**Left ventricular trabeculations in cardiac MRI: reference ranges and association with cardiovascular risk factors in UK Biobank**

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## Disclosure of Interest

Steffen E Petersen provides consultancy to Circle Cardiovascular Imaging, Inc., Calgary, Alberta, Canada. Other co-authors declare no conflicts of interest.


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## Data Availability Statement

Data generated or analyzed during the study are available from the corresponding author by request.

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Original Research

Summary Statement: Applying automated segmentation to UK Biobank MRI scans, hypertension, higher body mass index, and higher physical activity levels were associated with increased left ventricle trabeculations in healthy middle-aged White adults.

Key Results:

1. In a cross-sectional secondary analysis of prospectively collected data from the UK Biobank, applying automated segmentation to cardiac MRI scans, the trabeculated left ventricular (LV) mass was significantly higher in middle-aged White adults with established cardiovascular risk factors (n = 28 672) compared with a healthy reference group (n = 7384) for both men (median (IQR) of 6.8 g (5.1, 9.0) vs. 6.3 g (4.7, 8.5), P<.001) and women (5.1g (3.8, 6.7) vs. 4.6 g ( 3.4, 6.0) P<.001).
2. Hypertension (β=0.42, 95% CI: 0.36, 0.48, P<.001), higher body mass index (β=0.66, 95% CI: 0.63, 0.68, P<.001), and higher physical activity levels (β=0.15, 95% CI: 0.12, 0.17, P<.001), were associated with increased LV trabeculation.
3. Age- and sex-specific reference ranges of trabeculated LV mass values in a middle-aged healthy White population were established.

Abbreviations:

BMI, body mass index
CV, cardiovascular
LV, left ventricular
LVM, left ventricular mass
TMM, total myocardial mass

**Abstract**

**Background**: The extent of left ventricular (LV) trabeculation and its relationship with cardiovascular (CV) risk factors is unclear.

**Purpose**: To apply automated segmentation to UK Biobank cardiac MRI scans to (1) assess the association between CV risk factors and trabeculated LV mass and (2) to establish normal reference ranges in a selected group of healthy UK Biobank participants.

**Materials and Methods:** In this cross-sectional secondary analysis, prospectively collected data from the UK Biobank (2006-2010) was retrospectively analyzed. Automated segmentation of trabeculations was performed using a deep learning algorithm. After excluding individuals with known CV diseases, White adults without CV risk factors (reference group) and those with pre-existing CV risk factors (exposed group) were compared. Multivariable regression models, adjusted for potential confounders (age, sex and height) were fitted to evaluate the associations between cardiovascular risk factors (BMI, hypertension, hyperlipidemia, diabetes mellitus, physical activity, and smoking) and trabeculated LV mass.

**Results:** Of 43038 (mean age [SD] 64±8 years, 22360 women) White participants, 28672 individuals (66±7 years, 13754 women) and 7384 individuals (60±7 years, 4729 women) were included in the exposed and reference group, respectivelyHigher BMI (β=0.66, 95% CI=0.63, 0.68, P<.001), hypertension (β=0.42, 0.36, 0.48, P<.001), and higher physical activity levels (β=0.15, 0.12, 0.17, P<.001) were associated with higher trabeculated LV mass. In the reference group, the median (IQR) trabeculated LV mass was 6.3g (4.7, 8.5) for men and 4.6g (3.4, 6.0) for women. The trabeculated LV mass decrease with age for men (6.5g (4.8, 8.7) at 45-50 years to 5.9g (4.3, 7.8) at 71-80 years (P =.03) for men.

**Conclusions:** Higher trabeculated LV mass was observed with hypertension, higher BMI, and higher physical activity levels. Age- and sex-specific reference ranges of trabeculated LV mass values in a middle-aged healthy White population were established.

**Introduction**

The myocardium has two distinct layers: the outer compact layer and the inner trabeculated layer (1). Clinical interest in left ventricular (LV) trabeculations mainly arises from a cardiac phenotype of excessive trabeculation often referred to as LV non-compaction. However, the growth of LV myocardial compact wall is independent of trabecular development; thus, the term 'non-compaction' is likely a misnomer (2) and the term excessive trabeculation is preferred as it describes the phenotype (3). Features of excessive trabeculation have been observed in a wide spectrum of scenarios ranging from normal variation and adaptive response to altered pre-load or afterload to co-existence with myocardial dysfunction. There is mounting evidence to suggest that excessive trabeculation is not in itself pathological (4) (5).

As excessive trabeculation is frequently reported in cardiac MRI, a better understanding of its determinants would help clinicians to interpret the presence and extent of excessive trabeculation. Existing diagnostic criteria need to be adjusted in light of such determinants. Many studies have proposed imaging diagnostic criteria (6) for so-called LV non-compaction cardiomyopathy or excessive trabeculation. The first cardiac MRI diagnostic method was proposed by Petersen et al. using a semi-quantitative method based on a non-compacted (NC)/compacted (C) ratio > 2.3 in diastolic long-axis images (7). Later, Jacquier et al. suggested a quantitative method based on diastolic trabeculation mass (8). A percentage of trabeculated mass higher than 20% of the total myocardial mass (TMM) was considered as the diagnostic cut-off. An improved myocardial delineation permitted by high-resolution imaging has led to the suggestion that previous diagnostic criteria developed in small, highly selected case-control studies may have low specificity and lead to overdiagnosis (9) (10).

A fully automated and quality-controlled artificial intelligence algorithm was recently applied to quantify LV trabeculation and papillary muscle with higher reproducibility and precision compared with human experts (11). This innovation enables accurate high throughput measurement of LV trabeculation in large datasets. This study aimed to apply automated segmentation to UK Biobank cardiac MRI scans

to (1) assess the association between cardiovascular (CV) risk factors and trabeculated LV mass and (2) to establish normal reference ranges in a selected reference group of healthy UK Biobank participants.

## Materials and Methods

### *Study Design and Participants*

This cross-sectional secondary analysis of prospectively collected data from the UK Biobank is covered by the UK Biobank ethical approval from the NHS National Research Ethics Service on 17th June 2011 (Ref 11/NW/0382), which was extended on 18 June 2021 (Ref 21/NW/0157). This research did not receive financial or material support from the medical industry.

The UK Biobank (https://www.ukbiobank.ac.uk) is a large prospective population-based cohort study of more than 500000 individuals living in the United Kingdom (12). Detailed information on the participants' demographics, lifestyle factors, physical measurements, biological samples, and medical information including linkage to hospital records and national registries have already been used in numerous publications, which can be found here: https://www.ukbiobank.ac.uk/enable-your-research/publications. A subset of UK Biobank participants is undergoing imaging enrichment with a whole-body MRI study including a cardiac MRI evaluation (13). Consecutive UK Biobank participants with cardiac MRI data were considered (https://www.ukbiobank.ac.uk/enable-your-research/about-our-data/imaging-data). As the UK Biobank imaging study was predominantly comprised of White individuals (98%), the selected sample was restricted to only White individuals named entire White group. Ethnicity information was self-reported by the participants. A subgroup of White individuals with established CV risk factors such as current or previous tobacco smoking history, presence of diabetes, hypertension, or hyperlipidemia but no cardiac disease were selected as the exposed (index) group. This exposed group was selected to assess the relationship between CV risk factors and trabecular measurements. Another subgroup of healthy White participants named reference group was selected to create the normal reference ranges. This reference group was free from CV risk factors, cardiac disease, and obesity (body mass index (BMI) $\leq$ 30, calculated as weight in kilograms divided by height in

squared meters). The full list of exclusion criteria is available in Supplementary Table 1. Physical activity was measured by the metabolic equivalent of task minutes per week as previously detailed (14) using the information of a self-reported International Physical Activity Questionnaire (15).

*Cardiac MRI protocol*

The UK Biobank cardiac MRI protocol has been described in detail elsewhere (16). All cardiac MRI examinations were performed using a wide-bore 1.5 Tesla scanner (MAGNETOM Aera, Syngo Platform VD13A, Siemens Healthcare). Assessment of cardiac function was performed using a combination of cine series: long axis cines (horizontal long axis, vertical long axis) and a complete short axis stack covering the left and right ventricles. All cine acquisitions used balanced steady-state free precession with typical parameters (subject to standard radiographer changes to planning), as follows: TR/TE = 2.6/1.1 ms, flip angle 80°, Grappa factor 2, voxel size 1.8 mm x 1.8 mm x 8 mm (6 mm for long axis). The actual temporal resolution of 32 ms was interpolated to 50 phases per cardiac cycle (~20 ms). No signal or image filtering was applied besides distortion correction.

*Image analysis*

A fully convolutional neural network trained and tested in a previously published expert-annotated dataset (17) was used to automatically produce LV volumetric parameters and LV mass (excluding trabeculation and papillary muscle) in all cardiac MRI studies (18).

Trabeculations and papillary muscles segmentation was performed using a bespoke automatic deep-learning model previously described (11). This five-step pipeline allows end-diastolic LV anatomical structure segmentation including trabeculations and papillary muscle as shown in Figure 1 (19). Segmentation of trabeculae and papillary muscle was performed in the end-diastolic frame of the short-axis cine cardiac MRIs. The trabeculated LV mass (g) and LV papillary muscle mass (g) were calculated from these segmentation contours. This technique was validated histologically on a mouse model (20).

Blood in trabeculations recesses was excluded from trabecular quantification. The TMM was the sum of LV mass (LVM), LV papillary muscle mass, and trabeculated LV mass. The trabeculation mass–to-TMM ratio was calculated. Automatic segmentation was performed on a high-performance computer workstation (96-core CPU, 500Gb RAM and NVIDIA RTX A6000 GPU with 48Gb memory).

The UK Biobank individual-level data are made available to any bona fide researchers around the world via a standard access procedure outlined at https://www.ukbiobank.ac.uk/enable -your-research/apply-for-access. The code of the trabeculation segmentation software can be shared based on an End User License Agreement (http://www.sattse.com/). It allows the software to be used based on a collaboration agreement.

*Statistical analysis*

Statistical analysis were performed by NA and SC. The baseline characteristics were presented as mean (SD) or median (IQR) for continuous variables and proportion for categorical values. Normality of data distribution was assessed by inspecting the histograms and quantile-quantile plots. Inter-group differences were assessed by independent samples t-test for normally distributed continuous variables and Mann-Whitney U test for non-normal continuous variables, and Chi-square test for categorical variables. In the primary analysis, multivariable regression models were fitted to evaluate the associations between CV risk factors and trabeculated LV mass, LV papillary muscle mass, and trabeculation mass-to-TMM ratio. Given the right-skewed distributions of response variables (Supplementary Figure 1), a generalized linear model (GLM) with a Gamma distribution and an 'identity' link function was used to fit the regression models. In the sensitivity analysis, additional adjustment with compacted LVM was performed for the same multivariable models for trabeculated LV mass and LV papillary muscle mass, to assess the confounding effect of LVM. Multicollinearity of covariates was identified by a variance inflation factor cut-off of 3. After excluding outliers according to Tukey's method (any values below quartile 1 – 1.5 x IQR or above quartile 3 + 1.5 x IQR), mean ± SD, median (IQR) as well as reference intervals which represent 2.5% and 97.5% percentile limits (i.e. 95% interval)

were calculated for age groups stratified by sex in the reference group (21). The reference intervals were computed by a non-parametric method using 'referenceIntervals' R package (https://cran.r-project.org/web/packages/referenceIntervals). We followed the minimum sample size requirement for reference intervals (n>120 per group) as recommended by the Clinical and Laboratory Standards Institute (CLSI) (22). All statistical analyses were conducted in R (version 4.0.3) (23). All P-values were adjusted for multiple testing by Bonferroni correction and a Bonferroni-corrected $P < .05$ was considered to be significant.

**Results**

*UK biobank Sample characteristics*

Of 44892 consecutive UK Biobank participants with cardiac MRI data, participants whom trabeculation segmentation quality was deemed low as indicated by the built-in automatic quality control algorithm (n = 49) as well as images with no corresponding LV volumetric parameters due to image quality issues (n = 289) were excluded from analyses. Only White individuals were selected (n=43038) (Figure 2). Participant characteristics are summarized in Table 1. After exclusion criteria, the exposed group included 28672 individuals (13754 women) and the reference group included 7384 individuals (4729 women). Median LVM, LV volume and LV ejection fraction (LVEF) were all within normal limits for the entire group of White individuals (n=43038) and the subgroups (exposed and reference) (24). The participants in the reference group were younger than the exposed group (mean (SD) of 60.4 (7.4) years vs. 66.1 (7.5) years, P <.001 for men and 59.9 (6.9) years vs. 64.9 (7.3) years, P <.001 for women) and had lower BMI (median (IQR) of 24.6 (22.8, 26.5) kg/$m^2$ vs. 26.9 (24.7, 29.5) kg/$m^2$, P <.001 for men and 23.6 (21.7, 25.7) kg/$m^2$ vs. 25.8 (23.1, 29.1) kg/$m^2$, P <.001 for women). LVM was lower in the reference group than in the exposed group for both men (median (IQR) of 95.8 (85.7, 106.5) g vs. 101.5 (90.5, 113.8) g; P < .001) and women (65.8 (59.6, 72.8) g vs. 70.5 (63.0, 79.3) g; P < .001). Trabeculated LV mass was higher in the exposed group than in the reference group for both men (median (IQR) of 6.8 (5.1, 9.0) g vs. 6.3 (4.7, 8.5) g; P < .001) and women (5.1 (3.8, 6.7) g vs. 4.6 (3.4, 6.0) g; P < .001).

*Association with cardiovascular risk factors*

In multivariable regression models adjusted for age, sex, height, BMI, hypertension, smoking status, hyperlipidemia, diabetes mellitus, and physical activity in the entire group of White individuals (n=43 038), higher height (β=0.72, 95% CI= 0.68, 0.75, P < .001) higher BMI (β=0.66, 0.63, 0.68, P < .001), hypertension (β=0.42, 0.36, 0.48, P < .001), higher physical activity (β=0.15, 0.12, 0.17, P < .001) and current smoking status (β=0.24, 0.1, 0.39, P = .003) were all associated with higher trabeculated LV mass (Table 2). These observations, except for the associations of current smoking status with

trabeculated LV mass, remained significant after additional adjustment with LVM (Supplementary Table 2). Diabetes mellitus (β=-0.27, 95% CI= -0.37, -0.17, P < .001) and hyperlipidemia (β=-0.09, -0.14, -0.04, P < .001) were associated with lower LV papillary muscle mass, while higher BMI (β=0.37, 95% CI= 0.35, 0.4, P < .001), higher physical activity (β=0.15, 0.12, 0.17, P < .001) and hypertension (β=0.20, 0.15, 0.25, P < .001) were associated with higher LV papillary muscle mass. After additional adjustment for LVM, only the associations of diabetes mellitus and physical activity with LV papillary muscle mass, remained significant with concordant effect directions. Higher BMI (β=0.19, 95% CI= 0.16, 0.21, P < .001), hypertension (β=0.07, 0.02, 0.128, P = .02), and higher physical activity levels (β=0.03, 0.01, 0.05, P = .02), were all associated with higher trabeculation mass–to-TMM ratio in the multivariable model.

*Reference normal ranges*

The normal ranges of LV parameters, stratified by age for men and women in the reference group are presented in Tables 3 and 4, respectively. LVM measurements that excluded trabeculation and papillary muscle were lower in older age groups, from median (IQR) of 102.8 (88.9, 113.6) g at 45-50 years to 88.7 (80.0, 98.2) g at 71-80 years for men and from 67.5 (60.8, 74.1) g at 45-50 years to 61.8 (56.5, 69.0) g at 71-80 years for women (Figure 3). Similarly, LV papillary muscle mass was lower in older age for men (median (IQR) of 8.1 (6.8, 9.4) g at 45-50 years to 6.7 (5.2, 8.1) g at 71-80 years, P < .001) and women (6.0 (4.7, 7.3) g at 45-50 years to 5.0 (3.6, 6.4) g at 71-80 years, P < .001). The trabeculated LV mass values were lower in older age categories (6.5 (4.8, 8.7) g at 45-50 years to 5.9 (4.3, 7.8) g at 71-80 years, P = .03) for men but there was no evidence of lower trabeculated LV mass values in older age categories for women (4.7 (3.3, 6.0) at 45-50 years to 4.3 (3.2, 5.8) at 71-80 years, P > .99). In contrast, while the trabeculation mass-to-TMM ratio was higher with older age groups in both men (5.5 (4.5, 7.0) % at 45-50 years to 6.0 (4.4, 7.6) % at 71-80 years, P = .22) and women (5.9 (4.4, 7.7) % at 45-50 years to 6.2 (4.7, 8.1) % in 71-80 years, P = .02), only the association with age in women remained significant after multiple testing correction. The body surface area-indexed trabeculated LV mass values showed no evidence of significant associations with age in both men (3.3 (2.5, 4.2) g/m$^2$ at 45-50 years

to 3.1 (2.3, 4.0) g/m$^2$ at 71-80 years, P = .68) and women (2.8 (2.0, 3.5) g/m$^2$ at 45-50 years to 2.7 (1.9, 3.5) g/m$^2$ at 71-80 years, P > .99).

**Discussion**

We evaluated the associations between common CV risk factors and trabeculae mass and established the normal ranges for LV trabeculation and papillary muscle mass in a community-based adult population. This study was conducted with a validated deep learning segmentation tool that allowed rapid and reproducible segmentation of LV structures. We found that, hypertension (β=0.42, 95% CI: 0.36, 0.48, *p*<.001), higher BMI (β=0.66, 95% CI: 0.63, 0.68, *p*<.001), and higher physical activity levels (β=0.15, 95% CI: 0.12, 0.17, *p*<.001) had the most consistent associations with greater trabeculated LV mass.

Different approaches to measure cardiac trabeculations have been described using the trabecular layer thickness, trabecular volume or mass and fractal dimension (7) (8) (25). The presented method has the advantage to allow scalable and reproducible measurement of LV structures differentiated into papillary muscles, inter-trabecular blood and trabeculations. Captur et al. used fractal dimension to measure trabecular complexity (26). However, this technique still requires a dedicated software that is not widely available in clinical practice (25). Furthermore, fractal dimension as applied by Captur et al. did not distinguish LV papillary muscle from trabeculation unlike our method, which allows more granular assessment by direct quantification of trabecular and papillary muscle mass.

The extent of LV trabeculation was higher with hypertension even after adjusting for LVM. This finding was concordant with the data from Captur et al. and could be related to an increased afterload (26). Likewise, higher BMI was associated with greater trabeculated LV mass, in line with a previous report by Cai et al. using fractal analysis in 180 Chinese individuals (27). The association between LV trabecular measurements and physical activities had been inconsistently reported in prior studies. One of the earlier studies by Gati and colleagues found a higher prevalence of increased LV trabeculation quantified by echocardiography in athletes compared with healthy controls (28). In a smaller subset of

the UK Biobank cardiac MRI cohort (n = 1030), physical activity did not alter LV trabeculation measured in the so-called non-compaction to compaction ratio (14). Contrary to this report, in a study of 4184 middle-aged individuals, accelerometer-measured vigorous physical activity was associated with a higher prevalence of excessive trabeculation phenotype (29). Our current study found higher trabeculated LV mass with higher physical activity levels. A direct comparison of our analysis with previous literature is difficult due to the differences in trabecular quantification criteria, study populations, and differences in exposure definition. Given the small effect size (0.15g higher trabecular mass for every SD increment in total metabolic equivalent of task minutes per week), it is plausible that we have uncovered the subtle relationship between physical activity and LV trabeculation with the help of high precision measurements in a very large sample size..

Our results demonstrated that men have higher trabecular and papillary muscle mass than women. In the age group stratification, older men had a lower LV trabeculation mass than younger men. Trabeculated mass-to-TMM ratio is marginally higher in older women although there is a wide overlap in confidence interval of measurements in different age groups. One prior study on 140 healthy volunteers reported mean indexed trabeculations mass of $4.0 \pm 2.3$ g/m$^2$ for women and $5.4 \pm 2.3$ g/m$^2$ for men and were higher than the values presented here (30). This could be explained by the segmentation technique based on a voxel threshold that is more prone to partial volume effect and can lead to over integrate blood voxel in the trabeculated mass. Andre et al. observed that men had a higher trabeculated volume than women (31). Kawel et al. found a greater trabeculated layer thickness in men compared with women but the ratio of trabeculated layer thickness to compact myocardium was similar between sexes (32).

Our study had limitations. First, our data primarily focused on healthy individuals and those with cardiovascular risk factors in a community-based population. The generalizability of our results in patients with established cardiac diseases is uncertain. Second, our study group was largely comprised of White individuals. Third, the selected UK biobank sample consists of participants aged over 40 years old, although most of cardiomyopathy screenings occurs in a younger population. Finally, the temporal

association between risk factors and the extent of trabeculation and cause-and-effect relationship was not under the scope of this study.

In conclusion, deep learning-based automated segmentation enabled accurate, high-throughput quantification of LV trabeculation and papillary muscle in a large population-based biomedical database, the UK Biobank. We described the normal variation of LV trabeculation with age stratified by sex and highlighted that higher trabecular mass was observed with hypertension, higher BMI, and higher physical activity levels. Future studies should also evaluate the long-term impact of cardiovascular risk factors on changes in trabecular architecture and subsequent prognostic implications in both healthy hearts and cardiomyopathies.

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Tables

Table 1. Demographic characteristics, cardiovascular risk factors, and left ventricular measurements for the reference group and exposed group

| Variable | Entire White group Male | Entire White group Female | Reference Male | Reference Female | Exposed Male | Exposed Female | Reference vs. Exposed Male | Reference vs. Exposed Female |
|---|---|---|---|---|---|---|---|---|
| **n** | 20678 | 22360 | 2655 | 4729 | 14918 | 13754 | | |
| **Age, mean (SD)** | 64.9 (7.8) | 63.5 (7.5) | 60.4 (7.4) | 59.9 (6.9) | 66.1 (7.5) | 64.9 (7.3) | <.001 | <.001 |
| **Age range, years** | 45 to 80 | 45 to 80 | 45 to 80 | 45 to 80 | 46 to 80 | 46 to 80 | | |
| **Height, cm, mean (SD)** | 176.2 (6.6) | 162.9 (6.2) | 177.7 (6.7) | 164.1 (6.2) | 175.8 (6.5) | 162.4 (6.2) | <.001 | <.001 |
| **Weight, kg, median (IQR)** | 82.0 [74.5, 91.0] | 66.9 [60.0, 75.5] | 77.4 [71.1, 84.3] | 63.4 [57.9, 69.8] | 83.0 [75.3, 92.1] | 68.0 [60.7, 77.0] | <.001 | <.001 |
| **BMI, median (IQR)** | 26.4 [24.3, 29.0] | 25.2 [22.7, 28.4] | 24.6 [22.8, 26.5] | 23.6 [21.7, 25.7] | 26.9 [24.7, 29.5] | 25.8 [23.1, 29.1] | <.001 | <.001 |
| **BSA, m², mean (SD)** | 2.00 (0.2) | 1.7 (0.2) | 2.0 (0.1) | 1.7 (0.1) | 2.0 (0.2) | 1.7 (0.2) | <.001 | <.001 |
| **SBP, mmHg, mean (SD)** | 141.9 (17.3) | 136.5 (19.5) | 126.4 (8.8) | 122.3 (10.5) | 143.6 (17.4) | 139.4 (19.8) | <.001 | <.001 |
| **DBP, mmHg, mean (SD)** | 79.7 (10.2) | 76.0 (10.5) | 74.0 (7.5) | 71.1 (8.1) | 80.0 (10.3) | 76.8 (10.6) | <.001 | <.001 |
| **Smoking status, n (%)** | | | | | | | <.001 | <.001 |
| ***Never*** | 11958 (58.4) | 14513 (65.6) | 2642 (100.0) | 4713 (100.0) | 6278 (42.4) | 6019 (44.2) | | |
| ***Previous*** | 7719 (37.7) | 6985 (31.6) | 0 (0.0) | 0 (0.0) | 7719 (52.1) | 6985 (51.3) | | |
| ***Current*** | 808 (3.9) | 621 (2.8) | 0 (0.0) | 0 (0.0) | 808 (5.5) | 621 (4.6) | | |
| **Regular alcohol intake = Yes, n (%)** | 11002 (53.6) | 8739 (39.4) | 1211 (45.8) | 1707 (36.2) | 8267 (55.7) | 5735 (41.9) | <.001 | <.001 |
| **Total METs minutes per week, median (IQR)** | 2075.0 [1055.0, 3753.0] | 2044.0 [1004.0, 3705.0] | 2146.0 [1140.5, 3813.0] | 2190.0 [1132.5, 3870.0] | 2017.5 [1029.0, 3672.0] | 1999.5 [982.5, 3657.0] | .02 | <.001 |
| **Activity score, n (%)** | | | | | | | <.001 | <.001 |
| ***Low*** | 2518 (12.6) | 2720 (12.9) | 280 (10.8) | 473 (10.4) | 1906 (13.2) | 1750 (13.5) | | |
| ***Moderate*** | 8219 (41.2) | 9279 (43.9) | 1033 (39.9) | 1948 (42.7) | 6035 (41.9) | 5766 (44.5) | | |
| ***High*** | 9232 (46.2) | 9156 (43.3) | 1278 (49.3) | 2146 (47.0) | 6466 (44.9) | 5431 (41.9) | | |
| **Hypertension = Yes, n (%)** | 8089 (39.1) | 5718 (25.6) | 0 (0.0) | 0 (0.0) | 8089 (54.2) | 5718 (41.6) | <.001 | <.001 |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Hyperlipidemia = Yes, n (%)** | 8671 (41.9) | 6561 (29.3) | 0 (0.0) | 0 (0.0) | 8671 (58.1) | 6561 (47.7) | <.001 | <.001 |
| **Diabetes = Yes, n (%)** | 1562 (7.6) | 877 (3.9) | 0 (0.0) | 0 (0.0) | 1562 (10.5) | 877 (6.4) | <.001 | <.001 |
| **LVT mass, g, median (IQR)** | 6.8 [5.0, 8.9] | 5.0 [3.6, 6.6] | 6.3 [4.7, 8.5] | 4.6 [3.4, 6.0] | 6.8 [5.1, 9.0] | 5.1 [3.8, 6.7] | <.001 | <.001 |
| **LVPM mass, g, median (IQR)** | 7.5 [5.8, 9.2] | 5.8 [4.5, 7.2] | 7.6 [6.1, 9.0] | 5.7 [4.5, 7.0] | 7.5 [5.7, 9.2] | 5.8 [4.4, 7.2] | >.99 | >.99 |
| **T/TMM, %, median (IQR)** | 5.9 [4.5, 7.4] | 6.2 [4.7, 7.8] | 5.8 [4.5, 7.4] | 6.0 [4.5, 7.7] | 5.9 [4.6, 7.5] | 6.3 [4.8, 7.9] | >.99 | <0.001 |
| **LVEDV, mL, median (IQR)** | 165.4 [146.1, 186.5] | 126.9 [113.1, 142.5] | 167.8 [150.0, 188.4] | 127.0 [113.6, 141.5] | 164.3 [144.9, 185.4] | 126.3 [112.4, 142.0] | <.001 | >.99 |
| **LVESV, mL, median (IQR)** | 69.0 [58.6, 81.5] | 49.0 [41.7, 57.1] | 71.0 [61.1, 82.2] | 49.5 [42.9, 57.0] | 68.4 [57.9, 81.2] | 48.4 [41.1, 56.8] | <.001 | <0.001 |
| **LVSV, mL, median (IQR)** | 95.1 [83.4, 108.3] | 77.4 [68.3, 87.5] | 96.5 [84.8, 109.1] | 76.9 [68.1, 86.5] | 94.5 [82.8, 107.6] | 77.1 [68.1, 87.4] | <.001 | >.99 |
| **LVEF, %, median (IQR)** | 57.9 [54.0, 61.9] | 61.2 [57.5, 64.9] | 57.5 [54.0, 61.2] | 60.7 [57.2, 64.2] | 58.0 [54.0, 62.0] | 61.4 [57.6, 65.2] | .03 | <.001 |
| **LVM, g, median (IQR)** | 100.7 [89.8, 113.0] | 69.5 [62.1, 77.9] | 95.8 [85.7, 106.5] | 65.8 [59.6, 72.8] | 101.5 [90.5, 113.8] | 70.5 [63.0, 79.3] | <.001 | <.001 |
| **LVMVR, g/mL, median (IQR)** | 0.6 [0.6, 0.7] | 0.6 [0.5, 0.6] | 0.6 [0.5, 0.6] | 0.5 [0.5, 0.6] | 0.6 [0.6, 0.7] | 0.6 [0.5, 0.6] | <.001 | <.001 |

Notes – BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); BSA, body surface area; SBP, systolic blood pressure; DBP, diastolic blood pressure; MET, metabolic equivalent of task; LVT, left ventricular trabecular mass; LVPM, left ventricular papillary muscles; T/TMM, trabecular mass-to-total myocardial mass ratio; LVEDV, left-ventricular end-diastolic volume; LVESV, left ventricular end-systolic volume; LVSV, left ventricular stroke volume; LVEF, left ventricular ejection fraction; LVM, left ventricular mass; LVMVR, left ventricular mass to end-diastolic volume ratio. Normally distributed variables were expressed in mean (SD) and non-normally distributed variables were expressed in median (IQR). All P values were adjusted for multiple testing by Bonferroni correction.

Table 2. Multivariable analysis showing the relationship between cardiovascular risk factors and LV trabecular mass, papillary muscle mass, and trabeculation mass- to- total myocardial mass ratio measurements in the entire group of White adults between 45 and 80 years old (n = 43038)

| Variable | LVT mass (g) | | | LVPM mass (g) | | | T/TMM (%) | | |
|---|---|---|---|---|---|---|---|---|---|
| | β | 95% CI | *P* | β | 95% CI | *P* | β | 95% CI | *P* |
| **Age (per SD change)** | 0.05 | 0.02, 0.08 | <.001 | -0.25 | -0.27, -0.22 | <.001 | 0.12 | 0.09, 0.14 | <.001 |
| **Sex (Male to Female)** | -0.68 | -0.75, -0.6 | <.001 | -0.58 | -0.64, -0.51 | <.001 | 0.56 | 0.49, 0.62 | <.001 |
| **Height (per SD change)** | 0.72 | 0.68, 0.75 | <.001 | 0.77 | 0.74, 0.8 | <.001 | 0.13 | 0.1, 0.16 | <.001 |
| **BMI (per SD change)** | 0.66 | 0.63, 0.68 | <.001 | 0.37 | 0.35, 0.4 | <.001 | 0.19 | 0.16, 0.21 | <.001 |
| **Hypertension** | 0.42 | 0.36, 0.48 | <.001 | 0.20 | 0.15, 0.25 | <.001 | 0.07 | 0.02, 0.12 | .02 |
| **Diabetes mellitus** | -0.11 | -0.23, -0.01 | .25 | -0.27 | -0.37, -0.17 | <.001 | -0.04 | -0.14, 0.06 | >.99 |
| **Hyperlipidemia** | -0.04 | -0.10, 0.01 | .43 | -0.09 | -0.14, -0.04 | <.001 | 0.001 | -0.05, 0.05 | >.99 |
| **Physical activity in total MET minutes per week (per SD change)** | 0.15 | 0.12, 0.17 | <.001 | 0.15 | 0.12, 0.17 | <.001 | 0.03 | 0.01, 0.05 | .02 |
| **Previous smoking history (vs. never smoking history)** | 0.03 | -0.03, 0.08 | >.99 | 0.05 | 0.001, 0.09 | .14 | 0.0003 | -0.05, 0.05 | >.99 |
| **Current smoking history (vs. never smoking history)** | 0.24 | 0.1, 0.39 | .003 | 0.11 | -0.01, 0.24 | .23 | 0.06 | -0.06, 0.19 | >.99 |

Notes – LVT, left ventricular trabecular; LVPM, left ventricular papillary muscle; T/TMM, trabeculation mass-to-total myocardial mass ratio; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); MET, metabolic equivalent of task. The P values were obtained from a generalized linear model with a Gamma regression. The P values were adjusted for multiple testing by Bonferroni correction.

Table 3. Normal reference ranges of left ventricular measurements for men

| Variable | Overall | Age groups (y) | | | |
|---|---|---|---|---|---|
| | | 45-50 | 51-60 | 61-70 | 71-80 |
| **n** | 2655 | 199 | 1214 | 952 | 290 |
| **LVT mass, g** | | | | | |
| **mean±SD** | 6.6 ± 2.7 | 7.0 ± 3.0 | 6.8 ± 2.7 | 6.5 ± 2.5 | 6.2 ± 2.5 |
| **median (IQR)** | 6.3 (4.7, 8.4) | 6.5 (4.8, 8.7) | 6.4 (4.7, 8.5) | 6.2 (4.6, 8.0) | 5.9 (4.3, 7.8) |
| **Reference Interval** | 2.3 - 12.7 | 2.6 - 13.9 | 2.3 - 12.8 | 2.3 - 12.0 | 2.0 - 12.1 |
| **LVT mass/BSA, g/m²** | | | | | |
| **mean±SD** | 3.4 ± 1.3 | 3.5 ± 1.3 | 3.4 ± 1.3 | 3.4 ± 1.3 | 3.2 ± 1.3 |
| **median (IQR)** | 3.2 (2.4, 4.2) | 3.3 (2.5, 4.2) | 3.3 (2.4, 4.3) | 3.2 (2.4, 4.2) | 3.1 (2.3, 4.0) |
| **Reference Interval** | 1.2 - 6.3 | 1.3 - 6.6 | 1.2 - 6.2 | 1.2 - 6.4 | 1.1 - 6.1 |
| **LVPM mass, g** | | | | | |
| **mean±SD** | 7.5 ± 2.2 | 8.1 ± 2.2 | 7.8 ± 2.2 | 7.3 ± 2.0 | 6.7 ± 2.2 |
| **median (IQR)** | 7.5 (6.1, 8.9) | 8.1 (6.8, 9.4) | 7.8 (6.3, 9.2) | 7.3 (6.0, 8.6) | 6.7 (5.2, 8.1) |
| **Reference Interval** | 3.3 - 12.0 | 4.2 - 12.8 | 3.5 - 12.1 | 3.4 - 11.4 | 2.0 - 11.7 |
| **LVPM mass/BSA, g/m²** | | | | | |
| **mean±SD** | 3.9 ± 1.1 | 4.1 ± 1.0 | 4.0 ± 1.1 | 3.8 ± 1.0 | 3.5 ± 1.0 |
| **median (IQR)** | 3.9 (3.1, 4.6) | 4.1 (3.4, 4.7) | 4.0 (3.2, 4.7) | 3.8 (3.1, 4.5) | 3.6 (2.8, 4.2) |
| **Reference Interval** | 1.7 - 6.0 | 2.2 - 6.0 | 1.8 - 6.1 | 1.8 - 5.8 | 1.2 - 5.6 |
| **LVM, g** | | | | | |
| **mean±SD** | 96.2 ± 14.7 | 102.7 ± 16.0 | 99.2 ± 15.2 | 93.7 ± 13.1 | 88.9 ± 13.5 |
| **median (IQR)** | 95.6 (85.6, 106.1) | 102.8 (89.9, 113.6) | 98.6 (88.0, 109.0) | 93.0 (84.6, 102.1) | 88.7 (80.0, 98.2) |
| **Reference Interval** | 69.3 - 126.8 | 75.7 - 140.7 | 72.7 - 133.3 | 69.1 - 122.0 | 62.9 - 114.3 |
| **LVM/BSA, g/m2** | | | | | |
| **mean±SD** | 49.1 ± 6.3 | 51.7 ± 6.6 | 50.0 ± 6.4 | 48.3 ± 5.8 | 46.6 ± 5.9 |
| **median (IQR)** | 48.8 (44.7, 53.2) | 51.4 (47.0, 55.9) | 49.5 (45.5, 54.0) | 48.0 (44.3, 51.9) | 46.4 (42.6, 50.3) |
| **Reference Interval** | 37.7 - 62.3 | 40.0 - 65.9 | 38.4 - 64.1 | 37.9 - 60.9 | 35.1 - 58.4 |
| **T/TMM, %** | | | | | |
| **mean±SD** | 5.9 ± 2.0 | 5.9 ± 2.1 | 5.9 ± 2.0 | 6.0 ± 2.1 | 6.0 ± 2.2 |
| **median (IQR)** | 5.8 (4.4, 7.3) | 5.5 (4.5, 7.0) | 5.7 (4.4, 7.2) | 5.8 (4.5, 7.4) | 6.0 (4.4, 7.6) |
| **Reference Interval** | 2.3 - 10.3 | 2.3 - 11.0 | 2.3 - 10.1 | 2.5 - 10.7 | 2.3 - 10.8 |

LVT, left ventricular trabecular; BSA, body surface area; LVPM, left ventricular papillary muscle; LVM, left ventricular mass; T/TMM, trabecular mass-to-total myocardial mass ratio. Reference intervals represent 2.5% and

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97.5% percentile limits (95% interval).

Table 4. Reference normal ranges of left ventricular measurements for women

| Variable | Overall | Age groups (y) | | | |
|---|---|---|---|---|---|
| | | 45-50 | 51-60 | 61-70 | 71-80 |
| **n** | 4729 | 313 | 2344 | 1708 | 364 |
| **LVT mass, g** | | | | | |
| **mean±SD** | 4.7 ± 1.9 | 4.9 ± 2.1 | 4.7 ± 1.9 | 4.7 ± 1.9 | 4.6 ± 1.8 |
| **median (IQR)** | 4.5 (3.3, 5.9) | 4.7 (3.3, 6.0) | 4.5 (3.3, 5.9) | 4.5 (3.3, 5.9) | 4.3 (3.2, 5.8) |
| **Reference Interval** | 1.7 - 8.9 | 1.6 - 10.0 | 1.7 - 9.0 | 1.7 - 8.8 | 1.6 - 8.7 |
| **LVT mass/BSA, g/m²** | | | | | |
| **mean±SD** | 2.8 ± 1.1 | 2.8 ± 1.2 | 2.8 ± 1.1 | 2.8 ± 1.1 | 2.8 ± 1.1 |
| **median (IQR)** | 2.7 (2.0, 3.5) | 2.8 (2.0, 3.5) | 2.7 (2.0, 3.5) | 2.7 (2.0, 3.5) | 2.7 (1.9, 3.5) |
| **Reference Interval** | 1.0 - 5.2 | 1.1 - 5.6 | 1.0 - 5.1 | 1.0 - 5.3 | 1.0 - 5.1 |
| **LVPM mass, g** | | | | | |
| **mean±SD** | 5.7 ± 1.8 | 6.1 ± 1.8 | 5.9 ± 1.8 | 5.6 ± 1.8 | 5.0 ± 1.9 |
| **median (IQR)** | 5.7 (4.5, 7.0) | 6.0 (4.7, 7.3) | 5.9 (4.7, 7.1) | 5.6 (4.3, 6.8) | 5.0 (3.6, 6.4) |
| **Reference Interval** | 2.4 - 9.4 | 2.8 - 9.8 | 2.6 - 9.4 | 2.2 - 9.2 | 1.2 - 8.7 |
| **LVPM mass/BSA, g/m²** | | | | | |
| **mean±SD** | 3.4 ± 1.0 | 3.5 ± 1.0 | 3.5 ± 1.0 | 3.3 ± 1.0 | 3.0 ± 1.1 |
| **median (IQR)** | 3.4 (2.7, 4.1) | 3.5 (2.8, 4.2) | 3.5 (2.8, 4.1) | 3.3 (2.6, 4.0) | 3.1 (2.3, 3.8) |
| **Reference Interval** | 1.4 - 5.4 | 1.6 - 5.4 | 1.6 - 5.5 | 1.4 - 5.5 | 0.8 - 5.1 |
| **LVM, g** | | | | | |
| **mean±SD** | 66.2 ± 9.3 | 67.9 ± 9.7 | 67.4 ± 9.4 | 65.0 ± 9.0 | 62.7 ± 9.1 |
| **median (IQR)** | 65.6 (59.5, 72.4) | 67.5 (60.8, 74.1) | 66.9 (60.8, 73.6) | 64.5 (58.5, 71.3) | 61.8 (56.5, 69.0) |
| **Reference Interval** | 49.3 - 85.9 | 51.1 - 89.4 | 50.4 - 87.7 | 48.8 - 84.3 | 46.4 - 83.2 |
| **LVM/BSA, g/m2** | | | | | |
| **mean±SD** | 39.1 ± 4.6 | 39.4 ± 4.4 | 39.4 ± 4.7 | 38.7 ± 4.5 | 38.0 ± 4.7 |
| **median (IQR)** | 38.8 (35.8, 42.2) | 39.4 (36.2, 42.6) | 39.1 (36.1, 42.5) | 38.4 (35.5, 41.7) | 37.8 (34.9, 41.2) |
| **Reference Interval** | 30.6 - 48.9 | 30.9 - 48.2 | 31.0 - 49.3 | 30.6 - 48.5 | 29.0 - 47.8 |
| **T/TMM, %** | | | | | |
| **mean±SD** | 6.2 ± 2.2 | 6.1 ± 2.3 | 6.1 ± 2.2 | 6.2 ± 2.2 | 6.4 ± 2.4 |
| **median (IQR)** | 6.0 (4.5, 7.6) | 5.9 (4.4, 7.7) | 6.0 (4.4, 7.5) | 6.0 (4.6, 7.7) | 6.2 (4.7, 8.1) |
| **Reference Interval** | 2.4 - 11.0 | 2.4 - 11.0 | 2.2 - 10.8 | 2.5 - 11.1 | 2.5 - 11.9 |

LVT, left ventricular trabecular; BSA, body surface area; LVPM, left ventricular papillary muscle; LVM, left ventricular mass; T/TMM, trabecular mass-to-total myocardial mass ratio. Reference intervals represent 2.5% and 97.5% percentile limits (95% interval).

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Figure Legends

Figure 1. Examples of automatic segmentation and quality control pipeline for left ventricular structures

A. Cardiac MRI images of left ventricular short-axis; B. Complete segmentation and quality control pipeline; C. Automatic segmentation of left ventricular trabeculations (LVT, light blue), papillary muscles (PM, yellow), myocardium (M, dark blue) and blood cavity (BC, green), corresponding to each image in panel A using the deep-learning model in B. LV, left ventricle; EDLV, end-diastolic left ventricle.

Figure 2. Study flow chart

SBP, systolic blood pressure; DBP, diastolic blood pressure; CV, cardiovascular; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared);
*Full exclusion criteria are provided in Supplementary Table 1.

Figure 3. Association between age and LV trabeculations, LV papillary muscle and T/TMM ratio in the reference group for men (**A**) and women (**B**).

LVM, left ventricular mass; LVM/BSA, left ventricular mass on body surface area; LVPM, left ventricular papillary muscle mass; LVPM/BSA: left ventricular papillary muscle mass on body surface area; LVT, left ventricular trabeculation mass; LVT/BSA, left ventricular trabecular mass on body surface area; T/TMM, trabecular mass-to-total myocardial mass ratio
The P values were obtained from a generalized linear model with a Gamma distribution using age as an exposure variable. The P values were adjusted for multiple testing by Bonferroni correction.

Supplementary Table 1. Exclusion criteria

| UKB Data-field ID | Category | Answer | N |
|---|---|---|---|
| 20002 | Non Cancer Illness Code Self Reported | hypertension | 11373 |
| 20002 | Non Cancer Illness Code Self Reported | high cholesterol | 7792 |
| 20002 | Non Cancer Illness Code Self Reported | diabetes | 1601 |
| 20002 | Non Cancer Illness Code Self Reported | essential hypertension | 1113 |
| 20002 | Non Cancer Illness Code Self Reported | angina | 1087 |
| 20002 | Non Cancer Illness Code Self Reported | heart attack/myocardial infarction | 875 |
| 20002 | Non Cancer Illness Code Self Reported | type 2 diabetes | 792 |
| 20002 | Non Cancer Illness Code Self Reported | atrial fibrillation | 700 |
| 20002 | Non Cancer Illness Code Self Reported | stroke | 524 |
| 20002 | Non Cancer Illness Code Self Reported | heart valve problem/heart murmur | 363 |
| 20002 | Non Cancer Illness Code Self Reported | transient ischaemic attack (tia) | 343 |
| 20002 | Non Cancer Illness Code Self Reported | heart arrhythmia | 326 |
| 20002 | Non Cancer Illness Code Self Reported | rheumatic fever | 156 |
| 20002 | Non Cancer Illness Code Self Reported | svt / supraventricular tachycardia | 125 |
| 20002 | Non Cancer Illness Code Self Reported | diabetic eye disease | 124 |
| 20002 | Non Cancer Illness Code Self Reported | type 1 diabetes | 80 |
| 20002 | Non Cancer Illness Code Self Reported | peripheral vascular disease | 75 |
| 20002 | Non Cancer Illness Code Self Reported | atrial flutter | 59 |
| 20002 | Non Cancer Illness Code Self Reported | pericarditis | 44 |
| 20002 | Non Cancer Illness Code Self Reported | heart failure/pulmonary odema | 37 |
| 20002 | Non Cancer Illness Code Self Reported | cardiomyopathy | 30 |
| 20002 | Non Cancer Illness Code Self Reported | aortic stenosis | 29 |
| 20002 | Non Cancer Illness Code Self Reported | hypertrophic cardiomyopathy (hcm / hocm) | 25 |
| 20002 | Non Cancer Illness Code Self Reported | leg claudication/ intermittent claudication | 22 |
| 20002 | Non Cancer Illness Code Self Reported | aortic aneurysm | 22 |
| 20002 | Non Cancer Illness Code Self Reported | mitral valve prolapse | 21 |
| 20002 | Non Cancer Illness Code Self Reported | ischaemic stroke | 21 |
| 20002 | Non Cancer Illness Code Self Reported | mitral regurgitation / incompetence | 21 |
| 20002 | Non Cancer Illness Code Self Reported | wolff parkinson white / wpw syndrome | 18 |
| 20002 | Non Cancer Illness Code Self Reported | pericardial problem | 17 |

| | | | |
|---|---|---|---|
| 20002 | Non Cancer Illness Code Self Reported | aortic regurgitation / incompetence | 16 |
| 20002 | Non Cancer Illness Code Self Reported | myocarditis | 15 |
| 20002 | Non Cancer Illness Code Self Reported | mitral valve disease | 10 |
| 20002 | Non Cancer Illness Code Self Reported | diabetic nephropathy | 7 |
| 20002 | Non Cancer Illness Code Self Reported | aortic valve disease | 5 |
| 20002 | Non Cancer Illness Code Self Reported | renal failure requiring dialysis | 4 |
| 20002 | Non Cancer Illness Code Self Reported | hyperaldosteronism/conn's syndrome | 4 |
| 20002 | Non Cancer Illness Code Self Reported | mitral stenosis | 3 |
| 20002 | Non Cancer Illness Code Self Reported | pericardial effusion | 3 |
| 20002 | Non Cancer Illness Code Self Reported | aortic aneurysm rupture | 3 |
| 20002 | Non Cancer Illness Code Self Reported | sick sinus syndrome | 2 |
| 20002 | Non Cancer Illness Code Self Reported | phaeochromocytoma | 1 |
| 20002 | Non Cancer Illness Code Self Reported | cushings syndrome | 1 |
| 20002 | Non Cancer Illness Code Self Reported | aortic dissection | 1 |
| 20002 | Non Cancer Illness Code Self Reported | cerebrovascular disease | 0 |
| 20116 | Smoking Status | Previous | 16413 |
| 20116 | Smoking Status | Current | 2950 |
| 2966 | Age High Blood Pressure Diagnosed | | 12716 |
| 2976 | Age Diabetes Diagnosed | | 2204 |
| 4056 | Age Stroke Diagnosed | | 760 |
| 3894 | Age Heart Attack Diagnosed | | 983 |
| 3627 | Age Angina Diagnosed | | 1224 |
| 2443 | Diabetes Diagnosed By Doctor | Yes | 2275 |
| 21001 | Body Mass Index (BMI) | BMI > 30 (calculated as weight in kilograms divided by height in meters squared) | 7623 |
| 30690 | Cholesterol | Total cholesterol >= 7 | 5570 |
| 30750 | Glycated Haemoglobin (HbA1C) | HbA1C >= 48 | 841 |
| 41270 | Diagnoses Icd10 | Hypertension ICD10 codes: I10, I11, I110, I119, I12, I120, I129, I13, I130, I131, I132, I139, I15, I150, I151, I152, I158, I159, O10, O100, O101, O103, O104, O109, O11 | 6721 |
| 41270 | Diagnoses Icd10 | Hyperlipidaemia ICD10 codes: E780, E781, E782, E783, E784, E785 | 3192 |
| 41270 | Diagnoses Icd10 | Diabetes Mellitus ICD10 codes: E100, E101, E102, E103, E104, E105, E106, E107, E108, E109, E110, E111, E112, E113, E114, E115, E116, E117, E118, E119, E140, E141, E142, E143, E144, E145, E146, E147, E148, E149, | 1452 |

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| | | | |
|---|---|---|---|
| | | G590, G632, H280, N083, O240, O241, O243, O244, O249 | |
| 1249 | Past Tobacco Smoking | Smoked on most or all days | 11602 |
| 1249 | Past Tobacco Smoking | Smoked occasionally | 7420 |
| 1239 | Current Tobacco Smoking | Yes, on most or all days | 1847 |
| 1239 | Current Tobacco Smoking | Only occasionally | 1315 |
| 3140 | Pregnant | | 19 |
| 3079 | Pace Maker | | 15 |
| 6177 | Medication For Cholesterol Blood Pressure Or Diabetes | Cholesterol lowering medication | 7092 |
| 6177 | Medication For Cholesterol Blood Pressure Or Diabetes | Blood pressure medication | 6372 |
| 6177 | Medication For Cholesterol Blood Pressure Or Diabetes | Insulin | 203 |
| 6153 | Medication For Cholesterol Blood Pressure Diabetes Or Take Exogenous Hormones | Blood pressure medication | 4183 |
| 6153 | Medication For Cholesterol Blood Pressure Diabetes Or Take Exogenous Hormones | Cholesterol lowering medication | 3660 |
| 6153 | Medication For Cholesterol Blood Pressure Diabetes Or Take Exogenous Hormones | Insulin | 141 |
| 6150 | Vascular Heart Problems Diagnosed By Doctor | High blood pressure | 9663 |
| 6150 | Vascular Heart Problems Diagnosed By Doctor | Angina | 811 |
| 6150 | Vascular Heart Problems Diagnosed By Doctor | Heart attack | 602 |
| 6150 | Vascular Heart Problems Diagnosed By Doctor | Stroke | 418 |
| 22508 | Amount Of Tobacco Currently Smoked | No cigarettes, only smoke cigars or pipes | 44 |
| 22508 | Amount Of Tobacco Currently Smoked | Less than one cigarette per day | 1 |
| 22506 | Tobacco Smoking | Person who previously smoked | 8272 |
| 22506 | Tobacco Smoking | Smokes on most or all days | 420 |
| 22506 | Tobacco Smoking | Occasionally | 344 |
| 20415 | Ongoing Addiction To Alcohol | | 281 |
| 20004 | Operation Code | coronary angioplasty (ptca) +/- stent | 504 |
| 20004 | Operation Code | coronary artery bypass grafts (cabg) | 220 |
| 20004 | Operation Code | cardiac ablation | 185 |

| | | | |
|---|---|---|---|
| 20004 | Operation Code | carotid artery angioplasty +/- stent | 106 |
| 20004 | Operation Code | aortic aneurysm/repair or stent | 57 |
| 20004 | Operation Code | leg artery angioplasty +/- stent | 43 |
| 20004 | Operation Code | haemodialysis access / fistula surgery | 33 |
| 20004 | Operation Code | lung removal/pneumonectomy/lobectomy | 26 |
| 20004 | Operation Code | other arterial surgery/revascularisation procedures | 25 |
| 20004 | Operation Code | carotid artery surgery/endarterectomy | 23 |
| 20004 | Operation Code | renal artery angioplasty +/- stent | 16 |
| 20004 | Operation Code | leg artery aneurysm repair | 14 |
| 20004 | Operation Code | non-coronary artery angioplasty +/- stent | 11 |
| 20004 | Operation Code | fem-pop bypass/leg artery bypass | 8 |
| 20004 | Operation Code | renal/kidney transplant | 6 |
| 20004 | Operation Code | fistula for dialysis | 6 |
| 20004 | Operation Code | heart valve surgery | 5 |
| 20004 | Operation Code | pericardial surgery | 4 |
| 20004 | Operation Code | peritoneal dialysis (capd) access surgery | 4 |
| 20004 | Operation Code | cerebral artery aneurysm surgery or clipping | 3 |
| 20004 | Operation Code | defibrillator/icd insertion | 3 |
| 20004 | Operation Code | pacemaker/defibrillator insertion | 1 |
| 20004 | Operation Code | mitral valve repair/replacement | 1 |
| 20004 | Operation Code | other valve repair/replacement | 1 |
| 20004 | Operation Code | cardiovascular | 0 |
| 20004 | Operation Code | heart transplant | 0 |
| 20004 | Operation Code | aortic valve repair/replacement | 0 |
| 20004 | Operation Code | lung transplant | 0 |
| 20004 | Operation Code | pacemaker insertion | 0 |
| 20004 | Operation Code | pacemaker battery change | 0 |
| 20004 | Operation Code | defibrillator/icd battery change | 0 |
| 20004 | Operation Code | dialysis access surgery | 0 |
| 20001 | Cancer Code Self Reported | heart / mediastinum cancer | 1 |

Note: N column represents the number meeting the criterion on the same row. Frequently, participants met multiple criteria.

Supplementary Table 2. Multivariable Analysis showing the relationship between cardiovascular risk factors and LV trabecular mass and LV papillary muscle mass in the entire group of White adults between 45 and 80 years old (n = 43038) after additionally adjusting for LVM

| Variable | LVT mass (g) | | | LVPM mass (g) | | |
|---|---|---|---|---|---|---|
| | β | 95% CI | *P* | β | 95% CI | *P* |
| **Age (per SD change)** | 0.09 | 0.07 to 0.11 | <.001 | -0.20 | -0.22 to -0.18 | <.001 |
| **Sex (Male to Female)** | 0.40 | 0.33 to 0.48 | <.001 | 0.65 | 0.59 to 0.72 | <.001 |
| **Height (per SD change)** | 0.24 | 0.2 to 0.27 | <.001 | 0.20 | 0.17 to 0.23 | <.001 |
| **BMI (per SD change)** | 0.29 | 0.26 to 0.31 | <.001 | -0.09 | -0.11 to -0.07 | <.001 |
| **Hypertension** | 0.12 | 0.07 to 0.18 | <.001 | -0.13 | -0.18 to -0.09 | <.001 |
| **Diabetes mellitus** | -0.05 | -0.16 to 0.06 | >.99 | -0.22 | -0.31 to -0.14 | <.001 |
| **Hyperlipidemia** | -0.01 | -0.07 to 0.04 | >.99 | -0.05 | -0.1 to -0.01 | .051 |
| **Physical activity in total MET minutes per week (per SD change)** | 0.04 | 0.02 to 0.07 | <.001 | 0.03 | 0.01 to 0.05 | .021 |
| **Previous smoking history** | 0.0002 | -0.05 to 0.05 | >.99 | 0.03 | -0.01 to 0.07 | .53 |
| **Current smoking history** | 0.08 | -0.05 to 0.21 | .74 | -0.10 | -0.21 to 0.02 | .29 |
| **LVM (per SD change)** | 1.33 | 1.29 to 1.38 | <.001 | 1.6 | 1.56 to 1.64 | <.001 |

LVT, left ventricular trabecular; LVPM, left ventricular papillary muscle; BSA, body surface area; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); MET, metabolic equivalent of task; LVM, left ventricular mass. The P values were adjusted for multiple testing by Bonferroni correction.

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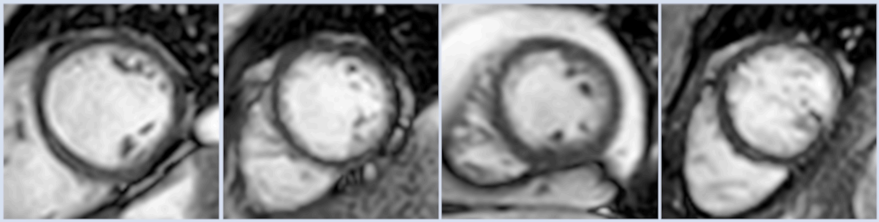
Supplementary Figure 1. Distributions of LV parameters

LVT, left ventricular trabecular mass; BSA, body surface area; LVPM, left ventricular papillary muscle mass; LVM, left ventricular mass; T/TMM, trabecular mass-to-total myocardial mass ratio.

A



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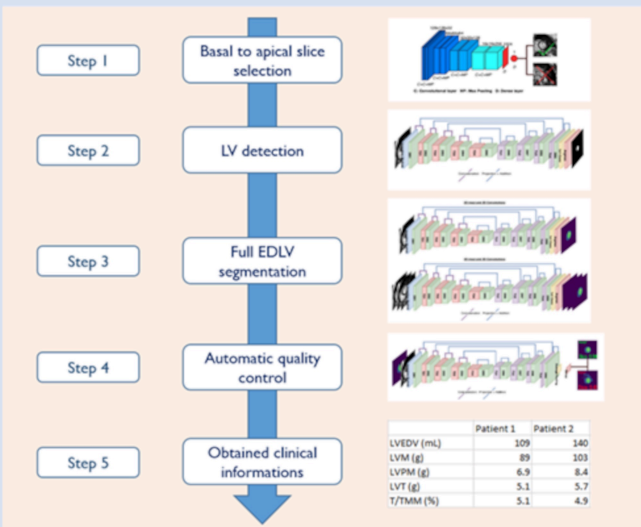
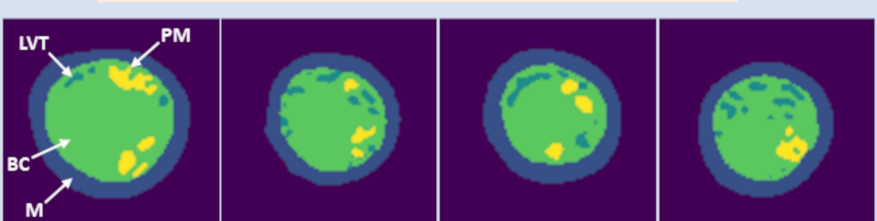
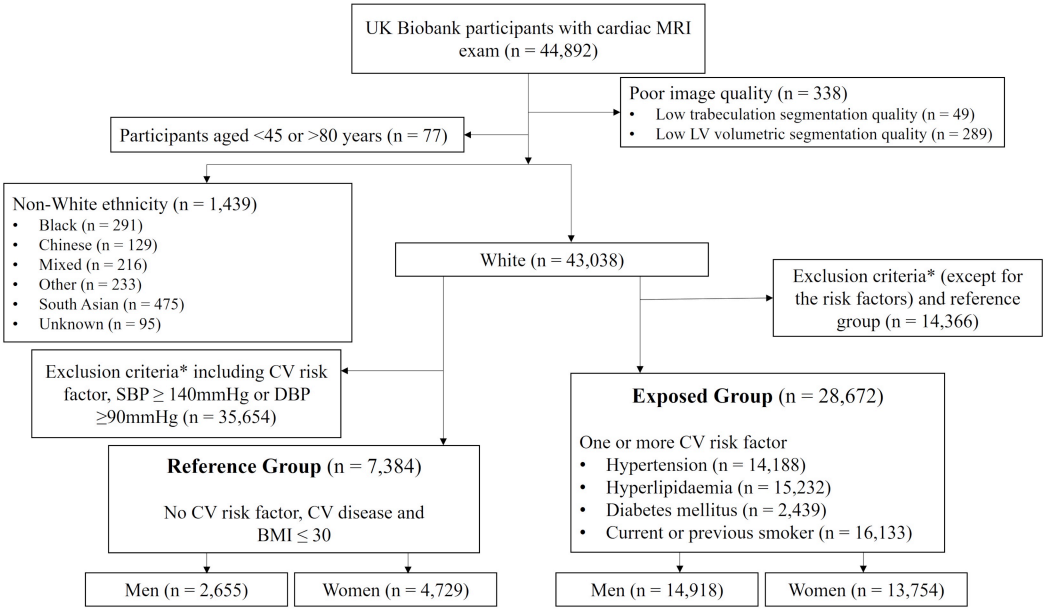
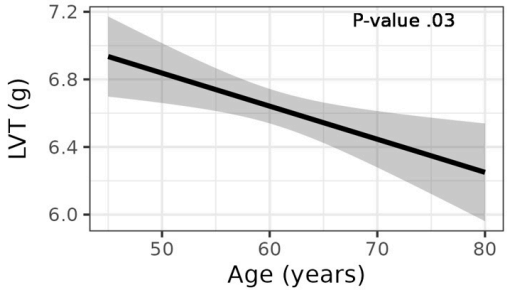


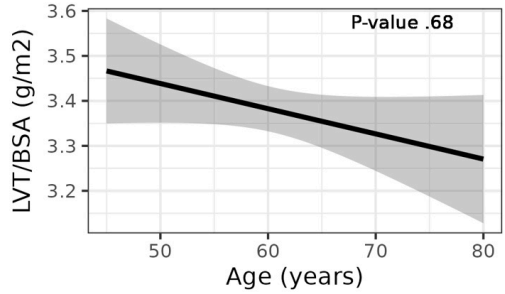

| | Patient 1 | Patient 2 |
|---|---|---|
| LVEDV (mL) | 109 | 140 |
| LVM (g) | 89 | 103 |
| LVPM (g) | 6.9 | 8.4 |
| LVT (g) | 5.1 | 5.7 |
| T/TMM (%) | 5.1 | 4.9 |

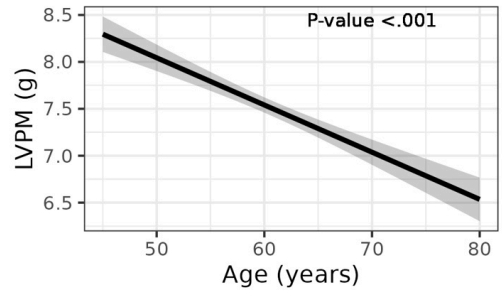
C

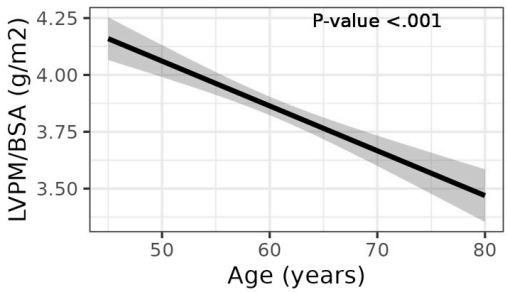


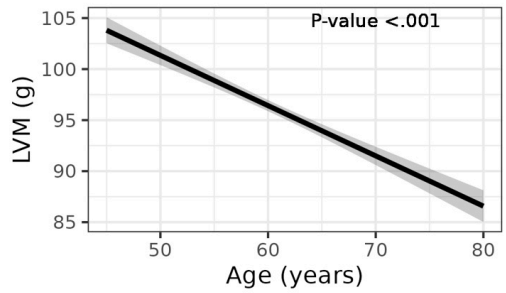

UK Biobank participants with cardiac MRI exam (n = 44,892)
Poor image quality (n = 338)
• Low trabeculation segmentation quality (n = 49)
• Low LV volumetric segmentation quality (n = 289)
Participants aged <45 or >80 years (n = 77)
Non-White ethnicity (n = 1,439)
• Black (n = 291)
• Chinese (n = 129)
• Mixed (n = 216)
• Other (n = 233)
• South Asian (n = 475)
• Unknown (n = 95)
White (n = 43,038)
Exclusion criteria* (except for the risk factors) and reference group (n = 14,366)
Exclusion criteria* including CV risk factor, SBP ≥ 140mmHg or DBP ≥90mmHg (n = 35,654)
Exposed Group (n = 28,672)
One or more CV risk factor
• Hypertension (n = 14,188)
• Hyperlipidaemia (n = 15,232)
• Diabetes mellitus (n = 2,439)
• Current or previous smoker (n = 16,133)
Reference Group (n = 7,384)
No CV risk factor, CV disease and BMI ≤ 30
Men (n = 2,655)
Women (n = 4,729)
Men (n = 14,918)
Women (n = 13,754)


P-value .03
LVT (g)
7.2
6.8
6.4
6.0
50
60
70
80
Age (years)


P-value .68
LVT/BSA (g/m2)
3.6
3.5
3.4
3.3
3.2
50
60
70
80
Age (years)


P-value <.001
LVPM (g)
8.5
8.0
7.5
7.0
6.5
50
60
70
80
Age (years)


P-value <.001
LVPM/BSA (g/m2)
4.25
4.00
3.75
3.50
50
60
70
80
Age (years)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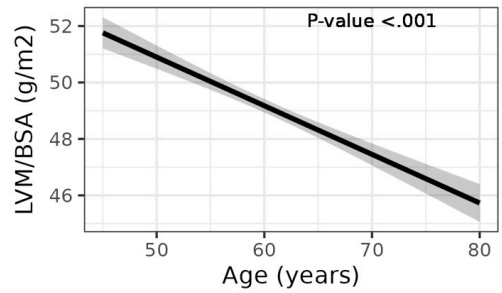
LVM (g)
105
100
95
90
85
50
60
70
80
Age (years)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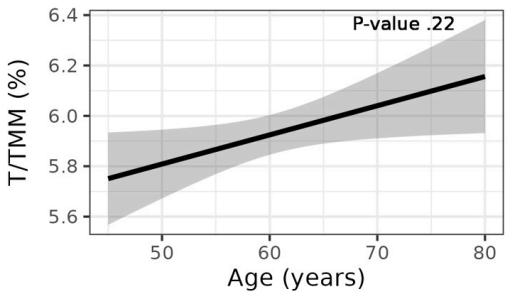
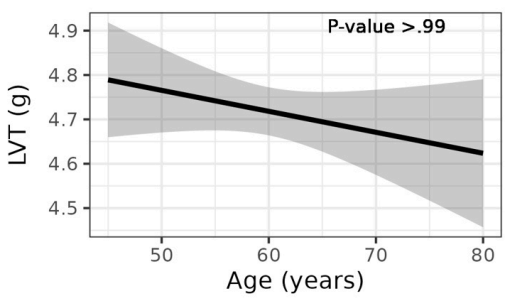
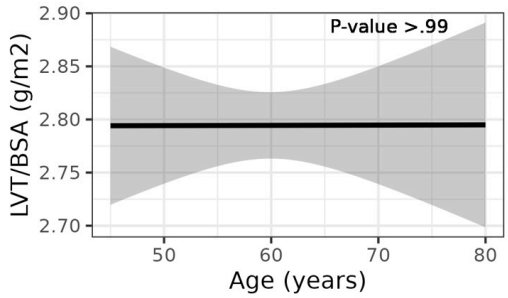
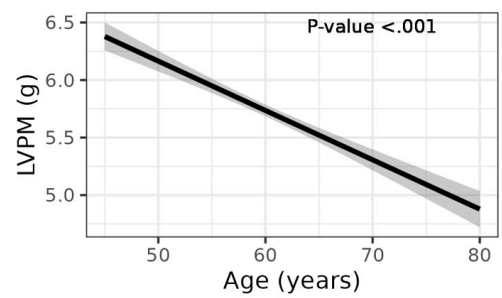
LVM/BSA (g/m2)
52
50
48
46
50
60
70
80
Age (years)


P-value .22
T/TMM (%)
6.4
6.2
6.0
5.8
5.6
50
60
70
80
Age (years)


P-value >.99
LVT (g)
4.9
4.8
4.7
4.6
4.5
50
60
70
80
Age (years)


P-value >.99
LVT/BSA (g/m2)
2.90
2.85
2.80
2.75
2.70
50
60
70
80
Age (years)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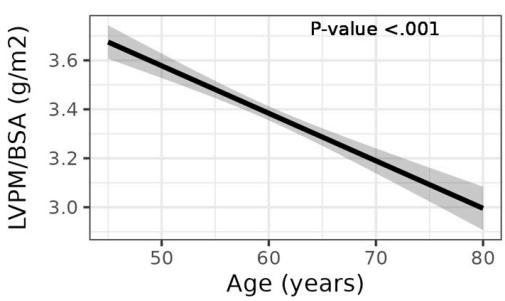
LVPM (g)
6.5
6.0
5.5
5.0
50
60
70
80
Age (years)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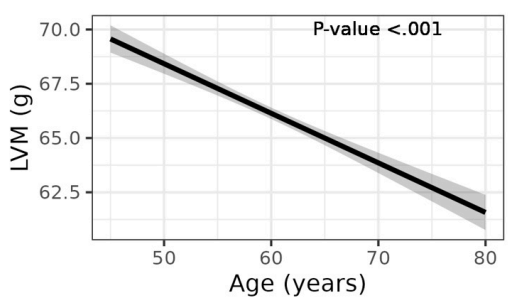
LVPM/BSA (g/m2)
3.6
3.4
3.2
3.0
50
60
70
80
Age (years)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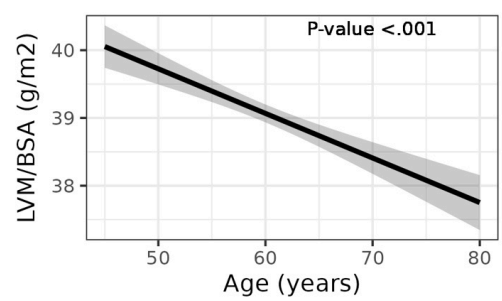
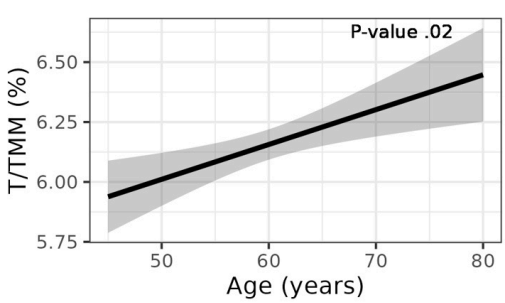
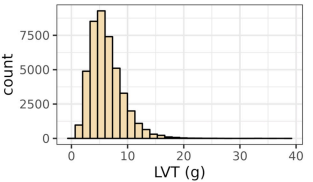
LVM (g)
70.0
67.5
65.0
62.5
50
60
70
80
Age (years)


P-value <.001
LVM/BSA (g/m2)
40
39
38
50
60
70
80
Age (years)


P-value .02
T/TMM (%)
6.50
6.25
6.00
5.75
50
60
70
80
Age (years)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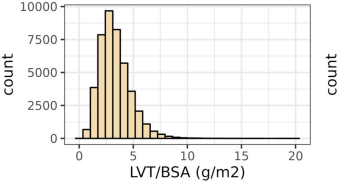
LVT (g)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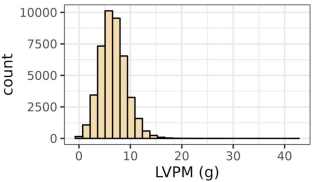
LVT/BSA (g/m2)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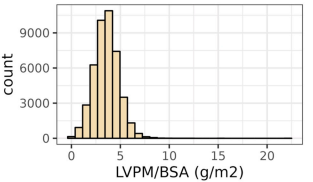
LVPM (g)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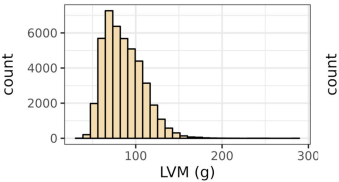
LVPM/BSA (g/m2)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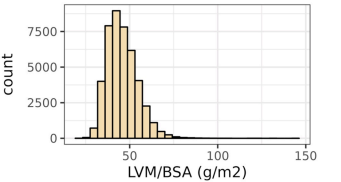
LVM (g)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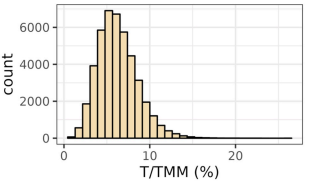
LVM/BSA (g/m2)


count
T/TMM (%)