assumption, were treated with drugs know to affect bone metabolism, underwent multiple vertebral collapses (2 or more) within 12 months prior to enrollment, femoral fracture within 6 months prior to enrollment, recent major surgery or prosthetic implant, or were affected by secondary osteoporosis, headache or migraine, cardiovascular or neuromuscular disease, diabetes mellitus, rheumatic disorders, hernias, urolithiasis or cholelithiasis, malignancy.
The recruited women randomly divided into a treatment and a control group (each composed of 15 subjects), without significant differences in age, height, weight, and body mass index (BMI) (Table 1). Women allocated in group A underwent a 6-month personalized drug therapy and focused mechano-acoustic vibration (2 sessions per week, each lasting 15 minutes); women allocated in group B underwent only 6-month personalized drug therapy.
*Intervention.* Focused mechano-acoustic vibration was administered by means of *Vibration Sound System®* (Vissman s.r.l., Rome, Italy). It consists of a 32,000-revolution turbine with a flow rate of 35 m$^3$/hour able to generate air waves with a pressure up to 250 mbar, and of a flow modulator which makes air vibrate with a pressure up to 630 mbar and a frequency up to 980 Hz (however, frequency within 300 Hz is recommended) producing mechano-acoustic waves (Figure 1).
Unlike traditional whole-body vibrating plates, the so-modified acoustic wave assumes a sinusoidal enlarged periodic waveform as a square wave type, in which the amplitude alternates at a steady frequency between fixed minimum and maximum values, with the same duration at minimum and maximum and an ideally instantaneous transition between minimum to maximum (Figure 2). This allows to reach the maximum wave amplitude instantly and to maintain it on constant values, as well as to stimulate the Pacinian corpuscles (which represent the vibration receptors for excellence) (31) in a continuous manner throughout the duration of the maximum.

Table 1 - Baseline characteristics of the subjects. Values are expressed as mean ± standard deviation (SD).

| Variable | Total (n = 30) | Group A (n = 15) | Group B (n = 15) | p value |
|---|---|---|---|---|
| Age (years) | 65.3 ± 5.4 | 63.4 ± 5.3 | 67.1 ± 4.7 | 0.642 |
| Height (cm) | 163.3 ± 7.8 | 167.2 ± 6.6 | 159.3 ± 8.9 | 0.512 |
| Weight (kg) | 63.4 ± 6.1 | 65.3 ± 7.8 | 61.4 ± 4.3 | 0.738 |
| BMI (kg/m$^2$) | 23.8 ± 1.5 | 23.4 ± 1.7 | 24.2 ± 1.2 | 0.825 |

Figure 1 - Vibration Sound System® (Vissman s.r.l., Rome, Italy).

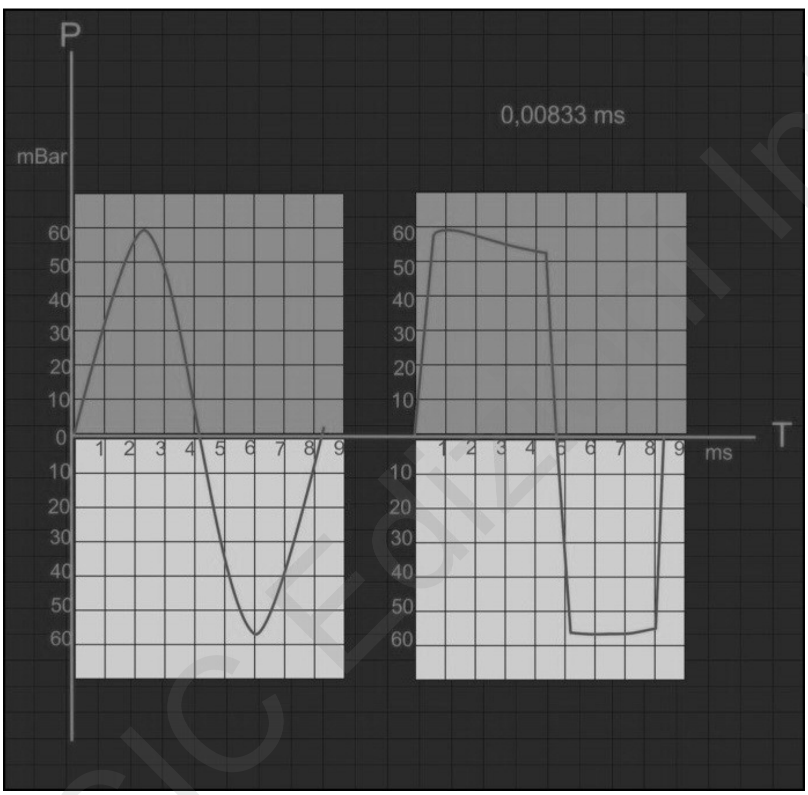


Figure 2 - Sinusoidal and sinusoidal enlarged periodic waveform as a square wave type.



Sites of application were the following muscles: superior fibers of the trapezius, triceps brachii, latissimus dorsi, rectus abdominis, gluteus maximus, rectus femoris, biceps femoris, and tibialis anterior.

*Clinical and instrumental assessment.* At the beginning (T0) and the end (T1) of the treatment all patients performed:

- DXA QDR-2000 fan-beam system (Hologic Inc., Waltham, Massachusetts, USA) to assess BMD and T-score at whole body, lumbar spine (L1-L4) and femoral neck;
- assessment of the hand grip strength with Jamar hydraulic dynamometer, which allows to explore the maximal isometric strength of the hand grip (kg) while performing two 5-sec measurements in each hand with the elbow flexed at 90°;
- assessment of the lower limb strength with isokinetic machine (Biodex Medical Systems, Inc., New York City, New York, USA), which allows to explore the maximal dynamic strength at the peak torque (N•m) while performing the movement of knee flexion and extension between 0-90° against the lever arm of the dynamometer (five maximal concentric repetitions were performed at 60°/s and 270°/s, with a 2-min rest period between tests);
- evaluation of balance and gait by administration of the

Tinetti scale (32) and of patient's health-related quality of life by administration of the ECOS-16 questionnaire (33-35).

*Data analysis.* Data obtained were analyzed with Number Cruncher Statistical System 9 (NCSS 9; Kaysville, Utah, USA) software for Windows. After checking for the normality of distribution (with the Shapiro-Wilk test), comparison between the two groups (treatment vs control) was made with unpaired Student's t-test and Mann-Whitney U-test (for normal and non-normal distribution, respectively). Statistical significance was set to values of $p \leq 0.05$. Values are expressed as mean ± standard deviation (SD).

## Results

At the end of the study, in both groups there was no drops-outs and no vibration-related adverse effects were observed.

The BMD changed as follows: in group A, from 0.886 ± 0.079 to 0.925 ± 0.034 (p = 0.027) at whole body, from 0.823 ± 0.057 to 0.872 ± 0.014 (p = 0.030) at lumbar spine, from 0.672 ± 0.016 to 0.783 ± 0.061 (p = 0.043) at femoral neck; in group B, from 0.893 ± 0.058 to 0.899 ± 0.076 (p = 0.053) at whole body, from 0.824 ± 0.043 to 0.826 ± 0.062 (p = 0.069) at lumbar spine, from 0.671 ± 0.021 to 0.566 ± 0.094 (p = 0.077) at femoral neck . The T-score changed as follows: in group A, from -1.91 ± 1.83 to -1.75 ± 1.26 (p = 0.036) at whole body, from -2.84 ± 1.63 to -2.67 ± 1.48 (p = 0.041) at lumbar spine, from -2.47 ± 1.87 to -2.32 ± 1.92 (p = 0.047) at femoral neck; in group B, from -1.97 ± 1.62 to -1.92 ± 1.73 (p = 0.065) at whole body, from -2.84 ± 1.82 to -2.81 ± 1.27 (p = 0.79 at lumbar spine, from -2.51 ± 1.49 to -2.68 ± 1.14 (p = 0.062) at femoral neck (Table 2).

The hand grip strength significantly improved in group A from 31.76 ± 9.24 to 33.42 ± 7.85 (p = 0.026) in the right hand and from 23.08 ± 10.36 to 25.59 ± 9.72 (p = 0.018) in the left hand, in group B changed from 30.97 ± 8.61 to 31.26 ± 8.39 (p = 0.067) in the right hand and from 23.53 ± 11.28 to 22.81 ± 7.63 (p = 0.334) in the left hand (Table 3).

The isokinetic strength of the knee estensors changed as follows: in group A from 21.82 ± 3.56 to 23.20 ± 4.13 (p = 0.039) in flexion at 60°/s, from 18.51 ± 2.73 to 19.41 ± 3.94 (p = 0.193) in flexion at 270°/s, from 23.40 ± 4.69 to 24.43 ± 5.21 (p = 0.047) in extension at 60°/s, from 19.56 ± 3.42 to 21.13 ± 5.48 (p = 0.028) in extension at 270°/s; in group B from 21.27 ± 2.89 to 20.98 ± 5.29 (p = 0.492) in flexion at 60°/s, from 18.46 ± 5.13 to 18.79 ± 4.37 (p = 0.0387) in flexion at 270°/s, from 23.77 ± 3.36 to 24.35 ± 2.19 (p = 0.254) in extension at 60°/s, from 20.41 ± 4.28 to 21.03 ± 6.12 (p = 0.265) in extension at 270°/s (Table 4).

In group A the average score of the Tinetti scale significantly increased from 21.37 to 25.26 (p = 0.023) and the ECOS-16 questionnaire significantly decreased from 3.82 to 3.17 (p = 0.046); in group B the Tinetti scale showed no change (from 22.03 to 22.95, p = 0.973) and the ECOS-16 questionnaire

Table 2 - Mean values of bone mineral density (BMD) and T-score at whole body, lumbar spine and femoral neck. Values are expressed as mean ± standard deviation (SD). Asterisk indicates statistical significance.

| | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| | T0 | T1 | p value | T0 | T1 | p value |
| **BMD (g/cm$^2$)** | | | | | | |
| **Whole body** | 0.886 ± 0.079 | 0.925 ± 0.034 | 0.027* | 0.893 ± 0.058 | 0.899 ± 0.076 | 0.053 |
| **Lumbar spine** | 0.823 ± 0.057 | 0.872 ± 0.014 | 0.030* | 0.824 ± 0.043 | 0.826 ± 0.062 | 0.069 |
| **Femoral neck** | 0.672 ± 0.016 | 0.783 ± 0.061 | 0.043* | 0.671 ± 0.021 | 0.566 ± 0.094 | 0.077 |
| **T-score** | | | | | | |
| **Whole body** | -1.91 ± 1.83 | -1.75 ± 1.26 | 0.036 * | -1.97 ± 1.62 | 1.92 ± 1.73 | 0.065 |
| **Lumbar spine** | -2.84 ± 1.63 | -2.67 ± 1.48 | 0.041* | -2.84 ± 1.82 | -2.81 ± 1.27 | 0.079 |
| **Femoral neck** | -2.47 ± 1.87 | -2.32 ± 1.92 | 0.047* | -2.51 ± 1.49 | -2.68 ± 1.14 | 0.062 |

Table 3 - Mean values of right and left hand grip strength. Values are expressed as mean ± standard deviation (SD). Asterisk indicates statistical significance.

| | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| **Hand grip strength (kg)** | | | | | | |
| | T0 | T1 | p value | T0 | T1 | p value |
| **Right hand** | 31.76 ± 9.24 | 33.42 ± 7.85 | 0.026* | 30.97 ± 8.61 | 31.26 ± 8.39 | 0.067 |
| **Left hand** | 23.08 ± 10.36 | 25.59 ± 9.72 | 0.018* | 23.53 ± 11.28 | 22.81 ± 7.63 | 0.334 |

Table 4 - Mean values of knee flexor and extensor peak torques at the angular speeds 60°/s and 270°/s. Values are expressed as mean ± standard deviation (SD). Asterisk indicates statistical significance.

| Knee peak torque(N•m) | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| | T0 | T1 | p value | T0 | T1 | p value |
| **Flexion at 60°/s** | 21.82 ± 3.56 | 23.20 ± 4.13 | 0.039* | 21.27 ± 2.89 | 20.98 ± 5.29 | 0.492 |
| **Flexion at 270°/s** | 18.51 ± 2.73 | 19.41 ± 3.94 | 0.193 | 18.46 ± 5.13 | 18.79 ± 4.37 | 0.387 |
| **Extension at 60°/s** | 23.40 ± 4.69 | 24.43 ± 5.21 | 0.047* | 23.77 ± 3.36 | 24.35 ± 2.19 | 0.254 |
| **Extension at 270°/s** | 19.56 ± 3.42 | 21.13 ± 5.48 | 0.028* | 20.41 ± 4.28 | 21.03 ± 6.12 | 0.265 |

not significantly decreased from 4.15 to 3.94 (P = 0.052). Even though the Study was not focused on prevention of falls, no one in the treatment group fell whereas one subject fell once during the course of the trial.

## Discussion

One of the most frequent diseases associated with ageing is osteoporosis, especially in post-menopausal women. It affects bone mass and muscle strength, with risk for falls, fractures and decline in quality of life.

It has been shown that vibration is an appropriate stimulus to generate bone formation and improve muscle strength, thus emerging over the last decades as a promising non-invasive treatment for osteoporosis, despite the several different protocols used, due to the numerous combinations of amplitudes and frequencies possible with the currently marketed devices.

Even though little is known about its exact mechanism(s) of action, according to most of Authors this treatment approach could cause an anabolic effect on bone mass, with significant increases in BMD at lumbar spine and femoral neck when compared with baseline; consistently with literature data, in our experience we found improvement in BMD and T-score values in the treatment group, and little non significant improvement or decrease in control group.

We also found significant increases in isokinetic strength of the knee extensors muscles in vibration treatment group. Although it is difficult to compare studies and standardize the application of the interventions on the skeletal and muscular systems, owing to the differences in vibration protocols used in the different studies, our results are in line with those published by other Authors. The reaffirmed transient and long-term enhancement of the muscle mechanical behavior (increase in sectional area and reduction in adipose tissue inside the muscle itself, increase in contractile velocity, force and power, improvement in vertical jumping ability, isometric lower-limb extension strength, and dynamic or static body balance) is strongly suggestive for a neurogenic adaptation that may occur in response to the vibration treatment.

Most importantly, it is remarkable that the results of this Study were obtained by means of a focal vibration protocol, in contrast to what reported by most other Authors. Indeed in our own experience, the high vibratory intensity achievable only with this type of stimulation is able to activate the Pacinian corpuscles besides muscle spindles eliciting the so-called tonic vibration reflex and other selected nervous networks (36, 37).

For example, using high-frequency focal vibration, we reached the normalization of the basal tone in two heads of the quadriceps femoris muscle (rectus femoris and vastus medialis) in ten sporting subjects (38). In another study, sarcopenic thigh muscles submitted to local vibrational training at 300 Hz for a period of 12 weeks, starting with a session of 15 min stimulation once a week and increasing to three sessions of 15 min per week, displayed enhanced maximal isometric strength and increased content of fast MyHC-2X myosin, without any change in cross-sectional area or in specific tension; analysis of transcriptional profiles by microarray revealed changes in gene expression after 12 weeks of local vibrational training, in particular pathways related with energy metabolism, sarcomeric protein balance and oxidative stress response were affected: thus, the mode of action of vibration is based on cellular and molecular changes which do not include increase in fiber or muscle size (39), but affects serum level of growth hormone, creatine phosphokinase (increase) and cortisol (decrease) (40). Moreover, using the focused mechano-acoustic vibration at 300 Hz, it has been also shown that a 12-week training is equivalent to a global sensorimotor and a resistance training (60-80% of maximum theoretical force, 10-12 repetitions for 3 sets, 2 sessions per week) in improving balance, with a reduction of sway area and of ellipse surface, and in increasing the length of half-step and reducing the width of the support at the gait analysis, with reduction of the risk of falls in the sarcopenic elderly subjects enrolled in the study (41).

Hence, the present study confirms the action of focal vibration on bone mass and muscle strength, and also strengthens the correlation (predictable but often not adequately highlighted) between the two effects (42-44).

Despite these results, a prolonged follow-up is needed to determine whether the effects of vibration therapy are transient or long-lasting, and therefore to confirm the actual superiority of the combined treatment compared to the sole pharmacological therapy, whose efficacy can be verified only in the medium and long term.

From this point of view, it would be desirable to design future studies that take into account the specific types of drug prescribed for patients with osteoporosis, and that correlate their mechanism of action to that of vibratory treatment.

## Conclusions

Results obtained show that combined treatment with focused mechano-acoustic vibration and pharmacological therapy has a beneficial effect on BMD and T-score as well as on the muscle strength and quality of life of osteoporotic subjects.
From a future perspective, the treatment with Vibration Sound System® could be used not only in the advanced stage of the osteoporosis but also as a preventive approach of the development of full- blown disease.

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