

**Contemporary Assessment of Left Ventricular Diastolic Function in Older Adults:  
The Atherosclerosis Risk In Communities Study**

**SUPPLEMENTAL MATERIAL**

Amil M Shah MD MPH,<sup>1</sup> Brian Claggett PhD,<sup>1</sup> Dalane Kitzman MD,<sup>2</sup> Tor Biering-Sørensen, MD, PhD,<sup>1,3</sup> Jan Skov Jensen, MD, PhD, DMSc,<sup>3</sup> Susan Cheng MD,<sup>1</sup> Kunihiro Matsushita MD PhD,<sup>4</sup> Suma Konety MD,<sup>5</sup> Aaron R. Folsom MD MPH,<sup>6</sup> Thomas H. Mosley PhD,<sup>7</sup> Jacqueline D. Wright DrPH,<sup>8</sup> Gerardo Heiss MD PhD,<sup>9</sup> Scott D. Solomon MD<sup>1</sup>

**Author Affiliations:**

<sup>1</sup>Division of Cardiovascular Medicine, Brigham and Women's Hospital, Boston, MA, USA; <sup>2</sup>Wake Forest University School of Medicine, Winston-Salem, NC; <sup>3</sup>Department of Cardiology, Herlev and Gentofte Hospital, University of Copenhagen, Denmark; <sup>4</sup>Johns Hopkins Bloomberg School of Public Health, Baltimore, MD; <sup>5</sup>Cardiovascular Division, University of Minnesota, Minneapolis, MN; <sup>6</sup>Division of Epidemiology and Community Health, School of Public Health, University of Minnesota, Minneapolis, MN; <sup>7</sup>Divisions of Geriatrics and Neurology, University of Mississippi Medical Center, Jackson, MS; <sup>8</sup>Division of Cardiovascular Sciences, National Heart, Lung, and Blood Institute, Bethesda, MD; <sup>9</sup>University of North Carolina Gillings School of Global Public Health, Chapel Hill, NC

## **Supplemental Tables and Figures**

Supplemental Figure 1. Scatter plots and restricted cubic splines demonstrating the continuous relationship between LV diastolic measures (TDI e', E/e' ratio, LA A-P dimension, and LAVi) and Log(NT-proBNP) levels assessed concomitantly at Visit 5 among ARIC participants without prevalent heart failure at Visit 5. Y-axis shows geometric mean values of NT-proBNP.

Supplemental Table 1. Prevalence of abnormalities of LV diastolic function, and the association of measure of LV diastolic function with incident HF hospitalization or death, stratified by sex.

	Hazard Ratio for Continuous Relationship			Dichotomous Categorization using ARIC Reference Limits					
				Percent Abnormal			Hazard Ratio		
	Women	Men	interact P	Women	Men	P	Women	Men	interact P
TDI e' <sub>septal</sub> (cm/sec)	1.20 (1.01-1.43), p=0.036	1.06 (0.93-1.21), p=0.40 <sup>f</sup>	0.34	20%	21%	0.20	1.54 (0.95-2.52), p=0.08	1.74 (1.13-2.67), p=0.01	0.65
TDI e' <sub>lateral</sub> (cm/sec)	1.16 (1.02-1.32), p=0.02	0.95 (0.87-1.03), p=0.24	0.009	19%	17%	0.02	2.21 (1.39-3.50), p=0.001	1.19 (0.73-1.94), p=0.49	0.07
E/e' <sub>septal</sub>	1.10 (1.06-1.13), p<0.001	1.10 (1.07-1.13), p<0.001	0.91	23%	27%	0.004	1.72 (1.09-2.73), p=0.02	2.46 (1.64-3.68), p<0.001	0.25
E/e' <sub>lateral</sub>	1.10 (1.06-1.14), p<0.001	1.09 (1.05-1.14), p<0.001	0.74	20%	22%	0.19	2.02 (1.27-3.20), p=0.003	2.15 (1.42-3.27), p<0.001	0.92
LA width (cm)	1.55 (0.98-2.46), p=0.06	2.76 (2.10-3.64), p<0.001	0.09	27%	30%	0.03	1.83 (1.17-2.86), p=0.009	3.07 (2.04-4.62), p<0.001	0.17

LAVi (ml/m <sup>2</sup> )	1.05 (1.02-1.07), p<0.001	1.03 (1.02-1.03), p<0.001 <sup>t</sup>	0.21	21%	25%	0.004	1.53 (0.94-2.50), p=0.09	3.31 (2.20-4.97), p<0.001	0.02
------------------------------	------------------------------	---	------	-----	-----	-------	-----------------------------	------------------------------	------

Abnormal defined using ARIC-based reference limits. P value for between sex comparison of prevalence of abnormal measures is adjusted for age and race. Cox proportional hazards models adjust for age and race. Interact P – P for interaction. <sup>t</sup>P for nonlinear trend = 0.01, P for overall trend=0.009; <sup>t</sup>P for nonlinear trend = 0.001, P for overall trend <0.0001

Supplemental Table 2. Prevalence of abnormalities of LV diastolic function, and the association of measure of LV diastolic function with incident HF hospitalization or death, stratified by race.

	Dichotomous Categorization using ARIC Reference Limits								
	Hazard Ratio for Continuous Relationship			Percent abnormal			Hazard Ratio		
	White	Black	interact P	White	Black	P	White	Black	interact P
TDI e' <sub>septal</sub> (cm/sec)	1.07 (0.94-1.21), p=0.30	1.29 (1.02-1.64), p=0.03	0.29	19%	25%	<0.001	1.33 (0.90-1.97), p=0.15	2.88 (1.56-5.30), p=0.001	0.05
TDI e' <sub>lateral</sub> (cm/sec)	0.97 (0.90-1.05), p=0.44	1.22 (1.03-1.44), p=0.02 <sup>§</sup>	0.03	18%	19%	0.12	1.23 (0.82-1.85), p=0.31	3.30 (1.79-6.11), p<0.001	0.01
E/e' <sub>septal</sub>	1.09 (1.06-1.11), p<0.001*	1.14 (1.09-1.19), p<0.001	0.14	25%	26%	0.05	1.81 (1.27-2.57), p=0.001	3.28 (1.78-6.03), p<0.001	0.15
E/e' <sub>lateral</sub>	1.07 (1.03-1.11), p<0.001	1.18 (1.12-1.25), p<0.001	0.02	21%	18%	0.11	1.57 (1.09-2.26), p=0.016	4.94 (2.68-9.09), p<0.001	0.003
LA width (cm)	2.16 (1.63-2.87), p<0.001	3.14 (1.69-5.84), p<0.001	0.12	30%	21%	<0.001	2.24 (1.59-3.14), p<0.001	3.08 (1.66-5.73), p<0.001	0.44

LAVi (ml/m <sup>2</sup> )	1.03 (1.02-1.03), p<0.001 <sup>‡</sup>	1.08 (1.04-1.12), p<0.001	0.01	23%	23%	0.39	2.29 (1.62-3.26), p<0.001	2.59 (1.39-4.82), p=0.003	0.99
------------------------------	---	------------------------------	------	-----	-----	------	------------------------------	------------------------------	------

Abnormal defined using ARIC-based reference limits. P value for between race comparison of prevalence of abnormal measures is adjusted for age and sex. Cox proportional hazards models adjust for age and sex. Interact P – P for interaction. \*P for nonlinear trend = 0.02, P for overall trend=0.009; <sup>‡</sup>P for nonlinear trend = 0.01, P for overall trend <0.0001; <sup>‡</sup>P for nonlinear trend = 0.04, P for overall trend =0.0001; <sup>§</sup>P for nonlinear trend = 0.01, P for overall trend =0.003

Supplemental Table 3. Reference values for cardiac structure and function in ARIC at Visit 5 compared with values from select healthy cohorts and American Society of Echocardiography guideline recommendations.

<b>LV STRUCTURE</b>														
	<b>ARIC</b>		<b>SHS/NYC sample*<sup>1</sup></b>		<b>NORRE<sup>2</sup></b>		<b>Guidelines<sup>†3</sup></b>							
<b>Publication year</b>	<b>2015</b>		<b>2001</b>		<b>2014</b>		<b>2015</b>							
	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men				
N	271	142	206	207	320	414	~300-700	~200-500						
Mean age	74.0 ± 4.4	75.5 ± 4.8	SHS: 58±8 NYC: 42±11	SHS: 59±8 NYC: 45±11	45.4±13.1	46.3±13.7	45±8 (parasternal views) 47±17 (apical views) <sup>‡</sup>							
LA width	3.20 ± 0.39	3.45 ± 0.45	3.00±0.36	3.28±0.47										
<b>LV DIASTOLIC FUNCTION</b>														
	<b>ARIC</b>	<b>FLEMENGO<sup>4</sup></b>			<b>de Sutter et al<sup>5</sup></b>			<b>HUNT<sup>6</sup></b>		<b>LOLIPOP<sup>7</sup></b>		<b>NORRE<sup>8</sup></b>		<b>Guidelines<sup>9</sup></b>
<b>Age category</b>	<b>Overall</b>	<b>Overall</b>	<b>≥60</b>	<b>65-74</b>	<b>&gt;74</b>	<b>Overall</b>	<b>&gt;60</b>	<b>Overall</b>	<b>65-75</b>	<b>Overall</b>	<b>&gt;60</b>	<b>&gt;60</b>		
N	413	239	24	35	17	1266	269	453	30	449	83	-		
Age	74.4±4.5	43.7±12.9	-	-	-	~49.5±13.6		51	69±3	45.8±13.7		-		
Female	65%	48%	-	-	-	52%	44%	44%	33%	56%	53%	-		
White	93%	-	-	-	-			43%	53%	-	-	-		
E wave	65 ± 16	-	-	77±21	74±20	F:75±16 M: 66±15	F:69±16 M:61±14	-	64.7±14.8	0.76±0.17	0.70±0.16	-		
A wave	73 ± 16	-	-	76±21	83±22	F: 58±18 M: 54±17	F:75±18 M: 65±18	-	71.8±16.7	0.60±0.17	0.74±0.16	-		
E/A ratio	0.92 ± 0.26	1.39 [1.19-1.70]	0.89 [0.81-1.12]	1.08±0.43	0.98±0.58	F: 1.42±0.62 M: 1.34±0.54	F:0.96±0.32 M:0.99±0.34	-	0.9±0.2	1.37±0.51	0.98±0.29	0.96±0.18		
S <sup>2</sup> <sub>septal</sub>	6.8 ± 1.2	-	-	-	-	8.0±1.2	-	8.1±1.5	7.6±1.2	8.1±1.4	7.5±1.3 (5.0-10.0)	-		
e <sup>2</sup> <sub>septal</sub>	6.2 ± 1.5	-	-	7±2.1	6.2±1.7	9.9±2.9	-	8.6±1.9	7.5±1.4	10.3±3.0 (8.0-12.0)	7.6±2.3 (3.0-13.0)	10.4±2.1		

E/e' <sub>septal</sub>	10.8 ± 3.1	-	-	11.5±3.1	12.4±3.3	7.5±2.4	9.0±3.1	8.7±2.2	8.9±2.3	7.9±2.4 (6.1-9.2)	9.7±2.8 (5.0-16.9)	-
s' <sub>lateral</sub>	7.4 ± 1.6	-	-	-	-	8.8±1.8	-	10.2±2.4	9.9±2.3	9.8±2.4	8.5±2.5 (4.0-15.0)	-
e' <sub>lateral</sub>	7.5 ± 1.9	-	-	-	-	12.5±3.7	-	12.2±3.0	10.5±1.9	13.5±4.0 (10.0-16.0)	9.6±2.8 (4.0-17.0)	12.9±3.5
E/e' <sub>lateral</sub>	9.1 ± 2.9	-	-	-	-	6.8±2.3	8.4±2.9	6.3±1.9	6.3±1.8	6.1±2.1 (4.6-7.3)	7.8±2.2 (4.2-12.8)	-

Values are mean ± standard deviation (SD) unless otherwise specified. \*Values are for white participants; †Based on unpublished data from the Asklepios study, FLEMENGHO study, CARDIA study, and Padua study incorporated in the guideline document. ‡Measures from parasternal views: LVEDD, LVESD, IVS, PW, LV mass, RWT; measures from apical views: LVEDV, LVESV.

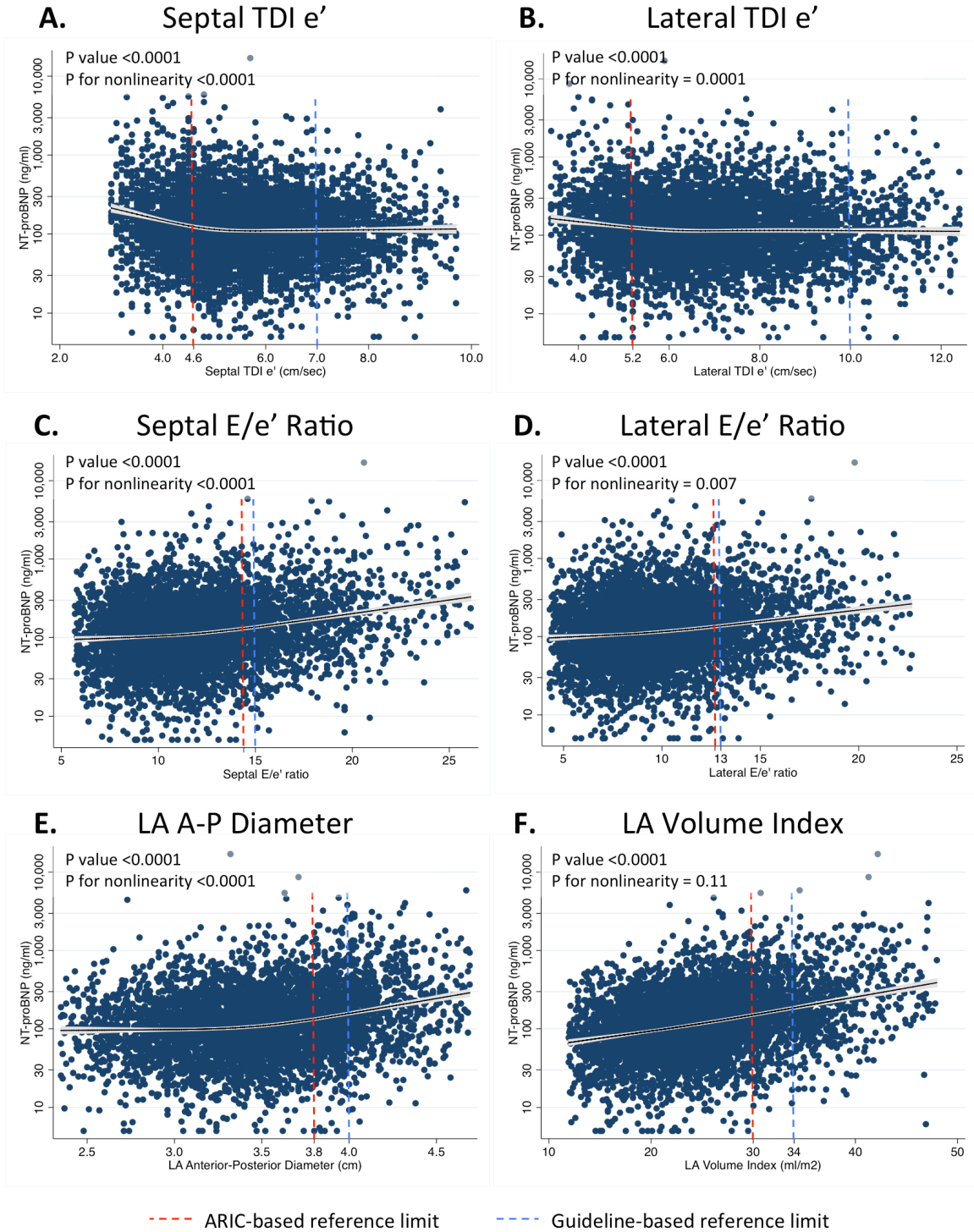


Supplemental Table 4. Percentile limits for the distribution of measures of LV diastolic function among the ARIC healthy subgroup restricted to participants with BMI of 18-25 kg/m<sup>2</sup> (n=206).

	<b>5%-ile</b>	<b>10%-ile</b>	<b>20%-ile</b>	<b>50%-ile</b>	<b>80%-ile</b>	<b>90%-ile</b>	<b>95%-ile</b>
	<b>(95% CI)</b>	<b>(95% CI)</b>	<b>(95% CI)</b>	<b>(95% CI)</b>	<b>(95% CI)</b>	<b>(95% CI)</b>	<b>(95% CI)</b>
<i>TDI e' septal (cm/sec)</i>							
Overall	4.1 ( 3.8 - 4.4)	4.5 ( 4.2 - 4.8)	5.0 ( 4.8 - 5.2)	6.2 ( 5.9 - 6.5)	7.7 ( 7.3 - 8.1)	8.5 ( 8.1 - 8.9)	9.1 ( 8.2 -10.0)
Female	4.1 ( 3.7 - 4.5)	4.5 ( 4.2 - 4.8)	5.0 ( 4.7 - 5.3)	6.2 ( 5.9 - 6.5)	7.9 ( 7.5 - 8.3)	8.7 ( 8.2 - 9.2)	9.3 ( 8.5 -10.1)
Male	4.1 ( 3.4 - 4.8)	4.8 ( 4.2 - 5.4)	5.2 ( 4.7 - 5.7)	6.0 ( 5.4 - 6.6)	7.3 ( 6.6 - 8.0)	7.9 ( 7.1 - 8.7)	8.1 ( 6.7 - 9.5)
<i>TDI e' lateral (cm/sec)</i>							
Overall	5.0 ( 4.6 - 5.4)	5.3 ( 5.1 - 5.5)	5.8 ( 5.5 - 6.1)	7.4 ( 7.1 - 7.8)	9.1 ( 8.7 - 9.6)	10.2 ( 9.5 -10.9)	11.1 (10.3 -11.9)
Female	4.9 ( 4.4 - 5.4)	5.2 ( 5.0 - 5.5)	5.8 ( 5.4 - 6.2)	7.4 ( 7.0 - 7.8)	9.2 ( 8.6 - 9.8)	10.5 ( 9.7 -11.3)	11.2 (10.3 -12.1)
Male	5.3 ( 4.4 - 6.2)	5.4 ( 5.0 - 5.8)	6.1 ( 5.5 - 6.7)	7.7 ( 7.0 - 8.4)	8.9 ( 7.9 - 10.0)	9.8 ( 8.4 -11.2)	10.4 ( 8.8 -12.0)
<i>E/e' septal</i>							
Overall	6.7 ( 6.0 - 7.5)	7.1 ( 6.8 - 7.5)	8.1 ( 7.7 - 8.6)	10.2 ( 9.6 -10.8)	13.1 (12.5 -13.8)	14.4 (13.4 -15.4)	16.2 (13.4 -19.0)
Female	6.7 ( 5.9 - 7.5)	7.1 ( 6.7 - 7.5)	8.1 ( 7.6 - 8.6)	10.6 ( 10.0 -11.3)	13.5 (12.7 -14.3)	15.0 (14.0 -16.0)	16.5 (14.1 -19.0)
Male	6.9 ( 5.5 - 8.3)	7.1 ( 6.5 - 7.7)	7.6 ( 6.7 - 8.5)	9.3 ( 8.2 -10.4)	11.6 (10.2 -13.0)	12.6 (10.9 -14.3)	13.2 ( 9.0 -17.4)
<i>E/e' lateral</i>							
Overall	5.4 ( 4.8 - 6.0)	6.1 ( 5.7 - 6.5)	6.7 ( 6.4 - 7.0)	8.6 ( 8.1 - 9.1)	10.9 (10.3 -11.5)	12.5 (11.5 -13.5)	13.9 (12.3 -15.5)

Female	5.6 ( 4.9 - 6.3)	6.2 ( 5.7 - 6.7)	7.0 ( 6.6 - 7.4)	9.0 ( 8.5 - 9.5)	11.4 (10.6 -12.2)	13.2 (12.0 -14.4)	14.9 (13.5 -16.3)
Male	5.0 ( 3.8 - 6.3)	5.5 ( 4.6 - 6.4)	6.1 ( 5.3 - 6.9)	7.3 ( 6.4 - 8.2)	9.6 ( 8.2 -11.0)	10.6 ( 8.5 -12.7)	11.9 ( 9.5 -14.3)
<i>LA A-P dimension (cm)</i>							
Overall	2.5 ( 2.3 - 2.7)	2.7 ( 2.6 - 2.8)	2.9 ( 2.8 - 2.9)	3.1 ( 3.1 - 3.2)	3.5 ( 3.4 - 3.5)	3.6 ( 3.5 - 3.7)	3.8 ( 3.7 - 4.0)
Female	2.4 ( 2.2 - 2.7)	2.7 ( 2.5 - 2.8)	2.8 ( 2.7 - 2.9)	3.1 ( 3.0 - 3.1)	3.4 ( 3.3 - 3.5)	3.5 ( 3.4 - 3.6)	3.6 ( 3.4 - 3.8)
Male	2.6 ( 2.2 - 3.1)	2.9 ( 2.7 - 3.1)	3.0 ( 2.9 - 3.2)	3.3 ( 3.2 - 3.4)	3.7 ( 3.6 - 3.9)	3.8 ( 3.7 - 4.0)	3.9 ( 3.6 - 4.3)
<i>LAVi (ml/m<sup>2</sup>)</i>							
Overall	13.1 (11.7 -14.6)	14.5 (13.2 -15.8)	17.6 (16.4 -18.8)	21.6 (20.6 -22.7)	26.7 (25.3 -28.0)	29.8 (28.3 -31.3)	31.5 (26.8 -36.3)
Female	12.8 (11.2 -14.5)	14.3 (12.7 -15.9)	17.2 (15.9 -18.5)	21.3 (20.2 -22.4)	26.2 (24.5 -27.8)	29.8 (27.8 -31.7)	31.4 (26.5 -36.3)
Male	13.1 (10.3 -15.9)	16.0 (13.2 -18.8)	18.7 (16.5 -21.0)	23.3 (21.4 -25.2)	28.4 (25.6 -31.2)	30.2 (26.9 -33.6)	32.0 (23.6 -40.5)

**Supplemental Figure 1.**



## Supplemental References

1. Ilercil A, O'Grady MJ, Roman MJ, Paranicas M, Lee ET, Welty TK, Fabsitz RR, Howard BV, Devereux RB. Reference Values for echocardiographic measures in urban and rural populations of differing ethnicity: The Strong Heart Study. *J Am Soc Echocardiogr* 2001;14:601-11.
2. Kou S, Caballero L, Dulgheru R, Voilliot D, De Sousa C, Kacharava G, Athanassopoulos GD, Barone D, Baroni M, Cardim N, Gomez De Diego JJ, Hagendorff A, Henri C, Hristova K, Lopez T, Magne J, De La Morena G, Popescu BA, Penicka M, Ozyigit T, Rodrigo Carbonero JD, Salustri A, Van De Veire N, Von Bardeleben RS, Vinereanu D, Voigt JU, Zamorano JL, Donal E, Lang RM, Badano LP, Lancellotti P. Echocardiographic reference ranges for normal cardiac chamber size: results from the NORRE study. *Eur Heart J Cardiovasc Imaging* 2014;15:680-90.
3. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L, Flachskampf FA, Foster E, Goldstein SA, Kuznetsova T, Lancellotti P, Muraru D, Picard MH, Rietzschel ER, Rudski L, Spencer KT, Tsang W, Voigt JU. Recommendations for cardiac chamber quantification by echocardiography in adults: An update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *J Am Soc Echocardiogr* 2015;28:1-39.
4. Kuznetsova T, Herbots L, Lopez B, Jin Y, Richart T, Thijs L, Gonzalez A, Herregods MC, Fagard RH, Diez J, Staessen JA. Prevalence of left ventricular diastolic dysfunction in a general population. *Circ Heart Fail* 2009;2:105-12.

5. De Sutter J, De Backer J, de Veire NV, Velghe A, De Buyzere M, Gillebert TC. Effects of age, gender, and left ventricular mass on septal mitral annulus velocity (E') and the ratio of transmitral early peak velocity to E' (E/E'). *Am J Cardiol* 2005;95:1020-3.
6. Dalen H, Thorstensen A, Vatten LJ, Aase SA, Stoylen A. Reference values and distribution of conventional echocardiographic Doppler measures and longitudinal tissue Doppler velocities in a population free from cardiovascular disease. *Circ Cardiovasc Imaging* 2010;3:614-622.
7. Chahal NS, Lim TK, Jain P, Chambers JC, Kooner JS, Senior R. Normative reference values for the tissue Doppler imaging parameters of left ventricular function: a population-based study. *Eur J Echocardiogr* 2010;11:51-6.
8. Caballero L, Kou S, Dulgheru R, Gonjilashvili N, Athanassopoulos GD, Barone D, Baroni M, Cardim N, Gomez de Diego JJ, Oliva MJ, Hagendorff A, Hristova K, Lopez T, Magne J, Martinez C, de la Morena G, Popescu BA, Penicka M, Ozyigit T, Rodrigo Carbonero JD, Salustri A, Van De Veire N, Von Bardeleben RS, Vinereanu D, Voigt JU, Zamorano JL, Bernard A, Donal E, Lang RM, Badano LP, Lancellotti P. Echocardiographic reference ranges for normal cardiac Doppler data: results from the NORRE Study. *Eur Heart J Cardiovasc Imaging* 2015;16:1031-41.
9. Nagueh SF, Appleton CP, Gillebert TC, Marino PN, Oh JK, Smiseth OA, Waggoner AD, Flachskampf FA, Pellikka PA, Evangelista A. Recommendations for the evaluation of left ventricular diastolic function by echocardiography. *J Am Soc Echocardiogr* 2009;22:107-33.