

**Heart Failure Stages Among Older Adults in the Community: The Atherosclerosis
Risk in Communities Study**

Shah: HF Stages in the Community

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SUPPLEMENTAL MATERIAL

Supplemental Tables and Figures.

Supplemental Figure 1. Prevalence of heart failure stages in the study sample overall when including LS and diastolic measures in the definition of Stage B HF. One participant was classified as Stage D on the basis of having an LVAD (prevalence <0.1%).

Supplemental Figure 2. Kaplan-Meier survival curves for death (panel A), and the composite of death or HF hospitalization (panel B), by HF Stage when including LS and diastolic measures in the definition of Stage B HF. Median follow-up time for the composite endpoint was 608 days (25th to 75th percentile range 469-761 days). Total number of events was 194. For the composite endpoint, estimates for HF Stage C2 are not provided as all participants in this stage had, by definition, experienced a previous HF hospitalization. Event rate is expressed per 100 person-years. Hazard ratios are adjusted for age, sex, race, and Field Center.

Supplemental Table 1. Comparison of ARIC-based limits for abnormal and American Society of Echocardiography guideline limits for measures of cardiac structure and function employed in this analysis.

		ARIC-based 95th percentile limit	Guideline-based limit
LVEF	Women	<57.4%	<54%
	Men	<59.0%	<52%
LVEDV/BSA	Women	>51.9 ml/m ²	>61 ml/m ²
	Men	>60.2 ml/m ²	>74 ml/m ²
LVM/height ^{2.7}	Women	>41.5 g/m ^{2.7}	>44 g/m ^{2.7}
	Men	>45.0 g/m ^{2.7}	>48 g/m ^{2.7}
TDI e' septal	Women	<4.1 cm/s	<7 cm/sec
	Men	<4.3 cm/s	
E/e' septal	Women	>17.4	>15
	Men	>14.8	
LAV/BSA	Women	>32.4 ml/m ²	>34 ml/m ²
	Men	>34.2 ml/m ²	

Supplemental Table 2. Association of HF stage with death, incident HF hospitalization, or the composite of death or HF hospitalization. Median follow-up for the composite endpoint was 608 days (25th to 75th percentile range 469-761 days). For incident HF hospitalization and the composite endpoint, estimates for HF Stage C2 are not provided as all participants in this stage had, by definition, experienced a previous HF hospitalization. Hazard ratios are based on multivariable Cox proportional hazards models. Model 1 adjusted for age, sex, race, and Field Center. Model 2 additionally adjusted for hypertension, diabetes, chronic kidney disease, obesity, prior stroke, myocardial infarction, and atrial fibrillation. For model 1 and model 2 analyses for all endpoints, adjusted P for trend across HF stages is <0.001.

HF Stage	N	Events	Rate per 100 person-years	Model 1		Model 2	
				Hazard Ratio	P value	Hazard Ratio	P value
<i>DEATH (events=145)</i>							
Stage 0	308	3	0.59 (0.19-1.83)	0.71 (0.22-2.27)	0.56	1.25 (0.32-4.79)	0.75
Stage A	3,192	52	0.97 (0.74 – 1.28)	Reference	-	Reference	-
Stage B	1,801	40	1.36 (1.00 – 1.85)	1.36 (0.90-2.06)	0.14	1.44 (0.93-2.24)	0.10
Stage C1	450	14	1.92 (1.13-3.23)	1.72 (0.95-3.12)	0.08	1.56 (0.82-2.97)	0.17
Stage C2	367	39	6.89 (5.03 – 9.43)	6.02 (3.95-9.20)	<0.001	4.27 (2.52-7.26)	<0.001
<i>HEART FAILURE</i>							

<i>(events=113)</i>							
Stage 0	305	0	0	-	-	-	-
Stage A	3,093	24	0.47 (0.31-0.70)	Reference	-	Reference	-
Stage B	1,721	58	2.12 (1.64-2.74)	4.51 (2.80-7.27)	<0.001	4.18 (2.47-7.08)	<0.001
Stage C1	419	28	4.21 (2.91-6.10)	7.48 (4.30-13.01)	<0.001	6.36 (3.39-11.94)	<0.001
<i>COMPOSITE (events=194)</i>							
Stage 0	305	3	0.59 (0.19-1.84)	0.51 (0.16-1.62)	0.25	0.85 (0.24-3.01)	0.80
Stage A	3,093	68	1.32 (1.04-1.68)	Reference	-	Reference	-
Stage B	1,721	85	3.11 (2.51-3.84)	2.29 (1.66-3.15)	<0.001	2.14 (1.51-3.03)	<0.001
Stage C1	419	35	5.27 (3.78-7.34)	3.44 (2.28-5.21)	<0.001	2.84 (1.78-4.53)	<0.001

Supplemental Table 3. Prevalence, biomarker levels, event rates, and hazard ratios for incident HF hospitalization or death among participants reclassified from Stage A to Stage B, not reclassified from Stage A, or existing Stage B with the inclusion of LS and diastolic measures in the definition of Stage B. *Adjusted for age, sex, race, and field center; *p<0.0001 compared to non-reclassified Stage A; ^p=0.003 compared to existing Stage B; #p=0.29 compared to existing Stage B

	N	NT-proBNP (ng/L)	hsTn-T (ng/L)	Events	Event Rate per 1000 person-yrs	Unadjusted HR (95% CI)	Adjusted* HR (95% CI)
Non-reclassified Stage A	2,331	101 [56,180]	9 [7,14]	45	12.1 (9.0, 16.2)	Reference	Reference
Reclassified stage B	861	133 [68,288]*^	12 [8,17]*#	23	16.3 (10.8,24.5)	1.34 (0.81-2.21)	1.11 (0.67-1.84)
Existing Stage B	1,801	158 [78,344]	12 [8,17]	85	31.1 (25.1,38.4)	2.59 (1.80-3.71)	2.37 (1.65-3.40)

Supplemental Table 4. Association between number of abnormal domains of LV structure and function (abnormal structure, systolic function, diastolic function) among HF Stage A and B participants and incident death or HF hospitalization at a median follow-up of 620 [IQR 465-774] days. Model 1 adjusted for age, sex, race, and Field Center. Model 2 additionally adjusted for hypertension, diabetes, chronic kidney disease, obesity, prior stroke, myocardial infarction, and atrial fibrillation. *No significant difference observed in risk of death or HF hospitalization between participants with isolated abnormality of LV structure, isolated systolic dysfunction, or isolated diastolic dysfunction.

	N	Events	Rate	Unadjusted		Model 1		Model 2	
				HR (95% CI)	P value	HR (95% CI)	P value	HR (95% CI)	P value
None	2,219	42	1.2 (0.9-1.6)	Reference		Reference		Reference	
One*	1,556	45	1.8 (1.3-2.4)	1.53 (1.01-2.34)	0.046	1.41 (0.93-2.15)	0.11	1.33 (0.85-2.09)	0.22
Isolated									
structural abnormality	650	18	1.7 (1.1-2.8)	1.51 (0.87-2.62)	0.14	1.54 (0.88-2.68)	0.13	-	-
Isolated									
systolic abnormality	282	9	1.9 (1.0-3.6)	1.62 (0.79-3.33)	0.19	1.53 (0.74-3.17)	0.25	-	-

Isolated									
diastolic	624	18	1.7 (1.1-2.8)	1.48 (0.85-2.57)	0.16	1.22 (0.69-2.13)	0.50	-	-
abnormality									
Two	723	36	3.1 (2.2-4.3)	2.69 (1.72-4.19)	<0.001	2.34 (1.49-3.67)	<0.001	2.18 (1.34-3.54)	0.002
Three	195	26	9.0 (6.1-13.1)	7.85 (4.82-12.81)	<0.001	6.30 (3.83-10.35)	<0.001	5.34 (3.08-9.25)	<0.001

Supplemental Table 5. Inverse probably attrition weighted estimates of the prevalence of HF Stages in the study population overall, and in subgroups defined by sex, race, and age category. Values provided at estimates with 95% confidence limits.

	Stage 0	Stage A	Stage B	Stage C1	Stage C2
Overall	4.5 (4.0-5.0)	51.9 (50.6-53.2)	29.3 (28.1-30.5)	7.7 (7.0-8.4)	6.6 (5.9-7.3)
≤70 years	6.2 (4.4-8.0)	58.8 (55.0-62.6)	26.3 (22.9-29.7)	5.5 (3.7-7.3)	3.1 (1.7-4.6)
70-75 years	6.1 (5.2-7.1)	52.9 (50.8-55.0)	29.0 (27.1-30.9)	7.5 (6.4-8.6)	4.5 (3.6-5.4)
75-80 years	4.2 (3.3-5.1)	51.8 (49.4-54.3)	30.7 (28.4-32.9)	6.4 (5.2-7.6)	6.9 (5.6-8.2)
>80 years	2.4 (1.6-3.2)	48.5 (45.8-51.2)	29.3 (26.9-31.7)	9.9 (8.2-11.6)	9.9 (8.3-11.5)
White women	6.9 (6.0-7.8)	54.3 (52.4-56.3)	27.9 (26.2-29.6)	5.0 (4.1-5.9)	5.7 (4.7-6.6)
Black women	1.0 (0.4-1.7)	52.4 (48.8-56.0)	21.3 (18.6-23.9)	12.9 (10.6-15.1)	10.9 (8.7-13.0)
White men	4.9 (4.0-5.7)	49.4 (47.3-51.6)	30.0 (28.0-32.0)	8.1 (6.9-9.3)	8.1 (6.9-9.3)
Black men	2.1 (0.7-3.5)	47.3 (42.5-52.2)	23.7 (19.5-27.9)	15.6 (12.3-18.8)	10.3 (7.4-13.3)

Supplemental Table 6. Inverse probably attrition weighted estimates of levels of NT-proBNP and high sensitivity troponin T by HF stage. Values provided are median and interquartile range.

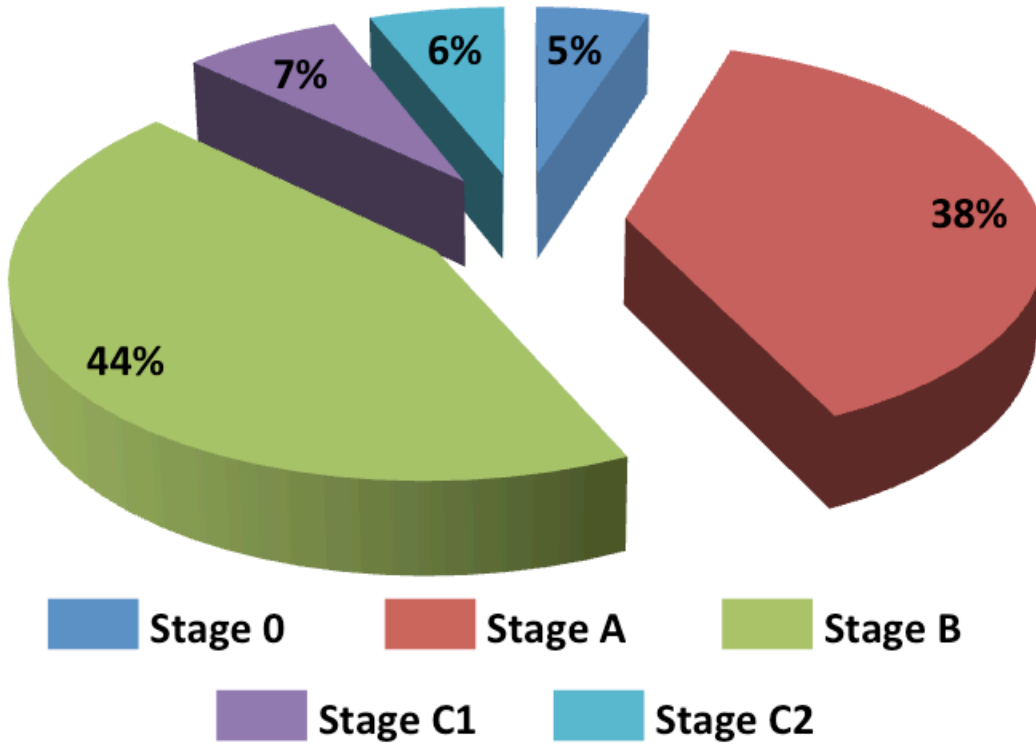
	Stage 0	Stage A	Stage B	Stage C1	Stage C2
NT-proBNP (ng/L)	85 (53-157)	112 (60-208)	167 (82-359)	247 (136-537)	504 (230-1380)
hs-TnT (ng/L)	7 (6-10)	10 (7-15)	12 (8-18)	14 (10-23)	19 (12-33)

Supplemental Table 7. Inverse probably attrition weighted estimates of measures of cardiac structure and function by HF stage at ARIC Visit 5. Values presented are n (%) for categorical variables and median [interquartile range] for continuous variables. Italics indicates that the variable was a criteria for Stage B assignment.

	Stage 0 (n=318)	Stage A (n=3736)	Stage B (n=1247)	Stage C1 (n=450)	Stage C2 (n=367)
<i>LV Structure</i>					
Wall thickness (cm)	0.88 (0.83-0.94)	0.94 (0.88-1.00)	1.05 (0.95-1.14)	1.02 (0.93-1.12)	1.06 (0.95-1.18)
<i>Mass/height^{2.7} (g/m^{2.7})</i>	30.3 (26.7-33.7)	33.4 (29.0-37.3)	45.8 (39.6-51.2)	41.3 (34.9-49.1)	46.4 (37.8-57.5)
<i>LVH</i>	0	0	68.7 (66.5-71.0)	42.8 (37.9-47.7)	58.3 (52.9-63.7)
<i>EDV/BSA (ml/m²)</i>	41.2 (35.5-46.3)	39.4 (34.3-45.4)	45.4 (37.9-55.3)	44.3 (37.5-52.8)	47.0 (38.8-60.7)
<i>LV enlargement</i>	0	0	23.6 (21.5-25.7)	17.4 (13.6-21.3)	31.0 (25.9-36.1)
<i>LV Systolic Function</i>					
LVEF (%)	66.6 (64.2-69.5)	66.7 (63.7-70.0)	63.9 (58.4-68.1)	64.2 (58.8-68.3)	61.5 (53.7-66.5)
<i>Abnormal LVEF</i>	0	0	25.6 (23.4-27.7)	22.1 (18.2-26.0)	34.1 (29.1-39.2)
<i>LVEF <50%</i>	0	0	5.4 (4.3-6.6)	8.4 (5.7-11.0)	18.9 (14.8-23.0)
LS (%)	19.0 (17.5-20.3)	18.5 (16.9-19.9)	17.6 (15.7-19.4)	17.4 (15.4-19.1)	15.9 (13.5-18.4)

Abnormal LS	3.1 (1.1-5.2)	7.3 (6.3-8.3)	18.1 (16.2-20.1)	21.3 (17.2-25.5)	39.3 (33.7-44.9)
<i>LV Diastolic Function</i>					
TDI e' (cm/s)	6.2 (5.3-7.3)	5.6 (4.8-6.6)	5.2 (4.4-6.1)	5.1 (4.2-6.0)	5.1 (4.1-6.1)
Abnormal e'	4.2 (0.2-6.6)	10.5 (9.4-11.7)	19.8 (17.9-21.8)	23.5 (19.2-27.8)	27.1 (22.1-32.0)
E/e' ratio	10.4 (8.5-12.7)	11.6 (9.5-14.0)	12.2 (9.9-15.5)	12.9 (10.3-16.6)	14.8 (11.2-19.3)
Abnormal E/e'	4.5 (2.0-7.1)	12.2 (11.0-13.4)	20.2 (18.2-22.2)	29.2 (24.6-33.8)	41.5 (36.1-46.9)
LAVi (ml/m ²)	21.5 (18.2-25.7)	22.9 (19.0-27.6)	26.7 (21.8-32.7)	27.3 (22.3-34.2)	30.9 (25.1-41.5)
Abnormal LAVi	4.8 (2.1-7.5)	8.6 (7.6-9.7)	23.6 (21.5-25.6)	26.0 (21.5-30.5)	42.4 (37.0-47.9)

Supplemental Figure 1.



Supplemental Figure 2.

