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Skeletal and functional status in patients with long-standing stroke

Jakość szkieletu i stan funkcjonalny u pacjentów po odległym udarze mózgu

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Abstract
Introduction: Skeletal and functional status can be affected after stroke, mainly due to subjects' immobilisation. The aim of our study was to assess the functional and bone status in post-stroke patients with hemiplegia. Quantitative ultrasound at hand phalanges and bone mineral density (BMD) in the wrist and the calcaneal bone were compared between the paralysed and the non-paralysed side. The study was performed at the Department of Rehabilitation in Nowa Sol.
Material and methods: The study included a group of 71 subjects (29 females and 42 males) who had suffered a stroke. Skeletal status was assessed by densitometry (Pixi, Lunar Corp., USA, forearm, calcaneus) and ultrasound (DBM Sonic 1200, IGEA, Italy, hand phalanges). Functional status was evaluated by the Barthel index.
Results: The mean values of forearm BMD and ultrasound measurements were significantly lower in the affected limbs versus the opposite site. The mean Barthel index value was 73 ± 21.5. Reduction of the time interval between stroke and standing up positively influenced the difference between wrist BMD in the affected versus the opposite limb, both in the whole group of patients ($r = 0.3$, $p < 0.05$) and females ($r = 0.41$, $p < 0.05$). Forearm BMD in males in the affected limb correlated with the Barthel index ($r = 0.35$, $p < 0.05$).
Conclusion: Fracture risk in post-stroke subjects may be increased due to disturbed skeletal and functional status. Reduction of the time interval between stroke and standing up improved wrist densitometric results.
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Key words: *Barthel index, bone densitometry, calcaneus, hand, male, female*

Streszczenie
Wstęp: Unieruchomienie spowodowane udarem mózgu może być przyczyną obniżonej jakości tkanki kostnej i funkcjonalnej sprawności chorego. Celem pracy była ocena stanu kostnego i funkcjonalnego pacjentów z niedowładem połowiczym będącym następstwem udaru. Dokonano obustronnego porównania pomiarów prędkości fali ultradźwiękowej paliczków rąk oraz gęstości mineralnej kości piętowych i przedramion. Badanie przeprowadzono na Oddziale Rehabilitacji Szpitala w Nowej Soli.
Materiał i metody: Zbadano 71 osób po przebytym udarze (29 kobiet i 42 mężczyzn). Pomiary densytometryczne aparatem PIXI (Lunar, Stany Zjednoczone) i ultradźwiękowe aparatem DBM Sonic (Igea, Włochy) zestawiono z oceną sprawności za pomocą skali Barthel.
Wyniki: Średnie wartości pomiarów ultradźwiękowych i gęstości mineralnej kości (BMD, *bone mineral density*) przedramion były znamiennie obniżone po stronie porażonej. Wskaźnik Barthel wynosił średnio 73 ± 21,5 pkt. Skrócenie czasu pomiędzy wystąpieniem udaru a pionizacją pozytywnie wpływało na różnice między BMD kości przedramion po stronie niedowładnej i przeciwnej w całej grupie ($r = 0{,}3$, $p < 0{,}05$) i u kobiet ($r = 0{,}41$, $p < 0{,}05$). Gęstość mineralna kości przedramion po stronie porażonej u mężczyzn korelowała ze wskaźnikiem Barthel ($r = 0{,}35$, $p < 0{,}05$).
Wnioski: Ryzyko złamań wśród pacjentów po udarze może być zwiększone z powodu zaburzeń tkanki kostnej i stanu funkcjonalnego. Skrócenie czasu między udarem a pionizacją poprawiało wartości densytometryczne przedramion.
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Słowa kluczowe: *wskaźnik Barthel, densytometria, pięta, ręka, mężczyźni, kobiety*

Introduction

Long-term immobilisation is an important factor influencing skeletal status [1]. Given that the number of stroke-immobilised subjects is steadily growing, a better understanding of the nature of skeletal changes may improve the patients' management. Bone changes in post-stroke patients have been evaluated in several studies [2–12]. In general, the authors observed progressive hemiosteoporosis, a significant clinical finding be-

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Table I. *Clinical characteristics of studied subjects (mean, SD, range)*
Tabela I. *Charakterystyka kliniczna badanych grup (średnia, odchylenie statystyczne, próba)*

	n	Age (years)	Weight [kg]	Height [cm]	Time interval after stroke (months)	Barthel index (point score)
Females	29	64.5 ± 8.3 49–79	71.8 ± 12.0 50–100	157.0 ± 6 146–170	28 ± 25 1–88	72 ± 23.7 20–100
Males	42	60.9 ± 11.1 33–82	77.3 ± 10.0 60–107	169.0 ± 7.1 152–190	34.8 ± 52.6 1–120	73.5 ± 20.0 25–100
All	71	62.8 ± 0.3 33–82	75.0 ± 11.1 50–107	164 ± 9.2 146–190	32.4 ± 43.5 1–120	73 ± 21.5 20–100

cause according to some reports, 4–15% of patients with hip fractures have had cerebrovascular disorders and 79–100% of the fractures occurred on the hemiplegic side [13, 14]. Usually, there is a significant bone loss on the paretic side, highest in patients with the most severe functional impairment. In some subjects, bone loss in the paretic arm during the first post-stroke year equals that over a period of > 20 years in healthy individuals of comparable age [12].

Recently, the prevention of hip fractures after stroke has been investigated [15]. A major problem in the interpretation of studies performed in post-stroke subjects is the presence of genetic and environmental factors influencing the current skeletal status, which can make selecting an adequate control group rather difficult. Therefore, we decided in this current study to use a solution already proposed in the medical literature [2, 6, 10]. This model gives an opportunity to compare results obtained in the paralysed and non-paralysed sides of the body and offers the advantage of proper control for involved cofactors.

Our study included peripheral bone mineral density (BMD) measurements and quantitative ultrasound (QUS) evaluations of hand phalanges. Quantitative ultrasound, a method of skeletal assessment, was introduced later than classical densitometry dual X-ray absorptiometry. QUS reveals both quantitative and qualitative (elasticity and microstructure) features of bone tissue and is used in pathological conditions and physiological evaluations.

The results of studies support the potential of QUS measurements to predict osteoporotic fractures [16–22]. QUS measurements demonstrate also an ability to detect skeletal growth and involution [23, 24].

Only rarely have QUS measurements been used to detect skeletal changes, due to physical activity [25] or immobilisation [26, 27] and so, the inclusion of sonographic imaging in our study was fairly novel. In one study, calcaneal QUS measurements have been used in patients following a stroke [28].

The purpose of our study was to assess skeletal and functional status in a group of long-standing patients after the first stroke.

Material and methods

All the evaluated patients were admitted for post-stroke rehabilitation to the Department of Rehabilitation, the entire group comprising 71 subjects (29 females and 42 males). The clinical characteristics of the patients are presented in Table I. All the women were post-menopausal, with menopause occurring at the age of 50.4 ± ± 2.9 years. Stroke diagnoses included brain infarct in 59 subjects, intracerebral haemorrhage in ten and stroke of unknown origin in two. In 45 subjects, hemiplegia was observed on the right hand side and in 26 on the left hand side.

Subjects were enrolled with no causes known to affect bone metabolism (e.g. chronic kidney, liver or thyroid diseases or prolonged medication with corticosteroids, anticonvulsants, thyroid hormones). Eleven subjects were excluded due to the presence of at least one of the above.

No patients received any medications, such as bisphosphonates, hormone replacement therapy or calcitonin, either before or during the study period. Four subjects had fractures after stroke (two patients presented with proximal femur fractures and two with ankle fractures). Of the studied subjects, 69 were right-handed and two were left-handed. Rehabilitation was managed and provided by a multi-disciplinary team, including physicians, physical therapists and experienced nurses. All the patients were managed in adherence with the current theory of neuro-plasticity and motor learning, designed by Berta Bobath [29].

The local Ethics Committee accepted the study protocol and all the enrolled subjects gave written consent before participation.

The skeletal status was assessed by densitometric measurements of the wrist and the calcaneus, their re-

Table II. *Results of densitometric and ultrasound measurements (mean, SD)*
Tabela II. *Średnie wyniki pomiarów densytometrycznych i ultradźwiękowych (średnia, odchylanie standardowe)*

	Forearm BMD [g/cm²]		Calcaneal BMD [g/cm²]		Ad-SoS [m/s]	
	Affected side	Non-affected	Affected side	Non-affected	Affected side	Non-affected
All n = 71	0.405 ± 0.13*	0.466 ± 0.13	0.452 ± 0.15	0.464 ± 0.13	1914 ± 88*	1963 ± 75
Females n = 29	0.327 ± 0.1*	0.368 ± 0.1	0.386 ± 0.13	0.381 ± 0.1	1875 ± 51*	1931 ± 63
Males n = 42	0.459 ± 0.11*	0.534 ± 0.11	0.497 ± 0.14	0.522 ± 0.11	1940 ± 98*	1986 ± 75

*results significantly lower than in the contralateral side, $p < 0.0$

sults being expressed in g/cm², using a Pixi densitometer (Lunar, USA), and by QUS at the hand phalanges, using a DBM Sonic 1200 (IGEA, Italy) model. A DBM Sonic ultrasound scanner consists of two probes mounted on an electronic caliper; one functions as an emitter and one as a receiver. The receiver records ultrasound energy after it crosses the phalanx. We determined the amplitude-dependent speed of sound (Ad-SoS [m/s]) in the distal metaphyses of the proximal phalanges in the second through the fifth finger of the dominant hand, considering the first signal at amplitude of, at least, 2 mV at the receiving probe; thus, the measured speed of sound was amplitude-dependent. Acoustic coupling was achieved with a standard ultrasound gel. All densitometric measurements were performed by the same operator and all the QUS scanning was done by a second operator on the same day, both on the affected and the non-affected side. The scanners were calibrated daily, according to the manufacturer's recommendations and with reference to phantom patterns. In order to precisely establish a possible error, serial measurements were conducted in the same group of subjects, covering all the three sites on the affected side and each measurement was repeated five times with repositioning of the scanned limb.

CV% was 0.43% for Ad-SoS, 0.7% for calcaneus BMD and 2.39% for wrist BMD.

The functional status was evaluated for primary, daily activities by the Barthel Index (BI) [30], where a score of 100 corresponds to functional independence and a score of 0 represents total dependence. All functional evaluations were performed on the same day as skeletal measurements by an experienced physician (F.P.).

Statistics

The results obtained on the paralysed body side were compared with the results obtained on the unaffected body side, with the latter acting as a control. Statistical analysis was performed using the Statistica programme. Data distribution was assessed by the Shapiro-Wilk test. Differences between variables were assessed by the Student's *t*-test or the Mann-Whitney U-test (in case of nonparametric data and distribution different from normal). Pearson's correlations and Spearman rank correlations were used in order to detect relationships between variables. Due to the small number of subjects with fractures in history, such cases were not analysed separately. All the results were considered as statistically significant at $p < 0.05$.

Results

Table II presents the results of skeletal and functional measurements. Since the reference data on densitometric and ultrasound Z-scores derived from the local population were not available, we decided to use only direct values of skeletal measurements. The mean values of forearm BMD and Ad-SoS were significantly lower in the affected limb versus the opposite limb in the whole group, males and females, and no differences were noted for calcaneus measurements. The time from stroke did not influence BI or skeletal variables. Time reduction between stroke and standing up decreased the difference between wrist BMD in the affected versus that in the opposite limb in the whole group ($r = 0.3$, $p < 0.05$) (Fig. 1) and among females ($r = 0.41$, $p < 0.05$) (Fig. 2). In males, a borderline significant correlation was noted ($r = 0.29$, $p = 0.08$) (Fig. 3). Calcaneal BMD and Ad-SoS were not influenced by time reduction between stroke and standing up. Among skeletal variables, only forearm BMD in the affected limbs of male subjects correlated with BI ($r = 0.35$, $p < 0.05$). Ad-SoS correlated significantly with forearm BMD (r ranged from 0.42 to 0.58, $p < 0.01$) and calcaneal BMD (r ranged from 0.45 to 0.46, $p < 0.01$).

Discussion

To the best of our knowledge, this study is the first to present data on the skeletal status in patients after stroke, using phalangeal ultrasound measurements.

The most significant finding of our study is that the skeletal status of the upper limbs was affected approx-

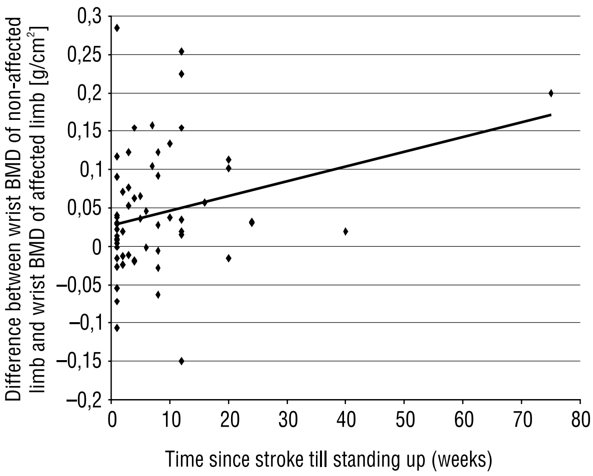

Figure 1. *Correlation of wrist BMD difference between affected and non-affected side and time since stroke till standing-up in the whole group*

Rycina 1. *Współzależność różnic BMD nadgarstka pomiędzy porażoną i nieporażoną stroną od czasu wystąpienia udaru a pionizacją w całej grupie*

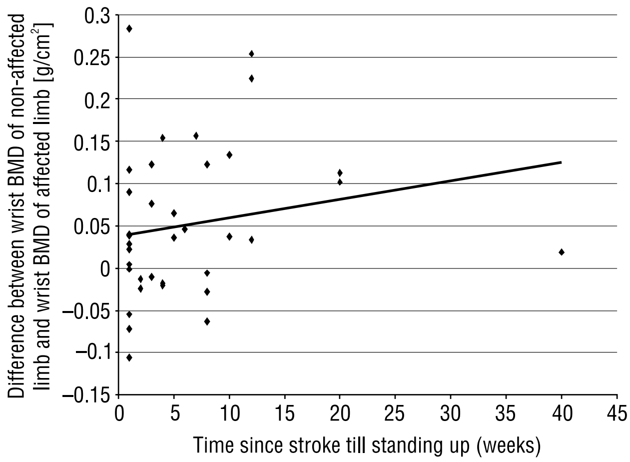

Figure 3. *Correlation of wrist BMD difference between affected and non-affected side and time since stroke till standing-up in men*

Rycina 3. *Współzależność różnic BMD nadgarstka pomiędzy porażoną i nieporażoną stroną od czasu wystąpienia udaru a pionizacją u mężczyzn*

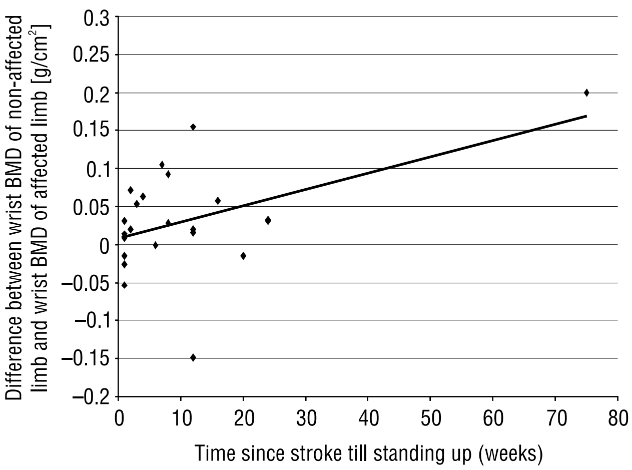

Figure 2. *Correlation of wrist BMD difference between affected and non-affected side and time since stroke till standing-up in women*

Rycina 2. *Współzależność różnic BMD nadgarstka pomiędzy porażoną i nieporażoną stroną od czasu wystąpienia udaru a pionizacją u kobiet*

imately three years after a stroke, something that may increase the future fracture risk. That observation applied to both men and women. Furthermore, we regard as clinically significant our observation that time reduction between stroke and standing up improved forearm densitometric results.

The Barthel Index in healthy subjects is around 100. So, its value of about 72 noted in our patients indicated functional status impairment. Therefore, additionally to disturbances in the skeletal status, a risk for falls may be increased. Generally, we found no influence of the time period from stroke on skeletal variables or functional status. However, time reduction between stroke and standing up decreased significantly the difference between forearm BMD in the affected versus the opposite side. In males, this association was weaker than in females. This is an important observation concerning the management of stroke patients. Other authors have proved that BMD in paraplegic patients, who do or do not perform standing, differs significantly at proximal femur [31] and a longitudinal study by Jorgenson et al. [4] found that in patients initially able to walk after stroke, BMD reduction was significantly smaller. The greatest changes in skeletal measurements are usually observed during the first months after cerebral accident [32] and, probably, in long-standing stroke patients, these factors cannot express their role. In some studies, skeletal measurements have been performed in subjects a long time after a stroke [7–9].

Despite different methodologies used in order to assess the skeletal status in stroke patients, a comparison of our study results with the results of other authors is interesting. Sato et al. [7], in a group of 93 patients, all of them more than four years after a stroke, noted significantly lower optical density of the metacarpal bone on the hemiplegic side. They noted also a positive correlation between the affected-non-affected side differences with the duration of illness, suggesting a continuous progression of osteopenia on the hemiplegic side. The current study did not confirm that observation, and the time interval from stroke did not correlate with the same data in our patients. In the study by Sato et al. [7], a correlation was also proven between clinical severity of hemiplegia, evaluated by Brunstrom's stages, and skeletal variables. We did not obtain any correlation between skeletal variables and functional status but BI does not express functional status separately for finger, upper and lower limbs as happens in Brunstrom's stages.

In another study by the same authors, metacarpal BMD and the functional status by BI were determined in 93 subjects an average of 4.6 years after a stroke [8]. BMD was significantly lower on the hemiplegic side than on the intact side, correlating significantly with the BI values, while the relationship between illness duration and BMD or BI were not given. The values of both studies, in comparison with the reported study, are also connected with the assessment of similar anatomic sites within upper limbs, what may explain generally common trends of skeletal changes. In still another study of 112 subjects, an average of nearly four years after a stroke, BMD values at the proximal femur were significantly decreased on the paretic versus the non-paretic side [9]. We did not observe such differences, which could suggest that the proximal femur is more sensitive to immobilisation than the calcaneus. This would be a rather unexpected observation since the calcaneus, consisting of almost trabecular bone, ought to show BMD decrease earlier than the proximal femur. We also found that improved daily activities could reduce the degree of skeletal deterioration.

In some recent studies, bone changes after stroke have been evaluated [10–12]. In a study of 41 post-stroke subjects, BMD values were decreased on the affected side in comparison to the intact contralateral side (forearm, proximal femur) [10]. Calcaneal BMD was not measured. Comparably to our study, BMD of the upper limbs was lower than that of the lower limbs but, unlike our results, the duration of hemiplegia negatively influenced bone status. The authors did not assess the functional status of their patients. In another interesting study [11], authors evaluated prospectively (eight and 52 weeks after a stroke) a group of 52 patients. Their methods included bone measurements (in the calcaneus, using the same device as in our study, the femoral neck and the entire hip) and the functional status (Tinetti and Barthel). Unfortunately, forearm BMD was not measured. A significant fall of BMD occurred on the stroke-affected side for the calcaneus and the proximal femur. Patients with a low initial Tinetti score (a measure of mobility and balance) developed a significant drop in femoral neck (14.5%) and calcaneus BMD (12.2%). BMD at the calcaneus and the femoral neck correlated both at baseline and follow-up, and the authors concluded that the calcaneus might be an appropriate site to search for bone changes after stroke. That article emphasised the need for long-term longitudinal studies, quantifying bone loss after stroke and assessing the role of functional deficits [12]. The authors also proposed that an assessment of skeletal health should be a standard component in the clinical management of all stroke survivors. Recently, there have been reviews as to how patients after stroke are commonly managed in order to maintain bone health and avoid fractures [33, 34]. In general, relatively few stroke patients used to take osteoporosis medications [33] and vitamin D and bisphosphonates tend to reduce bone loss, but larger longitudinal studies are required [34].

In a study using QUS in stroke patients [28], no differences were noted for the calcaneal Stiffness Index Z-score between affected and opposite sides in both sexes, (this aligns with our observations), concerning calcaneal BMD. That lack of difference between affected and opposite sides at the calcaneus was proven by two methods: QUS [28] and densitometry (current data), despite the fact that these methods express different features of bone tissue. The authors did not find any correlation between time interval from stroke and QUS variables but noted a significant correlation between the Stiffness Index and mobility after stoke (for stroke and non-stroke side), while we did not observe any relationship between Ad-SoS and functional status, expressed by BI. Another example of QUS measurements being used to detect skeletal changes due to immobilisation came in a study of patients after brain injury [27]. That found that the results of calcaneal QUS measurements had decreased by about 40% two years after injury.

Our study had several limitations: we observed patients with long-standing stroke and skeletal changes, expected to be the most excessive in the first period after stroke, could not be followed. Neither spine nor hip BMD measurements were available. We did not perform laboratory tests, and knowledge about bone resorption and formation markers could be helpful in better understanding the nature of skeletal changes after stroke.

Conclusions

In conclusion: in subjects after a long-standing stroke, skeletal and functional status is affected, which may increase the risk of future fractures. Reducing the time between stroke and standing up improves forearm densitometric measurements.

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