Supplementary Online Content

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This supplementary material has been provided by the authors to give readers additional information about their work.

eTable 1. Definitions of ACCF/AHA HF stages and criteria used to classify participants in the current study.

HF Stage	ACCF/AHA Guideline Definitions	Classification criteria in this employed
Stage 0	Free of criteria for Stages A, B, C	None of the following clinical risk factors: prevalent cardiovascular disease (coronary artery disease, stroke, or peripheral arterial disease), hypertension, diabetes mellitus, obesity, metabolic syndrome, or chronic kidney disease and none of the following cardiac structural or functional abnormalities: Abnormal LVEF, regional wall motion abnormality, LV enlargement based on LVEDV indexed to BSA, left ventricular hypertrophy based on LV mass indexed to height$^{2.7}$, moderate or greater aortic stenosis, aortic regurgitation, mitral regurgitation, or mitral stenosis
Stage A	At elevated risk for HF but without structural heart disease or symptoms of HF	At least 1 of the following clinical risk factors: prevalent cardiovascular disease (coronary artery disease, stroke, or peripheral arterial disease), hypertension, diabetes mellitus, obesity, metabolic syndrome, or chronic kidney disease, and none of the following cardiac structural or functional abnormalities employing ARIC-based reference limits: Abnormal LVEF, regional wall motion abnormality, LV enlargement based on LVEDV indexed to BSA, left ventricular hypertrophy based on LV mass indexed to height$^{2.7}$, moderate or greater aortic stenosis, aortic regurgitation, mitral regurgitation, or mitral stenosis.
Stage B	Structural heart disease but without signs or symptoms of HF	At least 1 of the following cardiac structural or functional abnormalities: abnormal LVEF, regional wall motion abnormality, LV enlargement based on LVEDV indexed to BSA, left ventricular hypertrophy based on LV mass indexed to height$^{2.7}$, moderate or greater aortic stenosis, aortic regurgitation, mitral regurgitation, or mitral stenosis.

Stage C	Structural heart disease with earlier or current symptoms of HF	Prevalent HF at ARIC Visit 5, defined as an adjudicated HF hospitalization since 2005, International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) 428 code for hospitalizations prior to 2005, or self-report of HF or treatment for HF among those without a prior hospitalization with at least one of the following: (a) subsequent confirmation of self-report by treating physician or the participant, or (b) an NT-proBNP>125pg/ml at Visit 4 or 5.

Definition of HF Stages

Stage A was defined by at least 1 of the following clinical risk factors: prevalent cardiovascular disease (coronary artery disease, stroke, or peripheral arterial disease), hypertension, diabetes mellitus, obesity, metabolic syndrome, or chronic kidney disease, and none of the following cardiac structural or functional abnormalities employing ARIC-based reference limits:[1] Abnormal LVEF, regional wall motion abnormality, LV enlargement based on LVEDV indexed to BSA, left ventricular hypertrophy based on LV mass indexed to height$^{2.7}$, moderate or greater aortic stenosis, aortic regurgitation, mitral regurgitation, or mitral stenosis. Stage B was defined by at least 1 of the following cardiac structural or functional abnormalities: abnormal LVEF, regional wall motion abnormality, LV enlargement based on LVEDV indexed to BSA, left ventricular hypertrophy based on LV mass indexed to height$^{2.7}$, moderate or greater aortic stenosis, aortic regurgitation, mitral regurgitation, or mitral stenosis. Stage C consisted of participants with prevalent HF at ARIC Visit 5. Stage D was defined based on therapy with a left ventricular assist device or chronic intravenous inotropes (milrinone or dobutamine), which were assessed at visit 5. In the present study, no participant met criteria of Stage D.

Prevalent hypertension and diabetes were based on blood pressure and glucose measured from study Visits 1 through 5, self-report of physician diagnosis, and medication use. ARIC

participants undergo surveillance for incident CHD events (including definite or probable MI, or coronary revascularization) as previously described in detail.[2] Atrial fibrillation was ascertained based on ECGs at the 5 study visits and hospital discharge records as previously described.[3] PAD was defined as ankle-brachial index (ABI) less than 0.9 for either leg at Visit 5. Prevalent HF at ARIC Visit 5 was defined as an adjudicated HF hospitalization after 2005; or International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) 428 code for hospitalizations prior to 2005; or self-report of HF or treatment for HF among those without a prior hospitalization with at least one of the following: (a) subsequent confirmation of self-report by treating physician or the participant, or (b) an NT-proBNP>125pg/ml at Visit 4 or 5.[1,4-6]

eTable 2. Participant characteristics at Visit 5 by measurable 3D RVEF.

	Participants at Visit 5 (n=6,538)	**RVEF available (n=1,004)**	**RVEF not available (n=5,534)**	p value
Age (year)	76±5	76±5	76±5	0.02
Female	41%	38%	42%	0.047
Black	24%	12%	26%	<0.001
Center				<0.001
Forsyth County	22%	47%	17%	
Jackson	22%	9%	24%	
Minneapolis	29%	21%	31%	
Washington County	27%	24%	28%	
Hypertension	84%	78%	85%	<0.001
Diabetes	39%	32%	40%	<0.001
CKD	23%	22%	23%	0.65
Ever smoker	61%	62%	61%	0.98
Current smoker	6%	6%	6%	0.66
CAD	15%	13%	16%	0.023
Prior MI	8%	7%	8%	0.14
Previous stroke	4%	3%	4%	0.17
Atrial fibrillation	10%	7%	10%	0.002
BMI (kg/m2)	28.7±5.8	27.1±5.0	29.1±5.9	<0.001
Systolic BP (mmHg)	131±19	131±18	131±19	0.52
Diastolic BP (mmHg)	66±11	66±11	66±11	0.47
Heart rate (bpm)	63±11	61±10	63±11	<0.001
eGFR (ml/min per 1.73 m2)	69.1±17.6	69.0±16.4	69.1±17.8	0.87
NT-proBNP (ng/L)	138 [70, 280]	135 [72, 244]	139 [70, 289]	0.13
hs-TnT (ng/L)	1.1[0.8, 1.7]	1.0 [0.7, 1.5]	1.1 [0.8, 1.7]	<0.001
2D echocardiography				
EDV/BSA (ml/m2)	43.4±11.3	44.8±10.5	43.1±11.5	<0.001
LV mass index (g/m2)	80.2±21.2	79.3±19.5	80.3±21.5	0.14
Wall thickness (mm)	0.99±0.14	0.98±0.13	0.99±0.14	0.002
LV EF (%)	65.1±6.9	66.5±5.8	64.8±7.0	<0.001
LV GLS (%)	-17.8±2.7	-18.1±2.4	-17.8±2.7	0.001
e' septal (cm/s)	12.6±4.7	12.8±4.5	12.5±4.8	0.044
LAVi (ml/m2)	26.3±9.5	26.9±8.8	26.2±9.6	0.016
RVEDA (cm2)	19.7±5.3	20.0±5.3	19.6±5.3	0.031
RVESA (cm2)	9.4±3.1	9.2±3.0	9.4±3.1	0.041
RVFAC (%)	0.52±0.08	0.54±0.08	0.52±0.08	<0.001

Abbreviations: BMI, body-mass index; BSA, body-surface area; BP, blood pressure; CAD, coronary artery disease; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; e', mitral early relaxation velocity; EDV, end-diastolic volume; EF, ejection fraction; GLS, global longitudinal strain; HR, heart rate; LAVi; left atrial volume indexed by BSA; MI, myocardial infraction; PAD, peripheral artery disease; RVEDA, right ventricular end-diastolic area; RVESA, right ventricular end-systolic area; RVFAC, right ventricular fractional area change.

eTable 3. Inverse probably attrition weighted estimates (with 95% confidence intervals) of measures of cardiac structure and function by 3D RVEF at ARIC Visit 5.

	Q1	Q2	Q3	Q4	P for trend
Age (years)	77.3 (76.4-78.1)	76.1 (75.2-76.9)	77.1 (76.2-77.9)	76.3 (75.6-77.1)	0.29
Male (%)	55 (47-62)	41 (33-48)	35 (27-42)	27 (20-33)	<0.001
Black (%)	27 (19-35)	21 (13-29)	24 (16-32)	27 (18-35)	0.97
HF Risk Factors					
Hypertension (%)	87 (83-91)	82 (77-87)	82 (78-87)	84 (79-89)	0.33
Diabetes (%)	40 (32-47)	39 (31-47)	33 (26-40)	40 (32-48)	0.78
Obesity (%)	26 (20-33)	27 (20-34)	28 (21-35)	22 (15-29)	0.49
Metabolic Syndrome (%)	59 (51-67)	55 (47-62)	62 (55-70)	55 (47-63)	0.75
CKD (%)	24 (18-30)	25 (18-32)	20 (14-27)	24 (17-30)	0.70
Ever smoker (%)	69 (63-76)	57 (50-65)	57 (49-65)	66 (58-73)	0.41
Current smoking (%)	7 (3-11)	8 (0.3-12)	2 (0.1-4)	6 (3.0-10)	0.40
Prevalent CVD					
CAD (%)	21 (14-27)	10 (5-14)	10 (6-14)	13 (8-18)	0.07
Prior MI (%)	16 (9-23)	7 (3-12)	7 (3-11)	4 (1-8)	0.003
PAD (%)	6 (2-11)	8 (2-13)	10 (4-15)	11 (5-17)	0.19
Stroke (%)	7 (3-11)	6 (2-10)	2 (0-4)	1 (0-2)	0.001
Atrial Fibrillation (%)	13 (8-18)	8 (4-13)	4 (1-7)	6 (2-9)	0.01
Physical Exam					
BMI (kg/m^2)	27.8 (27.2-28.5)	27.8 (26.8-28.8)	28.1 (27.0-29.2)	26.6 (25.8-27.4)	0.06
Systolic BP (mmHg)	131 (128-134)	131 (128-134)	132 (129-135)	135 (132-139)	0.08
Diastolic BP (mmHg)	66 (64-67)	66 (64-67)	66 (64-68)	64 (63-66)	0.50
HR (bpm)	62 (60-63)	62 (61-64)	61 (60-63)	61 (59-62)	0.31
Laboratory Values					
HbA1c (%)	6.1 (5.9-6.3)	5.9 (5.8-6.1)	5.9 (5.8-6.0)	5.9 (5.8-6.1)	0.086
eGFR (ml/min per 1.73 m^2)	68.5 (65.3-71.7)	67.7 (64.4-71.1)	68.3 (65.5-71.1)	68.6 (65.5-71.1)	0.92
LDL (mg/dL)	95 (90-100)	103 (98-107)	108 (103-113)	105 (99-111)	0.003
HDL (mg/dL)	50 (48-53)	54 (52-56)	53 (51-55)	55 (53-58)	0.007
hsCRP*	2.07 [1.69, 2.46]	1.81 [1.36, 2.26]	1.81 [1.38, 2.23]	1.87 [1.37, 2.36]	0.42
Cardiac Biomarkers					
NT-proBNP (ng/L)*	172 [129-216]	120 [100-140]	139 [119-159]	138 [115-162]	0.21
hs-TnT (ng/L)*	1.40 [1.23, 1.57]	1.00 [0.90, 1.10]	1.00 [0.85, 1.15]	1.00 [0.90, 1.10]	0.049
Left ventricular (LV) Structure					

EDV (ml)	92.6 (87.0-98.1)	84.1 (80.2-88.0)	80.9 (77.7-84.0)	81.7 (77.4-86.0)	0.001
ESV (ml)	34.4 (31.1-37.6)	29.3 (27.5-31.2)	26.6 (25.3-28.0)	27.0 (25.0-29.1)	<0.001
MWT (cm)	1.03 (1.01-1.05)	0.99 (0.97-1.01)	0.98 (0.96-1.01)	0.97 (0.95-0.99)	<0.001
LV mass (g)	165 (157-172)	147 (140-155)	143 (136-150)	138 (130-146)	<0.001
LV mass index (g/m^2)	87.5 (83.9-91.0)	79.8 (76.4-83.2)	78.5 (75.0-82.0)	77.8 (74.0-81.6)	<0.001
LV Systolic Function					
EF (%)	64.1 (62.9-65.3)	65.8 (64.8-66.7)	67.4 (66.7-68.2)	67.7 (66.9-68.5)	<0.001
GLS (%)	-17.1 (-16.7- -17.6)	-18.1 (-17.7- -18.5)	-18.3(-17.9- -18.6)	-18.4 (-18.0- -18.8)	<0.001
Twist (degree)†	12.2 (11.5-12.9)	12.2 (11.6-12.9)	13.7 (12.9-14.5)	13.6 (13.0-14.2)	<0.001
Torsion (degree/cm)†	1.62 (1.53-1.71)	1.64 (1.55-1.73)	1.85 (1.74-1.95)	1.84 (1.75-1.93)	<0.001
LV Diastolic Function					
E wave	69.9 (66.5-73.3)	69.8 (66.6-73.1)	68.7 (65.7-71.7)	72.9 (69.8-76.0)	0.32
e' septal (cm/sec)	5.54 (5.22-5.86)	5.79 (5.59-5.99)	5.86 (5.54-6.18)	5.74 (5.49-5.99)	0.28
E/e' septal	13.4 (12.6-14.1)	12.7 (11.9-13.5)	12.4 (11.8-13.0)	13.4 (12.6-14.3)	0.87
LA volume index (ml/m^2)	31.3 (28.7-33.9)	26.9 (25.7-28.1)	26.7 (25.5-27.9)	26.9 (25.4-28.4)	0.004

Values provided at estimates with 95% confidence limits (CIs).
*Estimated median values with 95%CIs.

3D RV measure non-availability was modeled among participants all ARIC participants alive at the initiation of visit 5 using the following covariates from Visit 1: age, gender, race, study center, systolic blood pressure, heart rate, body mass index, smoking and drinking status, diabetes mellitus, hypertension, and chronic kidney disease. The resulting calculated weights were incorporated into multivariable models for prevalence of abnormal and time-to-event analysis.

eTable 4. Inverse probably attrition weighted estimates (with 95% confidence intervals) of the prevalence of abnormal (based on the 90th or 10th percentile limits derived from the Stage 0 overall) across HF stages. Values provided at estimates with 95% confidence limits.

	Stage 0 (low risk)	**Stage A**	**Stage B**	**Stage C**
3D RVEF	13.1 (3.1-23.0)	15.9 (12.6-19.3)	25.3 (14.5-36.0)	26.6 (17.2-36.1)
3D RVLS	9.9 (2.8-17.0)	17.3 (13.9-20.8)	27.0 (16.3-37.8)*	36.4 (26.2-46.7)*
RV-PA coupling (3DRVEF/PASP)	10.8 (2.2-19.3)	33.4 (28.3-38.5)*	39.4 (25.2-53.7)*	58.9 (47.1-70.6)*

*P<0.05 for unadjusted and adjusted with age, sex, and race (reference=low risk)

3D RV measure non-availability was modeled among participants all ARIC participants alive at the initiation of visit 5 using the following covariates from Visit 1: age, gender, race, study center, systolic blood pressure, heart rate, body mass index, smoking and drinking status, diabetes mellitus, hypertension, and chronic kidney disease. The resulting calculated weights were incorporated into multivariable models for prevalence of abnormal and time-to-event analysis.

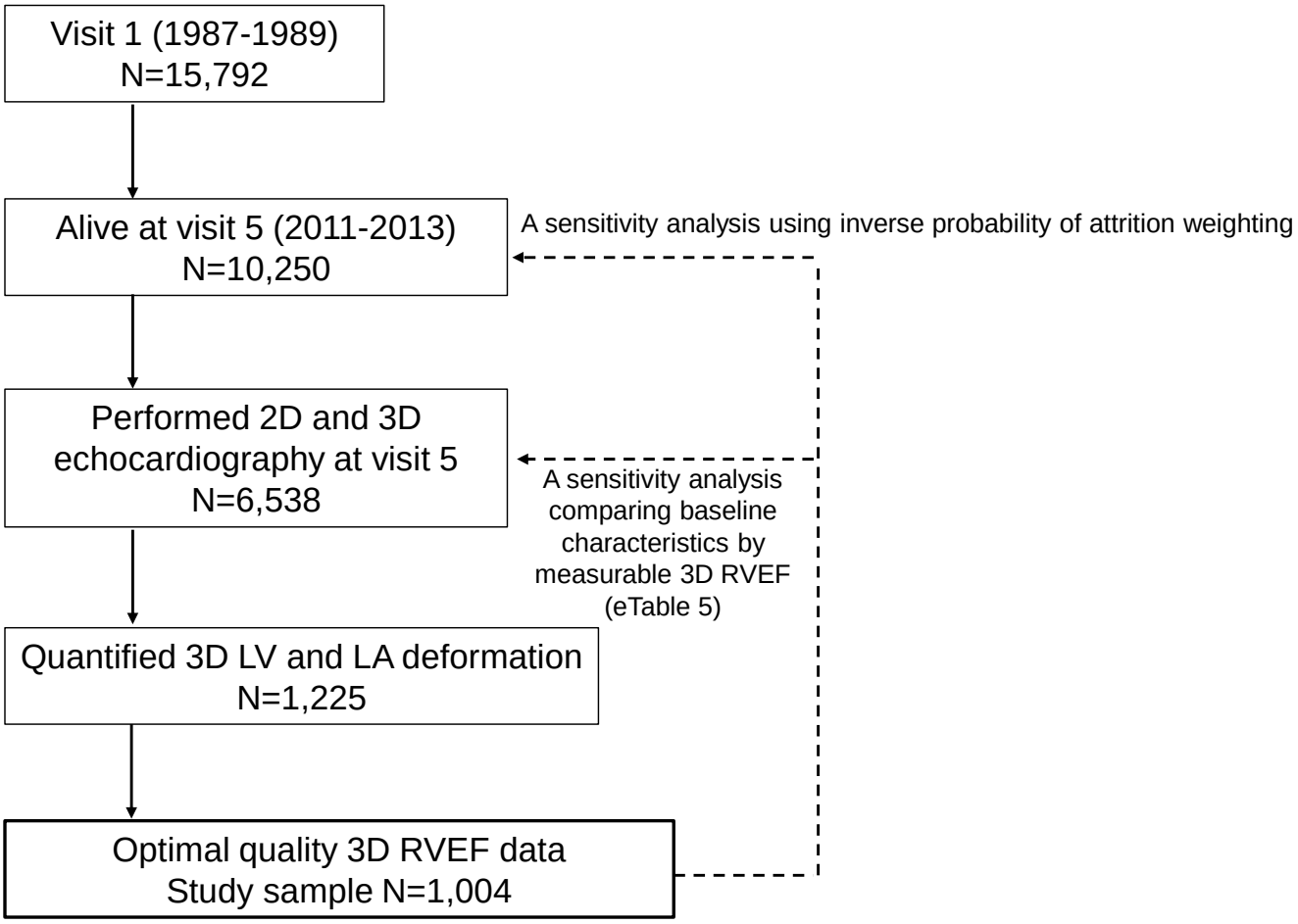
eTable 5. Inverse probably attrition weighted estimates of hazard ratios of 3D RVEF and RV-PA coupling (3D RVEF/PASP ratio) with incident heart failure (HF) hospitalization or all-cause mortality among participants free of prevalent HF at Visit 5.

	Model 1 Estimated HR (95%CI)	**P**	**Model 2 Estimated HR (95%CI)**	**P**
RVFAC	1.02 (0.97-1.06)	0.498	1.02 (0.97-1.06)	0.464
Tricuspid annular s'	1.08 (0.97-1.20)	0.185	1.08 (0.97-1.20)	0.182
3D RVEF	1.18 (0.98-1.42)	0.080	1.18 (0.98-1.42)	0.084
RV-PA coupling (3D RVEF/PASP)	1.60 (1.08-2.38)	0.020	1.59 (1.05-2.41)	0.028

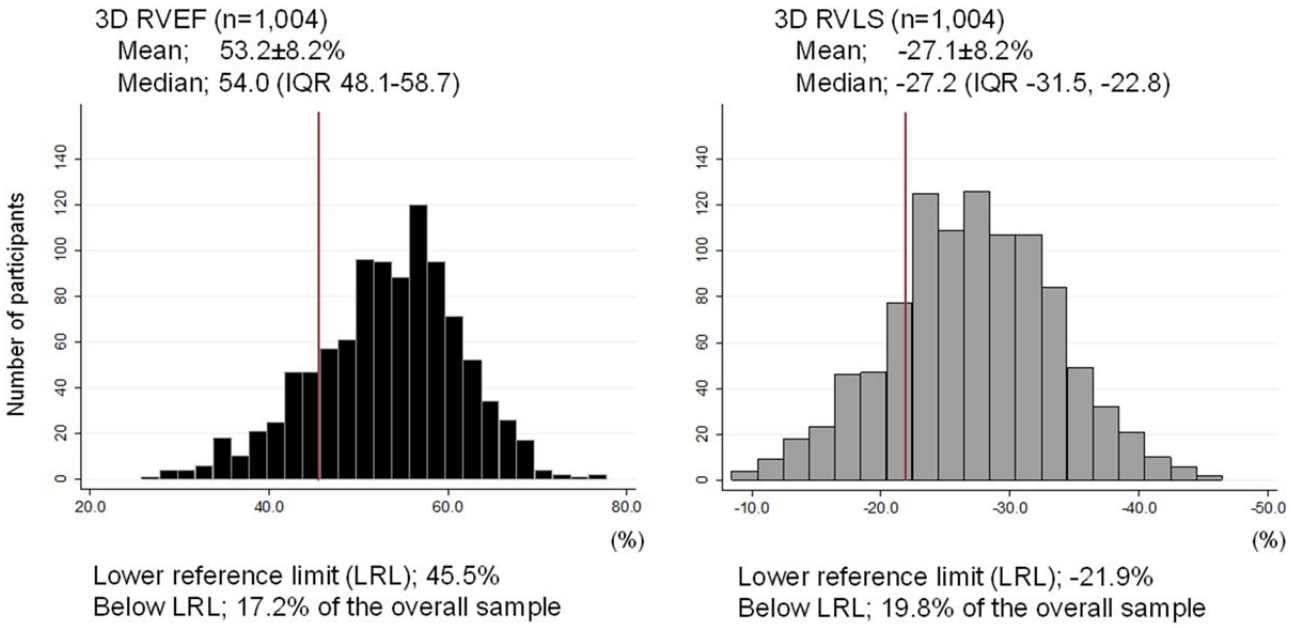
Model 1: Age, sex, race, LVEF, and NT-proBNP adjusted.
Model 2: Age, sex, race, LVEF, NT-proBNP, and LAVi adjusted.

3D RV measure non-availability was modeled among participants all ARIC participants alive at the initiation of visit 5 using the following covariates from Visit 1: age, gender, race, study center, systolic blood pressure, heart rate, body mass index, smoking and drinking status, diabetes mellitus, hypertension, and chronic kidney disease. The resulting calculated weights were incorporated into multivariable models for prevalence of abnormal and time-to-event analysis.

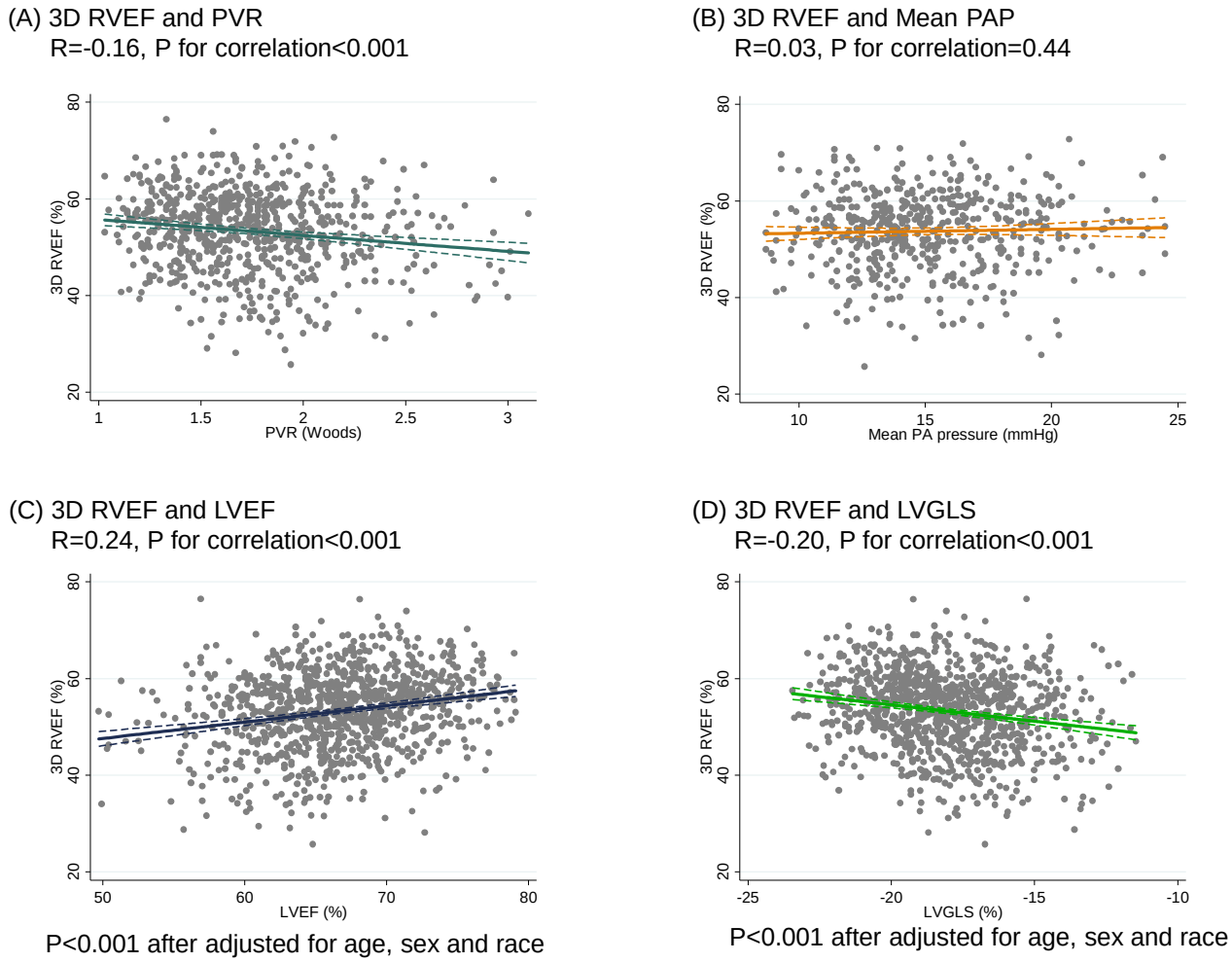
eFigure 1. Study diagram



eFigure 2. Histogram and descriptive statistics for 3D RVEF and RVLS. Vertical red line indicated the reference limit derived from the low-risk subgroup (HF stage 0).

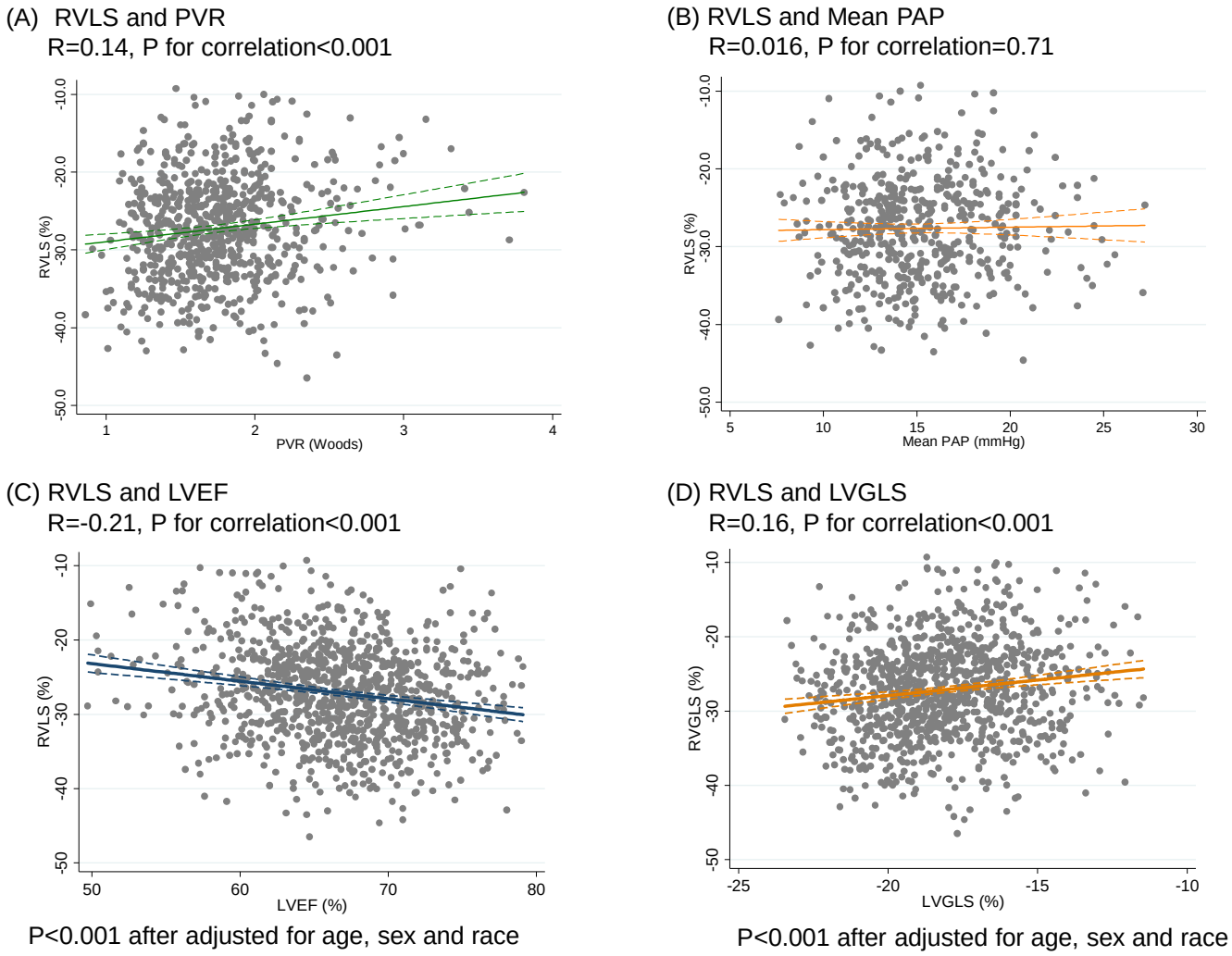


eFigure 3. The relationship of 3D RVEF with (A) PVR, (B) mean PA pressure, (C) LVEF and (D) LVGLS.



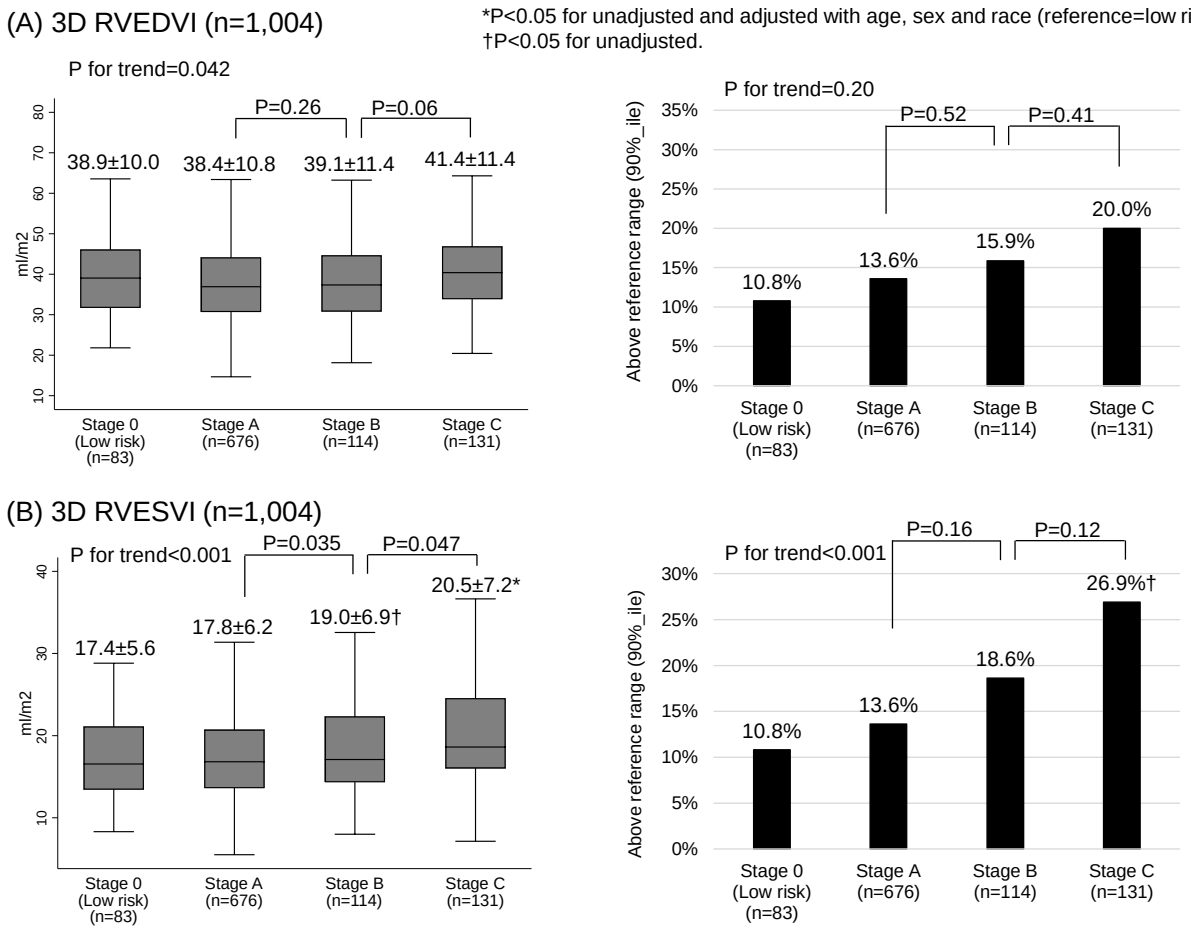
Caption: Linearity of the associations between RV functional measures (3D RVEF, RVLS) with PVR, mean PAP, LVEF, and LVGLS was assessed by fitting adjusted linear and restricted cubic spline models. The number of knots was selected based on the number of knots producing the lowest Baysian information criterion (BIC), with 3 to 6 knots tested. We assumed that the relationship was approximately linear if the linear model resulted in the lowest BIC. Using this approach, for no associations did the restricted cubic spline models improved the BIC beyond the linear model. Therefore, all associations were assumed to be approximately linear.

eFigure 4. Association of RVLS with (A) PVR, (B) mean PAP, (C) LVEF and (D) LVGLS.



Caption: Linearity of the associations between RV functional measures (3D RVEF, RVLS) with PVR, mean PAP, LVEF, and LVGLS was assessed by fitting adjusted linear and restricted cubic spline models. The number of knots was selected based on the number of knots producing the lowest Baysian information criterion (BIC), with 3 to 6 knots tested. We assumed that the relationship was approximately linear if the linear model resulted in the lowest BIC. Using this approach, for no associations did the restricted cubic spline models improved the BIC beyond the linear model. Therefore, all associations were assumed to be approximately linear.

eFigure 5. Mean values of 3D RV (A) EDVI and (B) ESVI, and the prevalence of abnormal (based on the 90th or 10th percentile limits derived from the Stage 0 overall) across HF stages. Comparison of the proportion with abnormal measures across HF stages was performed by trend testing using multivariable logistic regression models adjusting for age, sex, and race.



Supplemental Reference

1. Shah AM, Claggett B, Loehr LR, et al. Heart Failure Stages Among Older Adults in the Community: The Atherosclerosis Risk in Communities Study. Circulation. 2017;135(3):224-240.

2. White AD, Folsom AR, Chambless LE, et al. Community surveillance of coronary heart disease in the Atherosclerosis Risk in Communities (ARIC) Study: methods and initial two years' experience. J Clin Epidemiol. 1996;49(2):223-233.

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6. Loehr LR, Rosamond WD, Chang PP, Folsom AR, Chambless LE. Heart failure incidence and survival (from the Atherosclerosis Risk in Communities study). Am J Cardiol. 2008;101(7):1016-1022.