Occupation-dependent loading increases bone strength in men

E. Biver 1 · G. Perréard Lopreno 2 · M. Hars 1 · B. van Rietbergen 3 · J. P. Vallée 4 · S. Ferrari 1 · M. Besse 2 · R. Rizzoli 1

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Abstract
Summary Ex vivo analyses of humeri and radii from an anthropological collection and in vivo analyses of the distal radius of retired men indicate that occupation-dependent loading positively influences bone strength by an increase of bone size when young followed by a slowdown of the age-related endocortical and trabecular bone alteration.

Introduction Skeleton responds to mechanical stimuli, but it is not established whether chronic loading in the context of occupational activities (OA) influences bone properties. We assessed the impact of occupation-dependent loading on upper limb bone strength.

Methods Individuals were classified according to the intensity of physical loading associated with their OA in two models. Ex vivo, computed tomography scans of the humeri and radii of 219 male skeletons (age of death, 20–93 years) from an anthropological collection of the 20th century (Simon collection) were used to determine estimates of bone strength and cross-sectional geometry. In vivo, distal radius were analysed in 180 men enrolled in the Geneva Retirees Cohort study using high-resolution peripheral quantitative computed tomography and finite element analysis.

Results Heavy-loading OA was associated with higher bone strength in both models. This benefit was associated with higher total area (Tt.Ar), medullary area (Me.Ar) and cortical area (Ct.Ar) in young adult skeletons, but the difference decreased in older age. In older men, the humerus supporting heavy loading had a lower Me.Ar. This effect resulted in greater asymmetries of the Me.Ar and the Ct.Ar/Tt.Ar ratio between the humeri of men with unilateral versus bilateral heavy-loading OA. In vivo, an additional benefit of heavy-loading OA was observed on the distal radius trabecular density and microstructure.

Conclusion Repeated occupation-dependent loading positively influences bone strength by an increase of bone size when young followed by a slowdown of the age-related endocortical and trabecular bone alteration. These data supports the necessity to promote bone health in the context of sedentary occupation.

Keywords Bone cross-sectional geometry · Bone strength · HR-pQCT · Mechanical loading · Occupation

Introduction

Occupational activity (OA) represents a high proportion of lifelong physical activity, particularly in manual workers, but it remains unknown whether chronic loading in the context of OA may have an impact on bone strength. Very few studies have investigated the influence of OA on bone properties and...
fragility fracture risk in the general population. Only one study reported no clear and contradictory associations between physical workload on the hands and metacarpal cortical bone mass [1]. Conflicting results have been reported from cross-sectional studies about the association of bone mineral density (BMD) and OA. The association between bone and OA was classically reported in terms of epidemiologic associations with high-trauma fractures occurring during work time [2]. Epidemiological studies suggesting a possible protective influence of long-term exposure to heavy-loading OA on hip fragility fractures are biased by many confounding factors such as various nutritional, anthropometric and health-related patterns between groups [3–5]. These few heterogeneous data on the influence of OA and bone health reflect the methodological difficulties to consider the effects of lifelong OA and to distinguish leisure and home activities from OA [6].

Cortical bone is a major determinant of bone strength and fracture risk. It is influenced by genetic, physical, and nutritional factors [7, 8]. The increase in bone fragility with ageing results from reduced periosteal bone formation and increased endocortical resorption [9]. Exercise during growth increases bone size via periosteal apposition, whereas exercise at old age decreases endosteal bone loss in weight-bearing bone [10]. These positive effects of physical activity reflect the adaptation of bones to the loads they experience, as described by Wolff’s law [11]. This is well illustrated in athletes, such as baseball players who develop load-adaptive changes of cortical bone in the humerus of the overloaded limbs, or Olympic fencers in femurs [12–14]. However, this benefit may not be maintained throughout life. In a cross-sectional study, the high BMD observed in football players is no longer present in subjects aged over 60 years and retired for over 35 years, and fracture risk is not lower than predicted in older age [15]. Similarly, in professional baseball players, the benefits of loading on the humerus Ct.Ar and thickness decreases with ageing in former throwers, resulting in an increase of medullary bone, which markedly contributes to bone strength, should be more perceptible. We hypothesised that chronic mechanical stresses induced by heavy-loading OA influence the geometry and mechanical properties of bones throughout life.

Methods

The anthropologic bone collection (ex vivo study)

The Simon collection is housed at the University of Geneva, Switzerland, and consists of 494 identified skeletons, including 477 adults (282 men; 195 women) aged 20 to 93 years who died between 1905 and 1968. The individuals in this collection were buried in 27 cemeteries in the Canton of Vaud, a rural area on the northern side of the Lake of Geneva. Gender, date of birth, age at death, geographical origins, kinship, and professions were recorded from district registries and death certificates [20, 21]. Due to its rural origin, this collection provides a unique opportunity to investigate a high proportion of subjects with heavy-loading OA. We analysed 206 paired humeri and 190 paired radii from 219 adult male skeletons with apparent adequate preservation and no fracture callus by computed tomography (CT) (Fig. 1a) [21].

Participants of the Geneva retirees cohort (in vivo study)

One hundred and eighty healthy men from the Geneva Retirees Cohort (GERICO) study recruited at time of retirement, i.e. 65 years, with bone microstructure data at distal radius were included in the in vivo study [22, 23]. Dietary calcium and protein intake were assessed by frequency questionnaires [24]. OA was recorded and physical loading related to lifelong OA and leisure time was separately quantified on a scale from 1 to 4 at various life periods (<9 years, 9–14 years, 15–25 years, 25–50 years and >50 years) using a face-to-face-administered questionnaire, as previously reported [25]. Grades of physical activity are defined as follows in this questionnaire: (1) grade light - eg sitting, office work; (2) grade moderate, e.g. light work involving standing; (3) grade heavy, e.g. moderately painful work, lifting heavy loads; (4) grade very heavy, e.g. very tedious work, agricultural or construction workers, professional sports. Lifelong quantitative loading activities (scale 1–4) represents the mean score of physical activity levels adjusted for the duration of each life period. The study protocol was approved by the ethics committee of the
Geneva University Hospitals and all subjects provided written informed consent.

**Occupational activity classification**

Identical criteria were used to categorise the OA intensity of subjects in the ex vivo and in vivo studies. Individuals were classified according to physical loading applied on the upper limbs associated with their OA. We used the criteria defined during a workshop “Musculoskeletal Stress Markers (MSM): limitations and achievements in the reconstruction of past activity patterns” (Coimbra University, 2009: [http://www.uc.pt/en/cia/msm/](http://www.uc.pt/en/cia/msm/)) by an occupation working group of anthropologists [26]. Individuals were divided into light-loading and heavy-loading groups according to the intensity of physical loading applied on the upper limbs (based on the biomechanical criteria “manual”, “carrying of heavy loads”, “intensity” and “hard work” of the group). In the ex vivo study, the heavy-loading OA group was subdivided into unilateral or bilateral groups according to the lateralisation of heavy-loading OA. The asymmetry observed in a farrier (unilateral) is not observed in his brother of the same age, a farmer (bilateral). The age-related alteration of cortical bone is mainly observed at the non-dominant limb of the farrier (R, right; L, left).

86 years, respectively, illustrating the asymmetry of Cl.Ar and Me.Ar, according to the lateralization of heavy-loading OA. The asymmetry observed in a farmer (unilateral) is not observed in his brother of the same age, a farmer (bilateral). The age-related alteration of cortical bone is mainly observed at the non-dominant limb of the farrier (R, right; L, left).

Fig. 1 a: Flowchart of the 219 selected skeletons for humeri and radii scans from the Simon anthropologic collection. b Cross sections at 80 %, 65 %, 50 %, 35 % and 20 % of humerus length and 75 %, 60 %, 40 % and 20 % of radius length where geometrical and mechanical properties were measured and calculated from CT scans. c Corresponding cross-sections of the humeri and radii of two brothers who died at the age of 85 and
operators (94); unilateral heavy-loading OA baker (4), bricklayer (4), carpenter (1), cheese maker (2), cooper (1), farrier (4), locksmith (3), lumberjack (11), miller (2), roadman (2), sawyer (2), stonemason (1), tinsmith (1), winemaker (9) and wheelwright (1).

Bone geometry and strength assessment

**Ex vivo group**

Bone geometry, including the maximum length ($l$, mm) of the humerus and radius, the Tt.Ar (mm$^2$), Me.Ar (mm$^2$), Ct.Ar (mm$^2$) and the percentage of Ct.Ar (Ct.Ar/Tt.Ar), was assessed using a multi-detector row helical CT scanner (Philips Medical Systems MX8000 IDT 16, Hamburg, Germany, parameters of 16 slices, 120 kVp, 240 mAs, 16×0.75-mm collimation; pitch 2-mm and 1-mm slice thickness; voxel size 0.25 mm×0.25 mm×0.4 mm) on cross-sections at 80 %, 65 %, 50 %, 35 % and 20 % of the length of the two humeri and 75 %, 60 %, 40 % and 20 % of the length of the two radii (Fig. 1b and c). CT-derived measures enable to predict humeri and radii biomechanical properties [27, 28]. Estimates of bone strength were determined for each cross-section including the following: the cross-sectional moments of inertia (CSMI, mm$^4$) in the antero-posterior, medio-lateral, maximal and minimal diameter axis, representing the medio-lateral, antero-posterior, and minimal and maximal bending strength, respectively; the polar moment of inertia ($J$, mm$^4$) was obtained by adding the two maximum and minimum CSMI, reflecting torsional strength; the antero-posterior and medio-lateral section modulus ($Z$, mm$^3$), as the ratio of bending strength to its maximally distributed distance on the bending axis, was calculated as the CSMI divided by the distance to the centre of the shaft. To take into account the variability of anthropometric parameters between individuals, the ratio of areas to length$^2$, CSMI to length$^4$, $J$ to length$^4$ and $Z$ to length$^3$ were calculated to adjust for the humeri or radii length [29]. All geometric and mechanical parameters were analysed at each cross-section and by averaging all cross-section values for the humeri and the radii separately.

**In vivo group**

Volumetric bone mineral density (vBMD) and microstructure variables were determined at the distal radius by high-resolution peripheral quantitative computed tomography (HR-pQCT) using an Xtreme CT instrument (Scanco Medical, Bassersdorf, Switzerland) as previously described [24]. In brief, the HR-pQCT images were filtered and the bone was segmented using the standard method recommended by the manufacturer. The periosteal and endosteal boundaries were defined using an automated contouring method [30]. Cortical thickness was then defined by applying a distance transformation function to the cortical compartment. Cortical porosity (percentage) was calculated as the number of void voxels in each binary cortex image divided by the total number of voxels. Determinations were performed on the non-dominant limb, unless a fracture was reported in the region of interest. Recorded variables were as follows: total, cortical, and trabecular vBMD, expressed as milligrammes per cubic centimetre of...
calcium hydroxyapatite (mg/cm3); total area, cortical and trabecular areas (mm2); trabecular number (mm−1), thickness and spacing (μm); trabecular spacing standard deviation (SD), an estimate of the heterogeneity of the trabecular structure (μm); and mean cortical thickness (μm). A finite element model of the radius was created directly from the segmented HR-pQCT images to calculate bone stiffness (kilo-Newton per millimetre−kN/mm), estimated failure load (N) using the criterion described by Pistoia and colleagues [31], and apparent modulus (N/mm2), an estimate of stiffness corrected for Ti.Ar. All finite element analyses were done using the finite element solver integrated in the IPL software version 1.15 (Scanco Medical AG), as previously described [24].

**Skeleton asymmetry and handedness assessment**

Handedness induces a natural asymmetry of linear geometrical properties with higher values in the dominant limb [32]. Handness was determined for each skeleton according to the global directional asymmetry profile of linear geometrical properties of the humeri and radii, determined according to Mays and colleagues as asymmetry=([(right−left)/((right+left)/2)]×100, making it possible to take into account both its intensity and direction [33, 34]. For other analyses, absolute asymmetry of cross-section parameters were determined between the dominant and non-dominant limbs, as asymmetry=|[(dominant−non-dominant)/(non dominant)]|×100. For comparison between groups, asymmetry of geometric parameters was analyzed only at the humeri because the latter have larger bone areas than radii, providing thus data with lower variability.

**Statistical analyses**

Age at death of individuals from the anthropologic collection was divided into three categories: 20–45 years, 46–65 years, and 66–93 years. Data are reported as medians and interquartile ranges or numbers and percentages. As most variables were not normally distributed, nonparametric tests (Mann−Whitney and Kruskal−Wallis tests) were used to assess differences in continuous variables between groups. A chi-squared test was used for differences in frequency. Statistical analyses were performed using STATA software, version 12.1 (StataCorp LP, College Station, TX, USA).

**Results**

**Heavy-loading occupational activity is associated with greater calculated strength and higher total and cortical areas in young men**

The characteristics of individuals from the skeleton collection did not differ between OA groups (Table 1). One hundred eighty-three skeletons (84 %) were presumed right-handed men. Age was negatively associated with Ct.Ar and positively associated with Me.Ar (Fig. 2).

Table 2 shows the influence of heavy-loading OA on bone strength and geometry at the dominant upper limb. Men with heavy-loading OA had higher bending strength at the radius (antero-posterior and minimum CSMI +11.7 % and +10.3 %; p=0.035 and 0.037, respectively). Analyses according to age of death revealed that greater bone strength in the heavy-loading OA group was observed only in men who died between the age of 20 and 45 years. In this age class, all radii strength parameters were greater: higher bending strength (CSMI +14.4 to +27.2 %; p=0.014-0.005), torsional strength (J +23.8 %; p=0.006), and section modulus (+10.2 and +19.7 %; p=0.010–0.004). At humeri, medio-lateral, minimum and maximum CSMI, and medio-lateral section modulus were higher (+27.6 %, +18.5 %, +35.3 %, and +18.3 %, respectively, all p values <0.05). The greater mechanical properties in men with heavy vs light-loading OA in the age group 20–45 were associated with larger Tt.Ar at the humerus and radius (+10.1 %; p=0.027 and +10.6 %, p=0.004, respectively) and larger Me.Ar and Ct.Ar at the radius (+31 %, p=0.015 and +5.7 %; p=0.045, respectively). The Me.Ar increased in parallel with Tt.Ar, with no difference between groups in the Ct.Ar/ Tt.Ar ratio. These differences were not detected in men who were over 45 years at death, with values in the light-loading OA group gradually reaching those observed in the heavy-loading OA group, in which Tt.Ar at the humerus and radius did not significantly increase with age (Fig. 2). The differences in Tt.Ar and Ct.Ar between the heavy and light-loading OA groups at each of the nine cross-sections are shown in supplemental Table S1.

**Heavy-loading occupational activity slows down the age-related endocortical expansion**

Secondly, we focused on the heavy-loading OA group to investigate the asymmetry of geometrical parameters between the dominant and non-dominant limbs. We hypothesised that asymmetry should be higher in men with unilateral vs bilateral OA in a time-dependent manner. Asymmetry of humeri Tt.Ar, Me.Ar, and Ct.Ar/Tt.Ar ratio increased according to the age group, but this age-dependent increase of asymmetry was more marked in the unilateral group than the bilateral group (Table 3). Asymmetry was higher in the unilateral vs bilateral OA groups in men who died over the age of 65 years (Me.Ar asymmetry +15.2 % vs +9.1 %; p=0.007; Tt.Ar asymmetry +7.8 % vs +5.0 %, p=0.043; Ct.Ar/Tt.Ar ratio asymmetry +7.0 % vs +2.8 %, p=0.002). In this age group, values of geometric parameters at the dominant limb were similar in the unilateral and the bilateral heavy-loading OA groups. At the non-dominant distal humerus, Me.Ar was 18.4 % lower in the bilateral group (p=0.033) and associated with a 16.6 %
HUMERUS

Tt.Ar

\[ \beta = 0.23, p = 0.369 \]
\[ \beta = 1.05, p = 0.018 \]

Me.Ar

\[ \beta = 0.98, p < 0.001 \]
\[ \beta = 1.77, p < 0.001 \]

Ct.Ar

\[ \beta = -0.74, p < 0.001 \]
\[ \beta = -0.72, p = 0.005 \]

Ct.Ar/Tt.Ar

\[ \beta = -0.24, p < 0.001 \]
\[ \beta = -0.34, p < 0.001 \]

RADIUS

Tt.Ar

\[ \beta = -0.03, p = 0.776 \]
\[ \beta = 0.28, p = 0.133 \]

Me.Ar

\[ \beta = 0.49, p < 0.001 \]
\[ \beta = 0.25, p < 0.001 \]

Ct.Ar

\[ \beta = -0.28, p < 0.001 \]
\[ \beta = -0.21, p = 0.072 \]

Ct.Ar/Tt.Ar

\[ \beta = -0.17, p < 0.001 \]
\[ \beta = -0.27, p < 0.001 \]
higher Ct.Ar/Tt.Ar ratio ($p=0.020$) (supplemental Table S2). These data indicate that the increase of asymmetry is compatible with the hypothesis of an attenuation of age-related endocortical expansion by heavy-loading OA on the limb on which they are applied (most workers with heavy loading OA in the first part of the twentieth century continued to work hard after the current retirement age limit). This hypothesis is particularly well illustrated in Fig. 1c representing asymmetry of cross-sections of the humeri and radii of two elderly brothers with lateralized heavy-loading OA for one and non-lateralized heavy-loading OA for the other.

**Discussion**

These ex vivo and in vivo studies show that lifelong heavy-loading OA increase bone strength. This benefit is associated with two independent mechanisms influencing bone mass and strength: higher Tt.Ar and Me.Ar during early adulthood, and a slowdown of the age-related expansion in the Me.Ar and alteration of the Tb bone compartment.

The higher Tt.Ar observed in young manual workers suggests that OA-related mechanical stress promotes bone growth before peak bone size has been reached and during early adulthood. Heavy-loading OA, in particular farming, classically started early in youth in the twentieth century, a period during which the effect of OA on bone acquisition has been previously demonstrated [10]. In adults, Tt.Ar increases by periosseous apposition, which has been suggested to compensate endocortical bone loss observed with ageing and reduce the total net loss of bone [7, 35]. In the heavy-loading OA groups, the potential decrease of age-related bone resorption in elderly men, illustrated by the marked asymmetry of the medullary cavity and the lower alteration of Tb bone parameters, might explain the absence of Tt.Ar expansion. Manual OA (e.g. farmers) was usually maintained long after the age of 65 years in the twentieth century. In the light-loading OA group, no OA-related mechanical stress slowed bone loss and Tt.Ar continued to increase slowly until it caught up with the heavy-loading OA group, thus explaining why the early benefit on Tt.Ar attenuates with ageing. Thus, the benefit of heavy-loading OA on cortical bone results in the net difference between Tt.Ar and age-related endocortical expansion. In heavy-loading vs light-loading-OA, Tt.Ar and endocortical expansion are, respectively, higher and similar in young adult men, similar and lower in elderly men.

The impact of heavy OA on bone width observed in this study is consistent with previous anthropological studies in different ethnic groups. Differences in cross-sectional geometry parameters and structural adaptations according to physical activities were identified in long bones in these studies (humerus and femur mainly) [36–39], while this change has not been observed in metacarpal cortical bone [40].

We did not observe difference of asymmetry of areas between the bilateral and unilateral heavy-loading group in the age group 20–45, in contrast to previous reports in athletes.
Simon anthropologic collection is a remarkable homogeneous and environmental factors is probably limited. Moreover, the heavy-loading group suggest that the contribution of genetic dominant and non-dominant limbs of men from the unilateral collection of skeletons, the higher asymmetries between the factor contributing to bone health [43]. However, in the Simon heavy-loading OA had higher protein intake, a well-known lifestyle factors, which may reflect the sociocultural influence to environmental confounding factors, such as nutritional or ond, the benefit of heavy-loading OA might be partly related produce signals, such as sclerostin or periostin [41, 42]. Sec-

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ters of manual workers). Athletes provide an experimental model in which intensity of loading, muscle mass and strength surrounding the bones and nutritional intakes are amplified, leading to maximising the effects on bone geometry (Tt.Ar in this age
class). These data suggest that a longer time is needed to observe the effect of loading in the physiological conditions of manual workers of the general population, as compared to specific models.

Several mechanisms may be involved in these processes. First, a direct effect of mechanical stimuli on bone cells might be mediated by osteocytes, which sense mechanical loading to produce signals, such as sclerostin or periostin [41, 42]. Sec-

ond, the benefit of heavy-loading OA might be partly related to environmental confounding factors, such as nutritional or lifestyle factors, which may reflect the sociocultural influence of profession. Participants from the GERICO cohort with heavy-loading OA had higher protein intake, a well-known factor contributing to bone health [43]. However, in the Simon collection of skeletons, the higher asymmetries between the dominant and non-dominant limbs of men from the unilateral heavy-loading group suggest that the contribution of genetic and environmental factors is probably limited. Moreover, the Simon anthropologic collection is a remarkable homogeneous collection from a predominantly rural region in a well-defined area. In particular, calcium and protein intake were probably rich in local farm products, especially at the end of the nineteenth century and during the twentieth century. In addition, its genetic variability is reduced with little population migration and frequent kinships, obvious occupations may pass down through generations (sons of manual workers would tend to become manual workers themselves and marry daugh-
ters of manual workers).

A particular strength of our study is the use of unique datasets and methodologies to investigate the effects of life-
long OA on bone. Occupation classification categories were highly correlated with OA levels collected with a face-to-face-administered questionnaire in the GERICO cohort. By focusing on the humeri and radii, we eliminated the interference of OA-independent loading that may be observed in lower limb bones. Ex vivo data are in agreement with those observed in vivo at time of retirement in the GERICO cohort or specific conditions of various athletic sports [12, 13, 17]. Moreover, data from the GERICO cohort allowed determining which microstructural parameters were influenced by OA. Interest-

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<table>
<thead>
<tr>
<th>Table 2</th>
<th>Percent median difference (Δ) between the heavy- and light-loading occupational activity groups in mean values of geometric and mechanical properties of the five cross-sections of humeri and four cross-sections of radii at the dominant upper limb, according to age group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age group</td>
<td>All</td>
</tr>
<tr>
<td>N</td>
<td>206</td>
</tr>
<tr>
<td>Bone strength</td>
<td></td>
</tr>
<tr>
<td>CSMI</td>
<td></td>
</tr>
<tr>
<td>Antero-posterior</td>
<td>+7.9</td>
</tr>
<tr>
<td>Medio-lateral</td>
<td>+5.1</td>
</tr>
<tr>
<td>Minimum</td>
<td>+5.8</td>
</tr>
<tr>
<td>Maximum</td>
<td>+3.4</td>
</tr>
<tr>
<td>Polar moment of inertia (J)</td>
<td>+3.7</td>
</tr>
<tr>
<td>Section modulus (Z)</td>
<td>+2.3</td>
</tr>
<tr>
<td>Medio-lateral</td>
<td>+3.2</td>
</tr>
<tr>
<td>Geometric properties</td>
<td></td>
</tr>
<tr>
<td>Tt.Ar</td>
<td>+5.4</td>
</tr>
<tr>
<td>Ct.Ar</td>
<td>+4.2</td>
</tr>
<tr>
<td>Me.Ar</td>
<td>+4.0</td>
</tr>
<tr>
<td>Ct.Ar/Tt.Ar</td>
<td>+1.4</td>
</tr>
</tbody>
</table>

Items in italics are statistically significant p-values

Tt.Ar total area, Ct.Ar cortical area, Me.Ar medullary area, CSMI cross-sectional moments of inertia, OA occupational activity

[12, 13]. Differences of asymmetry were however observed in the oldest group in which loading was applied during a longer period of time. Physiological conditions in manual workers of the general population cannot be assimilated to those observed in athletes. Athletes provide an experimental model in which intensity of loading, muscle mass and strength surrounding the bones and nutritional intakes are amplified, leading to maximising the effects on bone geometry (Tt.Ar in this age
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changes in occupational and leisure time activities. Although probably less frequent in the first half of the twentieth century than nowadays, these changes may also be observed in a same professional group, a younger man tending to work harder than an older one because of different physical abilities and of workload changes (older workers with professional

Table 3  Asymmetry of mean values of geometric properties of the five cross-sections of humeri between the unilateral and bilateral heavy-loading occupational activity groups, according to age group

<table>
<thead>
<tr>
<th>Age group</th>
<th>20–45 years</th>
<th>46–65 years</th>
<th>66–93 years</th>
<th>P age trend for bilateral</th>
<th>P age trend for unilateral</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Bilateral</td>
<td>Unilateral</td>
<td>Bilateral</td>
<td>Unilateral</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(n=19)</td>
<td>(n=14)</td>
<td>(n=32)</td>
<td>(n=15)</td>
<td></td>
</tr>
<tr>
<td>Tt.Ar</td>
<td>4.3 [2.3]</td>
<td>3.9 [2.2]</td>
<td>4.8 [4.1]</td>
<td>3.9 [4.0]</td>
<td>-0.9</td>
</tr>
<tr>
<td></td>
<td>0.799</td>
<td>0.190</td>
<td>0.632</td>
<td>0.161</td>
<td></td>
</tr>
<tr>
<td>Cℓ.Ar</td>
<td>3.7 [3.1]</td>
<td>2.8 [2.3]</td>
<td>3.8 [3.5]</td>
<td>2.6 [3.6]</td>
<td>-1.1</td>
</tr>
<tr>
<td></td>
<td>0.190</td>
<td>0.229</td>
<td>0.632</td>
<td>0.161</td>
<td></td>
</tr>
<tr>
<td>Me.Ar</td>
<td>5.6 [4.9]</td>
<td>5.5 [8.2]</td>
<td>7.7 [7.2]</td>
<td>9.7 [10.3]</td>
<td>+2.0</td>
</tr>
<tr>
<td></td>
<td>0.588</td>
<td>0.489</td>
<td>0.837</td>
<td>0.488</td>
<td></td>
</tr>
<tr>
<td>Cr.Ar/Tt.Ar</td>
<td>1.4 [1.6]</td>
<td>1.8 [2.8]</td>
<td>2.7 [3.6]</td>
<td>2.6 [3.2]</td>
<td>-0.1</td>
</tr>
</tbody>
</table>

Items in italics are statistically significant *p*-values. Data are median (interquartile range)

Tt.Ar total area, Cℓ.Ar cortical area, Me.Ar medullary area

Table 4  Characteristics of men included in the GERICO cohort and geometric and mechanical properties at distal radius according to occupational activity group

<table>
<thead>
<tr>
<th></th>
<th>Light-loading OA (N=160)</th>
<th>Heavy-loading OA (N=20)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>65.1 [2.5]</td>
<td>66.0 [3.1]</td>
<td>0.287</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>175 [9]</td>
<td>174 [9]</td>
<td>0.542</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>80.7 [17.2]</td>
<td>80.2 [18.4]</td>
<td>0.759</td>
</tr>
<tr>
<td>Body mass index (kg/m2)</td>
<td>26.2 [4.4]</td>
<td>26.3 [7.1]</td>
<td>0.387</td>
</tr>
<tr>
<td>Clinical fracture in adult age</td>
<td>76 [47 %]</td>
<td>11 [55 %]</td>
<td>0.527</td>
</tr>
<tr>
<td>Calcium intake (mg/day)</td>
<td>1218 [555]</td>
<td>1374 [627]</td>
<td>0.062</td>
</tr>
<tr>
<td>Protein intake (g/day)</td>
<td>81.4 [28.4]</td>
<td>101.4 [30.0]</td>
<td>0.003</td>
</tr>
<tr>
<td>Lifelong quantitative loading activities (scale 1–4)</td>
<td>1.7 [1]</td>
<td>3.0 [1.3]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Occupational activity time</td>
<td>3.0 [0.7]</td>
<td>3.0 [0.7]</td>
<td>0.580</td>
</tr>
<tr>
<td>Leisure and sport time</td>
<td>1.7 [1]</td>
<td>3.0 [1.3]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Biomechanical parameters</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stiffness (kN/mm)</td>
<td>106.1 [29.3]</td>
<td>120.9 [36.3]</td>
<td>0.015</td>
</tr>
<tr>
<td>Estimated failure load (N)</td>
<td>3795 [933]</td>
<td>4226 [1161]</td>
<td>0.017</td>
</tr>
<tr>
<td>Apparent modulus (N/mm2)</td>
<td>1874 [580]</td>
<td>1931 [428]</td>
<td>0.178</td>
</tr>
<tr>
<td>Volumetric bone mineral density (mg HA/cm3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total BMD</td>
<td>324 [76]</td>
<td>338 [88]</td>
<td>0.171</td>
</tr>
<tr>
<td>Trabecular BMD</td>
<td>169 [46]</td>
<td>190 [59]</td>
<td>0.021</td>
</tr>
<tr>
<td>Cortical BMD</td>
<td>874 [56]</td>
<td>877 [62]</td>
<td>0.769</td>
</tr>
<tr>
<td>Tt.Ar (mm2)</td>
<td>360 [74]</td>
<td>361 [112]</td>
<td>0.339</td>
</tr>
<tr>
<td>Trabecular area (mm²)</td>
<td>280 [86]</td>
<td>298 [126]</td>
<td>0.551</td>
</tr>
<tr>
<td>Cortical area (mm²)</td>
<td>69.6 [18.7]</td>
<td>79.7 [18.4]</td>
<td>0.066</td>
</tr>
<tr>
<td>Cortical thickness (μm)</td>
<td>850 [220]</td>
<td>930 [270]</td>
<td>0.228</td>
</tr>
<tr>
<td>Cortical porosity (%)</td>
<td>2.8 [1.4]</td>
<td>3.3 [1.1]</td>
<td>0.037</td>
</tr>
<tr>
<td>Trabecular number (mm⁻¹)</td>
<td>2.04 [0.37]</td>
<td>2.19 [0.26]</td>
<td>0.084</td>
</tr>
<tr>
<td>Trabecular thickness (μm)</td>
<td>69 [16]</td>
<td>74 [11]</td>
<td>0.054</td>
</tr>
<tr>
<td>Trabecular spacing (μm)</td>
<td>417 [96]</td>
<td>387 [65]</td>
<td>0.049</td>
</tr>
<tr>
<td>Trabecular spacing standard deviation (μm)</td>
<td>175 [55]</td>
<td>157 [35]</td>
<td>0.065</td>
</tr>
</tbody>
</table>

Items in italics are statistically significant *p*-values. Data are median (interquartile range) or number of subjects (%)

OA occupational activity, BMD bone mineral density, Tt.Ar total area
experience will tend to teach or supervise younger workers). Regarding the statistical analysis, we did not apply a Bonferroni correction to take into account multiple comparisons because this correction assumes that all the tests performed are independent. This type of correction would be too restrictive to be applied in this study with strongly correlated variables [44].

To our knowledge, this is the first report showing the benefit of OA-dependent repeated loading on bone strength based on ex vivo and in vivo data. Cortical bone appears to be modulated by heavy-loading OA by two mechanisms: promotion of Tt.Ar and Me.Ar in young adulthood followed by slowdown of the age-related bone loss at endocortical and trabecular surfaces. From a general and public health point of view, these data provide a rationale to suggest that sedentary OA due to technological advancement observed in our current society will contribute to lifelong higher bone fragility and fracture risk with ageing and support the necessity to promote lifelong load-bearing physical activities for bone health.

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Compliance with ethical standards

Conflict of interest Dr. van Rietbergen reports personal fees from Scanco Medical AG, outside the submitted work; Emmanuel Biver, Geneviève Perréard Lopreno, Magaly Hars, Jean-Paul Vallée, Serge Ferrari, Marie Besse, and René Rizzoli declare that they have no conflict of interest.

References


