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Bone microarchitecture of the tibial plateau in skeletal health and osteoporosis

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ABSTRACT

Background: Impaired bone structure poses a challenge for the treatment of osteoporotic tibial plateau fractures. As knowledge of region-specific structural bone alterations is a prerequisite to achieving successful long-term fixation, the aim of the current study was to characterize tibial plateau bone structure in patients with osteoporosis and the elderly.
Methods: Histomorphometric parameters were assessed by high-resolution peripheral quantitative computed tomography (HR-pQCT) in 21 proximal tibiae from females with postmenopausal osteoporosis (mean age: 84.3 ± 4.9 years) and eight female healthy controls (45.5 ± 6.9 years). To visualize region-specific structural bony alterations with age, the bone mineral density (Hounsfield units) was additionally analyzed in 168 human proximal tibiae. Statistical analysis was based on evolutionary learning using globally optimal regression trees.
Results: Bone structure deterioration of the tibial plateau due to osteoporosis was region-specific. Compared to healthy controls (20.5 ± 4.7%) the greatest decrease in bone volume fraction was found in the medio-medial segments (9.2 ± 3.5%, $p < 0.001$). The lowest bone volume was found in central segments (tibial spine). Trabecular connectivity was severely reduced. Importantly, in the anterior and posterior 25% of the lateral and medial tibial plateaux, trabecular support and subchondral cortical bone thickness itself were also reduced.
Conclusion: Thinning of subchondral cortical bone and marked bone loss in the anterior and posterior 25% of the tibial plateau should require special attention when osteoporotic patients require fracture fixation of the posterior segments. This knowledge may help to improve the long-term, fracture-specific fixation of complex tibial plateau fractures in osteoporosis.

1. Introduction

The treatment of osteoporosis-associated tibial plateau fractures often poses a considerable challenge to achieve long-term fixation due to the diminished bone quality [1–3]. While in younger patients mainly high-energy trauma leads to fracture, the frequency of low-energy trauma increases in the elderly due to the increasing prevalence of osteoporosis with age, especially

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in females [4]. Rates of loss-of-fixation between 30% and 79% have been reported in patients older than 60 years [1,5]. In order to provide long-term fragment reduction, fixation devices should be placed in regions with sufficient bone quality. Therefore, next to the understanding of the fracture pattern, implant selection and the potential utilization of a bone graft substitute, a thorough appreciation of the structural specifics of the tibial plateau is critical. The tibial plateau has a unique internal microarchitecture as it has to cope with multiple strains due to its load-bearing function [6]. Although a number of studies have described the basic age-related bone structural decay of the proximal tibia, data on region-specific differences of the internal bone structure of the tibial plateau in patients with osteoporosis do not exist [3,6–11].

Hence, the aim of the present study was to characterize the region-specific changes of the internal bone structure of patients with osteoporosis compared to skeletally healthy controls. We hypothesize that the osteoporotic deterioration of the internal microarchitecture of the tibial plateau is region-specific. The understanding of region-specific architecture alterations of the tibial plateau may help to improve the treatment of pathologies around the proximal tibia.

2. Methods

2.1. Autopsy specimens

As part of the *ex vivo* "*Biomechanically founded individualized osteoporosis Assessment and treatment (BioAsset)*" study 21 fresh human right proximal tibiae were harvested from females (mean age: 84.3 ± 4.9 years) with postmenopausal osteoporosis (OPO) according to the World Health Organization (WHO) definition (Dual X-Ray absorptiometry *T*-Score of −2.5 or less at the radius, femur or lumbar spine) during autopsy at the Department of Legal Medicine, University Medical Center Hamburg-Eppendorf [12–16]. The primary goal of the BioAsset study was to explore the effect of bisphosphonate treatment compared to non-treated osteoporotic controls on different aspects of bone quality (structure, mechanics, diagnostics). In order to define distinct study groups, we excluded patients with any anti-osteoporotic treatment other than bisphosphonates. Exclusion criteria were bone cancer, immobility >1 year, renal transplantation or renal insufficiency III°, strontium or fluoride therapy, specific anti-osteoporotic medication other than bisphosphonates (BP) and BP therapy <1 year. All patients were categorized according to BP treatment prior to death as follows: (I) 10 females without documented history of BP treatment (tr-naïve OPO) and (II) 11 females with bisphosphonate treatment for 3.7 (±1.9) years (BP-tr OPO). All BP treated patients received Alendronate (ALN). Eight control biopsy specimens (mean age: 45.5 ± 6.9 years) were taken from skeletally intact, young female donors without manifestation of osteoporosis or osteopenia according to WHO definition (Dual X-Ray absorptiometry *T*-Score better than −1.0 at the femur or lumbar spine). Due to a high prevalence of osteoporosis among older females, patient age served as the primary search criterion to identify females without osteoporosis for the control group. All specimens were scanned by high-resolution peripheral quantitative computed tomography (HR-pQCT; XtremeCT, SCANCO Medical AG, Bruettisellen, Switzerland) using the default *in vivo* settings (60 kVp, 1000 μA, 100 ms integration time, resolution of 82 μm). A scan length of 90 mm was used that included at least five millimeters distal to the tibial tuberosity. With respect to the distance between the tibial eminentia and the distal end of the tibial tuberosity, the tibial plateau was divided into three equally high levels (proximal, middle, and distal). Subsequently, each level was digitally divided into different volumes of interest (VOI) based on a 10-segment classification of the tibial plateau (Figure 1) [17]. In the sagittal plane, the tibial plateau was divided into an anterior (A) and posterior column (P; first letter of a two/three digit code). In the axial plane, the medial (M) and lateral (L; second letter of a three digit code) tibial plateaux were divided into lateral (L) and central (C; third letter of a three digit code) segments for the lateral tibial plateau. The central section (antero-central [AC], postero-central [PC]) represents the tibial eminence and tibial spine. This resulted in overall 10 segments in the proximal and middle levels. Given the taper of the proximal tibia the distal level consisted of six VOI (Figure 1). Informed consent was obtained from the family members after comprehensive information on all related issues. The study was approved by the local Ethics Committee of the Medical Association Hamburg, Germany (PV3486).

2.2. HR-pQCT

The HR-pQCT datasets were evaluated using the standard *in vivo* patient evaluation protocol provided by the manufacturer, which has been described and validated in detail before [13,15,18]. Briefly, the periosteal surface of the proximal tibia was segmented with a semiautomated contouring scheme. Subsequently, a threshold-based algorithm was used to discriminate cortical and trabecular compartments. The standard analysis included measures of total bone mineral density (BMD) (D_{total} mg HA/cm^3), cortical BMD (D_{comp}) and trabecular BMD (D_{trab}). Trabecular bone volume fraction (BV/TV) was derived by dividing D_{trab} by the assumed density of fully mineralized bone (1200 mg HA/cm^3). Trabecular number (Tb.N, /mm) was determined using three-dimensional (3D) ridge extraction methods. Trabecular thickness (Tb.Th, mm) and separation (Tb.Sp, mm) were derived as follows: Tb.Th = (BV/TV)/Tb.N; Tb.Sp = (1 − BV/TV)/Tb.N using standard morphological relations based on traditional plate model assumptions [19].

2.3. Analysis of bone mineral density according to Hounsfield units based on larger case database

As HR-pQCT measurements revealed more sophisticated, region-specific alterations of the bony microarchitecture than anticipated by the 10-segment classification in our initial hypothesis, an additional analytical approach was chosen to visualize local general alterations of bone mineral density (BMD-CT), based on Hounsfield units (HU), in the tibial plateau with age. In order to increase general representability, a comprehensive database of clinical computed computer tomography (CT) scans of 168 human proximal tibiae was analyzed. Out of all females two groups were created based on patient age: Group 1 contained 58 patients between 30

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