The changing face of tuberculosis: Trends in tuberculosis-associated skeletal changes

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Abstract

Tuberculosis remains a major health problem in many areas of the world. Previous research suggested that the frequency of bone lesions has decreased in the modern (but pre-antibiotic) period, and that the predominantly spinal involvement have changed to affect other parts of the skeleton, in particular ribs. The purpose of this study was to investigate whether bone lesions associated with TB became more or less common in the post-antibiotic period, and if the pattern of skeletal involvement has changed. The skeletons of 147 individuals from South Africa who died from TB were assessed. These were divided into three groups - those dying before 1950 and presumed to have had no antibiotic intervention (n=52); those dying between 1950 and 1985 presumed to have been treated with antibiotics (n=34); and those dying after 1985 where co-infection with

HIV and drug-resistant disease emerged (n=61). Overall, 33.3% of all individuals showed signs that could be associated with TB, with corresponding figures in each of the three groups being 21.1%, 38.2% and 41.0%. The increase from group 1 to 3 was statistically significant. Rib lesions are becoming more common, while spinal lesions are decreasing. It may be suggested that patients are surviving for longer due to antibiotic treatment, allowing more time for the development of lesions.

Key words: Evolution of disease, antibiotics, South Africa

1. Introduction

Tuberculosis is a chronic infectious disease caused by *Mycobacterium tuberculosis*, and a multitude of publications have appeared that outline the history of this disease,[1-4] its rise and fall in different countries and across various time periods[5-7] and not the least its molecular evolution and genetic make-up.[8-11] TB remains a major health concern, such that it was declared a global emergency in 1993 by the WHO,[12] as at the time it was estimated that half of all individuals that developed the disease died within six to 24 months.[13]

Knowledge of past incidences and signs as well as the spread of TB can inform our understanding of this condition and health practices of today.[14] As is the case with many other diseases and micro-organisms, *Mycobacterium tuberculosis* undergoes continuous evolution. The genetic diversity of this microbe allows for any one variant, when placed in a changing host environment, to become a dominant form of the disease, allowing for such a strain to operate successfully between different species and geographical locations.[4] In doing so, the presentation of this disease also changes. Recently, for example, it has been argued that the frequency of bone involvement has decreased over time, and that bony lesions tend to become less common in the spine but more common elsewhere.[7]

Among the major events/influences in the long course of this disease are the development of immunizations, the development of antibiotics in the mid 1940's, and the emergence of HIV. In recent years the appearance of drug-resistant and highly drug-

resistant TB has also become particularly problematical. A combination of factors, including crowded living conditions and poor access to health care, have aided in the formation of drug-resistant TB. Poor compliance amongst patients to take the full course of medication which lasts six to 18 months has also contributed immensely to the development of drug-resistant strains. Even though a patient may feel better after only three months of treatment, full treatment lasting several months is needed to eradicate all the bacilli.[15] Possible reasons for failure to comply with treatment specifications include poor access to public health care, drug provisions, i.e. unavailability of drugs, and ignorance to and/or absence of knowledge regarding the disease.

A major factor that contributed to the increased incidence of tuberculosis in modern times is HIV infection. HIV was first recognized as a disease in 1985,[16] and co-infection with both HIV and TB has become common. HIV compromises the immune system, making it more susceptible to infection. An estimated 8 million people world-wide were co-infected with HIV and TB by 1998,[17] making HIV the single most important risk factor for contracting TB.[18] HIV is also frequently the cause of progression of dormant disease into full-blown TB and causes rapid progression of the disease.[19] HIV-related TB is most common in Sub-Saharan countries, making up 79% of such cases known world-wide.[20] TB is now the most common cause of HIV-related deaths, and occurs in at least a third of HIV positive people in sub-Saharan Africa.[17]

The emergence of drug-resistant TB and the spread of HIV are especially important in South Africa that ranks third in the world (after India and China) as far as the incidence of TB is concerned,[21] and where both co-infection with HIV and drug resistance are common. The first case of multidrug-resistant TB (MDR-TB) was recorded in the Western Cape in 1985,[22] whereas the first cases of extensively drug resistant TB (XDR-TB) were reported from Kwazulu Natal in 2006.[23]

These major events are very likely to have changed the skeletal expressions of this disease, which will be the focus of this paper.

The spine has been reported as the most commonly affected part of the skeleton, where lytic lesions are most often observed in the vertebral bodies of the thoracic and lumbar regions. Neural arches and other elements of the vertebrae are usually spared, and this condition has in the past sometimes resulted in kyphosis of the spine commonly

referred to as Pott's disease.[2,24] Various other parts of the skeleton, including the ribs, hip joint, long bones and other joints (e.g. knee and sacro-iliac) can also show signs of skeletal tuberculosis, but these lesions may be difficult to distinguish from lesions of other etiologies.[2,24] Previous research has reported on the incidence of skeletal tuberculosis, mostly relating to the pre-antibiotic era. In general, it has been reported that the skeleton is involved in about 3 - 5% of cases with TB,[25-27] although incidences as high as 30% have been reported.[28] Many sources quote the spine as being the most commonly involved area, followed by weight-bearing joints such as the hip and knee.

Recently several studies have been conducted to assess rib involvement,[1,29-34] showing much higher frequencies of skeletal involvement. Although not pathognomonic of TB, a clear correlation has been shown between rib lesions and TB, with reported incidences of up to 91%.[34] It was found that 8.8% of individuals with pulmonary TB in the Hamman-Todd Collection had lesions on the visceral side of their ribs,[35] but this figure was much higher at 61.6% in Terry Collection individuals.[36] Other reported figures for rib involvement are 85.2% (Coimbra),[34] 28.0% (Ute Mountain sample),[37] 2.0% (Aymyrlyg Cemetery complex)[38] and 1.0% (Wharram Percy village in northeast England).[33] Conversely, of individuals with rib lesions in the Coimbra Collection in Portugal, 85.7% had pulmonary or non-pulmonary TB as cause of death, whereas 17.8% of individuals with lesions had other causes of death. It is not clear why such highly variable numbers for rib involvement is found.

The purpose of this study was to assess the trends in tuberculosis-associated skeletal changes in modern South African individuals, in order to gain insight into the co-evolution of the pathogen and its host in recent times. Skeletons of individuals who died from TB in the pre- and post-antbiotic era were assessed and compared. These were also compared to frequencies of skeletal involvement in individuals dying after 1985, when co-infection with HIV became more common and drug resistant TB emerged. Two null hypotheses for this study will be tested; namely (a) the overall frequency of skeletal lesions has not changed through time and in particular in the post-antibiotic era, and (b) the distribution of lesions in the skeleton has not changed throughout the time periods observed.

2. Material and methods

Known cases of individuals who died from TB and whose remains are housed in the Pretoria Bone (University of Pretoria) and Raymond A Dart (University of the Witwatersrand) Collections were investigated.[39,40] One individual with no ribs and no vertebrae were excluded (this individual had no signs of pathology on the remainder of the bones). These individuals all have TB indicated as the cause of death, and most come from hospitals in the Gauteng region of South Africa. The vast majority of these individuals can be assumed to have been from low socio-economic status, in South Africa commonly referred to as "the poorest of the poor". In accordance with legislation, bodies of individuals who have died as paupers and are unclaimed can be donated to medical schools, and these individuals probably all fall in this category. As all remains were donated to the university from regional hospitals, the majority of individuals dying in the post-antibiotic era can be assumed to have been treated with antibiotics. However, it should be taken into account that Streptomycin was introduced in the late 1940's, and the date of 1950 used here as "post-antibiotic" is thus somewhat arbitrary. Some individuals dying in 1950, for example, may not have received antibiotics, whereas some dying in 1949 may have. Also there is no information as to the duration of treatment or the compliance of any of the individuals. The age, sex, and ancestry of these individuals are known, but unfortunately no detailed medical records are available.

All skeletons were systematically assessed for signs of TB and other skeletal abnormalities on the skull, ribs, vertebrae, long bones, os coxae, and hand and foot bones. No bone samples were taken and no destructive analyses were performed. Various authors have published detailed descriptions of skeletal signs of TB.[2,24,41] Visceral surfaces of ribs are commonly affected, mostly in the posterior region close to the vertebral column, but virtually every element can be involved.[5,29,30,42] After analysis, the dates of death were recorded for each individual, and according to this the sample was divided into three groups – those dying before 1950 (1925 – 1949) and presumed to have had no antibiotic intervention; those dying between 1950 and 1985 presumed to have been treated with antibiotics; and those dying after 1985 (1986 – 2003) where co-infection with HIV and drug-resistant disease came into play. Although these divisions are somewhat arbitrary, it corresponds (for the first group) to the development of

Streptomycin in the late 1940's and the institution of multiple drug regimes in the early 1950's. The 1985 date was chosen because that is when both AIDS and the first drug-resistant case in South Africa were reported, as outlined in the introduction.

Frequencies of skeletal involvement in the three groups were compared by means of a Kolmogorov-Smirnov analysis, and correlation coefficients were calculated to assess the relationship between age of individuals and skeletal changes. Following Holloway and colleagues' example,[7] skeletons with signs of skeletal TB were further subdivided into those with rib involvement only, spinal involvement only, both rib and "other" and spine and "other" involvement. The "other" group included changes in joints and endocranial fossa and individuals with widespread lesions reminiscent of pulmonary hypertrophic osteoarthropathy.[3,43-45] These two individuals will be discussed in more detail under the results section.

3. Results

It is extremely difficult to specifically diagnose any disease based on skeletal changes only, and TB is no exception. Bone has a limited response to insults, and therefore can react in a limited number of ways. Many of the bony changes are therefore non-specific, and cannot be attributed to a specific disease. In this study, many cases were noted where only non-specific signs of disease were present. These mostly occurred in the form of new (woven) bone deposition on the long bones, in particular the distal tibia and radius. Also, some of the observed cranial lesions had a circular appearance which may be more reminiscent of treponemal infection[2,24] although none of them had saber-shin tibiae or other definitive signs of treponemal disease. Possible co-infection with other disease thus complicated the analysis of the data. Taking this into account, the individuals in each of the date-of-death cohorts were divided into three sub-groups for further analysis. The first sub-group (sub-group A) included all individuals who had no skeletal signs of infectious disease. Sub-group B included all individuals with non-specific changes and changes that may have been due to other infectious diseases. All individuals with vertebral changes (Figure 1), new bone formation on the visceral sides of the ribs (Figure 2) and joint involvement (Figure 3) were included in Sub-group C, which was seen to represent individuals with skeletal signs of TB. In this sub-group were also

included endocranial lesions, e.g., one individual with a destructive lesion in the anterior cranial fossa (Figure 4), and individuals with massive bony changes which can most probably be described as pulmonary hypertrophic osteoarthropathy (Figure 5).

Preservation was in most cases excellent, as the material is derived from cadavers used for collection. In a few cases some of the major long bones or a skull was missing and was so noted.

A total of 147 individuals were included in the analysis, and their demographic composition is shown in Table 1. The vast majority of individuals were male (n = 134), with only 13 females. Ages ranged between 20 and 90, with a mean age of 47.2 years. The mean ages for the three groups were similar and ranged from 42.6 to 49.7. Only two individuals were of European descent, all others were of African descent. This skewed demography should not be seen to reflect mortality patterns, but rather as being the result of collection practices. In all South African skeletal collections African males are the best represented group, and many of the individuals under study can be assumed to have been migrant labourers at the mines around the Witwatersrand.

Table 2 shows the numbers of skeletons without any lesions, those with non-specific lesions, and those with lesions deemed to be associated with TB. As can be seen from this table, Group 2 contained the least number of skeletons (n = 34). The percentage of skeletons showing signs of TB increased from 21.1% in Group 1 (n = 52), to 38.2% in Group 2 and 41.0% in Group 3 (n = 61). Those without changes decreased similarly. The number of individuals with non-specific changes remained constant at around 23 – 24%. More information on each of the 49 individuals with skeletal changes deemed to be due to TB is shown in the Appendix.

Kolmogorov-Smirnov tests were conducted to assess whether there are any marked differences between the underlying distributions of the three groups. These results are summarized in Table 3. The most notable difference arose when only the cases showing skeletal signs of TB were taken into consideration (thus excluding the individuals with non-specific changes). The smallest p-value obtained was between groups 1 and 3 indicating that there is a marked difference (at an 84% level of significance) between these two groups. The difference between groups 1 and 3 were also statistically significant at $p<0.05$ using a Chi-squared analysis.

Furthermore, a Student's t-test for the equality of means was conducted - the results of which are shown in Table 4. These further reiterate that there are marked differences between groups 1 and 3 and a lesser (but still noticeable) difference between groups 1 and 2. The above analyses indicated that there is little significant difference between groups 2 and 3. For cases without TB (Sub-group B; non-specific changes) the same tests were done. It can be concluded that the effects between groups are more or less stable and no significant differences in the underlying distributions are observed.

A Pearson's correlation coefficient was calculated to assess whether there is a significant correlation between the presence of skeletal lesions and the age of individuals. This correlation was found to be 0.022125, which is close to zero, implying that there is little to no linear correlation between age at death of TB patients in this sample and the number with lesions present. For the correlation between the year of death and the number of individuals with lesions, a correlation coefficient of 0.134283 was calculated. This means that there is a 13.43% positive but weak linear correlation between the year of death and the number of individuals with lesions.

Table 5 shows the prevalence of skeletal lesions in the complete skeleton. Here, once again, co-infection with other disease may have confounded the results. For example, it is possible that a person may have had rib lesions (placing him into the group described as having skeletal changes attributable to TB), but also a cranial lesion caused by a different condition. This may explain the high number of individuals (Na = 10) who displayed cranial lesions. As expected, ribs were the bony elements most commonly involved. Very few individuals had vertebral lesions, and if it occurred it was most commonly found in the lumbar vertebrae. However, none had the classic Pott's disease. Also, six individuals had lesions (three unilateral and three bilateral) on the ventral side of the scapulae, and eight had pathological changes in the pelvis. Five individuals had changes in hand bones, and four in foot bones. Femora, tibiae and fibulae frequently showed subperiosteal bone deposition. Only three individuals had joint destruction – one in a hip joint, one in an elbow and another in both a knee and a wrist.

Out of the 49 individuals with signs of TB, 35 (71.4%) had rib lesions, of which 25 had unilateral and 10 bilateral lesions. As expected, rib lesions were more common on the right (59.2% of affected individuals) than left sides (32.7%).

Figures 6 & 7 show data for those skeletons (n = 49) with signs of TB. Figure 6 shows the relative proportions of individuals with lesions on the ribs only, lesions on the ribs and other areas of the skeleton and lastly, lesions only in other skeletal locations, in the three respective year-of-death groups. The percentage of individuals with rib lesions can be seen to increase from group 1 to group 2, again decreasing slightly in the most recent group. Conversely, in the pre-antibiotic era, vertebral lesions were common with more than 50% of affected individuals showing spinal involvement (Figure 7). This decreased in group 2 and again to less than 20% in group 3.

Two individuals had advanced, widespread bone deposition on several bones (Figure 5). Both were males, and both died after 1985 (both in 1991). It is interesting to note that in neither of the two cases the skull, vertebrae or ribs were affected, and the bony changes were mainly present on the appendicular skeleton. These changes are most probably due to hypertrophic pulmonary osteoarthropathy, a condition which results due to long-term disease, often related to lung infections. It is marked by massive periostitis of the long bones.[43-45] Two others had the same widespread changes, but to a lesser degree (see Appendix for more detail).

4. Discussion

The emergence and reemergence of infectious disease has been proposed to be due to 5 possible reasons: cross-species transfer, spatial diffusion, pathogenic evolution, new descriptions of pathogens that have been present for long but are "newly" recognized and a change in human-environment relationships.[46] Although never completely eradicated, the emergence of drug resistant disease (as in the case of TB) can be ascribed to both the evolution of the pathogen and a change in the human-environment relationship (with newer and different medications, increasing poverty, etc.). The changing clinical presentation of TB in South Africa is most likely due to both host genetics and changes in strain lineages. For example, it has been shown that Beijing strains have increased in recent years[47], and it is possible that other changes throughout the periods covered in this study may have played a role in the changing expressions of the disease. Future research should therefore also consider genotypic analysis of TB strains in skeletal samples with the aim of investigating different lineages, individual strains and diversity of strains.

Also, one should keep in mind that mixed infections may alter host resistance to TB and alter skeletal presentations thereof.

In this study it was shown that there is an increase (with time) in the prevalence of skeletal changes associated with TB. A weak but positive correlation was found between the date of death and the incidence of skeletal lesions. Individuals with skeletal involvement increased from 21% to 38% with the introduction of antibiotics, which may suggest that people lived longer and thus had more time to develop skeletal lesions. A similar and statistically significant (as compared to the pre-antibiotic group) increase to 41% was noted in the post-1985 period, and may possibly reflect a long treatment with drugs with the disease gradually gaining the upper hand, either through primary or secondary drug-resistance. The two individuals with the pulmonary hypertrophic osteoarthropathy, both dying in 1991, also lends limited support to the idea that treatment of long duration would lead to a protracted course for the disease, providing more opportunity for skeletal lesions to develop. However, no correlation could be found between age at death and presence of lesions. An increased life expectancy of individuals may therefore not be the only explanation for the observed higher incidences of skeletal involvement. It may also be possible that antibiotic intervention (and possibly HIV) changed the expression of the disease, but this of course cannot be confirmed from this study alone. This finding adds to that of Holloway and colleagues[7] who found that skeletal incidences in people dying from TB were declining, but their study did not include post-antibiotic individuals as was the case here. One of the problems mentioned in the meta-analysis of palaeopathological cases in the Holloway study is the fact that they had to rely on other authors' interpretation that skeletal changes were due to TB; this was not the case here as all individuals came from hospitals and all were documented to have died of TB. Unfortunately their HIV status was not known, which makes it difficult to comment specifically on the influence of HIV.

Similar to what was reported by Holloway and colleagues, trends in the differential involvement of various skeletal parts were found. Spinal TB is becoming less frequent, and in none of the cases anything even closely resembling a classic Potts disease was found. Rib lesions were the most common, with overall 23.8% of individuals in this sample affected. It is difficult to compare this with published figures of rib

involvement, as these range widely from about 1.0%[33] to 91%.[48] Extra-spinous / extra-rib involvement remained infrequent.

The large number (23-24%) of individuals presenting with non-specific signs of disease is worth mentioning. By far the most common of these lesions were subperiosteal new bone formation on the long bones – in almost all cases on the tibia and radius. Many of them can most probably be related to TB and may even represent early expressions of pulmonary hypertrophic osteoarthropathy, but this is difficult to say conclusively. What should be kept in mind here is that the individuals in the sample represent the lowest classes of society, where it can be surmised that malnutrition and poverty are common. Vitamin deficiencies and other infectious diseases may thus also have been responsible for these changes. If these inconclusive changes are taken into account, 44% – 66% (in the three groups) of individuals assessed here showed some skeletal changes, again suggesting that bony involvement in TB is becoming more common.

In this study no attempt was made to distinguish between active, healing and healed lesions. Although most of the lesions were probably active, it is not impossible that some of them may have healed initially with antibiotic treatment, but that the disease then progressed in other parts of the body such that eventually it lead to the demise of the individual.

This paper elucidated aspects of the evolution of disease and the co-evolution of host and organism. In the Holloway et al. paper[7] it was mentioned that their study was the only one to investigate the distribution of lesions over time, and the current paper contributes to our knowledge of trends in this important disease, despite shortcomings such as the relative small sample size and the selective nature of the sample. This paper fills the gap in our knowledge as to what happened after the introduction of antibiotics – whereas it was reported that in recent times (but before antibiotic intervention)[7,49] there was a decrease in TB bone lesions, this paper suggests that not only is the frequency of skeletal involvement increasing, but the distribution of the lesions are also changing. This, however, may only be true for the southern African regions and remains to be confirmed in other areas of the world. Through our human intervention with the development of drugs, the increased resistance of organisms, and subsequent

development of better drugs, patients are surviving for longer with this chronic disease, possibly providing more opportunity for the development of skeletal lesions

5. Conclusion

In conclusion, both null hypotheses for this study were rejected. It seems that the overall frequency of skeletal lesions has changed through time, and particular in the post-antibiotic era skeletal involvement is becoming more common. Additionally, the distribution of lesions in the skeleton has changed, such that rib lesions are becoming more common, as opposed to spinal lesions that are decreasing.

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Table 1
Demography of the sample. Group 1 = individuals dying before 1950; Group 2 = individuals dying 1950 – 1985; Group 3 = individuals dying after 1985

	N	N (males)	N (females)	Age range	Mean age	SD (age)
All	147	134	13	20-90	47.2	14.18
Group 1	52	52	0	20-90	44.6	15.17
Group 2	34	30	4	28-70	46.9	12.17
Group 3	61	52	9	22-84	49.7	14.14

Table 2
Frequency distribution of individuals displaying no signs of TB (Sub-group A), non-specific signs (Sub-group B) and signs that could be associated with TB (Sub-group C). Group 1 = individuals dying before 1950; Group 2 = individuals dying 1950 – 1985; Group 3 = individuals dying after 1985

	Total N	N (unaffected) Sub-group A	N (non-specific) Sub-group B	N (TB) Sub-group C
Group 1	52	29 (55.8%)	12 (23.1%)	11 (21.1%)
Group 2	34	13 (38.2%)	8 (23.6%)	13 (38.2%)
Group 3	61	21 (34.4%)	15 (24.6%)	25 (41.0%)
Total	147	63 (42.9%)	35 (23.8%)	49 (33.3%)

Table 3
p-values for Kolmogorov-Smirnov test (two-sample distribution). Group 1 = individuals dying before 1950; Group 2 = individuals dying 1950 – 1985; Group 3 = individuals dying after 1985

	All cases	TB cases only
Group 1 and 2	0.4918	0.2126
Group 1 and 3	0.3667	0.1601
Group 2 and 3	0.4259	0.8576

Table 4
p-values for Student's t-test for equality of means, assuming unequal variances. Group 1 = individuals dying before 1950; Group 2 = individuals dying 1950 – 1985; Group 3 = individuals dying after 1985

	All cases	TB cases only
Group 1 and 2	0.5441	0.03858
Group 1 and 3	0.07985	0.01484
Group 2 and 3	0.2768	0.779

Table 5
Sites of skeletal involvement, including only the individuals showing skeletal signs of TB (N = 49). Na = number affected

Skeletal location	N	Na	%
Skull	47	10	21.3
Mandible	41	0	0.0
Right ribs	49	29	59.2
Left ribs	49	16	32.7
Cervical vertebrae	28	0	0.0
Thoracic vertebrae	48	8	16.7
Lumbar vertebrae	48	9	18.8
Right scapula	49	4	8.2
Left scapula	48	5	10.4
Right clavicle	49	2	4.1
Left clavicle	47	2	4.3
Right humerus	48	7	14.6
Left humerus	48	5	10.4
Right radius	48	10	20.8
Left radius	47	8	17.0
Right ulna	48	8	16.7
Left ulna	48	7	14.6
Carpals	46	2	4.4
Metacarpals	47	4	8.5
Hand phalanges	47	2	4.3
Right os coxa	46	8	17.4
Left os coxa	46	8	17.4
Sacrum	46	3	6.5
Right femur	47	10	21.3
Left femur	49	8	16.3
Right tibia	47	18	38.3
Left tibia	48	20	41.7
Right fibula	48	15	31.3
Left fibula	48	17	35.4
Tarsals	49	3	6.1
Metatarsals	49	4	8.2
Foot phalanges	49	2	4.1

N = number of individuals with the specific skeletal component present
Na = number of individuals showing skeletal manifestations of TB

APPENDIX Information on the 49 individuals with skeletal changes associated with TB. Skeletons with "A" numbers are from the Raymond A Dart Collection, others from the Pretoria Bone Collection

DOD	Skeleton Number	Sex	Anc	Age	Bones affected
1925	A 15	M	B	46	skull
1926	A 80	M	B	38	ribs, scapula
1927	A 148	M	B	36	Vertebrae
1927	A 171	M	B	30	skull, ribs, vertebrae, scapula, pelvis
1927	A 175	M	B	50	skull, vertebrae
1928	A 165	M	B	45	vertebrae, fibula
1928	A 170	M	B	29	ribs, scapula
1945	A 1614	M	B	21	skull, ribs, tibia, fibula
1947	A 1486	M	B	49	Ribs
1948	A 1533	M	B	58	vertebrae, tibiae, fibulae
1949	A 1550	M	B	40	Vertebrae
1952	A 1786	M	B	55	ribs, vertebrae, scapulae, humeri, radius, ulna, femora, tibiae, fibulae
1953	A 1797	M	B	65	skull, ribs, humerus, radius, tibiae, fibulae
1953	A 1803	M	B	37	Ribs
1955	A 1949	M	B	56	Ribs
1955	A 1937	M	B	50	vertebrae, tibiae
1955	A 1876	M	B	68	ribs, radius, ulna, femorae, tibiae, carpals
1969	2905	F	B	49	ribs, radii, ulna, femorae, tibiae, fibulae
1978	4198	F	B	35	ribs
1979	4448	F	B	38	ribs, pelvis
1983	A 3364	M	B	50	scapulae, humeri, radii, ulnae, femora, tibiae, fibulae, pelvis, metacarpals, tarsals, metatarsals (?early PHOA)
1983	A 3368	M	B	69	skull, ribs, vertebrae, femora
1985	A 3446	M	B	52	ribs, tibiae, fibulae
1985	A 3490	M	B	33	ribs, tibiae
1987	A 3561	M	B	84	vertebrae
1987	A 3576	M	B	60	ribs, vertebrae, pelvis
1988	A 3588	M	B	49	skull, ribs, tibiae
1988	A 3629	M	B	70	ribs, tibiae, fibulae
1989	A 3713	M	B	36	ribs
1989	A 3789	M	B	55	ribs
1990	A 3652	M	B	53	ribs, scapula
1990	A 3699	M	B	40	ribs, radii, ulnae, tibia, fibulae
1990	A 3729	M	B	60	Ribs
1991	A 3716	M	B	26	humeri, radii, ulnae, femora, tibiae, fibulae, pelvis, metacarpals, metatarsals (PHOA)
1991	A 3792	M	B	49	scapulae, claviculae, humeri, radii, ulnae, femora, tibiae, fibulae, pelvis, metacarpals, tarsals, metatarsals, phalanges (PHOA)

1991	5532	M	B	54	ribs, vertebrae
1992	A 3779	M	B	58	ribs
1992	5670	M	B	40	ribs, femur
1992	5629	F	B	52	humerus, radii, ulna, tibia, fibula (?early PHOA)
1993	A 3857	M	B	42	ribs, humeri, radii, ulnae, femora, tibiae, fibulae, pelvis, tarsals, metatarsals
1994	A 3874	M	B	78	Ribs
1994	5906	M	B	unkn	skull, ribs, fibula
1994	5891	M	B	46	ribs, claviculae, femora, tibiae, fibulae, pelvis, carpals, metacarpals, phalanges
1995	A 3957	M	B	33	Ribs
1995	5962	M	B	72	skull, ribs, tibiae, fibulae
2001	6354	M	B	40	ribs
2001	6376	M	B	37	Skull
2001	6409	M	B	70	vertebrae, radius, ulna, tibia, fibula
2002	6438	M	B	40	ribs, tibiae, fibula

DOD – date of death; Anc – ancestry; M – male; F – female; B – black
PHOA =Pulmonary hypertrophic osteoarthropathy

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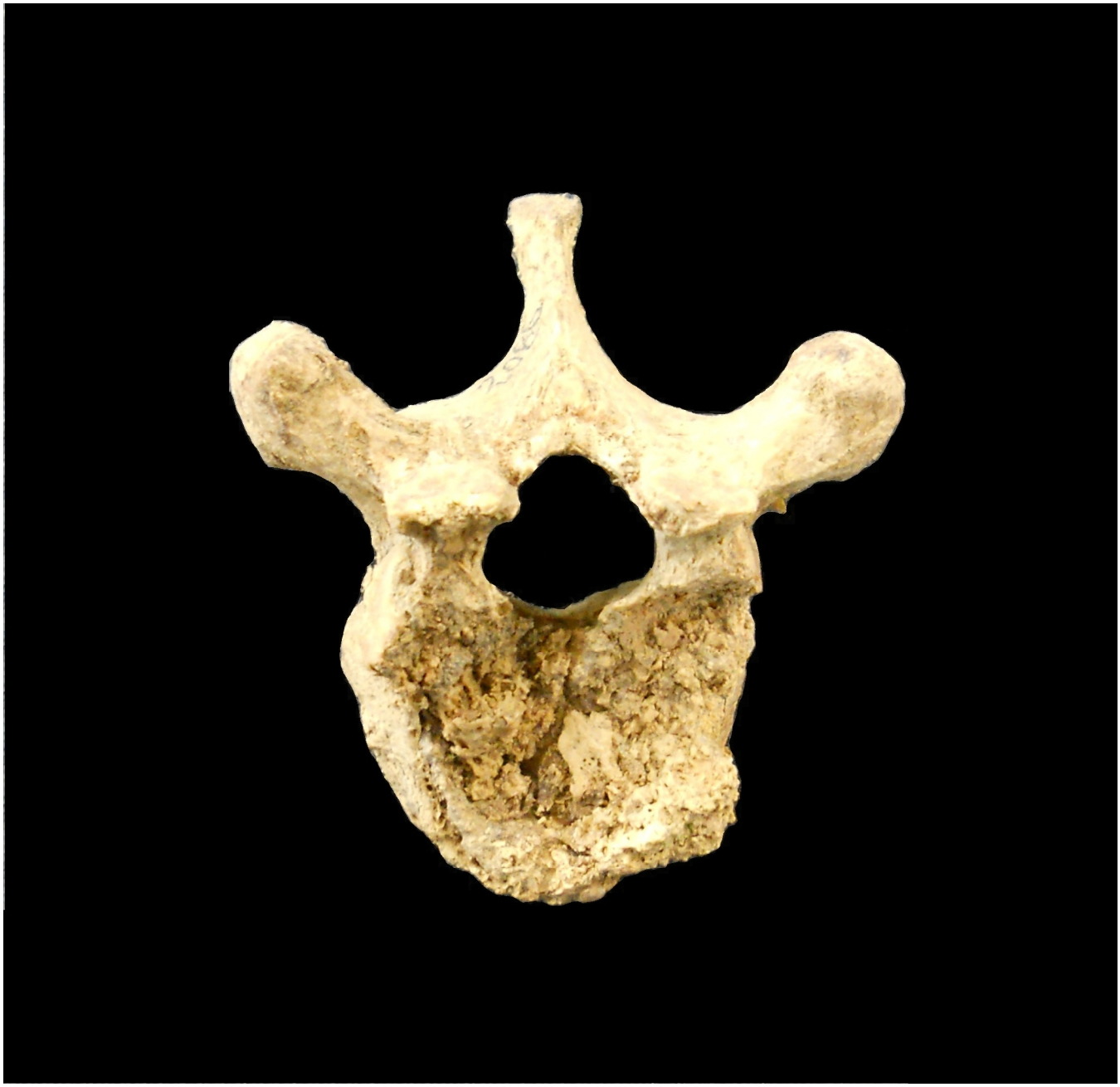

Figure 1. Example of changes in a vertebral body judged to be associated with tuberculosis (A1550; 40 year old African male). Some reactive new bone formation is visible, which may suggest attempts at healing

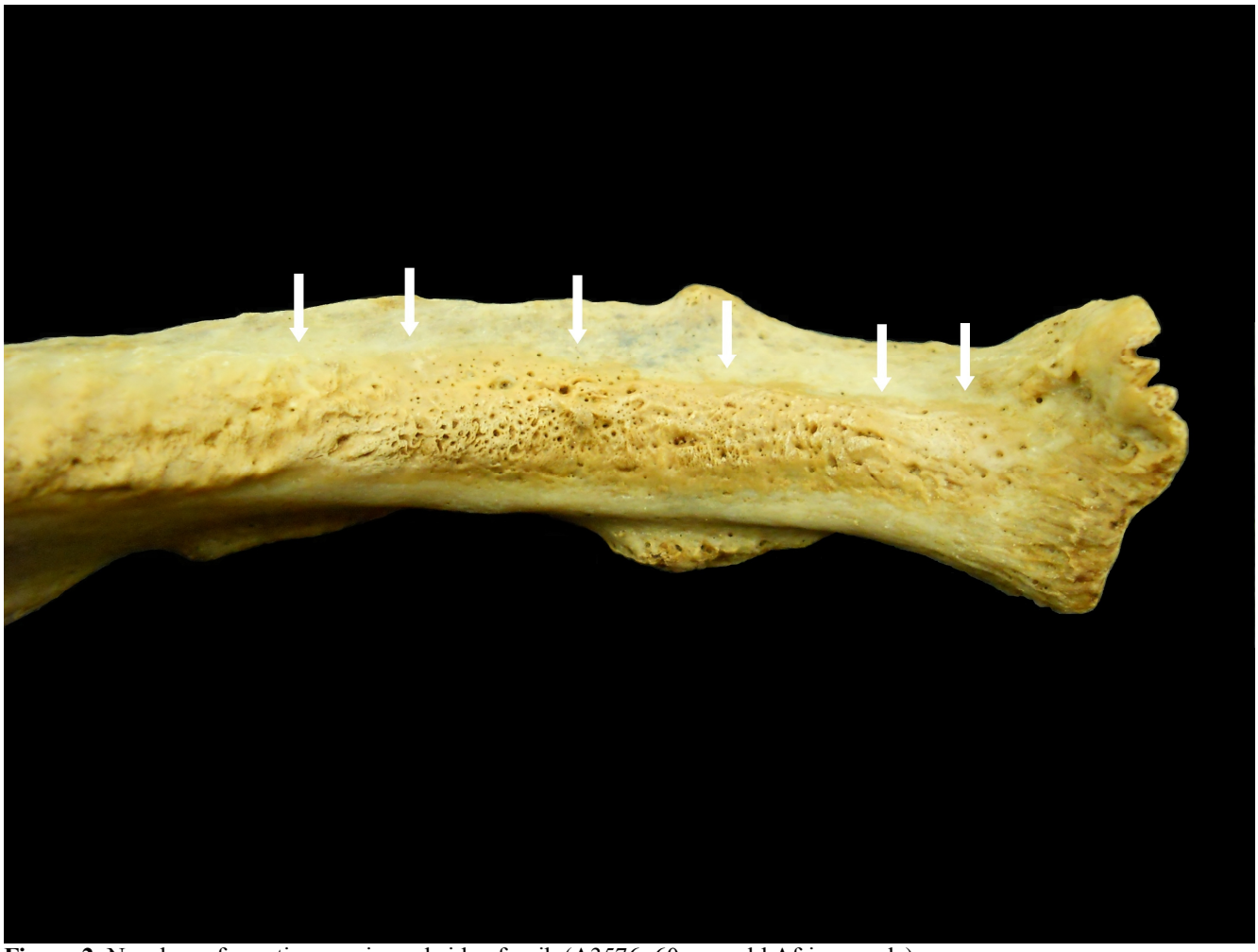

Figure 2. New bone formation on visceral side of a rib (A3576; 60 year old African male)

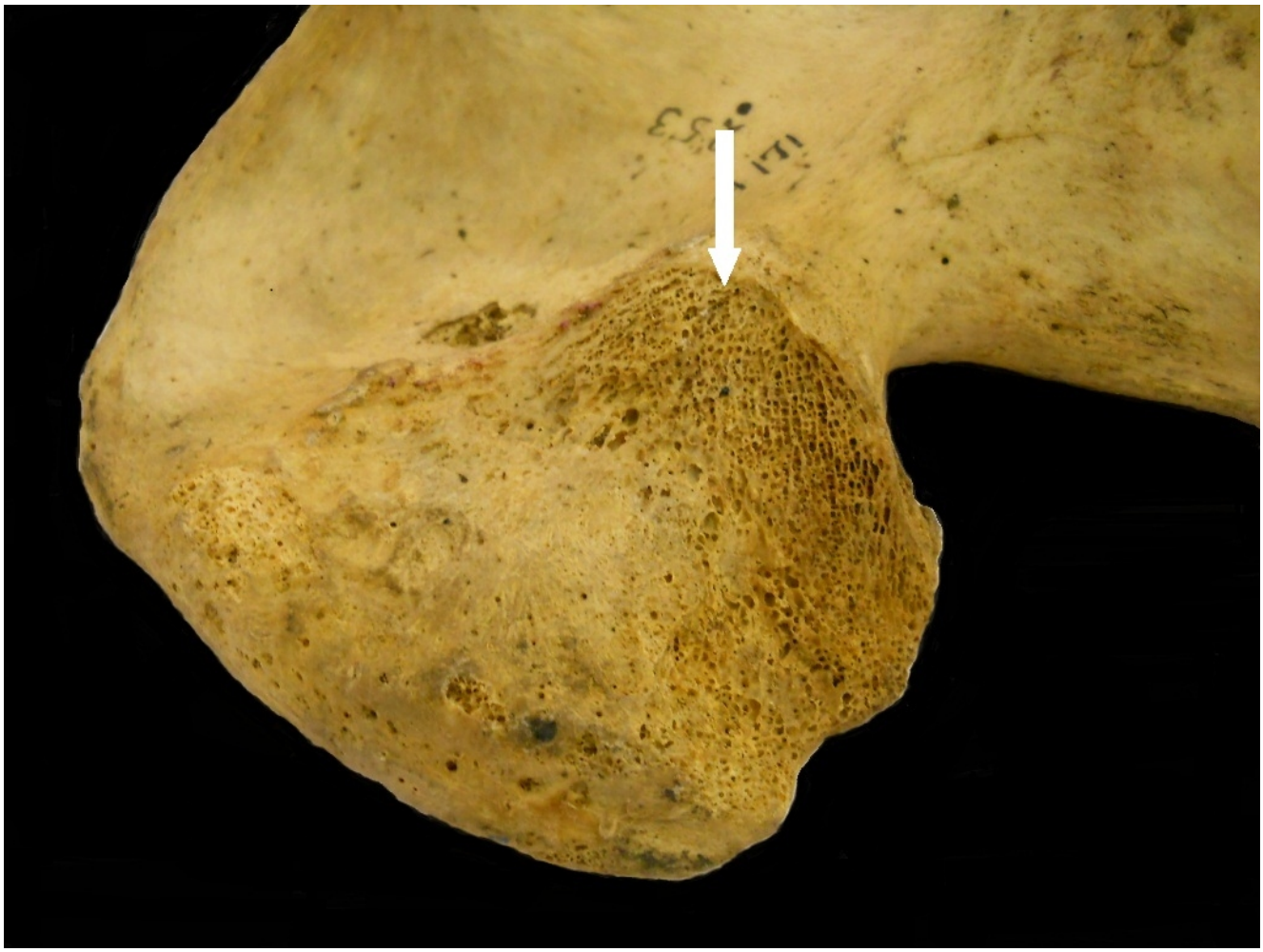

Figure 3. Infective changes in a sacro-iliac joint (A171; 30 year old African male)

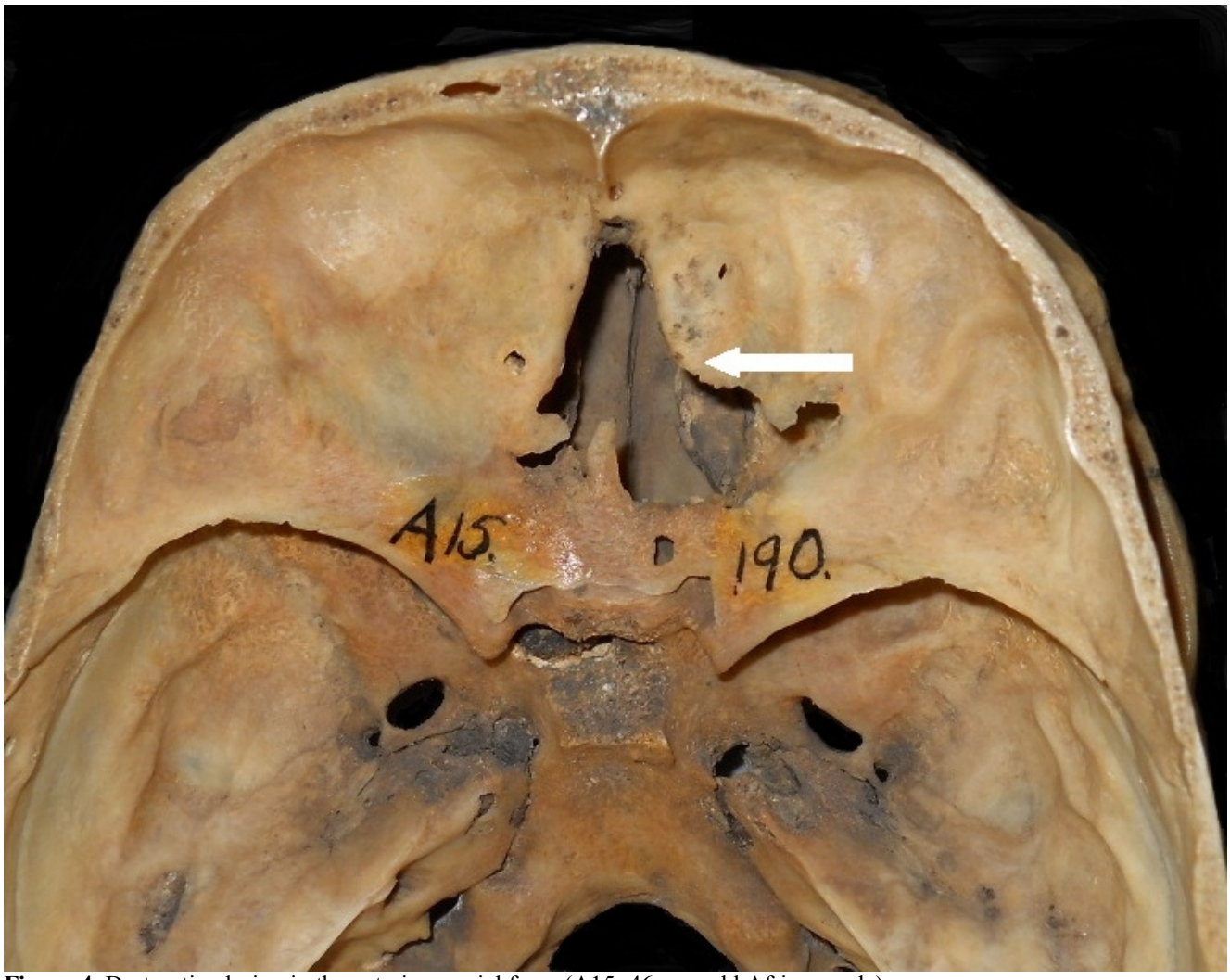

Figure 4. Destructive lesion in the anterior cranial fossa (A15; 46 year old African male)

Figure 5a&b. Skeleton showing signs of pulmonary hypertrophic osteoarthropathy (A3792; 49 year old African male). Fig. 5a shows the anterior surface of the right distal radius and ulna and 5b the antero-medial surface of the right tibia

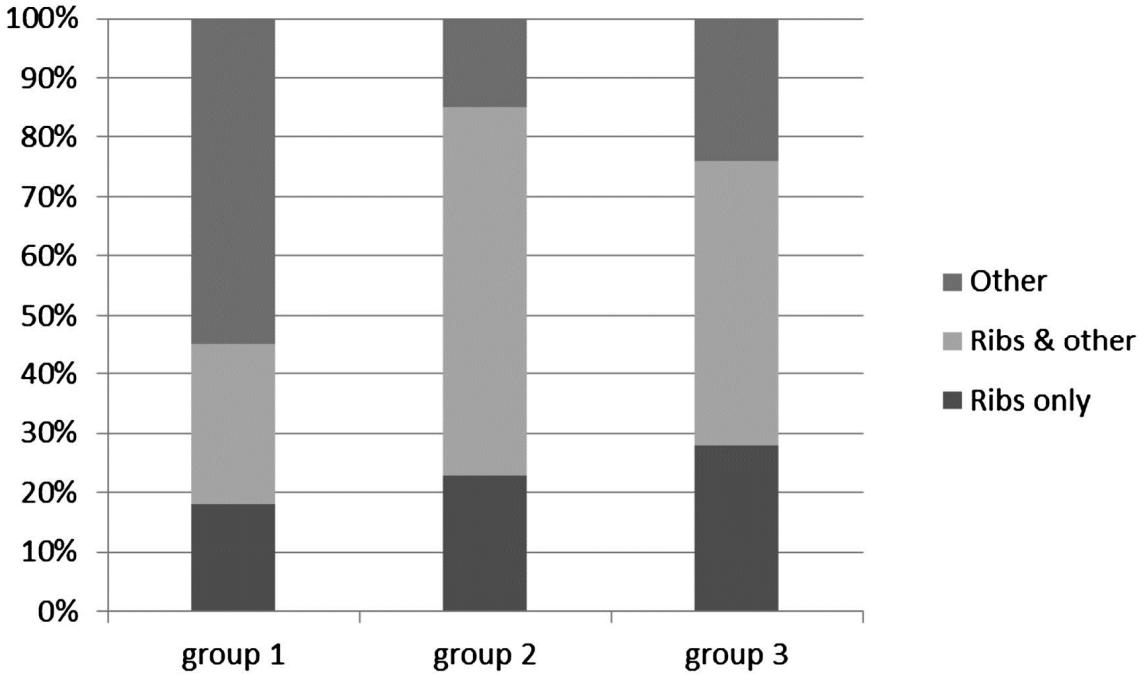

Figure 6. Distribution of skeletal lesions (n=49), showing relative involvement of ribs. Group 1 = individuals dying before 1950; Group 2 = individuals dying 1950 – 1985; Group 3 = individuals dying after 1985. "Other" refers to all bony changes not occurring in the ribs

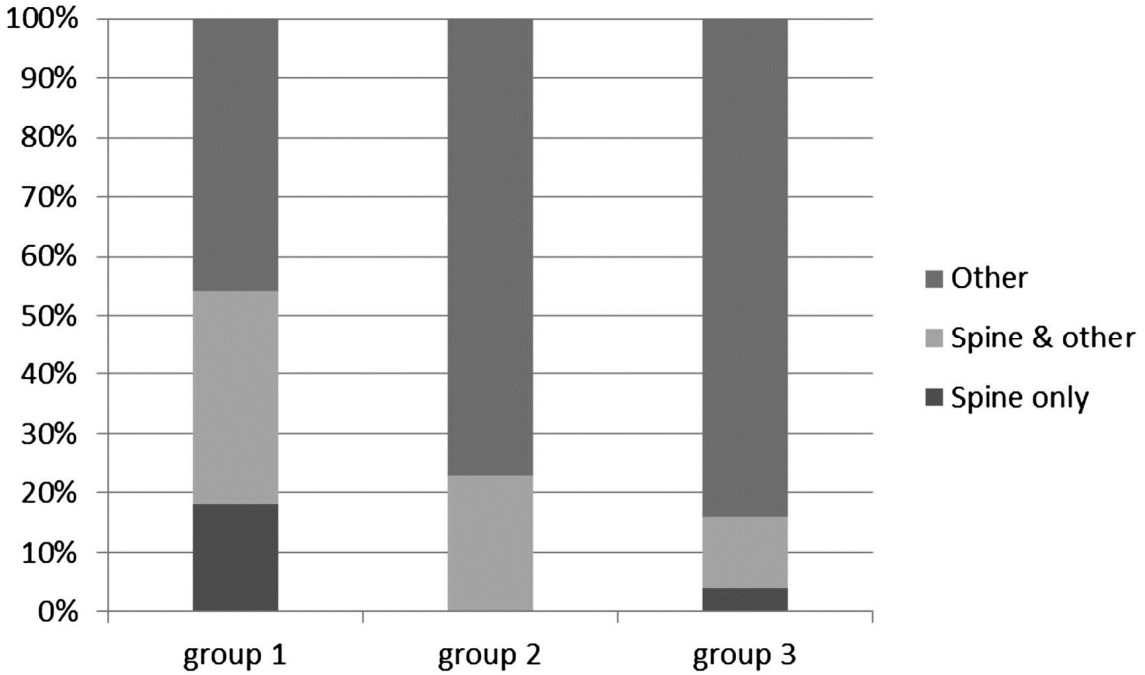

Figure 7. Distribution of skeletal lesions (n=49), showing involvement of spine. Group 1 = individuals dying before 1950; Group 2 = individuals dying 1950 – 1985; Group 3 = individuals dying after 1985. "Other" refers to all bony changes not occurring in the vertebrae