No evidence for left ventricular diastolic dysfunction in asymptomatic normotensive type 2 diabetic patients: a case-control study with new echocardiographic techniques

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Abstract

Objective. – We sought to determine whether abnormalities of left ventricular structure and function could be detected in asymptomatic type 2 diabetic patients free of cardiovascular complications.

Research design and methods. – We compared 48 subjects with type 2 diabetes (34 men, 50 ± 6 years) without hypertension, coronary artery disease and microangiopathic complications with 30 age-matched healthy controls. Left ventricular diastolic function was assessed by conventional Doppler echocardiography and new echocardiographic techniques (tissue Doppler imaging, color M-mode propagation velocity). A pseudonormal (PN) pattern of left ventricular filling was screened by several methods including Valsalva maneuver.

Results. – Systolic function was normal in all patients. There was no significant difference in conventional and new echocardiographic Doppler indices of diastolic function between patients and control subjects. A PN diastolic function frequently suggested by the Valsalva maneuver (20 patients) was excluded using the new parameters.

Conclusions. – Diastolic dysfunction is not as frequent as previously described in selected patients with type 2 diabetes free of microangiopathic complications. New Doppler echocardiographic methods provide, in contrast with the Valsalva maneuver, a reliable estimate of diastolic function and should be incorporated in the non-invasive screening for diabetic cardiomyopathy.

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Résumé

Préervation de la fonction diastolique ventriculaire gauche chez le diabétique de type 2, asymptomatique, normotendu : étude cas témoins intégrant de nouvelles techniques d’échocardiographie.

But de l’étude. – Évaluer la fonction ventriculaire gauche des diabétiques de type 2, asymptomatiques, sans antécédent cardiovasculaire.

Patients et méthode. – Chez 48 diabétiques de type 2 (34 hommes, âge moyen 50 ± 6 ans) normotendus, non coronariens, sans microangiopathie et 30 témoins non diabétiques appariés pour l’âge, nous avons évalué la fonction systolique et diastolique ventriculaire gauche par échocardiographie transthoracique. L’étude de la fonction diastolique a fait appel à des méthodes classiques (doppler, manœuvres de Valsalva) et récentes (doppler tissulaire, vitesse de propagation du flux de remplissage ventriculaire gauche ou \( V_p \)).

Résultats. – La fonction systolique ventriculaire gauche était dans les limites de la normale dans les deux groupes. Les indices de fonction diastolique ventriculaire gauche étaient comparables entre les deux groupes. Un profil pseudonormal de remplissage ventriculaire gauche (doppler, manœuvre de Valsalva), marqueur de dysfonction diastolique a été observé chez 20 diabétiques et volontaires sains. L’analyse par doppler tissulaire et par \( V_p \) ne permet pas finalement de retenir ce diagnostic.

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Conclusion. – Dans notre travail, l’utilisation des nouvelles méthodes d’échocardiographie de type doppler tissulaire et \( V_p \) infirme les résultats d’études antérieures qui étaient en faveur d’une fréquence élevée de dysfonction diastolique chez les diabétiques de type 2 asymptomatiques, normotendus, non compliqués de micro- et de macroangiopathie. Chez ce type de diabétique notamment, ces techniques non invasives devraient être utilisées systématiquement en appoint des méthodes classiques d’échocardiographie pour une évaluation plus précise de la fonction diastolique ventriculaire gauche.

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Keywords: Type 2 diabetes; Diastolic function; Echocardiography; Tissue Doppler imaging

Mots clés : Diabète de type 2 ; Fonction diastolique ventriculaire gauche ; Échocardiographie ; Doppler tissulaire ; Vitesse de remplissage ; Manœuvre de Valsalva

1. Introduction

There is now growing evidence for an increased incidence of heart failure in diabetic patients [1]. Left ventricular diastolic dysfunction has been described as an early preclinical manifestation of a specific cardiomyopathy in diabetic patients without hypertension and known coronary artery disease [2]. The prevalence of left ventricular dysfunction in asymptomatic diabetic patients reported in previous studies have yielded variable results [3,4]. Moreover, some studies even failed to demonstrate either systolic or diastolic dysfunction [5,6]. Nevertheless, a very high prevalence of left ventricular dysfunction in selected type 2 diabetic patients has been recently suggested [7, 8]. Impairment of left ventricular diastolic function in diabetic patients has been mainly described using conventional mitral valve inflow pattern from pulsed Doppler [9–11]. However, this method is known to be influenced by numerous parameters (age, heart rate, preload and afterload conditions) independently of diabetes itself. Tissue Doppler imaging (TDI) and color M-mode propagation velocity (\( V_p \)) have been validated as new non invasive methods for the evaluation of left ventricular relaxation essentially as they are independent from preload [12–20]. Therefore, the present study was conducted to assess left ventricular structure and function in a well-characterized population of asymptomatic, normotensive type 2 diabetic patients using conventional echocardiography and novel echocardiographic techniques.

2. Research design and methods

2.1. Study group

Forty-eight patients (34 men, 14 women), aged 38–60 years with type 2 diabetes mellitus from the outpatient diabetes unit of Lariboisière Teaching Hospital were prospectively studied. Exclusion criteria were diabetic microvascular complications (retinopathy, neuropathy, nephropathy), history of cardiac disease or coronary artery disease and abnormal 12-lead ECG. Silent ischemia was excluded using treadmill exercise testing or thallium scintigraphy or both. Patients with systemic hypertension (systolic blood pressure \( \geq \) 140 and/or diastolic blood pressure \( \geq \) 90 mmHg) or under antihypertensive therapy were also excluded. In case of suspected borderline hypertension, a 24-h ambulatory blood pressure monitoring was performed to rule out this condition.

2.2. Control group

Thirty age and sex-matched (20 men, 10 women), healthy controls from the hospital staff, were prospectively studied during the same period. None had a history of cardiac disease. Physical examination and 12-lead ECG were in the normal range.

All subjects gave written informed consent to participation.

2.3. Biology

Fasting plasma glucose was measured by the glucose oxidase method. The HbA1c levels were measured by high-performance liquid chromatography (normal range: 4.3–6.2%). Plasma B-type natriuretic peptide (BNP) dosage was performed as a screen for LV dysfunction [21,22]. An immunoradiometric assay kit (Shionogi, Osaka, Japan) was used as previously described in [23]. The detection limit of the assay was 2.0 pg/ml.

2.4. Echocardiography

Echocardiograms were performed with Sonos 5500 instruments (Hewlett-Packard, Andover, MA) equipped with a 2.5 MHz transducer and TDI. A single investigator (SC) performed all echo-Doppler recordings. Left ventricular internal dimension, thickness of interventricular septal and posterior wall were measured at end-diastole and end-systole according to the American Society of Echocardiography recommendations [24]. Left ventricular mass was determined according to the formula introduced by Devereux et al. [25]. To take into account the known relation between left ventricular mass and body size, left ventricular mass was indexed for body surface area [26]. Left ventricular hypertrophy was defined as left ventricular mass index > 116 g/m² in men and > 104 g/m² in women [27]. Relative wall thickness was calculated as the ratio 2 × posterior wall thickness in diastole/left ventricular internal diameter. A partition value of 0.44 for relative wall thickness was used for both men and women. Ejection fraction was calculated according to Simpson’s rule biplane method [28] with the use of second harmonic imaging. Left atrium diameter was measured from long axis parasternal view and area from apical four-chamber view at the end of systole. Averaged values of five cardiac cycles were used for analysis.
2.5. Conventional Doppler indices

All Doppler signals were recorded with a chart recorder set at 100 mm/s. Mean values of at least five cardiac cycles were used for each parameter. Mitral flow velocities were recorded from the apical four-chamber view using pulsed Doppler. A 1.7-mm sample volume was placed between the tips of mitral leaflets during diastole. Peak early (E) and late (A) mitral inflow velocities, E/A ratio, mitral A wave duration, and deceleration time (DT) of E velocity were measured at end-expiration.Isovolumic relaxation time (IVRT) was measured as the interval from the end of the aortic flow to the onset of mitral inflow with use of the pulsed Doppler recordings. In order to detect a pseudonormal (PN) filling pattern in patients with a baseline E/A ratio > 1, mitral flow velocities (E-wave, A-wave, E/A ratio, E-wave DT) were also measured during phase II of the Valsalva maneuver. Patients were instructed to strain again to a closed glottis and measurements were obtained when the decrease in E velocity was maximum. Care was taken to keep the sample volume placed between the tips of the mitral leaflets. Three separate attempts were performed and the mean of the two best recordings were used for analysis. Pulmonary venous flow velocities were obtained by placing the sample volume 1–2 cm into the upper right pulmonary vein guided by color Doppler imaging. Peak velocity of systolic (S), diastolic (D) and atrial reversal (Ap) waves and Ap wave duration were recorded. The difference between the mitral and pulmonary A wave duration (A – Ap) was calculated.

2.6. New Doppler indices

2.6.1. TDI

Pulsed wave TDI of the mitral annulus was obtained from the apical four-chamber view. A 1.7 mm sample volume was placed at the lateral side of the mitral annulus. Early (Ea) and late (Aa) peak diastolic velocities and the Ea/Aa ratio were obtained. The combined indice E/Ea was calculated as proposed by Nagueh et al. [12]. Patients with a baseline E/A ratio > 1 were considered to have a PN filling if peak early diastolic velocity of the lateral annulus was < 8 cm/s and E/Ea ratio > 10 [12,16].

2.6.2. Color M-mode Doppler flow propagation velocity

Color M-mode Doppler echocardiography was performed in the apical four-chamber view by positioning the M-mode cursor aligned parallel with LV inflow. Flow propagation velocity (Vp) was measured as the slope of the first aliasing velocity from the mitral annulus in early diastole to 4 cm distally into the LV cavity (19). E/Vp was calculated as proposed by Garcia et al. [19]. Patients with a baseline E/A ratio > 1 were considered to have a PN filling if Vp was < 45 cm/s and E/Vp ratio ≥ 1.5 [16].

2.7. Statistical analysis

Continuous data are presented as mean ± S.D. The unpaired t-test (two-tailed) was used to assess differences between continuous variables. The chi-square test was used to compare categorical variables between groups. A value of P < 0.05 was considered significant.

3. Results

3.1. Clinical characteristics

The clinical characteristics and laboratory results in diabetic patients and control subjects are summarized in Table 1. No significant difference was observed between groups regarding age, sex, heart rate, blood pressure and body mass index. Fasting glucose and HbA1c were significantly higher in diabetic subjects. Fasting glucose was less than 6 mmol/l and HbA1c level was in the normal range in every control subject. BNP levels were in the normal range (< 18 pg/ml) and not significantly different between diabetic patients and controls.

3.2. Left ventricular structure and systolic function

The M-mode and bidimensional measurements are reported in Table 2. All dimensions were within normal limits. Septal wall thickness, posterior wall thickness, LV mass did not differ between the diabetic patients and control subjects. No LV hypertrophy or LV remodeling were detected in any diabetic

### Table 1

<table>
<thead>
<tr>
<th>Clinical characteristics</th>
<th>Controls (n = 30)</th>
<th>Diabetics (n = 48)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>50 ± 5</td>
<td>50 ± 6</td>
<td>NS</td>
</tr>
<tr>
<td>Male (%)</td>
<td>23 (77%)</td>
<td>34 (71%)</td>
<td>NS</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>24.8 ± 3.2</td>
<td>26.0 ± 3.7</td>
<td>NS</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>66 ± 10</td>
<td>70 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP (mmHg)</td>
<td>125 ± 11</td>
<td>123 ± 13</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP (mmHg)</td>
<td>76 ± 9</td>
<td>72 ± 8</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>7.7 ± 4.5</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fasting glucose (mmol/l)</td>
<td>5.3 ± 0.4</td>
<td>9.1 ± 2.9</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>5.3 ± 0.5</td>
<td>8.5 ± 2.1</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

### Table 2

<table>
<thead>
<tr>
<th>Left ventricular structure and systolic function</th>
<th>Controls (n = 30)</th>
<th>Diabetics (n = 48)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Septal wall thickness (mm)</td>
<td>8.57 ± 1.38</td>
<td>8.85 ± 1.01</td>
<td>NS</td>
</tr>
<tr>
<td>Posterior wall thickness (mm)</td>
<td>8.08 ± 1.13</td>
<td>8.11 ± 1.13</td>
<td>NS</td>
</tr>
<tr>
<td>LV end-diastolic dimension (cm)</td>
<td>4.83 ± 0.39</td>
<td>4.84 ± 0.44</td>
<td>NS</td>
</tr>
<tr>
<td>LV end-systolic dimension (cm)</td>
<td>3.00 ± 0.36</td>
<td>3.05 ± 0.43</td>
<td>NS</td>
</tr>
<tr>
<td>LV mass (g)</td>
<td>135.9 ± 29.3</td>
<td>140.0 ± 29.7</td>
<td>NS</td>
</tr>
<tr>
<td>LV mass/body surface area (g/m²)</td>
<td>71.3 ± 12.2</td>
<td>75.1 ± 12.7</td>
<td>NS</td>
</tr>
<tr>
<td>Relative wall thickness</td>
<td>0.34 ± 0.06</td>
<td>0.34 ± 0.06</td>
<td>NS</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>37.9 ± 4.9</td>
<td>37.2 ± 4.9</td>
<td>NS</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>64.0 ± 5.1</td>
<td>63.9 ± 7.7</td>
<td>NS</td>
</tr>
<tr>
<td>Left atrium dimension (mm)</td>
<td>34.2 ± 4.5</td>
<td>35.0 ± 4.5</td>
<td>NS</td>
</tr>
<tr>
<td>Left atrium end-systolic area (cm²)</td>
<td>16.0 ± 2.4</td>
<td>16.1 ± 2.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation; BP = blood pressure.
patients and control subjects. No subject had regional wall motion abnormality or significant valvular disease. Indexes of systolic function (fractional shortening, ejection fraction) and left atrium dimensions were similar and in the normal range in both groups.

3.3. Left ventricular diastolic function

3.3.1. Conventional Doppler indices

Transmitral recordings were obtained in all subjects. The results of conventional Doppler indices for evaluation of diastolic left ventricular function are reported in Table 3. There was no difference in E wave velocity, E/A ratio, DT and IVRT between groups. Peak A wave velocity was significantly increased in diabetic patients. Forty-six patients (96%) had adequate recordings of pulmonary venous flow. There was no difference in S/D ratio, Ap velocity and duration, A – Ap duration between groups. No patient had (Ap – A) duration over 20 ms. Significant decreases in S and D waves velocities were observed in diabetic patients.

3.3.2. New Doppler indices

TDI velocities were obtained in all subjects. The results of new Doppler indices for evaluation of diastolic left ventricular function are reported in Table 4. There was no difference in myocardial tissue Doppler parameters. Color M-mode Doppler parameters were similar in both groups.

3.3.3. Detection of PN diastolic function

Twenty-nine diabetic patients (60%) and 21 control subjects (70%) had a resting E/A ratio between 1 and 2. All the diabetic patients were able to perform a Valsalva maneuver. As shown in Table 5, the Valsalva maneuver induced a significant increase in heart rate and DT and a significant decrease in other parameters in both groups. Inversion of E/A ratio during Valsalva maneuver was obtained in 71% of diabetic patients and in 95% of controls. However, all these patients and controls had other parameters suggesting a normal diastolic function (Ea > 8 cm/s and E/Ea < 10, Vp > 45 cm/s and E/Vp < 1.5, (Ap – A) duration > 20 ms).

4. Conclusions

The present study demonstrates the absence of significant difference in left ventricular structure and function between a selected population with type 2 diabetes free of detectable cardiovascular disease and healthy control subjects. This was achieved by a non-invasive echocardiographic evaluation including new echocardiographic techniques. This study also underscores the limitations of the inversion of E/A ratio during Valsalva maneuver, which used alone, would identify as abnormal subjects with a normal diastolic function.

4.1. Diastolic function in diabetic patients

Type 2 diabetes mellitus is associated in most cases with hypertension, obesity, high prevalence of coronary artery disease and microangiopathic complications which are known to early impair left ventricular diastolic function [29]. In this study, we therefore excluded these factors with potential influence on left ventricular function. Nevertheless, some studies have demonstrated an impairment in left ventricular diastolic function in diabetic patients independently of hypertension and coronary artery disease, suggesting that this abnormality could be an early manifestation of a specific diabetic cardiomyopathy. Most of the available data refer to type 1 diabetes mellitus [2,3,5,6]. Few studies have been performed regarding diastolic function in type 2 diabetes [4,7–11]. Most of these studies have been performed in small sample sized populations. Moreover, patients’ selection criteria were inhomogeneous regarding age, duration of diabetes and presence of microangiopathy. While some studies reported significant abnormalities of diastolic function [4], other demonstrated no differences from healthy control subjects [5,6]. By the way, evidence of an intrinsic diastolic dysfunction in diabetes mellitus remains questionable. A relation between left ventricular diastolic functional abnormalities in asymptomatic patients with type 2 diabetes and microvascular complications has been suggested but is still controversial. Di Bonito et al. [10] demonstrated an impairment of left ventricular diastolic function in 16 normotensive type 2 diabetic patients free of microangiopathy. Inversely, Takenaka et al. [9] reported a normal left ventricular dia-
Table 5
Transmitral Doppler parameters during Valsalva maneuver in subjects with a baseline E/A ratio > 1

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 21)</th>
<th>Diabetics (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Rest</td>
<td>Valsalva</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>63 ± 10</td>
<td>73 ± 10*</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>68.5 ± 8.4</td>
<td>37.6 ± 7.1*</td>
</tr>
<tr>
<td>A (cm/s)</td>
<td>55.1 ± 6.0</td>
<td>49.9 ± 6.7*</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.25 ± 0.14</td>
<td>0.76 ± 0.12*</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>178 ± 25</td>
<td>270 ± 62*</td>
</tr>
</tbody>
</table>

Data are mean ± standard deviation; *p < 0.01 versus resting value.

Diastolic function in a normotensive population of type 2 diabetic patients (n = 60) free of microangiopathy. One hypothesis to explain these discrepancies observed between those studies might be, apart from variations in clinical selection, related to technical limitations. Most of the studies dealing with the diastolic function in diabetic patients have been performed by using the transmitral flow as the unique diagnostic tool in the evaluation of diastolic function. However, the mitral inflow velocity profile, although widely used to evaluate left ventricular diastolic function, is known to be influenced by age, heart rate, loading conditions, and other potentially interrelated factors that may have confounding effects on the interpretation of Doppler flow signals [29]. To overcome these limitations, new non-invasive echocardiographic methods have been recently validated for the evaluation of left ventricular relaxation. We therefore included these new echocardiographic tools in our study to improve the reliability of our results.

TDI is a new ultrasound method that records regional systolic and diastolic velocities within the myocardium. A good correlation has been found between the initial diastolic peak velocity and the ventricular relaxation measurements obtained through invasive methods [12–14]. Previous studies have shown that the early diastolic velocity recorded at the mitral annulus is reduced in patients with a relaxation abnormality [13,15]. The mitral annulus motion appears less load dependent than conventional mitral flow variables [13] and is sensitive to changes not identified by conventional mitral Doppler indexes [30]. To date, only few studies have used this new Doppler method in the assessment of subclinical myocardial disease in diabetes mellitus [31–33]. Fang et al. [31] have recently reported that regional diastolic myocardial function (peak early diastolic velocity obtained at the septal annulus) is significantly reduced in a population of 93 diabetic patients (predominantly type 2) compared with controls. However, most of patients included in this study had hypertension and a high prevalence of diabetic complications. In our study, we did not include patients with these complications to determine the impact of diabetes itself on the left ventricular function. To our knowledge, the present study is the first to show that patients with type 2 diabetes, without hypertension and microangiopathic complications, evaluated with a new indice of left ventricular relaxation are similar to a control population.

Color M-mode \( V_p \) has been proposed as a reliable, preload independent, new index of global left ventricular relaxation [16–18]. In patients with a delayed relaxation, \( V_p \) is often reduced [16]. Still, scanty data are available on the application of this new echocardiographic parameter in studies specifically dealing with diabetic subjects. Andersen et al. [32] recently studied 32 normotensive patients (53 ± 7 years) with type 2 diabetes mellitus without clinical signs of ischemic heart disease and microangiopathic complications. They found a significantly decreased \( V_p \) compared with their control population (55 ± 17 vs. 67 ± 16 cm/s). Shishehbor et al. [34] reported in a small group (n = 25) of patients with type 1 diabetes with a long diabetes duration and microangiopathic complications a significant reduced \( V_p \) compared with non-diabetic controls. In our study, however, the application of this method provided no evidence for a left ventricular diastolic dysfunction in the diabetic group.

4.2. PN function

Based on Doppler transmitral flow, a grading system for diastolic dysfunction has been proposed. Indeed, it has been demonstrated that the transmitral flow shows a progression over time with diseases involving the myocardium. Three different abnormal patterns of mitral filling have been described (impaired relaxation, pseudonormalization and restriction) [35]. The pattern representing abnormalities of both relaxation and compliance has been termed pseudonormalization, because of an apparently normal mitral filling pattern (E/A ratio > 1). This results from an increase in left atrial pressure compensating for slow relaxation. The PN filling pattern, while indicating a moderate left ventricular diastolic dysfunction, cannot be recognized without additional measurements. This is a common example of a major limitation in Doppler echocardiographic assessment of left ventricular diastolic function derived from transmitral flow. Among several echocardiographic methods, E/A reversal during Valsalva maneuver has been proposed to be an indicator of a pseudonormal filling pattern [36]. In two recent studies, identification of a non previously reported PN filling pattern in 17–28% of asymptomatic, normotensive type 2 diabetic patients has been reported [7,8]. The Valsalva maneuver was used in these studies as a method of differentiating between normal and PN left ventricular function. High prevalence of diastolic dysfunction in type 2 diabetes with no clinically detectable heart disease has been suggested throughout the results of these studies. However, because no control population was evaluated in these studies, a confounding effect of aging could not be excluded. In addition, the limitations of the Valsalva maneuver were not discussed in the interpretation of the results. By performing a study including a control population, we are able to demonstrate that an inversion of the E/A ratio during Valsalva maneuver is not specific for an abnormal
left ventricular diastolic function. Indeed, this maneuver induced an inversion of the E/A ratio in the vast majority of our control subjects. This finding is consistent with a recent study where inversion of E/A ratio in response to Valsalva maneuver occurred in every subject [37]. It is also supported by studies, which have addressed the accuracy of the Valsalva maneuver in defining a PN left ventricular diastolic function [37–39]. Therefore, recent reliable methods, superior to the classical Valsalva maneuver, have been proposed to identify a PN diastolic function [16,38,40,41]. By using these parameters in our study, no difference could be detected between diabetic patients and controls, more specifically in subjects with a baseline E/A ratio > 1 who might have a masked abnormal function. The values observed in our study population point out the absence of any PN diastolic function. In the study of Poirier et al. [7], a decrease of at least 25% of E/A ratio during Valsalva maneuver was used to define a PN filling pattern. By applying these criteria to our population, the Valsalva maneuver would suggest a prevalence of 20 diabetic patients (42%) with a PN pattern while no other Doppler parameter would suggest this abnormality. Therefore, by using only the variation of mitral flow during Valsalva maneuver there is a great potential to overestimate the prevalence of diastolic dysfunction in a population of asymptomatic, type 2 diabetic patients. These data have implications for interpretation of the myocardial function with the Valsalva maneuver as we document that in clinically normal diabetic subjects an “abnormal” response will frequently be observed. Using conventional Doppler echocardiography at rest and during Valsalva maneuver, TDI and color M-mode echocardiography, Boyer et al. have recently pointed out a higher prevalence of LV diastolic dysfunction in 61 consecutive, asymptomatic, normotensive, type 2 diabetic patients without significant coronary artery disease. Diastolic dysfunction was found in 43 of 57 (75%) patients when all of the above techniques were used. TDI detected diastolic dysfunction more often (63%) than any other and was thought as an improvement in the echocardiographic detection of diastolic dysfunction in asymptomatic patients in type 2 diabetes [42]. Although their conclusion comes in contrast with our study, there is evidence that new echocardiographic techniques should be incorporated in the non-invasive assessment of diastolic function in diabetic patients.

4.3. Study limitations

Cardiac catheterization is the method of reference to evaluate diastolic function and left ventricular filling pressures. In particular, it allows identifying a PN function which combines elevated filling pressures and an abnormal relaxation. Because of ethical reasons, we did not perform invasive hemodynamic measurements in our asymptomatic study population without any cardiovascular complication. Thus, we used non-invasive new Doppler indices of left ventricular relaxation and combined indices of LV filling pressure, which have been validated by previous hemodynamic studies [12–14,18–20,40,41]. In addition, we used the BNP dosage, as a biochemical marker of high left ventricular diastolic pressures to strengthen the accuracy of the echocardiographic results. Indeed, this dosage can be reliably used to rule out significant diastolic abnormality in the setting of normal systolic function, in particular in diabetic patients [21,22]. Similar normal levels of BNP in our two populations further support the absence of advanced diastolic dysfunction in our study, especially a PN function. We excluded diabetic patients with complications frequently associated in this population.

In conclusion, our study is the first to demonstrate, using new Doppler techniques, the absence of diastolic dysfunction in normotensive, type 2 diabetic patients, free of microvascular complications. New Doppler echocardiographic methods provide, in contrast with the Valsalva maneuver, a reliable estimate of diastolic function and should be included in the non-invasive assessment of diastolic function in patients with diabetes mellitus.

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