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Short Communication

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Clinical Characteristics and Bone Mineral Density Score in Post-Stroke Neuromuscular Deficit

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Abstract

Background: Disuse osteoporosis in hemiparetic patients often results in significant morbidity, decreased quality of life, and different clinical characteristics. The study aimed to investigate the effect of these clinical factors on bone mineral density (BMD).

Methods: This was an analytical observational study with a cross-sectional method evaluating hemiparetic patients at Cipto Mangunkusumo Hospital from 2018 to 2019. BMD (g/cm^2) was assessed using dual energy X-ray absorptiometry (DXA) on the spine and both sides of the body. The relationship and correlation between BMD and delta BMD scores with clinical characteristics were analyzed. A linear regression test was used to assess the correlation between variables.

Results: A total of 34 participants were recruited for this study. There was a difference between the healthy and paretic side of BMD of both hip and wrist ($P < 0.001$), strong positive correlation between the onset of hemiparesis and wrist and hip delta BMD ($r = 0.779$, $P = 0.001$ and $r = 0.791$, $P = 0.001$), and significant association between delta BMD and age and motor strength. Multivariate analysis shows that the onset of hemiparesis was a strong predictor of delta BMD (aR^2 wrist = 0.486, aR^2 hip = 0.614). There was a 7.36% decrease in the mean BMD score of the paretic side compared to the non-paretic side.

Conclusion: A low BMD score is prevalent in seven out of 10 patients with post-stroke neuromuscular deficit. Age, limb strength, the onset of hemiparesis, and rehabilitation compliance are associated with decreased BMD among patients with post-stroke neuromuscular deficit.

Keywords: Bone density; Hemiparesis; Hemiplegia; Osteoporosis; Stroke

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Introduction

Osteoporosis is a condition characterized by reduced bone mass, deteriorated bone structure, and increased fracture risk. The primary osteoporosis occurs as a natural part of aging or life stages, without an identifiable secondary cause. Osteoporosis has various forms beyond age-related primary osteoporosis such as corticosteroid-induced osteoporosis (CIO). Corticosteroids impair bone metabolism by inhibiting osteoblast activity, promoting osteoclast-mediated resorption, reducing calcium absorption, and impairing vitamin D metabolism. Other secondary forms of osteoporosis include those caused by chronic illnesses (e.g., rheumatoid arthritis), endocrine disorders (e.g., hyperthyroidism), and lifestyle factors (e.g., smoking, excessive alcohol use). Preventative strategies, including calcium and vitamin D supplementation, lifestyle modifications, and, when necessary, bone-protective medications, are critical for managing these conditions [1].

Osteoporosis affects around 10 million population in the United States and is predicted to affect 80% of people above 65 years old [2]. Prevalence of osteoporosis in Indonesia is 10.3% with fracture risk of more than 40%. Osteoporosis can happen due to physiological process or secondary process, such as chronic kidney disease, prolonged steroid consumption, hormonal disturbance, and prolonged immobilization [3].

Patients who suffer from stroke are often followed by a loss of extensive bone mass, which triggers an increased risk of fractures. Bone deficit often starts directly on the first day after injury to brain cells and increases rapidly during the first 3 - 4 months after stroke. Fracture in the paralyzed extremity is one of the most feared complications as it causes significant morbidity in patients. During the first year after stroke, pa-

Table 1. Example of Delta BMD Calculation Using Data of Age and Stroke Onset

A 55-year-old man with a history of stroke 18 months before examination	
Delta BMD of wrists	= -0.205 + 0.009 × (onset of hemiparesis in months) + 0.002 × (age in years)
	= -0.205 + 0.009 × 18 + 0.002 × 55
	= 0.067 adjusted R squared 48.6%
Delta BMD of hip	= 0.053 + 0.010 × (onset of hemiparesis in months)
	= 0.053 + 0.010 × 18
	= 0.233 adjusted R squared 61.4%

BMD: bone mineral density.

tients can lose bone mineral density (BMD) up to 14% in the proximal femur and 17% in the upper extremity. After a longer period of time (up to 484 weeks after a stroke), bone mineral content has been reported to decrease by 21% in the upper extremities and 4.5% in lower extremitries [4].

Although disuse osteoporosis in stroke patients is a well-documented phenomenon, the reduced BMD in stroke is multifactorial. Pharmacological therapies can also significantly influence bone health, especially in patients on long-term medications like anticoagulants or anticonvulsants. To mitigate these risks, stroke patients should undergo a comprehensive evaluation of both their physical rehabilitation needs and their medication regimen. However, at the moment, long-term studies about the risk of post-stroke osteoporosis in Indonesia are still scarce. There is also no consensus regarding treatment of osteoporosis in stroke patients and when is the right time to start treatment. This study aimed to measure BMD in stroke patients and evaluate its relationship with several factors, including age, sex, onset pattern, motoric function, and different rehabilitation status.

Materials and Methods

This was an observational analytic study using a cross-sectional study design. Participants were patients with neuromuscular deficit due to stroke who visited Neurorestoration Clinic in Cipto Mangunkusumo Hospital from June 2018 to March 2019. Patients admitted into the study were females less than 60 years old and males less than 70 years old, with a history of hemiparesis for 3 months or more, and a Medical Research Council motoric strength scale of 4 or less. We excluded patients who have bilateral neuromuscular deficit; history of bisphosphonate, steroid, and alcohol consumption; history of oophorectomy and fractures of the hip, wrist, and lumbar bodies; abnormal body mass index (BMI); history of chronic kidney disease and history of bone infection and malignancy [5].

Data were obtained through interview and physical examination. BMD of bilateral wrist and hip and lumbar body was measured using GE Lunar Prodigy bone densitometry dual X-ray absorbtiometry (DXA). To provide more accurate comparison, delta BMD was calculated as the difference between BMD in healthy side and paretic side [6]. Afterwards, we analyzed the relationship between BMD and demographical and clinical characteristics including age, sex, hemiparesis duration, participation in rehabilitation program, motoric strength, and hand dominance. An example of delta BMD calculation is shown in Table 1. Data testing was carried out using ordinal regression tests to assess the correlations between variables.

Standard protocol approvals, registrations, and patient consents

This study was approved by the Faculty of Medicine University of Indonesia Ethics Committee of the University of Indonesia (approval code no. 0312/UN2.F1/ETIK/2018). Written informed consents have been given to all research participants on their participation.

Results

A total of 34 participants (16 males and 18 females) were included in this study. In most cases, hemiparesis occurred in the dominant side (19 cases; 56 BMD scores). Clinical characteristics distribution of patients is shown in Table 2.

Bone density was measured in both paretic and unaffected sides of the hip and wrists. The mean BMD score of paretic hip and wrists was lower than the unaffected side ($P \leq 0.001$). The average percentage of BMD decrease in the wrists and hip was 7.36.

Bivariate analysis between age and delta BMD score showed moderate positive correlation (correlation coefficient r

Table 2. Clinical Characteristics of Subjects

Characteristics	Mean (SD)	P score
Age	54.71 (7.522)	0.011
Hemiparesis onset (months)	17.32 (4.388)	0.63
BMD healthy wrist	0.802 (0.149)	0.328
BMD paretic wrist	0.741 (0.15)	0.595
BMD healthy hip	0.833 (0.15)	0.228
BMD paretic hip	0.770 (0.15)	0.44
BMD spine	1.005 (0.20)	< 0.001

BMD: bone mineral density; SD: standard deviation.

Table 3. Multivariate Analysis of Hip Delta BMD

Predictor variables	Parameter estimation	95% confidence interval	P value
Constant	0.053	0.004 - 0.102	0.034
Duration after stroke onset	0.010	0.007 - 0.013	< 0.001
Age			0.154
Motoric strength of lower extremities			0.705

BMD: bone mineral density.

= 0.461 and 0.441, P = 0.006 and 0.009, consecutively). Negative correlation was found between age and BMD score of the paretic hip and wrist (correlation coefficient r = -0.526, P = 0.001). Comparison between sex revealed higher wrists BMD score in men. Duration after stroke onset was correlated with delta BMD of the wrist and hip (P = 0.001). Patients who complied with the rehabilitation program had higher BMD score of the paretic wrist (P = 0.037). Motoric strength also affected delta BMD of the wrist and hip, where delta BMD was higher in the paretic side (P = 0.003 and 0.033, consecutively). In contrast, hand dominance did not affect BMD score and delta BMD. The result of multivariate analysis of duration after stroke onset, age, and motoric strength is shown in Tables 3 and 4.

Discussion

As stated by Wolff, bone resorption is associated with axial loading. The less weight loads the bones have to sustain, the quicker the bones are resorbed. Disorders or pathological conditions causing the patient to be bedridden, such as hemiparesis following stroke, are proven to cause progressive bone loss [7]. Palermo et al stated that 40% of all stroke patients have osteoporosis, especially on the bones of paretic extremities in the first year after the onset of stroke [4]. Beside axial loading, decrease of BMD is also attributed to inactivity of affected extremitries [8]. Moreover, BMD score of unaffected extremities tends to increase due to increased activity and bone mineral redistribution [8]. The degree of bone density reduction in paretic side is correlated with the degree of functional deficits. Beaupre et al found that bone loss in the upper extremities during the first year after stroke was comparable to 20 years of bone loss in healthy people of the same age [9].

Our study produced similar result showing lower BMD score of the paretic extremities. Previous studies by Brealey et al revealed the same result showing lower BMD score of the upper extremities compared to BMD score of vertebral bones and lower extremities [10, 11].

The effect of demographical factors on BMD

Statistical analysis showed positive correlation between age and delta BMD, and negative correlation between age and BMD of paretic side. Although International Osteoporosis Foundation (IOF) advocates for BMD sreening using DXA in all women above 65 and men 70 years old, screening of patients who are younger than the recommended age might be beneficial as the effect of hemiparesis on BMD occurred early despite the age [12]. In the study by Liu et al, decrease in BMD of stroke patients happened as young as 36 years old [13].

Comparison between sex showed a small difference in the BMD of paretic side (mean BMD score of paretic wrists in males was 0.005 g/cm^2 higher than females). However, there was no difference between BMD and delta BMD values at other sites. Other than the risk of osteoporosis due to hormonal changes in females, Pang et al [14] described that bone resorption in males and females differs in the resorption pattern. Bone resorption in males occurs predominantly by endosteal reaction, while bone resorption in females mostly happens through periosteal reaction [15].

The effect of clinical factors on BMD

Hemiparesis duration

Duration after stroke onset is positively correlated with BMD and delta BMD scores of the wrists (correlation coefficient r = 0.779) and the hip (correlation coefficient r = 0.791). In our study, the earliest bone loss following stroke is detected at 10 months after the onset of stroke. Kim et al reported in their study that the decline of bone density happens earlier at 3 months after stroke. According to Lam et al, bone loss occurs rapidly during the first 24 months after the onset of stroke. After 2 years, the rate of bone resorption slowly declines until becoming steady. This plateau condition may occur faster in the hip and tibial diaphysis [16].

Other than detecting osteoporosis, BMD screening could be

Table 4. Multivariate Analysis of Wrist Delta BMD

Predictor variables	Parameter estimation	95% confidence interval	P value
Constant	-0.205	-0.325 to -0.084	0.002
Duration after stroke onset	0.009	0.005 - 0.012	< 0.001
Age	0.002	0.001 - 0.004	0.047
Motoric strength of lower extremities			0.558

BMD: bone mineral density.

useful to determine the right time to initiate appropriate therapy to prevent secondary morbidities, such as pathological fracture. In a prospective study performed by Forster and Young, 73% of stroke patients fell down in 6 months after discharge [17]. Furthermore, these patients are seven times more susceptible to hip fractures than normal population, if their BMD scores decline for 2 standard deviations (SDs) or more [18].

Compliance to rehabilitation program

Patients who followed rehabilitation program had better overall BMD scores. This result is in line with a previous study which showed that return to daily activities and normal function increases the bone density of stroke patients [6]. The rehabilitation programs should include gait training since certain gait characteristics are correlated with BMD of chronic stroke patients [19]. In addition, nutritional support should also be incorporated into the rehabilitation program as the concentration of serum 25-hydroxyvitamin D and 1,25-dihydroxyvitamin D is proven to affect bone resorption [20].

Motoric strength of the extremities

Higher delta BMD score was found in patients with lower motoric strength. This is due to the decrease in weight-bearing and functional activities on the paretic side, which ultimately leads to muscle atrophy [21]. A study by Pang et al compared motoric strength of extremities in stroke patients which was measured with hand-held dynamometry. They suggested that muscle atrophy and decrease in motoric strength reduced mechanical stimuli necessary for bone formation [22]. Additionally, weight-bearing capacity which creates mechanical loading is also related to BMD on hip [23].

Hand dominance

Immobilization of non-dominant extremities aggravated the initial low BMD score at this site, especially in upper extremity. The risk of bone loss in non-dominant extremities is 3.35 times higher than that on the dominant side. It was found that dominant hand had greater BMD score than the contralateral side [24-26]. Our study showed no difference between BMD score of dominant wrist and non-dominant wrist.

BMD of vertebral bones

In our study, the mean BMD score of the spine was greater than the mean BMD of paretic extremities and unaffected extremities. This showed that the decrease in BMD did not occur simultaneously and was in different degrees. This phenomenon of spine sparing was also found by Yavuzer et al and Biering-Sorensen et al. It was suggested that predilection of bone resorption in stroke patients was in peripheral bones [27]. Reduced burden on the skeleton is also thought to be the cause of limb osteopenia, hence BMD of vertebral bones is preserved due to gravitational loads during sitting in a wheelchair [28].

The BMD measurements in our study were obtained using DXA, which allowed precise and site-specific evaluation of the BMD. By analyzing multiple skeletal regions, including spine, hip, and the wrist, we could identify the differential impact of immobilization and weight-bearing on bone particularly in stroke patients.

Multivariate analysis of BMD predictors

Multivariate analysis of demographical and clinical factors produced two significant predictors of bone loss, which are age and duration of hemiparesis. These two factors can be used to estimate delta BMD score. The formula is as follows:

$$\text{Delta BMD of Wrists} = -0.205 + 0.009 \times (\text{duration of hemiparesis}) + 0.002 \times (\text{age})$$

$$\text{Delta BMD of Hip} = 0.053 + 0.010 \times (\text{duration of hemiparesis})$$

Duration of hemiparesis is calculated in months, while age is in years.

Conclusion

In stroke patients, BMD on the hemiparetic side is lower than the unaffected side. Several factors, including age of the patient, hemiparesis duration, motoric strength, and rehabilitation compliance are correlated with BMD loss. In particular, age and onset of hemiparesis are proven to be major predictors of accelerated BMD loss in stroke patient. We found that there is sparing effect in the spine as BMD value of the spine is higher than BMD of both extremities (paretic or non-paretic side).

The effect of immobilization takes place soon after the onset of stroke. Rehabilitation program in stroke patients addressed on functional motor recovery can prevent further bone loss. Diagnostic and treatment of disuse osteoporosis in stroke patients should also consider age and onset of hemiparesis to provide personalized treatment. We hope that this evidence of osteoporosis in stroke patients can be the basis of BMD screening and anti-osteoporotic drug administration and/or calcium and vitamin D supplementation to prevent osteoporotic fracture. Further studies involving larger number of sample and multiple centers may give better view on the prevalence of disuse osteoporosis among stroke patients.

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Conflict of Interest

The authors have no conflict of interest to declare.

Informed Consent

Informed consent for publication was obtained from all participants in this study.

Author Contributions

Ifran Saleh, Harris S. Hasan and Nyimas D. Yulisa designed the study; Ifran Saleh and Auliya Akbar performed the experiments and analyzed the data; Ifran Saleh, Harris S. Hasan and Nyimas D. supervised the experiments; Ifran Saleh and Auliya Akbar wrote the manuscript; Dina Aprilya reviewed and revised the manuscript.

Data Availability

All data generated during this study are included in this article. Further enquiries can be directed to the corresponding author.

Abbreviations

BMD: bone mineral density; BMI: body mass index; CIO: corticosteroid-induced osteoporosis; DXA: dual energy X-ray absorptiometry; IOF: International Osteoporosis Foundation; SD: standard deviation

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