#### **Original Article**

# Bone Density Loss Following Ankle Fusion Persists at Long-Term Follow-Up

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# Abstract

**Introduction:** The aim of ankle fusion is to create a stable and pain-free hind foot. A decrease in bone density secondary to postoperative immobilization is well established. It is commonly accepted that bone density is restored toward normal values when normal weight bearing is permitted. To the current authors' knowledge, this restoration of bone density has not been definitively established via clinical studies. **Subjects and Methods:** Patients who underwent an isolated ankle fusion between January 1998 and March 2015, to address advanced degenerative or posttraumatic osteoarthrosis or rheumatoid arthritis were included. Clinical and radiological examination, Foot Function Index (FFI), and American Orthopedic Foot and Ankle Society-Score (AOFAS) scoring systems were utilized. Pain intensity was calculated using the Visual analogue scale (VAS). We use semiquantitative ultrasound osteodensitometry to measure bone density of the calcaneus was significantly lower in the treated foot compared to the contralateral side (-1.4 vs.-0.4; P = 0.001). With the numbers available, a reduction in bone density was found without a significant difference in the AOFAS score (P = 0.875), FFI (P = 0.655), VAS (P = 0.804), and body mass index (P = 0.272). Seven (12%) developed a nonunion. **Conclusions:** These results demonstrate that a reduction in bone density as a consequence of immobilization while bone union was achieved did not completely return to baseline values even at 10 years postoperative. This persistent reduction in bone density does not correlate in a statistically significant way with higher pain scores, inferior AOFAS scores or nonunion rates. Postoperative partial weight bearing should be instigated as soon as possible to minimize bone loss.

Keywords: Ankle fusion, bone density, long-term follow-up, osteoarthrosis, weightbearing

## INTRODUCTION

There are various surgical treatment options for degeneration of the ankle joint.<sup>[1]</sup> Ankle fusion has been used successfully for end-stage osteoarthrosis to relieve pain and improve quality of life.<sup>[2,3]</sup>

However, ankle arthrodesis requires postoperative partial weight bearing until there is sufficient bony union at 6–12 weeks. Reduced weight bearing leads to a loss of bone mineral density (BMD), whilst increased activities involving full weight bearing such as running, increase the bone density of the calcaneus.<sup>[4-6]</sup>

Local bone density may also be affected by hypo- and hypervascularization, diabetic neuropathy, neurological and renal diseases, palsy, rheumatoid diseases, osteomalacia, and osteoporosis.<sup>[7-10]</sup>

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There does not exist a true consensus in the literature on the etiology and the influence of osteoarthritis on bone density of the bones of the foot. Some authors posit that the development of arthrosis of the ankle joint is related to bone changes which are associated with pain.<sup>[11]</sup> Others report cartilage degeneration associated with a change in bone density at the talus.<sup>[12]</sup> These may result in a reduction<sup>[13]</sup> or an increase bone density.<sup>[14]</sup>

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The parameter most used to measure bone density is the BMD. $^{[8,15]}$ 

Alternative nonionizing methods such as (semi)-quantitative ultrasound densitometry (QUS) have also been used for bone density evaluation. In addition to the absence of radiation exposure, it is also more cost-effective and requires less space than quantitative computed tomography (QCT) and dual-energy X-ray Absorptiometry (DEXA).<sup>[16,17]</sup> Additional information may also be gleaned such as the structure and elasticity of the bone.<sup>[17-19]</sup> The two central parameters that are collected are the speed of sound (SOS, unit m/s) and the broadband ultrasound attenuation (BUA, unit dB/MHz).<sup>[20]</sup>

To our knowledge, there are no long-term studies on the changes in bone density after ankle fusion *in vivo*.

We investigated the difference of bone density of the calcaneus by semi-QUS after ankle fusion compared to the contralateral healthy foot over the long-term. We correlated these data to the functional outcome, pain level and the nonunion rate.

# SUBJECTS AND METHODS

All adults, treated with isolated unilateral ankle fusion without any further surgery for degenerative, posttraumatic and rheumatoid changes in our trauma department were included (minimum follow-up of 24 months). Patients <18 years of age, those with other joint fusions of the ipsilateral foot before ankle fusion, dementia, inactivity due to reasons other than the foot, with extended fusion or amputation at time of recruitment and language barriers were excluded. No patient received treatment for osteoporosis before.

Patient reported outcomes were evaluated using the Foot Function Index (FFI) and the American Orthopedic Foot and Ankle Society-Score (AOFAS). Furthermore, the patients were asked four questions, related to pain, through a visual analog scale (VAS; scale 1–10).

Dorsoplantar and lateral plain weightbearing radiographs of the foot, an oblique view of the foot, and anteriorposterior and lateral views of the ankle joint were performed. Union was defined as radiographic evidence of fusion at last follow-up using plain radiographs and partial CT scans. Using the Kellgren – Lawrence Score, degenerative changes in the related subtalar and Chopart joints were graded.

The bone density of both calcanei was measured semi-quantitatively with ultrasound densitometry using the Pegasus<sup>TM</sup> smart according to the manufacturer's instructions (Medilink, Inc., Mauguio, France). Pegasus<sup>TM</sup> is automatically calibrated at a phantom before use. This calibration enables compensation for any drift from the electrodes or the probes, thus producing stable measurements, even after many years of use.

Calcaneal width, BUA, SOS, stiffness index (SI), *T*-score and *Z*-score are calculated from the ultrasound signal transmitted through the calcaneus. The range and accuracy of the BUA

was 30–120 dB/MHz  $\pm$  2% reproducibility and of the SOS was 1000–2000 m/s  $\pm$  2% reproducibility.

BUA correlates to bone density. The measurement of the attenuation corresponds with the measurement of the reduction of the ultrasound signal power through the bone. The BUA corresponds with the slope of attenuation related to the frequency. This measurement is realized over the frequency range 0.2–0.6 MHz. SOS is increased in rigid materials but decreased in heavy materials. In bone, the SOS value is higher than in soft tissues, and it is correlated with bone density and strength. A reliable correlation of BUA with bone density has been demonstrated in adults and children.<sup>[16,18,21]</sup>

The SI, an index established by Lunar combines both BUA and SOS and was defined as SI =  $0.67 \times BUA \pm 0.28 \times SOS - 420$ .<sup>[17]</sup> The SI was also expressed as *Z*-score and *T*-score based on a US reference database using the following equations: *Z*-score = (SI-age-matched mean SI)/16.6, where age-matched mean SI =  $68 \pm 31.6/(1\pm [age/55.9]) \times 10.1$ , and for *T*-score = (SI-100/16).

The *T*-score compares a patient's result with the mean value of healthy young same-sex adult, expressed in number of standard deviations from the reference group. The actual normal value used as a reference is that which provides the highest value, generally obtained between 20 and 40 years of age. The *Z*-score is the difference between the result of a patient and the mean value of a normal same-sex subject of the same age, expressed in number of standard deviations of the reference group. Both were based on a large European/United States reference database for BMD.<sup>[19,22]</sup> The patients were categorized as "osteoporotic" (*T*-score of -2.5 or below), "osteopenia" (*T*-score between -1.0 and 2.5) and "normal bone density" (*T*-score -1.0 and above) according to the conventional World Health Organization definition.<sup>[23]</sup> The width of the heel was measured in mm.

All analyses were performed with the Statistical Package for the Social Sciences program (SPSS), version 26.0 (SPSS, Chicago, Illinois, USA).  $P \le 0.05$  was considered statistically significant. Bilateral measurements at the calcaneus were performed for all patients and related to the follow-up after surgery, applying two-tailed paired Student's *t*-test (continuous variables). The relationship between the mean QUS values and radiologic and clinical outcome was explored using Pearson's correlation coefficient. Means and standard deviation were generated for all variables.

Informed consent was obtained written from all individual participants included in the study. This retrospective study was performed with approval from the local Ethics and Research Committee (No. 6927).

## RESULTS

#### **Characteristics of the patient**

One hundred and thirty-seven patients underwent ankle fusion between January 1998 and March 2015 at the current authors'

university-affiliated trauma department, which is a level one trauma center. Ten patients did not meet the inclusion criteria. Eleven patients had died and another 11 patients were lost to follow-up. Nineteen patients underwent further surgery to the ipsilateral foot. The remaining 86 patients were invited to participate in the follow-up examination. Six patients declined to participate or<sup>[16]</sup> only answered the questionnaire. From the remaining 64 patients, another four with incomplete data were excluded. At the end, complete data of 60 (m/f 30/30; age 62 (range 22–87 years) patients were eligible for statistical analysis [Figure 1].

In 68% of patients, posttraumatic osteoarthrosis was the leading diagnosis [Table 1].

The demographic, disease-related characteristics, and variables of the cohort are shown in Table 2.

#### **Bone density**

The mean (semi)-QUS T-score of the treated foot was significantly lower compared to the contralateral foot (-1.4 vs. - 0.4; P = 0.001) [Table 3]. For QUS measurements, the reduction was -21.4 (95% CI - 32.7 to -9.1) for SOS, -15.8 (95% CI - 20.1 to - 11.4) for BUA, and-16.6 (95% CI - 21.3 to - 11.6) for SI.

Of 60 patients undergoing QUS measurement, 10 (17%) patients were classified as osteoporotic based on dual X-ray absorptiometry (DXA) criteria, whereas 31 (52%) had low BMD (osteopenia) and 19 (32%) patients showed normal bone mass [Figure 2].

The follow-up after surgery was <10 years in 37 and more than 10 years in 23 ankle fusions. More than half of the patients in these two groups showed a decreased in bone density at the



Figure 1: Study participation. Number of patients examined and excluded

treated side. The *T*-score in the group with  $\geq 10$  years follow-up was higher, but there was no significant difference compared to the patients with < 10 years of follow-up [Table 4].

#### Factors associated with bone measurement reduction

Bone union at the ankle was achieved in 53 of 60 (88%) patients. Seven (12%) developed pseudarthrosis, which was confirmed by a CT scan. Four out of these seven patients did not require any further treatment. After revision ankle arthrodesis because of pain another two patients achieved bony union. One patient needed revision arthrodesis of the ankle joint, combined with a subtalar fusion for osteoarthrosis.

The mean QUS *T*-score in the nonunion group was -1.5 (95% CI -2.3 to -0.8) compared to -1.3 (95% CI -1.7

# Table 1: Preoperative indications for ankle fusion. Number of patients with degenerative related joints and need for surgery

Diagnosis	n (%)
Posttraumatic arthritis	41 (68)
Gout-arthritis	11 (18)
Degenerative osteoarthritis	2 (3)
Osteochondrosis dissecans	3 (5)
Rheumatoid arthritis	2 (3)
Club foot	1 (2)
Total	60 (100)

# Table 2: Demographic variables, lifestyle, and bone characteristics of patients with ankle arthrodesis

Demographic variables	Subjects mean (n=60), n (%)
Age (years)*	62 (12; 22-87)
Male sex	30 (50)
BMI (kg/m <sup>2</sup> )*	29 (6; 18-47)
Current smoker	22 (38)
Diabetic	4 (7)
Follow-up (years)*	9 (6; 1-18)
Bone nonunion	7 (12)

\*The values are given as the mean (SD) and range. BMI: Body mass index, SD: Standard deviation



**Figure 2:** Distribution of quantitative ultrasound of treated calcaneus *T*-score results, n = 60

Table 3: Bone density measures of the treated and untreated side								
	Treated side ( $n=60$ ), $n$ (%)	Untreated side ( $n=60$ ), $n$ (%)	Δ	$\Delta$ (95% CI)	Р			
Calcaneus thickness (mm)	53.2 (6.5)	51.9 (5.7)	1.3	(0.3-2.4)	0.014			
SOS (m/s)	1356.8 (47.2)	1378.2 (47.2)	-21.4	(-32.7-9.1)	< 0.001			
BUA (dB/MHz)	66.0 (20.6)	81.8 (20.5)	-15.8	(-20.1-11.4)	< 0.001			
QUS T-score	-1.4 (1.1)	-0.4 (1.2)	-0.9	(-1.1-0.6)	< 0.001			
QUS Z-score	-0.8 (1.2)	0.03 (1.1)	-0.9	(-1.1-0.6)	< 0.001			
SI	4.1 (24.7)	20.7 (26.2)	-16.6	(-21.3-11.6)	< 0.001			
SI T-score	-5.9 (1.5)	129.8 (164.3)	-135.8	(-176-95.0)	< 0.001			
SI Z-score	-29.9 (3.6)	6.9 (25.9)	-33.0	(-37.8-27.7)	< 0.001			

Mean (SD) QUS measures in 60 patients in the two groups of treated and untreated side. Paired two-tailed student's *t*-test used testing differences in bone measurements between treated and untreated sides. CI: Confidence interval, SOS: Speed of sound, BUA: Broadband ultrasound attenuation, SI: Stiffness index, QUS: Quantitative ultrasound, SD: Standard deviation

Table 4: Bone density measures of the treated side below and above 10 years after operation								
	Follow up <10 years, <i>n</i> (%)	Follow up >=10 years, $n$ (%)	Δ	$\Delta$ (95% CI)	Р			
BD reduced <i>n</i> (% of total number)	24 (40)	17 (28)						
BD nonreduced $n$ (% of total number)	9 (15)	10 (17)						
Calcaneus thickness (mm)	54.3 (7.5)	51.1 (4.9)	3.2	(-5.8-0.9)	0.092			
SOS (m/s)	1349.7 (46.0)	1365.7 (48.1)	-16.0	(-8.3-40.4)	0.910			
BUA (dB/MHz)	63.6 (18.3)	69.0 (23.1)	-5.4	(-5.3-16.0)	0.137			
QUS T-score	-1.5 (1.0)	-1.2 (1.2)	0.3	(-0.3-1.0)	0.286			
QUS Z-score	-1.0 (1.2)	-0.7 (1.3)	0.3	(-0.4-0.9)	0.729			
SI	0.6 (22.3)	8.6 (27.1)	-8.0	(-4.7-20.9)	0.530			
SI T-score	-6.2 (1.4)	-5.7 (1.7)	0.5	(-0.3-1.3)	0.530			
SI Z-score	-29.6 (22.1)	-21.6 (26.8)	8.0	(-4.6-20.6)	0.475			

Distribution and mean (SD) QUS measures of 60 patients and treated side in the two groups of arthrodesis below and above 10 years after operation. BD nonreduced is defined *T*-score >-1.0. BD reduced is defined *T*-score <-1.0 or below. Unpaired two-tailed student's *t*-test used testing differences in *T*-score between the ages. QUS: Quantitative ultrasound, BD: Bone density, SOS: Speed of sound, BUA: Bone ultrasound attenuation, SI: Stiffness index, CI: Confidence interval, SD: Standard deviation

to -1.0) in the group with bony healing, which is not significant (P = 0.693).

FFI pain, VAS, body mass index, and AOFAS-score were not significantly correlated to bone density [Table 5].

*T*-score, *Z*-score, SI, BUA, and SOS did not exhibit any statistically significant correlation to the AOFAS, FFI pain, VAS preoperative, and VAS postoperative [Table 6].

# DISCUSSION

The changes in the density of adjacent bones on the foot in osteoarthrosis or osteoarthropathy and after surgery have already been described and several reasons for this phenomenon have been discussed in the literature.<sup>[7,8,24-28]</sup> To our knowledge, studies to investigate the bone density of the calcaneus following ankle arthrodesis *in vivo*, with follow-up of up to 10 years, do not exist in the literature.

The bone density reduction we found did not have a significant influence on the nonunion rate nor implant failure, despite a lower QUS *T*-score in the nonunion group. No significant correlation between the clinical scores and the reduced bone density was found in our cohort. In contrast, Lee found the opposite effect after calcaneus fractures.<sup>[28]</sup> They found a significant correlation of a higher bone density in the calcaneus

Table 5: Score values of the treated side									
	BD reduced (n=41)	BD nonreduced (n=19)	95% CI	Р					
AOFAS	62 (17)	61 (12)	(-9-8)	0.875					
FFI pain	22 (15)	25 (13)	(-7-11)	0.655					
VAS	3.8 (2)	3.6 (3)	(-2-1.3)	0.804					
BMI (kg/m <sup>2</sup> )	30 (6)	28 (4)	(-5-1.5)	0.272					
VAS BMI (kg/m <sup>2</sup> )	3.8 (2) 30 (6)	3.6 (3) 28 (4)	(-2-1.3) (-5-1.5)	0.804 0.272					

Mean (SD) score values in 60 patients with reduced or nonreduced BD in the treated side. Unpaired two-tailed student's *t*-test used testing differences in score values between reduced and nonreduced group. AOFAS: American Orthopedic Foot and Ankle Score, FFI: Foot function index, VAS: Visual Analog Scale, BD: Bone density, CI: Confidence interval, BMI: Body mass index, SD: Standard deviation

with superior clinical and radiological outcomes. Their data were based on Hounsfield units (HU) calculation through CT scans after the treatment of calcaneus fractures. Patients with decreased preoperative bone density displayed a significant correlation with a decreased Böhler's angle, widening of calcaneal width and inferior short-term clinical outcomes after operation.

Like us, Jirkovská *et al.* measured a significantly lower *T*-score and lower bony stiffness in the calcaneus by comparing Charcot feet with noncharcot feet. They assume, calcaneal ultrasonometry seems to be useful for diagnosing a Charcot osteoarthropathy and assessing fracture risk.<sup>[7]</sup>

outcomes (n=60	)									
	QUS T-score		QUS Z-score		SI		BUA		SOS	
	Pearson r	p-Wert	Pearson <i>r</i>	p-Wert						
AOFAS	0.057	0.332	0.071	0.295	0.082	0.267	0.107	0.207	0.041	0.378
FFI Schmerz	0.069	0.325	-0.021	0.446	0.099	0.256	0.045	0.383	0.134	0.188
VAS preoperative	-0.024	0.436	0.064	0.331	0.032	0.413	-0.059	0.343	0.122	0.201
VAS postoperative	-0.027	0.427	0.110	0.226	-0.014	0.462	-0.052	0.360	0.028	0.423

Table 6: Correlation between quantitative ultrasound densitometry measurements in the treated side and clinical outcomes (n=60)

Correlation analysis performed using Pearson correlation between clinical outcomes and mean QUS measurements for treated side. AOFAS: American Orthopedic Foot and Ankle Score, FFI: Foot function index, VAS: Visual Analog Scale, QUS: Quantitative ultrasound, SOS: Speed of sound, BUA: Bone ultrasound attenuation, SI: Stiffness index

Since we did not measure any values preoperatively and several times after the operation, we cannot conclude whether there was a reduction in bone density as a result of the arthrodesis or whether it remained unchanged and was already present at the time of operation. Possible reasons for the persistent reduction in bone density might be a lack of regeneration of the bone structure, a change of gait patterns or pain, which may lead to reduced weightbearing on the affected foot or to changes in local bone metabolism.

QCT and DEXA have been established as methods for measuring BMD demonstrated correlation with bone strength. Both are indirect methods and can generate varying global measurements, especially in heterogeneous regions like the calcaneus.<sup>[8,29]</sup> CT scanning with calculation of HU may also provide information regarding bone density.<sup>[28,30]</sup>

Controversy exists regarding the use of QUS and bone density studies, as there are known limitations in the use of *T*-scores based on DXA, nevertheless DXA and QUS values were found comparable.<sup>[7,17,19,31]</sup> The International Society for Clinical Densitometry states that peripheral measurements of bone density such as QUS are useful for assessment.<sup>[32]</sup>

Collinge *et al.*<sup>[17]</sup> have determined cutoff values for QUS according to ROC analysis of QUS and DXA measurements as recommended by the International Society for Clinical Densitometry (*T*-score cut-off level of -1.6 or less). In addition, QUS is cheaper and easier to use in clinical practice.<sup>[31]</sup> Another advantage is the lack of radiation exposure to the patients.

The results of this study are limited by the retrospective design and the small sample size in a very specific patient population. *A priori* sample size calculation was not done. A quality assessment on the basis of published literature was only possible to a very limited extent, since the results with regard to the primary endpoint were only partially available or slightly deviating collectives were considered and the follow-up periods were of different lengths. Therefore, our data must be proven in larger cohorts. In addition, unaccounted confounding variables may exist. Measurement of bone density before surgery may help to decide whether the differences in bone density were preexisting or caused by postoperative weightbearing restrictions. A final limitation is that the data derived in this study are device-specific and the results were not proven by other QUS devices.

## CONCLUSIONS

In our cohort, quantitative values of the bone density of the treated feet were significantly lower when compared to the healthy feet [Table 4]. This difference persists up to 10 years postoperatively. This difference in bone density and T-score decreases over time but never returns to the values of the untreated foot [Table 5]. Although we have not observed any correlation with implant failure, nonunion or postoperative outcome with decreased bone quality, the result of significantly lower bone density compared to the healthy feet may reflect something more systemic. An important consideration for future studies is to further investigate this result in larger cohorts, to quantify patients' bone density using a preoperative measurement and the investigation of a possible connection between these changes and correlations with bone metabolism. Ultimately, the cause of the decreased unilateral bone density remains unknown. Therefore, recommendations for treatment cannot be made currently.

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#### **Conflicts of interest**

There are no conflicts of interest.

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