CMR-Derived Basal Septal Curvature is a Measurable Early Marker of Hypertensive Heart Disease: Evidence from 38,830 UK Biobank Participants

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Abstract

Basal septal hypertrophy (BSH) occurs in up to 20% of hypertensive patients, but no quantitative marker exists for detecting early geometric changes preceding overt BSH. We investigated whether CMR-derived basal septal curvature (BSC) captures early hypertensive remodelling and predicts cardiovascular events.

In 38,830 UK Biobank participants, BSC was automatically derived from a 3D shape model, correlated with cardiac parameters, and tested in survival models for associations with incident hypertension and MACE.

BSC correlated with basal septum thickness (r=0.39), age (r=0.35), and LV remodelling (r=0.34), and inversely with aortic distensibility, LA reservoir volume and LV filling (r=-0.24 to -0.31) (p<0.001 for all). Hypertensive participants had higher BSC (p<0.001). BSC independently predicted incident hypertension in both sexes (HR 1.10–1.33, strongest under 65, p<0.05) but was not independently associated with incident MACE. Low BSC/low septal thickness was associated with a 4-fold lower 5-year hypertension incidence than high values in both (98.2% vs 93.1%). Septal thickness remained the stronger predictor of long-term events.

CMR-derived BSC is a reliable early biomarker of hypertensive cardiac remodelling that independently predicts incident hypertension, while basal septal thickness remains the stronger marker of subsequent cardiovascular events; together they may complement conventional risk stratification.

1. Introduction

Systemic hypertension is a major driver of cardiovascular disease and heart failure. Hypertension-mediated LV hypertrophy increases cardiovascular risk 2- to 4-fold [1,2], yet concentric remodelling and hypertrophy occur relatively late in disease progression [3,4]. Sensitive early markers are needed to improve mechanistic understanding and enable timelier intervention [2,4].

The basal interventricular septum is particularly vulnerable to biomechanical stress due to its greater radius of curvature, biventricular pressure exposure, and late activation [5], making basal septal measurements sensitive markers of hypertensive heart disease [6]. Basal septal hypertrophy (BSH) occurs in ~1.5% of the general population but rises to 20% in hypertensive elderly patients [5,7].

BSH diagnosis remains challenging due to inconsistent definitions and measurement techniques [8]. Basal septal thickness (BST), the conventional marker, does not capture geometric change. Basal septal curvature (BSC) has been proposed as a more robust alternative, showing greater reproducibility and stronger correlation with functional parameters on echocardiography [8], as it captures changes in shape rather than thickness alone [7,8]. BSC is calculated as the inverse radius of curvature along the LV endocardial contour, classified as concave or convex depending on the centre of curvature's position relative to the LV cavity [8] (Figure 1). BSC has not previously been evaluated against hypertension and incident events using cardiovascular magnetic resonance (CMR).

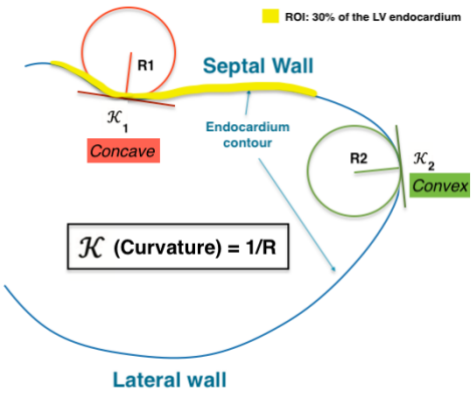

Figure 1. BSC calculation. Blue curve: endocardial contour in four-chamber view (septum top, apex right). Yellow curve: region (basal 30% of arc, excluding base) over which negative curvature is averaged.

We therefore investigated the significance of BSC and BSH in hypertension development using the UK Biobank CMR cohort, developing a novel 3D shape-modelling method to estimate BSC in 38,830 participants and comparing BSC and BST associations with prevalent hypertension, risk factors, incident hypertension, and major adverse cardiovascular events (MACE).

2. Methods

2.1. Study Population and 3D Shape Modelling

This study used UK Biobank data (application 2964) [9], a prospective cohort of ~500,000 participants aged 40–69 at recruitment; imaging protocols have been described previously [10]. CMR long- and short-axis images were segmented using fully automated contouring (CVI42 v5.11), and a biventricular 3D subdivision-surface mesh was customised to end-diastole via non-rigid diffeomorphic registration, as previously described [11,12]. Quality control excluded incomplete segmentations and statistical outliers [11], leaving 38,830 participants for analysis.

2.2. 2D LV Contour Extraction and Curvature Quantification

Four-chamber contours were derived from the 3D shape models to enable comparison with echocardiographic studies [8]. A virtual four-chamber plane, defined through the mitral and tricuspid annular centroids and the LV apex, was intersected with the LV endocardial mesh to generate a closed 3D contour, which was projected onto 2D and re-parameterised (~140 ordered points). Contours were interpolated using a radial basis function and resampled to 500 equidistant points for stable curvature estimation. Curvature outliers were excluded using non-standard Tukey's fences (3×IQR, 15th–85th percentile). BSC was calculated as the magnitude of mean negative curvature across the basal 30% of the septal contour (noisy near-basal points excluded); higher values indicate greater septal concavity (Figure 1).

Basal septal thickness (BST) was calculated as the mean of basal anteroseptal and inferoseptal thicknesses, automatically contoured by a deep-learning algorithm on end-diastolic short-axis cine images, using the maximum distance between layers per segment [14]. BSC and BST were standardised (z-scores) before analysis.

2.3. Outcomes

Hypertensive status was defined using self-report, hospital admission records (ICD-9/ICD-10: 401, 403; I10–I15), death registry data, and antihypertensive medication use, classified as prevalent or incident relative to the CMR date. MACE was a composite of myocardial infarction, stroke, or cardiovascular death, identified from hospital episode statistics and death registry ICD codes.

2.4. Statistical Analysis

Continuous variables are reported as mean ± SD or median (IQR); categorical variables as n (%). Associations between BSC and continuous variables were assessed using Pearson's correlation. Participants were stratified into four groups by BSC/BST z-score (>0 vs ≤0): High/High, High/Low, Low/High, Low/Low. Cumulative incidence was estimated from the CMR date to the first event or censoring, with group differences assessed by the log-rank test (Bonferroni-adjusted α=0.008). Multivariable Cox models evaluated associations of BSC and BST (entered separately due to their correlation, r=0.39) with incident hypertension and MACE, stratified by sex and adjusted for age, BMI, height, diabetes, high cholesterol, smoking status, and an age × BSC interaction term; VIFs<5 were considered acceptable [13]. Where age interactions were significant, analyses were stratified by age (<65, ≥65 years).

3. Results

3.1. Study Sample

Out of 38,830 participants, 53% were female, and the mean age was 63.9 ± 7.7 years. Prevalent hypertension was present in 27% of participants (10,644), with a higher prevalence in males (34%) than females (21%). Participants with hypertension had significantly higher BSC (2.14 ± 0.77 dm^{-1} vs 1.83 ± 0.74 dm^{-1}, P<0.001) and BST (9.22 ± 1.47 mm vs 8.18 ± 1.38 mm, P <0.001) compared to those without hypertension.

3.2. Associations Between Basal Septal Geometry and Cardiovascular Risk Factors

BSC positively correlated with BST (r = 0.39), age (r = 0.35), and LV mass-to-end-diastolic volume ratio (r = 0.34; P<0.001 for all). Conversely, BSC was negatively correlated with LV peak filling rate (LVPFR) (r = −0.31), left atrial reservoir volume (LARV) (r = −0.28), and ascending aortic distensibility (AoD) (r = −0.24; P < 0.001 for all).

3.3. Basal Septal Geometry and Incident Diagnosed Hypertension during follow-up

After excluding 10,644 participants (27%) with prevalent hypertension and 158 with missing covariates, 28,028 participants remained. Over a median 5.7-year follow-up, 1,257 (4.5%) developed incident hypertension, with a clear gradient across BSC–BST groups: Low BSC/Low BST had the lowest risk and High BSC/High BST the highest (5-year hypertension-free survival: 98.2% vs 93.1%; log-rank χ^2=364.63, P<0.001), with pairwise comparisons significant after Bonferroni correction for all group combinations except High BSC/High BST vs Low BSC/High BST (P<0.001; Figure 2), suggesting synergistic effects. In adjusted Cox models, BSC independently predicted incident hypertension, most strongly among females and males under 65 (HRs of 1.33 and 1.30 per SD, respectively; both P<0.001). BST was independently associated with incident hypertension across all subgroups, with hazard ratios ranging from 1.27 (older males) to 1.93 per SD (females under 65) (Figure 3).

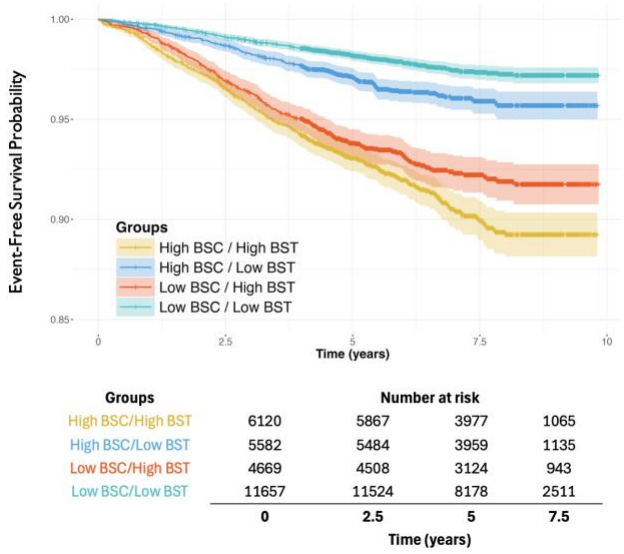

Figure 2. Kaplan–Meier hypertension-free survival by BSC/BST group (n = 28,028; median follow-up 5.7 years). Shaded areas = 95% CI.

3.4. Basal Septal Geometry and Incident Major Adverse Cardiovascular Events

After excluding 214 participants with missing covariates, 38,616 remained. Over a median 5.7-year follow-up, 823 MACE events occurred, with rates ranging from 1.0% (Low BSC/Low BST) to 3.3% (High BSC/High BST) (5-year cumulative incidence 0.9% vs 2.9%; log-rank χ^2=163.6, P<0.0001). Pairwise comparisons after Bonferroni correction were significant across most group combinations (P<0.001), except High BSC/High BST vs Low BSC/High BST. In adjusted Cox models, BSC was not independently associated with incident MACE in any subgroup (females HR 1.04, P=0.58; females <65 HR 1.16, P=0.183; females ≥65 HR 1.11, P=0.097; males HR 1.08, P=0.148; males <65 HR 1.16, P=0.095; males ≥65 HR 1.01, P=0.82), though point estimates trended higher in participants under 65 in both sexes. BST, in contrast, was independently associated with MACE across all subgroups (all P<0.001), with hazard ratios ranging from 1.32 (older males) to 1.98 (younger females) (Figure 3).

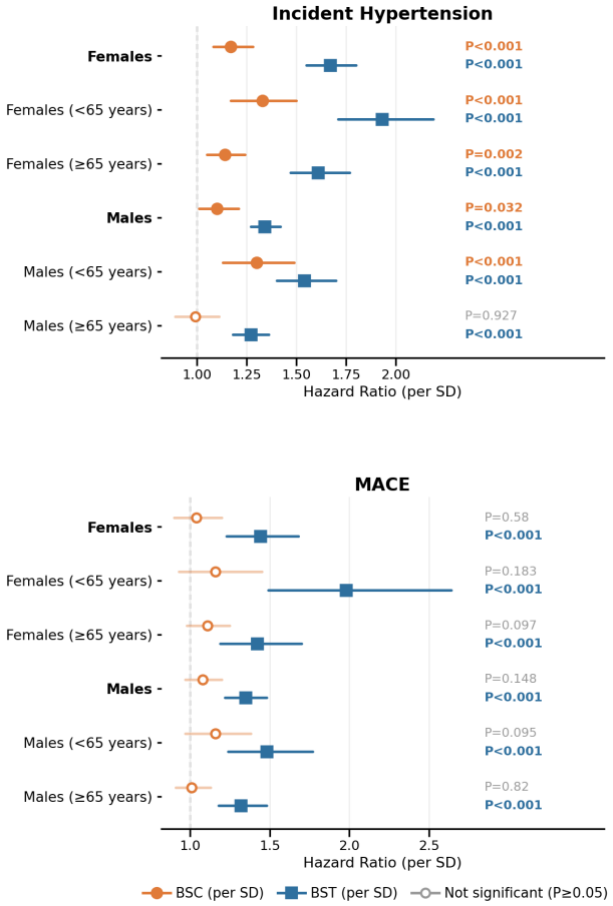

Figure 3. Cox proportional hazards results for incident hypertension and MACE outcomes by sex and age subgroup for the BSC and BST.

4. Discussion

In this cohort of 38,830 UK Biobank participants, septal geometry independently predicted hypertension diagnosis and adverse events for the first time. BSC predicted incident hypertension after adjustment for traditional risk factors, most strongly under age 65; BST predicted MACE across all sex and age groups. Low BSC/low BST were associated with markedly lower risk for both outcomes, supporting automated quantification of BSC/BST in routine CMR reporting.

BSC's correlation with higher blood pressure, LV remodelling, reduced filling, and lower aortic distensibility supports its role as a hypertensive

remodelling marker, consistent with prior work showing curvature better captures functional remodelling than thickness ratios [8]. The basal septum's greater radius of curvature makes it disproportionately sensitive to rising wall stress, thereby driving compensatory hypertrophy [15]. BSC elevation preceded hypertension diagnosis independent of traditional risk factors, likely reflecting subclinical hypertension and/or arterial stiffening prior to overt blood pressure elevation [16].

BST was the stronger MACE predictor overall (HR 1.32–1.98), consistent with its progression from an adaptive marker to clinical disease [6], whereas BSC showed no independent association with MACE despite its role in incident hypertension. Combining both markers added value: Low BSC/Low BST identified the lowest-risk group, while high BST consistently clustered with higher risk regardless of BSC. The stronger BSC associations with incident hypertension in midlife may reflect greater plasticity of remodelling and sex-specific differences in arterial stiffening, whereas BST's consistent MACE significance across all subgroups reflects its role as a marker of established disease. Automated quantification also removes inter-observer variability inherent to subjective LVH assessment [8].

5. Limitations

The UK Biobank is a relatively healthy, largely White (98%) cohort, limiting generalisability. Single-timepoint assessment precludes evaluating longitudinal change, and residual confounding cannot be excluded. Sex and age differences require further biomechanical and independent cohort validation.

6. Conclusions

BSC provides a geometric signature of hypertensive remodelling that independently predicts incident hypertension, particularly in midlife, whereas BST remains the stronger and more consistent marker of adverse cardiovascular events. Prospective studies should test whether BSC- and BST-guided evaluation improves clinical decision-making.

Acknowledgments

Conducted in the UK Biobank under access application 2964. We thank participants and UKBB staff. TS was supported by the Centre for Doctoral Training in Digital Twins for Healthcare, King's College London. Part-funded by EPSRC grant Z533762 (AAY).

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