

ABSTRACT

The cardiothoracic ratio (CTR) is commonly used as an indicator of cardiomegaly in clinical radiology. CTR is generally calculated using measurements from chest radiographs. More recently, a number of studies have used computed tomography (CT). This has not been attempted using with post-mortem ventilation, which would more closely mimic the inspiratory breath hold phase chest radiograph used for clinical CTR.

The aim of this study was to determine whether CTR can be measured on post-mortem CT (PMCT), whether it correlates with heart weight at autopsy and suggests cardiomegaly, and what effect ventilated PMCT (VPMCT) has on CTR measurements. CTR (%) was measured on PMCT scans pre and post ventilation using a method designed to mimic the deep inspiration and breath hold clinical thoracic CT, and compared with heart weights measured at autopsy with cardiomegaly defined from normal heart weight tables scaled for body size and sex.

Forty-two cases with both PMCT and VPMCT were consented for research. Results showed excellent measurement repeatability. VPMCT reduced heart diameter and CTR. The best CTR threshold to correlate cardiomegaly was 50% for PMCT (sensitivity & specificity (S&S) = 89 & 71%) and 44% for VPMCT (S&S = 79 & 71%). The heart diameter thresholds were 130 mm for PMCT (S&S = 89 & 93%) and 114 mm for VPMCT (S&S = 93% & 86%). Both CTR and heart diameter, using both PMCT and VPMCT, correlated well with heart weight at autopsy. However, using VPMCT and CTR did not give any advantage to measuring heart size on standard PMCT in this study.

Introduction

Cardiothoracic ratio (CTR) is used clinically to assess heart size, as an increased heart size has been associated with risk of cardiovascular disease [1,2]. The use of the CTR was first described using plain-film x-ray in 1919 by Danzer [3]. This method is still widely used today and states that a CTR ratio of >0.5 (50%) is abnormal on an inspiratory breath-hold chest radiograph. The threshold of 50% was based on statistical rather than prognostic grounds and some studies have looked at changing the threshold for abnormality [3,4]. Similar problems with setting thresholds have been noted for defining normal heart weight at autopsy, and how to account for body height, weight or sex to determine cardiomegaly [5,6]. However, cardiomegaly is now normally determined at autopsy by using pre-determined tables, considering the heart weight, height, body weight, body mass index (BMI) and sex of the individual.

Although originally developed for chest radiographs of living patients, some studies have successfully used CTR on post-mortem chest radiology with regard to finding a cause of death [7]. A number of studies have also shown that CTR can be applied to computed tomography (CT) and therefore post-mortem CT (PMCT) [1,2]. However, this has not been done with ventilated post-mortem computed tomography (VPMCT) [8], which can be used to replicate the inspiratory breath-hold chest radiograph that is normally used for CTR. This being said, since the heart is not beating in a post-mortem setting, compression of the heart will be more or less distinctive and the diameter of the heart will be reduced, which must be taken into consideration, as discussed by Germerott *et al.* [9]. If a method was developed to calculate CTR using post-mortem computed tomography (PMCT) in conjunction with post-mortem ventilation (PMV), it may more accurately correlate with cardiomegaly than calculating CTR on non-ventilated patients.

In this retrospective study we calculate CTR in cases that have undergone both pre- and post-ventilated PMCT to consider: 1) whether ventilation affects the measurement of CTR, 2) whether the CTR measured on pre- or post-ventilation scans better matches heart weight at autopsy, and 3) which CTR threshold is the most appropriate to diagnose cardiomegaly using PMCT.

Materials & Methods

Cases having both pre- and post-ventilation PMCT scans were identified from the anonymised image database stored at the East Midlands Forensic Pathology Unit. The research was conducted

with the approval of the local research ethics committee (amendment to original approved submission ref: 04_Q2501_64) and was supported by the local coroners' offices [8]. Informed consent was obtained from the next-of-kin for all VPMCT procedures. Pre- and Post- ventilation PMCT for the cases had been conducted as previously reported [8, 10], a method that was based on the work by Germott et al [9,11, 12]. Each case was anonymised with a unique identification code. Each case underwent an autopsy and weighing of the heart the following day without knowledge of the results of the PMCT. The autopsy was carried out under current United Kingdom autopsy guidelines [13]. The absence or presence of blood clots, and the extent of rigor of the heart are not normally recorded in UK autopsy practice. Cardiomegaly was diagnosed by comparing heart weight at autopsy in relation to body height to the normal heart weight tables generated by Zeek *et al.* [5].

The resulting 42 cases consisted of 16 females and 26 males, with an age range of 25-93 years and a post mortem interval of between 12 to 99 hours. None of the cases showed signs of decomposition, at levels that would have affected the results of this investigation, according to the post-mortem radiological alteration index (RA Index) [14]. All forms of natural and non-suspicious unnatural deaths were included. Exclusion criteria were known transmittable disease (for example tuberculosis, HIV or hepatitis C), weight over 210kg or shoulder width of >65cm; these criteria were based on CT scanner table limits, safety of intubation and body handling factors. Thoracic pathologies were then divided into 'major' or 'minor' depending on whether the abnormality would reduce pulmonary ventilation (rather than the clinical significance). No cases with 'major pathologies (e.g. bilateral extensive pneumonia consolidation) were included in this investigation, and only 11 of the 42 cases had 'minor' pathologies (e.g. segmental or lobar pneumonia consolidation or unilateral pathology or trauma).

The image data was analysed using OsiriX 3D imaging software (version 3.7.1; distributed freely as open-source software under the GNU licensing scheme at the following Web site: <http://homepage.mac.com/rossetantoine/osirix>. Pixie: Switzerland).

CTR Method: Using 10mm Multiplanar Reconstructions (MPR) in the coronal plane, images were oriented in the anatomical position by drawing a line through the estimated mid-point of the sterno-clavicular joint (figure 1A) and orientating the CT using the *rotate tool* (figure 1B), similar to the method used when assessing plain film chest x-rays. The cardiac diameter was measured on

each slice in the series, in order to determine the maximum cardiac diameter. Where pericardial fluid or fat were present, this was not measured. All measurements were done using the *rectangle tool* (figure 1C), to ensure that all of the lines were parallel. The thoracic diameter was measured from the widest internal surface of the pleura/rib above the costodiaphragmatic join. The internal surface of the thorax is more difficult to establish where pleural effusion is present. In general, the widest part tends to be immediately above the diaphragm. The cardiac diameter and maximum thoracic diameter were measured and recorded to the nearest millimetre on both the pre and post-ventilation scans.

The CTR was then calculated using the Danzer method [15]. The thoracic diameter was divided by the cardiac diameter and given as a percentage.

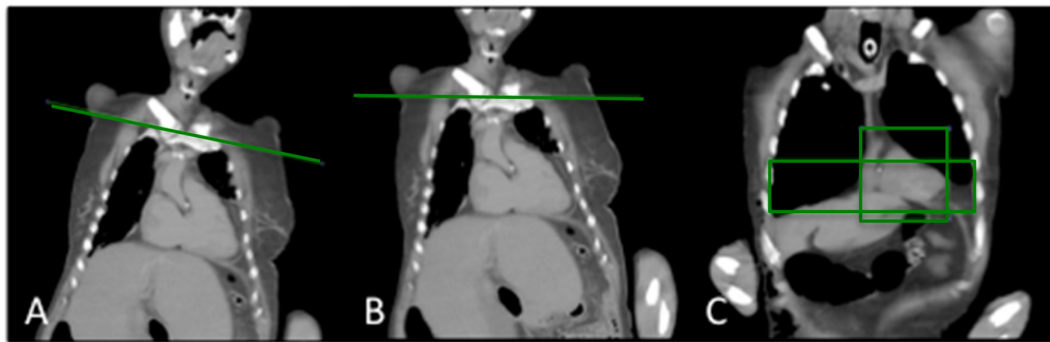


Figure 1. A) On the coronal view, line the axis to mid-point of the manubrium B) use the *rotate tool* to orientate the body into the anatomical position C) measure the cardiac diameter and maximum thoracic diameter, using the *rectangle tool*.

Analysis: Statistical analysis was performed using IBM SPSS Statistics Desktop 22.0 (IBM United Kingdom Limited, Hampshire, UK). Measurement data is presented as mean with 95% confidence intervals (CI). Where pre- and post-ventilation measurements are compared the ‘paired’ student’s t- test is used. Repeatability of CTR measurements by two different operators independently is shown using a Bland-Altman plot. Pre- and post-ventilation CTR and heart diameters were correlated with heart weight using Pearson correlation coefficient method. Receiver operating characteristic (ROC) curves were then plotted to compare the ability of CTR and diameter measurements to suggest cardiomegaly, based on heart weight at autopsy. Based on these data, CTR and diameter thresholds are suggested based on equal weight to sensitivity and specificity.

Results

Forty-two cases having both pre- and post-ventilation PMCT were identified. The average cardiac diameter for pre- and post-ventilation was 137 (95% CI \pm 7.1) and 123 (95% CI \pm 7.7) mm respectively. The thoracic diameter was found to be 253 and 263 mm respectively, and CTR was 0.54 (95% CI \pm 0.03) and 0.47 (95% CI \pm 0.03), respectively (paired t-test $P < 0.0001$ for both heart diameter and CTR difference).

A second observer repeated measurements independently. Bland & Altman plot of inter-observer difference for CTR, showed excellent repeatability of the measurements.

The average weight of the heart at autopsy was 420g, with a range of 190-650g. Twenty-eight cases were identified as cardiomegaly using Zeek's normality tables.

Figure 2 shows the CTR (%) for pre- and post-ventilation scans against heart weight at autopsy. Correlation coefficients for the pre- and post-ventilation measurements were not significantly different at 0.59 (95% CI 0.35 to 0.76) and 0.55 (95% CI 0.30 to 0.73) respectively. Assessing the difference in CTR between pre- and post-ventilation scans against heart weight showed no significant correlation.

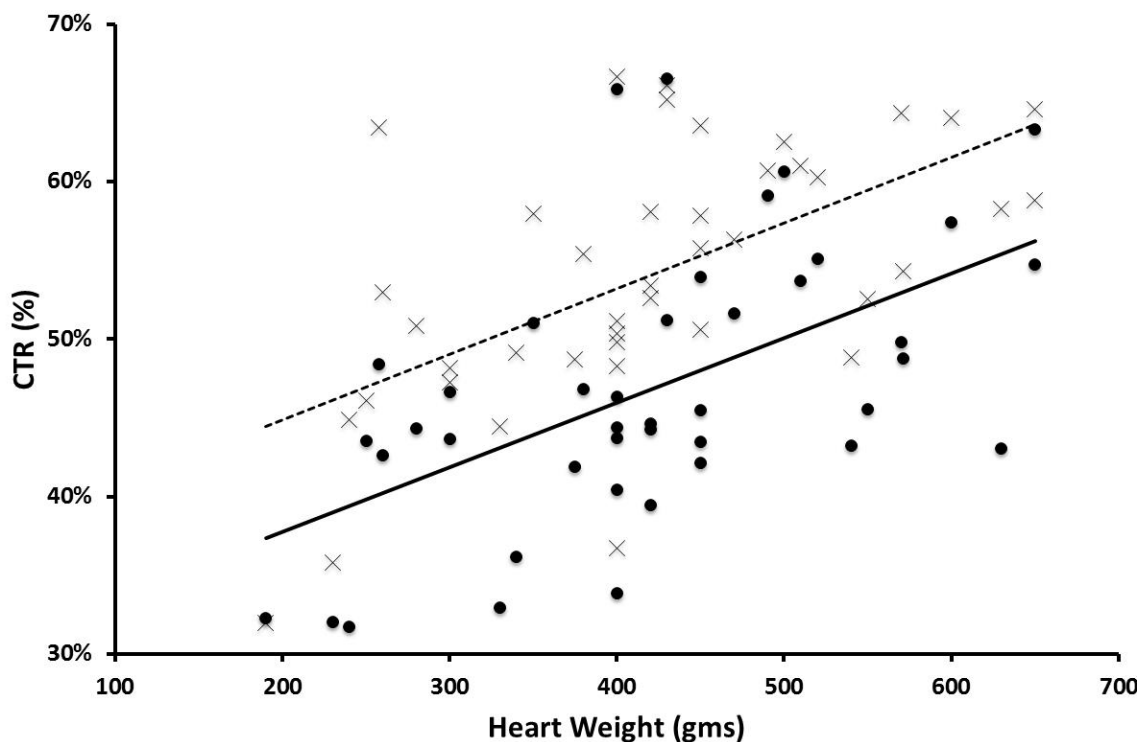


Figure 2: Plot of CTR (%) against heart weight at autopsy (pre ventilation X and dashed trend line, post ventilation ● and solid trend line).

The heart diameter for pre- and post-ventilation scans against heart weight at autopsy is shown in Figure 3. Correlation coefficient (CC) for the pre- and post-ventilation measurements was not significantly different at 0.79 (95% CI 0.64 to 0.88) and 0.74 (95% CI 0.56 to 0.85), respectively. Heart diameter therefore shows an increased correlation with heart weight than CTR but not statistically significant in this series ($p=0.1$).

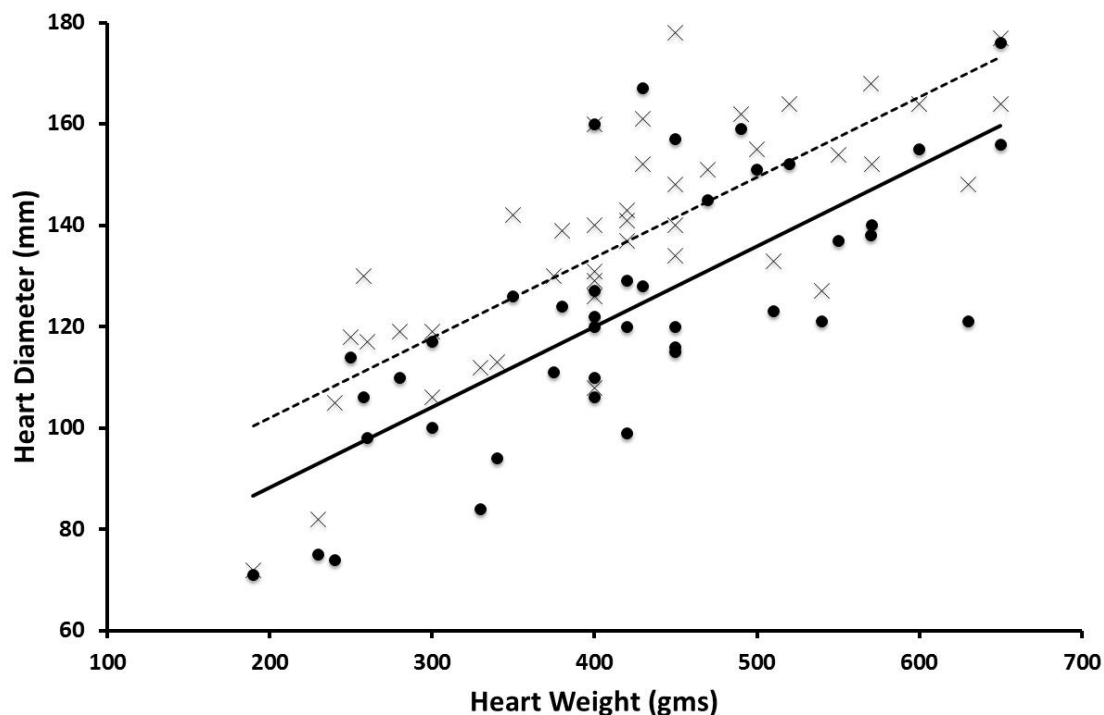


Figure 3: Plot of heart diameter (mm) against heart weight at autopsy (pre ventilation X and dashed trend line, post ventilation ● and solid trend line).

Figure 4A shows ROC curve generated for CTR measurements for both pre- and post- ventilation scans to suggest cardiomegaly, defined by heart weight at autopsy. ROC analysis shows significant ability to indicate cardiomegaly ($p<0.001$ for both curves) but no significant difference between the two curves. Figure 4B shows the ROC generated for heart diameter measurements for both pre- and post- ventilation scans to predict cardiomegaly, defined by heart weight at autopsy. ROC analysis shows significant ability to indicate cardiomegaly ($p<0.001$ for both curves) but no significant difference between the two curves. Heart diameter shows greater area under the ROC

curve to CTR measurements but this is not statistically significant. Area under the ROC curve was not improved by correcting the heart diameter for height, weight or body mass index.

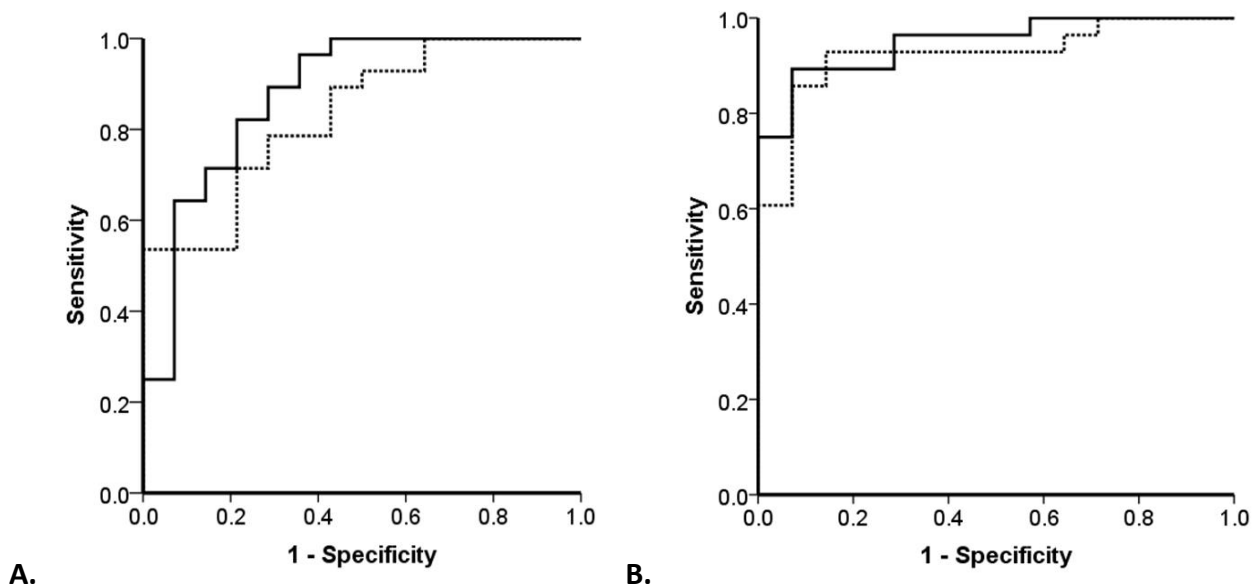


Figure 4. A) ROC curve for pre- (solid line) and post- ventilation (dashed line) CTR measurement showing significant indication of cardiomegaly as defined by increased heart weight at autopsy ($p < 0.001$). The Areas under the two ROC curves are 0.88 and 0.83 respectively and are not significantly different. **B)** ROC curve for pre- (solid line) and post- ventilation (dashed line) heart diameter measurement showing significant indication of cardiomegaly as defined by increased heart weight at autopsy ($p < 0.001$). The Areas under the two ROC curves are 0.95 and 0.92 respectively and are not significantly different.

A CTR threshold of 50% for pre-ventilation CTR measurements gave the best sensitivity and specificity of 89% and 71% respectively. For the post-ventilation CTR measurements a threshold of 44% gave best sensitivity and specificity of 79% and 71% respectively. For heart diameter best pre-ventilation threshold was 130 mm (sensitivity and specificity, 89 & 93%) and post ventilation was 114 mm (sensitivity and specificity, 93% & 86%).

Discussion

In this study we found a significant difference in CTR and heart diameter between ventilated and non-ventilated PMCT, and that both VPMCT and non-ventilated PMCT correlated well to heart weight at autopsy. This study agrees with previous studies, which illustrate that the cardiothoracic ratio can be measured reliably on PMCT. Not surprisingly there is a significant difference between the CTR and heart diameter pre- and post-ventilation, as is seen between inspiratory and expiratory chest radiographs. Ventilated CTR correlates well with heart weight at autopsy and can

indicate cardiomegaly with reasonable sensitivity and specificity, but with different thresholds than for clinical practice (44% on ventilated PMCT against 50% on inspiratory chest radiographs). This may imply our ventilation protocol is reducing heart diameter more than inspiration on a chest radiograph. However, this difference in thresholds could also be caused by a combination of the following factors; a post-mortem body does not have an active circulation, the body is scanned in a supine position (unlike a routine chest radiograph in a living person, which is taken in a standing position), and/or post-mortem changes may influence the heart and lung volumes. Non-ventilated PMCT shows equally good correlations and indication of cardiomegaly, but with an optimum threshold 50%. There is no obvious advantage to using VPMCT.

This study also shows that the diameter of the heart on CT measured in the coronal plane also shows good, if not better, correlation with heart weight and indication of cardiomegaly, with a threshold of 130 mm for PMCT and 114 mm for VPMCT. These correlations are not improved by scaling by height or weight of the cadaver. This is not totally surprising as the use of the CTR on chest radiographs is a scaling method, not only for dealing with variations in body size, but also for exposure factors, magnification and the lack of an accurate scale.

This study does have weaknesses. The Danzer method for measuring CTR has been criticised by some practitioners [3, 16] and some alterations to this method have been suggested [3, 4, 16, 17]. However, it remains the most widely used in clinical practice and was therefore considered the best method for this study. Similarly, the Zeek method to define cardiomegaly at autopsy is considered out-dated by some authors, but is still a commonly referenced technique [18]. Furthermore, when other tables are used [19] the same cases are classified as cardiomegaly as in this study. Although measuring heart weight at autopsy is considered a good method of assessing cardiomegaly, the autopsies performed in this study are part of routine service and weights may not have all been measured with the care of a scientific study.

A larger study with accurate heart weights at autopsy would be required to decide whether our threshold heart sizes are accurate and whether scaling heart diameter body parameters such as height has any advantage. It could also address whether heart volume offers any advantage to heart diameter.

Summary

CTR can be measured with excellent repeatability. VPMCT reduces heart diameter and CTR. Both CTR and heart diameter, using both PMCT and VPMCT, correlated well with heart weight at autopsy. Using VPMCT and CTR did not bestow any advantage to measuring heart size on standard PMCT in this study.

Key points

- Post-mortem ventilation reduces heart diameter and CTR.
- A CTR threshold of 50% for PMCT and 44% for VPMCT correlates to cardiomegaly.
- A heart diameter threshold of 130 mm for PMCT and 114 mm for VPMCT suggests cardiomegaly.
- Both PMCT and VPMCT can be used to measure heart size to indicate cardiomegaly but thresholds need to be altered accordingly.

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