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In Search of a Cause: An Etiological Analysis of Manubrial Porosity

Jose Sanchez, *The University of Western Ontario*

Supervisor: Dr. Andrew Nelson, *The University of Western Ontario*

Joint Supervisor: Dr. El Molto, *The University of Western Ontario*

A thesis submitted in partial fulfillment of the requirements for the Master of Arts degree in Anthropology

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IN SEARCH OF A CAUSE: AN ETIOLOGICAL ANALYSIS OF MANUBRIAL
POROSITY

Monograph

by

Jose Sanchez

Graduate Program in Anthropology

A thesis submitted in partial fulfillment
of the requirements for the degree of
Master of Arts

The School of Graduate and Postdoctoral Studies
The University of Western Ontario
London, Ontario, Canada

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Abstract

Few studies in paleopathology focus on the sternum as a unit of analysis to determine how it can contribute to disease diagnosis in the past. This thesis tested the null hypothesis that manubrial porosity was not associated with respiratory disease or pulmonary tuberculosis. One hundred fifty-four individuals from the Luis Lopes Skeletal Collection were assessed for manubrial porosity. This study sought to be as comprehensive as possible, and thus tested several variables to identify any significant associations with manubrial porosity. Using the odds ratio, 95% confidence interval, and chi-square tests, significant associations exist between manubrial porosity, adolescence, and a type II sternal body shape at the $p = 0.05$ confidence level, but associations do not exist with disease. This research showed that the sternum could not be used to aid in the diagnosis of respiratory disease or pulmonary tuberculosis, and that the etiology and/or significance of manubrial porosity remains to be definitively ascertained.

Keywords

Pulmonary tuberculosis, normal variation, sternum, manubrium, paleopathology, odds ratio, Luis Lopes Skeletal Collection

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Table of Contents

Abstract.....	ii
Acknowledgments.....	iii
Table of Contents.....	v
List of Tables.....	viii
List of Figures.....	x
List of Appendices.....	xiii
Chapter 1.....	1
1 Introduction.....	1
Chapter 2.....	6
2 Biology of the Sternum.....	6
2.1 Anatomy of the Thorax.....	7
2.2 Biomechanics of the Thorax.....	10
2.3 Growth and Development of the Sternum.....	12
2.4 Normal Variants of the Sternum.....	14
Chapter 3.....	25
3 Paleopathology Introduction.....	25
3.1 Paleopathology.....	26
3.2 Tuberculosis Pathology.....	30
3.3 Clinical Diagnosis of Tuberculosis.....	32
3.4 Tuberculosis Skeletal Changes.....	34
3.5 Pathological Conditions Affecting the Sternum.....	39
3.6 Documented Sternal Porosity.....	40
Chapter 4.....	45
4 Methods and Materials.....	45

4.1 Early 20 th century Portugal	45
4.2 Study Sample	51
4.3 Scoring systems	55
4.4 Statistical analysis.....	58
Chapter 5.....	65
5 Results.....	65
5.1 Cause of Death.....	65
5.2 Age and disease correlations.....	69
5.3 Sex.....	72
5.4 Biomechanics.....	73
5.5 Sternal Variations.....	76
5.6 Thoracic lesion co-existence.....	79
Chapter 6.....	81
6 Discussion	81
6.1 The Sternum and Paleopathology	81
6.2 Manubrial Porosity and Age	86
6.3 Manubrial Porosity, Sex, and Biomechanics	89
6.4 Manubrial Porosity and Sternal Variations.....	90
6.5 Coexistence of thoracic lesions.....	92
Chapter 7.....	96
7 Conclusion	96
7.1 Hypotheses Addressed.....	97
7.2 Possible Etiology of Manubrial Porosity	97
7.3 Contributions to Paleopathology and Bioarchaeology	99
7.4 Future Research	100
References.....	103

Appendices.....	114
Curriculum Vitae	117

List of Tables

Table 2.1: Descriptions for other sternal variations described in Barnes (2012).....	24
Table 3.1: Bone reactions to disease processes	28
Table 4.1: Sample distribution of males and females per age cohort	53
Table 4.2 Sanchez et al. (2012) scoring system for sternal porosity	56
Table 4.3: Robusticity score summary as described in Hawkey and Merbs (1995).....	58
Table 4.4 Descriptions of stress lesion scores as provided by Hawkey and Merbs (1995)....	58
Table 4.5: Sample 2x2 contingency table for odds ratio	60
Table 4.6: Sample 2x2 contingency table for phi-coefficient.....	62
Table 5.1: Odds ratio results when testing the strength of association between cause of death groups and the presence/absence of manubrial lesions.....	69
Table 5.2: Odds ratio results when testing the strength of association between the presence and absence of manubrial lesions in pulmonary tuberculosis against non-pulmonary causes of death	69
Table 5.3: Results of odds ratio and 95% confidence statistical tests when comparing the presence of manubrial lesions in the adolescence cohort against other age cohorts.	70
Table 5.4: Results of odds ratio and 95% confidence statistical tests when comparing the presence of manubrial lesions in all other age cohorts.	71
Table 5.5: Odds ratio and 95% confidence interval results assessing the strength of association between the younger age cohorts against older adults and having tuberculosis as a cause of death.....	72
Table 5.6: Odds ratio and 95% confidence interval results assessing the strength of association between age and having tuberculosis as a cause of death.....	72

Table 5.7: Results of odds ratio and 95% confidence interval statistical tests assessing the strength of association between sex and manubrial lesions.....	73
Table 5.8: Odds ratio and 95% confidence interval results for strength of association between pronounced MSMs for the pectoralis major on the left humerus and manubrial lesions.	75
Table 5.9: Odds ratio and 95% confidence interval results assessing the strength of association between presence of muscular microfractures and manubrial lesions.	76
Table 5.10: Results of odds ratio and 95% confidence interval for the relationship between the shape of the sternum and the presence of manubrial lesions	77
Table 5.11: Odds ratio and 95% confidence interval results for manubrium-body fusion and the presence of manubrial lesions	78
Table 5.12: 2x2 contingency table for phi-coefficient assessing the co-occurrence of tuberculous rib lesions and manubrial lesions in individuals with pulmonary tuberculosis...	79

List of Figures

Figure 1.1: Example of manubrial porosity investigated.....	2
Figure 2.1: Image illustrating the positioning of the heart in relation to the sternum.	9
Figure 2.2: Illustration of the lungs in relation to the sternum. The dashed outline indicates the extent of the lungs and pleurae. Heart is located at the centre.....	9
Figure 2.3: Image of a sternal foramen/aperture redrawn from Barnes (2012).....	15
Figure 2.4: Sternal body shape resulting from ossification pattern I. Image is redrawn from Barnes (2012).....	16
Figure 2.5: Sternal body shape resulting from ossification pattern II. Image is redrawn from Barnes (2012).....	17
Figure 2.6: Sternal body shape resulting from ossification pattern III. Image redrawn from Barnes (2012).....	18
Figure 2.7: Example of suprasternal ossicles that fuse to the manubrium. Image redrawn from Barnes (2012). Arrows point to suprasternal ossicles.....	19
Figure 2.8: Illustration of caudal clefting redrawn from Fokin et al. (2009).....	20
Figure 2.9: Illustration depicting cranial clefting (bifurcation) with the inferior sternum still in tact. Image redrawn from Fokin et al. (2009).	21
Figure 2.10: Illustration depicting a mild form of pectus excavatum redrawn from Barnes (2012). Anterior is to the left of the image, posterior is on the right.	22
Figure 2.11: Illustration of a mild form of pectus carinatum after Barnes (2012). Anterior is to the right, posterior is to the left.....	23
Figure 4.1: Map of Portugal.....	46
Figure 4.2 All individuals available for analysis in the Luis Lopes Collection.....	50

Figure 4.3: Distribution of all individuals analyzed by age cohort and sex	53
Figure 4.4: Images of all 5 scores taken by the author during the creation of the scoring system (2012). A: shows a score 0, B: depicts a score of 1, C: shows a score of 2, D: depicts a score of 3, E: shows a score of 4.....	57
Figure 5.1: Absolute frequencies depicting the number of individuals with and without manubrial lesions in the Luis Lopes Collection regardless of age and sex	66
Figure 5.2: Absolute frequencies of individuals with and without manubrial lesions by cause of death, regardless of age and sex	67
Figure 5.3 Absolute frequencies of individuals with and without manubrial lesions within the pulmonary cause of death group, regardless of age and sex.....	67
Figure 5.4: Absolute frequencies of individuals in the non-pulmonary cause of death category with and without manubrial lesions regardless of age or sex	68
Figure 5.5: Distribution of individuals with and without manubrial lesions by age categories	70
Figure 5.6: Absolute frequencies of males and females that do and do not exhibit manubrial lesions.	73
Figure 5.7: Absolute frequencies of individuals with and without manubrial lesions in relation to pronounced pectoralis major MSM on the left humerus	74
Figure 5.8: Absolute frequencies of individuals with and without manubrial lesions with respect to the presence of micro-fractures on the left humerus	75
Figure 5.9: Absolute frequencies of individuals with and without manubrial lesions with respect to the shape of the sternal body	76
Figure 5.10: Absolute frequencies illustrating the presence and absence of manubrial lesions based on whether or not the manubrium is fused to the sternal body.....	78

Figure 6.1: Individual #220, a 52-year-old female who died of heart failure exhibiting a manubrial porosity score of 2 84

Figure 6.2: An example of a manubrial porosity score 3, Individual #405 was a 32-year-old male whose cause of death was recorded as brain laceration 84

List of Appendices

Appendix A: Sample of Data Collection Form.....	114
Appendix B: Raw data on presence of “classic” tuberculous lesions based on respiratory disease.....	115

Chapter 1

Introduction

The field of paleopathology, the study of ancient disease, attempts to recognize and understand bony changes that are anatomical alterations due to disease and it explores the singular and/or multifactorial causes of those alterations (Grauer, 2012).

Paleopathological research ultimately examines the relationship between ancient disease and the health of a society in order to understand the experiences of past peoples with disease (Angel, 1981; Boldsen and Milner, 2012; Grauer, 2012).

The purpose of this research is to determine the most probable etiology of web-like porosity on the internal (posterior) surface of the manubrium (Figure 1.1). This will be done by examining the relationship between bone changes on the posterior aspect of the sternum, specifically the manubrium, and disease in a documented population. The sternum is rarely included in paleopathological studies, and preliminary research by Sanchez et al. (2012) was the first study to focus solely on the sternum in a paleopathological context. This thesis is an expansion of this work since Sanchez et al.'s (2012) results were inconclusive, and takes recommendations proposed by the earlier authors into account to produce a thorough and comprehensive study. By understanding the relationship between sternal porosity and disease, this research attempts to determine if sternal changes can be used in the differential diagnosis of respiratory disease in paleopathological analyses. This is particularly important when conducting pathological assessments of comingled collections, such as ossuaries, where individual skeletal elements have lost their context and cannot confidently be associated with one another. A correlation between sternal porosity and disease has the potential to provide a means of reassessing disease prevalence in past populations, which can assist examine changes in the geographical distribution of a disease and understand the way diseases change and adapt throughout time (Barnes, 2012). This can then provide possible explanations regarding why we experience the reemergence of some diseases, such as the current reemergence of tuberculosis. Furthermore, determining the number of individuals

affected by a disease can help us make inferences about the experience a society had with disease, particularly those diseases known to have debilitating effects. Thus, the overall goal of this research is to assess whether or not the sternum could be utilized as a means to diagnose respiratory diseases in past populations, with a specific focus on pulmonary tuberculosis.



Figure 1.1: Example of manubrial porosity

This research also examines potential interrelationships between sternal porosity and other skeletal lesions in the thoracic region, namely on the thoracic vertebrae and ribs. Identifying patterns in the distribution of lesions throughout the thoracic region may help with understanding how the thorax is involved with pulmonary diseases, and may potentially elucidate patterns of pathogenesis throughout the thoracic cavity. Additionally, relationships between sternal porosity and well-known morphological variations that occur on the sternum will be examined. The co-occurrence of normal variants in sternal morphology could suggest that a genetic component may be partly responsible for differing degrees of sternal porosity or it may be the remnant of developmental defects of surrounding soft tissues, such as the heart.

Hypotheses

This research tests two null hypotheses. The primary null hypothesis (H_0^1) is that sternal porosity is not associated with pulmonary disease. The alternative hypothesis (H_A^1) is

that sternal porosity has an association with pulmonary disease. Due to its close proximity to the lungs and associated soft tissue such as the pulmonary pleura, dissemination of bacilli affecting the lungs or pleura has the potential to affect the sternum. Rejection of the null hypothesis will occur if results from an odds ratio and 95% confidence interval tests show that a strong positive correlation between sternal lesions and pulmonary diseases exists and has a p-value that falls below a 0.05 confidence level. A p-value above this confidence level will suggest that no association exists between the two variables; therefore the null hypothesis will not be rejected.

The secondary null hypothesis (H_0^2) being tested is that pulmonary tuberculosis will not be more likely to be associated with sternal lesions when compared to other pulmonary diseases. The alternative hypothesis (H_A^2) is that pulmonary tuberculosis will have a stronger association with sternal porosity compared to any other pulmonary disease. Pulmonary tuberculosis is known to affect the skeleton and produce lesions throughout the thorax to a greater extent than other pulmonary diseases, such as pneumonia and bronchitis, which do not often affect the skeleton (Kelley and Micozzi, 1984; Roberts et al. 1994; Aufderheide and Rodriguez-Martin, 1998). Since tuberculosis causes near destruction of the manubrium in severe cases, it is proposed that the web-like porosity investigated here may be an early manifestation of manubrial involvement. This secondary null hypothesis will be rejected if a strong positive relationship with a p-value falling below the 0.05 confidence level is determined when odds ratio and 95% confidence interval statistical tests are conducted.

Brief Paleopathology Overview

Prior to the 1960s, paleopathologists focused on descriptive analyses of diseases in archaeological populations (Goodman, 1998). By the 1970s, a shift in bioarchaeology focused on anthropological and ecological correlations of disease (Goodman, 1998). Instead of simply reporting relative frequencies of diseases in past populations, bioarchaeologists attempted to recognize patterns of disease prevalence to ultimately understand the social, cultural, and ecological variables that affect the observed disease patterns. However, an evolutionary-ecological approach to paleopathological studies is

only as good as the diagnoses that are used to understand lesion patterns. Descriptive paleopathological studies, therefore, remain equally important to further the understanding of where lesions manifest on the skeletal in relation to different diseases. In the early 1990s, Rothschild changed the way research was conducted by attempting to associate skeletal lesions with a particular disease by examining skeletons with known disease (or causes of death) from the Hamann-Todd Skeletal Collection (Rothschild, 1990, 1995, 1997). Despite the fact that there are many paleopathological texts that have provided in-depth descriptions of skeletal lesions caused by different pathological conditions (e.g. Ortner and Putschar, 1981; Aufderheide and Rodriguez-Martin, 1998; Ortner, 2003; Roberts and Manchester, 2005; Waldron, 2009; Grauer, 2012), the ability to positively diagnose disease from a skeleton remains problematic. Moreover, the paleopathological texts available to help identify pathological conditions only provide examples of severe “classic” skeletal lesions that diseases produce and not a spectrum of how lesions may appear at any given point of disease involvement.

Paleopathological research requires a thorough understanding of the morphological variation that exists in the human skeleton and each of its individual elements. These morphological variants in skeletal elements can occur as a result of growth and development differences that occur during skeletal maturation (Mann and Hunt, 2005; Barnes, 2012) or as a result of muscular stresses acting on, and subsequently remodeling and altering, a bone and its appearance (Washburn, 1951; Ruff, 2008). A clear understanding of normal variation is vital as the distinction between what is considered “normal” bone from that altered by a pathological condition is the cornerstone of disease identification in skeletal remains. Paleopathological analysis also relies on the identification of patterns of skeletal lesions produced by specific diseases to conduct a differential diagnosis, a diagnostic method used to differentiate one disease, or disease category, from another (Ortner, 2003; 2008). Differential diagnoses are imperative because bone reacts in limited ways, and can react similarly to different diseases. Incorporating as many skeletal elements as possible to generate a differential diagnosis is crucial in an archaeological context given that the preservation of complete skeletons in the archaeological record does not always occur. Understanding the specific skeletal lesion patterns initiated by infectious pathogens can help diagnose the most likely cause

of a pathological bone reaction, and can ultimately allow us to better understand the impact of a pathological condition on the individual and their society. This thesis will test the above hypotheses using a modern skeletal sample, the Luis Lopes Skeletal Collection.

Thesis Outline

This thesis is divided into seven chapters. Chapter 2 outlines the anatomical position of the sternum in relation to soft-tissue organs that may contribute to the expression of manubrial porosity. Information on the muscles that anchor to the sternum, how the sternum grows, and documented variations of sternal morphology are also presented. Chapter 3 provides a brief overview on the discipline of paleopathology and outlines the pathology of tuberculosis. This chapter also provides background as to how tuberculosis is diagnosed clinically as well as the skeletal lesions that help diagnose tuberculosis archaeologically. Chapter 3 ends with a discussion on recorded pathological conditions that are known to affect the sternum and a presentation of three studies that document the presence of web-like porosity on the sternum. Chapter 4 “Methods and Materials” provides background to the social and health conditions in Portugal and Lisbon during the late 19th and early 20th centuries, which coincides with the time frame when the people of the Luis Lopes Collection were alive. Chapter 4 also presents the methodology used for data collection (i.e. method of sample selection and scoring systems used) and statistical tests used to analyze the data collected. Chapter 5 presents the results of all statistical tests conducted to determine the most likely etiology of manubrial porosity, while Chapter 6 provides a detailed discussion of what the results may mean and possible explanations for the results. Chapter 7 summarizes the thesis by proposing the possible etiologies of manubrial porosity, and demonstrates what this thesis contributes to the paleopathological and bioarchaeological literature. It also outlines future avenues of investigation into manubrial porosity.

Chapter 2

2 Biology of the Sternum

In order to understand and investigate how a disease process may potentially affect the sternum, the sternum is contextualized anatomically in terms of its relationship to surrounding soft tissue organs. This will help our understanding of how microbial diseases disseminate in a host (for example via blood vessels or pleurae), and will also help exclude pathogens that do not affect, or are not known to spread to, neighboring organs or tissues. The anatomical context of the thorax can also elucidate confounding factors, such as biomechanical forces, that have the potential to alter the macroscopic appearance of the sternum. By knowing what muscles insert to, or originate on, the sternum and the actions those muscles are responsible for, abnormal bone formation or destruction of the sternum can be assessed.

Conversely, anomalous bone appearance may be the result of genetic variability within and between populations. On an evolutionary basis, populations exist with a large gene pool in order to thrive and adapt to their environment. A large gene pool results in a large amount of genetic variation within a population, and it is that genetic variation that has the potential to produce varying frequencies of skeletal anomalies. Skeletal anomalies, or variants, have variable forms of expressions that are usually not detrimental to a person's health, and are believed to have an underlying genetic or epigenetic basis (Saunders, 1977; Barnes, 2012). While a population may contain genes that allow for one type of skeletal anomaly to exist, another population may have the same or similar gene causing the same anomalous skeletal appearance but at a lower frequency. This, in turn, would account for varying expressions of skeletal anomalies between populations.

Variation in a skeletal element's macroscopic appearance can also be a reflection of growth disturbances during embryonic maturation (Barnes, 2012). Factors such as maternal health or exposure to external toxins can disrupt growth and development of the skeleton (Barnes, 1994), thereby leading to an altered appearance of a bone. Since genetic and environmental factors can affect the growth, and subsequently the appearance of a

bone, an understanding of the process by which a bone grows and its known variations in morphology will help differentiate between normal variations and pathological alterations.

This chapter provides the anatomical context of the sternum and its relationship to soft tissues of the thoracic cavity. A review of muscular anatomy is provided to illustrate the extent to which muscular activity may affect the macroscopic appearance of the sternum. This chapter also details the growth and development of the sternum, and a number of known and documented normal variants that occur in the morphology of the sternum.

2.1 Anatomy of the Thorax

A prerequisite to understanding pathological processes is knowledge of normal anatomical contexts of the sternum. The thoracic cavity is a conically shaped cage primarily composed of bone and cartilage that contains and protects vital organs necessary for respiration and circulation of blood. The posterior boundary of the thoracic cavity is comprised of 12 thoracic vertebrae and the vertebral (or posterior) ends of the associated ribs. The sternum and costal cartilage comprise the anterior surface of the thoracic cage, which is slightly flat and convex (Scheuer and Black, 2000). Twelve ribs on both the left and right sides comprise the lateral boundaries of the thorax. The lateral surfaces are convex and contain intercostal spaces that, in life, are filled by intercostal muscles anteriorly and posteriorly (Martini and Nath, 2009).

The sternum is a flat bone that is composed of three parts: the manubrium, the mesosternum (or body), and the xiphoid process. The manubrium is a roughly triangular shaped bone with a thick and broad superior margin that slightly thins out inferiorly. The anterior surface of the manubrium is convex, usually exhibiting evidence of muscle attachments. The posterior surface of the manubrium is slightly concave and relatively featureless. The left and right sides of the superior border have articular notches for the clavicles. The lateral surfaces have depressed areas for articulation with the first costal cartilage superiorly, and a half facet for the articulation with the second costal cartilage. Inferiorly, the manubrium has a depressed area for articulation with the mesosternum.

The mesosternum is longer, narrower, and thinner than the manubrium. Anteriorly, the mesosternum is flat with an upward and forward orientation. Occasionally, three transverse lines can be seen on the anterior surface of the mesosternum, which outline where segments of the mesosternum fused during growth (Standring, 2008). The mesosternum is slightly concave posteriorly with transverse lines also occasionally visible. The lateral surfaces of the mesosternum contain four full depressions, or notches, that articulate with the third to sixth costal cartilages and a half depression superiorly for articulation with the second costal cartilage (Scheuer and Black, 2000; Martini and Nath, 2009). The xiphoid process is the smallest of the three sternal segments. It is thin with variable lengths and appearances and can, at times, fuse to the mesosternum, generally at advanced age. The xiphoid process tapers distally.

In the living, the manubrium is positioned at the level of the third and fourth thoracic vertebrae (Standring, 2008). The superior posterior portion of the manubrium is in close anatomical relation to the thymus, left brachiocephalic vein, left common carotid, and left subclavian artery (Scheuer and Black, 2000; Standring, 2008; Martini and Nath, 2009). The lower portion of the manubrium has close association to the aortic arch (Figure 2.1). Due to the close relationship with major soft tissue arteries, the manubrium can exhibit evidence of arterial pathological conditions, such as an aortic aneurysm (Kelley, 1979; Scheuer and Black, 2000). The lateral portions of the manubrium are in direct contact with the parietal pleurae, a smooth membrane that lines the inner chest cavity and covers the diaphragm (Standring, 2008). Furthermore, the manubrium lies anterior to the upper lobes of the left and right lungs (Figure 2.2). Therefore, the possibility exists that upper lobe infections of the lungs could affect, in some manner, the manubrium.

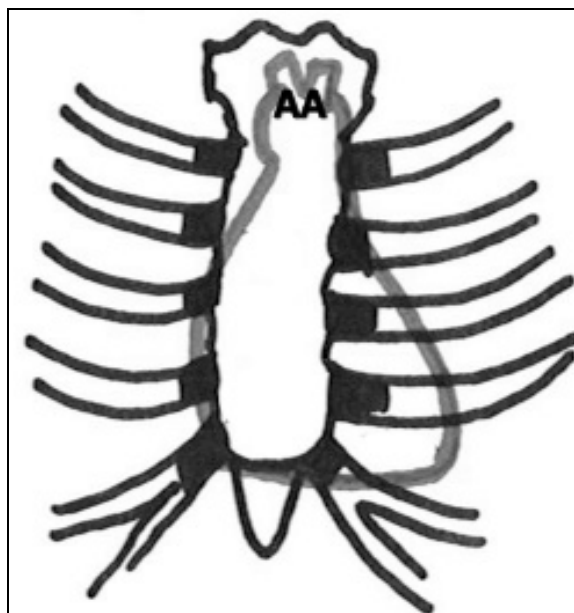


Figure 2.1: Image illustrating the positioning of the heart in relation to the sternum. AA indicates where the aortic arch is in relation to the manubrium.

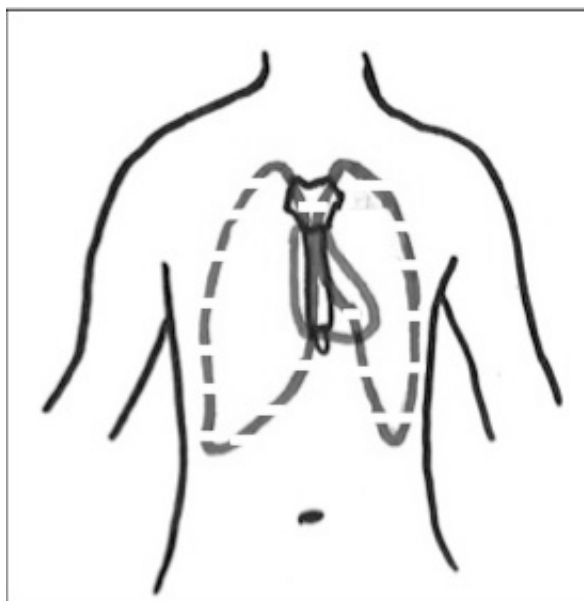


Figure 2.2: Illustration of the lungs in relation to the sternum. The dashed outline indicates the extent of the lungs and pleurae. Heart is located at the centre of the image.

The mesosternum is parallel to the fifth to ninth thoracic vertebrae during life.

Posteriorly, the mesosternum is in contact with the parietal pleurae on both sides laterally and to the left it is in contact with the pericardium (Figure 2.1), which is a double-layered fibrous membrane that surrounds the heart (Standring, 2008; Martini and Nath, 2009).

The middle lobes of the left and right lungs, and the lower lobe of the right lung, lie posterior to the mesosternum (Figure 2.2). Given that the sternum is closely associated with circulatory and respiratory organs, it is possible that cardiovascular or pulmonary pathological conditions can affect the sternum. For this reason, cardiovascular and respiratory diseases are two disease categories that merit further investigation here.

2.2 Biomechanics of the Thorax

Bone is a dynamic tissue that is constantly remodeling and adapting to forces that act upon it. The concept that bone adapts to its mechanical environment during life, which accounts for some skeletal variation existing between individuals, is widely accepted in bioarchaeological research (e.g. Washburn, 1951; Ruff et al, 2006; Weiss, 2003). While habitual use of a muscle may not cause drastic bone changes to the sternum, repetitive over-exertion resulting from physically demanding and laborious work, may have the potential to create bony changes.

Since the sternum delineates the anterior border of the thoracic cavity, several muscles anchor to the anterior and posterior surfaces of the sternum. The sternocleidomastoid has two branches (or heads), where the sternal head originates from the anterior surface of the manubrium superiorly and the clavicular head originates from the superior medial aspect of the clavicles (Standring, 2008). When branches on both sides of the sternocleidomastoid muscle are in use, the sternocleidomastoid flexes the neck. When used unilaterally, the muscle rotates the head contralaterally and bends the neck to one side (Standring, 2008; Martini and Nath, 2009). In addition to the sternocleidomastoid muscles, the sternohyoid and sternothyroid muscles attach to the manubrium on the posterior surface. Both the sternohyoid and the sternothyroid muscles function to depress the hyoid and larynx (Martini and Nath, 2009). The manubrium is also affected indirectly by muscles that do not originate or insert on its surface. For example, flexion of the vertebral column forces the manubrium backwards (Scheuer and Black, 2000).

The anterior surface of the mesosternum provides the site of origin for the pectoralis major, which is responsible for flexion, adduction, and medial rotation of the shoulder (Abrahams et al. 2003; Hamilton et al. 2008; Martini and Nath, 2009). Evidence of

excessive use of the pectoralis major can also be seen on the humerus, with robusticity and stress scores available for analysis (Hawkey and Merbs, 1995). As a result, humeral robusticity at the pectoralis major insertion site can be used as a proxy to provide evidence of excessive muscular use, which in turn can reveal information about the biomechanical stresses also exerted on the sternum. The anterior lateral borders of the mesosternum allow for the attachment of the external intercostal membranes. The muscle that these membranes attach to is responsible for elevating the ribs during respiration (Martini and Nath, 2009). The transversus thoracis muscle, which depresses the ribs during respiration (Martini and Nath, 2009), originates from the lateral borders of the posterior surface of the mesosternum. The numerous muscles that anchor to the sternum and manubrium are all of interest because pus and/or disease agents have the potential of channeling along muscle fascia, as is seen with the psoas muscles of the spine in tuberculosis (Aufderheide and Rodriguez-Martin, 1998; Roberts and Buikstra, 2003).

Despite being the smallest and thinnest segment of the sternum, the xiphoid process provides an anchoring site for several muscles or associated soft tissues. The anterior surface of the xiphoid allows for the attachment of the rectus abdominis, a muscle that depresses ribs, flexes the vertebral column, and allows for compression of the abdomen (Martini and Nath, 2009). The xiphoid process also allows for the attachment of the aponeuroses (layers of flat broad tendons) of the external and internal oblique muscles, which compress the abdomen, depress the ribs, and bend the spine (Martini and Nath, 2009). The inferior portion of the xiphoid provides an attachment site for the linea alba, a band of connective tissue composed primarily of collagen that runs down the midline of the abdomen to the pubic symphysis (Martini and Nath, 2009). In addition to the linea alba, the aponeuroses of the internal oblique and transversus abdominis, two muscles that facilitate abdominal compression (Martini and Nath, 2009), attach to the inferior portion of the xiphoid process. Posteriorly, the xiphoid process is a site of origin for two anterior muscle slips of the diaphragm which, when they contract, expand the thoracic cavity, and are responsible for compressing the abdominopelvic cavity (Martini and Nath, 2009).

In a study of 36 children whose sterna were examined radiographically and microscopically, Ogden and colleagues (1979) encountered two children with

asymmetrical mesosterna. Both children exhibiting asymmetrical sternal bodies also showed evidence of scoliosis. The authors state that it is possible that the irregular muscular forces being transmitted from the vertebrae to the sternum may cause the asymmetry, but the reverse may be true as well (Ogden et al. 1979). This study by Ogden and colleagues (1979) provides evidence of the fact that musculoskeletal forces, whether direct or indirect, have the potential to affect the macroscopic appearance of the sternum.

All three segments of the sternum act as anchors to many different muscles. It is possible, then, that the different biomechanical forces acting on the sternum can alter its shape and may cause slight modifications to the overall morphology of the bone. Therefore, biomechanical forces on the sternum may act as confounding factors contributing to the presence of porosity on the sternum, specifically the manubrium, and will be investigated.

2.3 Growth and Development of the Sternum

In addition to understanding the anatomy of the thorax as a whole and knowing what muscles have the potential to alter the morphology of the sternum, understanding how the sternum grows is vital to differentiate between “normal” appearance of the sternum and morphological changes that are abnormally produced.

The sternum develops from the same embryogenic structure that also gives rise to the pectoral muscles. Therefore, the sternum is a derivation from appendicular cellular ontogeny as opposed to axial (Scheuer and Black, 2000). The undifferentiated cellular precursors of the sternum develop anterior to the clavicle and ribs, but develop independently from the aforementioned skeletal elements. Lateral sternal plates can be seen embedded anteriorly in the chest at six fetal weeks, but are independent of each other and the neighbouring developing ribs (Scheuer and Black, 2000). The lateral sternal plates are located medial to the ribs and, as the ribs grow in length the sternal plates move towards each other at the midline and become cartilage (Ogden, 1979; Scheuer and Black, 2000; van der Merwe et al. 2013). At approximately nine fetal weeks, the two sternal plates begin to fuse together at the midline in a cranio-caudal direction. An

extension of the sternal bars caudally produces the xiphoid process. The fusion of the sternal plates should only occur once the heart has dropped into the thorax.

In addition to the lateral sternal plates appearing at the sixth fetal week, three mesenchymal masses appear superior to the lateral sternal plates (Scheuer and Black, 2000). The first is called the presternal mass, which lies above the lateral plates at the midline, or mediocranially to the sternal plates. The other two masses are the suprasternal masses, located superior and on each side of the presternal mass. The presternal mass subsequently fuses with the medial portions of the suprasternal masses to form the manubrium and to the superior portion of the sternal plates (Scheuer and Black, 2000; van der Merwe et al. 2013). The lateral portions of the suprasternal masses form the sternoclavicular joint.

When the sternal plates fuse and chondrify, the sternum is one continuous structure made of cartilage that is not segmented (Barnes, 2012; van der Merwe et al. 2013). Once the sternum begins to ossify, the sternum becomes a segmented structure, with each segment referred to as a sternebra. The ribs and their attachment to the mesosternum influence the segmentation of the mesosternum (van der Merwe et al. 2013). The manubrium is the first sternal segment to begin ossification in the fourth to fifth fetal month, while the sternal body segments begin ossification approximately a month later in a craniocaudal direction (Saunders, 1977; Ogden et al. 1979; Crubézy, 1992; Scheuer and Black, 2000; Barnes, 2012; van der Merwe et al. 2013). Ossification may begin prior to the fusion of the sternal plate, in which case an ossification center will develop within each sternal plate (Scheuer and Black, 2000; Barnes, 2012; van der Merwe et al. 2013). Fusion of the ossified sternal segments begins in a caudal-cranial direction, where the third and fourth mesosternal segments fuse between four to ten years of age. Fusion of all sternal segments into one sternal body usually occurs in individuals older than 15 years of age (van der Merwe et al. 2013). Ossification of the xiphoid process can begin after three years of age, but tends to be quite variable.

2.4 Normal Variants of the Sternum

Variations in the morphology of post-cranial elements have been documented and skeletal variations of the post-cranium are known to abound (Saunders, 1977; Crubézy, 1992; Saunders and Rainey, 2008; Barnes, 2012). Nonmetric traits are morphological variants of anatomy, usually of a feature or an anatomical landmark (Saunders and Rainey, 2008). These traits are minor skeletal and dental variations that may or may not be present (Saunders and Rainey, 2008). Development of skeletal elements is influenced by the anatomy and development of the surrounding soft tissue. In many cases, these variations do not affect the function of the skeletal element (Saunders and Rainey, 2008). The following non-metric traits or normal variations of the sternum have been documented and well researched:

Sternal aperture/foramen: Due to errors in ossification, the sternum may have a hole on the mesosternum with smooth edges (Figure 2.3), which may occasionally be confused as a bullet wound (Saunders, 1977; Crubézy, 1992; Saunders and Rainey, 2008). Sternal foramina are usually located on the lower third portion of the sternal body along the mid-line of the sternum (Saunders, 1977; Crubézy, 1992; Saunders and Rainey, 2008; Verna et al. 2013). The lower sternebrae usually arise from two ossification centers during growth and development. The two ossification centers that become the affected sternebrae do not fuse properly, resulting in the presence of a sternal foramen (Saunders, 1977). An alternate explanation is that the sternal foramen is believed to be the result of a passage for a massive vascular bundle through the cartilaginous precursor during the fetal period (Kohler and Zimmer, 1968). Saunders (1977) and Crubézy (1992) strongly believe that the sternal foramen is the result of a hypostotic defect in ossification, and not the result of vascular bundles perforating the sternal cartilaginous precursor. The presence of a sternal foramen is believed to be quite rare with relative frequencies being as low as 1.9% and as high as 10.2% (Saunders, 1977; Crubézy, 1992). However, the frequencies at which sternal foramina are present differ from one population to another depending on different allele frequencies for the trait. The size of a sternal aperture is variable and the form or outline of sternal apertures are distinct from one another (Crubézy, 1992). Although the sternal aperture is a hypostotic trait, it does not have a statistically

significant relationship with biological sex, which is believed to be due to the low frequency of individuals with a sternal foramen (Saunders, 1977; Verna et al. 2013).

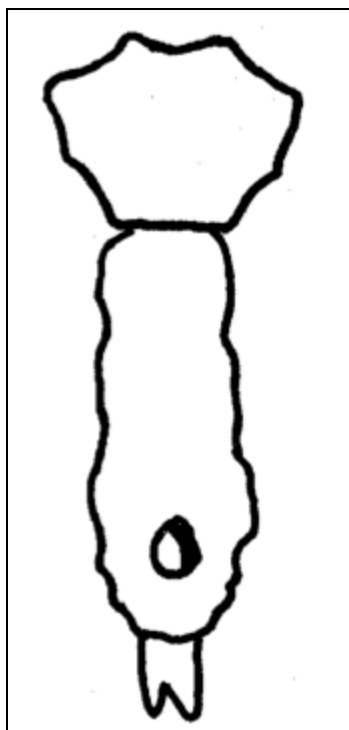


Figure 2.3: Image of a sternal foramen/aperture redrawn from Barnes (2012).

Sternal anomalies generally occur during two stages of development. The first stage is during the formation and development of the sternal cartilaginous bundles. The heart is developing around the same time as the cartilaginous bundles are (Crubézy, 1992). During the development of the heart, the arterial supply to the lungs is being differentiated from the aorta (Crubézy, 1992). The second stage is when sternal anomalies occur in the ossification of the sternum. Sternal foramina are believed to occur because of a defect in the ossification of multiple nuclei between the third and fourth mesosternum segments (Saunders, 1977; Crubézy, 1992). Sternal foramina are likely to be under strong genetic influence (Saunders, 1977; Crubézy, 1992; Saunders and Rainey, 2008). As a result, the presence of a sternal foramen in multiple individuals may suggest there is a biological relationship between those individuals.

Sternal shape: In addition to the sternal foramen, variations in the overall shape of the sternum occur during growth and development. Ashley (1965) conducted a study where

three distinct sternal body shapes were found and determined to be the result of different sternal ossification patterns with differing numbers of ossification centers. The ossification patterns are as follows:

Ossification pattern I: each of the first three sternal body segments has a single ossification center along the midline. There may be two ossification centers vertically, but they will always be along the midline. This results in a shape where the sternal body has the same width superiorly-inferiorly but is not as wide as the manubrium (Figure 2.4).

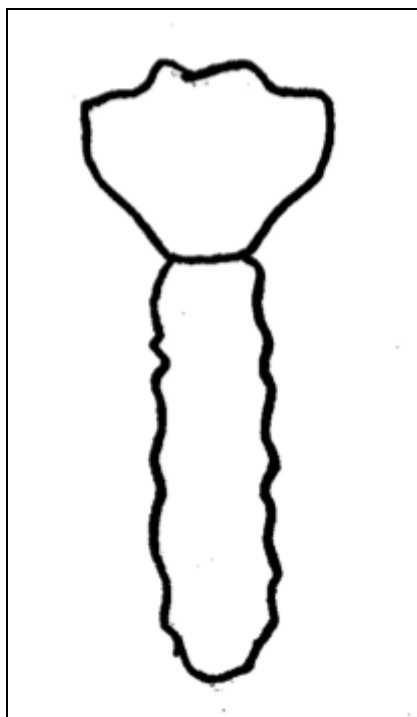


Figure 2.4: Sternal body shape resulting from ossification pattern I. Image is redrawn from Barnes (2012).

Ossification pattern II: either the first or the first and second sternal body segments have a single ossification center along the midline. In some individuals the second, and in most, if not all, individuals the third and fourth mesosternum segments have two ossification centers that are bilaterally placed. This results in a sternal body that is less wide superiorly (at the first and second sternal segments) and becomes broader inferiorly (or at the third and fourth sternal segments) [Figure 2.5].

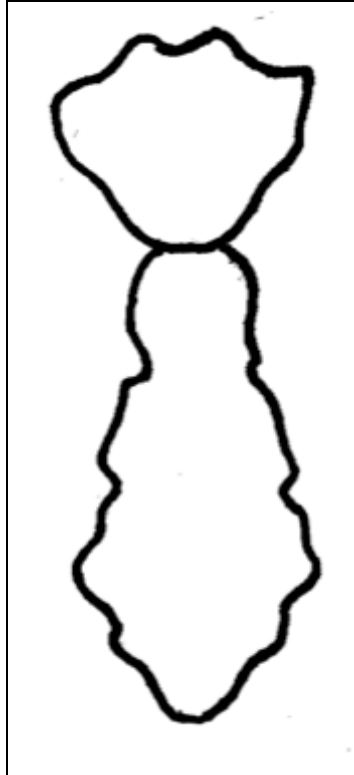


Figure 2.5: Sternal body shape resulting from ossification pattern II. Image is redrawn from Barnes (2012).

Ossification pattern III: The first three sternal body segments have two ossification centers bilaterally placed; while the fourth segment is variable, having one or two ossification centers. The resulting shape is similar to the first ossification pattern, where the mesosternum had a uniform width throughout, but has a similar breadth as the manubrium (Figure 2.6).

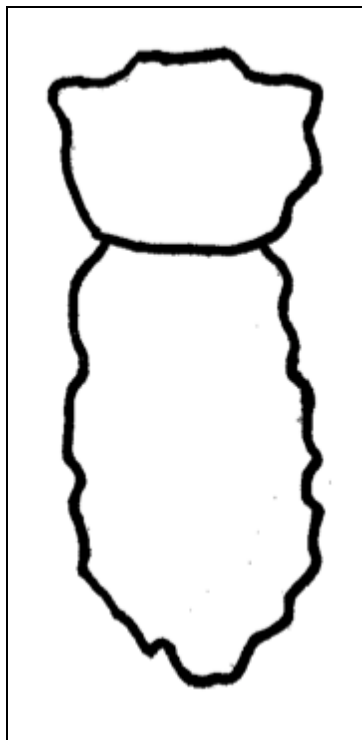


Figure 2.6: Sternal body shape resulting from ossification pattern III. Image redrawn from Barnes (2012).

The patterns of sternal ossification, and therefore shape, are the result of different developmental patterns. The single midline ossification is believed to occur when sternal cartilage bands grow together and are complete before conditions are suitable for ossification to begin (Ashley, 1965). Conversely, bilateral ossification likely results when sternal bands fail or partly fail to grow simultaneously before ossification begins (Ashley, 1965). Given that the sternum has a substantial amount of variation in shape and morphology (sternal foramen), porosity on the posterior surface of the manubrium may potentially be another morphological variant associated with the sternum. If this is the case, relationships between sternal porosity and the three sternal shapes outlined by Ashley (1965) will be assessed. Investigating such a relationship will help further develop an understanding of how the sternum develops and the possible variants that may result from growth disruptions.

Suprasternal ossicles: Suprasternal ossicles result from a failure of the suprasternal masses to reach their destination between the clavicular sternal ends and the growing membranous manubrium. The absence of suprasternal masses at their designated location

does not prevent the development of a proper sternoclavicular joint (Barnes, 2012). When unattached, the suprasternal masses become separate cartilaginous structures and subsequently ossify into nodules often fusing to the manubrium at the juglar notch (Barnes, 2012). Suprasternal ossicles can occur bilaterally, unilaterally, or may ossify as separate elements within the interclavicular ligament (Figure 2.7). Bilateral expression of suprasternal ossicles occurs more frequently than unilateral expression (Yekeler et al. 2006; Barnes, 2012), although no clear percentages are reported. The presence of suprasternal ossicles does not cause adverse effects and is usually incidentally identified in 1-7% of individuals clinically (Kohler and Zimmer, 1968; Yekeler et al. 2006).

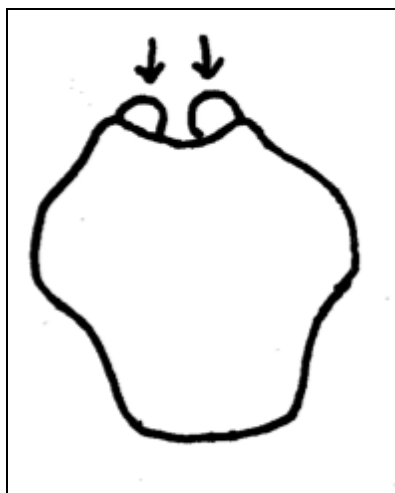


Figure 2.7: Example of suprasternal ossicles that fuse to the manubrium. Image redrawn from Barnes (2012). Arrows point to suprasternal ossicles.

Sternal cleft: Sternal clefting can manifest in two manners, the first being caudal clefting (Figure 2.8) and the second being cranial bifurcation (Figure 2.9). Caudal clefting manifests when the caudal ends of the sternal plates are too slow when meeting up at the midline (Barnes, 2012). Minor delay in fusion is usually seen, where there is a cleft on the inferior border of the last sternal segment. A wide caudal cleft resulting from non-union of the sternal plates is very rare. Inferior or caudal clefting is often associated with thoracoabdominal *ectopia cordis*, which is complete or partial displacement of the heart outside of the thoracic cage covered by a thin-pigmented membrane (Shamberger and Welch, 1990; van der Merwe et al. 2013). Inferior or caudal clefting is often associated

with other abdominal defects on the diaphragm, pericardium, as well as ventral hernias (Shamberger and Welch, 1990).



Figure 2.8: Illustration of caudal clefting redrawn from Fokin et al. (2009).

Cranial clefting of the sternum is a very rare condition and is considered to be an isolated abnormality (van der Merwe et al. 2013). Superior or cranial clefting results from a malformation of the manubrium as this inhibits craniocaudal fusion of the sternal plates normally seen during growth, which results in the fusion of inferior sections but inhibits fusion of the superior sections (van der Merwe et al. 2013). Sternal clefting can be either partial or complete. Complete clefting divides the sternum into two parts superiorly to inferiorly to the xiphoid process, which usually remains intact (Barnes, 2012). A fibrocartilaginous tissue fills the gap, maintaining contact of the two segments. Complete clefting affects cardiopulmonary function and causes discoloration to the skin surface as a result of low oxygen saturation (or cyanosis) (Barnes, 2012; van der Merwe et al. 2013). In clinical situations, patients with partial cranial clefting are asymptomatic and have no related functional problems. However, patients with partial cranial clefting are prone to develop recurrent respiratory infections and may have difficulty breathing (van der Merwe et al. 2013).

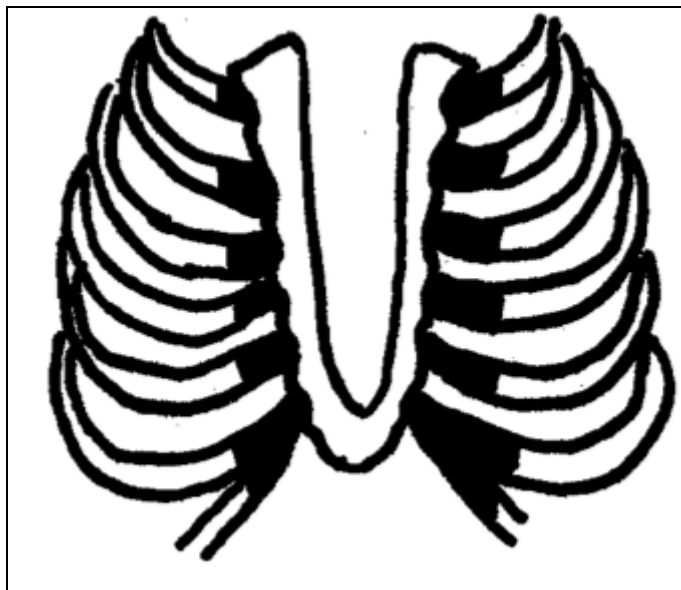


Figure 2.9: Illustration depicting cranial clefting (bifurcation) with the inferior sternum still intact. Image redrawn from Fokin et al. (2009).

Funnel Chest: Funnel chest, or pectus excavatum, occurs when the mesosternum has an inward misdirection during growth (Figure 2.10). Figure 2.10 shows a mild form of funnel chest where only the xiphoid process is deflected inward. The misdirection inward is caused by a shortened central tendon of the diaphragm that inserts to the posterior surface of the xiphoid process (Fokin et al. 2009; Barnes, 2012). Similarly shortened tendon fibers inserting on the distal lateral portion of the mesosternum can further contribute to the inward displacement of the sternum and affects adjacent costal cartilage. Funnel chest is believed to occur in 1 in 400 to 1 in 1,000 live births where males are affected 3-5 times more than females (Fokin et al. 2009). The displacement of the sternum can occur symmetrically or asymmetrically, where asymmetric cases have a right-side predominance. Growth and development of the sternum is not affected in individuals with funnel chest, only the direction of growth is altered. The inward deflection of the sternum can be mild to severe, where mild cases are asymptomatic and only affected the xiphoid process (Barnes, 2012). Severe cases of funnel chest have a deeply depressed lower third mesosternum, where respiration is affected and the heart can be displaced. The severity of funnel chest is determined by the degree of reduction of the distance between the sternum and vertebrae (Fokin et al. 2009).

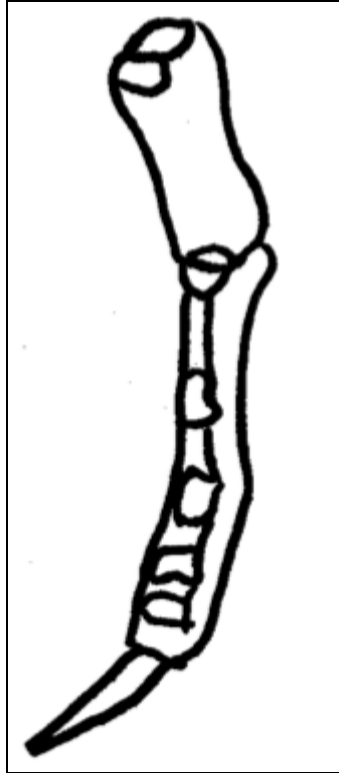
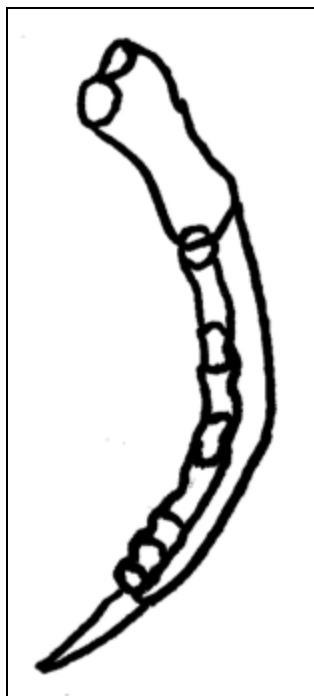


Figure 2.10: Illustration depicting a mild form of pectus excavatum redrawn from Barnes (2012). Anterior is to the left of the image, posterior is on the right.

Pigeon breast: Pigeon breast, or pectus carinatum, is similar to funnel chest except the sternum is misdirected anteriorly (or forward) in these individuals (Figure 2.11). Figure 2.11 illustrates a mild expression of pigeon breast, where the mesosternum is bowed or projecting forward. This contrasts to the mild expression of funnel chest, where the mesosternum is not affected, but the xiphoid process is deflected posteriorly. Pigeon breast is caused by anomalous growth of adjacent ribs and costocartilage (Lester, 1961; Fokin et al. 2009; Barnes, 2012). Similar to pectus excavatum, pectus carinatum does not affect the growth and development of the sternum, it is merely the direction that is affected. Mild anterior misdirection of the sternum, known as arcuate sternum, is an asymptomatic condition that has a familial relationship (Barnes, 2012). Drastic expression of pectus carinatum show pronounced anterior arching of the anterior/midportions of the sternum and can cause respiratory problems (Lester, 1961; Fokin et al. 2009).



**Figure 2.11: Illustration of a mild form of pectus carinatum after Barnes (2012).
Anterior is to the right, posterior is to the left.**

This list of sternal variants does not constitute an exhaustive list of sternal variations that have been documented, but represents variations that have been studied in detail in bioarchaeological, clinical, and forensic anthropological contexts. Other variations do exist and are reported in Barnes (2012) and are briefly outlined in Table 2.1. Sternal variants, however, appear to have links with living conditions such as protein malnutrition, early pregnancies, and childhood diseases that lead to ossification malformations (Zivanovic, 1982 cited in Barnes, 1994). Therefore, the presence of sternal porosity with a lattice-like morphology may have a pathological link that did not contribute to morbidity or mortality, even if considered a normal variant.

Clinical research has demonstrated that most, if not all, sternal abnormalities are associated with cardiac defects (Crubézy, 1992). Therefore, it is possible that manubrial porosity may be associated with cardiac defects as well.

Table 2.1: Descriptions for other sternal variations described in Barnes (2012)

Sternal Variant	Brief Description
Manubrium-mesosternal joint fusion	Occurs when a cartilaginous separation develops between the manubrium and mesosternum instead of a fibrous lamina. When the sternebrae fuse, the manubrium fuses as well (Barnes, 2012).
Displaced manubrium-mesosternal joint	The fibrous lamina usually developing between the manubrium and first sternebra develops between the first and second sternebrae instead. This leads to a disjointed mesosternum at the first and second sternebrae (Barnes, 2012).
Mesosternal hypoplasia	Normally occurring at the last sternebrae and xiphoid, this results in a short or asymmetrical mesosternum with a very small or absent xiphoid (Barnes, 2012).
Sternal Hyperplasia	Sternal bands are longer than normal and produce an extra sternebra, resulting in a longer than usual mesosternum. The xiphoid process may be longer than normal as well (Barnes, 2012).

Chapter 3

3 Paleopathology. Introduction

The analysis of evidence of disease on human skeletal remains is an integral component for the reconstruction of how populations and communities lived in the past. It is by looking at diseases in past populations, that bioarchaeologist can begin to reconstruct how an individual and population experienced disease. Bioarchaeologists can also examine how interactions between humans and pathogens have evolved throughout time and space. Subsequently, comparative analysis of geographically and temporally distinct populations in the past can provide inferences about the adaptiveness or maladaptiveness of differing cultural strategies (Zuckerman et al. 2012).

Tuberculosis is an infectious disease that is known to have been in existence since at least 9200 B.P in Jordan (Roberts and Buikstra, 2003; Roberts and Manchester, 2005). The World Health Organization (WHO) estimated that in 2012 alone, approximately 8.6 million people developed the disease worldwide, of which 1.3 million died from it (WHO, Global Tuberculosis Report, p. 1). An understanding of the pathogenesis of tuberculosis and how it affects the skeleton can provide valuable information for understanding how the pathogen's interaction with humans has changed over time. Furthermore, knowing the evolution of the disease and its interaction with humans can help address the issue of the current re-emergence of tuberculosis and how the tuberculous bacterium is becoming resistant to antibiotics (Roberts and Buikstra, 2003; Roberts, 2012; Wiley and Allen, 2012). Incorporating bones that may have previously been overlooked, such as the sternum, in the diagnosis of tuberculosis or other diseases can potentially help examine the evolution of this pathogen. Having a deeper understanding of all areas of the skeleton that can be affected by tuberculosis or other diseases can allow for the reassessment of prevalence rates in archaeological contexts, particularly in commingled contexts.

This chapter provides a brief overview of the emergence of the study of disease in past populations and how it is currently practiced, outlines how diseases are diagnosed from skeletal remains, and discusses the limitations that exist when trying to diagnose a disease in archaeological populations. It also provides a description of the pathogenesis of tuberculosis as it is currently understood and outlines the skeletal lesion patterns that manifest in reaction to the pathogen. Since tuberculosis is not the only disease that can affect the sternum, a review of other diseases known to cause destructive lesions on the sternum, specifically the manubrium, is provided. Finally, known studies that address pronounced porosity on the manubrium, though few, are presented in order to also consider the disease differential diagnoses that are provided.

3.1 Paleopathology

Paleopathology, or the scientific study of disease in the past, began as a heavily descriptive discipline where paleopathological studies focused on reporting the presence, absence, and frequency with which diseases were encountered. Furthermore, these early studies also relied heavily on single case studies describing skeletal lesions and focused on an individual's, as opposed to population's, experience (Ortner, 1998; Aufderheide and Rodriguez-Martin, 1998; Roberts and Manchester, 2005; Buzon, 2012). Research during this descriptive stage of paleopathology generally failed to incorporate and consider the archaeological context in which the skeletal remains were found (Buzon, 2012). Thus, studies of this nature failed to address what the distribution of skeletal lesions meant for a population and what factors could have affected, and contributed to, the prevalence of a disease in a population.

In the 1960s, paleopathology experienced what Buikstra and Cook (1980), Angel (1982), and Ubelaker (1982) deemed as the renaissance of the field. Questions shifted from what was present or absent to what the prevalence of skeletal lesions was in the population, also known as paleoepidemiology. There was also a shift in paleopathology from being a descriptive discipline to one that was more interpretive and that increased its focus on ecological, evolutionary, and epidemiological interpretations. This paralleled the transition towards a processual paradigm in archaeology that investigated the relationship between the environment and cultural systems (Binford and Binford, 1968; Zuckerman et

al. 2012). In paleopathology, this led to greater interest in ecological and biocultural perspectives, hypothesis testing, and region-level analysis (e.g. Leatherman and Goodman, 1997; Goodman 1998; Armelagos and Van Gerven, 2003; Zuckerman et al. 2012). As a result, paleopathology has become a discipline that is situated in a way that not only provides information on the presence or absence of disease, but also addresses the social, cultural, environmental, and evolutionary factors that make a population more susceptible to disease (Schell, 1997; Dufour, 2006; Zuckerman et al. 2012). In addition, inferences made on how a community experienced disease can be accomplished by examining the number of individuals who were affected and what that meant in terms of how they contributed to the society, labour, care, and subsequent spread of disease to other individuals in the community.

Evolutionary-ecological and biocultural approaches to paleopathological studies, however, are only as good as the diagnoses that are used to understand lesion patterns. Bone can only react in a finite number of ways in response to a pathogen (see Table 3.1); therefore, lesion types can result from, and have similar appearance in, multiple disease categories. For this reason, differential diagnoses become an integral component of analysis in paleopathology. The use of differential diagnoses, a diagnostic method used to differentiate one disease or disease category from another (Ortner, 2008), becomes important when attempting to identify pathognomonic lesions or lesion patterns of a disease to reliably diagnose it in a population. Without the ability to identify pathognomonic lesions or lesion patterns, tracing the global distribution of a disease and understanding a pathogen's evolution throughout time becomes difficult. Descriptive paleopathological studies, therefore, remain fundamentally important for the understanding of the lesion patterns manifested throughout the skeleton by different diseases. Moreover, a deeper understanding of skeletal lesion patterns can provide the potential to incorporate bones that may have previously been overlooked. This research attempts to do this by identifying whether or not the manubrium, specifically, can be incorporated and/or used to identify associations with particular diseases. Incorporating more bones to identify disease would allow for a reassessment of disease prevalence in populations globally, particularly in archaeological contexts where human remains are found in commingled burials.

Table 3.1: Bone reactions to disease processes

Reaction	Description
Abnormal bone growth	Disruption in normal osteoblastic activity often associated with chronic conditions (Steinbock, 1976). Abnormal bone growth ranges from poorly organized bone to well organized woven bone appearance. Poorly organized woven bone, which takes on a plaque like appearance, is the most common type of bone to appear during a pathological process (Ortner, 2012). The most common stimuli that will prompt abnormal bone growth are inflammatory processes and vascular conditions (Ortner and Putschar, 1981).
Abnormal bone destruction	Normal existing bone is destroyed by osteoclastic activity and fails to be replaced during the bone modeling and remodeling process (Ortner, 2003; Brickley and Ives, 2006). Abnormal bone destruction can range from fine porosity on cortical bone to larger areas of bone destruction, which can be single or multi-focal. Abnormal bone destruction is often associated with acute conditions (Ortner, 2012).
Combination of both	Increased activity of both osteoclasts and osteoblasts. The combination can be seen as healed lamellar bone with porosity or woven bone on one area of the skeleton with resorptive lesions on another (Resnick et al. 1995; Ortner, 2012). The combination can also be found in instances where there are sclerotic margins on erosive lesions (Resnick et al. 1995; Ortner, 2012).

Despite the plethora of research aimed at associating skeletal lesions with a specific disease in an attempt to provide definite differential diagnoses for diseases (e.g. Hackett, 1976; Pfeiffer, 1991; Aufderheide and Rodrigues-Martin, 1998; Mays et al. 2002; Ortner, 2003; Lewis, 2004; Matos and Santos, 2006; Lagia et al. 2007; Waldron, 2009; Walker et al. 2009), several limitations exist that complicate disease diagnoses in archaeological contexts. Being able to differentiate between normal and abnormal appearance of bone is integral to diagnosing a disease. Abnormal bone addition or destruction occurring in areas of the skeleton and during ages that are not expected, can be key indicators of a pathological process. The expression of disease, however, cannot be expected to manifest the same way in every environment, population, or throughout time (Ortner, 1992; Zuckerman et al. 2012). Skeletal expression of a disease is likely to differ throughout time because pathogens evolve, and consequently so do host-pathogen interactions. As a

result, the varying expressions of diseases throughout time and geography can complicate diagnosis and confound comparative population studies.

The possibility of co-infections can also obscure and confound diagnosis of a disease based solely on skeletal lesions. Some diseases may coexist in a host (e.g. tuberculosis and leprosy or the human immunodeficiency virus) (Donoghue et al. 2005; Steyn et al. 2013). Therefore, skeletons may not exhibit “classic” expressions of a disease. It is possible that if a combination of classic and “abnormal” lesions in a skeleton are observed, the “abnormal” or “non-classic” lesions may be the result of the co-existing pathogen. While ancient DNA (aDNA) analysis can help detect a co-infection (as seen in Donoghue et al. 2005), in the absence of aDNA analysis, macroscopic diagnosis alone cannot provide such information. A further complication in diagnosing diseases from archaeological remains is the inconsistent use of terminology and issues with recording skeletal lesions. Although standards for documenting and recording skeletal lesions exist (Buikstra and Ubelaker, 1994; Brickley and McKinley, 2004; Steckel et al. 2011), these standards do not consider all skeletal elements (e.g. the sternum) or provide descriptive terms that help with accurately describing a lesion. While the absence of skeletal elements and terms can be well justified, not having standardized ways to document the various forms of lesion expressions on all skeletal elements provides the opportunity to create inconsistent terminology in an attempt to describe a lesion, rendering diagnosis of a disease challenging.

Diagnosis in paleopathology has relied heavily on radiological and clinical studies of modern populations (Miller et al. 1996; Waldron, 2009; Mays, 2012). However, in modern clinical studies, a skeletal condition must be advanced and symptomatic in order to merit doing radiographic analysis (Miller et al. 1996). This poses a problem for pathological cases in archaeological contexts that exemplify mild and asymptomatic conditions, since such cases likely do not have an analogue in clinical studies. Therefore, unless a condition is symptomatic even at its mild stage, the clinical literature cannot help with understanding the complete spectrum of ways in which bones are affected by disease. An added problem with using clinical studies for archaeological diagnoses is that clinical radiological studies cannot provide images of the subtle changes that are

primarily seen on dry bone. This is because a change in bone density of a 40 percent minimum is needed for bony changes to become visible on plain film radiographs (Ortner, 1991; Miller et al. 1996). Moreover, clinical diagnoses start with a patient's symptoms and proceed down a well directed course on the basis of those symptoms. In paleopathology, there is no access to a patient's symptoms therefore, there is no initial direction to investigate.

A final, but important, challenge for diagnosing disease from archaeological skeletal remains is the fact that the absence of evidence is not evidence of absence. Most diseases do not have skeletal expressions and those that do, tend to be in the minority (Roberts and Manchester, 2005; Zuckerman et al. 2012). Furthermore, as addressed in the "Osteological Paradox" (Wood et al. 1992) individuals with skeletal lesions likely lived with a disease long enough for lesions to develop, suggesting a healthy or strong immune system. Conversely, individuals exhibiting no skeletal lesions are not necessarily healthier individuals, but may also represent individuals that were quick to succumb to a disease (Wood et al. 1992). Therefore, the true prevalence of a disease in any archaeological population is likely underestimated. Moreover, the full spectrum of how a disease affects the skeleton is not known since examples of "classic" manifestations of several diseases tend to exemplify severe manifestations of a disease (Mays, 2012). Despite these limitations, research remains necessary to examine skeletal lesion patterns to help with diagnosis. For this reason, documented skeletal collections from anatomical, medical, and/or cemetery contexts are used to examine dry bones in order to observe associations between skeletal lesions and disease.

3.2 Tuberculosis Pathology

In 1882 Robert Koch isolated the *Mycobacterium tuberculosis* bacillus, identifying it as the causative agent of tuberculosis (Roberts and Buikstra, 2003; Curvo-Semedo et al. 2005; De Backer et al. 2006). Of the six strains known to cause tuberculosis, *Mycobacterium tuberculosis* and *M. bovis* are the two strains of the *Mycobacterium tuberculosis* complex that are the most infectious in humans (Roberts and Buikstra, 2003; Roberts and Manchester, 2003; Ortner, 2003; Waldron, 2009). Transmission of the tuberculous bacterium can occur through the respiratory system, via infected droplets

and/or sputum, or the gastrointestinal system, from contaminated milk or meat products (Ortner, 2003; Roberts and Manchester, 2005). The primary mode by which the mycobacterium is transferred, whether from human to human or from bovine to human, is through the respiratory route (De Backer et al. 2006; Waldron, 2009). The bovine strain of tuberculosis is suggested to be approximately ten times more likely to produce skeletal lesions in humans than the tuberculosis strain (Roberts and Manchester, 2005). However, Waldron (2009) has contested this claim. Waldron's (2009) opposition is on the basis that there is no clear indication as to which of the two strains of tuberculosis is more common skeletally since, in humans, *M. bovis* infections are indistinguishable from *M. tuberculosis* in pathogenesis and lesion morphology. While *M. tuberculosis* was previously believed to have evolved from *M. bovis*, Brosch and colleagues (2002) demonstrated that *M. bovis* has undergone several gene deletions compared to *M. tuberculosis*. These results suggest that cattle, and therefore the bovine strain of tuberculosis, contracted the tuberculous bacterium from humans (*M. tuberculosis*), which may account for the broader host range of *M. bovis*.

Ninety percent of infected individuals will have the tuberculous infection contained in a primary lesion, known as the Ghon focus. The Ghon focus is initiated when a person has a strong enough immune response, and the bacilli are walled off, calcified, and survive in infected necrotic or dead tissue (Waldron, 2009). This primary scar tissue is produced as a result of immunological response by macrophages (Ortner, 2003; Waldron, 2009). If the host's immune response is not strong, the tuberculous bacteria primarily spread throughout the host's body through the blood stream (Aufderheide and Rodriguez-Martin, 1998; Mays et al. 2002; Roberts and Buikstra, 2003; Ortner, 2003). Pulmonary and intestinal infections cause primary foci in the lungs and intestinal wall respectively, with potential subsequent spread to neighbouring lymph nodes (Roberts and Buikstra, 2003; Waldron, 2009). Once affected, lymph nodes enlarge and have the potential to discharge pus and the bacilli can spread throughout the host's lymphatic system.

The development of tuberculosis is a two-stage process. The primary infection occurs when an individual is first infected with the mycobacterium. This stage has an approximate duration of five years (Roberts and Buikstra, 2003; Waldron, 2009). The

secondary infection is a reinfection or reactivation stage, which occurs after an individual has been infected by the bacterium for more than five years (Roberts and Buikstra, 2003; Waldron, 2009). Reactivation of the bacillus occurs either because the host's immunity begins to fade (due to infection, poor nutrition, etc.) or because the bacteria replicate again, predominantly occurring during adolescence or adulthood of the host (de Backer et al. 2006; Saunders and Britton, 2007; Wilbur et al. 2008; Waldron, 2009). Bone changes related to tuberculosis occur during the secondary infection.

Tuberculosis is considered a disease of poverty, malnutrition, and overpopulation/overcrowding (Roberts and Buikstra, 2003; Waldron, 2009; Wiley and Allen, 2012). There is a complex relationship between host, pathogen, and environment where a change in one variable will engender a change in another (Roberts and Buikstra, 2003; Wilbur et al. 2008). Overcrowding can result in poor sanitation, particularly in past populations, which provides ideal environmental conditions for the tuberculous bacterium to thrive. Furthermore, domestication of cattle increases the vectors that can spread the bacterium to more hosts. Individuals with compromised immune systems will likely contract and succumb to the disease much more quickly than those without. For example, individuals with the human immunodeficiency virus (HIV) often easily contract tuberculosis (Roberts and Buikstra, 2003; Wiley and Allen, 2012; Steyn et al. 2013). Knowledge of the social and environmental factors that increase a person's chance of contracting tuberculosis is important to understand all the variables that predispose a population or community to have a high prevalence of tuberculosis.

3.3 Clinical Diagnosis of Tuberculosis

Clinically, there are numerous ways in which a patient can be diagnosed with tuberculosis. The diagnostic methods available have a varying range of efficacy. Therefore, even with contemporary methods of diagnosis, there are many challenges that can lead, or contribute, to the misdiagnosis of tuberculosis.

Many clinical diagnoses of tuberculosis begin with a symptomatic diagnosis. Primary pulmonary tuberculosis is often asymptomatic, but can occasionally cause mild respiratory tract infections (Davies and Pai, 2008). Therefore, diagnosis of patients with

primary pulmonary tuberculosis becomes difficult when there are no symptoms to investigate. Secondary tuberculosis can be asymptomatic during the early stages. Once the disease has advanced, symptoms include coughing with occasional bloody discharge, fever, weight loss, night sweats, shortness of breath, and chest pains (Davies and Pai, 2008). Only weight loss and night sweats are symptoms that have a statistically significant relationship to tuberculosis compared to other symptoms. Accurate symptomatic definitions are required for clinicians to suspect, and subsequently investigate whether or not tuberculosis is the cause of the symptoms. Failure to provide accurate definitions of symptoms can lead to a misdiagnosis since the most common symptoms experienced by patients with tuberculosis can mimic other pulmonary conditions (Marais and Pai, 2006; Davies and Pai, 2008).

Chest radiography is another often used method for the diagnosis of tuberculosis. Clinicians look for evidence of a Ghon focus, Ranke Complex (the combination of the Ghon focus and enlarged calcified lymph nodes), Simon focus (apical nodules that are often calcified resulting from hematogenous seeding during initial infection), and/or pleural fluid (Leung, 1999). Radiography, however, is not universally available. This poses a problem for conducting an initial assessment of patients believed to have tuberculosis in such places. A further complication is that chest radiographs are a non-specific way to investigate and diagnose tuberculosis (Palomino, 2005; Marais and Pai, 2006; Davies and Pai, 2008). Despite these issues, chest radiography remains the most widely used method to diagnose TB (Marais and Pai, 2006). Accurate diagnosis of tuberculosis can be achieved from chest radiographs but only when the radiographs are interpreted by an experienced clinician.

In general, cases of tuberculosis can only be ascertained by bacterial culture growth, and sputum smear tests can assist with that. The technique used to obtain smear samples influences the ability to detect tuberculosis (Davies and Pai, 2008). Three sputum samples are usually collected on three different days to ensure accurate results (Davies and Pai, 2008). While smear tests are better for diagnosing tuberculosis compared to diagnosis based on symptoms or chest radiographs, smear tests can also pose problems with diagnosis. Sputum smear tests produce positive results in less than 10-15% of

infected child patients (Marais and Pai, 2006). In adults, the sensitivity of smear tests is approximately 34-80% (Davies and Pai, 2008) but is usually dependent on a patient being at an advanced stage of the infection. The culture yield in sputum smears tends to be low, usually less than 30-40% (Marais and Pai, 2006). As a result, a negative smear test does not eliminate the diagnosis of active tuberculosis, especially if the suspicion is high.

The gold standard for diagnosing tuberculosis in clinical contexts is the cultivation of the *M. tuberculosis* bacterium (Palomino, 2005; Marais and Pai, 2007; Davies and Pai, 2008). Samples for bacterial cultivation are usually collected when sputum smear samples are collected (Davies and Pai, 2008). Cultivation of the bacterium only requires a sample of 10-100 organisms, which will produce a test sensitivity of 80-95% and a specificity of 98% (Davies and Pai, 2008). Culture tests, however, are very expensive and cannot be afforded in developing countries or by patients of a low-socioeconomic status.

It is clear that contemporary clinical methods have many issues and can contribute to a misdiagnosis in the absence of bacterial culture tests. Therefore, the misdiagnosis of tuberculosis clinically is a confounding factor that must be recognized and considered.

3.4 Tuberculosis Skeletal Changes

Tuberculosis is an infectious disease that has garnered much attention because of the debilitating effects it has, and the skeletal lesions it produces are well known (Aufderheide and Rodriguez-Martin, 1998; Ortner, 2003; Roberts and Buikstra, 2003; Roberts and Manchester, 2005; Waldron, 2009). The effect of tuberculosis on the skeleton is primarily a lytic process in which the bone around the infected area is destroyed (Steinbock, 1976; Mays et al. 2002; Ortner, 2003). Therefore, tuberculosis is almost exclusively associated with the presence of resorptive destructive lesions. Once an individual is infected by the mycobacterium, lesions can develop anywhere throughout the skeleton (Roberts and Manchester, 2005; Ortner, 2003), with some areas more commonly affected than others. Tuberculous lesions in the skeleton occur in approximately three to five percent of individuals during the secondary infection (estimates derived from clinical/radiological studies) (Ortner, 2003; Roberts and Buikstra, 2003; Waldron, 2009; Roberts and Manchester, 2005). Understanding what

skeletal elements are affected by tuberculosis is important in order to provide a probable diagnosis in an individual demonstrating skeletal evidence of the disease.

Vertebral Lesions. Studies suggest that half of individuals that develop tuberculous lesions on the skeleton will have their spine, specifically the lumbar spine, affected (Waldron, 2009). The majority of spinal tuberculosis cases affect children and young adults, but spinal tuberculosis can occur at all ages (Waldron, 2009). The tuberculous infection can spread to other vertebrae through the intervertebral discs, behind the anterior longitudinal ligament, and/or the psoas muscles via abscesses beneath the fascia (Waldron, 2009). Given that the psoas muscles can act as a conduit to transport the tuberculous bacterium from the lungs, the possibility exists that a similar mode of spread may occur to the sternum via thoracic muscles that anchor to the manubrium. This illustrates the importance of understanding the gross muscular anatomy associated with the sternum and surrounding organs. The involvement of three to four contiguous vertebrae is typically reported in individuals with spinal tuberculosis, although clinical and autopsy data suggest that this occurs in 10% of cases, while 80% of cases have two adjacent vertebrae involved (Ortner, 2003).

Tuberculosis exclusively affects the vertebral body, specifically the anterior portion of the centrum (Roberts and Manchester, 2005; Ortner, 2003). Extension of tuberculous lesions to the neural arches is uncommon (Ortner, 2003). Abscesses can occur within the vertebral body, destroying the trabecular bone of the centrum. The loss of trabecular bone causes the vertebral body to collapse, and a small wedge of what remains of the vertebral body is present (Ortner, 2003). The collapsed vertebrae, which usually result in an angular kyphosis, subsequently fuse after a prolonged period of time and is more commonly known as Pott's disease (Roberts and Manchester, 2005; Ortner, 2003; Aufderheide and Rodriguez-Martin, 1998). Tuberculosis has the distinctive feature of having unilateral or bilateral abscesses along the vertebral body, such that the abscesses are located on areas associated with psoas muscle attachment (Ortner, 2003).

Rib Lesions. Research has attempted to associate skeletal lesions to a specific form of tuberculosis with the use of documented skeletal collections. Documented skeletal

collections are uniquely situated to assist with associating patterns of skeletal lesions with particular diseases, primarily when cause of death is known for all or the majority of individuals. Lesions on the visceral surface of the ribs have been considered to be indicative of pulmonary tuberculosis (Kelley and Micozzi, 1984; Pfeiffer, 1991; Roberts et al, 1994; Santos and Roberts, 2001, 2006; Lambert, 2002; Mays et al. 2002; Matos and Santos, 2006; Nicklisch et al. 2012). There are three manners in which rib lesions resulting from tuberculosis arise: the first, being an extension of spinal lesions, the second from hematogenous spread from a tuberculous foci unrelated to the thorax (e.g. gastrointestinal tuberculosis), and last, from a direct extension of adjacent organs affected by tuberculosis, namely the lungs, pleura, or chest-wall lymph nodes (Asnis and Niegowska, 1997; Mays et al. 2002; Ortner, 2003). The latter mode of lesion creation is often associated with proliferative lesions instead of lytic lesions. Studies suggest that rib involvement in tuberculosis occurs in approximately 10% of the individuals that develop skeletal lesions, most often affecting the middle ribs of the left side (Kelley and Micozzi, 1984; Waldron, 2009).

The type of lesion produced on the ribs is dependent on the pathway the tuberculous bacterium took to reach the ribs. Rib lesions due to spinal extension and hematogenous spread produce destructive or lytic lesions with little to no reactive bone (Mays et al. 2002). The locations of the lytic rib lesion differ between the two pathways. Spinal extension lesions tend to concentrate on the head and neck of the rib. Lesions that form following hematogenous spread originate in the trabecular bone of ribs and result in fusiform enlargement of the involved area with perforations of the cortex that lead to chest wall abscesses (Asnis and Niegowska, 1997; Mays et al. 2002; Ortner, 2003). Rib lesions associated with soft tissue tuberculous involvement have evidence of periosteal bone thickening, likely due to osteoperiostitis on the rib surface (Eyler et al. 1996; Mays et al. 2002). Conflicting relative frequencies of rib involvement between dry bone studies and clinical studies is likely a result of radiographs not having the ability to pick up on minute plaque-like growth and/or because radiologists and doctors do not look for rib lesions.

The association between rib lesions and pulmonary tuberculosis suggests that other skeletal elements of the thorax, such as the sternum, may also be affected by pulmonary tuberculosis. The sternum can then potentially be included in the diagnosis of tuberculosis that has been transmitted through the respiratory system.

Pelvic lesions

Acetabular lesions. The hip joint is the second most common area in the skeleton to demonstrate tuberculous lesions apart from the vertebral column (Ortner, 2003). The majority of hip tuberculosis cases tend to begin during childhood. The mycobacterium can spread to this area of the hip through the hematogenous route, but can also spread through contact with abscesses from vertebral or pelvic tuberculosis (Ortner and Putschar, 1981). The femoral head is primarily affected and infection is identified by the presence of small cavitating lesions (Ortner and Putschar, 1981; Aufderheide and Rodriguez-Martin, 1998; Ortner, 2003). When the destruction of the hip joint becomes severe and extensive, the acetabulum may become displaced (Ortner, 2003). The displacement of the acetabulum may result in the formation of a pseudo-acetabulum on the lateral aspects of the ilium, and ankylosis of the joint can occur (Ortner, 2003).

Sacroiliac lesions. The sacroiliac joint is the second most common area of the pelvis affected by tuberculosis. Involvement of the sacroiliac joint is most often observed in young adults as opposed to children (Ortner, 2003). Isolated cases of sacroiliac tuberculosis are rare, therefore individuals with sacroiliac lesions that are the result of tuberculosis are almost always found with other tuberculous lesions (Ortner, 2003). Sacroiliac involvement results in the extension of a lumbosacral focus unilaterally or bilaterally (Ortner, 2003). There may be a considerable amount of destruction to the sacral alae with some reactive sclerosis (Ortner, 2003; Aufderheide and Rodriguez-Martin, 1998). When sacroiliac tuberculous lesions are healed, the healing process may result in asymmetric pelvic deformity (Ortner, 2003).

Knee Lesions. Most cases of tuberculosis of the knee begin in infancy, childhood, or adolescence (Ortner, 2003). The majority of the cases of knee tuberculosis begin as synovial tuberculosis (Ortner, 2003; Aufderheide and Rodriguez-Martin, 1998), meaning

that the surrounding synovium becomes infected, fills with fluid, and has muscular deterioration before the bones become affected (Peabody, 1927). Tuberculosis of the knee results in cortical erosion and undermining destruction of the adjacent portions of the articular surface (Ortner, 2003). Destruction of the femoral condyles and tibial plateau occurs only if an osseous hematogenous tuberculous focus is present (Ortner, 2003). Healing of tuberculous knee lesions results in ankylosis of the joint.

Cranial Lesions. Tuberculous involvement of the cranium has been documented, but at a low frequency of 0.1% (Waldron, 2009). The vault is the most common location for tuberculous lesions to manifest on the cranium. Tuberculous infections of the cranium spread primarily through the hematogenous route (Ortner, 2009; Aufderheide and Rodriguez-Martin, 1998). The bacterium first affects the inner table of the cranial vault. Therefore, the destructive lesion is larger on the inner table of the cranial vault than the outer table, a pattern that is diagnostic of tuberculosis (Waldron, 2009). The cranial lesions have a round lytic focus, with or without a central sequestrum, and ultimately result in the complete perforation of the inner and outer cranial tables (Waldron, 2009; Ortner, 2003). Furthermore, the margin of typical cranial lesions show active bone resorption (Ortner, 2003) and cranial lesions can cross sutures.

Sternal Lesions. Sternal involvement in individuals with tuberculosis has been reported, albeit with differing frequencies. Roberts and Buikstra (2003) report a frequency of sternal involvement of 3.9% from a study consisting of 160 individuals with tuberculosis as a known cause of death. Ortner (2003) reports a frequency of 1.2% from a study conducted by Alfer (1892) on a sample of 1752 individuals. Finally, Kelley and El-Najjar (1980) report that 15.4% of 26 individuals in the Hamann-Todd collection exhibiting tuberculosis had sternal involvement. While the sternum has varying frequencies of involvement, Ortner (2003) notes that the most frequent location affected by tuberculosis on the sternum is the manubrium. These above studies (Ortner, 2003; Roberts and Buikstra, 2003; Kelley and El-Najjar, 1980) provide a few cases where the sternum is involved, but none of the studies describe the appearance of the lesion or provide examples of what *early* manifestation of sternal involvement would look like. As a result, the lack of descriptive data on sternal tuberculous lesions merits more investigation,

particularly in regards to the potential of identifying web-like manubrial porosity as an early manifestation of tuberculosis.

Given that tuberculosis is characterized by lytic lesions and is known to affect the sternum to some degree, the presence of pronounced lattice-like porosity on the posterior surface of the manubrium could have potential associations with tuberculosis, and will be the primary focus for this research. It is also possible that tuberculous lesions of the sternum might mimic those that manifest on the cranium given the structural similarity (i.e. two layers of cortical bone enclosing trabecular bone).

3.5 Pathological Conditions Affecting the Sternum

While skeletal lesions associated with tuberculosis have been described on the sternum, primarily affecting the manubrium, tuberculosis is likely not the only pathological condition that has the ability to affect the sternum. Tayles and Buckley (2004) briefly proposed that pronounced porosity in the form of web-like pores on the manubrium might be the result of an inflammatory process of associated blood vessels, which can be caused by a multitude of conditions. A review of paleopathological research resulted in very few mentions of conditions that are known to cause changes to the sternum. Two pathological conditions known to produce lytic skeletal changes to the sternum include aneurysmal erosion and reticulum cell sarcoma.

Aneurysmal erosion. Aneurysmal erosion is a cardiovascular condition that is stimulated by the enlargement of the aorta (Mann and Murphy, 1990). The most common sites affected by the enlargement of the aorta are the vertebrae, ribs, and sternum. The pulsating nature and increased pressure of aortic aneurysms are likely to cause erosion seen on the vertebrae, ribs, and/or sternum (Kelley, 1979). Kelley (1979) reported on a case from the Hamann-Todd collection in which an individual had an aneurysm of the ascending aorta associated with severe bone destruction on the posterior surface of the manubrium. Aneurysmal skeletal erosion results in well-rounded margins with smooth depressions (Kelley, 1979). This provides evidence that lytic lesions on the sternum can be the result of other pathological conditions.

Reticulum cell sarcoma. Radiographically, reticulum cell sarcomas of bone are characterized by destructive lesions. Fouche and Freeman (1956) provided a case study in which a 51-year-old man had a reticulum cell sarcoma on the manubrium. The patient stated that after a couple of years of chest pain, a small nodule on the upper portion of his sternum was noticed (Fouche and Freeman, 1956). The upper portion of the manubrium was analyzed macroscopically, where a tumor was discovered at the centre of the manubrium. The tumor on the manubrium had an irregular outline and caused bone destruction (Fouche and Freeman, 1956). The nodule on the anterior surface of the manubrium seemed to have affected the posterior surface of the manubrium by causing a slight thickening of the periosteum.

Since there are pathological conditions known to affect the sternum apart from tuberculosis, the present research will consider all types of pathological conditions, which are equally likely to cause destructive lesions on the sternum and manubrium. Other pathological conditions to be considered include cardiovascular disease, neoplasm, and non-tuberculous infections.

3.6 Documented Sternal Porosity

Paleopathological studies seldom incorporate the sternum as a unit of analysis. Furthermore, there is little research investigating pronounced porosity on the sternum and manubrium. However, three studies provide clear images and report on pronounced sternal porosity.

A study by Tayles and Buckley (2004) reported a male between 16-20 years of age (Individual B107) with many pathological skeletal changes, from an Iron Age site close to the Mun River in Thailand. One of the lesions reported was on the posterior aspect of the manubrium, which had a latticework appearance. Individual B107 also had bony changes on the hands, feet, tibiae, fibulae, and possibly face (Tayles and Buckley, 2004). Tayles and Buckley (2004) concluded that the lesions on Individual B107 were likely caused by leprosy or psoriatic arthritis, with leprosy being the most probable diagnosis. Tayles and Buckley (2004) stated that the porosity seen on the posterior surface of the manubrium was likely the result of increased vascularity due to chronic inflammation of

blood vessels since branches from the internal thoracic artery supplies the manubrium with blood via numerous foramina on the posterior surface. Since Tayles and Buckley (2004) did not comment more on the sternal lesion, the lesion on the sternum remains anomalous and unaccounted for. Furthermore, Tayles and Buckley (2004) indicated that there is no literature on the nature of the lesion on the manubrium. This thesis project sought to remedy such an issue by investigating the nature of pronounced sternal porosity to determine the most probable etiology of the lattice lesion. By doing so, this research will be able to either confirm or refute Tayles and Buckley's suggestion that some sort of inflammatory process results in the porosity seen on Individual B107 (see section 7.3 of this thesis).

Mann and Tuamsuk (2013) presented a case study of a 58-year-old male skeleton (Individual 698) from the Khon Kaen University skeletal collection in Thailand. The skeleton had evidence of extensive cortical resorption with osteoporosis and marrow hyperplasia, which contributed to several bones having a "lacy", "woven", or "wicker basket" appearance perforating the cortex (Mann and Tuamsuk, 2013). The authors also noted the presence of coarse bars of bone in hematopoietic, or blood producing, areas of the skeleton. While associated patient records and histories accompanied most individuals in the collection, the Individual 698 did not have associated records, which made a diagnosis or probable diagnosis difficult.

The "lacy" or "wicker basket" lesions were diffuse throughout the skeleton. Pertinent to the current study were the lesions on the sternum, ribs, vertebrae, sacrum, and clavicles. The sternum had resorptive lesions without sclerotic margins and erosion of the cortical bone, which resulted in coarse strands of bone. Mann and Tuamsuk (2013) noted that all cortical surfaces of the sternum, except for the clavicular joints, were affected. The most affected area on the rib was the pleural surface, which exhibited the "lacy" bone resorption. All vertebrae had severe bone resorption and "wicker basket" lesions with the lumbar vertebrae affected the most (Mann and Tuamsuk, 2013). The sacrum had the most severe destruction of any other bone, where the ventral surface was affected with the lacy lesion more so than the dorsal surface. The clavicles only exhibited localized small amounts of porosity on the medial and lateral ends (Mann and Tuamsuk, 2013).

Differential diagnoses listed by Mann and Tuamsuk (2013) included: thalassemia, Gaucher's disease, hemangioma/lymphangioma, multiple myeloma, chronic leukemia, lymphoma, Hodgkins disease, and metastatic carcinoma. Despite these possible causes of the "lacy" lesions, the authors and other well-respected pathologists consulted were unable to agree on a diagnosis. The difficulty in producing a diagnosis is due to the fact that macroscopic and radiographic analysis found numerous similarities and dissimilarities with any one of the previously mentioned pathological conditions (Mann and Tuamsuk, 2013). Further examination of the Khon Kaen University skeletal collection revealed a second individual, a 33-year-old male, exhibiting the same "lacy" or "wicker basket" lesions as Individual 698. The 33-year-old male was diagnosed as having had thalassemia, he died of congestive heart failure, and had expanded ribs near the vertebral border. The latter is associated with thalassemia (Mann and Tuamsuk, 2013).

Mann and Tuamsuk (2013) referred to a study conducted by Lagia and colleagues (2007) that reported on the skeleton of a 14-year-old female from a skeletal collection at the University of Athens that presented a similar lesion pattern and morphology; the individual was believed to have had thalassemia. In the case study presented by Lagia and colleagues (2007), the 14-year-old girl exhibited thickening of the cranial vault associated with diploic expansion with hair-on-end appearance, which is characteristic of thalassemia. While Lagia and colleagues (2007) did not provide detailed descriptions of the sternal lesions, the clavicles, sternum, vertebrae, and sacrum were said to have had skeletal changes similar to marrow hyperplasia. Although there was evidence to suggest the lesions seen on Individual 698 could have been associated with thalassemia, Mann and Tuamsuk (2013) were cautious to not reach this conclusion.

Last, in a preliminary study that forms the basis of this current research, Sanchez and colleagues (2012) investigated the possibility of lattice-like sternal porosity on the posterior surface of the manubrium being associated with tuberculosis. Eighty-one individuals with known age, sex, and cause of death from the JCB Grant Skeletal collection in Toronto, Canada, were analyzed for lattice-like porosity on the manubrium. Sanchez and colleagues (2012) devised a five-point scoring system from absence (score 0) to severe (score 4), corresponding to patterns in which the lattice lesion may be

expressed (the scoring system will be provided in detail in Chapter 4). The 81 individuals examined were divided into pulmonary and non-pulmonary groups based on cause of death. The pulmonary group was further divided into tuberculosis and non-tuberculosis causes of death. Tests of association between age and sex were also conducted.

The lattice lesions with scores from 1-4 were present in 34.6% of the 81 individuals examined. When divided into pulmonary and non-pulmonary groups, 34.5% of individuals with a pulmonary cause of death exhibited lattice-lesions, and 35.3% of individuals in the non-pulmonary group had lattice-lesions. Forty-three percent of individuals with lattice lesions in the pulmonary group had tuberculosis as a cause of death, while only 27% had a pulmonary cause of death other than tuberculosis (Sanchez et al. 2012). Chi-square tests of significance determined that there were no statistically significant associations between the lattice-lesion, cause of death, or sex. A statistically significant relationship was determined with age, where adolescents had significantly more sternal lesions than early, middle, or late adults (Sanchez et al. 2012). All but one individual in the adolescent category, however, had tuberculosis as a cause of death, confounding the results. Sanchez and colleagues' (2012) results suggested that there is no statistically significant association between lattice-lesions on the manubrium and tuberculosis. The authors, however, noted that there were certain limitations that may have been confounding the results. The limitations outlined included: the relatively small number of manubria available for analysis, a general lack of lattice-lesions in the collection, a relatively low sample size of individuals available for assessment with tuberculosis compared to the collection (14/202), and an age and sex bias towards older males (Sanchez et al. 2012). The authors suggested that further research be conducted in a similar manner on a skeletal collection with a larger number of manubria available for analysis, a higher prevalence of tuberculosis, an equal male to female ratio, and an extensive age distribution.

The studies by Tayles and Buckley (2004), Mann and Tuamsuk (2013), and Sanchez and colleagues (2012) provided evidence that lattice lesions on the manubrium are likely associated with some sort of pathological process. However, all three studies showed difficulty with associating lattice lesions on the manubrium with a specific disease. For

this reason, this current research expanded on the preliminary work conducted by Sanchez and colleagues (2012) and used a skeletal collection that met the criteria suggested. While tuberculosis was the primary disease of interest due to its primary area of infection and lytic process, the above review of studies examining sternal porosity addressed a plethora of other possible pathological conditions that may be associated with lattice lesions on the manubrium, and therefore, all possible causes of death were considered and separated into specific categories (see Chapter 4.2 page 54-55).

Chapter 4

4 Methods and Materials

This chapter provides background on the skeletal collection used in this research and situates the collection in the broader environmental and health conditions experienced by the people in the collection. The chapter also provides a description of how the sample used in this study was selected, the methods used to collect all necessary data, and the statistical analyses undertaken in an attempt to determine the most probable etiology of sternal porosity.

4.1 Early 20th century Portugal

The collection that was utilized for this research, the Luis Lopes Skeletal Collection, is located in Portugal. Tuberculosis was a major concern in the country, and in other parts of Europe such as Poland, during the late 19th and early 20th century due to the outbreak of a tuberculosis epidemic, which coincided with the end of World War II. For this reason, the Luis Lopes Skeletal Collection was believed to be an ideal collection to utilize for this research. In order to provide context to the lives of the people that comprised the collection, information about Portugal's geography and the health conditions experienced by Portuguese citizens in the late 19th and early 20th centuries will be provided.

Geography

Portugal is located at the southwestern tip of continental Europe, and is bordered by the Atlantic Ocean on the south and west and by Spain on the north and east (Figure 4.1) (Cardoso, 2005; Holland, 2013). The northern part of Portugal is mountainous with a cooler and rainy climate, and landscape is dominated by small-scale farming. The southern portion of the country, in contrast, is primarily a rolling plains landscape with a warmer and drier climate, which is dominated by large landowners and landless peasants (Cardoso, 2005). The country's population was always more concentrated in coastal areas, particularly during the 1960s period of urbanization. The cities of Lisbon (a coastal

city and the capital of Portugal) and Porto (another coastal city) and their surrounding areas have always been the most populated areas of Portugal. Lisbon, the city where the Luis Lopes collection is located, is situated next to the Tagus River, a major Iberian river in the south central portion of Portugal (Cardoso, 2005). Lisbon, known as the city of seven hills, is a dry and warm city with hills opening to the river, with the highest peak being 226 meters in altitude (Cardoso, 2005). Urbanization of Lisbon occurred along the river, and after the late 19th century, spread northward away from the Tagus River. Although Lisbon experienced significant urbanization, large portions of the city held a rural atmosphere for the majority of the 20th century (Cardoso, 2005).



Figure 4.1: Map of Portugal

source: www.maps.com

Health in early 20th century Portugal

Portugal faced some of the worst health conditions in Western Europe in the early 20th century. Lisbon reflected social inequalities seen throughout the country that were caused by large wage disparities, low levels of education, and low levels of social insurance and health facilities (Cardoso, 2005). Throughout the 20th Century, there were repeated migrations of people from rural towns to large cities, such as Lisbon, which significantly

increased the city's population. Deep inequalities between the slowly modernizing and capitalist-driven urban society and the deeply traditional rural society were the main reasons for the migrations, where people searched for better living conditions (Cardoso, 2005). Rapid population growth in late 19th to early 20th century Lisbon was not met with equally fast housing development. There were two primary ways in which the growth of working class housing was addressed: the first being an overpopulation of older areas in city centres, and the second being the construction of new houses for the working class (Moreira, 1950; Teixeira, 1996). The new houses mainly took the form of abandoned buildings and monasteries that were converted into apartments, which were normally overcrowded with bad living conditions. Even by 1960, only about 30-40% of Lisbon's population had access to basic facilities (Pereira, 1966). Despite a national attempt to implement an economic housing program for the poorer classes, most of the lower class resided in overpopulated old areas of the city or in slums around the cities' peripheries.

During the 1920s, life expectancy at birth in Portugal was 35.5 and 40 years for males and females respectively (Cardoso, 2005; Holland, 2013). While infant mortality at the beginning of the 1930s decreased from 200 deaths per 1000 live births to 142 deaths per 1000 live births (Bandeira, 1996), infant mortality was still high in comparison to other developed European countries (e.g. France). Approximately 50% of children died before 15 years of age in 1900, which further highlights the poor health conditions in Portugal. Infectious disease was rampant in the first half of the 20th century and was the most common cause of death during this time (Morais, 2002; Holland, 2013). The most common cause of death in adults was tuberculosis, while the most common causes of death for children were diarrhea and enteritis (Santos, 2000; Morais, 2002; Holland, 2013). Tuberculosis was a national problem that was exacerbated by crowded and unsanitary living conditions in all major urban centers of the country, including Lisbon. Since tuberculosis is an airborne disease in which individuals can contract it by inhaling sputum or droplets from an infected individual, contracting the disease was likely not limited to individuals of the lower-middle class. Brief interactions between an infected person of low economic status and a non-infected person of high economic status would have been sufficient to transmit the bacteria from person to person. It was not until the 1940s that the antibiotic era began, although mass vaccination did not start until the

1960s for common childhood ailments or infectious diseases (Gomes et al. 1999; Santos, 2000; Holland, 2013). Before the antibiotic era, the only treatment for tuberculosis that was available was the placement of infected persons in a sanatorium, which was primarily afforded by the upper class, where patients would rest in open-air locations, and had carefully controlled diets (Santos, 2000; Wilbur et al. 2008; Holland, 2013).

Luis Lopes Skeletal Collection

The Luis Lopes Skeletal Collection, also referred to as the Lisbon Collection or the new Lisbon Collection, is housed in the Department of Zoology at the National Museum of Natural History in Lisbon, Portugal. The collection was initially started by Francisco Ferraz de Macedo, a physician in Lisbon, and was primarily comprised of skulls that were donated shortly before his death (Cardoso, 2006). In 1978, the collection was almost entirely destroyed in a fire that damaged the National Museum. To replace the destroyed Ferraz de Macedo collection, a second collection was initiated in the 1980s by Luis Lopes, a technician at the Bocage Museum and assistant professor of anthropology at the University of Lisbon (Cardoso, 2005; Cardoso, 2006). The skeletal material of the new collection was acquired from cemeteries. It was standard practice in Portugal that when a person died, they were buried in a public cemetery plot for approximately five years. When space in the cemetery became scarce and another grave was required, the family of the current occupant of a grave was to be informed. The family was required to receive the exhumed remains and arrange and pay for a new resting place in the cemetery (Holland, 2013). If arrangements were not made, the person was placed in a large communal burial. In 1981, the National Museum requested permission from the Lisbon City Hall to collect the remains of individuals that were abandoned by relatives and destined for communal graves (Cardoso, 2006). The skeletal material comprising the Luis Lopes collection comes from several cemeteries including: Alto de São João, Prazeres, Benfica (the three cemeteries where the bulk of the skeletal remains come from), Ajuda, and Lumiar (Cardoso, 2005). All individuals of the Luis Lopes collection are identified via cemetery registers, coffin plates, and grave numbers, thus a significant amount of biographical information is available. In 1991, the same year Luis Lopes retired from his position as a technician at the National Museum, the collection process ceased and the

curation of the skeletal collection suffered. In 2000, curation of the skeletal collection and the acquisition of more skeletons were initiated by Dr. Hugo Cardoso, then the collection's curator. Hugo Cardoso targeted the new acquisition of skeletons to underrepresented age groups, which included young adults and subadults (Cardoso, 2006). This differs from the skeletal acquisition of the 1980s and 1991 where Luis Lopes retrieved all and any available skeletons. The skeletal acquisition protocol and process, however, was the same as when Luis Lopes initiated the collection in 1981.

Approximately 1,692 skeletons are curated at the museum, where 1,552 identified individuals were collected between the late 1980s and 1991 and 140 are new acquisitions (Cardoso, 2006). Of the 1,692 individuals of the collection, approximately 699 are readily available for study since their demographic information has been integrated into the collection's database thus far (Figure 4.2) (Cardoso, 2006). The year of death for individuals in the collection ranges between 1880-1975, with the majority of people dying between 1941-1960. Age, sex, cause of death, occupation, date of birth and death, are amongst the information known for each individual. Ages at death of individuals from the collection range from birth to 98 years of age, and there is a slight overrepresentation of females (a 1:1.14 male:female ratio) (Cardoso, 2006). Thirty-three percent of all individuals' cause of death was related to problems of the circulatory system, 15% died from tuberculosis (of which 82% are of the pulmonary type), and 13% died of cancer. The collection likely represents a low to middle socioeconomic stratum of an urban population as inferred by reported occupation of the males. Thirty percent of the males worked in the sales industry and 23% worked as skilled workers, craftsmen, or some similar occupation. The majority of females in the collection (85%) have a reported occupation as housewife and the remaining 15% include maids, teachers, or students (Cardoso, 2006). The preservation of the skeletal remains varies considerably, however, the skeletons are all essentially complete and well preserved. Cause of death for each individual is derived from death certificates signed off by the doctor overseeing the person during the illness. When there was doubt pertaining to the cause of death or when there was no family physician involved, the death certificate was issued as a result of an autopsy performed by a local or regional medical examiner (Cardoso, 2005). Diagnoses of cause of death were likely determined on the basis of symptoms the patient

experienced when alive, when an autopsy was not performed, which may result in inaccurate diagnosis.

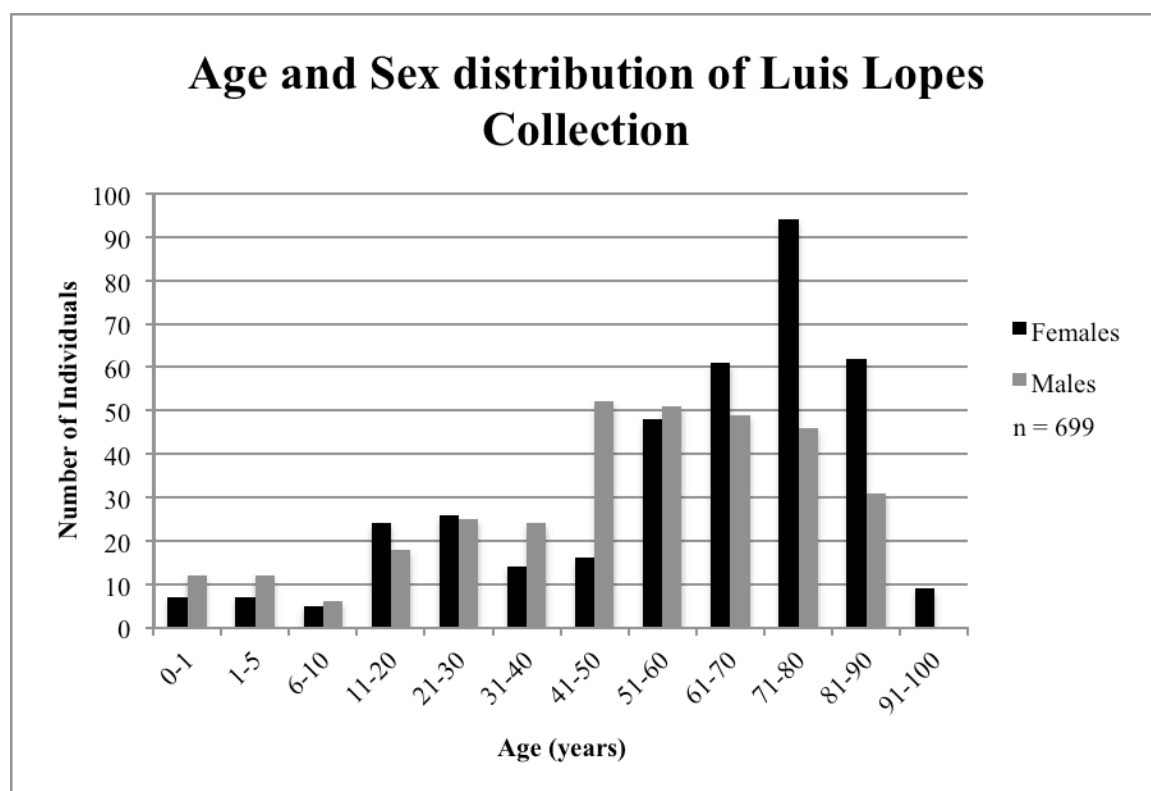


Figure 4.2 All individuals available for analysis in the Luis Lopes Collection

Due to the thorough documentation available for each individual, the Luis Lopes Skeletal Collection has been heavily used for many research endeavours. The collection has been used to inform research about stature assessment (Cardoso, 2009), pathology (Cardoso, 2007; Matos and Santos, 2006; Matos, 2009; Macak, 2013), age estimation (Cardoso, 2008; Rios et al. 2008; Rios and Cardoso, 2009; Cardoso et al. 2013; Cardoso et al. 2014), juvenile sex assessment (Albanese et al. 2005; Rogers, 2009; Vlak et al. 2008; Veroni et al. 2010; Wilson et al. 2011), and markers of occupational stress (Campacho and Santos, 2013).

4.2 Study Sample

Sample Selection

The primary criteria for sample selection for this study are known age and sex of individuals and the presence of a complete or almost complete manubrium with minimal taphonomic damage. All 699 individuals of the Luis Lopes collection were sorted into ten age groups of ten years (e.g. 0-9, 10-19, 20-29 etc.). This was done in order to closely account for changes in the manubrium's cortex that may occur throughout skeletal development and/or during skeletal degeneration in older age groups. Once separated by age cohorts, all individuals were divided into male and female for each cohort. When separated by age and sex, 20 individuals (10 males and 10 females per age category) were selected from each age cohort. Individuals in the collection who did not have known age or sex recorded in the museum's database were excluded from the selection process. Maintaining an equal male to female ratio and an even number of individuals per age cohort helps control for age and sex.

The selection of the 20 individuals per age cohort was semi-randomly conducted. Each individual, represented by a catalogue number, was assigned a number from 1 – n, where n equals the total number of females or males within an age cohort. Using the randomization function on Microsoft Excel, 10 numbers for each sex of every age cohort were randomly selected from 1 – n to select the 10 males and 10 females to be analyzed. During analysis, any individuals that: (1) did not have a manubrium present, (2) had a manubrium that was less than 50% complete, (3) had a manubrium with the posterior surface damaged/missing, or (4) had a manubrium with significant taphonomic damage, were excluded from the sample. In instances where multiple individuals were selected, but they did not meet the criteria to be included in the analysis, an adjacent catalogue number (either the catalogue number that preceded or followed the randomly chosen number) was selected.

Methodology

The sample used herein is comprised of 154 individuals, 77 males and 77 females, ranging from 2-94 years of age (Figure 4.3; Table 4.1). Most age cohorts do not have exactly 20 individuals because of the absence of a manubrium from most individuals in the collection. Analysis of all individuals included in this study was done in blind, where only the catalogue number and sex were known prior to examining the skeletal remains. This reduces the potential for bias when assigning a sternal lesion score and assessing for rib and vertebral lesions associated with tuberculosis. Each individual was scored for the presence of sternal porosity on the manubrium using the scoring system devised by Sanchez and colleagues (2012). A complete description of the scoring system will be provided in section 4.3 of this chapter. Photographs of the posterior surface of the manubria were taken with a Sony Cyber-Shot DSC-W690 16.1MP point and shoot camera using the macro setting for optimal clarity. Photographs were taken in the event that post-hoc analysis was required to determine if other patterns could be identified associated with porosity on the manubrium.

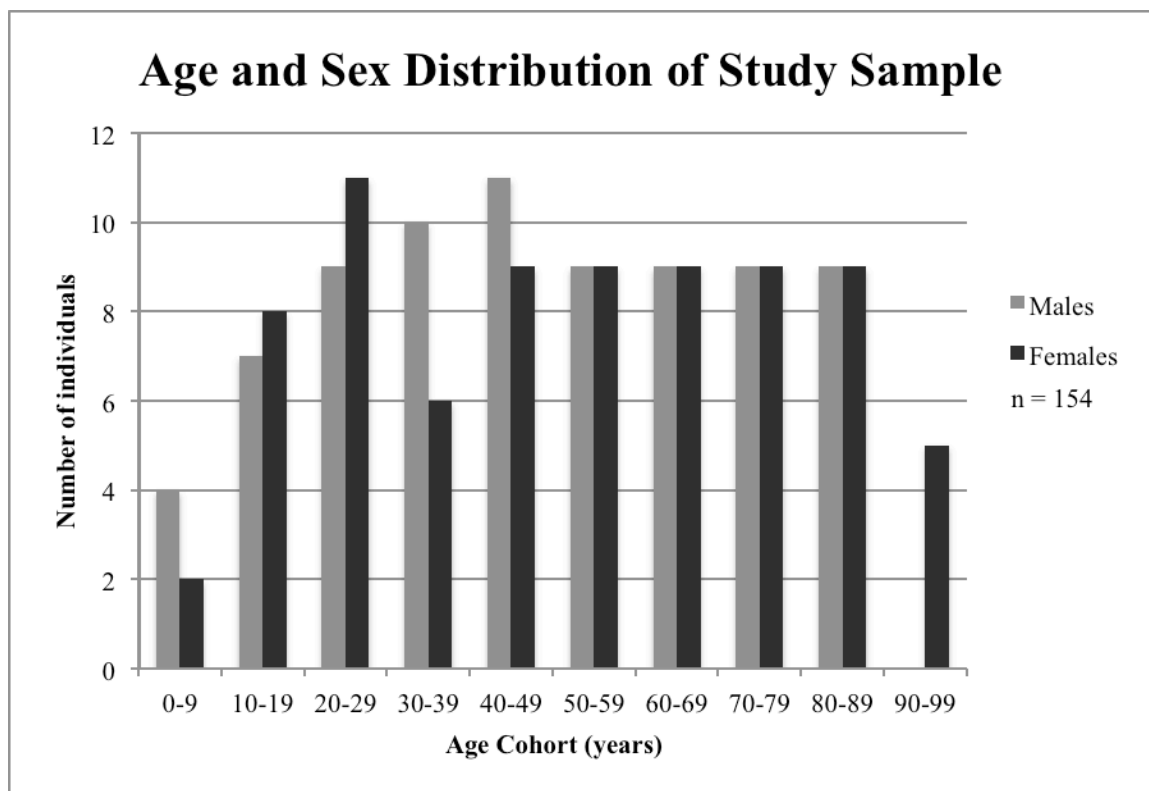


Figure 4.3: Distribution of all individuals analyzed by age cohort and sex

Table 4.1: Sample distribution of males and females per age cohort

Age range	n	# of males	# females
0-9	6	4	2
10-19	15	7	8
20-29	20	9	11
30-39	16	10	6
40-49	20	11	9
50-59	18	9	9
60-69	18	9	9
70-79	18	9	9
80-89	18	9	9
90-99	5	0	5
Total	154	77	77

The ribs and vertebrae were assessed for any lesions indicative of tuberculosis. Rib and vertebral lesions were primarily scored as present or absent and where possible, the affected rib(s) or vertebra(e) were specifically identified. Rib and vertebral assessments were conducted in order to determine if there is a relationship between porosity on the manubrium and tuberculous rib and/or vertebral lesions and subsequently, where

manubrial lesions lay in the sequence of tuberculous expression within the thorax. The presence of the lower thoracic and lumbar vertebrae were the minimal requirement for this portion of analysis since they are more likely to exhibit tuberculous lesions compared to other vertebrae (Ortner, 2003; Roberts and Buikstra, 2003; Roberts and Manchester, 2005; Waldron, 2009). In order to assess for rib lesions, the presence of the left middle ribs (R4-8) were required given that these ribs are believed to be more likely to exhibit evidence of tuberculosis compared to the right ribs (Kelley and Micozzi, 1984; Waldron, 2009). Given that the investigation into the etiology of manubrial porosity took precedence in this study, absence of, or poorly preserved, vertebrae or ribs did not affect the overall sample size of the entire study, but merely affected the number of individuals that were included in this portion of analysis.

An assessment of the sternal body shape and normal variants of the sternum was conducted to determine if porosity on the manubrium has an association with normal variations of sternal morphology. The sternal body was examined for its shape and was assigned a category as per the description in Ashley (1965). Additionally, examination of other normal sternal variations was conducted, such as suprasternal ossicles and/or presence of a sternal foramen.

The pectoralis major is the largest and most active muscle whose origin is located on the sternal body and lateral margins of the manubrium (Henry et al. 1974). Severe scores for muscular stress exerted by the pectoralis major and the presence of porosity on the manubrium may provide an indication that sternal porosity is a reactive mechanism to excessive biomechanical stress. Since there is no scoring system available for assessing muscular stress on the sternum, the humerus was used as a proxy to assess the extent of muscular stress exerted by the pectoralis major. The humeri were assessed for evidence of excessive muscular stress (musculoskeletal markers) exerted by the pectoralis major. The humerus was scored using the system developed by Hawkey (1988) and used by Hawkey and Merbs (1995). This scoring system will be further elaborated on in Section 4.3 of this chapter.

Finally, age, occupation, and cause of death were recorded from the museum's collection database. Demographic information, such as occupation and cause of death, was translated based on linguistic knowledge of a similar language (Spanish) and with the use of an online translation website (translate.google.ca). Cause of death was separated into two broad categories: pulmonary and non-pulmonary. The pulmonary category was further divided into two categories: tuberculosis and non-tuberculosis infection. In order to compare whether or not a stronger association exists between manubrial lesions and pulmonary tuberculosis compared to non-pulmonary diseases, the non-pulmonary group was divided into five categories: cardiovascular (e.g. myocarditis, coronary thrombosis, etc), extra-pulmonary tuberculosis (e.g. meningeal tuberculosis), neoplastic (e.g. rectal cancer or stomach carcinoma), non-TB infection (e.g. meningitis, leprosy, etc.), organ (e.g. cirrhosis, uraemia), and other (e.g. senility). All data were collected on standardized data collection forms (see Appendix A for an example).

For statistical analysis, the 154 individuals were separated into four age categories: Child (birth-12), Adolescent (13-20), Young Adult (21-35), and Older Adult (36+). These age cohorts loosely follow the age cohorts outlined by Buikstra and Ubelaker (1994). In this study, the "Middle Adult" and "Older Adult" cohorts designated by Buikstra and Ubelaker (1994) have been amalgamated to create a more robust sample size for older individuals for statistical testing. The child and adolescent cohorts were left as separate cohorts to closely account for sternal growth and development.

4.3 Scoring systems

The use of two scoring systems was integral to this project in order to ensure information was collected in a manner that would allow for later comparative population analysis. Lesions on the posterior surface of the manubrium were scored based on a system developed by Sanchez et al. (2012). This scoring system was devised using the JCB Grant Skeletal Collection curated at the University of Toronto's Department of Anthropology in Toronto, Canada. While standards for recording pathological lesions exist (Buikstra and Ubelaker, 1994; Brickley and McKinley, 2004; Steckel et al. 2011), none of the existing standards for assessing pathology from skeletal remains were adequate to document changes to the manubrium. None of the three standards available

provide documentation standards for the manubrium or sternum specifically, nor do the descriptions for bone loss adequately describe the lattice-appearance of the porosity in question. Sanchez et al. (2012) addressed this shortcoming by devising a 5-point scoring system that documents the patterns that sternal porosity may take (Figure 4.4). Table 4.2 outlines the criteria for each score. The scores specifically describe porosity located on the posterior surface of the manubrium.

Table 4.2 Sanchez et al. (2012) scoring system for sternal porosity

Score	Description
0	Sternal lesion is absent.
1	Minimal porosity is present but lattice appearance is <i>not</i> distinguishable.
2	Sternal lesion is present with two or less foci, no vigorous bone resorption but lattice appearance is distinguishable
3	Bone resorption is coalesced into one centralized focus, lattice appearance is pronounced but no bone growth is present
4	Advanced bone resorption, lattice lesion is pronounced, deep, and extends to the lateral margins of the manubrium. Bone growth is also present

Slightly adapted from Sanchez et al. 2012

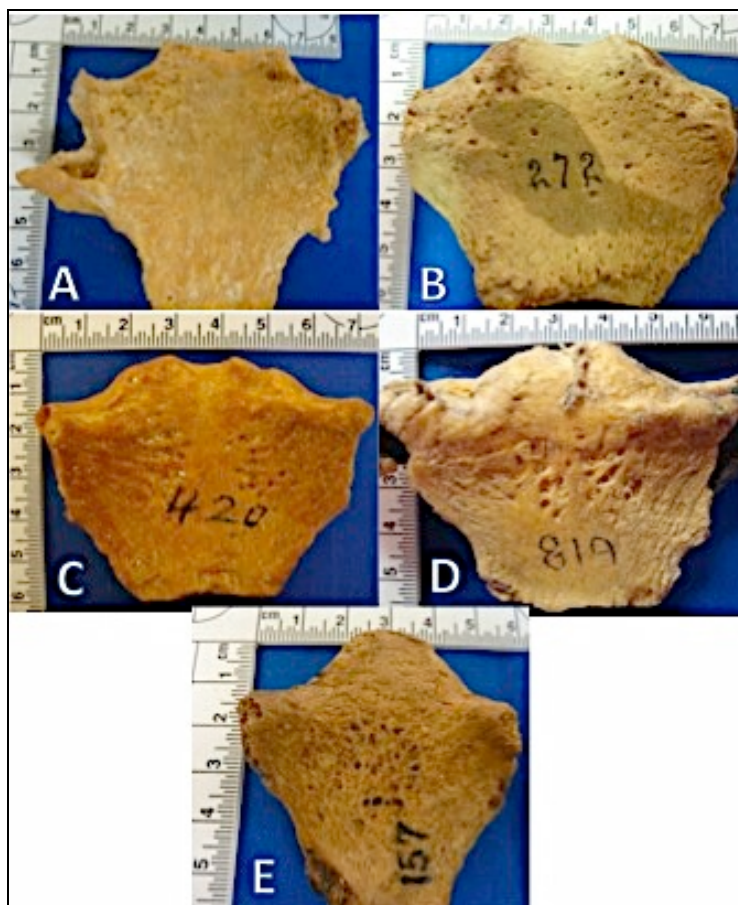


Figure 4.4: Images of all 5 scores taken by the author during the creation of the scoring system (2012). A: shows a score 0, B: depicts a score of 1, C: shows a score of 2, D: depicts a score of 3, E: shows a score of 4

This method of scoring for sternal porosity is the best system to use for this study because all the manubria assessed in the preliminary study conducted by Sanchez et al. (2012) could be separated into one of the five categories.

To assess biomechanical forces that act on the sternum that could potentially alter the macroscopic appearance of cortical bone, musculoskeletal stress markers (MSMs) on the humerus were scored. The system devised by Hawkey (1988) and expanded on by Hawkey and Merbs (1995) was used. Two scores were assigned to the left and right humeri of every individual. The first score was a robusticity score, which ranged from a score of R0-R3 (Table 4.3). Robusticity scores assess the normal reaction that habitual muscle usage has on the skeleton, which reflects daily activities that are responsible for building rugged markings at muscle attachment sites (Hawkey and Merbs, 1995).

Table 4.3: Robusticity score summary as described in Hawkey and Merbs (1995)

Robusticity Score	Description
R0	Absent
R1	Faint. The cortical bone is slightly rounded and not visible without the use of strong light. The elevation is apparent to the touch, but no distinct crests or ridges have formed.
R2	Moderate. The cortical bone is uneven and a mound-shaped elevation is easily observable. There are no sharp ridges or crests that have formed.
R3	Strong. There are distinct sharp crests or ridges that have formed. There may often be a slight depression between the two crests or ridges, but the depression does not extend into the cortical bone.

The second score assigned to the humeri was a stress score, which ranges from S0-S3 (Table 4.4). Stress scores assess the amount of pitting into the cortical bone at the MSM site to the extent that it resembles a lytic lesion (Hawkey and Merbs, 1995). Since this type of pitting occurs only at muscle attachment sites, it is likely not disease related, but instead activity induced resulting from continual micro-trauma to the attachment site (Hawkey and Merbs, 1995). A high robusticity score (e.g. R3) does not always coincide with a high stress score (Hawkey and Merbs, 1995). In instances where there is a high robusticity score but a low stress score, or vice versa, the stress score was given more weight to infer excessive muscular use of the pectoralis major because micro-trauma at an insertion site is a better indicator of muscular over-exertion than robusticity alone.

Table 4.4 Descriptions of stress lesion scores as provided by Hawkey and Merbs (1995)

Stress lesion score	Description
S0	Absent
S1	Faint. There is a shallow furrow and a pitting into the cortical surface that has a lytic appearance. The furrow is less than 1mm in depth.
S2	Moderate. The pitting covers more of the cortical surface and is deeper. The pitting is greater than 1mm, but less than 3mm deep. The length of the pitting may vary, but it is not longer than 5mm.
S3	Strong. There is marked pitting that is greater than 3mm in depth and more than 5mm in length.

The left middle ribs (R4-8) were examined for lesions that may be indicative of tuberculosis. Examination of rib lesions followed criteria outlined by Kelley and Micozzi

(1984), Roberts et al. (1994), and Santos and Roberts (2001, 2006). Rib lesions on the visceral surface were scored as either present or absent, and when possible, the exact rib that was affected was identified.

Finally, the presence of any sternal variants was noted. Sternal variants were identified based on those outlined by Barnes (2012).

4.4 Statistical analysis

Odds Ratio

The odds ratio is a statistical test that assesses the association between two binary variables. In epidemiology, the odds ratio is used to determine if an association exists between a particular disease and some sort of exposure (Waldron 2009, 262). Although used infrequently in bioarchaeology, the odds ratio test of association has been used to determine if associations exist between the risk of dying from combative trauma and having a pre-existing condition, such as infections, arthritis, and previous trauma (Steadman et al. 2009) or to determine the rates of stress in two different populations (Klaus and Tam, 2009).

The odds ratio is a useful test because it measures the *strength* of association between two variables and also calculates the likelihood of one variable occurring compared to a second variable (Bland and Altman, 2000; Minsky-Rowland, 2009). An odds ratio with a value of one suggests that the two variables are statistically independent, but the further the odds ratio is from a value of one, there is a greater association between both variables (Waldron, 2009). Waldron (2009) suggests that odds ratio values larger than 2 are considered to be substantial enough to require further investigation. However, a large (>2) odds ratio may not be significant if it includes unity (value of 1) when the 95% confidence interval is calculated. Compared to the chi-square test of significance, the odds ratio provides information about the degree of association and not merely if an association is present or not. A negative association is represented by an odds ratio value that is between 0 and 1, a positive association is indicated by an odds ratio greater than 1,

and a value of 1 is indicative of no association or unity. Using standard values provided by the 2x2 contingency table from Table 4.5, the odds ratio formula is:

$$\text{Odds ratio} = \frac{(a/b)}{(c/d)}$$

Where (a/b) = the odds that variable 1 is present in group 1,

(c/d) = the odds that variable 1 is absent in group 2.

Table 4.5: Sample 2x2 contingency table for odds ratio

		Variable 1		
		Present	Absent	Total
Variable 2	Group 1	a	b	a+b
	Group 2	c	d	c+d
	Total	a+c	b+d	a+b+c+d

In clinical literature, the odds ratio is often confused with relative risk. Odds ratio is a ratio of ratios, or compares events with non-events (Last and Wilson, 2004). For example, the odds of rolling a 4 on a 6-sided die would be 1:5. Relative risk is the ratio of probability, or the probability of an event occurring in relation to all possible events (Last and Wilson, 2004; Grimes and Schulz, 2008). For example, the probability of rolling a 4 on a 6-sided die would be 1/6. Using standard values provided by the 2x2 contingency table from Table 4.5, the relative risk formula is:

$$\text{relative risk} = \frac{(a/a + c)}{(b/b + d)}$$

When the diseases studied are rare, the odds ratio and relative risk have a comparable value (Last and Wilson, 2004).

In the present study, several odds ratio tests were conducted to determine the strength of association between: cause of death and the presence or absence of manubrial porosity; sex and the presence or absence of porosity; age and the presence or absence of porosity; co-occurrence of sternal variants and sternal porosity; and finally humeral MSMs and sternal porosity. Since this research tested for any associations that exist with manubrial porosity, the variable or cohort with the highest prevalence of manubrial porosity was

tested against those with a lower prevalence. As such, the group with the highest prevalence was always the numerator in the above formula. For example, if the adolescent age cohort had the highest prevalence of manubrial porosity, then adolescents (numerator) were compared to all other age cohorts (demoninator) to determine if an association existed and the strength of said association. The results of the odds ratio in this study, therefore, represent the number of times it is more likely that manubrial porosity will appear with one variable/cohort (e.g. adolescents) compared to another (e.g. children). For example, an odds ratio of 2.5 between pulmonary disease (broadly) and manubrial porosity when compared to the non-pulmonary group would suggest that individuals with pulmonary disease are two and a half times more likely to have manubrial porosity compared to those with a non-pulmonary cause of death. The odds ratio was conducted using SPSS Statistics Desktop 21.0.

95% confidence interval

In order to determine whether or not an association is statistically significant, a 95% confidence interval for the odds ratio was calculated. The 95% confidence interval is a test that determines if a calculation were to be repeated with multiple samples, the confidence interval calculated would include the true value produced by the odds ratio test 95% of the time (Drennan, 2009). The 95% confidence interval can be calculated as follows:

$$\text{Odds ratio estimate} \pm \text{the confidence coefficient} \times \text{SE}$$

Where, SE is the standard error. The confidence coefficient at the 95% confidence interval for the sample size of this study is 1.98 (Drennan, 2009) based on the degrees of freedom. The confidence interval can then be calculated as a natural logarithm scale variable with the following equation:

$$\text{Ln}(OR) \pm 1.98 \times \sqrt{\left(\frac{1}{a}\right) + \left(\frac{1}{b}\right) + \left(\frac{1}{c}\right) + \left(\frac{1}{d}\right)}$$

A correlation will be considered statistically significant if the 95% confidence interval does not include a value of one. Overt discrepancies between odds ratio values and significance will be evaluated carefully to avoid erroneous reporting. The 95% confidence interval will be used to determine the statistical significance for every odds ratio calculated.

Phi-Coefficient

The phi-coefficient is another statistical test that is used to measure the strength of association between two binary categorical variables (Sjøvold, 1984; Brown, 2013). Additionally, the phi-coefficient measures the agreement between the two variables for classifying the variant as being the same (Molto, 1979), or occurring together. In essence, the phi-coefficient measures how strongly the presence of one variable (e.g. manubrial lesion) will predict the presence of another (e.g. rib lesions). In this study, the phi-coefficient measured the extent to which thoracic lesions (e.g. manubrial lesions and rib lesions) are associated with one another. Similar to the odds ratio, the phi-coefficient can only be used for 2x2 contingency tables (see Table 4.6 for an example).

Table 4.6: Sample 2x2 contingency table for phi-coefficient

		Variable 1		
		Present	Absent	Total
Variable 2	Present	a	b	a+b
	Absent	c	d	c+d
	Total	a+c	b+d	a+b+c+d

From the 2x2 contingency table above (Table 4.6), phi is calculated with the following formula:

$$\Phi = \frac{ad - bc}{\sqrt{(a + d)(a + c)(b + d)(c + d)}}$$

For this study, a, b, c, and d represented cell frequencies for the presence and absence of each thoracic lesion investigated (manubrial, rib, and vertebral lesions). Since phi is expressed as a correlation coefficient (r), phi has a theoretical range between -1 and +1,

where a value of zero indicates that an association between the two variables does not exist (Molto, 1979; Brown, 2013). A score of -1 or +1 would indicate a perfect correlation between the two variables assessed such that a score of -1 would suggest that the two variables never occur together and a score of +1 would indicate that the two variables always occur together (Thomas, 1976; Brown, 2013).

The phi-coefficient was used specifically for testing the correlation existing between manubrial lesions and other thoracic lesions indicative of tuberculosis, such as rib lesions and vertebral lesions. The phi-coefficient tests, when sufficient data were available, were done to detect correlations at the 0.05 confidence level. The phi-coefficient was conducted using SPSS Statistics Desktop 21.0.0.

Chi-square

The chi-square statistical test uses categorical data (or nominal data) and proportions of raw counts (Drennan, 2010) to determine whether or not an association exists between variables. Unlike the odds ratio and the phi-coefficient, the chi-square test is not limited to a 2x2 contingency table. A set of observations is divided into mutually exclusive categories and proportions for each category are calculated (Shennan, 1997; Drennan, 2010). The chi-square statistic is similar to a standard deviation, but instead of deviations from a mean, it is a measure of how much deviation there is between observed values from expected values (Shennan, 1997; Moores et al. 2009). The expected values are based on theoretically derived expectations. The assumption with chi-square is that the sample must be randomly selected (Shannan, 1997). Chi-square is calculated as follows:

$$\chi^2 = \sum \frac{(O_i - E_i)^2}{E_i}$$

where O_i = the observed value of a cell in a contingency table, and E_i = the expected value for that same cell in a contingency table. In the event of any discrepancies between the odds ratio and 95% confidence interval (i.e. odds ratio of 2 and higher but a 95% confidence interval encompassing (or marginally encompassing) a 1), the chi-square was

used as a second manner to test whether an odds ratio value was statistically significant or not. The chi-square tests were run to detect statistical significance at the 0.05 confidence level. The chi-square test was conducted using SPSS Statistics Desktop 21.0.0

Summary

This chapter has provided an overview of the Luis Lopes skeletal collection and has situated the geographic and health conditions the people in this collection lived in. The detailed demographic documentation and good preservation of skeletal material of the skeletal collection have proven why the Luis Lopes skeletal collection is more than suitable for the present study. The manner in which the sample was selected shows that each individual was randomly selected and the means of skeletal analysis shows that this study is done in blind (with reference to disease diagnosis), minimizing the amount of bias during analysis. This chapter has also provided a brief overview of the statistical methods that will be used to determine the associations linked to sternal porosity, thereby elucidating the possible etiology of lattice porosity on the posterior surface of the manubrium.

Chapter 5

5 Results

This chapter provides the results of the macroscopic analysis conducted to assess the relationship between manubrial porosity and disease. Two primary null hypotheses are being tested in this chapter. The first null hypothesis (H_0^1) is that there will be no association between pulmonary disease (as a general category) and the presence of manubrial lesions. The second null hypothesis (H_0^2) is that pulmonary tuberculosis will not have a stronger association with manubrial lesions compared to other pulmonary diseases.

First, prevalence data on the presence of manubrial porosity in the Luis Lopes Collection will be provided, as well as the prevalence of manubrial porosity with respect to cause of death. The results of statistical tests determining the strength of association between cause of death and porosity on the posterior surface of the manubrium will be presented. Other variables such as age, sex, biomechanics, and normal variations in sternal morphology, have the possibility of confounding the results pertaining to cause of death. Therefore, prevalence data and strength of association for each confounding variable are provided in this chapter. The results examining whether or not manubrial lesions co-occur with tuberculous rib and vertebral lesions will also be presented. Detailed analysis of the results presented in this chapter will be discussed further in Chapter 6 in addition to inferences on the possible etiology of manubrial lesions.

5.1 Cause of Death

Manubrial porosity is present in 39% (60/154) of the sample in the Luis Lopes Collection (Figure 5.1). For the purpose of this (and subsequent) chapter(s), a manubrial lesion score of 2 and higher represents the presence of abnormally appearing manubrial porosity and scores of 0 and 1 represent the absence of abnormally appearing manubrial porosity, as per Sanchez et al. (2012). The data were separated into presence and absence because the

odds ratio test of association can only be calculated for a 2 by 2 contingency table. The 154 individuals analyzed were separated into two broad causes of death categories: pulmonary and non-pulmonary causes of death. The pulmonary category was further divided into a tuberculosis category, which included all individuals that died specifically from pulmonary tuberculosis, and non-tuberculosis, which included individuals that died from all other pulmonary related diseases such as pneumonia and bronchitis. The non-pulmonary cause of death group was further divided into: cardiovascular, extra-pulmonary tuberculosis, neoplasm (e.g. colon cancer), non-tuberculous infection (e.g. typhoid fever, meningitis, etc.), organ (e.g. cirrhosis), and other (e.g. senility).

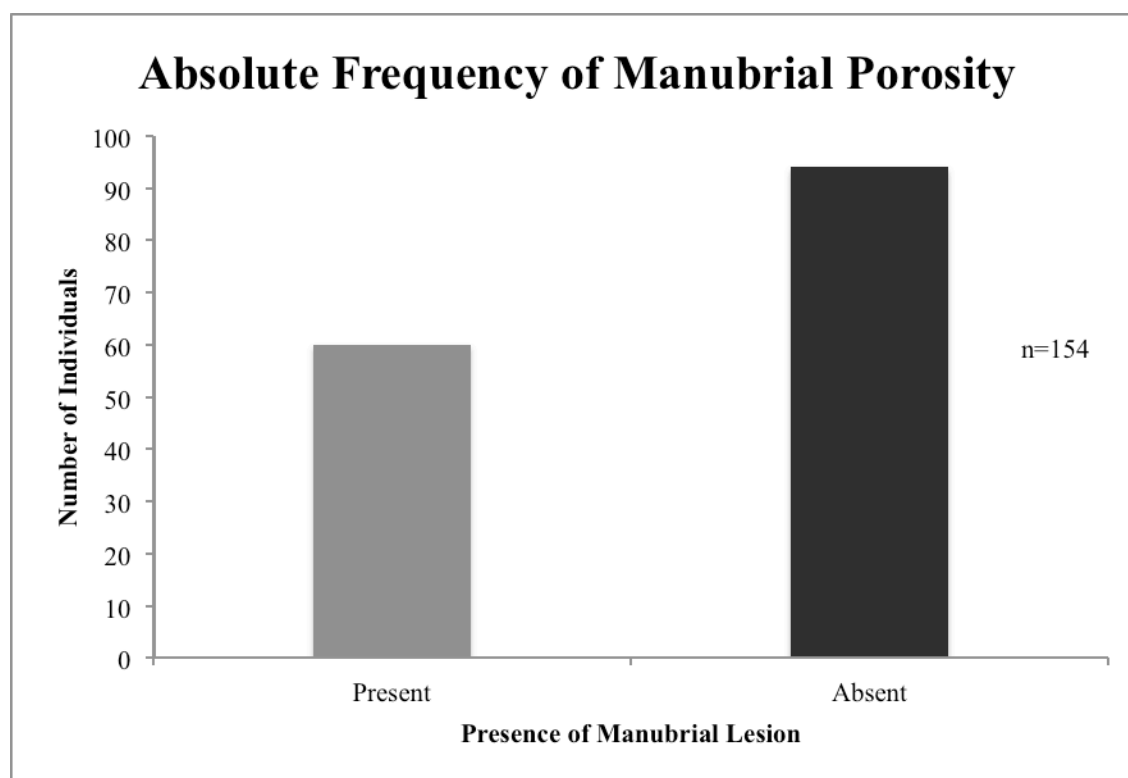


Figure 5.1: Absolute frequencies depicting the number of individuals with and without manubrial lesions in the Luis Lopes Collection regardless of age and sex

The pulmonary cause of death group exhibited manubrial lesions at a relative frequency of 40.5% (17/42), while the relative frequency of individuals with a non-pulmonary cause of death that exhibited manubrial lesions was 37% (40/108) (Figure 5.2). Of 29 individuals whose cause of death was recorded as pulmonary tuberculosis, a relative frequency of 34.5% (10/29) of individuals had manubrial lesions compared to 54% (7/13) of individuals with non-pulmonary tuberculous causes of death (Figure 5.3).

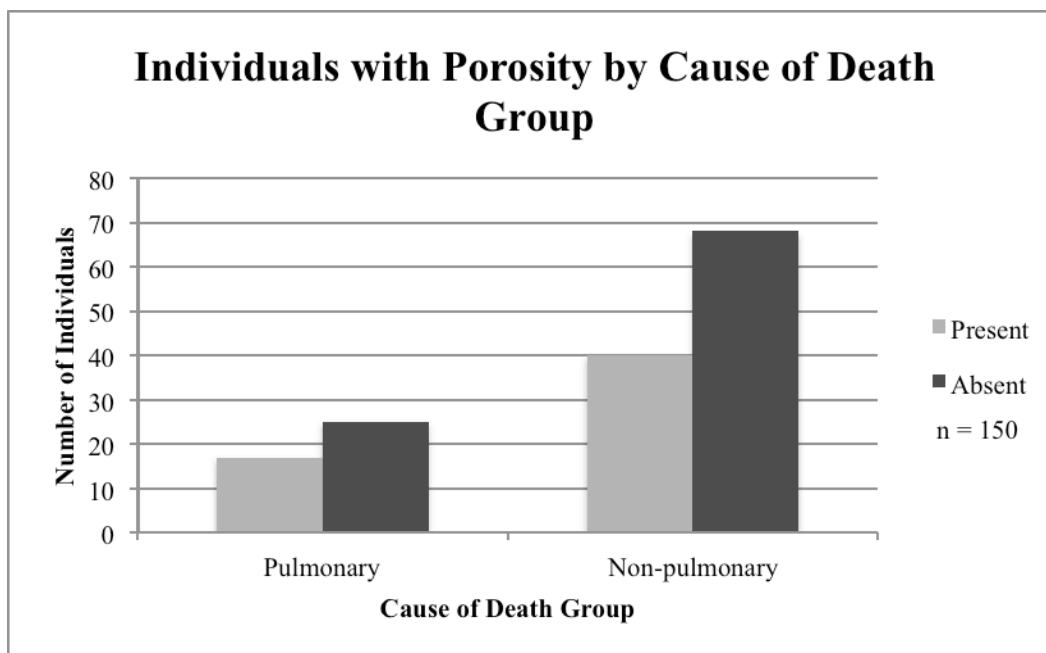


Figure 5.2: Absolute frequencies of individuals with and without manubrial lesions by cause of death, regardless of age and sex

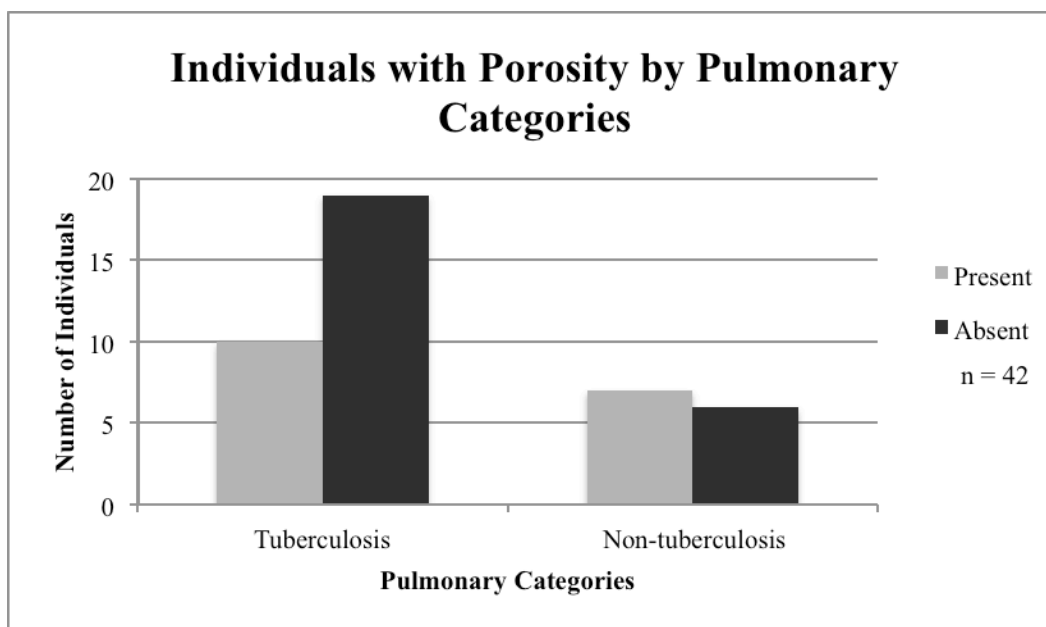


Figure 5.3 Absolute frequencies of individuals with and without manubrial lesions within the pulmonary cause of death group, regardless of age and sex

Within the six non-pulmonary cause of death categories, the relative frequencies of individuals with manubrial lesions are: 29% (2/7) for individuals with extra-pulmonary tuberculosis, 34% (11/32) of individuals in the cardiovascular group, 43% (6/14) percent

of individuals with some form of cancer (neoplasm), 38.5% (5/13) of the non-tuberculosis infection group, 32% (8/25) of the organ group, and 47% (8/17) of the other category (Figure 5.4).

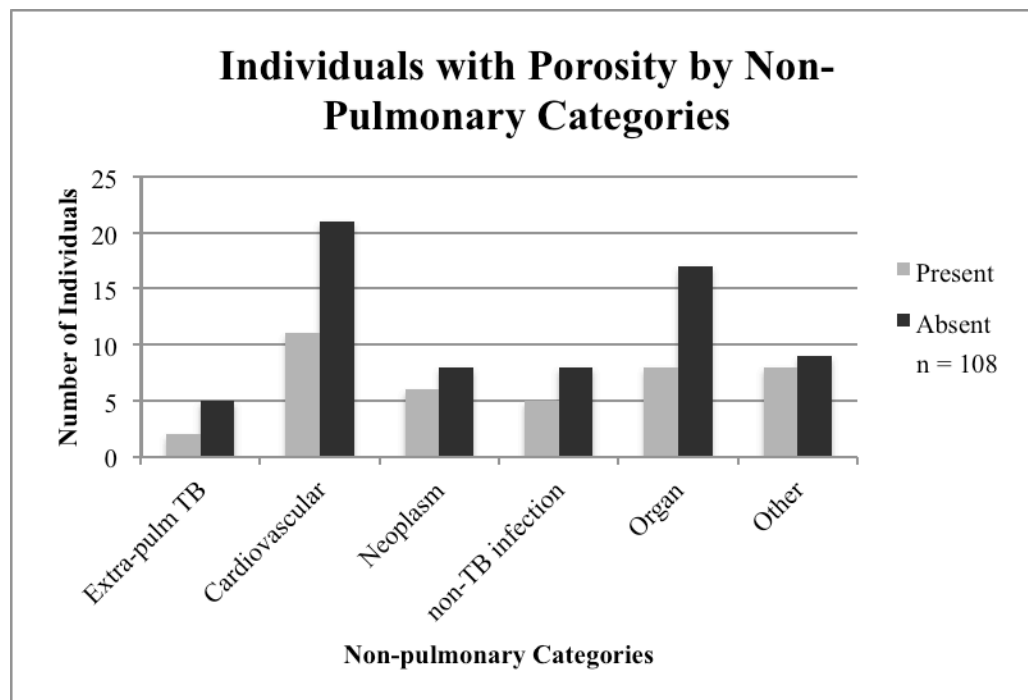


Figure 5.4: Absolute frequencies of individuals in the non-pulmonary cause of death category with and without manubrial lesions regardless of age or sex

In order to determine the strength of association between the cause of death categories and manubrial lesions, odds ratio and 95% confidence interval statistical tests were conducted. There were no statistical associations between cause of death groups (pulmonary vs. non-pulmonary groups) or pulmonary groups (tuberculosis vs. non-tuberculosis groups) and the presence of manubrial lesions (Table 5.1). A chi square test of significance was conducted for the pulmonary group since the confidence interval encompasses a value of 1.00, which would suggest unity, but the odds ratio has a value over 2. The result of the chi-square test suggests that the association between the non-tuberculous pulmonary disease and manubrial lesions is not statistically significant ($\chi^2 = 1.40$, p -value = 0.237). When testing for strength of association between individuals with pulmonary tuberculosis and the various non-pulmonary causes of death (e.g. cardiovascular or neoplastic groups), no associations were observed (Table 5.2).

Table 5.1: Odds ratio results when testing the strength of association between cause of death groups and the presence/absence of manubrial lesions

Cause of Death group	Odds Ratio	95% confidence interval	
		Lower	Upper
Pulmonary vs. non-pulmonary	1.16	0.56	2.40
Non-tuberculosis vs. tuberculosis	2.2	0.59	8.40

Table 5.2: Odds ratio results when testing the strength of association between the presence and absence of manubrial lesions in pulmonary tuberculosis against non-pulmonary causes of death

Non-Pulmonary Cause of Death	Odds Ratio	95% confidence interval	
		Lower	Upper
Cardiovascular	1.01	0.35	2.89
Non-tuberculous infection	0.84	0.22	3.26
Neoplasm	0.70	0.19	2.59
Extra-pulmonary TB	1.32	0.22	8.04
Organ	1.12	0.36	3.49
Other	0.59	0.17	2.01

5.2 Age and disease correlations

The 154 individuals examined for this thesis were separated into four age categories for statistical testing: child (birth-12), adolescent (13-20), young adult (21-35), and older adult (35+). Manubrial porosity was present in 22% (2/9) of children, 69% (11/16) of adolescents, 38% (11/29) of young adults, and 35% (35/100) of older adults (Figure 5.5).

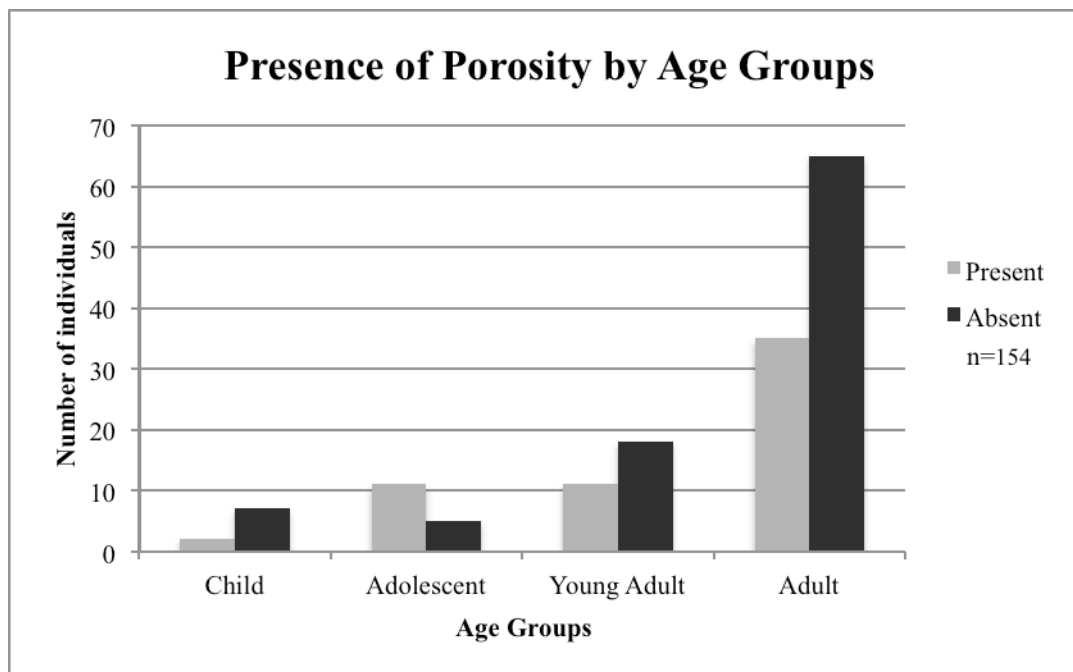


Figure 5.5: Distribution of individuals with and without manubrial lesions by age categories

Odds ratio and 95% confidence interval statistical tests were conducted to assess the strength of association between age cohorts and the presence of manubrial lesions. A strong statistically significant association was determined to exist between the adolescent age group and manubrial lesions when compared to all other age groups (Table 5.3), but no other age cohort demonstrated a statistically significant association (Table 5.4). A chi square test of significance was used for the adolescent versus young adult cohort since the 95% confidence interval marginally encompasses a value of 1.00, which would suggest unity, but has an odds ratio well over 2. The result of the chi-square test suggests that the strong association between the adolescent cohort and manubrial lesions is statistically significant ($\chi^2 = 3.92$, $p = 0.048$) when compared to young adults.

Table 5.3: Results of odds ratio and 95% confidence statistical tests when comparing the presence of manubrial lesions in the adolescent cohort against other age cohorts.

Age Group	Odds Ratio	95% confidence interval	
		Lower	Upper
Adolescent vs. Child	7.7*	1.16 ^a	51.17

Adolescent vs. Young Adult	3.6*	0.99	13.16
Adolescent vs. Older adult	4.09*	1.31 ^a	12.70

*Strong association

^a Statistically significant

Table 5.4: Results of odds ratio and 95% confidence statistical tests when comparing the presence of manubrial lesions in all other age cohorts.

Age Group	Odds Ratio	95% confidence interval	
		Lower	Upper
Young Adult vs. Child	2.14*	0.38	12.20
Young Adult vs. Older Adult	1.14	0.48	2.67
Older Adult vs. Child	1.88	0.37	9.56

* Strong association

Fifty-six individuals assessed in this research died from some sort of infectious disease. The strength of association between age and having died from tuberculosis was assessed to test the hypothesis that tuberculosis is predominantly contracted in childhood. Seventy-one percent (5/7) of children died of pulmonary tuberculosis, 92% (11/12) of adolescents had pulmonary tuberculosis as a cause of death, 80% (12/15) of young adults died of pulmonary tuberculosis, and 36% (8/22) of adults had pulmonary tuberculosis listed as a cause of death.

The odds ratio and 95% confidence interval suggest that a strong association exists between all younger cohorts having a greater probability of dying from tuberculosis compared to older adults (Table 5.5). This strong association is statistically significant at the 0.05 confidence level for the adolescent and young adult cohorts since the confidence intervals do not encompass a value of 1.00, which would suggest unity. While a strong association was determined to exist between the child cohort and having tuberculosis when compared to the older adult cohort (OR = 4.38), this relationship is not statistically significant as determined by the 95% confidence interval. A chi-square test of significance confirms the lack of statistical significance ($\chi^2 = 2.64$, $p = 0.104$). Although the adolescent cohort has a strong association with having tuberculosis as a cause of death when compared to the child and young adult cohorts (Table 5.6), these results are

not statistically significant as determined by the 95% confidence interval. A chi-square test of significance confirms the lack of statistical significance ($\chi^2 = 1.36$, $p = 0.243$; $\chi^2 = 0.719$, $p = 0.396$, respectively).

Table 5.5: Odds ratio and 95% confidence interval results assessing the strength of association between the younger age cohorts against older adults and having tuberculosis as a cause of death

Age Group	Odds Ratio	95% confidence interval	
		Lower	Upper
Child vs. Older Adult	4.38*	0.68	27.98
Adolescent vs. Older Adult	19.25*	2.08 ^a	177.92
Young Adult vs. Older Adult	7.0*	1.51 ^a	32.48

*Strong association

^a Statistically significant results

Table 5.6: Odds ratio and 95% confidence interval results assessing the strength of association between age and having tuberculosis as a cause of death

Age Group	Odds Ratio	95% confidence interval	
		Lower	Upper
Adolescent vs. Child	4.4*	0.32	60.61
Adolescent vs. Young Adult	2.75*	0.25	30.51
Young Adult vs. Child	1.6	0.20	12.69

*Strong association

5.3 Sex

When assessing the presence of manubrial lesions by sex, females exhibited porosity on the posterior surface of the manubrium at a relative frequency of 37.7% (29/77). Males exhibited manubrial porosity at a comparable relative frequency to females, 39.0% (30/77).

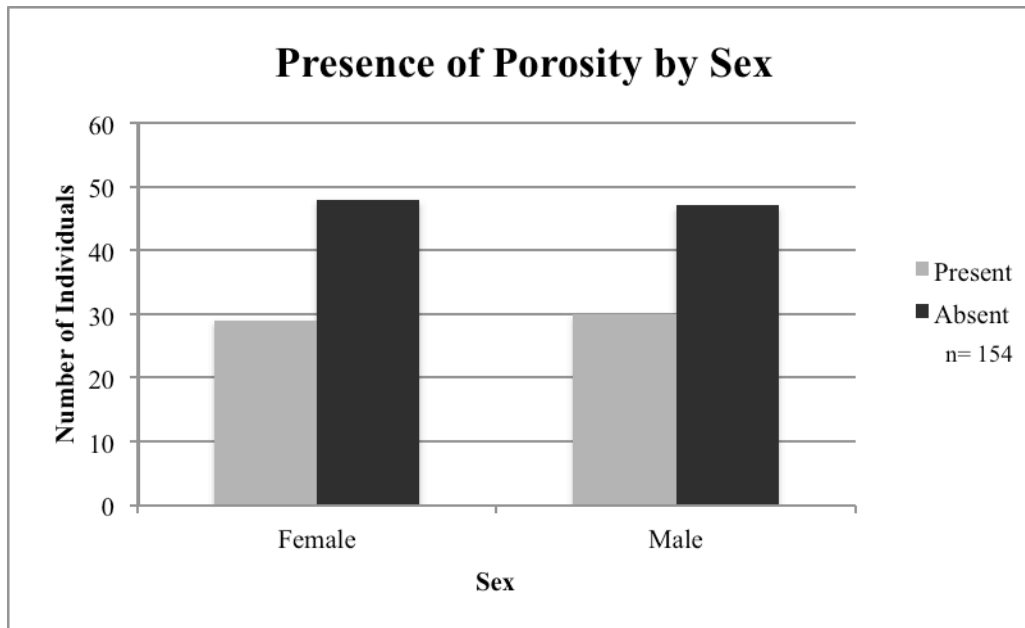


Figure 5.6: Absolute frequencies of males and females that do and do not exhibit manubrial lesions.

The results of the odds ratio and 95% confidence interval tests of association suggest that no association exists between the sex of an individual and the presence of manubrial lesions (Table 5.7).

Table 5.7: Results of odds ratio and 95% confidence interval statistical tests assessing the strength of association between sex and manubrial lesions

Sex	Odds Ratio	95% confidence interval	
		Lower	Upper
Male	1.06	0.55	2.02
Female			

5.4 Biomechanics

In order to control for potential biomechanical influences that may result in web-like porosity on the manubrium, the presence of manubrial lesions was assessed for each robusticity score of the pectoralis major insertion site on the humerus. Thirty-six percent (4/11) of individuals with a robusticity score of zero had manubrial lesions, 50% (12/24) of individuals with a R1 robusticity score had manubrial lesions, 42% (14/33) of individuals with a score of R2 exhibited manubrial lesions, and 35% (23/66) of individuals with a R3 score had manubrial lesions present. As illustrated in Figure 5.7,

there is a slight increase in the absolute frequency of individuals with manubrial lesions as the robusticity score increases.

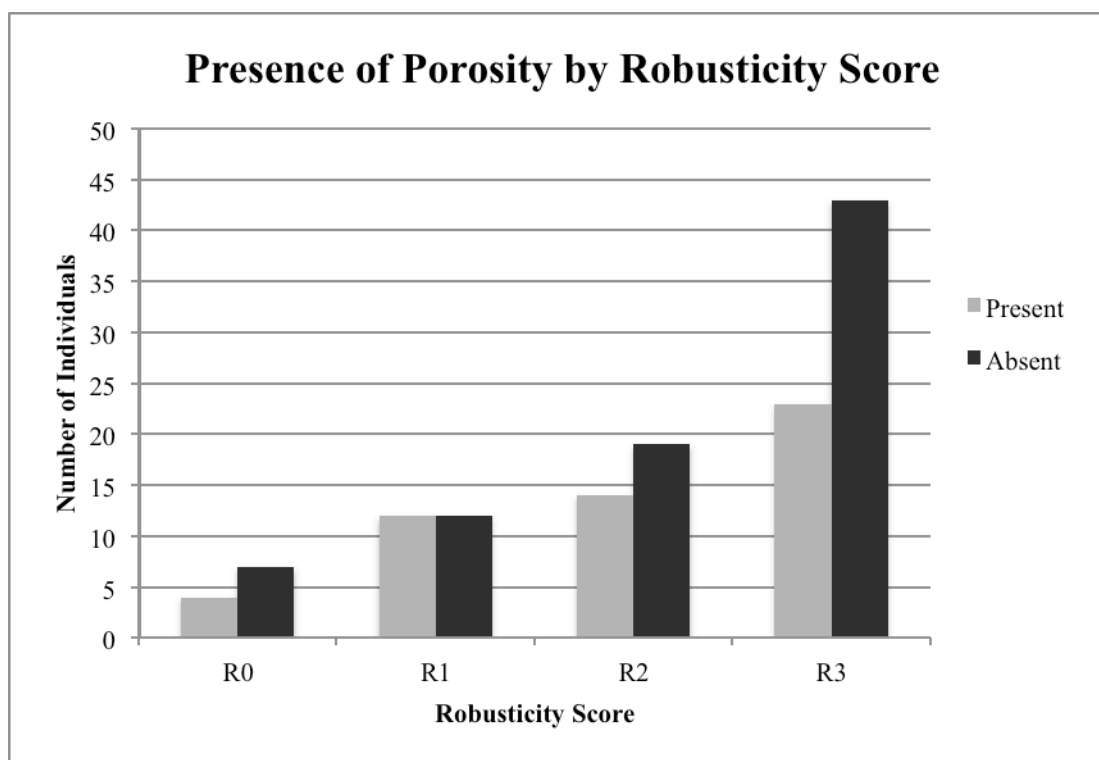


Figure 5.7: Absolute frequencies of individuals with and without manubrial lesions in relation to pronounced pectoralis major MSM on the left humerus

Similarly, the presence of manubrial lesions was assessed in relation to each stress lesion score associated with the pectoralis major MSM on the humerus. Forty-seven percent (29/62) of individuals with a stress score of zero had manubrial lesions, 36% (13/36) of individuals with a S1 stress score exhibited web-like porosity on the posterior surface of the manubrium, 39% (7/18) of individuals with a stress lesion score of S2 also had manubrial lesions, and 30% (3/10) of individuals with a S3 stress score exhibited manubrial lesions. Figure 5.8 illustrates a slight decrease in the absolute counts of individuals with manubrial lesions and increasing stress lesion score severity.

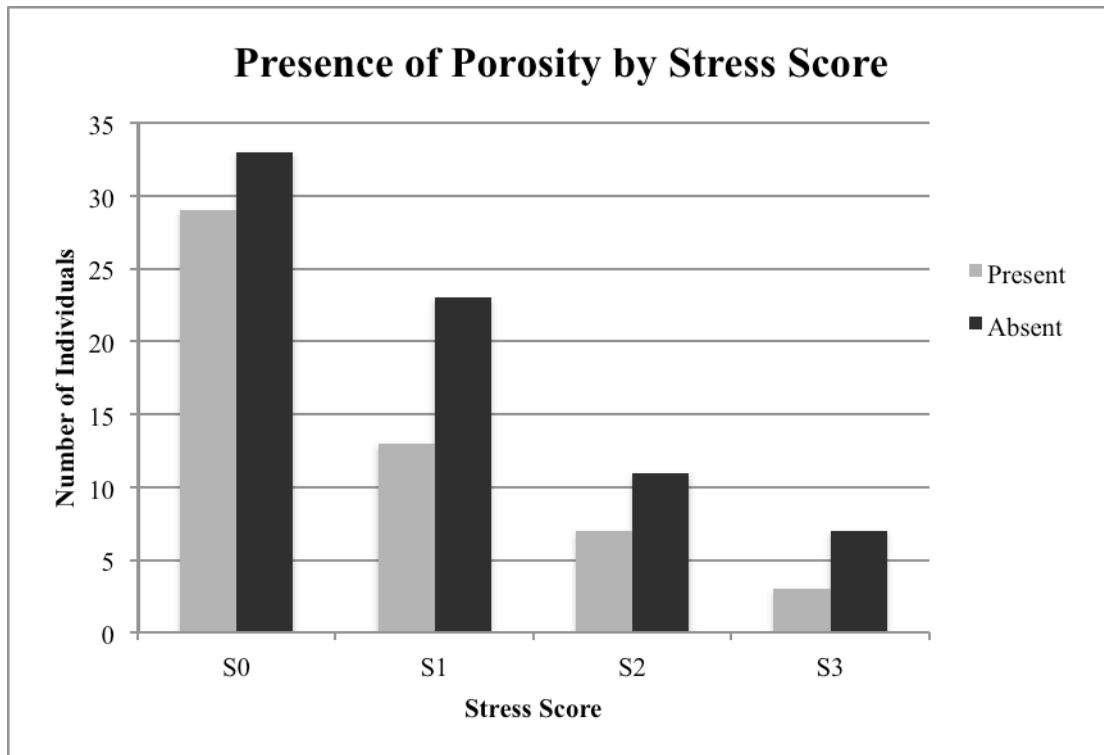


Figure 5.8: Absolute frequencies of individuals with and without manubrial lesions with respect to the presence of micro-fractures on the left humerus

The results of the odds ratio and 95% confidence interval for the pectoralis major MSMs on the humerus demonstrates that there is no association existing between robusticity score or stress score and the presence of manubrial lesions. The results of the odds ratio and 95% confidence interval for robusticity score and stress lesion score are presented in Table 5.8 and Table 5.9 respectively.

Table 5.8: Odds ratio and 95% confidence interval results for strength of association between pronounced MSMs for the pectoralis major on the left humerus and manubrial lesions.

Robusticity Score	Odds Ratio	95% confidence interval	
		Lower	Upper
R0 vs. R1	0.57	0.13	2.48
R1 vs. R2	1.36	0.47	3.91
R2 vs. R3	1.38	0.59	3.24

Table 5.9: Odds ratio and 95% confidence interval results assessing the strength of association between presence of muscular microfractures and manubrial lesions.

Robusticity Score	Odds Ratio	95% confidence interval	
		Lower	Upper
S0 vs. S1	1.56	0.67	3.61
S1 vs. S2	0.89	0.28	2.85
S2 vs. S3	1.49	0.29	7.74

5.5 Sternal Variations

Sternal Shape

One hundred and eighteen individuals had a complete sternum available to assess for sternal shape. Forty-four percent (23/52) of individuals with a sternal shape I exhibited manubrial lesions, 50% (18/36) of individuals exhibiting a sternal shape II also exhibited manubrial lesions, and 13% (4/30) of individuals with a sternal shape III had web-like porosity on the posterior surface of the manubrium (Figure 5.9).

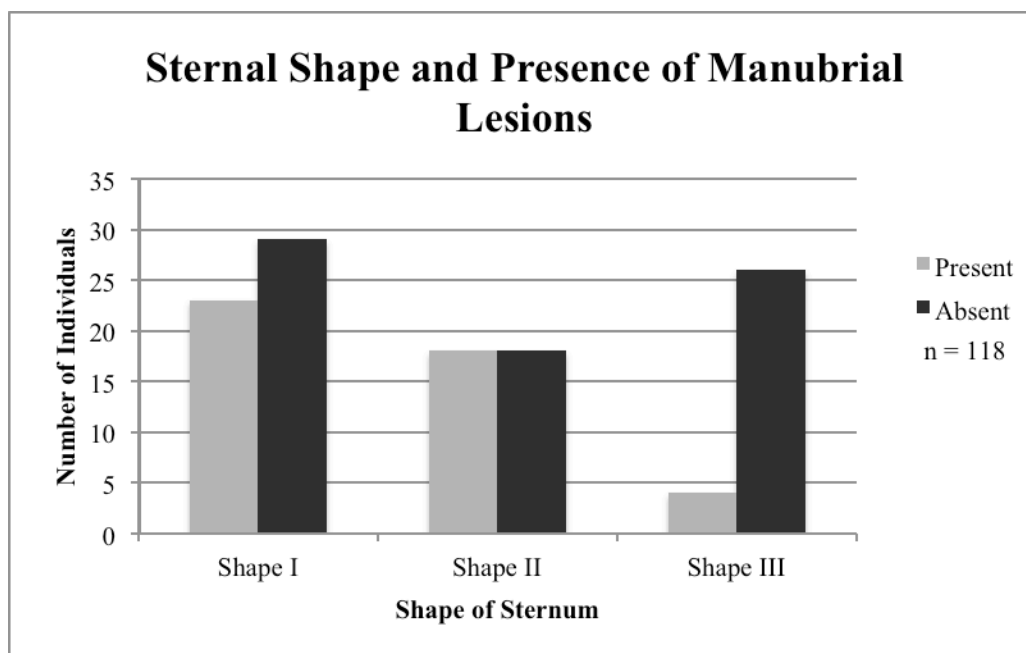


Figure 5.9: Absolute frequencies of individuals with and without manubrial lesions with respect to the shape of the sternal body

The results of the odds ratio test of association and 95% confidence interval suggest that a strong positive association exists between sternal body shapes I and II and the presence of manubrial lesions when compared to sternal body shape III (Table 5.10). The associations between the sternal shapes I and II and manubrial lesions is statistically significant at the $p=0.05$ level since the confidence interval does not encompass a value of 1.00, which would suggest unity. Given these results, as well as the fact that the prevalence of sternal porosity in individuals with a sternal shape III is much lower than in those individuals with sternal shapes I and II, it is evident that there is a marked lack of manubrial porosity expression in sternal shape III.

Table 5.10: Results of odds ratio and 95% confidence interval for the relationship between the shape of the sternum and the presence of manubrial lesions

Sternal body shape	Odds Ratio	95% confidence interval	
		Lower	Upper
Shape II vs. Shape I	1.26	0.54	2.96
Shape II vs. Shape III	6.5*	1.88 ^a	22.44
Shape I vs. Shape III	5.16*	1.57 ^a	16.89

*Strong association

^a Statistically significant

Fusion of Sternum

In order to determine if fusion between the manubrium and the sternal body has any effect on the presence of manubrial lesions, the strength of association between these two variables was assessed. Seventeen percent (4/23) of individuals exhibiting manubrial-body fusion also exhibited manubrial lesions, while 42% (55/131) of individuals without manubrial-body fusion showed evidence of manubrial lesions (Figure 5.9).

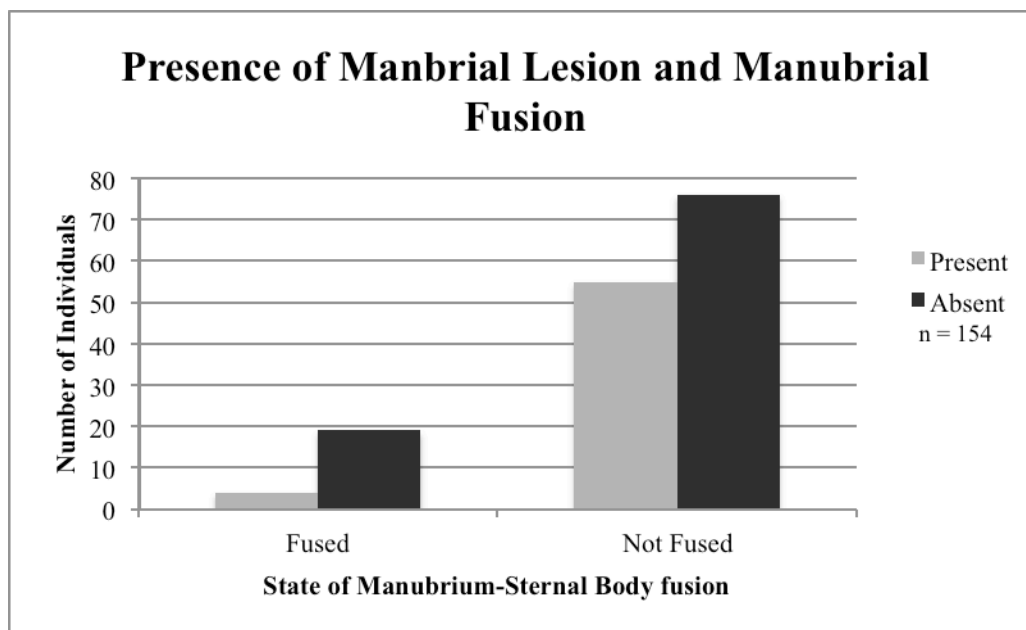


Figure 5.10: Absolute frequencies illustrating the presence and absence of manubrial lesions based on whether or not the manubrium is fused to the sternal body

Statistical tests assessing the strength of association between the fusion of the manubrium to the sternal body and the presence of manubrial lesions suggests that there is no association existing between the two variables (Table 5.11). The 95% confidence interval further demonstrates the extent of the weak association between the two variables.

Table 5.11: Odds ratio and 95% confidence interval results for manubrium-body fusion and the presence of manubrial lesions

Fusion state	Odds Ratio	95% confidence interval	
		Lower	Upper
Manubrium-body fusion	0.29	0.094	0.90
Manubrium-body non-fusion			

Other Sternal Variants

Of the 118 individuals with a complete manubrium and sternal body, only three individuals had a sternal foramen, none of which exhibited manubrial lesions. From the 154 individuals with a manubrium, eight individuals had the presence of suprasternal ossicles, four of which also exhibited web-like porosity on the posterior surface of the

manubrium. Given the low number of individuals with each trait, odds ratios and 95% confidence intervals were not calculated to assess the strength of association between sternal foramen or suprasternal ossicles and manubrial lesions.

5.6 Thoracic lesion co-existence

In order to assess the co-existence of thoracic lesions indicative of tuberculosis and manubrial lesions, the phi-coefficient was used. Analysis of all individuals who died from tuberculosis shows that no one exhibited “classic” tuberculous lesions in the thorax (e.g. Pott’s disease). Individuals with tuberculosis do exhibit non-specific lesions believed to have some degree of association with tuberculosis, such as rib lesions on the visceral surface. However, individuals who died from other pulmonary diseases unrelated to tuberculosis also exhibit rib lesions on the visceral surface (see Appendix B). Table 5.12 illustrates a 2x2 contingency table with absolute frequencies of individuals with both left rib lesions and manubrial lesions, with neither type of lesion, and with only one type of lesion. The association between left rib lesions on individuals with tuberculosis and manubrial lesions being present in unison resulted in a non-statistically significant relationship at the $p = 0.05$ level ($\phi = 0.141$, $p\text{-value} = 0.081$). An odds ratio and 95% confidence interval assessing the relationship resulted in a non-statistically significant association (Odds Ratio = 2.74, 95% CI = 0.85, 8.81).

Table 5.12: 2x2 contingency table for phi-coefficient assessing the co-occurrence of tuberculous rib lesions and manubrial lesions in individuals with pulmonary tuberculosis

		Left Ribs Lesions		
		Absent	Present	Total
Manubrial Lesions	Absent	89	5	94
	Present	52	8	60
	Total	141	13	154

A phi-coefficient was not calculated for the presence of both manubrial and vertebral lesions because there was an absence of vertebral lesions indicative of tuberculosis (e.g. Pott’s disease).

Summary

By using the odds ratio, 95% confidence interval, and chi square statistical tests, this chapter has demonstrated that statistically significant relationships exist between manubrial porosity and adolescence compared to all other age groups and between manubrial porosity and type I and II sternal shapes compared to type III sternal shape. In terms of a relationship between age and dying from tuberculosis compared to other infectious diseases, the odds ratio and 95% confidence interval showed that a statistically significant relationship exists with all the younger cohorts compared to the older adult cohort. Apart from the tests aforementioned, no statistically significant relationships were found with manubrial porosity. These results will be discussed in detail in the following chapter.

Chapter 6

6 Discussion

Paleopathological studies continue to develop and refine diagnostic criteria for the skeletal identification of diseases in order to identify the presence of specific diseases, such as pulmonary tuberculosis, in past populations. Investigations into the incorporation and utilization of skeletal elements not often considered useful for garnering evidence of disease may in fact prove to be fruitful. The use of multiple skeletal elements to diagnose diseases in the past is especially important in archaeological contexts of commingled burials, where complete articulated skeletons cannot be assembled, and for taphonomic conditions that result in the poor preservation of skeletal remains.

Taking the results presented in Chapter 5 into consideration and the null hypotheses proposed in Chapter 1 of this thesis, this chapter discusses the utility the sternum may have in paleopathology with regard to the diagnosis of pulmonary tuberculosis. This chapter addresses the results of the relationship between manubrial lesions and disease as seen in the Luis Lopes Skeletal Collection. The relationship between the presence of manubrial porosity and confounding factors such as age, sex, biomechanics, and growth and development will be discussed and interpreted. Finally, a discussion regarding the likelihood of encountering multiple lesions throughout the thorax (e.g. rib lesions, manubrial lesions, and/or vertebral lesions) in individuals with tuberculosis will be provided. By discussing all factors potentially affecting the level and severity of porosity on the posterior surface of the manubrium, this chapter attempts to shed light on the etiology of web-like porosity on the manubrium.

6.1 The Sternum and Paleopathology

Web-like porosity on the posterior surface of the manubrium was present in the Luis Lopes Skeletal Collection at a relatively moderate prevalence (38%). The prevalence of manubrial lesions observed in the Luis Lopes Collection is comparable to the prevalence

assessed in a preliminary study conducted by Sanchez et al. (2012) on the Grant Skeletal Collection, also of European origin (prevalence = 30%) but with a smaller sample size (n=80). The overall pattern of this study suggests that individuals with a pulmonary disease as a cause of death have a slightly higher, but not statistically significant, prevalence of manubrial lesions compared to individuals with a non-pulmonary cause of death (~41% and 37% respectively). Sanchez et al. (2012) observed a similar trend, but to a lesser extent, where the prevalence of manubrial lesions in the Grant Collection was only 2% higher in the pulmonary group compared to the non-pulmonary group (31% and 29% respectively). Despite the apparent difference in this study, the difference is not statistically significant, thus individuals with pulmonary disease are not more likely to have manubrial lesions compared to individuals with non-pulmonary diseases, as demonstrated through the odds ratio and 95% confidence interval tests.

Within the pulmonary cause of death group, it was demonstrated that individuals with a non-tuberculous pulmonary cause of death have a higher (but not significant) prevalence of manubrial lesions compared to individuals with tuberculosis (54% and ~35% respectively). This trend contrasts to that found by Sanchez et al. (2012), where individuals with tuberculosis had a higher prevalence of manubrial lesions compared to individuals with non-tuberculous pulmonary diseases (~36% and 27% respectively). The trend observed in this study, however, is not statistically significant as demonstrated by the results from the odds ratio and 95% confidence interval tests. The lack of a significant relationship between manubrial lesions and disease (pulmonary disease broadly speaking and tuberculosis specifically) is consistent with what was found by Sanchez et al. (2012).

Furthermore, the odds ratio and 95% confidence intervals in Table 5.2 (found in Chapter 5) demonstrate that individuals with pulmonary tuberculosis are no more likely to have manubrial lesions when compared to individuals with cardiovascular diseases, non-tuberculous infections, neoplasm, extra-pulmonary tuberculosis, organ failure/complications, or other categories of cause of death. This suggests that pulmonary tuberculosis is not associated with manubrial lesions, not only compared to other pulmonary diseases, but also to diseases that are not associated with the respiratory system.

Based on the results of this study and integrating them with those from Sanchez et al.'s (2012) preliminary research, it appears that the web-like porosity on the manubrium is not associated with pulmonary disease (as a broad category) or pulmonary tuberculosis at a statistically significant level and, thus, is not likely to be an early manifestation of pulmonary tuberculosis. Therefore, it is more likely that the presence of web-like porosity on the posterior surface of the manubrium is the result of morphological variation that can occur normally between individuals. If this is the case, this study, in conjunction with Sanchez et al. (2012), has demonstrated that manubrial porosity can be expressed in various ways, which are outlined in the scoring system devised by Sanchez et al. (2012) (see Table 4.2 in Chapter 4). In this study, however, it was only possible to assign manubria to one of four porosity scores (scores 0-3), as a porosity score of 4 was not encountered in the Luis Lopes Collection. The absence of a manubrial porosity score of 4 may indicate that there is something different occurring between individuals of the Luis Lopes Collection and those of the Grant Collection.

The web-like porosities that are scored as a 2 or 3 (Figures 6.1 and 6.2), however, clearly demonstrate that some processes is occurring, such as an increase in vascularity (as noted by Tayles and Buckley, 2004) or a pathological process resulting in abnormal bone growth, resulting in such pronounced pores on the cortical surface of the manubrium. As a result, the possibility remains that manubrial lesions still represent, and are associated with, some sort of pathological process. For example, manubrial porosity may have an association with a secondary, or co-existing, pathological condition that would contribute to a person's morbidity but not necessarily mortality (e.g. an anemia of some sort). A scenario of this nature could explain the lack of statistical association between manubrial porosity and specific disease categories, particularly if the increased vascularity is the result of said co-occurring condition that contributes to, but does not directly cause, a person's death. Therefore, manubrial porosity still has the potential to provide information about a person's health by acting as a non-specific indicator of disease and become an indicator of some sort of nutritional insufficiency.

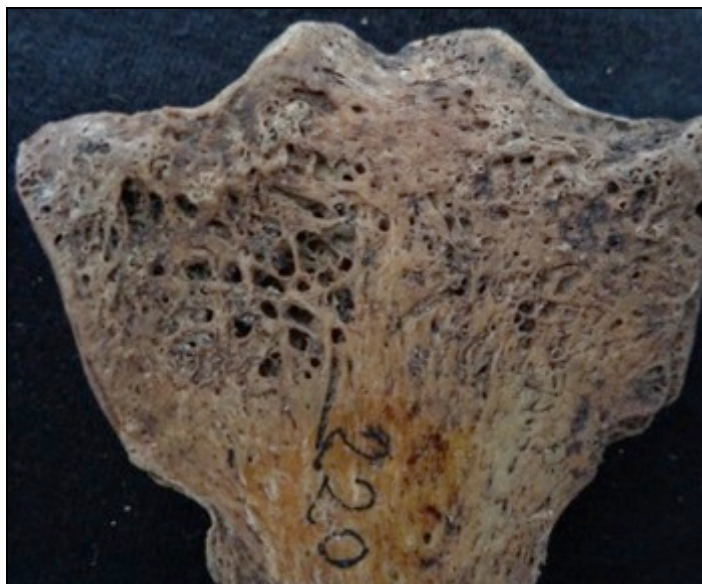


Figure 6.1: Individual #220, a 52-year-old female who died of heart failure exhibiting a manubrial porosity score of 2



Figure 6.2: An example of a manubrial porosity score 3, Individual #405 was a 32-year-old male whose cause of death was recorded as brain laceration

Another factor that could account for the statistically non-significant relationship between manubrial porosity and tuberculosis is differences in diagnosis of tuberculosis in the past and present. In the absence of commonly used methods to diagnose a patient with tuberculosis, such as sputum smear, bacterial cultures, and chest radiographs (Palomino,

2005; Marais and Pai, 2005; Davies and Pai, 2008; Lange and Mori, 2010), the diagnosis of tuberculosis based on symptoms alone can prove to be difficult. Symptoms exhibited by individuals with tuberculosis are considered to be non-specific and can mimic, and be mimicked by, a plethora of other respiratory conditions (Lange and Mori, 2010). Even if chest radiographs are used, diagnosis of tuberculosis cannot be definitely ascertained. The most common method of positively diagnosing tuberculosis in a patient is through sputum smears or bacterial cultures; therefore, radiography is also considered to be a non-specific method for assessing tuberculosis (Davies and Pai, 2008). While the exact method of diagnosis (e.g. chest radiography) in the Luis Lopes Collection is unclear, the individuals with tuberculosis were most likely diagnosed on the basis of their symptoms while hospitalized or during an autopsy if one was required or requested.

The misdiagnosis of individuals with tuberculosis in the Luis Lopes Collection could therefore confound the results observed in this study in two manners: the first by having an overestimated number of individuals with tuberculosis and the second by having an underestimated number of individuals with tuberculosis by diagnosing a tuberculous person with a non-tuberculous pulmonary disease. In either scenario, the misdiagnosis of tuberculosis could be contributing to the lack of association between manubrial porosity and tuberculosis. This limitation and confounding factor is unfortunately inherent in the collection and difficult to overcome because diagnosis of cause of death was conducted during or around the time of death for each individual. If tuberculosis can be misdiagnosed symptomatically by today's standards, it is more than possible that tuberculosis could have been misdiagnosed in late 19th to mid 20th century Portugal.

If the diagnosis of tuberculosis recorded on death certificates and medical records is accurate, it is possible that some of the 19 individuals with tuberculosis that did not exhibit manubrial porosity represent acute cases of tuberculosis. This would be an example of individuals succumbing to a disease quickly before exhibiting skeletal manifestations, exemplifying the problem with assessing the prevalence of a disease from skeletal lesions as addressed in Wood et al.'s (1992) seminal paper. Further evidence of possible cases of acute tuberculosis in the Luis Lopes Collection will be elaborated on in section 6.5 of this chapter.

6.2 Manubrial Porosity and Age

As a means of being comprehensive in this research, the association between manubrial porosity and other demographic or epigenetic factors was assessed. The results from this study have demonstrated that age is an important factor when assessing manubrial porosity. Adolescent individuals are 7.7 times more likely to exhibit manubrial porosity compared to children, 3.6 times more likely compared to young adults, and approximately 4 times more likely compared to older adults. These relationships contrast to the young adult cohort compared to the child and older adult cohorts and the older adult cohort compared to the child cohort. While the relationship between the young adult cohort exhibiting manubrial porosity compared to the child cohort is not statistically significant, young adults are still two times more likely to exhibit manubrial porosity than children. The adolescent individuals exhibiting manubrial lesions have an equal distribution of porosity scores of 2 and 3 ($n = 6$ and 5 respectively). Five of the six adolescents with a manubrial porosity score of 2 had pulmonary tuberculosis listed as a cause of death, and two of the five adolescents with a score of 3 had a pulmonary disease listed as cause of death. Since pulmonary disease accounts for 7 out of the 11 cases of manubrial porosity in adolescents, and pulmonary tuberculosis accounts for 6 cases, this age related association might not be as clear as anticipated. However, further complicating matters arise in the fact that all adolescents ($n=5$) who scored a 0 or 1 for manubrial porosity had pulmonary tuberculosis listed as a cause of death.

The spike in the adolescent cohort indicates that whatever the condition was, it likely was contracted in childhood, developing through childhood and into adolescence, subsequently killing most of the adolescent victims. This would help explain the decline in manubrial lesions prevalence in the young adult and adult cohorts. The pattern observed in this study parallels the reactivation stage of a tuberculous infection, where reactivation of the bacillus occurs during adolescence or adulthood (de Backer et al. 2006; Waldron, 2009). It is possible that the hormonal changes that occur during adolescence, in addition to the lower to middle class status of these individuals, could result in the rupture of the Ghon focus, thereby causing a reactivation of tuberculosis in

this age cohort. This would account for the high prevalence of adolescents having tuberculosis as a cause of death.

Here I argue for two possibilities occurring that could account for the high association between manubrial porosity and adolescence. The first possibility is that manubrial porosity is a result of the growth and development process of the manubrium. The manubrium generally arises from one primary ossification centre, usually located at the centre (Scheuer and Black, 2000) of what later becomes the fully formed manubrium. While more than one ossification center may occur, these “accessory” ossification centres quickly coalesce into one. Furthermore, as mentioned in Chapter 2 of this thesis, the sternum (generally speaking) is a red blood cell producing bone. In the manubrium, red marrow can be located at the center of bone, or the origin of the manubrium. Therefore, it is possible that manubrial porosity, particularly scores of 2 and 3, could represent the remnant of some sort of growth disruption that may contribute to a web-like appearance. This could provide an explanation for the manubrial porosity score of 3, given that the webbing occurs at the center of the manubrium, where the primary ossification center appears and where red bone marrow is located. Since the manubrium continues to form at age 13 (the beginning of the adolescent age cohort), with growth completing by 20 (the end of the adolescent age cohort), the proposed explanation could stand true.

The high number of adolescents with pulmonary tuberculosis as a cause of death cannot be dismissed. The second possible explanation for this statistically significant association, as mentioned previously, is that manubrial porosity may be a non-specific indicator of stress or ailment. Adolescence by today’s standard is likely different compared to what adolescence meant in late 19th to early 20th century Portugal. Indeed, three of the 11 adolescents were no longer students but had already been introduced to the work force. This observation, compounded by the fact that the individuals of the Luis Lopes Skeletal Collection represent the low to middle socioeconomic status and most adolescents had pulmonary tuberculosis, indicates that these adolescents could very likely have had some sort of nutritional deficiency, health problem(s) that did not cause death, growth faltering, a series of stressful episodes, or a combination thereof. Since this was not investigated in this study, subsequent research on manubrial porosity should seek to investigate

relationships between manubrial porosity with non-specific evidence of stress. Given any of the aforementioned possibilities, it is possible that the manubrium could react in a similar manner to skeletal elements with a similar structure, such as the cranium (a flat bone with two layers of cortical bone enclosing a layer of trabecular bone), to a pathological condition that would contribute to morbidity but not cause mortality (e.g. anemia). Since the web-like porosity is not as vigorous as that presented by Mann and Tuamsuk (2013) with the possible case of thalassemia (a genetic anemia), the porosity investigated in this thesis may represent an acquired anemia. The fact that the pronounced porosity investigated in this study is located at the center of the manubrium on the posterior surface, the general location in which red marrow is located, further supports the possibility that manubrial porosity can reflect a non-specific indicator of stress for a condition like acquired anemia.

A study by Morgan (2014) of porotic hyperostosis (interpreted to represent episodes of anemia) demonstrated a similar age profile being affected as is shown in this study. Of 13 subadult individuals (anyone <18 years old) in Morgan's (2014) study, 10 individuals had active cranial vault lesions, two had partially healing vault lesions, and only one individual had healed vault lesions. Of 24 adult individuals sampled (anyone >18 years of age), only three individuals had active vault lesions, while 21 individuals had partially or completely healed vault lesions. While the age ranges are not exactly comparable (since adolescence in this study extends to 20 years of age), the general pattern of a higher prevalence of active lesions in younger individuals may suggest that manubrial lesions may be a form of porotic hyperostosis manifesting itself on the sternum.

Age and infectious disease interact with one another, where the youngest and oldest members of a community are more susceptible and vulnerable to succumbing to disease. It has been found that the prevalence of tuberculosis is highest in childhood (Buikstra and Roberts, 2003; Roberts and Manchester, 2005). This study has demonstrated that, among all individuals dying from an infectious disease, all younger age groups are more likely to have (and succumb to) tuberculosis than older adults. The child cohort is approximately 4.4 times more likely to succumb to tuberculosis than the older adult cohort, adolescents are approximately 19 times more likely to succumb compared to older adults, and young

adults are 7.0 times more likely to succumb to tuberculosis compared to older adults. While not statistically significant, adolescents are still 4.0 and 2.75 times more likely to succumb to tuberculosis compared to children and young adults respectively. While I am not arguing that tuberculosis is *not* a childhood disease, as the tuberculosis the adolescents died from was likely contracted during childhood, the results of this study show that it is more likely that adolescents succumbed to the disease compared to children, young adults, and older adults, but that all of the younger cohorts were more likely to succumb to tuberculosis compared to older adults at a statistically significant level.

6.3 Manubrial Porosity, Sex, and Biomechanics

The statistical analysis presented in Chapter 5 demonstrated that there is no association between the sex of a person and the presence of manubrial porosity. Manubrial porosity is present in males and females at relatively similar relative frequencies (39% and 37.7% respectively). In terms of normal variations in skeletal morphology, this is to be expected since the only difference in growth and development between males and females is the rate and timing of skeletal maturity, and in the expression of secondary sex characteristics.

As described in Chapter 2, section two, the sternum as a unit anchors many muscles of the thoracic cavity and their associated soft tissues. Therefore, this study investigated the possibility that biomechanical forces exerted on the sternum by muscles could have some sort of affect on the morphology of the manubrium. Using the musculoskeletal markers on the humerus as a proxy to assess the effects that the pectoralis major could have on the manubrium's cortical bone, it was determined that no association exists between exhibiting evidence of pronounced pectoralis major use and manubrial porosity. The odds ratio and 95% confidence intervals showed that neither repetitive use (robusticity score) nor overexertion (stress score) have an affect on the cortical bone of the manubrium. This, however, is not unexpected. The pectoralis major's origin spans the entire length of the sternum and extends towards the clavicles superiorly and costal cartilage inferiorly. This broad origin likely distributes the biomechanical forces evenly throughout the origin site of the muscles, thereby not altering the morphology of the sternum in one

concentrated area. Since the insertion site of the tendon for the pectoralis major is concentrated to the lateral portion of the bicipital groove on the humerus, most of the muscular forces will act on and affect that area of the humerus. As a result, it is not surprising that the pectoralis major will primarily cause morphological alterations to the humerus and not the sternum, especially the manubrium.

6.4 Manubrial Porosity and Sternal Variations

The individuals of the Luis Lopes Skeletal Collection exhibited few variations known to exist with respect to the sternum. These variations include: the presence of all three sternal shape types, sternal foramen, suprasternal ossicles, and differing states of sternal fusion, that is manubrium-body fusion. It was demonstrated in Chapter 5.5 that a strong association exists between Type I and II sternal shapes and porosity compared to Type III sternal shape. The odds ratio showed that individuals with Type I sternal shape are approximately five times more likely to exhibit manubrial porosity compared to those individuals with Type III sternal shape. Type II sternal shapes are six and a half times more likely to exhibit manubrial porosity compared to individuals with Type III sternal shape. Conversely, it was determined that individuals with Type II are no more likely to exhibit manubrial porosity compared to individuals with Type I sternal shape (OR = 1.26). Based on the higher likelihood of having manubrial porosity with Type I or II sternal shapes compared to a Type III sternal shape, in addition to the low number of individuals with Type III sternal shape exhibiting manubrial porosity (4/30), it is evident that there is a marked lack of expression of porosity in sternal shape III.

Given that there is a strong relationship between manubrial porosity and a Type I and II sternal shape, these sternal shapes *may* help predict the presence of web-like porosity on the manubrium. Conversely, the presence of a Type III sternal body may likely predict the absence of manubrial porosity. Moreover, the presence of manubrial porosity, in addition to the presence of a Type II sternal body shape, can elucidate information about the ossification pattern of a person's sternum. A Type II sternal shape has been shown to result when the first and second sternal segments are derived from a single, mid-sagittally placed ossification center. The third and fourth sternal segments are derived from two bilaterally or obliquely placed ossification centers. Ashley (1956) provided a series of line

drawings that were traced from radiographs to demonstrate the “ideal”, but also variations of “ideal”, ossification patterns. The line drawings of Type II sternal shapes (both “ideal” and variant ossification patterns) presented in Ashley (1956) usually depict the manubrium of Type II sternal shapes having more than one ossification center. If Type II sternal shapes are associated with multiple ossification centers for the manubrium, it may explain the abundance of individuals with a manubrial porosity score of 2 (where there are usually two foci of web-like porosity separated by unaffected cortical bone) when having a sternal body shape of II (16/18). Should this hypothesis hold true, it would serve as evidence towards classifying manubrial porosity as normal variation. However, given the overall abundance of a manubrial porosity score of 2 ($n = 52$), the number of ossification centers of the manubrium may not fully explain the presence of manubrial porosity.

When assessing if a relationship exists between the fusion of the manubrium to the sternal body and manubrial porosity, a weak association was determined to exist (Odds Ratio = 0.29). Given that the fusion of the three separate sternal segments is quite variable (Barnes, 2012), the weak association is not unexpected. Individuals with a fused manubrium varied in age (between 15-94 years of age), showing the variable nature of manubrium fusion.

Suprasternal ossicles were exhibited at a relatively low prevalence (5%). Due to the low occurrence of suprasternal ossicles, odds ratio and 95% confidence interval tests were not conducted to determine the association between morphological variations. The low occurrence of suprasternal ossicles, however, could be a misrepresentation of their actual prevalence in the Luis Lopes Skeletal Collection. As Barnes (2012) notes, suprasternal ossicles can remain unfused to the manubrium and instead be separate bones within the interclavicular ligament. Therefore, the separated suprasternal ossicles are unlikely to be recovered during excavation. This would definitely be the case given that the workers who exhumed the individuals of the Luis Lopes Collection did not have an archaeological or bioarchaeological background (Cardoso, 2005). Consequently, there is the possibility that there could be more individuals who had suprasternal ossicles, but were not recovered during exhumation.

Last, the prevalence of a sternal foramen in this sample was lower than that of the suprasternal ossicles (2.5% or 3/118). This likely reflects one of two possibilities. The first is that it may reflect Saunders (1978) and Crubezy's (1992) claim that the sternal foramen is a relatively rare non-metric or hypostotic trait, which is why it may be used in genetic distance studies. While the rarity of the sternal foramen is likely population dependent, it would appear to be a rare trait in this particular Portuguese population. As there are no expected frequencies available for population, this cannot be assessed. The second possible explanation for the low prevalence of the sternal foramen could reflect a sampling bias. This study sampled approximately 22% of the entire Luis Lopes Collection, but approximately 44% of all individuals believed to have a complete sternum ($n = \sim 350$; Cardoso, 2013, personal communication). A larger number of individuals with a sternal body could have yielded a slightly higher number of sternal foramen than what is reported in this study.

6.5 Coexistence of thoracic lesions

The last portion of this research was to determine what relationship, if any, exists between manubrial porosity and other skeletal lesions of the thorax that are thought to be indicative of tuberculosis. For this, the phi-coefficient, odds ratio, and 95% confidence interval were all used to test whether or not an association exists between these variables and/or the strength of said association. When assessing for an association between manubrial lesions and the presence of rib lesions on the left side of the thorax in individuals with pulmonary tuberculosis, the phi-coefficient was not statistically significant at the $p = 0.05$ level. The odds ratio and 95% confidence interval also demonstrated the non-statistical significance.

This research has demonstrated that rib lesions on the visceral surface are not exclusively related/associated with tuberculosis. The lack of association between left rib lesions in individuals with pulmonary tuberculosis and manubrial porosity is likely an indication that rib lesions exhibited by individuals with pulmonary tuberculosis do not exclusively occur on the left side. This would support studies by Roberts et al. (1994) and Santos and Roberts (2001, 2006) who also found that there is no exclusive pattern between left rib lesions and pulmonary tuberculosis. While this study did not identify the exact rib where

lesions occurred, ribs were categorized as upper (ribs 1-4), middle (ribs 5-8), and lower (ribs 9-12). Rib lesions in individuals with pulmonary tuberculosis were primarily located on the mid-lower ribs, as was found by Kelley and Micozzi (1984) and Santos and Roberts (2001, 2006) who found that ribs lesions commonly occur on the middle ribs. Since the rib lesions observed in the Lisbon Collection follow this pattern, it is possible that the tuberculous infection occurred in the mid-lower lobes of the lungs. If this association is typical, then it is unlikely that there would be direct contact between the site(s) of tuberculous infection and the manubrium. This would help support the fact that manubrial porosity is not related to pulmonary tuberculosis, and is certainly not involved with direct diffusion of the tuberculous bacilli from the site of infection.

Of the 29 individuals who had pulmonary tuberculosis listed as a cause of death, no one exhibited “classic” skeletal signs of tuberculosis therefore, no statistical analysis was undertaken of vertebral or sacroiliac lesions. As represented in Appendix B, only two individual exhibited lesions on the lumbar vertebrae. One individual with vertebral lesions only had one lumbar vertebra (L5) affected and exhibited multiple (at least 4) abscesses. The second individuals had one abscess on the inferior surface of the L1 vertebra and one abscess on the superior surface of their L2 vertebra. Therefore, the only clear evidence of infection in the lumbar vertebrae is the presence of abscesses in two individuals, which is indicative of a non-specific infection. Many individuals exhibited clustered and relatively large circumferential lesions, or pores, on the lateral sides of the thoracic and lumbar vertebral bodies. As Baker (1999) proposes, the presence of circumferential lesions on the thoracic and lumbar vertebrae may represent an early manifestation of tuberculosis, as they may be associated with the tuberculous bacilli being transported to the vertebrae via the psoas muscles. However, since very little research has been done on circumferential lesions, and this pronounced vertebral porosity was not limited to individuals with tuberculosis, I argue that lesions of that nature are non-specific indicators of a *potential* pathological process beginning to occur. Due to the lack of more indicative tuberculous lesions, it is very possible that the individuals assessed in this study represent acute cases of tuberculosis. Individuals with tuberculosis did exhibit evidence of rib lesions on the visceral surface, but individuals with non-tuberculous pulmonary diseases showed similar rib lesions as well (see Appendix B).

While some tuberculous individuals exhibit rib lesions on the visceral surface, there has yet to be a concrete consensus that ribs lesions are definitely associated with pulmonary tuberculosis (Pfeiffer, 1991; Roberts et al. 1994; Santos and Roberts, 2001, 2006; Matos and Santos, 2006). No sacroiliac lesions were observed.

The evidence provided in this section points to the potential that most cases of tuberculosis analyzed from the Luis Lopes collection were cases of acute tuberculosis. It is possible then, that the individuals assessed in this study succumbed to the infection during the primary infection or shortly after the secondary or reinfection stage of the disease. If the cases of tuberculosis assessed in this study were cases of a primary tuberculous infection, the skeleton would not have been affected, thereby rendering the results pertaining to cause of death inconclusive. If the individuals experienced an acute case of a reinfection or reactivation of tuberculosis and succumbed to the disease shortly after, the skeleton, again, would not have been affected, thereby rendering the results pertaining to cause of death inconclusive.

Summary

This chapter has provided a discussion of the results found in this study. As proposed in this chapter, the lack of association between manubrial porosity and disease, the statistically significant relationship with age, and the statistically significant association with sternal shape indicate that manubrial porosity could likely be the result of normal variation. In this scenario, this research suggests that manubrial porosity can be expressed in one of four ways in the Luis Lopes Collection: 1) Not be present, 2) Take the form of pores randomly dispersed along the posterior surface, 3) Assume a web-like porosity with two foci separated by a “bridge” of unaffected cortical bone, or 4) Have one concentrated focus of web-like porosity at the center of the manubrium on the posterior surface. These morphological expressions represent the first four porosity scores devised by Sanchez et al. (2012). It has also been proposed here that the potential of a relationship between manubrial porosity and a co-occurring disease/condition contributing to morbidity cannot be dismissed. This could account for the increased and pronounced vascularity, expressed in a web-like porosity, seen in the latter two porosity scores (refer to Figure 6.1 and 6.2

above). Therefore, another possible explanation is that manubrial porosity could represent a non-specific indicator of stress/ill-health, such as acquired anemia.

Chapter 7

7 Conclusion

The main aim of this research was to determine whether or not the sternum could be incorporated into paleopathological analysis as a means of diagnosing respiratory disease, specifically pulmonary tuberculosis. This was done by assessing the relationship between a web-like porosity on the posterior surface of the manubrium and disease at the Luis Lopes Skeletal Collection. Whenever attempting to diagnose an individual with a disease, whether it is clinically or archaeologically, the ability to conduct a thorough differential diagnosis is an imperative part of the process in order to ascertain as closely as possible the disease a person was infected with, and therefore what disease or diseases a population was faced with.

Tuberculosis is a disease that has garnered much attention and its expression in terms of lesion patterns throughout the skeleton is well known. Since the primary sites of tuberculous infections are the lungs, skeletal elements of the thorax are often assessed for skeletal lesions associated with tuberculosis. The lower thoracic and lumbar vertebrae are affected by tuberculosis and lesions are identified as Pott's disease (Aufderheide and Rodriguez-Martin, 1998; Ortner, 2003; Roberts and Buikstra, 2003). Lesions on the visceral surface of ribs have been studied extensively to determine whether or not these lesions are associated with tuberculosis (Kelley and Micozzi, 1984; Pfeiffer, 1991; Roberts et al, 1994; Santos and Roberts, 2001, 2006; Lambert, 2002; Mays et al. 2002; Matos and Santos, 2006). Although the sternum is part of the skeletal "scaffolding" that encloses the thoracic cavity, it has not been studied extensively with respect to tuberculosis and has oft-been excluded from paleopathological analysis in general. With the exception of the preliminary study by Sanchez et al. (2012) that forms the basis of this current research, the sternum has not been the sole focus of a paleopathological study. However, as illustrated throughout this research, the anatomical location of the sternum and manubrium alludes to the possibility that evidence of disease, particularly

pulmonary disease, could be manifested on the sternum. This thesis, then, attempted to address the lack of research on the sternum and how it could contribute to the study of disease.

7.1 Hypotheses Addressed

This research addressed two primary null hypotheses. The first null hypothesis stated that there is no association between manubrial porosity and pulmonary disease. When testing for the strength of association between manubrial porosity and pulmonary disease, results from odds ratio and the 95% confidence interval proved that no association exists between manubrial porosity and disease on a statistical level. As a result, the null hypothesis could not be rejected.

The second null hypothesis tested in this study stated that manubrial lesions are not specifically associated with pulmonary tuberculosis. Odds ratio and 95% confidence interval statistical testing indicated that tuberculosis and manubrial porosity were not associated with one another. Therefore, the second null hypothesis investigated could also not be rejected.

7.2 Possible Etiology of Manubrial Porosity

Based on the results of the two hypotheses tested, this research proposes two etiological possibilities for manubrial porosity manifesting specifically on the posterior surface of the manubrium. Since null hypothesis 1 and 2 were not rejected through statistical testing, the first “etiology” proposed here is normal variation. Given this scenario, it is proposed that manubrial porosity can have a range of expressions when present in the Luis Lopes Collection. The porosity can be exhibited by randomly distributed porosity through the posterior surface of the manubrium as small pores. This manner of expression does not have concentrated areas of porosity. Another expression of manubrial porosity is as two foci of web-like porosity separated by a bridge of unaffected cortical bone. This form of expression can have variations where only one focus is present that is off-center and more laterally placed. Finally, another form expressed is as a single concentrated focus of web-like porosity at the center of the manubrium. These three manubrial

porosity variations represent sternal porosity scores 1-3 proposed by Sanchez et al. (2012).

Even if manubrial porosity is a result of normal variation, there must be some sort of mechanism associated that results in the creation and variable expression of the porosity. It is possible that the variations may be the result of some external factor(s) disrupting or altering the growth and development of the manubrium between individuals. Conversely, and likely more probable, there may be some sort of genetic component responsible for disrupting the growth process of the manubrium and resulting in the presence of manubrial porosity. It is also possible that the bone remodeling process creating the porosity does not have a mechanism that would help predict the form of expression the porosity will take.

The second etiology proposed as a result of this research is that manubrial porosity is caused by a pathological condition that contributes to morbidity but does not cause mortality. It is therefore possible that manubrial porosity could be a non-specific indicator of stress. This could likely account for the lack of a clear statistical association with any disease category, but instead manubrial porosity may provide evidence of synergistic relationship between mal- or under-nutrition and disease. This would explain why the porosity has an abnormal web-like appearance. Since this was not investigated in this study, future research should investigate this hypothesis. Manubrial porosity could then be used in a similar manner as enamel hypoplasias to identify stressful episodes or as porotic hyperostosis to indicate some sort of nutritional deficiency such as hyperplastic marrow conditions. Because of the issue with non-specificity, the normal variation etiological explanation cannot be ascertained to be the sole cause of the porosity.

However, as proposed in section 6.5 of this thesis, the lack of “classic” skeletal indicators of tuberculosis in those individuals with tuberculosis examined in this study suggests two possible scenarios; 1) the individuals represent acute cases of secondary tuberculosis or 2) the individuals succumbed during the primary infection stage. In either scenario, there would be no skeletal involvement and would, therefore, preclude any definitive conclusions with respect to the results pertaining to cause of death.

7.3 Contributions to Paleopathology and Bioarchaeology

This research has clearly demonstrated the importance and necessity of having a thorough understanding of the morphological variations that exist throughout the skeleton and on each of its separate elements. As illustrated in Chapter 2 of this thesis, there already are many variants in sternal morphology that are well known and documented. Should the first etiological explanation postulated here hold true, this research has served to contribute to a further understanding and documentation of another sternal variation that has been overlooked in the bioarchaeological literature. This study now acts as a model to clearly document manubrial porosity, which is necessary to eliminate the possibility of manubrial porosity being a sign of a specific pathological condition. With the knowledge now available regarding manubrial porosity and the patterns in which it can be expressed, this research is beginning to understand that even minute variations in the skeleton that can be confused for a pathological process.

This research also contributes to the paleopathological literature by being the first extensive and comprehensive study examining the role that the sternum could play in the diagnosis of disease in archaeological populations. This research attempted to contribute to Tayles and Buckley's (2004) passing suggestion that manubrial porosity was the result of increased vascularity that is the result of inflammation of blood vessels that supply the manubrium with blood. Since the etiology of manubrial porosity remains to be ascertained, this study can neither confirm nor reject Tayles and Buckley's (2004) suggestion. This thesis has demonstrated that the manubrial porosity seen in the Luis Lopes Collection has the potential of being a less severe but relatively similar condition (e.g. acquired anemia) to the probable case of thalassemia presented by Mann and Tuamsuk (2013). Finally, this research has expanded on Sanchez et al.'s (2012) preliminary research into the etiology of manubrial porosity. This thesis has elucidated variables that have significant associations to manubrial porosity that were not found by Sanchez et al. (2012) because of their smaller sample size.

7.4 Future Research

Further research is necessary to better understand the etiology of manubrial porosity, as two or more possible etiological explanations exist. The use of non-destructive imaging techniques, such as radiography, clinical computed tomography (CT), and/or micro-CT could assist with further understanding the etiology of manubrial porosity. Radiographs of manubria exhibiting the web-like porosity could provide a quick and cost-efficient way to determine the extent of the porosity throughout the manubrium. Clinical CT and micro-CT could provide digital cross-sections of the manubrium to determine if the porosity is in fact a destructive process or if a proliferative process produces the webbing. Furthermore, micro-CT can provide the opportunity to examine the underlying trabecular bone at a high resolution to see the extent to which the manubrium is affected by the web-like porosity (e.g. Morgan, 2014). The use of micro-CT could also assist with examining how the trabecular bone is affected, thereby elucidating whether or not a pathological process is occurring. A comparison study of all three imaging techniques could determine if similar information can be garnered by any one of the three techniques mentioned above.

Cross population analysis assessing the prevalence of manubrial porosity could provide valuable information pertaining to the etiology of the porosity. An extensive cross-population study of manubrial porosity could reveal geographical and temporal changes in the occurrence of manubrial porosity that may exist. A study of this nature could elucidate which populations have a higher prevalence of manubrial porosity compared to others and whether one form of expression (manubrial porosity score) is more common in one population over another. Similar, or even equal, prevalence of manubrial porosity between geographically and temporally distinct populations may further support and validate the argument of normal variation. Conversely, if there is a high prevalence and higher severity of manubrial porosity present in certain archaeological populations, it is possible that the porosity is the result of a pathological condition that cannot be reconstructed in more contemporary populations, such as the Luis Lopes Collection.

While this study assessed relationships between manubrial porosity and disease categories (pulmonary disease)/ specific diseases (e.g. pulmonary tuberculosis), another

avenue of research would be to examine if any relationships exist with non-specific indicators of stress. Determining if a relationship exists between manubrial porosity and non-specific indicators of stress (such as enamel hypoplasias or porotic hyperostosis) could support the second argument put forth in this study. Doing so would provide another avenue to assess stress experience not just by a person, but also on a population level. This could then contribute to having a “history of health” of an individual if used in tandem with other non-specific indicators of stress. It is also possible that the accumulation of non-specific indicators of stress for a condition, such as anemia, could serve as evidence for a clearer diagnosis. The use of non-destructive imaging (e.g. micro-CT) in addition to multiple indicators of anemia could allow for the diagnosis of a specific anemia.

Since most individuals with tuberculosis in this study exhibited manubrial porosity and/or rib lesions, only two individuals showed evidence of infection in the vertebrae, and no individuals showed sacroiliac involvement, future investigations could be conducted on a skeletal collection known to have evidence of “classic” tuberculous lesions and conduct a thorough analysis attempting to “seriate” tuberculous lesions with the hopes of identifying a sequence of presence and absence of tuberculous lesions. A study of this nature could help identify whether or not manubrial porosity and rib lesions are signs of early skeletal manifestations of tuberculosis. Furthermore, a study like this could also help elucidate information about pathogenesis of tuberculosis and shed light on how the bacteria may spread throughout the host and their skeleton.

Last, further investigation is required into the etiology of circumferential vertebral lesions and the associations they have with tuberculosis. The use of micro-CT could help with this by examining the internal trabecular structure around the lesions to assess if there is destruction of trabeculae occurring. Given the location of circumferential lesions (lateral sides of vertebral body/site of psoas muscle attachment), analysis of this nature will test Baker’s (1999) hypothesis that circumferential lesions are indicators of early manifestation of tuberculosis. If this holds true, then analysis of co-occurring thoracic lesions may provide patterns that are not observed in macroscopic analyses, such as this one, that merit further investigation.

This study took into account the recommendations proposed by Sanchez et al. (2012) and has attempted to incorporate the oft-forgotten sternum into the paleopathological literature. The research presented here acts as another stepping-stone to understanding the etiology of web-like porosity on the posterior surface of the manubrium.

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Appendices

Appendix A: Sample of Data Collection Form

Sternal Lesion Data Sheet

Observer Name: J. Sanchez Date: July 25 2013
 Recorder Name: J. Sanchez
 Catalogue Number: 436
 Sex: F
 Age: 79
 Cause of Death: Arteriosclerosis
 Occupation: Domestica

Sternal Lesion Present: Yes / No
 Severity of Lesion: 0 1 2 3 4

Scoring

0: sternal lesion is absent

1: Minimal porosity is present but latticework appearance is not distinguishable. Porosity is likely due to normal variation but also the beginning of porous cavitation

2: sternal lesion is present with two or less foci, no vigorous bone resorption but latticework lesion is distinguishable

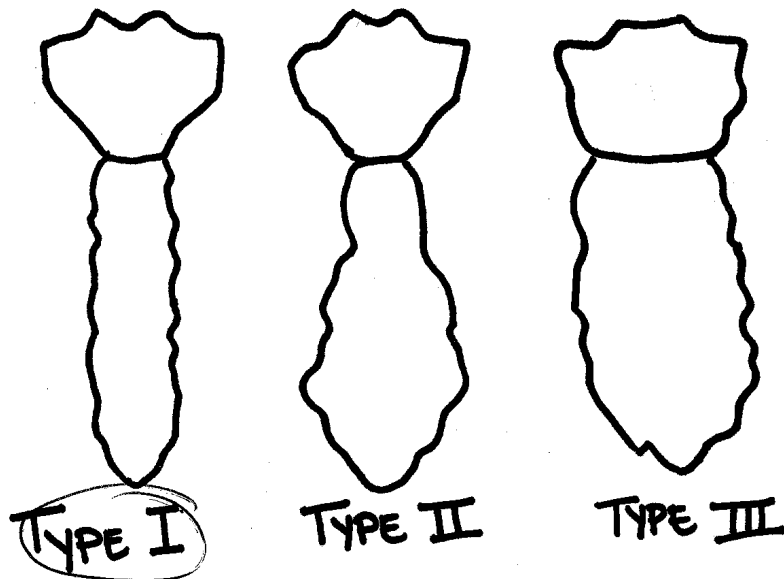
3: centralized/concentrated bone resorption, latticework lesion is pronounced but no bone growth

4: vigorous bone resorption, latticework lesion is pronounced, deep, and diffused (extends to the lateral margins of the manubrium). Bone growth is also present.

	Left Humerus				Right Humerus			
Rob. Score	R0	R1	R2	<input checked="" type="radio"/> R3	R0	R1	R2	<input checked="" type="radio"/> R3
Stress Score	S0	<input checked="" type="radio"/> S1	S2	S3	S0	<input checked="" type="radio"/> S1	S2	S3

Vertebral tuberculous lesions: Present _____ Absent
 Rib Lesions: Present _____ Absent

Sternal Shape:



Appendix B: Raw data on presence of “classic” tuberculous lesions based on respiratory disease

Individuals with pulmonary tuberculosis who exhibit “classic” tuberculous lesions

Cat #	Age	Sex	Manubrial Lesion	Rib Lesion	Vertebral Lesion	Sacroiliac Lesion
83	14	F	✓	✓	×	×
452	15	F	×	✓	×	×
258	16	M	×	×	×	×
759	17	F	×	×	×	×
8	18	F	×	✓	×	×
39	19	F	✓	×	×	×
394	19	M	✓	×	×	×
221	20	F	✓	×	×	×
301	20	M	×	×	×	×
391	20	M	✓	×	×	×
361	21	F	✓	×	×	×
422	21	M	×	✓	×	×
177	23	F	✓	✓	×	×
474	23	M	×	×	×	×
498	24	F	×	×	×	×
495	25	M	×	✓	×	×
488	26	M	×	×	×	×
115	28	F	✓	✓	×	×
476	31	M	×	×	×	×
154	35	M	×	✓	×	×
238	35	M	×	×	×	×
706	35	F	×	×	×	×
596	39	M	×	×	×	×
404	43	F	✓	×	×	×
503	46	F	×	×	×	×
572	48	F	×	×	×	×
245	50	M	✓	×	×	×
27	67	M	×	×	×	×
313	75	M	×	×	×*	×

*Individual has an abscess on a vertebra but is being considered as non-specific infection

Individuals with extra-pulmonary tuberculosis who exhibit “classic” tuberculous lesions

Cat #	Age	Sex	Manubrial Lesion	Rib Lesion	Vertebral Lesion	Sacroiliac Lesion
522	4	M	×	×	×	×
600	5	M	×	×	×	×

719	5	F	×	×	×	×
365	11	F	×	×	×	×
516	11	F	✓	×	×	×
314	20	F	✓	×	×*	×
605	44	F	×	×	×	×

* Individual has one abscess on 2 vertebrae but is being considered as non-specific infection

Individuals with non-tuberculous pulmonary disease who exhibit “classic” tuberculous lesions

Cat #	Age	Sex	Manubrial Lesions	Rib Lesions	Vertebral Lesions	Sacroiliac Lesions
466	2	M	×	×	×	×
136	19	M	✓	×	×	×
305	30	M	✓	✓	×	×
69	40	M	×	×	×	×
497	47	M	✓	×	×	×
63	48	F	×	×	×	×
755	49	M	✓	×	×	×
37	56	M	✓	×	×	×
504	59	M	✓	✓	×	×
119	64	F	✓	×	×	×
166	75	M	×	✓	×	×
585	86	F	×	×	×	×
97	87	M	×	×	×	×

Curriculum Vitae

Name: Jose Sanchez

Post-secondary Education and Degrees: University of Toronto
Mississauga, Ontario, Canada
2007-2012 B.Sc (Hons)

The University of Western Ontario
London, Ontario, Canada
2012-present M.A.

Honours and Awards: Western Graduate Research Scholarship
2012-2014

Related Work Experience Teaching Assistant
The University of Western Ontario
2012-2014

Conference Presentation:

Sanchez, J, Holland, E.J., Rogers, T.L. 2012. Normal Variation or Abnormal Situation: A Preliminary Paleopathological Study of the Sternum. *Poster presented at the 40th annual meeting of the Canadian Association of Physical Anthropology*. Victoria, BC.