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Usefulness of Biventricular Volume as a Predictor of Mortality in Patients with Diabetes Mellitus (From the Diabetes Heart Study)

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Abstract

Individuals with type 2 diabetes mellitus (DM) are at increased risk of cardiovascular disease (CVD) and mortality. Beyond traditional CVD risk factors, novel measures reflecting additional aspects of disease pathophysiology, such as biventricular volume (BiVV), may be useful for risk stratification. This study examined the relationship between BiVV and risk for mortality in European Americans with type 2 DM from the Diabetes Heart Study. BiVV was calculated from 771 non-contrast computed tomography scans performed to image coronary artery calcified plaque (CAC). Relationships between BiVV and traditional CVD risk factors were examined. Cox proportional hazards regression was performed to determine risk for mortality (all-cause and CVD-mortality) associated with increasing BiVV. Area under the curve analysis was used to

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assess BiVV utility in risk prediction models. During 8.4 ± 2.4 years (mean $\pm$ SD) of follow-up, 23% of the sample were deceased. In unadjusted analyses, BiVV was significantly associated with increasing body mass index, height, CAC, history of hypertension and prior myocardial infarction ($p < 0.0001$ – 0.012). BiVV was significantly associated with all-cause (HR: 2.45; CI: 1.06–5.67; $p = 0.036$) and CVD-mortality (HR: 4.36; CI: 1.36–14.03; $p = 0.014$) in models adjusted for other known CVD risk factors. Area under the curve increased from 0.76 to 0.78 ($p = 0.04$) and 0.74 to 0.77 ($p = 0.02$) for all-cause and CVD-mortality on inclusion of BiVV. In conclusion, in the absence of echocardiography or other noninvasive imaging modalities to assess ventricular volumes, or when such methods are contra-indicated, BiVV from computed tomography may be considered as a tool for stratification of high-risk individuals, such as those with type 2 DM.

Keywords

cardiovascular disease; heart size; diabetes; risk-prediction

Coronary artery calcified plaque scores (CAC), determined by computed tomography scanning, are an independent predictor of all-cause mortality¹ and CVD-mortality² in the Diabetes Heart Study, a family based study enriched for type 2 diabetes mellitus (DM). In addition to CAC, other reported cardiovascular-related predictors of all-cause and CVD-mortality include arterial stiffness³, conduction wave abnormalities (as determined by electrocardiography)^{4–6} and left ventricular hypertrophy.^{7–9} More recently, biventricular volume (BiVV) determined from non-contrast computed tomography scans (as used for measurement of CAC) has been identified as a safe, non-invasive and cost-effective surrogate of left ventricular mass with correlation coefficients >0.8 when compared with magnetic resonance imaging-derived left ventricular mass.¹⁰ Several methods have been described to calculate ventricular volumes^{11–13}, however, relationships between BiVV and other traditional markers of CVD risk remains unclear. In addition, whether BiVV is similarly predictive of mortality has not been investigated. The aim of the current investigation was to assess the relationships between BiVV and traditional cardiac risk factors and to examine the ability of BiVV to predict risk for all-cause and CVD-mortality in patients with DM from the Diabetes Heart Study.

METHODS

This investigation included 771 self-described European American individuals (from 352 families) with overt type 2 DM from the Diabetes Heart Study. Briefly, the Diabetes Heart Study includes siblings concordant for type 2 DM without advanced renal insufficiency. Type 2 DM was clinically defined as diabetes developing after the age of 35 years and treated with insulin and/or oral agents, in the absence of historical evidence of ketoacidosis. Ascertainment and recruitment have been described in detail previously.^{14, 15}

Study protocols were approved by the Institutional Review Board at Wake Forest School of Medicine, and all participants provided written informed consent prior to participation. Participant examinations were conducted in the General Clinical Research Center of the Wake Forest Baptist Medical Center, and included interviews for medical history and health behaviors, anthropometric measures and resting blood pressure were recorded, fasting blood sampling for laboratory analyses and spot urine collection. Standard laboratory analyses included fasting glucose, glycated hemoglobin, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides and C-reactive protein concentrations. Individuals reported history of prior CVD based on prior event (angina, myocardial infarction, stroke) and/or intervention (coronary angiography, coronary artery bypass grafting, carotid endarterectomy). Individuals were classified as hypertensive if

prescribed anti-hypertensive medication or had blood pressure measurements exceeding 140 mmHg (systolic) or 90 mmHg (diastolic), and dyslipidemic based on the criteria established in the Third Report of the National Cholesterol Education Program Expert Panel Detection, Evaluation and Treatment in Adults (ATP III)¹⁶.

Participant examinations included measurement of carotid artery intima-media thickness by high-resolution B-mode ultrasonography with a 7.5-MHz transducer and a Biosound Esaote (AU5) ultrasound machine (Biosound Esaote, Inc., Indianapolis, IN) as previously described.¹⁷ In addition a resting 12-lead electrocardiography was performed using a Marquette MAC 500 ECG instrument (Marquette Electronics, Milwaukee, WI, USA) as described previously.¹⁸ All data were transmitted electronically to a central reading center for processing (EPICARE Inc., Winston-Salem, NC, USA). Electrocardiographic left ventricular hypertrophy (ECG-LVH) was determined according to the Minnesota code criteria (<http://www.sph.umn.edu/epi/ecg/>).

The imaging protocol has been reported previously.¹⁹ In brief, images to calculate BiVV were captured using fast-gated helical computed tomography. All cardiac computed tomography examinations were performed on a single-slice helical computed tomography or a four-channel multidetector computed tomography both with cardiac gating and capable of 500 ms temporal resolution (HiSpeed LX and LightSpeed QXi with the SmartScore Cardiac scan package; General Electric Medical Systems, Waukesha, WI). After a scout image of the chest, the heart was imaged during suspended respiration at end inspiration. Scan parameters were 3 mm slice thickness, 26 cm display field of view, retrospective cardiac gating, 120 KV, 240 mA, and computed tomography scan pitch adjusted to heart rate for the single-slice system and 2.5-mm slice thickness in four-slice mode, 26 cm display field of view, prospective cardiac gating at 50% of the RR interval, 120 KV, and 240 mA for the multidetector computed tomography. BiVV was calculated using the modified Simpson's formula¹⁰:

$$(\text{Max short axis area} + \text{Mid-ventricular area}) * (\text{Ventricular Length} / 3) + (\text{Area at apex} \times \text{Ventricular Length}^2 \times \pi) / 108.$$

BiVV has been highly correlated ($r=0.804$) with left ventricular mass obtained from magnetic resonance imaging.¹⁰ Determinations of CAC, carotid artery calcified plaque (CarCP) and infra-renal abdominal aortic calcified plaque (AACP) were also made from computed tomography scan images as previously described²⁰ and reported as Agatston scores.

For all participants, vital status was determined from the National Social Security Death Index maintained by the United States Social Security Administration. For participants confirmed as deceased, length of follow-up was determined from date of the initial study visit to date of death. For deceased participants, death certificates were obtained from relevant county Vital Records Offices to confirm cause of death. For all other participants length of follow-up was determined from the date of the initial study visit to the end of 2011. Cause of death was categorized based on information contained in death certificates as CVD-mortality (myocardial infarction, congestive heart failure, cardiac arrhythmia, sudden cardiac death, peripheral vascular disease, and stroke) or either cancer, infection, end-stage renal disease, accidental, or other (including obstructive pulmonary disease, pulmonary fibrosis, liver failure and Alzheimer's dementia).

Summary statistics were calculated including means and standard deviations (SD) for continuous variables and count and percentages for categorical variables. Due to the inclusion of related individuals in this study, marginal models with incorporation of generalized estimating equations were used to describe associations between BiVV and

cardiovascular risk factors. First, analysis of the simple univariate associations between BiVV and each individual risk factor/demographic trait were performed, where BiVV was treated as the outcome variable. Second, each of these associations was adjusted for age, sex and body mass index (BMI) (for the analysis with height the BMI adjustment was not performed). For the analysis with ECG-LVH, individuals with electrocardiography readings failing to meet the minimum accepted quality standard were excluded (n=13). Continuous variables (including both BiVV and CAC) were log-transformed to better approximate the normality assumption as appropriate. The statistical inference (i.e. p-value) was reported based on the log-transformed BiVV analysis, however, to allow easier interpretation, the beta coefficients for untransformed BiVV are reported. This approach is reasonable when the p-values from the transformed and untransformed analyses are similar.

To evaluate the association between BiVV and mortality, BiVV was considered as both a continuous (log-transformed) and categorical variable derived from quartile ranges (Q1–4 based on increasing BiVV). The curves of cumulative incidence of all-cause mortality and CVD-mortality for each quartile of BiVV were plotted for exploratory analysis. Cox proportional hazards models were used to assess the ability of BiVV to predict all-cause mortality and CVD-mortality. To account for the correlated family structure, a robust sandwich covariance estimate was calculated. The robust standard error for the parameter estimates were used for statistical inference. Follow-up duration started from the beginning of the study to the last updated assessment of vital status. When the endpoint is all-cause mortality, censoring may occur if one is alive. When the endpoint is CVD-mortality, censoring may occur if one is alive or the death is due to other causes. Models were adjusted for (i) age and sex (model 1) (ii) age, sex, height and known CVD risk factors including current smoking, hypertension, dyslipidemia, and history of prior myocardial infarction (MI) (model 2); and (iii) age, sex, height, known CVD risk factors, ECG-LVH and CAC (model 3). The test for trend across increasing BiVV quartiles was also performed. SAS version 9.2 (SAS Institute Inc., Cary, NC) was used for the analysis.

Receiver operating characteristic (ROC) curves were computed for the basic (model 1) and fully adjusted models (model 3) and progressive addition of continuous measures of CAC and BiVV. The areas under the curves were used to assess the ability of BiVV to predict all cause mortality or CVD-mortality after adjusting for other confounding variables and the known predictor CAC. The difference in area under the curve between two models was tested using Delong's method.²¹ Stata software, version 8.2 (StataCorp, College Station, TX), was used for the ROC analysis. Statistical significance was accepted at $p < 0.05$.

RESULTS

The demographic and clinical characteristics of the participants are presented in Table 1. A predominance of known CVD risk factors, including high body mass, hypertension and abnormal lipid concentrations was evident. Vascular calcified plaque scores for CAC, CarCP and AACP reflect a substantial burden of subclinical CVD in these diabetes-affected individuals. Based on available data, 4.3% of the sample had ECG-LVH defined using Minnesota Code criteria. The cohort was followed for 8.4 ± 2.4 years (mean $\pm$ SD) with 180 participants found to be deceased (23.3% of the sample) during this period. Among those individuals with documented cause of death information (n=152), 82 individuals (53.9%) had a documented CVD related cause of death.

In unadjusted analyses BiVV was significantly associated with increasing BMI, height, CAC, and histories of hypertension and prior MI (Table 2). Following adjustment for age, gender and BMI, BiVV remained associated ($p < 0.01$) with hypertension, prior MI, CAC and

left ventricular hypertrophy (Table 2). BiVV was not significantly associated with dyslipidemia or current smoking status.

Cumulative incidence of all-cause and CVD-mortality increased across increasing BiVV quartiles (Figure 1). A linear relationship was observed where risk for all-cause and CVD-mortality increased with greater heart size, although only the comparison between the highest quartile of BiVV values versus the lowest quartile is significant (Table 3). A formal test for trend of BiVV as an ordinal measure (using quartiles as cut-points) supported an overall trend for increasing BiVV values (based on quartiles) to be associated with increased risk for both all-cause (HR: 1.28; 95% CI: 1.12–1.47; $p=0.0005$) and CVD mortality (HR: 1.31; CI: 1.07–1.61; $p=0.011$) in a univariate analysis.

When treated as a continuous measure, BiVV was associated with a significant increase in risk for both all-cause and CVD-mortality in univariate models; each SD unit increase in log transformed BiVV was associated with a >2.5-fold increase in all-cause mortality and a >3.5-fold increase in risk for CVD-mortality (Table 4, unadjusted). BiVV remained associated with CVD-mortality following adjustment for age and sex (Table 4, model 1), and other known CVD risk factors (Table 4, model 2). In models adjusted for known CVD risk factors, CAC (predictor of mortality in T2D¹) and ECG-LVH, BiVV remained a significant predictor of both all-cause and CVD-mortality (Table 4, model 3).

Area under the curve analysis confirmed the utility of BiVV in models for risk prediction (Figure 2 and Table 5). For models including age, sex and CAC only, the area under the ROC curve for prediction of all-cause mortality increased from 0.76 to 0.78 ($p=0.04$) for all-cause mortality and from 0.74 to 0.77 ($p=0.02$) for CVD-mortality upon inclusion of BiVV. For the fully adjusted models including CAC, the area under the curve increased from 0.79 to 0.80 ($p=0.04$) for all-cause mortality and from 0.77 to 0.78 ($p=0.12$) for CVD-mortality upon with inclusion of BiVV.

DISCUSSION

Individuals with type 2 DM, have elevated rates of cardiovascular complications and CVD-mortality. Improved risk prediction may better inform clinical management. This study was designed to evaluate the relationships between BiVV and traditional CVD risk factors, including CAC. We have previously shown that CAC is a powerful predictor of mortality in this cohort¹, improves prediction compared to conventional risk factors and reclassifies a significant percentage of type 2 DM subjects to higher or lower risk categories². Non-contrast computed tomography scans to determine CAC are increasingly common and we evaluated the ability of BiVV, derived from the computed tomography scans for CAC, to add to prediction of all-cause and CVD-mortality. BiVV was associated with conventional CVD risk factors: male sex, BMI, hypertension, prior MI, CAC and ECG-LVH. Accounting for these relationships BiVV was an independent predictor of both all-cause and CVD-mortality in this high-risk sample with type 2 DM.

BiVV has been well correlated previously with left ventricular mass.¹⁰ Left ventricular hypertrophy is a predictor of adverse cardiovascular outcomes including sudden arrhythmic death⁹, congestive heart failure^{22, 23}, MI²⁴ and stroke.²⁵ Diverse mechanisms have been proposed to explain the relationship between left ventricular hypertrophy and adverse CVD outcomes including a causal role of left ventricular hypertrophy via contributions to diastolic dysfunction⁹ and reduced coronary flow reserve.⁸ Alternatively left ventricular hypertrophy may simply reflect underlying disease processes such as hypertension⁸, valvular heart disease⁷ or atherosclerosis.⁹ Whether BiVV, as an alternative measure of left ventricular mass, similarly reflects elements of the underlying pathophysiology contributing to CVD

risk remains unclear. In this study BiVV was associated with a 2.4 and 4.4-fold increased risk of all-cause and CVD-mortality, respectively. These associations persisted following adjustment for traditional CVD risk factors and CAC, suggesting an independent contribution of heart size to adverse CVD outcomes in type 2 DM, and supporting the utility of BiVV in risk stratification models.

Although BiVV was strongly correlated with left ventricular hypertrophy in this study, it is not a surrogate for left ventricular hypertrophy and may be capturing other underlying processes. The magnitude of increased risk conferred by BiVV for mortality is consistent with prior examinations of left ventricular hypertrophy as a risk factor for cardiac death. Increased left ventricular hypertrophy has been associated with an approximate 2-fold greater risk for all-cause mortality and an approximate 3-fold increase in risk for sudden arrhythmic death in the largely male, U.S. Heart and Soul Study.⁹ Likewise, in the Framingham cohort, left ventricular hypertrophy was associated with an approximate 1.5-fold increased risk of sudden death⁸ with hazard ratios between 1.5 and 2.0 also reported in the National Health and Nutrition Examination Survey II.⁷

We do not know if these observations are generalizable to other population samples, e.g. other ethnicities, non-diabetic individuals. Traditional CVD risk factors are increased in the Diabetes Heart Study and likely contribute to increased BiVV. Further, the electrocardiography determination of LVH described here is not the gold standard for determination of LVH and may have contributed additional variance to the reported risk prediction. While there are limitations to our study design an important counterpoint is that it likely reflects a general population of type 2 DM-affected individuals in the U.S., and thus the underlying CVD risk for such individuals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Cumulative incidence curves for (A) all-cause and (B) CVD-mortality based on increasing BiVV quartiles (Q1–Q4).

Figure 2.

Receiver operator characteristic curves for (A) all-cause and (B) CVD-mortality for fully adjusted (age, sex, height, hypertension, current smoking, dyslipidemia, prior MI, and LVH) models with sequential additional of CAC and BiVV.

Table 1

Demographic Information for n=771 European Americans with type 2 diabetes mellitus and available Biventricular Volume from the Diabetes Heart Study.

Variable	Mean $\pm$ SD (range; median [*]) or %		
	All (n=771)	Living (n=591)	Deceased (n=180)
Demographic Information			
Age (years)	61.9 $\pm$ 8.9 (36.3–86.0)	60.5 $\pm$ 8.4	66.7 $\pm$ 9.0
Male	49.2%	47.2%	55.6%
Smoking (current or prior)	44.0%	43.5%	45.6%
Metabolic Syndrome	89.0%	89.0%	88.9%
Diabetes Duration (years)	10.6 $\pm$ 7.1 (1.0–41.1)	9.6 $\pm$ 6.3 (1.0–30.8)	13.6 $\pm$ 8.5 (1.0–41.1)
Self-reported CVD History	44.0%	38.9%	60.6%
Self reported prior MI	21.4%	16.4%	37.8%
Deceased – CVD causes	9.3%	n/a	40.0%
Body Composition			
Height (cm)	168.8 $\pm$ 9.7 (122.8–195.8)	168.8 $\pm$ 9.8 (122.8–195.8)	168.8 $\pm$ 9.5 (147.4–189.0)
Weight (kg)	92.3 $\pm$ 20.1 (40.8–209.2)	92.8 $\pm$ 20.0 (44.1–209.2)	90.5 $\pm$ 20.6 (40.8–152.1)
Body Mass Index (kg/m ²)	32.4 $\pm$ 6.6 (17.1–58.0)	32.6 $\pm$ 6.5 (17.1–58.0)	31.7 $\pm$ 6.8 (17.5–56.9)
Blood Pressure			
Systolic BP (mmHg)	140 $\pm$ 19 (98–260)	140 $\pm$ 17 (98–214)	141 $\pm$ 23 (99–260)
Diastolic BP (mmHg)	72 $\pm$ 10 (37–102)	73 $\pm$ 10 (37–102)	69 $\pm$ 10 (45–101)
Pulse Pressure (mmHg)	68 $\pm$ 17 (28–159)	67 $\pm$ 16 (28–124)	71 $\pm$ 19 (32–159)
Hypertension	88.7%	87.1%	93.9%
Anti-hypertensive Use	78.7%	76.1%	87.2%
Blood Biochemistry			
Fasting Glucose (mg/dL)	150 $\pm$ 57 (16–463)	148 $\pm$ 54 (16–463)	156 $\pm$ 68 (46–436)
HbA1c (%)	7.5 $\pm$ 1.6 (4.3–16.6)	7.4 $\pm$ 1.5 (4.6–15.4)	7.8 $\pm$ 1.8 (4.3–16.6)
Cholesterol (mg/dL)	186 $\pm$ 43 (74–427)	186 $\pm$ 43 (74–427)	187 $\pm$ 43 (105–386)
LDL (mg/dL)	103 $\pm$ 32 (14–236)	103 $\pm$ 32 (14–236)	104 $\pm$ 32 (33–228)
HDL (mg/dL)	43 $\pm$ 12 (8–98)	43 $\pm$ 12 (18–98)	41 $\pm$ 12 (8–86)
Triglycerides (mg/dL)	208 $\pm$ 133 (30–1068)	204 $\pm$ 127 (30–1068)	221 $\pm$ 152 (38–1065)
Dyslipidemia	94.3%	93.6%	96.7%
C-reactive protein (mg/L)	6.3 $\pm$ 9.7 (0.05–96)	5.7 $\pm$ 8.3 (0.05–96)	8.4 $\pm$ 12.8 (0.08–90)
Cardiovascular Disease Severity			
CAC>0	96.0 %	94.6%	98.9%
Mean CAC	2096 $\pm$ 3557 (0–50415; 604)	1640 $\pm$ 3412 (0–50415; 374)	3586 $\pm$ 3622 (0–21725; 2506)
CarCP>0	79.3%	74.6%	93.9%

Variable	Mean $\pm$ SD (range; median [*]) or %		
	All (n=771)	Living (n=591)	Deceased (n=180)
Mean CarCP	390 $\pm$ 745 (0–6122; 97)	296 $\pm$ 656 (0–6122; 51)	692 $\pm$ 916 (0–5605; 299)
AACP>0	96.7%	96.2%	98.3%
Mean AACP	13644 $\pm$ 17113 (0–94156; 6766)	10998 $\pm$ 15046 (0–75567; 4525)	23482 $\pm$ 20497 (0–94156; 18732)
Carotid IMT (mm)	0.687 $\pm$ 0.137 (0.451–1.569)	0.671 $\pm$ 0.132 (0.451–1.569)	0.739 $\pm$ 0.140 (0.498–1.316)
Ventricular Volume			
Biventricular Volume (mL)	384.5 $\pm$ 112.1 (156.6–884.5)	374.6 $\pm$ 105.5 (156.6–884.5)	416.8 $\pm$ 128.7 (188.1–798.3)
Biventricular Volume Quartile			
Ranges			
Q1	156.6–300.9	156.6–297.5	188.1–332.2
Q2	300.9–375.6	297.5–364.1	332.2–395.9
Q3	375.6–448.8	364.1–438.6	395.9–495.3
Q4	448.8–884.5	438.6–884.5	495.3–798.3

CVD = cardiovascular disease; MI = myocardial infarction; BP = blood pressure; HbA1c = glycated hemoglobin; LDL = low density lipoprotein cholesterol; HDL = high density lipoprotein cholesterol; CAC = coronary artery calcified plaque; CarCP = carotid artery calcified plaque; AACP = abdominal aortic calcified plaque; IMT = intima-media thickness.

* median values included only for measures of vascular calcification

Table 2

Associations between Biventricular Volume and cardiovascular disease risk factors in unadjusted and adjusted models.

	Unadjusted		Adjusted (age, sex, BMI)	
	β -coefficient	p-value	β -coefficient	p-value
Age	-1.13	0.01	n/a	n/a
Gender (male)	119.33	<0.0001	n/a	n/a
BMI	2.77	<0.0001	n/a	n/a
Height	5.96	<0.0001	2.82	<0.0001
Hypertension	32.97	0.01	34.98	0.0003
Current Smoking	5.64	0.61	-7.94	0.37
Dyslipidemia	5.92	0.41	-2.05	0.89
Prior Myocardial Infarction	54.05	<0.0001	28.05	0.0024
Coronary Artery Calcium	13.66	<0.0001	7.12	0.0010
ECG-LVH	47.31	0.07	56.41	0.0074

BMI = body mass index; ECG-LVH = Electrocardiographic left ventricular hypertrophy

Table 3

Relationship between Biventricular volume quartiles and risk for all-cause and cardiovascular disease (CVD) mortality using Cox proportional hazard models partially and fully adjusted for known CVD risk factors.

				Unadjusted		Partially adjusted [*]		Fully Adjusted [†]	
Mortality	Quartile	# Events	Events / 100 person years	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
All-cause	Q1 (Ref)	31	2.1	1.00	-	1.00	-	1.00	-
	Q2	36	2.2	1.05 (0.63–1.72)	0.86	1.05 (0.64–1.73)	0.85	0.93 (0.56–1.56)	0.80
	Q3	46	2.8	1.34 (0.84–2.11)	0.22	1.47 (0.84–2.57)	0.18	1.22 (0.64–2.30)	0.55
	Q4	67	4.1	1.98 (1.29–3.05)	0.002	2.31 (1.35–3.97)	0.002	1.82 (1.02–3.25)	0.04
CVD	Q1 (Ref)	15	1.0	1.00		1.00	-	1.00	-
	Q2	15	0.9	0.90 (0.44–1.83)	0.77	0.85 (0.42–1.71)	0.64	0.69 (0.32–1.47)	0.33
	Q3	19	1.1	1.136 (0.59–2.19)	0.70	1.08 (0.50–2.35)	0.84	0.90 (0.36–2.25)	0.81
	Q4	33	2.0	2.014 (1.11–3.64)	0.02	2.19 (1.10–4.37)	0.03	1.78 (0.83–3.83)	0.14

^{*} adjustment for age, sex, height, current smoking, hypertension, dyslipidemia, prior myocardial infarction.

[†] adjustment for age, sex, height, current smoking, hypertension, dyslipidemia, prior myocardial infarction, electrocardiographic left ventricular hypertrophy and coronary artery calcium.

Table 4

Biventricular volume prediction of all-cause and cardiovascular (CVD) mortality using Cox proportional hazard models.

Models	All-cause Mortality		CVD-Mortality	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Unadjusted	2.80 (1.56–5.01)	0.0005	3.85 (1.64–9.05)	0.002
1	4.17 (1.980–8.78)	0.0002	6.83 (2.443–19.08)	0.0002
2	3.63 (1.674–7.86)	0.001	5.66 (1.993–16.10)	0.001
3	2.45 (1.06–5.67)	0.036	4.36 (1.356–14.03)	0.014

Models adjusted as follows (1) age and sex; (2) age, sex, height, current smoking, hypertension, dyslipidemia, prior myocardial infarction; (3) age, sex, height, current smoking, hypertension, dyslipidemia, prior myocardial infarction, electrocardiographic left ventricular hypertrophy and coronary artery calcium.

Table 5

Area under the curve (AUC) analysis for basic (age and sex) and fully adjusted (age, sex, height, current smoking, hypertension, dyslipidemia, prior myocardial infarction, and electrocardiographic left ventricular hypertrophy) models predicting all-cause and cardiovascular disease (CVD) mortality with sequential addition of coronary artery calcium (CAC) and biventricular volume (BiVV).

Models	All-cause mortality		CVD-mortality	
	AUC	p-value*	AUC	p-value*
Basic	0.71	-	0.69	-
Basic + CAC	0.76	<0.0001	0.74	0.0005
Basic + CAC + BiVV	0.78	0.0001	0.77	0.005
Full	0.76	-	0.75	-
Full + CAC	0.79	0.004	0.77	0.031
Full + CAC + BiVV	0.80	0.001	0.78	0.058

*
p-values are for comparisons of subsequent models to either basic or full models without CAC and BiVV