

Differences in Diastolic Function and Global Longitudinal Strain on Stress Echocardiography Between Elderly Diabetic and Non-Diabetic Patients

Diferencias entre el comportamiento de la función diastólica y el strain longitudinal global en el ecocardiograma de estrés de paciente ancianos diabéticos versus no diabéticos

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ABSTRACT

Background: Diabetes mellitus (DM) is a disease with increasing prevalence due to population aging. According to the Framingham study, DM is associated with an increased risk of heart failure in both women and men, regardless of the presence of concomitant coronary artery disease. In its early stages, diabetic cardiomyopathy is characterized by an almost always preserved left ventricular ejection fraction (LVEF), with reduced global longitudinal strain (GLS) and diastolic dysfunction.

Objective: The following study was conducted to describe alterations in diastolic function and GLS and their associations in a population of elderly diabetic patients.

Methods: This was an observational cohort study including consecutive patients undergoing a stress echocardiogram in our department, excluding those diagnosed with coronary artery disease. Diastolic function variables (E velocity, e' velocity and E/e' ratio) were measured, and patients were categorized as presenting normal diastolic function or mild (Grade 1), moderate (Grade 2), or severe (Grade 3) diastolic dysfunction. Speckle tracking was used to measure global longitudinal strain. 6 years Diabetic patients were compared with non-diabetic patients. Multivariate analysis was performed to identify the predictors of significant diastolic dysfunction (moderate or severe) and GLS. A p-value <0.05 was considered statistically significant.

Results: The study included 176 diabetic patients and 771 non-diabetic ones, with a mean age of 73 ± 6 years. Diabetic patients exhibited greater diastolic function parameter abnormalities at rest and during exercise compared with non-diabetic patients, as well as a significant reduction in GLS. The group with DM had a higher percentage of significant diastolic dysfunction both at rest (12.5% vs. 7.5%, $p < 0.001$) and during exercise (35% vs. 23%, $p < 0.001$). Left ventricular ejection fraction was normal and similar in both groups ($p = 0.417$). Global longitudinal strain was lower in patients with DM (-15.20% vs. -16.21% in patients without DM; $p < 0.001$). In logistic regression analysis, DM was an independent predictor of significant diastolic dysfunction and an independent predictor of GLS. Only one patient in the diabetic group presented with LVEF <50%.

Conclusion: In this population of elderly patients without ischemic heart disease, DM was independently associated with a higher prevalence of diastolic dysfunction, both at rest and during exercise, and with a reduction in stroke volume despite preserved left ventricular ejection fraction. These findings are consistent with the concept of a predominantly subclinical diastolic diabetic cardiomyopathy.

Key words: Diabetes mellitus - Heart failure - Ventricular dysfunction - Diastolic dysfunction.

RESUMEN

Introducción: La diabetes mellitus (DM) es una enfermedad cuya prevalencia va en aumento conforme el envejecimiento de la población. De acuerdo con el estudio Framingham, la DM implica un aumento del riesgo de insuficiencia cardíaca en mujeres y hombres más allá de la presencia de enfermedad coronaria concomitante. En estadios iniciales la miocardiopatía diabética se caracteriza por una fracción de eyección del ventrículo izquierdo (FEVI) casi siempre preservada, con disminución del strain longitudinal global (SLG) y disfunción diastólica.

Objetivo: El siguiente estudio se realizó con el objetivo de describir las alteraciones de la función diastólica y el SLG y sus asociaciones en una población de pacientes diabéticos añosos.

Material y métodos: Estudio de cohorte observacional en el cual se incluyeron pacientes consecutivos que acudieron a realizarse un ecocardiograma de estrés en nuestro servicio, excluyendo los pacientes con diagnóstico de enfermedad coronaria. Se midieron

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variables de función diastólica (Vel E, Vel e', relación E/e') y se categorizó a los pacientes como función diastólica normal y disfunción diastólica leve (Grado 1), moderada (Grado 2) o grave (grado 3). Se midió el SLG mediante speckle tracking. Se compararon los pacientes diabéticos versus no diabéticos. Se realizó análisis multivariado para establecer los determinantes de disfunción diastólica significativa (moderada o grave) y del SLG. Se consideró estadísticamente significativa una $p < 0,05$.

Resultados: Se incluyeron 176 pacientes diabéticos y 771 pacientes no diabéticos, con una edad media de 73 años. Los pacientes diabéticos presentaron mayor alteración de los parámetros de función diastólica en reposo y esfuerzo con respecto a los no diabéticos, y también una significativa disminución del SLG. El grupo con DM presentó mayor porcentaje de disfunción diastólica significativa tanto en reposo (12,5% vs 7,5%, $p < 0,001$) como en esfuerzo (35% vs 23%, $p < 0,001$). La FEVI fue normal y similar en ambos grupos ($p = 0,417$). El SLG fue menor en los pacientes con DM (-15,20% vs. -16,21% en pacientes sin DM; $p < 0,001$). En análisis de regresión logística la DM fue predictor independiente de disfunción diastólica significativa, y predictor independiente del SLG. Solo un paciente en el grupo de pacientes diabéticos presentó FEVI $< 50\%$

Conclusión: En esta población de pacientes añosos sin cardiopatía isquémica, la DM se asoció de manera independiente con una mayor prevalencia de disfunción diastólica, tanto en reposo como durante el esfuerzo, y con una reducción del SLG en presencia de FEVI preservada. Estos hallazgos son consistentes con el concepto de miocardiopatía diabética subclínica de predominio diastólico.

Palabras clave: Diabetes mellitus - Insuficiencia cardíaca - Disfunción ventricular - Disfunción diastólica

INTRODUCTION

The incidence and prevalence of diabetes mellitus (DM) is steadily increasing due to population aging, obesity, and physical inactivity (1) and is associated with the development of macro and microvascular coronary artery disease. (2) It has also been reported that type 2 DM may be associated with cardiomyopathy, particularly with heart failure regardless the presence of associated coronary artery disease, especially in women. (3,4) Heart failure is also related to a poorer prognosis in diabetic patients. (5) In this context, diastolic dysfunction often represents the first manifestation of structural and functional myocardial compromise and is considered more common than systolic dysfunction in diabetic patients without overt ischemic heart disease. (6,7) This pattern has led to the concept of diabetic cardiomyopathy, characterized in early stages by preserved left ventricular ejection fraction (LVEF) and early alterations in ventricular relaxation and distensibility. (8) In recent years, global longitudinal strain (GLS) assessed by echocardiography has emerged as a sensitive marker of subclinical systolic dysfunction, reflecting the involvement of longitudinal myocardial fibers. Several studies have shown that GLS may be reduced in diabetic patients even in the presence of preserved LVEF, suggesting early myocardial damage undetectable by conventional methods. (7,8)

OBJECTIVES

The objective of the present study was to assess differences in echocardiographic systolic and diastolic function and GLS parameters in elderly diabetic versus non-diabetic patients without evidence of ischemic heart disease. A secondary objective was to evaluate the prevalence of significant diastolic dysfunction and associated variables.

METHODS

An observational cohort study was conducted, including consecutive patients referred to the echocardiography service for resting and exercise stress echocardiography. Patients

with a history of known coronary artery disease, peripheral vascular disease, stroke, and those unable to exercise were excluded from the study, as were patients with significant (moderate or severe) valvular heart disease. Additionally, patients with a positive test for myocardial ischemia were excluded. The population was divided into two groups based on the clinical history of DM: patients with treated diabetes (DM) and patients without diabetes (No DM). A Vinno E 35 ultrasound system with a 2.4 MHz phased-array transducer was used to perform the study.

The following measurements were acquired at baseline and immediately post-exercise: in the mitral flow graph obtained with pulsed-wave Doppler at the tips of the mitral valves: peak E velocity (E velocity) at rest and immediately post-exercise; in the tissue Doppler recording at the level of the basal septum: e' velocity at rest and immediately post-exercise (e' velocity); E/e' ratio at rest and post-exercise (Figures 1–3); LVEF by the Simpson method in apical 4, and 2-chamber views, averaging both values at rest and immediately post-exercise; GLS (assessed by speckle tracking), averaging the apical 4-, 3-, and 2-chamber views at rest. Exercise testing was performed on a treadmill using the Bruce protocol. Measurements were acquired 1–2 minutes post-exercise when the A and E waves were no longer fused. Significant diastolic dysfunction was defined as moderate (grade 2) or severe (grade 3) diastolic dysfunction according to the definition of the American Society of Echocardiography (9) (Figures 1–3) or an E/e' ratio greater than 14.

Statistical analysis

For descriptive statistics, quantitative data are presented as mean \pm standard deviation (SD), and categorical data as frequency and percentage. Means in both groups were compared using Student's t-test, and proportions were compared using the chi-square test. A p-value < 0.05 was considered statistically significant. Univariate associations are expressed as odds ratios (OR) with their respective 95% confidence intervals (95% CI). A multiple logistic regression analysis was performed in which significant diastolic dysfunction (moderate or severe) was the dependent variable, and the following predefined variables were included in the model: advanced age (over 73 years), male sex, diabetes, hypertension, dyslipidemia, and smoking. A multiple regression analysis was also performed in which GLS was the dependent variable and diabetes, hypertension, male sex, age, dyslipidemia, and smoking were the independent variables.

Fig. 1. A. Mild diastolic dysfunction (grade 1). Pulse Doppler mitral filling. The mitral Flow pattern shows peak “E” velocity of 44.86 cm/s and peak “A” velocity of 58.74 cm/s. The corresponding E/A ratio is 0.76. This is the most frequent filling pattern in our study and is very prevalent in subjects over 60 years of age and in initial stage of heart diseases. **B.** Mild diastolic dysfunction (grade 1). Mitral annulus tissue Doppler. This image is related to Figure 1 and shows “e’” velocity of 5.52 cm/s , corresponding to an E/e’ ratio of 8.12. These values are associated with low pulmonary capillary pressure and absence of cardiac dyspnea.

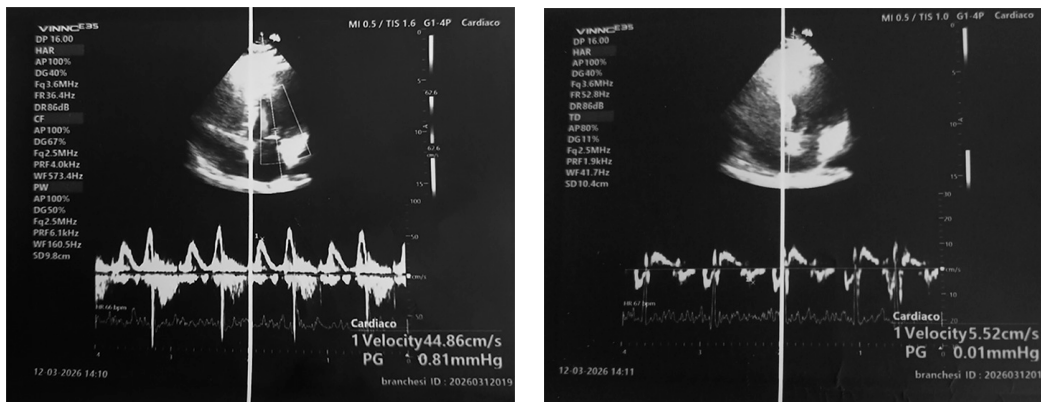


Fig. 2. A. Moderate cardiac dysfunction (grade 2). Pulsed Doppler mitral filling. The image shows peak E velocity of 78.21 cm/s and peak A velocity of 71.01 cm/s, with an E/A ratio of 1.10. This pattern is also called pseudonormal. **B.** Moderate diastolic dysfunction (grade 2). Mitral annulus tissue Doppler. This image is related to Figure 2. The E/e’ ratio is 11.90. These patients usually have a slightly raised capillary pressure and occasional symptoms of stress dyspnea.

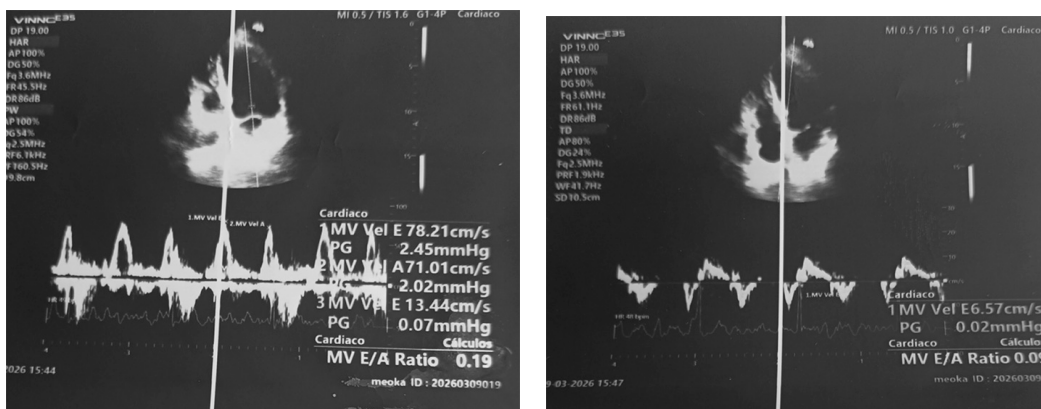
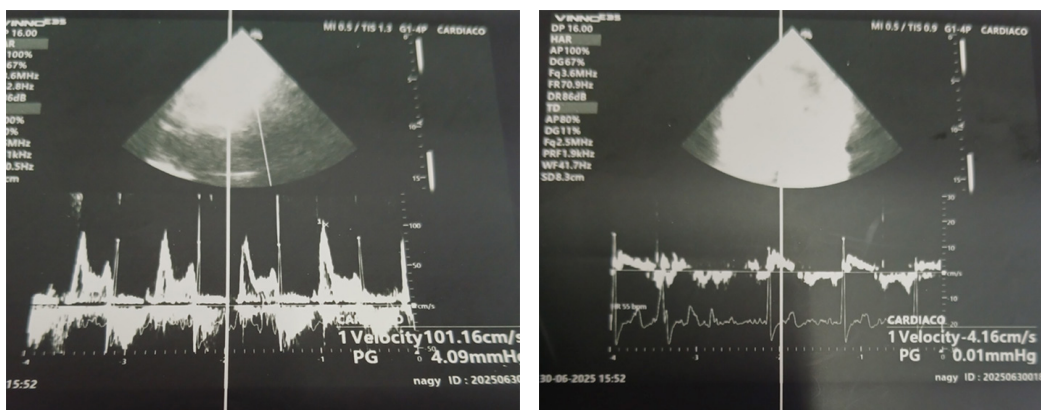


Fig. 3. A. Severe diastolic dysfunction (grade 3). Altered ventricular compliance. The mitral flow pattern shows peak “E” velocity of 101 cm/s and peak A velocity of 33 cm/s, with an E/A ratio of 3.06. This pattern is observed in advanced or decompensated heart diseases. **B.** Severe diastolic dysfunction (grade 3). Mitral annulus tissue Doppler. e’ velocity is 4.16 cm/s and the E/e’ ratio is 24 , indicating high pulmonary capillary pressure. This pattern is observed in frequently symptomatic patients.



RESULTS

A total of 1384 patients were evaluated in the stress echocardiography unit between March 2023 and December 2025; of these, 437 were excluded from the analysis due to coronary artery disease. A total of 947 patients with a mean age of 73 ± 6 years were included, 176 of which had diabetes (18.5%). The demographic characteristics and risk factors of patients with and without DM are presented in Table 1.

The group with DM consisted of a higher number of male patients and a greater incidence of hypertension, dyslipidemia, and smokers. The prevalence of moderate or severe diastolic dysfunction was significantly higher in the diabetic group, both at rest and immediately post-exercise. In addition, patients with DM had a significantly higher E/e' ratio both at rest and post-exercise due to a lower e'. There were no significant differences in LVEF at rest or immediately after exercise, and the GLS at rest was significantly lower in diabetic patients. (Table 2).

In a logistic regression model (in which diastolic dysfunction was the dependent variable and the independent variables were advanced age, male sex, diabetes, hypertension, dyslipidemia, and smoking), advanced age, diabetes, and male sex independently predicted moderate or severe diastolic dysfunction at rest. Advanced age, diabetes, and male sex also independently predicted moderate or severe diastolic dysfunction during exercise. (Tables 3 and 4)

Global longitudinal strain was significantly reduced in diabetic patients (Table 2), and in a multiple regression analysis, diabetes ($p=0.031$), hypertension ($p<0.001$), and male sex ($p=0.013$) were independent predictors of GLS, whereas age, dyslipidemia, and smoking were not.

DISCUSSION

Our case series includes a group of elderly patients with type 2 DM and without coronary artery disease. Although there were no inclusion or exclusion criteria

Table 1. Population characteristics

Variables	DM (n=176, 18.5%)	Non-DM (n=771, 81.5%)	p
Age, years, mean \pm SD	72 ± 7	73 ± 6 years	0.270
Male sex, n (%)	73 (41,5)	208 (27,0)	<0.001
Hypertension, n (%)	147 (83,5)	521 (67,6)	<0.001
DLP, n (%)	83 (47,2)	301 (39,0)	0.047
TS or ex-TS, n (%)	87 (49,4)	245 (31,8)	0.001

DLP: dyslipidemia; DM: diabetes; TS: tobacco smoker.

Table 2. Echocardiographic parameters of systolic function, diastolic function, and strain in diabetic and non-diabetic patients

Parameters	DM (n=176, 18.5%)	Non-DM (n=771, 81.5%)	p
Resting LVEF, %	59 ± 8	60 ± 7	0.255
Exercise LVEF, %	68 ± 9	69 ± 7	0.240
Resting peak E velocity, m/s	0.69 ± 0.20	0.67 ± 0.20	0.318
Resting peak e' velocity, m/s	0.061 ± 0.011	0.065 ± 0.012	<0.001
Resting E/e' ratio	12.4 ± 1.1	10.9 ± 5.5	<0.001
Exercise peak stress E velocity, m/s	0.88 ± 0.2	0.85 ± 0.2	0.018
Exercise peak stress e' velocity, m/s	0.071 ± 0.03	0.074 ± 0.02	0.640
Exercise E/e' ratio	13.9 ± 8	12.1 ± 5	< 0.001
Global longitudinal strain, %	-15.20	-16.21	< 0.001
Resting diastolic dysfunction, n (%)	22 (12.5)	55 (7.1)	< 0.001
Exercise-induced diastolic dysfunction, n (%)	62 (35)	177 (23)	< 0.001

LVEF: Left ventricular ejection fraction; DM: Diabetes mellitus

Table 3. Prediction of resting diastolic dysfunction. Univariate and multivariate analysis.

Independent variables	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Male	2.28 (1.6–3.2)	0.001	2.24 (1.54–3.26)	<0.001
Advanced age	1.48 (1.04–2.10)	0.025	1.44 (1.00–2.05)	0.045
Diabetes	1.90 (1.27–2.85)	<0.001	1.70 (1.11–2.59)	0.013
Hypertension	1.56 (1.04–2.33)	0.029	1.33 (0.87–2.01)	0.177
Dyslipidemia	1.05 (0.73–1.49)	0.658	1.11 (0.77–1.60)	0.562
Smoking	0.94 (0.65–1.36)	0.524	0.76 (0.52–1.13)	0.188

Table 4. Prediction of moderate-to-severe exercise-induced diastolic dysfunction. Univariate and multivariate analysis.

Independent variables	Univariate OR (95% CI)	p	Multivariate OR (95% CI)	p
Male	3.5 (1.75–7)	< 0.001	3.03 (1.45–6.32)	0.003
Advanced age	2.45 (1.18–5.07)	0.015	2.42 (1.15–5.10)	0.019
Diabetes	3.93 (1.97–7.84)	< 0.001	3.31 (1.60–6.85)	0.001
Hypertension	1.78 (0.77–4.14)	0.280	1.27 (0.53–3.04)	0.590
Dyslipidemia	1.16 (0.58–2.31)	0.781	1.23 (0.60–2.52)	0.555
Smoking	1.25 (0.62–2.50)	0.765	0.86 (0.41–1.82)	0.700

in the study that specifically addressed age, it is justified to consider the population as elderly given their mean age of 73 years and the fact that 95% of patients were over 60 years of age.

We found that these patients did not have significant abnormalities in left ventricular systolic function as assessed by LVEF at rest and during exercise, although in some studies the LVEF of diabetic patients is found to be slightly reduced. (10) On the other hand, several parameters of diastolic function were consistently significantly altered in this group of diabetic patients, and there was also a significant reduction in GLS, indicating an abnormal myocardial fiber function. (11)

The pathophysiological mechanisms implicated in diabetic cardiomyopathy (3–12) include impaired cardiac insulin signaling, mitochondrial dysfunction, increased oxidative stress, reduced nitric oxide availability, elevated advanced glycation end products, impaired myocardial calcium handling, inflammation, activation of the renin-angiotensin-aldosterone system, cardiac autonomic neuropathy, and microvascular dysfunction. (13,14)

Although there was a difference in the prevalence of other risk factors in the group of diabetic patients (more hypertension, dyslipidemia, and smoking), the multivariate analysis showed that DM is independently associated with diastolic function, as are advanced age and male sex, but not the other factors mentioned. Diabetes mellitus was also independently associated with GLS.

Moderate or severe diastolic dysfunction at rest

was found in 12.5% of diabetic patients, and moderate to severe diastolic dysfunction during exercise in 35%. It is known that exercise can reveal greater degrees of diastolic dysfunction, that is, a lower functional reserve of diastolic function.

Based on these findings, we conclude that our observations support the existence of cardiomyopathy with diastolic dysfunction in a small but statistically significant group of diabetic patients studied, and that diabetes is a determinant of this condition. This finding is consistent with several previously published series. (15)

In our study, this cardiomyopathy is characterized by preserved LVEF at rest and during exercise, and a mild but significant decrease in GLS, in addition to altered diastolic parameters on Doppler, consistent with several published series. (16)

In contrast, only one diabetic patient in our series presented with a low LVEF (systolic dysfunction), demonstrating a very low prevalence of diabetic-related systolic dysfunction in our series (it should be noted that patients with ischemic heart disease were excluded). The term “diabetic cardiomyopathy” was initially introduced based on postmortem findings in four diabetic adults with heart failure in the absence of coronary artery disease. (17) This condition —diabetic dilated cardiomyopathy in the absence of coronary artery disease— is described in case series, but its existence is more controversial. (18)

In summary, based on previous publications and the results of our study, we can conclude that diabetic cardiomyopathy with isolated diastolic dysfunction is

relatively common in asymptomatic elderly diabetics, but that the prevalence of diabetic dilated cardiomyopathy, whose existence is controversial, is very low, if it exists at all. This diastolic dysfunction in diabetic patients, beyond the presence of coronary artery disease, is associated with a higher incidence of heart failure in this population. Although the risk of heart failure is thought to be higher in diabetic women, in our study, male sex was associated with the presence of significant diastolic dysfunction. The significance of this finding is unclear, but it could be explained by the fact that diastolic dysfunction is not synonymous with diastolic heart failure.

Limitations

Our case series was limited to elderly patients with type 2 diabetes. Moreover, cardiomyopathy as a complication of type 1 diabetes is a condition of very low prevalence. (19)

The cross-sectional nature of our study does not allow us to draw conclusions regarding the development of heart failure during the course of this diastolic dysfunction, which is evident at rest and during exercise in a subgroup of diabetic patients. It has been described that more than one factor is involved in the development of heart failure in diabetics, some of which are extra myocardial, such as the phenomenon of hyperfiltration and increased blood volume in these patients. (20) Prospective follow-up of these patients would be necessary to clarify the prognostic significance of diastolic dysfunction in elderly diabetic patients.

Conflicts of interest

None declared.

(See authors' conflict of interests forms on the web).

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