

Contralateral comparison of bone geometry, BMD and muscle function in the lower leg and forearm after stroke

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Abstract

Objective: The aim of the study was to investigate the side-to-side differences of the upper and lower limbs in chronic stroke patients by means of peripheral quantitative computed tomography (pQCT). **Methods:** Twenty-three subjects (12 males and 11 females) who had previously suffered a stroke were recruited. Bone parameters and muscle cross-sectional areas were measured by pQCT in the forearm and the lower leg on the paretic and non-paretic side. Muscle function tests included hand grip dynamometry and sit-to-stand on force plates. **Results:** Relative side-to-side differences in bone parameters at the radius were twice to three times the relative differences at the tibia. At the forearm the muscle-bone relationship was stronger on the non-paretic than the paretic side, while at the lower leg the muscle-bone relationship was similar on both sides. **Conclusions:** Side-to-side differences in bone parameters were much smaller than differences between individuals, and bone mass deficits on the paretic side were greater at the radius than at the tibia. Therapies to restore muscle force and function, which may also help to decrease the risk of falls, are recommended.

Keywords: Bone, Muscle, pQCT, Stroke, Hemiparesis

Introduction

People who survive a stroke are confronted with numerous consequences. One of the most serious complications is a hip fracture which increases the level of disability and dependence¹. It has been reported that stroke survivors are at a 2-4 fold higher risk of hip fracture². Studies have shown that 10-20% of patients admitted with hip fracture have a history of previous stroke³⁻⁵ with the majority of hip fractures occurring on the paretic side^{5,6}.

Bone loss has also been observed on the paretic side after stroke⁷ which is at least in part the cause of an increased frac-

ture rate in this population^{5,8}, with the other cause being increased risk of falls^{9,10}.

Several studies have documented bone loss in the paretic arm and leg in stroke survivors with DXA measurements^{7,11-13}. Large changes in lean and fat mass on the paretic side were also observed^{7,13}. Areal BMD (aBMD) is overestimated by DXA when the fat/lean ratio of the surrounding soft-tissue is large, whereas aBMD is underestimated when the ratio is small. This is due to a systematic error inherent in DXA measuring technology¹⁴ which poses a problem when comparing extremities with different fat/lean ratios. Likewise, when the fat/lean ratio of the surrounding tissue changes over time, longitudinal measurements of aBMD are also problematic. Furthermore, bone data from DXA measurements cannot be separated into trabecular and cortical bone compartments and do not reveal bone geometric properties. To date, only a few studies have assessed side-to-side differences in stroke survivors by means of peripheral quantitative computed tomography (pQCT) at the tibia¹⁵⁻¹⁷ and the radius^{18,19}. However, none of these pQCT studies have compared the bone mass and architecture deficits between the arm and legs within the same subjects.

The aim of our study was to investigate the side-to-side differences of the upper and lower limbs in chronic stroke patients

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by means of pQCT, allowing the separate assessment of trabecular and cortical bone as well as bone geometry. Within the same subjects, we compared the paresis-related deficits in bone mass and architecture between the epiphyses and diaphyses, and between the radius and tibia. This study also investigated muscle cross-sectional area and muscle function in order to assess the muscle-bone relationship on both sides of the body.

Methods

Participants

Participants who had suffered a stroke were recruited through the Royal Talbot Rehabilitation Centre and through flyers sent to stroke support groups within the Melbourne metropolitan area. Participants with recent or chronic stroke were included. Exclusion criteria were bisphosphonate therapy within the previous 24 months, fractures of the radius or tibia within the previous 12 months, and periods of acute bed rest of more than 2 weeks within the previous 12 months. The study was approved by the Austin Health Human Research Ethics Committee in Heidelberg, Victoria, and written consent was obtained from all participants.

Anthropometric measurements

Body weight was measured to the nearest 0.1 kg, with the participant wearing light clothing and without footwear. Standing height was measured using a stadiometer to the nearest 0.1 cm. Bone lengths of the tibia and ulna were measured using an anthropometric tape (measure to the nearest 0.5 cm). Ulna bone length was measured from the ulnar styloid process to the olecranon. The tibial length was measured from the distal edge of the medial malleolus to the medial joint cleft of the knee.

Demographics

Details regarding participants' stroke and recovery, fracture history, medication, smoking history, as well as past and present physical activity levels were collected on a standard form.

Kinetics

A sit-to-stand test was performed from a height-adjustable chair with armrests. The chair was positioned on one force plate, and the subject had each foot on a separate additional force plate; a total of 3 plates were used (OR6-7 force platform, Advanced Medical Technology Inc., Waterford, MA, USA). Participants were seated with their knees and hips at 90°. They were instructed to stand up and sit down five consecutive times as quickly as possible. If necessary, they were allowed to use the armrests to push off. The trial was repeated once. Ground reaction forces (GRF) measured by each of the three separate force plates were recorded at 1000 Hz. The Vicon™ 612 System (Oxford Metrics, Oxford, UK) was used for data analysis.

Grip force was measured with a Hydraulic Hand Dynamometer (North Coast Medical, Morgan Hill CA, USA) while the participants were seated in a chair with hip and knee joint angles at 90°. The tested arm was resting on the armrest of the chair with the elbow at 90°. The dynamometer was sup-

Parameter	N / Mean ± SD
N (male/female)	23(12/11)
Age (yrs)	68±11
Height (cm)	166.4±10.2
Weight (kg)	77.3±16.3
Paretic side (right(*)/left(*)	10(2)/13(0)
Time post stroke (yrs)	5.4±3.2
Ambulant / non-ambulant	21/2
Use of mobility aid ¹ 0/1/2/3/4/5/6	2/2/1/6/12

* number of persons with left arm as the dominant arm before stroke

¹ Use of mobility aid: 0: using a wheelchair - person cannot walk without help from another person; 1: able to walk very short distances, but mainly using a wheelchair; 2: using a walker; 3: using a stick; 4: no walking aid required.

Table 1. Anthropometric data of stroke patients (means ± standard deviations).

ported by the investigator, so that the participant did not have to lift the device. Both hands were tested three times in alternating order. Pinch force of both hands was also measured three times in alternating order using a Hydraulic Pinch Gauge (North Coast Medical, Morgan Hill, CA, USA), and with participants in the same position as for grip force measurements.

Bone measurements

All measurements were performed with a Stratec XCT 2000 scanner (Stratec Medical, Pforzheim, Germany). This pQCT apparatus measures attenuation of x-rays, which are linearly transformed into hydroxylapatite (HA) densities. Unlike some other pQCT scanners, the Stratec XCT 2000 is calibrated with respect to water which is set at 60 mg HA, so that fat results in 0 mg HA²⁰.

HA equivalent densities are automatically calculated from the attenuation coefficients by employing the manufacturer's phantom, which itself is calibrated with respect to the European Forearm Phantom (EFP; QRM, Erlangen, Germany)²⁰.

A scout view was performed at the distal end of the radius and at the distal and proximal ends of the tibia. At the distal radius the automatic placement provided by the manufacturer was used, and at the distal tibia the reference line was placed on the distal end of the lateral half of the tibia. At the proximal tibia, the reference line was placed on the most distal part of the medial tibial plateau.

At the radius, scans were performed at 4% and 66% of the bone's total length measured from the reference line. At the distal tibia a scan was performed at 4%, measured from the distal reference line, and at the tibial shaft, a scan was placed at 34% from the proximal reference line, corresponding to 66% measured from the distal reference line. This procedure had to be used because with the XCT 2000 it is not possible to access the 66% shaft site from the distal tibial end (translational movement of the gantry is limited to 230 mm). Slice thickness was 2 mm, and voxel size was set at 0.5 mm with a scanning speed of 20 mm/s.

		Non-paretic Mean ± STD	Paretic Mean ± STD	Abs. diff.	Rel. diff. [%]	p-value
Radius						
4%	BMC (g/cm)	1.26±0.42	1.09±0.41	-0.17	-13.52	0.000
	Total CSA (mm ²)	415.19±74.96	403.73±79.03	-11.47	-2.76	0.141
	Total vBMD (mg/cm ³)	299.49±74.20	265.78±71.86	-33.72	-11.26	0.002
	Trabecular vBMD (mg/cm ³)	182.15±46.20	161.56±47.89	-20.59	-11.31	0.007
66%	BMC (g/cm)	1.11±0.33	0.99±0.37	-0.12	-11.05	0.001
	Total CSA (mm ²)	167.19±36.35	163.13±34.99	-4.07	-2.43	0.332
	Cortical CSA (mm ²)	85.88±27.90	75.36±29.29	-10.51	-12.24	0.001
	Cortical Wall Thickness (mm)	2.24±0.71	1.96±0.78	-0.28	-12.36	0.001
	Cortical vBMD (mg/cm ³)	1098.50±80.81	1065.76±91.92	-32.75	-2.98	0.002
	SSIpol (mm ³)	340.16±115.35	311.99±116.11	-28.18	-8.28	0.085
	Muscle CSA [mm ²]	3462.66±224.53	3240.99±222.26	-221.67	-6.40	0.010
	Fat CSA [mm ²]	1664.56±161.09	1749.75±167.53	85.19	5.12	0.467
Tibia						
4%	BMC (g/cm)	3.28±0.87	3.07±0.95	-0.22	-6.57	0.001
	Total CSA (mm ²)	1235.48±202.92	1220.65±197.60	-14.82	-1.20	0.200
	Total vBMD (mg/cm ³)	265.99±55.96	250.87±63.66	-15.12	-5.69	0.001
	Trabecular vBMD (mg/cm ³)	210.23±44.80	203.46±49.51	-6.77	-3.22	0.120
66%	BMC (g/cm)	3.81±1.10	3.69±1.18	-0.12	-3.07	0.024
	Total CSA (mm ²)	581.55±100.62	580.29±95.66	-1.26	-0.22	0.736
	Cortical CSA (mm ²)	290.58±100.47	277.04±111.53	-13.53	-4.66	0.018
	Cortical Wall Thickness (mm)	4.02±1.31	3.82±1.51	-0.20	-4.94	0.032
	Cortical vBMD (mg/cm ³)	1102.39±53.79	1097.88±54.70	-4.50	-0.41	0.363
	SSIpol (mm ³)	2337.05±800.55	2272.09±834.81	-64.96	-2.78	0.164
	Muscle CSA [mm ²]	5795.13±285.21	5502.59±277.70	-292.54	-5.05	0.050
	Fat CSA [mm ²]	3158.21±229.77	3218.72±219.16	60.51	1.92	0.388

* $p < 0.01$, ** $p < 0.001$

Table 2. Parameters obtained from the pQCT-measurements (means and standard deviations) of the paretic and non-paretic side, as well as absolute differences (abs. diff.) and relative differences (rel. diff.) between the paretic and the non-paretic side. P-values for paired t-tests are also indicated.

Measuring parameters

Epiphyseal scans (4%): The periosteal surface of each bone's epiphysis was found by a contour algorithm based on thresholding at 180 mg/cm³. Bone mineral content (BMC) per cm of slice thickness, cross-sectional area (CSA) and total bone mineral density (BMD) were determined. Concentric pixel layers were then peeled off from the bone's perimeter until a central area covering 45% of the total bone CSA remained. From this central area trabecular BMD was determined.

Diaphyseal scans (66%): The periosteal surface of the bone's diaphysis was found by a contour algorithm based on a threshold of 280 mg/cm³. BMC, total CSA, and the polar bone strength strain index (SSIpol) were calculated. Cortical bone was selected by thresholding at 710 mg/cm³. Of the selected area, cortical CSA and cortical BMD were calculated. Cortical wall thickness was calculated, based on the assumption that bone shaft was cylindrical from total CSA, which included the bone marrow CSA, and cortical CSA, which excluded the bone marrow CSA. Subcutaneous fat CSA was determined by selecting the area with thresholds -40 to +40 mg/cm³ HA density, and muscle CSA was determined by subtracting the total

bone CSA (threshold 280 mg/cm³) and subcutaneous fat CSA from the total limb CSA.

In a more recent study on depressive subjects we performed a reproducibility study on repeated measurements in 5 subjects with 4 repeat measurements (manuscript under preparation). We found the following coefficients of variations: 0.7-2.0% in bone parameters measured at the radius and 0.3-1.4% at the tibia.

Data analysis

Kolmogorov-Smirnov tests were performed on all bone and force data to verify the normality of the data. Of the repeated muscle function tests the best trial was used. Paired t-tests were performed between paretic and non-paretic side for all pQCT derived bone and soft-tissue data as well as for force data. Linear regressions were performed between muscle CSA and BMC at the epiphyses as well as diaphyses (including radius and ulna at the forearm and tibia and fibula at the lower leg) in the affected and non-affected limbs. All statistical analyses were completed using SPSS for Windows (version 12.0.1). Due to the large number of tests, statistical significance was adjusted at an alpha of 0.01.

	Non-paretic		Paretic		Abs. diff.	Rel.diff	
	Mean	SD	Mean	SD		[%]	P-value
Grip Force (kg)	32.53	15.53	20.82	15.75	-11.71	-35.99	0.002
Pinch Force (kg)	7.94	3.34	5.31	4.05	-2.64	-33.19	0.001
GRF (N)	574.35	142.08	451.65	137.39	-122.70	-21.36	0.000

* $p < 0.01$, ** $p < 0.001$

Table 3. Grip force, pinch force and ground reaction force (GRF) of the non-paretic and paretic side (means and standard deviations), as well as absolute differences (abs. diff.) and relative differences (rel. diff.) between the paretic and the non-paretic side. P-values for paired t-tests are also indicated.

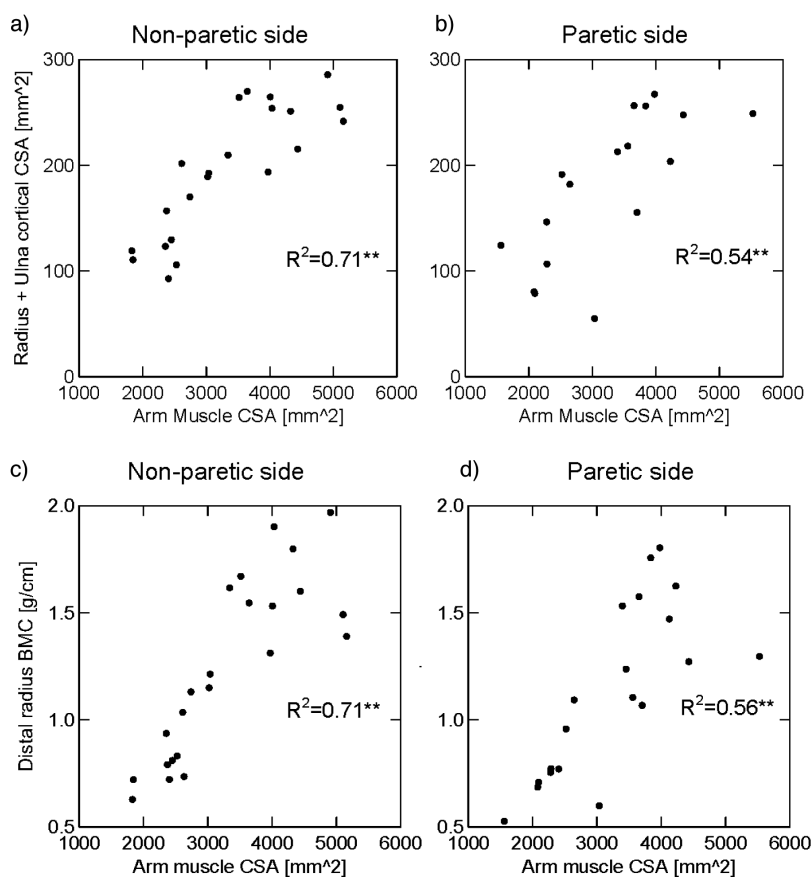


Figure 1. Muscle-Bone-Relationship on the non-paretic and paretic side of the forearm at the diaphysis (a, b) and epiphysis (c, d). The x-axis shows the muscle cross-sectional area (CSA) of the forearm and the y-axis the cortical CSA of the radius and ulna shaft and the bone mineral content (BMC) of the distal radius respectively. R^2 is the linear regression coefficient with probabilities * $p < 0.01$, ** $p < 0.001$.

Results

Twenty-three participants, 12 males and 11 females, were recruited. They were between 49 and 84 years of age and had suffered a stroke between 1 and 13 years ago (Table 1). Thirteen participants were paretic on the left side and 10 participants were paretic on the right side. The level of mobility ranged from being able to walk almost normally to being

wheelchair bound. Arm function ranged from having almost normal function to total paresis.

Radius pQCT-scans of three participants were excluded from analysis due to artefacts caused by movement or inability to position the arm correctly for scanning (due to contractures). At the radius, all densitometric as well as geometric bone parameters were significantly compromised on the paretic side compared to the non-paretic side (Table 2) except for the bone

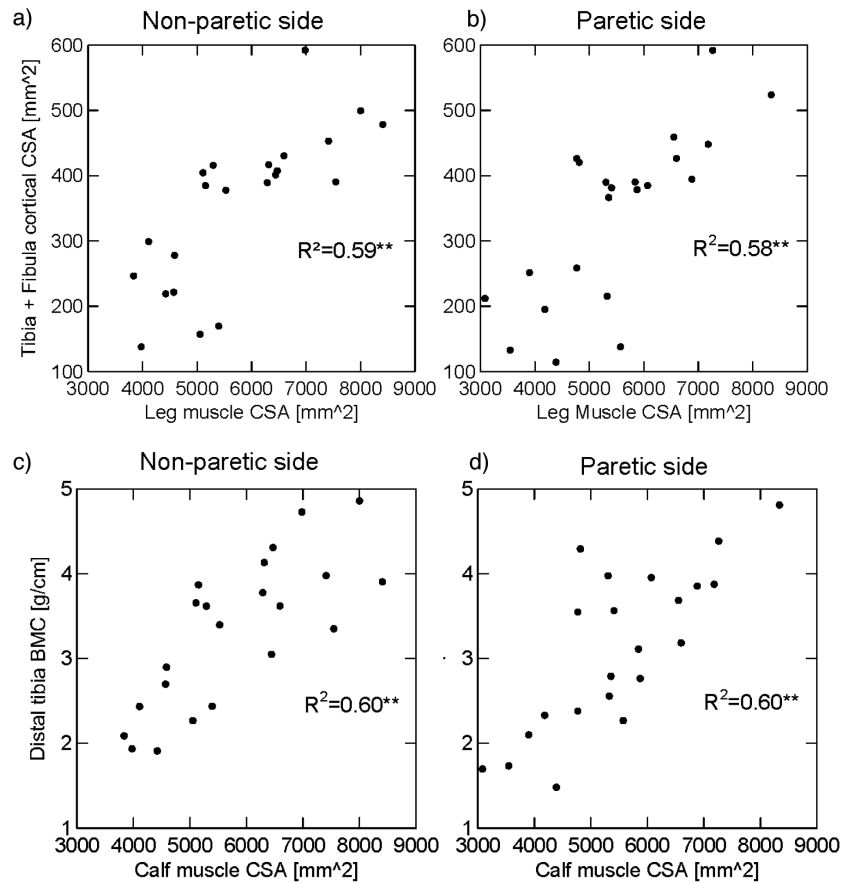


Figure 2. Muscle-bone relationship on the non-paretic and paretic side of the lower leg at the epiphysis (a, b) and diaphysis (c, d). The x-axis shows the muscle CSA of the lower arm and the y-axis the BMC of the distal radius and the cortical CSA of the tibia and fibula shaft respectively. R^2 is the linear regression coefficient with probabilities * $p < 0.01$, ** $p < 0.001$.

outer dimensions (total CSA) and SSIpol which showed a trend to being smaller on the paretic side. At the tibia, only BMC and total BMD of the epiphysis were significantly compromised, while all other parameters showed a trend to being smaller on the paretic side. When the side-to-side differences were compared between the upper and lower extremities, the relative differences at the radius were two to three times the relative differences at the tibia.

The deficit in muscle CSA was similar on the paretic side at the forearm and lower leg (6% and 5%, respectively, however, non-significantly at the lower leg) whereas fat CSA was only marginally greater. Mean grip and pinch force of the paretic side were reduced by 33% (range 100 to -13% for grip force; 100 to -8% for pinch force) compared to the non-paretic side, while mean ground reaction force of the paretic leg was -21% lower (range 72 to -1%, Table 3).

The mean absolute differences of all bone parameters between the paretic and non-paretic sides were much smaller than the standard deviations for the whole population, indicating that side-to-side differences were small compared to inter-individual differences of both the paretic and non-paretic side

(Table 2). At the forearm the muscle-bone relationship was stronger on the non-paretic than the paretic side (Figure 1), while at the lower leg the muscle-bone relationship was similar on both sides (Figure 2). Figure 3 shows cortical CSA at the diaphyses of the lower leg (a) and forearm (b) as well as trabecular BMD at the distal tibia (c) and radius (d) of each participant's paretic limbs versus their non-paretic limbs, in order to depict side-to-side differences. Figure 3 shows again that side-to-side differences were greater in the forearm than the lower leg, and that between-subject differences were much greater than within-subject differences.

Discussion

Bone parameter deficits in the paretic limbs were found. This included lower trabecular and total BMD at the epiphyses and lower cortical wall thickness in the bone shafts of the forearm and lower legs (differences were significant at the radius and by trend at the tibia). While the outer bone dimensions of the paretic limbs were comparable across sides, the cortical wall thickness was compromised by endosteal resorption on

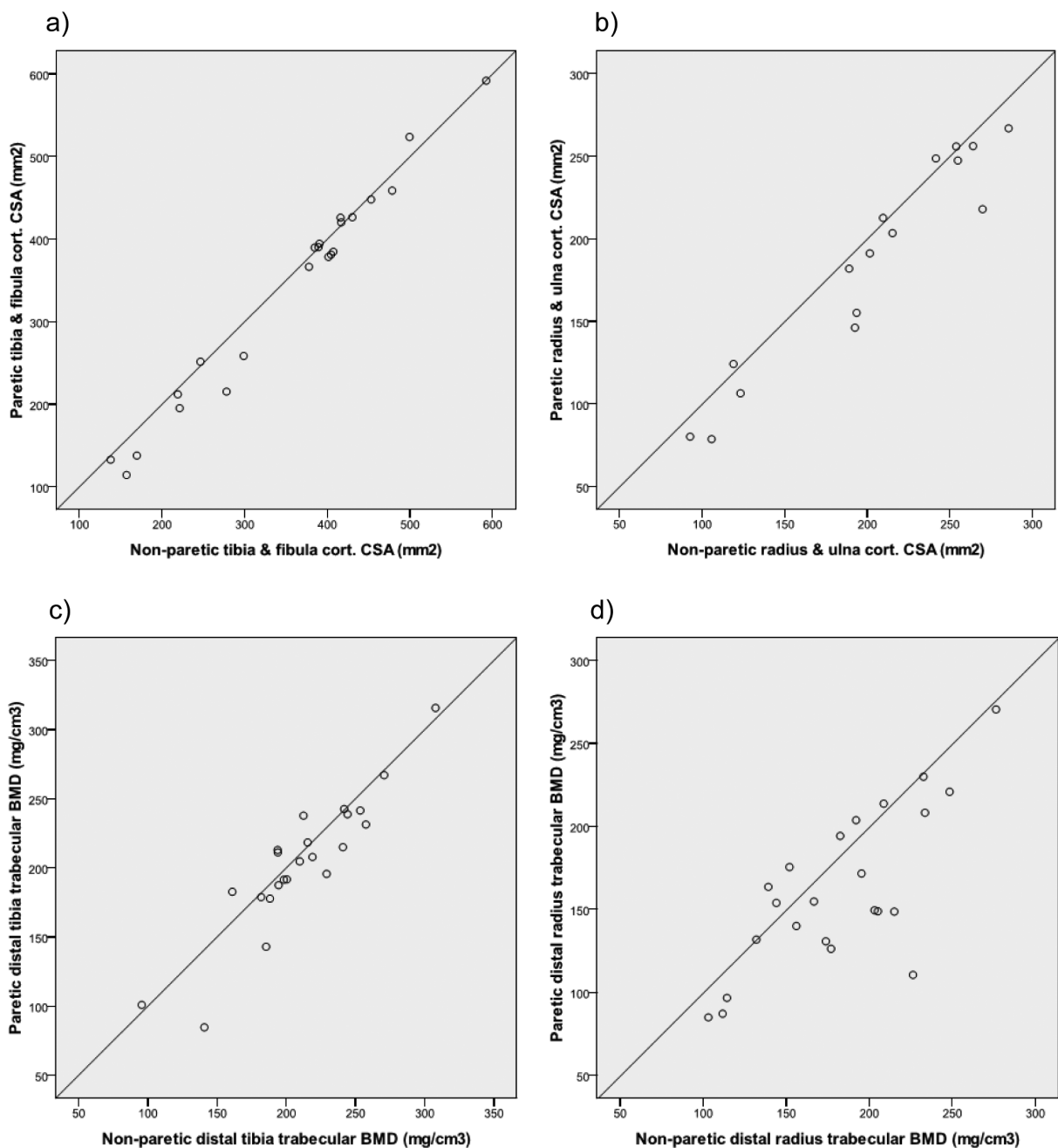


Figure 3. Relationship between the paretic and non-paretic side for cortical CSA of the tibia and fibula (a), and of radius and ulna (b), as well as trabecular BMD in the distal tibia (c) and distal radius (d). These graphs show values for the non-paretic limb on the x-axis and the paretic limb on the y-axis. The diagonal lines are lines of equity, meaning that dots on this line depict a subject with same values on paretic and non-paretic side

the paretic side. Side-to-side differences were greater at the forearm than at the lower leg, hence the difference in significance. It is noteworthy, that side-to-side differences in bone parameters were small relative to inter-individual differences in bone parameters and in some individuals bone parameters of the paretic side showed no deficit at all. The muscle-bone relationship persisted on the paretic side, however, at the fore-

arm it was weaker than on the non-paretic side.

This investigation is the first known study to use pQCT to examine and compare the densitometric and geometric bone properties of the upper and lower extremities of a group of stroke patients. Previous pQCT studies have only assessed bone parameters either in the paretic arm^{18,19,21} or the leg¹⁵⁻¹⁷. Their findings regarding side-to-side differences were similar

to ours, especially the large inter-individual differences described by Runge et al.¹⁵. Pang and colleagues¹⁷ found an almost identical result at the distal tibia with a deficit in trabecular BMD of 2.7% (3.2% in our study). Ashe and colleagues²¹ found a side-to-side BMC difference of 11% at the distal radius whereas this investigation found a 13.5% difference. In other investigations of the diaphysis of the tibia¹⁶ and radius¹⁸ scans were placed at 30% in contrast to our measurements at 66%. This may explain why we have found more pronounced side-to-side differences.

Our finding of greater differences in the forearms than the lower legs are in agreement with findings by Ramnemark et al.⁷ who measured bone properties with DXA. Bone loss after stroke was found in both legs immediately after stroke while patients are often confined to bed. Depending on the degree of regained mobility, recovery of bone status in the non-paretic lower limb was reported to be common. In the arm, the situation has been found to be different in that the non-paretic arm tended to gain bone strength¹³. This could be one explanation why, in the present study, deficits in bone parameters of the paretic limb were greater at the radius than at the tibia. Another possible reason may lie in the fact that even a severely affected leg is mechanically loaded to some degree when walking with a walking aid, whereas the differences in activity and mechanical loading can be much greater at the arms at a comparable level of dysfunction when the affected arm is not used. A higher symmetry of bone status of the lower leg in the present study could also be due to the fact that activity after stroke and hence loading may be decreased in the non-paretic leg as well and bone loss may still be progressing on both sides due to a reduction in physical activity levels. On the other hand, some of our subjects with considerable functional deficits of the paretic leg had hardly any bone deficits at the paretic lower limb. Last but not least, there is often a greater neurological deficit in the paretic arm than the paretic leg¹².

We found higher correlations between bone parameters and muscle CSA than with force data acquired by grip dynamometer and force plates (data not shown). We interpret this as population-inherent difficulty to measure maximal forces by grip and pinch tests. With the Chair Rising Test we did not intend to measure maximal forces but rather we used it as an approximation for the side-to-side difference in loading of the paretic and non-paretic leg.

The persisting muscle-bone relationship in the paretic limbs found in our study is in accordance with other studies. Pang et al.²² also found that lean mass in the paretic leg was a major predictor of areal BMD of the paretic proximal femur and that lower leg lean mass correlated with BMC of the distal tibia¹⁷ and the bone strength index of the tibia¹⁶. Similarly, a persisting relationship between muscle CSA and bone strength has been found in the paralysed legs of spinal cord injured people with spastic paralysis²³. However, we would like to point out that the muscle-bone relationship is weaker in the paretic limb than the non-paretic limb after stroke. We do not have an explanation for this, but a neural drive to maintain symmetry in muscle force may be involved²⁴.

Limitations of the present study were the relatively small number of participants and the large range of impairment. Further, the study had a cross-sectional design and the status of the non-paretic side cannot be assumed to reflect status before the stroke incident. Temporary or permanent immobilisation can also lead to bone loss in the non-paretic limb^{19,25}. Increased use of the non-paretic arm, on the other hand, can lead to an increase in BMD¹³. Spasticity, which we did not measure, may also have had some influence on bone parameters, as previous studies have found a negative correlation between spasticity and bone strength parameters in the arms²⁶ and legs^{16,17} of stroke survivors. We also have not assessed stroke severity, whether stroke was ischemic or hemorrhagic, comorbidities, medications or physical activity level, which may have affected the findings on the contralateral comparisons.

Conclusions

The main findings of this study were that in stroke patients, bone strength deficits of the paretic versus the non-paretic limb were generally greater in the forearm than the lower leg. Side-to-side differences in bone parameters were small compared to differences between individuals, indicating that, for the tibia, only those subjects with poor bone status on the non-paretic side may be at risk of developing poor bone status on the paretic side. This may not alleviate their fracture risk to any great degree as stroke survivors are at higher risk of falling^{9,10}. The strong relationship between muscle CSA and bone status supports the use of therapy to restore muscle force and function, which may also reduce the risk of falls.

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