



# Comparing the influence of 2009 versus 2016 ASE/EACVI diastolic function guidelines on the prevalence and echocardiographic characteristics of preclinical diastolic dysfunction (stage B heart failure) in a Hispanic population with type 2 diabetes mellitus

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## ABSTRACT

**Aims:** To identify prevalence and predictors of undetected pre-clinical diastolic dysfunction (PDD) in a cohort of adult Hispanic patients with type 2 diabetes (T2D), and compare variations in epidemiology and echocardiographic characteristics between categorization based on the 2009 versus 2016 guidelines.

**Methods:** From 2013 to 2016, a cross-sectional cohort study of adults with T2D was performed. Patients without signs/symptoms of heart failure (HF) underwent 2D/Doppler echocardiographic screening, and were grouped into two subcohorts: 1) normal diastolic function, and 2) PDD, defined by the 2009 or 2016 ASE/EACVI criteria. **Results:** Among 307 Hispanic subjects, by 2009 criteria, 193 (62.9%) had normal diastolic function, 113 (36.8%) diastolic dysfunction and 1 (0.3%) indeterminate. Those that had diastolic dysfunction (DD) were older (mean age  $59.1 \pm 12.7$  vs  $52.2 \pm 12.2$  years,  $p < 0.0001$ ), with higher proportion female (69.0 vs 53.9%,  $p = 0.0092$ ), and higher systolic blood pressure ( $136.5 \pm 18.6$  vs  $131.7 \pm 19.9$ ,  $p = 0.0372$ ). By 2016 criteria, 261 (85%) had normal diastolic function, 22 (7.2%) diastolic dysfunction and 24 (7.8%) indeterminate. Among those that had normal diastolic function ( $n = 261$ ) by 2016 criteria, 29% ( $n = 76$ ) had DD by 2009 criteria, and they were more likely to have higher E/e' and left atrial volume index (LAVI).

**Conclusions:** By applying the 2016 versus the 2009 diastolic function criteria to a Hispanic population with T2D, the prevalence of PDD decreased significantly from 37% to 7%. These findings are consistent with recent studies demonstrating that the 2016 ASE/EACVI guidelines are more specific for diagnosing DD and hence less sensitive leading to lower prevalence of diastolic dysfunction.

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## 1. Introduction

Type 2 diabetes (T2D) and heart failure (HF) are predicted to impose significant health and economic burdens across the globe well into the 21st century, and global prevalence of T2D is increasing.<sup>1–5</sup> Advanced glycation end-product production, abnormal metabolic signaling, inflammation, and ventricular remodeling are believed to contribute to the development of diastolic dysfunction and results in increased all-cause mortality.<sup>6–13</sup> Previous epidemiological studies have reported that preclinical diastolic dysfunction (PDD, Stage B HF), defined as

diastolic dysfunction with normal systolic function and no HF symptoms, is common in T2D and portends high risk for development of symptomatic HF (Stage C and D).<sup>8–10,14</sup>

Assessment of diastolic dysfunction noninvasively remains challenging, and in 2016, the American Society of Echocardiography and European Association of Cardiovascular Imaging (ASE/EACVI) released updated criteria for echocardiographic definition of diastolic dysfunction, which is significantly different from the 2009 criteria.<sup>15,16</sup> Recent studies have reported that the new 2016 ASE/EACVI recommendations resulted in much lower prevalence of DD when applied to the general population, when compared to the 2009 recommendations.<sup>17</sup> However, prevalence of PDD and subject characteristics based on the 2009 versus 2016 diastolic dysfunction guidelines in the Hispanic population remains undefined.

The objective of this study is to: 1) identify the prevalence and predictors of stage B PDD in a cohort of adult Hispanic patients with T2D

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based on the 2009 diastolic function guidelines; 2) identify the prevalence and predictors of stage B PDD in a cohort of adult Hispanic patients with T2D based on the 2016 diastolic function guidelines; and 3) identify differences in epidemiology and echocardiographic parameters in a cohort of adult Hispanic patients with T2D, comparing diastolic function based on 2009 and 2016.

## 2. Methods

### 2.1. Study setting, subjects, and data collection

A registry-supported, observational, cross-sectional study was performed from January 2013 through May 2016 on 307 consecutive Hispanic patients, aged 18 years or older and with a documented diagnosis of T2D (as defined by criteria established by the American Diabetes Association<sup>18</sup>) who were referred to the integrated practice unit (IPU) team at Western Diabetes Institute (WDI) of Western University of Health Sciences, Pomona, CA, USA. As part of the initial comprehensive multidisciplinary IPU evaluation, all patients underwent screening 2D and Doppler echocardiography using a Philips iE33 system performed by an experienced cardiac sonographer at the WDI Heart and Vascular Center. None had signs or symptoms suggestive of HF. De-identified images and measurements were independently reviewed by an experienced echocardiographer (H.H.C.) at the Cardiovascular Research Center, Mayo Clinic, Rochester, MN, USA.

All patients gave their written, informed consent and permission to have their past, present, and future health record information placed into the WDI Diabetes Research Registry, which is approved by the Institutional Review Board (IRB) of Western University of Health Sciences (Protocol #13/IRB/017). Baseline characteristics and data collected at the initial IPU evaluation included: age, gender, ethnicity, smoking status, glycated hemoglobin, blood pressure, lipid profile, urine albumin-creatinine ratio (UACR), serum creatinine, body mass index (BMI), and the use of glucose-lowering and antihypertensive medications.

Obesity was defined as a BMI  $\geq 30$  kg/m<sup>2</sup>. Overweight was defined as a BMI between 25 kg/m<sup>2</sup> and 29.99 kg/m<sup>2</sup>. Chronic kidney disease (CKD) was defined as an estimated glomerular filtration rate (eGFR, calculated by the CKD-EPI equation<sup>19</sup>)  $< 60$  ml/min/1.73 m<sup>2</sup> (i.e., Stages 3A–5). Subjects were grouped into subcohorts: normal diastolic function and PDD.

The 2009 criteria for diastolic dysfunction and estimation of left atrial pressure in those with normal ejection fraction were used. Diastolic dysfunction categorization was based on septal E/e' and left atrial volume index. If septal E/e'  $\leq 8$ , or  $8 < E/e' < 15$  and left atrial volume index (LAVI)  $< 34$  ml/m<sup>2</sup>, then subjects were categorized as having normal diastolic function. If septal E/e'  $\geq 15$ , or  $8 < E/e' < 15$  and LAVI  $> 34$  ml/m<sup>2</sup>, then subjects were categorized as having diastolic dysfunction.<sup>20</sup> We defined indeterminate diastolic dysfunction by 2009 criteria when medial or lateral e' was unable to be reliably obtained by Doppler echocardiography.

The 2016 criteria for diastolic dysfunction in those with normal ejection fraction were used. Diastolic dysfunction categorization was based on four parameters: E/e'  $> 14$ , septal e'  $< 7$  cm/s or lateral e'  $< 10$  cm/s, tricuspid regurgitation (TR) velocity  $> 2.8$  m/s, and LAVI  $> 34$  ml/m<sup>2</sup>. If  $< 50\%$  of these parameters were positive, subjects were classified as having normal diastolic function. If  $50\%$  of these parameters were positive, subjects were classified as having indeterminate diastolic function. If  $> 50\%$  of these parameters were positive, subjects were classified as having diastolic dysfunction.<sup>16</sup>

### 2.2. Statistical analysis

All statistical analyses were conducted using the SAS software for Windows version 9.3 (Cary, North Carolina). Descriptive statistics were presented as means and standard deviations for continuous variables, and frequencies and proportions for categorical variables.

Independent *t*-test was used to identify whether the continuous variables were different between the PDD and normal diastolic function. Chi-square analyses were conducted to identify the association between categorical variables and the binary diastolic function groups (PDD vs normal diastolic function). Fisher's exact tests were conducted if the expected cell count were  $< 5$ . Multivariable logistic analysis was performed to identify factors associated with the presence of PDD. All statistical analyses were two-sided. *p*-Value  $< 0.05$  was considered to be statistically significant.

## 3. Results

### 3.1. Prevalence and characteristics of pre-clinical diastolic dysfunction: the 2009 criteria

307 Hispanic subjects had sufficient echocardiographic data for classification in the 2009 and 2016 diastolic dysfunction guidelines and were included in the final analysis. The cohort was divided into two sub-cohorts: those with normal diastolic function and those with PDD.

By the 2009 criteria, the prevalence of PDD was 37% in this cohort. The baseline clinical and echocardiographic data from these two groups were compared (Table 1). PDD was present in 113 (36.8%) subjects, while 193 (62.9%) had normal diastolic function, and 1 (0.3%) was indeterminate. When compared to patients with normal diastolic function, those with PDD were more likely to be female (69.0% vs 53.9%, *p* =

**Table 1**  
Baseline clinical characteristics between those with diastolic dysfunction (DD) and those with normal diastolic function by 2009 criteria.

	Normal diastolic function, n = 193 (63%)	Diastolic dysfunction, n = 113 (37%)	<i>p</i> -Value
Mean age (years)	52.2 ± 12.2 <sup>a</sup>	59.1 ± 12.7	<0.0001
Female	104/193 (53.9%)	78/113 (69.0%)	0.0092
Smoking status			0.4782
Never smoker	76/143 (53.2%)	44/83 (53.0%)	
Ex-smoker	52/143 (36.4%)	34/83 (41.0%)	
Current smoker	15/143 (10.5%)	5/83 (6.0%)	
Alcohol consumption			0.1168
Never used alcohol	43/138 (31.2%)	28/79 (35.4%)	
Ex-drinker	46/138 (33.3%)	16/79 (20.3%)	
Current drinker	49/138 (35.3%)	35/79 (44.3%)	
History of coronary artery disease, n	12/180 (6.7%)	7/110 (6.4%)	0.9194
History of hypertension	140/193 (72.5%)	86/113 (76.1%)	0.4931
Insulin usage	86/193 (44.6%)	49/113 (43.4%)	0.8388
Duration of diagnosed diabetes (years)	10.0 ± 7.7	12.2 ± 10.4	0.0435
CKD stage			0.6727
Stage 1	106/182 (58.2%)	73/110 (66.4%)	
Stage 2	39/182 (21.4%)	17/110 (15.5%)	
Stage 3	27/182 (3.9%)	15/110 (13.6%)	
Stage 4	7/182 (1.7%)	3/110 (2.7%)	
Stage 5	3/182 (1.7%)	2/110 (1.8%)	
Baseline BMI			0.4749
Normal	20/193 (10.4%)	11/113 (9.7%)	
Overweight	38/193 (19.7%)	29/113 (25.7%)	
Obese	135/193 (70.0%)	73/113 (64.6%)	
HbA1C (%)	8.37 ± 2.03	8.25 ± 1.84	0.5994
BMI (kg/m <sup>2</sup> )	33.9 ± 8.4	33.7 ± 8.3	0.8504
Heart rate (bpm)	71.6 ± 11.1	69.7 ± 11.2	0.1489
Systolic BP (mmHg)	131.7 ± 19.9	136.5 ± 18.6	0.0372
Diastolic BP (mmHg)	77.3 ± 9.5	77.7 ± 10.4	0.7279
Mean arterial pressure (mmHg)	95.4 ± 11.1	97.3 ± 11.4	0.1606
LDL cholesterol (mg/dL)	97.4 ± 31.1	106.2 ± 41.2	0.0689
HDL cholesterol (mg/dL)	48.8 ± 22.7	47.3 ± 11.9	0.4659
Serum creatinine (mg/dL)	0.86 ± 0.76	0.86 ± 0.55	0.9970
eGFR (ml/min/1.73 m <sup>2</sup> )	89.2 ± 26.3	84.7 ± 28.3	0.2772

Abbreviations: CKD = chronic kidney disease, BMI = body mass index, HbA1C = hemoglobin A1C, eGFR = estimated glomerular filtration rate.

<sup>a</sup> All values were presented as mean ± standard deviation, or n/column total (%).

**Table 2**

Echocardiographic characteristics between those with DD and those with normal diastolic function by 2009 criteria.

	Normal diastolic function, n = 193 (63%)	Diastolic dysfunction, n = 113 (37%)	p-Value
Ejection fraction (%)	64.2 ± 5.7 <sup>a</sup>	64.0 ± 6.3	0.8380
Mass index (g/m <sup>2</sup> ) 2D	80.2 ± 25.1	86.5 ± 27.1	0.0458
Relative wall thickness	0.51 ± 1.0	0.47 ± 0.2	0.5793
E/e' medial	13.5 ± 5.1	15.7 ± 5.0	0.0003
E/e' lateral	10.0 ± 4.1	12.0 ± 4.4	0.0001
E/A	1.03 ± 0.32	1.01 ± 0.36	0.6375
LA volume index (ml/m <sup>2</sup> )	21.9 ± 8.3	24.5 ± 8.7	0.0092
Left ventricular hypertrophy	39/189 (20.6%)	35/113 (31.0%)	0.0856 <sup>b</sup>

<sup>a</sup> All values were presented as mean ± standard deviation, or n/column total (%).<sup>b</sup> Based on Fisher's exact test.

0.0092), had higher systolic blood pressure (136.5 ± 18.6 vs 131.7 ± 19.9,  $p = 0.0372$ ), and older in age (59.1 ± 12.7 vs 52.2 ± 12.2 years,  $p < 0.0001$ ).

Table 2 shows the echocardiographic characteristics of the study population with PDD and with normal diastolic function by 2009 criteria. Compared to patients with normal diastolic function, those with PDD had no difference in left ventricular ejection fraction (64 ± 6% vs 64 ± 6%,  $p = 0.8380$ ) or relative wall thickness (0.47 ± 0.2 vs 0.51 ± 1.0,  $p = 0.5793$ ) but did have a greater left ventricular mass index, LVMI (86.5 ± 27.1 vs 80.2 ± 25.1 g/m<sup>2</sup>,  $p = 0.0458$ ). Those in the PDD subgroup had a greater medial E/e' (15.7 ± 5.0 vs 13.5 ± 5.1,  $p = 0.0003$ ), lateral E/e' (12.0 ± 4.4 vs 10.0 ± 4.1,  $p = 0.0001$ ) and LA volume index (24.5 ± 8.7 vs 21.9 ± 8.3 ml/m<sup>2</sup>,  $p = 0.0092$ ) but had no difference in E/A (1.01 ± 0.36 vs 1.03 ± 0.32,  $p = 0.6375$ ) as compared to those with normal diastolic function. There was a trend for greater prevalence of left ventricular hypertrophy in the diastolic dysfunction group (31.0% vs 20.6%,  $p = 0.0856$ ).

Univariable analysis showed that older age (OR 1.25 [1.13, 1.38],  $p < 0.0001$ ), female gender (OR 1.91 [1.17, 3.11],  $p = 0.0097$ ), duration of diagnosed diabetes (OR 1.03 [1.00, 1.06],  $p = 0.0309$ ), and history of hypertension (OR 2.62 [1.46, 4.71],  $p = 0.0013$ ) were all significant predictors of PDD. Both unadjusted and adjusted odds ratio predicting the presence of PDD are shown in Table 3. Using multivariable logistic analysis, significant predictors of PDD in adults with T2D included older age (adjusted odds ratio (AOR) 1.21 [1.08, 1.35],  $p = 0.0013$ ) and female gender (AOR 2.05 [1.20–3.49],  $p = 0.0086$ ).

### 3.2. Prevalence and characteristics of pre-clinical diastolic dysfunction: the 2016 criteria

By the 2016 criteria, the prevalence of PDD was 7% in this cohort. The baseline clinical and echocardiographic data from these two groups were compared (Table 4). PDD was present in 22 (7.2%) subjects, while 261 (85%) had normal diastolic function, and 24 (7.8%) were indeterminate. There was no significant difference in gender or age between the normal diastolic function versus PDD groups.

Table 5 shows the echocardiographic characteristics of the study population with PDD and with normal diastolic function. There was no significant difference in left ventricular ejection fraction, relative wall thickness, left ventricular mass index, medial E/e', lateral E/e', LA volume index, or left ventricular hypertrophy between the normal diastolic function versus PDD groups. E/A was higher in the PDD group (1.47 ± 0.66 vs 1.0 ± 0.27,  $p = 0.0045$ ) as compared to those with normal diastolic function.

Univariable analysis did not demonstrate any significant variables that were predictors of PDD. Using multivariable logistic analysis, there were no significant predictors of PDD in adults with T2D.

### 3.3. Comparing the characteristics of pre-clinical diastolic dysfunction between the 2009 and 2016 criteria

Among those that had normal diastolic function ( $n = 261$ ) by 2016 criteria, 29% ( $n = 76$ ) had DD and 70% ( $n = 184$ ) had normal diastolic function by 2009 criteria, while 0.4% ( $n = 1$ ) was indeterminate by

**Table 3**

Odds ratio (OR) and 95% confidence interval (CI) for DD by 2009 criteria.

	Unadjusted			Adjusted		
	OR	95% CI	p-Value	OR <sup>a</sup>	95% CI	p-Value
Age (based on 5 years increment)	1.25	1.13–1.38	<0.0001	1.21	1.08–1.35	0.0013
Duration of known diagnosis of diabetes (based on 1 year increment)	1.03	1.00–1.06	0.0309	1.02	0.99–1.05	0.3130
BMI group			0.4766			0.3303
Normal BMI	Referent			Referent		
Overweight	1.39	0.58–3.35		1.3	0.49–3.45	
Obese	0.98	0.45–2.16		0.8	0.34–1.92	
CKD stage			0.6758			0.3621
Stage 1	Referent			Referent		
Stage 2	0.63	0.33–1.20		0.53	0.26–1.08	
Stage 3	0.81	0.40–1.62		0.54	0.21–1.37	
Stage 4	0.62	0.16–2.49		0.42	0.08–2.11	
Stage 5	0.97	0.16–5.94		0.78	0.11–5.46	
Insulin usage at baseline (yes vs no)	0.95	0.60–1.52	0.8389	1.23	0.73–2.09	0.4407
Gender (female vs male)	1.91	1.17–3.11	0.0097	2.05	1.20–3.49	0.0086
Baseline eGFR (ml/min/1.73 m <sup>2</sup> )			0.7160			0.8932
<60	1.14	0.55–2.41		1.07	0.38–3.00	
≥60	Referent			Referent		
History of hypertension (yes vs no)	2.62	1.46–4.71	0.0013	1.83	0.96–3.52	0.0686

Abbreviations: CKD = chronic kidney disease, BMI = body mass index, eGFR = estimated glomerular filtration rate.

<sup>a</sup> Adjusted ORs and CIs were calculated based on the logistic regression while keeping other factors in the regression model.

**Table 4**

Baseline clinical characteristics between those with DD and those with normal diastolic function by 2016 criteria.

	Normal diastolic function, n = 261 (85%)	Diastolic dysfunction, n = 22 (7%)	p-Value
Mean age (years)	54.0 ± 12.4 <sup>a</sup>	56.8 ± 17.8	0.4798
Female	150/261 (59.8%)	14/22 (63.7%)	0.7221
Smoking status			0.3640
Never smoker	106/191 (55.5%)	7/17 (41.2%)	
Ex-smoker	68/191 (35.6%)	9/17 (52.9%)	
Current smoker	17/191 (8.9%)	1/17 (5.9%)	
Alcohol consumption			0.5654
Never used alcohol	61/185 (33.0%)	5/16 (31.3%)	
Ex-drinker	54/185 (29.2%)	3/16 (18.8%)	
Current drinker	70/185 (37.8%)	8/16 (50.0%)	
History of coronary artery disease	17/246 (6.9%)	1/21 (4.8%)	0.7062
History of hypertension	189/261 (72.4%)	16/22 (72.7%)	0.9006
Insulin usage	116/261 (44.4%)	8/22 (36.4%)	0.4632
Duration of diagnosed diabetes (years)	10.7 ± 8.6	12.8 ± 10.6	0.2706
CKD stage			0.4223
Stage 1	151/247 (61.1%)	14/22 (63.6%)	
Stage 2	46/247 (18.6%)	2/22 (9.1%)	
Stage 3	38/247 (15.4%)	3/22 (13.6%)	
Stage 4	8/247 (3.2%)	2/22 (9.1%)	
Stage 5	4/247 (1.6%)	1/22 (4.6%)	
Baseline BMI group			0.1193
Normal BMI	28/261 (10.7%)	1/22 (4.6%)	
Overweight	49/261 (18.8%)	8/22 (36.4%)	
Obese	184/261 (70.5%)	13/22 (59.1%)	
HbA1C (%)	8.3 ± 2.0	8.3 ± 1.9	0.9967
BMI (kg/m <sup>2</sup> )	34.0 ± 8.3	31.5 ± 4.4	0.0234
Heart rate (bpm)	70.9 ± 10.8	69.3 ± 14.7	0.6258
Systolic BP (mmHg)	132.5 ± 19.6	139.3 ± 20.4	0.1230
Diastolic BP (mmHg)	77.4 ± 9.6	76.6 ± 11.9	0.7429
Mean arterial pressure (mmHg)	95.7 ± 11.2	97.5 ± 12.3	0.4801
LDL cholesterol (mg/dL)	100.0 ± 35.7	115.1 ± 36.9	0.0774
HDL cholesterol (mg/dL)	48.6 ± 20.4	47.0 ± 12.8	0.6004
Serum creatinine (mg/dL)	0.85 ± 0.68	1.12 ± 1.03	0.2569
eGFR (mL/min/1.73 m <sup>2</sup> )	87.0 ± 27.3	86.1 ± 28.3	0.9034

Abbreviations: CKD = chronic kidney disease, BMI = body mass index, HbA1C = hemoglobin A1C, eGFR = estimated glomerular filtration rate.

<sup>a</sup> All values were presented as mean ± standard deviation, or n/column total (%).

2009 criteria. Among those that had normal diastolic function by 2016 criteria, those that had DD vs those that had normal diastolic function by 2009 criteria were more likely to be older (57.5 ± 12.3 vs 52.5 ± 12.1 years,  $p = 0.0028$ ) and female (73.7% vs 53.4%,  $p = 0.0038$ ) and trended to have greater prevalence of left ventricular hypertrophy (33.0% vs 21.1%,  $p = 0.1351$ ) (Table 6). Echocardiographic differences show a higher E/e' (medial 16.0 ± 4.9 vs 13.6 ± 5.2, lateral 11.9 ± 4.3 vs 10.0 ± 4.1,  $p = 0.0005$  and  $p = 0.0015$ , respectively) and higher LAVI (24.4 ± 8.6 vs 21.9 ± 8.4 years,  $p = 0.0331$ ) (Table 7).

#### 4. Discussion

Previously with the 2009 ASE/EACVI diastolic dysfunction criteria, PDD has been reported to be common among those with T2D.<sup>8,9</sup> In

**Table 5**

Echocardiographic characteristics between those with DD and normal diastolic function by 2016 criteria.

	Normal diastolic function, n = 261 (85%)	Diastolic dysfunction, n = 22 (7%)	p-Value
Ejection fraction (%)	64.2 ± 6.0 <sup>a</sup>	63.9 ± 6.5	0.8531
Mass index (g/m <sup>2</sup> ), 2D	81.4 ± 26.3	89.3 ± 25.9	0.1972
Relative wall thickness, 2D	0.5 ± 0.85	0.46 ± 0.15	0.5318
E/e' medial	14.3 ± 5.2	14.9 ± 5.7	0.6052
E/e' lateral	10.6 ± 4.2	12.2 ± 5.1	0.0840
E/A	1.0 ± 0.27	1.47 ± 0.66	0.0045
LA volume index (ml/m <sup>2</sup> )	22.6 ± 8.5	25.4 ± 8.9	0.1496
Left ventricular hypertrophy	63/257 (24.5%)	6/22 (27.3%)	0.8152 <sup>b</sup>

<sup>a</sup> All values were presented as mean ± standard deviation, or n/column total (%).<sup>b</sup> Based on Fisher's exact test.**Table 6**

Comparison of clinical characteristics between patients with DD based on 2009 and 2016 criteria.

	No DD by 2016 criteria but DD by 2009 criteria (n = 76)	No DD by 2009 and 2016 criteria (n = 184)	p-Value
Mean age (years)	57.5 ± 12.3 <sup>a</sup>	52.5 ± 12.1	0.0028
Female	56/76 (73.7%)	100/184 (53.4%)	0.0038
Smoking status			0.6051
Never smoker	31/52 (59.6%)	75/138 (54.4%)	
Ex-smoker	18/52 (34.6%)	49/138 (35.5%)	
Current smoker	3/52 (5.8%)	14/138 (10.1%)	
Alcohol consumption			0.0714
Never used alcohol	19/52 (36.5%)	42/132 (31.8%)	
Ex-drinker	9/52 (17.3%)	45/132 (34.1%)	
Current drinker	24/52 (46.2%)	45/132 (34.1%)	
History of coronary artery disease	5/74 (6.8%)	12/171 (7.0%)	0.9412
History of hypertension	57/76 (75.0%)	135/184 (73.4%)	0.7856
Insulin usage	33/76 (43.4%)	83/184 (45.1%)	0.8034
Duration of diagnosed diabetes (years)	12.2 ± 10.3	10.2 ± 7.8	0.1262
CKD stage			0.3481
Stage 1	50/73 (68.5%)	100/173 (57.8%)	
Stage 2	9/73 (12.3%)	37/173 (21.4%)	
Stage 3	12/73 (16.4%)	26/173 (15.0%)	
Stage 4	1/73 (1.4%)	7/173 (4.1%)	
Stage 5	1/73 (1.4%)	3/173 (1.7%)	
Baseline BMI group			0.9886
Normal BMI	8/76 (10.5%)	20/184 (10.9%)	
Overweight	14/76 (18.4%)	35/184 (19.0%)	
Obese	54/76 (71.1%)	129/184 (70.1%)	
HbA1C (%)	8.1 ± 1.8	8.3 ± 2.0	0.4290
BMI (kg/m <sup>2</sup> )	34.2 ± 8.1	33.9 ± 8.5	0.7951
Heart rate (bpm)	69.2 ± 10.4	71.6 ± 10.9	0.1047
Systolic BP (mmHg)	135.5 ± 18.3	131.3 ± 20.0	0.1223
Diastolic BP (mmHg)	78.1 ± 9.9	77.0 ± 9.6	0.4259
Mean arterial pressure (mmHg)	97.2 ± 11.2	95.1 ± 11.2	0.1745
LDL cholesterol (mg/dL)	106.4 ± 44.7	97.1 ± 31.0	0.1143
HDL cholesterol (mg/dL)	48.6 ± 12.3	48.7 ± 23.0	0.9607
Serum creatinine (mg/dL)	0.8 ± 0.3	0.9 ± 0.8	0.3990
eGFR (mL/min/1.73 m <sup>2</sup> )	82.3 ± 28.8	88.9 ± 26.6	0.1829

Abbreviations: CKD = chronic kidney disease, BMI = body mass index, HbA1C = hemoglobin A1C, eGFR = estimated glomerular filtration rate.

<sup>a</sup> All values were presented as mean ± standard deviation, or n/column total (%).

our cohort of Hispanic adults with T2D, the prevalence of PDD/stage B HF varied from 7% to 34%, depending on whether the 2009 or 2016 guidelines were applied. Based on univariable and multivariable analyses in the 2009 guidelines, those with PDD were more likely to be female and older in age with greater left ventricular mass than those with normal diastolic function. These differences were not found when applying the 2016 guidelines.

Comparing the 2009 and 2016 recommendations revealed that among those with normal diastolic function by 2016, 29% had DD by 2009 criteria and these subjects were more likely to be older, female

**Table 7**

Comparison of echocardiographic characteristics between patients with DD based on 2009 and 2016 criteria.

	No DD by 2016 criteria but DD by 2009 criteria (n = 76)	No DD by 2009 and 2016 criteria (n = 184)	p-Value
Ejection fraction (%)	64.2 ± 6.7 <sup>a</sup>	64.2 ± 5.7	0.9812
Mass index (g/m <sup>2</sup> ), 2D	83.9 ± 29.2	80.3 ± 25.1	0.3333
Relative wall thickness, 2D	0.46 ± 0.16	0.52 ± 1.02	0.5147
E/e' medial	16.0 ± 4.9	13.6 ± 5.2	0.0005
E/e' lateral	11.9 ± 4.3	10.0 ± 4.1	0.0015
E/A	0.98 ± 0.27	1.02 ± 0.28	0.2517
LA volume index (mL/m <sup>2</sup> )	24.4 ± 8.6	21.9 ± 8.4	0.0331
Left ventricular hypertrophy	25/76 (33.0%)	38/180 (21.1%)	0.1351 <sup>b</sup>

<sup>a</sup> All values were presented as mean ± standard deviation, or n/column total (%).<sup>b</sup> Based on Fisher's exact test.

and had higher LAVI when compared to those with normal DD by 2009 criteria.

This study is one of the first to assess the prevalence, clinical and echocardiographic parameters of PDD in a Hispanic population with T2D, comparing the 2009 and 2016 diastolic function guidelines. Applying the 2009 guidelines revealed that adults with T2D and PDD/vstage B HF are more commonly older, overweight or obese females with higher blood pressure, and these findings are consistent with those of prior studies.<sup>21–23</sup> However, when applying the 2016 guidelines, the prevalence of diastolic dysfunction decreases significantly, consistent with the strict definition of the 2016 criteria. This is consistent with prior research demonstrating a lower prevalence of diastolic dysfunction when applying the 2016 versus 2009 guidelines among the general population.<sup>17</sup>

PDD, defined as diastolic dysfunction with normal systolic function and no symptoms of HF, has emerged as an important precursor to the development of overt heart failure with preserved ejection fraction (HFpEF). Early detection of at-risk patients with stage B HF/PDD is likely to be beneficial and cost-effective.<sup>8,9,12,24</sup> Early screening of patients at risk of heart failure (stage B) and aggressive management of risk factors have been shown to reduce the rate of LV dysfunction and heart failure progression, and improve outcomes.<sup>25,26</sup>

Based on prior studies by From et al., there is evidence that those with diabetes are at greater risk of diastolic dysfunction development.<sup>8,9</sup> There has unfortunately not been a large amount of data for Hispanics and other minorities, as these populations are often underrepresented in large trials. Mehta et al showed in ECHO-SOL that approximately 50% of the general Hispanic population had left ventricular diastolic dysfunction, and 96% of this was subclinical or unrecognized.<sup>27</sup> Adapted 2009 diastolic criteria were used in that study. Similarly, Russo et al. compared diastolic function in different racial-ethnic groups, with increased prevalence of diastolic dysfunction among Hispanics and Blacks, although the authors concluded that many of these differences may be related to sociodemographic factors.<sup>28</sup>

While the purpose of the 2016 diastolic function guidelines was to simplify the identification of diastolic dysfunction via noninvasive assessment, it is essential both for clinical practice and future cardiovascular research that there is a consistent and reproducible set of criteria for diastolic function that also correlates with long term outcomes. The 2016 criteria resulted in lower prevalence of PDD in our study population. However, those that had normal diastolic function per 2016 criteria but diastolic dysfunction in 2009 had underlying structural abnormalities as evidenced by increased LAVI, which has previously been shown to be associated with worse outcomes among the T2D and HF populations.<sup>29–33</sup>

With the new 2016 guidelines on diastolic dysfunction, prospective studies are needed to better understand the burden and progression of PDD defined by the 2016 criteria to clearly define what is normal and abnormal on noninvasive assessment. While this study was not designed to assess outcomes or progression to symptomatic HF, future

studies may incorporate heart failure risk scores such as the ABC HF risk score to identify if there is differential HF progression risk using the 2016 versus 2009 diastolic function criteria.<sup>34</sup>

#### 4.1. Limitations

There are several limitations of this study that warrant consideration when interpreting the results. There may be referral bias when patients with established T2D are referred to a specialty practice for further evaluation and detailed echocardiographic evaluation. This study was cross-sectional and not designed to assess outcomes or prospectively determine the progression to symptomatic HF. There were only 22 individuals diagnosed with PDD with the 2016 criteria, which diminishes statistical power for comparisons. Additionally, technical limitations in obtaining all needed measurements on echocardiography limited inclusion of some subjects in the final analyses.

#### 5. Conclusions

The prevalence of pre-clinical diastolic dysfunction (stage B HF) varied widely (7% to 37%) depending on whether the 2009 or 2016 diastolic function criteria were applied. The 2009 criteria led to significantly higher prevalence of DD and a subpopulation that is older and more likely to be female. The findings are consistent with recent studies demonstrating the 2016 ASE/EACVI guidelines are more specific and less sensitive for DD.

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