

Research Article

## Echocardiographic Assessment of Left Ventricular Diastolic Dysfunction In Adult Patients with Diabetes Mellitus and Hypertension Above 30 Years

Syed Shah Hussain Miran, Muhammad Azeem, Faisal Shah, Syed Amir Gilani, Raham Bacha,  
Syed Muhammad Yousaf Farooq\*, Hafiz Syed Arsalan Gilani

<sup>1</sup>The University of Lahore, Lahore, Pakistan

\*Corresponding Author: Syed Muhammad Yousaf Farooq, Research In charge, The University of Lahore, Pakistan, E-mail:  
[Yousafgelani@gmail.com](mailto:Yousafgelani@gmail.com)

Received: 27 December 2019; Accepted: 21 January 2020; Published: 30 January 2020

**Citation:** Syed Shah Hussain Miran, Muhammad Azeem, Faisal Shah, Syed Amir Gilani, Raham Bacha, Syed Muhammad Yousaf Farooq, Hafiz Syed Arsalan Gilani. Echocardiographic Assessment of Left Ventricular Diastolic Dysfunction In Adult Patients with Diabetes Mellitus and Hypertension Above 30 Years. Journal of Radiology and Clinical Imaging 3 (2020): 022-030.

### Abstract

**Objective:** The target of the present investigation is to echocardiographic grade of left ventricular diastolic dysfunction in grown-up patients with diabetes mellitus and hypertension over 30 years.

**Methodology:** This was cross-sectional analytical study with sample size of 149, performed at Punjab Institute of Cardiology Lahore, for 03 months. The patients was underlying heart diseases such as: Myocardial Infarction, Angina Pectoris, Congenital Heart Diseases, Valvular Heart Diseases, Pericardial Disease – by history, chest X-ray (CXR) postero-anterior (PA) view, and echocardiography

(Echo) and patients with regional wall motion abnormalities are excluded by Echo and Age above 30. Machine was performed with convex transducer of Aplio & Ge.

**Result:** Total 149 patients were taken a crack at the investigation, in which out of 149 patients 53(35.6%) were female and 96(64.5%) were male. 37 patients were analyzed ordinary, 86 were analyzed as grade 1, 22 patients were analyzed as grade 2, and 4 were analyzed as grade 3. Out 149 patients 141 were hypertensive. 86 were finding LVDD, 26 patients were determination LVSD and 37 were conclusion ordinary. 82 patients were not diabetic and 67

were diabetic. The mean of the age of the patients was 54 years and Std. deviation was 10.64%.

**Conclusion:** In present study examination exhibits that hypertension and diabetes mellitus have an independent positive impact on left ventricular diastolic dysfunction. The occurrence of grade 3 left ventricular diastolic dysfunction and left ventricular systolic dysfunction increased with diabetes mellitus.

**Keywords:** Echocardiographic; Diastolic Dysfunction; Diabetes Mellitus; Hypertension

## **1. Introduction**

Diastolic dysfunction is one of the most widely recognized cardiovascular issue which prompts clinical crisis, the mass of left ventricle is thickened with insufficient filling of ventricles raising the weight inclination of blood in the aspiratory vessels which brings about the transudate liquid spillage into the lung alveoli causing pneumonic edema which lessens the degree of oxygen in blood creating brevity of breath and even passing if not identified and treated promptly [1]. Diastole is the period during which the myocardium does not have its capacity to deliver power and continues to an unstressed measurement and quality bringing about deficiency of these courses causing diastolic dysfunction and the progressions in diastolic capacity can be available without cardiovascular breakdown with or without systolic function [2].

The recurrence of diabetes mellitus is enormously expanding on the planet about 40% of patients with diabetes present with diastolic dysfunction and pervasiveness of diabetes in grown-ups overall was assessed to be 4% in 1995 and to ascend to 5.4% continuously 2025 and will be a 42% expansion in diabetic patients in the created nations and 70% expansion in the

creating nations constantly 2025 [3]. Diastolic dysfunction is related with low mortality which represents roughly 8% however high horribleness, in this manner the death rate hazard is expanded by two to four folds [4]. Aging, corpulence, diabetes mellitus, cardiovascular ischemia, hypertension, aortic stenosis, myocardial illnesses, endomyocardial clutters, pericardial emission and constrictive pericarditis are different normal reasons for left ventricular diastolic dysfunction [5]. The higher predominance of diastolic dysfunction and cardiovascular breakdown with saved discharge part (HFpEF) in type-2 diabetes patients appears to show the effect of diabetes in the improvement of these conditions and is related with changes in heart digestion, structure, work and the instruments adding to myocardial dysfunction in diabetes incorporate hyperglycemia, lipotoxicity, insulin obstruction and weight is a high hazard marker, an increment in weight, moreover associate with diabetes, hypertension, hyperlipidemia and impacts heart capacity and structure with developing age [6].

There is an expanded pervasiveness of hypertension among diabetic patients and is likewise connected with hindered diastolic filling yet there is additionally high inclination among hypertensive patients to create type-2 diabetes [7]. Possible components for diastolic dysfunction incorporate interstitial gathering of glycoprotein, slow sarcoplasmic calcium reuptake, inordinate myocardial fibrosis or modified arrival of middle people, for example, nitric oxide and endothelin from a useless coronary endothelium and practical irregularities happens prior contrasted and systolic dysfunction in coronary illness as a result of left ventricular unwinding process is more reliant on vitality than ventricular contraction [8]. It is hard to separate diastolic and systolic cardiovascular breakdown dependent on physical discoveries alone so sign and manifestations helps a ton in separating between them as, patients with diastolic

dysfunction generally present with Fatigue, Jugular Venous Distension (JVD), Exertional Dyspnea, Orthopnea, Tachycardia, third and fourth Heart Sounds and Nocturnal dyspnea [9]. The pathophysiology of diastolic dysfunction includes deferred unwinding, weakened left ventricular filling or expanded stiffness [10].

Echocardiography, Pulse Waves Doppler and Tissue Doppler Imaging (TDI), Magnetic Resonance Imaging (MRI), Cardiac catheterization and Cardiac scintigraphy are different imaging modalities for diagnosing left ventricle diastolic dysfunction [11]. Cardiac catheterization is the best quality level obtrusive indicative strategy for the grade of diastolic capacity comprises of estimating the mean pneumatic fine wedge weight and LV end-diastolic pressure [12]. Pulse Waves Doppler and Tissue Doppler Imaging (TDI) parameters in typical working heart are: E wave taller than A wave. E/A proportion ought to be more prominent than 1.0. DT=160 ms - 200 ms and E' more noteworthy than 8.0 ms [13]. Doppler echocardiography is a straightforward, non-obtrusive strategy that can be utilized for the appraisal of diastolic capacity giving dependable information on diastolic performance [14]. Trans-mitral speed design is made out of E wave (happening during the quick filling stage) and lower A wave (emerging from atrial compression) and the stream design quickly goes through the phases of ordinary unwinding ( $E > A$ ), postponed (hindered) unwinding ( $E < A$ ), and prohibitive ( $E \gg A$ ) filling patterns [15]. Left ventricular diastolic dysfunction may speak to the primary phase of diabetic cardiomyopathy, strengthening the significance of early grade and thus early treatment of diastolic capacity at asymptomatic stage in people with diabetes in this manner, ID of patients with diastolic cardiovascular breakdown is significant on the grounds that these patients nearly have a poor guess as patients with systolic cardiovascular breakdown and even asymptomatic

patients with diastolic dysfunction are under the expanded danger of antagonistic cardiovascular events [16]. The point of our investigation is to assess the recurrence of left ventricular diastolic dysfunction utilizing echocardiography which is a non-intrusive analytic imaging apparatus that furnishes a dependable information in patients with type-2 diabetes mellitus and hypertension.

## 2. Methodology

This was cross-sectional analytical study with sample size of 149, performed at Punjab Institute of Cardiology Lahore, for 03 months. The patients was underlying heart diseases such as: Myocardial Infarction, Angina Pectoris, Congenital Heart Diseases, Valvular Heart Diseases, Pericardial Disease – by history, chest X-ray (CXR) postero-anterior (PA) view, and echocardiography (Echo) and patients with regional wall motion abnormalities are excluded by Echo and Age above 30. Machine was performed with convex transducer of Aplio & Ge.

## 3. Result

Total 149 patients were enrolled in the study, 65 patients were diagnosed as grade 1 LVDD in which 34 (52.3%) were non diabetic and 31 (47.7%) were diabetic, while 19 patients were diagnosed as grade 2 LVDD in which 7 (36.8%) patients were non diabetic and 12 (63.2%) were diabetic and just 2 patients were diagnosed as grade 3 LVDD and both were diabetic. Whereas 21 patients were diagnosed as grade 1 LVSD in which 12 (57.1%) were non diabetic and 9 (42.9%) patients were diabetic while 3 patients were diagnosed as grade 2 LVSD 1 (33.3%) was non diabetic and 2 (66.7%) were diabetic and 2 (100%) patients were diagnosed as grade 3 LVSD. Whereas 37 patients were normal in while 28 (75.7%) patients were normal as well as not suffering from diabetes mellitus and 9 (24.3%) patients were suffering from diabetes mellitus (Table 1).

Diagnosis				DM		Total
				NO	YES	
LVDD	grade	1.00	Count	34	31	65
			% within grade	52.3%	47.7%	100.0%
	2.00	Count	7	12	19	
		% within grade	36.8%	63.2%	100.0%	
	3.00	Count	0	2	2	
		% within grade	0.0%	100.0%	100.0%	
	Total		Count	41	45	86
			% within grade	47.7%	52.3%	100.0%
LVSD	grade	1.00	Count	12	9	21
			% within grade	57.1%	42.9%	100.0%
	2.00	Count	1	2	3	
		% within grade	33.3%	66.7%	100.0%	
	3.00	Count	0	2	2	
		% within grade	0.0%	100.0%	100.0%	
	Total		Count	13	13	26
			% within grade	50.0%	50.0%	100.0%
N	grade	.00	Count	28	9	37
			% within grade	75.7%	24.3%	100.0%
Total	grade	.00	Count	28	9	37
			% within grade	75.7%	24.3%	100.0%
	1.00	Count	46	40	86	
		% within grade	53.5%	46.5%	100.0%	
	2.00	Count	8	14	22	
		% within grade	36.4%	63.6%	100.0%	
	3.00	Count	0	4	4	
		% within grade	0.0%	100.0%	100.0%	
	Total		Count	82	67	149
			% within grade	55.0%	45.0%	100.0%

Table 1 : Grade \* DM \* Diagnosis Crosstabulation.

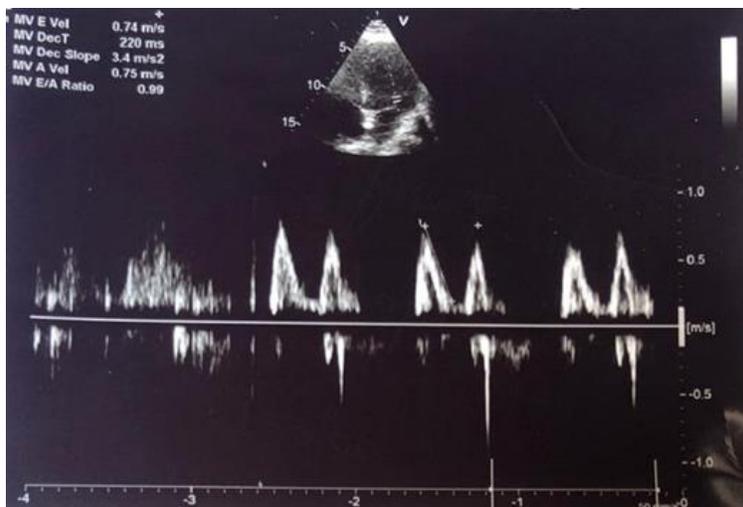


Figure 1: Grade 1 left diastolic dysfunction.

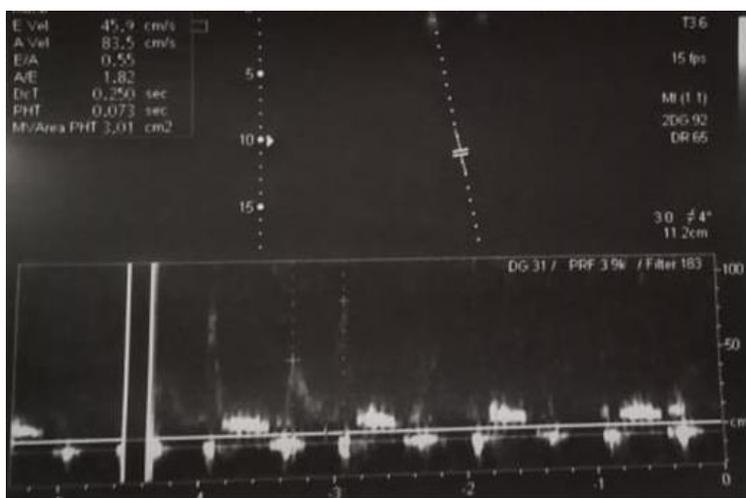


Figure 2: Grade 2 left diastolic dysfunction.

#### 4. Discussion

Left Ventricular Diastolic dysfunction is a hazard factor for the improvement of congestive cardiovascular breakdown. In our examination, we exhibited that in a network diabetes, and hypertension have an autonomous positive effect on LV diastolic capacity. We demonstrated that diabetes and hypertension were freely connected with a higher E/E' proportion, a record of LV end-diastolic weight. The finding of a higher LV end-diastolic weight when diabetes and hypertension exist together, contrasted and either condition alone, could clarify to some extent the extra

danger of creating cardiovascular breakdown in patients with joined diabetes and hypertension contrasted and patients with hypertension alone [17,18]. In this regard, the avoidance, from our examination, of subjects with proof of coronary supply route ailment or with strange LV systolic capacity enabled us to determine significant data on the impact of the two most common cardiovascular hazard factors on diastolic capacity at beginning periods of malady (Stages An and B of the American Heart Association arrangement of cardiovascular breakdown improvement). To all the more likely separate the impact of diabetes and hypertension, just as to survey their joined impact, we

assessed the diastolic capacity in bunches with just diabetes, just hypertension, or both, contrasted and subjects without either condition. The predominance of diastolic dysfunction was higher in HT, DM, and HT + DM than in HT-/DM-. At the point when we considered the extent of subjects with raised LV end-diastolic weight, we saw it as essentially more noteworthy in the HT + DM bunch than in HT and DM bunches. True to form, the HT + DM bunch was more seasoned and had higher BMI, while the HT and DM bunches were in a middle of the road position between HT + DM and HT-/DM-. Strikingly, LVM record was higher in the gatherings with hypertension, yet was not altogether unique between HT-/DM- and DM gatherings. This discovering is predictable with past investigations that detailed no expansion in LVM in diabetic contrasted and non-diabetic subjects when the impact of hypertension is removed [19, 20]. After modification for all the covariates, we found that the gathering with both hypertension and diabetes had altogether more awful diastolic capacity than the others. E' speed was lower in HT + DM than in HT-/DM-, yet not essentially unique in relation to HT and DM, while the E/E' proportion was fundamentally higher in HT + DM than in HT and DM, recommending an added substance impact of hypertension and diabetes on the LV end-diastolic weight free of different covariates. Nonetheless, despite the fact that the E/A proportion indicated a pattern toward lower esteems in patients with hypertension and additionally diabetes, no critical contrasts were found among the four gatherings. This perception may seem astounding, however it is steady with the pathophysiology of the LV diastolic elements. The E/A proportion is firmly reliant on heart load, and pursues a U-formed bend in the characteristic history of LV diastolic dysfunction, with a decrease in the previous phases of dysfunction. In this stage, the unwinding of the LV is postponed and the early diastolic stream (E-wave) turns out to be more slow; accordingly, as a compensatory

instrument, the atrial commitment to the LV filling increments, and the E/A proportion diminishes (diastolic dysfunction, Stage 1). With the movement of diastolic dysfunction, the expanding pressure angle between the left chamber and the LV goes about as an impelling power, causing an expansion in the E-wave speed. As a result, the E/A proportion increments too, getting vague from a typical stream pattern [21]. In such manner, the investigation of other Doppler stream determined parameters (mitral isovolumic unwinding time and E-wave deceleration time) that are load-subordinate isn't helpful for distinguishing the obvious inversion of the mitral inflow to a typical example (otherwise called 'pseudo-standardization' of the mitral inflow) as real movement of the sickness (diastolic dysfunction, Stage 2). The mitral annulus early diastolic speed evaluated by beat TDI (E') has been demonstrated to be less pre-load ward, and its reduction with the dynamic debilitation of the LV diastolic mechanics permits the distinguishing proof of LV unusual unwinding and diminished LV consistence, and can recognize diastolic dysfunction even within the sight of a pseudo-ordinary mitral flow [22].

In old populaces with high cardiovascular hazard profile, a few cofactors are frequently related to the two conditions. Specifically, heftiness is carefully connected to both hypertension and insulin-obstruction and diabetes. We had the option to show that the synergistic impact of hypertension and diabetes on LV diastolic capacity is available in both lean and overweight/corpulent patients. We additionally exhibited that a BMI  $\geq 25$  kg/m<sup>2</sup> was related with more terrible diastolic capacity, even in the HT-/DM- gathering. In this manner, our information affirm the beneficial outcome of expanded BMI on LV diastolic mechanics [23, 24], yet additionally show that the effect of hypertension and diabetes on LV diastole perceives illness explicit instruments that go past the basic

impact of corpulence. These discoveries recommend a few contemplations. To start with, it is realized that diabetes is related with changes in myocardial digestion and structure that add to diastolic variations from the norm. Various metabolic adjustments have been distinguished that add to diabetic cardiomyopathy. In diabetic hearts, glucose digestion is diminished for vitality creation from beta-oxidation of free unsaturated fats. The changed glucose digestion brings about a gathering of harmful intermediates that influence calcium taking care of, advance apoptosis, and influence myocardial mechanics [25, 26].

Shockingly, our finding of a diminished diastolic capacity when hypertension and diabetes coincided was not related with a parallel increment in LA size in the HT + DM gathering. Left atrial size is identified with LV diastolic capacity and is viewed as a pointer of a ceaseless presentation to raised LV filling pressures [27]. In any case, as the principle determinant of LA size is the body size, and given the raised mean BMI in the HT, DM, and HT + DM gatherings, a noteworthy cover in the appropriation of the LA size exists in those gatherings that may have averted the location of malady explicit impacts on LA breadth. Additionally, it is realized that LA antero-lateral breadth, albeit prognostically applicable in the populace, isn't a precise proportion of LA size, on the grounds that the extension of the LA in the antero-lateral hub is restricted by the anatomical imperatives of the spine and sternum. In this manner, atrial developments over the latero-horizontal and cranio-caudal tomahawks are not distinguished by the LA antero-lateral measurement. In such manner, the assessment of LA volumes may be progressively touchy in identifying littler contrasts in LA size than the antero-lateral measurement.

Past examinations have researched the relations of LV diastolic capacity with diabetes and hypertension. These

investigations, notwithstanding, utilized more established criteria for the meaning of diabetes [28, 29] or didn't utilize TDI for the evaluation of diastolic function [30], or didn't alter the correlations for significant covariates, for example, LVM [31, 32]. A report from the Strong Heart Study indicated that the mix of hypertension and diabetes was related with more noteworthy weakness of diastolic unwinding subsequent to changing for covariates, for example, age and LVM [33]. That review, in any case, utilized transmitral stream parameters no one but, which couldn't recognize a pseudo-ordinary example from genuinely typical LV diastolic capacity, bringing about an underestimation of the predominance of diastolic dysfunction. Truth be told, a pseudo-ordinary diastolic filling design has been seen in a noteworthy extent of asymptomatic hypertensive and diabetic subjects [34]. Another investigation demonstrated that in hypertensive patients the nearness of diabetes was related with more regrettable diastolic capacity, however the absence of a benchmark group without hypertension and the high pervasiveness of coronary supply route illness made the outcomes hard to translate.

## **5. Conclusion**

In present study demonstrates that hypertension and diabetes mellitus have an independent positive impact on left ventricular diastolic dysfunction. The occurrence of grade 3 left ventricular diastolic dysfunction and left ventricular systolic dysfunction increased with diabetes mellitus.

## **References**

1. Nasir M, Hyder SN, Hassan A. Frequency of Left Ventricle Diastolic Dysfunction in Asymptomatic Type II Diabetic Patients. *Pakistan Journal of Medical & Health Sciences* 10 (2016): 905-908.

2. Josephson ME. Josephson's Clinical Cardiac Electrophysiology. Lippincott Williams & Wilkins (2015).
3. Hameedullah., Faheem, M., Khan, S. B.& Hafizullah, M. Prevalence of asymptomatic left ventricular diastolic dysfunction in normotensive type 2 diabetic patients. *JPMI* 24 (2010): 188-192.
4. Biering-Sørensen T, Biering-Sørensen SR, Olsen FJ, et al. Global longitudinal strain by echocardiography predicts long-term risk of cardiovascular morbidity and mortality in a low-risk general population: the Copenhagen City Heart Study. *Circulation: Cardiovascular Imaging* 10 (2017): e005521.
5. Laflamme D. *Cardiology: A Practical Handbook*. CRC Press (2018).
6. Paulus WJ, Tschöpe C. A novel paradigm for heart failure with preserved ejection fraction: comorbidities drive myocardial dysfunction and remodeling through coronary microvascular endothelial inflammation. *Journal of the American College of Cardiology* 62 (2013): 263-271.
7. Dogar HN, Ghani MH, Javed M. Frequency of Pre-Mature Diastolic Dysfunction in Obesity. *Age (years)* 2 (2018): 1-4.
8. Maiello M, Zito A, Carbonara S, et al. Left ventricular mass, geometry and function in diabetic patients affected by coronary artery disease. *Journal of Diabetes and its Complications* 31 (2017): 1533-1537.
9. Araz M, Bayrac A, Ciftci H. The impact of diabetes on left ventricular diastolic function in patients with arterial hypertension. *Northern clinics of Istanbul* 2 (2015): 177.
10. Formenti P, Brioni M, Chiumello D. Left Diastolic Function in Critically Ill Mechanically Ventilated Patients. In *Annual Update in Intensive Care and Emergency Medicine* (2019): 139-153.
11. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the grade of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. *European Journal of Echocardiography* 17 (2016): 1321-1360.
12. Flachskampf FA, Biering-Sørensen T, Solomon SD, et al. Cardiac imaging to evaluate left ventricular diastolic function. *JACC: Cardiovascular Imaging* 8 (2015): 1071-1093.
13. Mascherbauer J, Zotter-Tufaro C, Duca F, et al. Wedge pressure rather than left ventricular end-diastolic pressure predicts outcome in heart failure with preserved ejection fraction. *JACC: Heart Failure* 5 (2017): 795-801.
14. Panesar DK, Burch M. Assessment of diastolic function in congenital heart disease. *Frontiers in cardiovascular medicine* 4 (2017): 5.
15. Dugo C, Rigolli M, Rossi A, et al. Assessment and impact of diastolic function by echocardiography in elderly patients. *Journal of geriatric cardiology: JGC* 13 (2016): 252.
16. Moorjani N, Rana BS, Wells FC. Echocardiography of the Mitral and Tricuspid Valves. In *Operative Mitral and Tricuspid Valve Surgery* (2018): 21-55.
17. Kannel WB, Hjortland M, Castelli WP. Role of diabetes in congestive heart failure: The Framingham study. *Am J Cardiol* 34 (1974): 29-34.
18. Gottdiener JS, Arnold AM, Aurigemma GP, et al. Predictors of congestive heart failure in the elderly: the Cardiovascular Health Study. *J Am Coll Cardiol* 35 (2000): 1628-1637.
19. Di Bonito P, Moio N, Cavuto L, et al. Early detection of diabetic cardiomyopathy: usefulness of tissue Doppler imaging. *Diabet Med* 22 (2005): 1720-1725.

20. Fang ZY, Yuda S, Anderson V, et al. Echocardiographic detection of early diabetic myocardial disease. *J Am Coll Cardiol* 41 (2003): 611-617.
21. Nishimura RA, Tajik AJ. Evaluation of Diastolic Filling of Left Ventricle in Health and Disease: Doppler Echocardiography Is the Clinician's Rosetta Stone. *J Am Coll Cardiol* 30 (1997): 8-18.
22. Nagueh SF, Middleton KJ, Kopelen HA, et al. Doppler tissue imaging: a noninvasive technique for evaluation of left ventricular relaxation and estimation of filling pressures. *J Am Coll Cardiol* 30 (1997): 1527-1533.
23. Peterson LR, Waggoner AD, Schechtman KB, et al. Alterations in left ventricular structure and function in young healthy obese women: assessment by echocardiography and tissue Doppler imaging. *J Am Coll Cardiol* 43 (2004): 1399-1404.
24. Wong CY, O'Moore-Sullivan T, Leano R, et al. Association of Subclinical Right Ventricular Dysfunction With Obesity. *Circulation* 110 (2004): 3081-3087.
25. Zhou YT, Grayburn P, Karim A, et al. Lipotoxic heart disease in obese rats: implications for human obesity. *Proc Natl Acad Sci USA*. 97 (2000): 1784-1789.
26. Young ME, Guthrie PH, Razeghi P, et al. Impaired Long-Chain Fatty Acid Oxidation and Contractile Dysfunction in the Obese Zucker Rat Heart. *Diabetes* 51 (2002): 2587-2595.
27. Tsang TS, Barnes ME, Gersh BJ, et al. Left atrial volume as a morphophysiologic expression of left ventricular diastolic dysfunction and relation to cardiovascular risk burden. *Am J Cardiol* 90 (2002): 1284-1289.
28. Liu JE, Palmieri V, Roman MJ, et al. The impact of diabetes on left ventricular filling pattern in normotensive and hypertensive adults: the Strong Heart Study. *J Am Coll Cardiol* 37 (2001): 1943-1949.
29. Mogelvang R, Sogaard P, Pedersen SA, et al. Cardiac dysfunction assessed by echocardiographic tissue Doppler imaging is an independent predictor of mortality in the general population. *Heart J* 30 (2009): 731-739.
30. Liu JE, Palmieri V, Roman MJ, et al. The impact of diabetes on left ventricular filling pattern in normotensive and hypertensive adults: the Strong Heart Study. *J Am Coll Cardiol* 37 (2001): 1943-1949.
31. Di Bonito P, Moio N, Cavuto L, et al. Early detection of diabetic cardiomyopathy: usefulness of tissue Doppler imaging. *Diabet Med* 22 (2005): 1720-1725.
32. Kosmala W, Kucharski W, Przewlocka-Kosmala M, et al. *Am J Cardiol* 94 (2004): 395-399.
33. Zabalgoitia M, Ismaeil MF, Anderson L, et al. Prevalence of diastolic dysfunction in normotensive, asymptomatic patients with well-controlled type 2 diabetes mellitus. *Am J Cardiol* 87 (2001): 320-323.
34. Wachter R, Lüers C, Kleta S, et al. Natriuretic peptides in the detection of preclinical diastolic or systolic dysfunction. *Eur J Heart Fail* 9 (2007): 469-476.



This article is an open access article distributed under the terms and conditions of the [Creative Commons Attribution \(CC-BY\) license 4.0](https://creativecommons.org/licenses/by/4.0/)