Phenotypic Characterization of Echocardiographic Abnormalities in Patients with Diabetic Cardiomyopathy

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BACKGROUND

Diabetic Cardiomyopathy (DbCM) is diagnosed as the presence of cardiac dysfunction in patients with diabetes in the absence of other causes of cardiac dysfunction such as coronary artery disease (CAD), clinically relevant arrhythmias, severe valvular heart disease, and uncontrolled blood pressure.

PURPOSE

To use baseline data from the ARISE-HF trial (an ongoing placebo-controlled phase 3 clinical trial evaluating the safety and efficacy of a novel highly selective aldose reductase inhibitor on cardiac functional capacity in individuals with DbCM) to explore the patient characteristics among subgroups of DbCM based on the nature and number of echocardiographic abnormalities.

METHODS

662 patients with DbCM defined as either elevated cardiac biomarker (NT-proBNP and/or high-sensitivity cardiac troponin) or structural/functional cardiac abnormalities along with impaired exercise tolerance were enrolled. Participants were allocated to previously-defined clusters. Systolic dysfunction or hypertrophy was defined by global longitudinal strain (GLS) <16% and/or increased LV mass (LVMi >95g/m2 for females and >115g/m2 males). The diastolic cluster was defined as the presence of at least one diastolic abnormality on echocardiography (elevated LV filling pressures [E/e' >13], left atrial volume index (LAVI)> 34 ml/m2 and right ventricular systolic pressure (RVSP)>35 mmHg). An overlap cluster was included for participants with a combination of diastolic, systolic, or LV geometric abnormalities.

RESULTS

Baseline characteristics of individuals with DbCM across the four groups are shown in Table 1. Patients with solely diastolic abnormalities were most commonly female, treated with beta blockers, and less commonly treated with GLPRA.

Patients with diastolic and mixed abnormalities had higher NT-proBNP and lower cardiac functional capacity.

	Elevated biomarkers of heart disease N=278	Systolic/LVH cluster N= 177	Diastolic cluster N= 160	Overlap cluster N= 47	p
Age, yrs	67.6 ± 6.6	67.0 ± 7.4	68.7 ± 7.2	67.7 ± 6.7	0.98
Male, n (%)	150 (54%)	102 (58%)	62 (39%)	21 (45%)	<0.001
Race, n (%)					
White	238 (86%)	140 (79%)	129 (81%)	39 (83%)	
Black or African American	19 (7%)	16 (9%)	7 (4%)	1 (2%)	0.11
Others	20 (7%)	20 (11%)	24 (15%)	7 (15%)	
BMI, kg/m²	30.5 ± 4.6	30.7 ± 4.2	30.6 ± 4.8	30.2 ± 4.4	0.61
SBP, mmHg	129.8 ± 13.0	128.5 ± 11.6	130.9 ± 13.3	131.4 ± 14.8	0.39
Medical History					
Duration of T2DM, yrs	13.5 ± 8.9	14.3 ± 8.9	14.8 ± 10.1	14.9 ± 9.2	0.54
Hypertension, n (%)	184 (66%)	127 (72%)	112 (70%)	35 (75%)	0.48
Dyslipidemia, n (%)	40 (14%)	33 (19%)	26 (16%)	8 (17%)	0.69
Concomitant medications, n (%)					
ACEI-ARBs	185 (66%)	122 (69%)	114 (71%)	28 (60%)	0.45
B-blockers	48 (17%)	29 (16%)	52 (33%)	8 (17%)	<0.001
SGLT2 inhibitors	72 (26%)	47 (27%)	47 (29%)	15 (32%)	0.77
GLP1-RA	55 (20%)	45 (25%)	23 (14%)	13 (28%)	0.04
Laboratory test					
NT-proBNP, ng/L	69 (35-122)	59 (27-118)	82 (44-150)	84 (58-197)	0.04
Hs-Tnt, ng/L	9 (6-12)	8 (6-11)	9 (6-12)	8 (7-13)	0.39
HbA1c, %	6.97 ± 0.77	7.01 ± 0.78	6.94 ± 0.81	7.0 ± 0.78	0.77
Hgb, g/dl	13.8 ± 1.3	13.8 ± 1.4	13.5 ± 1.3	13.2 ± 1.6	<0.001
eGFR, ml/min/1.73m²	80.4 ± 15.3	81.5 ± 16.5	79.0 ± 16.9	80.3 ± 17.2	0.99
Echocardiogram					
LVEF, %	63.3 ± 5.2	61.2 ± 4.7	62.1 ± 5.4	60.0 ± 8.5	<0.001
GLS, %	-19.5 ± 2.0	-14.9 ± 1.9	-19.0 ± 2.4	-15.2 ± 3.2	<0.001
LAVI, ml/m²	22.3 ± 5.2	22.0 ± 5.4	29.4 ± 8.5	31.1 ± 10.0	<0.001
LVMI, g/m²	70.9 ± 14.0	85.3 ± 24.8	73.3 ± 14.7	101.5 ± 28.2	<0.001
E/e'	8.7 ± 1.9	9.1 ± 2.0	13.4 ± 5.8	14.8 ± 7.6	<0.001
RVSP, mmHg	21.5 ± 6.1	22.2 ± 6.5	26.0 ± 8.8	27.8 ± 7.4	<0.001
CPET					
PeakVO₂, ml/min/kg	16.1 ± 3.7	16.2 ± 3.7	15.0 ± 4.1	14.4 ± 3.5	<0.001
VE/VCO₂ slope	30.6 ± 4.7	31.8 ± 5.0	30.5 ± 5.6	30.9 ± 4.4	0.66
PASE score	164.6 ± 99.7	151.9 ± 80.9	146.4 ± 76.4	134.3 ± 77.6	0.12

RESULTS

Patients with DbCM and elevated biomarkers of heart disease showed similar cardiac functional capacity compared to those with systolic dysfunction/hypertrophy documented at a baseline echocardiogram (Table 2).

	Systolic/LVH cluster N= 177	Diastolic + Overlap N= 207	p	Diastolic + Overlap N= 207	Elevated Biomarkers of heart disease N= 278	p	Systolic/LVH cluster N= 177	Elevated Biomarkers of heart disease N= 278	p
Age, yrs	67.0 ± 7.4	68.4 ± 7.1	0.05	68.4 ± 7.1	67.6 ± 6.6	0.19	67.0 ± 7.4	67.6 ± 6.6	0.32
Male, n (%)	102 (58%)	83 (40%)	<0.001	83 (40%)	150 (54%)	<0.001	102 (58%)	150 (54%)	0.47
Race, n (%)									
White	140 (79%)	168 (81%)		168 (81%)	238 (86%)		140 (79%)	238 (86%)	
Black or African American	16 (9%)	8 (4%)	0.09	8 (4%)	19 (7%)	0.01	16 (9%)	19 (7%)	0.18
Others	20 (11%)	31 (15%)		31 (15%)	20 (7%)		20 (11%)	20 (7%)	
BMI, kg/m²	30.7 ± 4.2	30.5 ± 4.5	0.64	30.5 ± 4.5	30.5 ± 4.6	0.91	30.7 ± 4.2	30.5 ± 4.6	0.54
SBP, mmHg	128.5 ± 11.6	131.0 ± 13.6	0.06	131.0 ± 13.6	129.8 ± 13.0	0.34	128.5 ± 11.6	129.8 ± 13.0	0.27
Medical History									
Duration of T2DM, yrs	14.3 ± 8.9	14.8 ± 9.9	0.58	14.8 ± 9.9	13.5 ± 8.9	0.09	14.3 ± 8.9	13.5 ± 8.9	0.29
Hypertension, n (%)	127 (72%)	147 (71%)	0.87	147 (71%)	184 (66%)	0.25	127 (72%)	184 (66%)	0.20
Dyslipidemia, n (%)	33 (19%)	34 (16%)	0.57	34 (16%)	40 (14%)	0.55	33 (19%)	40 (14%)	0.23
Concomitant medications, n (%)									
ACEI-ARBs	122 (69%)	142 (69%)	0.95	142 (69%)	185 (66%)	0.61	122 (69%)	185 (66%)	0.58
B-blockers	29 (16%)	60 (29%)	<0.001	60 (29%)	48 (17%)	<0.001	29 (16%)	48 (17%)	0.79
SGLT2 inhibitors	47 (27%)	62 (30%)	0.46	62 (30%)	72 (26%)	0.34	47 (27%)	72 (26%)	0.90
GLP1-RA	45 (25%)	36 (17%)	0.05	36 (17%)	55 (20%)	0.49	45 (25%)	55 (20%)	0.16
Laboratory test									
NT-proBNP, ng/L	59 (27-118)	83 (45-155)	<0.001	83 (45-155)	69 (35-122)	<0.001	59 (27-118)	69 (35-122)	0.10
Hs-Tnt, ng/L	8 (6-11)	9 (6-12)	0.33	9 (6-12)	9 (6-12)	0.89	8 (6-11)	9 (6-12)	0.25
HbA1c, %	7.01 ± 0.78	6.95 ± 0.80	0.49	6.95 ± 0.80	6.97 ± 0.77	0.75	7.01 ± 0.78	6.97 ± 0.77	0.65
Hgb, g/dl	13.8 ± 1.4	13.4 ± 1.4	<0.001	13.4 ± 1.4	13.8 ± 1.3	<0.001	13.8 ± 1.4	13.8 ± 1.3	0.67
eGFR, ml/min/1.73m²	81.5 ± 16.5	79.3 ± 16.9	0.10	79.3 ± 16.9	80.4 ± 15.3	0.44	81.5 ± 16.5	80.4 ± 15.3	0.50
Echocardiogram									
LVEF, %	61.2 ± 4.7	61.6 ± 6.2	0.48	61.6 ± 6.2	63.3 ± 5.2	<0.001	61.2 ± 4.7	63.3 ± 5.2	<0.001
GLS, %	-14.9 ± 1.9	-17.8 ± 3.1	<0.001	-17.8 ± 3.1	-19.5 ± 2.0	<0.001	-14.9 ± 1.9	-19.5 ± 2.0	<0.001
LAVI, ml/m²	22.0 ± 5.4	29.8 ± 8.9	<0.001	29.8 ± 8.9	22.3 ± 5.2	<0.001	22.0 ± 5.4	22.3 ± 5.2	0.63
LVMI, g/m²	85.3 ± 24.8	79.9 ± 22.1	<0.001	79.9 ± 22.1	70.9 ± 14.0	<0.001	85.3 ± 24.8	70.9 ± 14.0	<0.001
E/e'	9.1 ± 2.0	13.7 ± 6.2	<0.001	13.7 ± 6.2	8.7 ± 1.9	<0.001	9.1 ± 2.0	8.7 ± 1.9	0.05
RVSP, mmHg	22.2 ± 6.5	26.3 ± 8.5	<0.001	26.3 ± 8.5	21.5 ± 6.1	<0.001	22.2 ± 6.5	21.5 ± 6.1	0.34
CPET									
PeakVO₂, ml/min/kg	16.2 ± 3.7	14.9 ± 4.0	<0.001	14.9 ± 4.0	16.1 ± 3.7	<0.001	16.2 ± 3.7	16.1 ± 3.7	0.9
VE/VCO₂ slope	31.8 ± 5.0	30.6 ± 5.4	0.46	30.6 ± 5.4	30.6 ± 4.7	0.14	31.8 ± 5.0	30.6 ± 4.7	0.37
PASE score	151.9 ± 80.9	143.0 ± 76.6	0.32	143.0 ± 76.6	164.6 ± 99.7	0.02	151.9 ± 80.9	164.6 ± 99.7	0.17

CONCLUSIONS

- The current analysis provides unique insights into the morphological and functional changes of patients with DbCM.
- Diastolic dysfunction (alone or in combination) is present in 31%, and these patients have lower cardiac functional capacity and higher natriuretic peptide levels.
- The ARISE-HF study (NCT04083339) is evaluating the safety and efficacy of AT-001 to improve or prevent the decline of cardiac functional capacity in individuals with DbCM.