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Postmortem heart weight modelled using piecewise linear regression in 27,645 medicolegal autopsy cases

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ABSTRACT

The interpretation of postmortem heart weight is often difficult, and references for normal heart weight are important. However, to assess the cause of death at a medicolegal autopsy it is also important to have references based on an unselected population of medicolegal autopsy cases with non-natural causes of death (not due directly to disease). We aimed at studying and deriving references for adult heart weight by considering sex, age and body size in cases with an external cause of death. We identified all medicolegal autopsies in Sweden from 1999 to 2013 ($n = 79,778$) and included 27,645 cases. We applied multivariate piecewise linear regression models in three strata of body mass—underweight, normal-/overweight and obesity. We observed that approximately 50% of the variation in heart weight was explained by age, sex and body size. These variables were slightly less important in explaining the variation in heart weight in the underweight and obese compared to in those normal or overweight. Based on the linear regression models we present equations to calculate the predicted heart weight with reference intervals using age, sex, body weight and height. We provide an online heart weight calculator (http://lundforensicmedicine.com) based on these equations. In the forensic interpretation of postmortem heart weights, we suggest that heart weight references derived in cases with an external cause of death is an important complement to references solely based on healthy and normal hearts. Furthermore, the heart weight references presented are derived from a large population, with sufficient numbers for separate models in underweight, normal-/overweight and obese populations.

1. Introduction

Interpretation of postmortem heart weight is often difficult, and references for normal heart weight are important to assist physicians. An increased heart weight is an unspecific marker of disease and is caused by several conditions such as cardiomyopathies, valvular diseases, ischemic- and hypertensive cardiovascular disease. The association between an increased heart weight and death is considered to be by mechanisms such as heart failure or arrhythmias [1,2]. Several papers have studied the distribution of heart weight and the selection criteria have varied from populations without microscopic and macroscopic cardiovascular disease to individuals specifically affected by diseases such as cancer or cardiovascular disease [2–7], see Vanhaebost et al. [8] for an overview. In a study published in 1899 an association between the weight of the heart and age, body weight and sex was presented and an association between socioeconomic factors and heart weight was observed [2]. To add further complexity the normal size of the heart shows variation both temporally and across populations [8]. A couple of recent studies [8,9] have studied heart weight using linear models in autopsy populations of less than 500 individuals and by applying disease related exclusion criteria's [8,9]. Studying heart weights in populations selected either on basis of disease or exclusion thereof is likely not representative of the general medicolegal autopsy population. Also, when assessing the importance of an increased heart weight to the cause of death, and when passing expert opinions in a legal setting of similar matters, it is valuable to have references based on a cross-section of the general population. The non-natural deaths, i.e. deaths not directly caused by disease, are considered to be representative of such a cross-section of the general population. This group of deaths should have a distribution of illnesses similar to that of the general population, when dying from non-disease related causes. We believe this to be the most accurate population for studying heart weights compatible with life.

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In this study we model adult heart weight using piecewise linear regression models separate in strata of body mass index, in a large adult population ($n = 27{,}645$) of medicolegal autopsy cases with an external cause of death. By studying the association in strata of BMI we also fill in existing knowledge gaps concerning heart weights in the lower and upper intervals of BMI [9,10]. Using the multivariate piecewise models we set out to create equations estimating heart weight using measures of body size, age and sex in the population of routine medicolegal autopsy cases dying of external causes. Based on these equations we supply a heart weight reference calculator for particular use in a caucasian medicolegal autopsy material.

2. Materials and methods

2.1. Study population

In Sweden, all medicolegal autopsies are performed at one of the six departments of the Swedish National Board of Forensic Medicine. Using the autopsy register maintained by this agency we identified all cases 18 years and older in which a medicolegal autopsy took place in Sweden from 1999 to 2013 ($n = 76{,}778$) (Fig. 1). We excluded cases without a valid code for the cause of death. We identified cases with an external underlying cause of death, i.e. deaths not directly caused by disease. To avoid including cases with advanced decomposition, we excluded those cases in which the autopsy had not been performed within 10 days after their passing or in which a plausible date of death had been determined with the highest resolution within a calendar month.

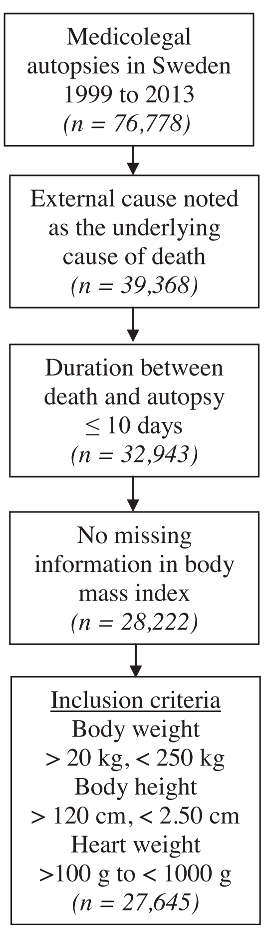

Fig. 1. The selection process of the population included in the study starting with all medicolegal autopsy cases in Sweden 18 years and older from 1999 to 2013.

We also excluded cases in which BMI was not possible to calculate due to missing information in either weight or height. We excluded cases with implausible body weights (<20 kg and >300 kg), body heights (<120 cm and >250 cm) and heart weights below 100 g or more than 1000 g. In total we included 27,645 cases fulfilling the inclusion criteria (Fig. 1).

2.2. Assessment of variables

Body weight (kg) was included as a continuous variable in the analyses. When calculating the heart weight to body weight ratio, we included body weight measured in grams.

Heart weight (g) was included as a continuous variable and we transformed it into the logarithmic scale, since previous studies had indicated a better fit in linear models using transformations [4,9].

Body height (m) was included in the models as a continuous variable.

Body mass index was calculated using the formula (weight [kg]/height [m]^2), and we categorized the results into three groups: (i) underweight (<18.5 kg/m^2), (ii) normal-/overweight (18.5 to <30 kg/m^2) and (iii) obesity (≥30 kg/m^2) [11].

The heart weight to body weight ratio (HW/BW-ratio) was calculated using the formula (heart weight (g)/body weight (g)) × 100.

We calculated body surface area (BSA) using the Mosteller's formula (BSA = $\sqrt{}$(weight (kg) × height (cm))/3600)) [12,13].

The duration in days between the date of death and the medicolegal autopsy was calculated in cases with complete information on the date of death.

We included sex as a dichotomous variable in the analyses, using women as reference.

Age (years) was included as a continuous variable in the analyses.

2.3. Methods

In each BMI group we applied univariate linear regression models and studied the explanatory power of different measures of body size as well as of age and sex in the variance of heart weight transformed into the logarithmic scale. In a bivariate model we studied the combination of height and weight. Based on the results of these models we constructed a multivariate model also considering sex and age separately in each stratum of BMI, a piecewise modelling approach. In the multivariate models we evaluated the standardized residuals to avoid including obvious outliers in the model. We a priori set out to exclude those with large standardized residuals (>3, <−3). After excluding the outliers the final multivariate linear regression models were obtained. Using the regression coefficients and the standard deviation obtained from the final multivariate linear regression models we aimed at presenting an equation calculating the predicted heart weight, predicted heart weight plus 1 SD and the upper 95%CI (single sided) limit of heart weight and to provide a calculator to make these equations easily accessible for the user. We also obtained the median HW/BW-ratio separately in strata of BMI.

All of the independent factors included in the study have previously been associated with the weight of the heart [2,5,8]. Also, heart weight has been transformed into the logarithmic scale in previous studies [9].

We report the results of the linear regression models using the regression coefficients, 95% confidence intervals (CI), standard deviation (SD), and R^2. The data was analysed using IBM SPSS version 22.0.0.0.

The study was approved by the ethics committee in Lund, Sweden.