



Smaller long bone cross-sectional size in people who died of tuberculosis: Insights on frailty factors from a 19th and early 20th century Finnish population

Liina Mansukoski^{a,b,*}, Vitale Stefano Sparacello^c

^a Department of Anthropology, Durham University, Dawson Building South Road, Durham, DH1 3LE, United Kingdom

^b School of Sport, Exercise and Health Sciences, Loughborough University, Ashby Road, Loughborough, Leicestershire, LE11 3TU, United Kingdom

^c UMR5199 PACEA, Univ. Bordeaux, Batiment B8, Avenue Geoffroy Saint Hilaire, CS 50023, 33615 Pessac Cedex, France

ARTICLE INFO

Keywords:

Cross-sectional geometry
Robusticity
Ontogeny
Vitamin-D deficiency
Identified individuals

ABSTRACT

There is little research on how individuals suffering from tuberculosis may differ from those not infected in terms of overall skeletal morphology. Tuberculosis was endemic in 19th and early 20th century Finland making documented skeletal collections of Finns ideal to study effects of the disease on bone. The present study compares long bone cross-sectional total area between individuals who died of tuberculosis and those with another recorded cause of death in a Finnish sample. Adult male individuals (N = 105) were selected for analysis. Complete humeri (N = 56), femora (N = 66) and tibiae (N = 64) were 3D scanned using a laser scanner and total cross-sectional areas calculated with AsciiSection software. Individuals who died of tuberculosis (N = 24, 15 humeri, 14 femora, 13 tibiae) had, when standardized for body size, significantly smaller total cross-sectional femoral and humeral, but not tibial, areas. The mechanisms behind the observed relationship may reflect a combination of biological ‘frailty’ in terms of susceptibility to infection, reduced childhood activity and/or vitamin D deficiency, which possibly influenced both subperiosteal development during adolescence and, later, susceptibility to contracting and dying of TB. Due to the relatively small sample future studies are needed to further investigate the relationship between TB and bone cross-sectional size.

1. Introduction

In the recent past, tuberculosis (TB) was one of the leading causes of death (Roberts and Buikstra, 2003) and, despite the availability of antibiotic treatment, tuberculosis is currently a re-emerging disease that still causes millions of deaths every year (WHO, 2016). Tuberculosis was endemic in 19th and early 20th century Finland, and it was the main identified cause of death in 16% of the population (Harjula, 2007). Documented collections of the Finns are therefore ideal for investigating the effects of TB on bones, as well as the possible indicators of susceptibility to TB recorded in the skeleton.

Changes to the skeleton due to tuberculosis are usually due to the infection spreading from its primary focus (Roberts and Buikstra, 2003). Tuberculosis leaves traces in the skeleton in approximately 3–5% of cases, with lesions occurring particularly in the vertebrae (Holloway et al., 2011; Resnick and Niwayama 1995), although rates appear to be higher, up to 30%, for extrapulmonary tuberculosis (Jaffe, 1972). In children, TB may hinder bone growth through osteomyelitis of the growth plates (Aufderheide and Rodriguez Martin, 1998), and in

adults, radiography has revealed marked demineralisation of long bones (Tuli, 2016). Direct metabolic effects on the bone occur when infection reaches skeletal sites via vascular channels (Tuli, 2016). Indirect effects may occur due to the link between the body’s inflammatory response and hypothalamic–pituitary–adrenal (HPA) axis function, because as a bacterial disease TB causes an immune response and thus promotes the release of cytokines (Bozza et al., 2007; Etna et al., 2014). These in turn could lead to reduced bone growth due to cortisol secretion (Walsh, 2015). In addition, TB leads to malnutrition (i.e. “consumption”), especially involving problems in protein absorption (Macallan, 1999; Schwenk and Macallan, 2000), which may affect bone growth and their normal turnover in adult life.

Despite the above, there is little research on how individuals suffering from TB may differ from those who are not infected in terms of overall skeletal morphology, that is, in traits other than TB related lesions. In particular, it would be relevant for bioarchaeological studies to understand how this disease may alter the mechanical competence of long bones, which is usually assessed through the study of their diaphyseal cross-sections. In developing individuals, long-term metabolic

* Corresponding author at: School of Sport, Exercise and Health Sciences, Loughborough University, Ashby Road, Loughborough, Leicestershire, LE11 3TU, United Kingdom.
E-mail address: l.mansukoski@lboro.ac.uk (L. Mansukoski).

insults significantly alter bone development by slowing down subperiosteal apposition and accelerating medullary expansion (Garn et al., 1964, 1969; Himes et al., 1975). In adults, long-term severe malnutrition and inactivity can lead to significant decreases in bone mass (Bourrin et al., 2000; Garn et al., 1964, 1969; Tuli, 2013). This decrease is mainly due to variations in bone mineral density and trabecular bone density rather than cortical bone area (Nordström and Nordström, 2011; Tervo et al., 2009), and cortical thinning is generally due to an expansion in the medullary area (Bass et al., 2002; Garn et al., 1964, 1969; Himes et al., 1975; Hummert, 1983; Huss-Ashmore, 1981).

The relationship of TB and bone mechanical competence through the study of cross-sectional geometry properties (CSG) was investigated by Sparacello et al. (2016). The study found that one adolescent individual from the Neolithic of Italy (Liguria region) who died of TB was relatively gracile in comparison to his peers, suggesting a period of compromised periosteal apposition during growth. In contrast, an adult individual with Pott's spine did not show any apparent changes in upper and lower limb structure. This would suggest that, while significantly disrupting bone development, TB does not have a major impact on adult long bones, or at least not enough to be detectable via CSG in a bioarchaeological setting.

However, in palaeopathological studies sufficient sample sizes are difficult to obtain and the diagnosis of the disease from bony changes remains uncertain as conditions other than TB may cause very similar lesions (Holloway et al., 2011). The present study expands on these findings by using a larger sample size of individuals whose cause of death was recorded as TB by a medical examiner in a post-mortem examination, termed here "TB sample". The relationship between skeletal robusticity and tuberculosis was investigated by comparing late 19th and early 20th century Finnish adult males who died of TB with those with another recorded cause of death ("non-TB sample"). The aim was to assess whether there is a difference in robusticity – measured as size-standardized bone cross-sectional total area (TA) – between the TB and non-TB Finnish samples. We expected no differences, after controlling for body dimensions and age, especially considering that subperiosteal area should be the bone property that would be the least affected by the long-term consequences of the disease in adult life.

2. Materials and methods

2.1. Study sample

Throughout the study, the ethical guidelines of the British Association for Biological Anthropology and Osteoarchaeology were followed (BABAO, 2015). The sample belongs to a skeletal collection of identified individuals, housed at the Finnish Museum of Natural History in Helsinki. The individuals in the sample were born between 1850 and 1914, and died between 1915 and 1937. Written post-mortem records accompanying the individuals include information on names, years of birth, occupations, recorded living statures and causes of death (Söderholm, 2002; Telkkä, 1950). The collection consists principally of low and medium social status individuals whose remains were sent to the University of Helsinki by local medical examiners (Söderholm, 2002).

Any bones showing signs of healed fractures or other clear alterations were excluded from analysis. In total 105 male individuals were included (N = 56 humeri, N = 66 femora and N = 64 tibiae). No data were collected on female individuals; there are only four females in the collection with TB listed as cause of death, an insufficient sample size. The name of each individual in the collection is known and was used to assign sex; there were no individuals for whom the recorded name was ambiguous. The name data indicate all individuals were ethnic Finns, but this is not conclusive evidence, as the accompanying records make no reference to ethnicity. Only adult individuals were included in this study with ages at death ranging from 18 to 81. Biological maturity was estimated using the recorded age at death of the individuals together

Table 1

Study sample sizes, mean ages, age ranges and standard deviations by bone and cause of death category (TB or not TB).

	Cause of death TB	Cause of death not TB
Humerus		
Sample size	15	41
Mean age at death	44.73	43.95
Age range (years)	23–77	22–81
SD (years)	14.41	16.83
Femur		
Sample size	14	52
Mean age at death	36.07	44.75*
Age range (years)	21–77	18–81
SD (years)	14.02	17.07
Tibia		
Sample size	13	51
Mean age at death	32.92	44.76**
Age range (years)	21–45	18–81
SD (years)	7.91	17.24

* Mann-Whitney *U* Test: difference with the "cause of death TB" sample significant at the $p = 0.1$ level.

** Mann-Whitney *U* Test: difference with the "cause of death TB" sample significant at the $p = 0.05$ level.

with assessing epiphyseal fusion of present limb long bones. Sample sizes and mean ages at death by bone and by cause of death category are detailed in Table 1.

Though well preserved, the collection does not comprise complete skeletons and for most individuals only a few long bones are present (often either upper or lower limbs, but not both), with the humerus sample consisting of largely different individuals than the samples for femur and tibia. For each individual with a present tibia (N = 64) there is also a femur, and for 15 of those, there is also a humerus. If different bones were present for the same individual (humerus, femur and/or tibia) all were included in their respective samples. Individuals were assigned to two categories for each bone (humerus, femur, tibia): (1) cause of death TB (15 humeri, 14 femora, 13 tibiae), and (2) cause of death not TB (41 humeri, 52 femora, 51 tibiae). The early 20th century medical examiners did not use modern disease classifications to assign a diagnostic code for cause of death, and those classified as having died of TB (N = 24) either had a cause of death "tuberculosis" or "keuhkotauti" (a historically used Finnish name for the disease; see supplementary materials for a summary of other causes of death in this sample). For most individuals, bones from the left side of the body were chosen, except in the few cases when they were absent (N = 2 humeri, N = 4 femora, N = 3 tibiae), where the right side was analysed instead.

2.2. Measurement protocol

The maximum lengths of humeri, femora and tibiae were measured manually using an osteometric board following White et al. (2011). Vertical femoral head diameter (M18; Bräuer, 1988) measurements were taken using a Sylvac digital sliding caliper following Ruff and Scott (1991).

Total cross-sectional area (TA, in mm^2) was calculated from 3D models in AsciiSection (instructions for acquiring the program are available from the PAVE research group <http://www.pave.arch.cam.ac.uk/index.html>) following the method by Davies et al. (2012). Using 3D models increases accuracy in reconstructing cross sections by requiring fewer passages compared to periosteal silicon moulds, and 3D models make data collection faster especially when multiple sections are extracted (Davies et al., 2012). For femur and tibia, TA was calculated at midshaft (50% of bone length), while for the humerus, the mid-distal section was considered (35% of bone length) following the standard practice in the field of CSG (Ruff, 2002). Body mass was estimated using the vertical femoral head diameter measurements and the formula by

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