



Diastolic Dysfunction in Preoperative Normotensive Normoglycemic Patients Older than 50 years-A Hospital Based Prevalence Study

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JAMMR/2018/41081

Editor(s):

(1) Fatma Mohammad Nasr, Theodor Bilharz Research Institute, Warraq El-hadar, Imbaba, Giza, Egypt.

Reviewers:

(1) Shailendra Singh, West Virginia University, USA.

(2) Chiara Lazzeri, Azienda Ospedaliero-Universitaria Careggi, Italy.

(3) Franco Mantovan, University of Verona, Italy.

Complete Peer review History: <http://www.sciencedomain.org/review-history/24661>

Original Research Article

Received 5th March 2018

Accepted 11th May 2018

Published 17th May 2018

ABSTRACT

Introduction: Preoperative assessment of heart function has typically focused on evaluating left ventricular ejection fraction (LVEF) which measures the systolic function of the heart. Recent evidence suggests that diastolic dysfunction is reported in more than 50% of geriatric patients undergoing cardiac and non-cardiac surgery, which may cause substantial increase in morbidity and mortality in perioperative period.

Diastolic dysfunction (DD) is usually asymptomatic at rest, but as it progresses with age, it can become unmasked by exercise or when the cardiovascular system is stressed beyond its physiological reserve such as in those undergoing surgery. The aim of our research was to study the prevalence of diastolic dysfunction with the help classic and new doppler parameters in preoperative patients.

Methods: Two hundred and sixty patients older than 50 years attending preoperative assessment

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clinic were divided into three groups, group A 50-60 years, group B 60-70 years, group C 70-80 years underwent transthoracic echocardiography. Two-dimensional (2-D), pulse wave and tissue doppler imaging were performed according to a standardized protocol.

Results: In the group C, shorter deceleration time, higher velocity of mitral in flow atrial phase (A), and lower early mitral inflow velocity(E), and (E/A) ratio less than one were observed and it was statistically significant compared to group A and B. Left atrial volume index was more in Group C and there was no change in ejection fraction between groups. Mitral annular velocity (E/e^1) in group C (average 13.2 ± 1.1) was elevated compared to other two groups.

Conclusions: Isolated focus on normal LVEF may not be sufficient to describe the overall heart function in preop patients. DD has been associated with increased perioperative risk so early recognition, is mandatory and possible with modern echographic indices.

Keywords: Diastolic function; mitral inflow; tissue doppler echocardiography; heart failure with preserved ejection fraction.

1. INTRODUCTION

Diastolic dysfunction (DD) is an important cause of heart failure (HF) with preserved ejection fraction (HFpEF) and a major public health issue [1,2].

It is well known that LV function and structure are influenced by age in healthy subjects. Aging itself results in an increase in heart weight and myocyte size as well as in an increase in the collagen content of the heart. Aging has been shown to preserve systolic function, whereas an alteration of filling patterns with a reduced early and an increased late filling rate has been reported. Studies have documented an increased myocardial stiffness in the aging heart [2,3]. So we chose a age group of 50 to 80 for our study.

Diastole hemodynamically refers to the phase during the cardiac cycle in which the ventricles acquire the stroke volume for the next cardiac cycle [4,5]. Diastolic dysfunction which is the forerunner of diastolic heart failure refers to an abnormality of diastolic distensibility, filling, or relaxation of the left ventricle regardless of whether the ejection fraction is normal or abnormal and the patient is symptomatic or asymptomatic. Patients with diastolic dysfunction, perioperatively have the potential to develop a hypertensive crisis, pulmonary congestion, hemodynamic lability, poor tolerance of volume shifts, cardiac arrhythmia [6] In the early postoperative period, patients with known diastolic heart disease should be watched over closely. They can acutely decompensate secondary to hypoxemia or atrial fibrillation as a consequence of volume overload. Thus, in addition to conventional perioperative risk quantification, it is important to consider the

results of diastolic assessment for predicting the postoperative outcome and making better decisions. Left ventricle DD is still underestimated in preoperative risk assessment and few clinical data supporting its importance are available [7] Clinical assessment of left ventricular diastolic function is principally based on echocardiographic findings. Recently, echocardiographic assessment of diastolic function has incorporated new measurements such as propagation of mitral inflow or pulsed, tissue doppler, which are particularly valuable for noninvasive evaluation diastolic function [8]. The availability of newer diagnostic tools such as tissue doppler imaging has informed the need to assess all components of diastolic function.

2. METHODOLOGY

After approval of Institute ethics committee, two hundred and sixty patients older than 50 years attending preoperative assessment clinic were grouped into three groups A,B,C (Clinical Trial Registry India CTRI REF/2017/03/013577). They were screened with transthoracic echocardiography after informed, written consent. With a 2.5-MHz transducer, two-dimensional (2-D), pulse wave and tissue doppler imaging were performed by a registered echocardiography technician using Philip cardiac ultrasound unit according to a standardized protocol. Examinations were done in the left-lateral posture during quiet breathing.

All patients greater than 50 years were included in the study.

Specific exclusion criteria included hypertension, diabetes, overt heart failure, and coronary artery disease, obesity and congenital cardiac defects.

2.1 Primary Objectives

1. To quantify diastolic dysfunction using echographic indices
 - a. Mitral inflow patterns: E/A
 - b. Mitral annulus velocities on tissue Doppler : E/e'(septal,lateral and average) ratio

E - Peak velocity of mitral inflow early wave (cm/s)
A -peak velocity of mitral inflow atrial wave (cm/s);

2.2 Secondary Objectives

1. To measure Deceleration time
2. To assess the left atrial volume index and ejection fraction

Five cardiac beats were chosen, and their average value calculated. The left ventricle diastolic filling pattern of the mitral inflow was recorded from the apical transducer position, with the sample volume situated between the mitral leaflet tips during diastole. The peak velocity of early rapid filling (E wave) and the peak velocity of atrial filling (A. wave) was recorded, and the E-to-A ratio (E/A) calculated (Fig. 1).

The deceleration time (DT) the interval between the peak of the E wave and the point at which the descending segment of the E wave crosses the zero-velocity line was measured. As the size of the left atrium can reflect LV diastolic function, it was included as a measure of diastolic function.

Tissue Doppler imaging (TDI). at of the mitral annulus was done at both the septal and lateral annulus and corresponding peak velocities known as **e** prime (e') and **a** prime (a ') were measured. Higher E/e' there is increase chance of diastolic dysfunction.

TDI at of the mitral annulus reveals a waveform that is similar in shape to the PW trans-mitral (inflow) E and A waves but, in the opposite direction, and the corresponding peak velocities are known as e prime (e') and a prime (a ') (Fig. 2) Measurements were taken from both septal and lateral annulus, and then averaged .E/e' has been shown to reflect LV filling pressure in patients with both preserved and reduced ejection fraction HFpEF and HfrEF [9].

In normal diastolic filling E:A ratio is >1 and DT is 220ms

Diastolic filling abnormalities is graded as follows [10]

- Grade 1: Impaired relaxation pattern with normal filling pressures E:A<1 and DT is >220ms
- Grade 2: Pseudonormalized pattern E:A ratio >1-2 and DT is 150 to 200ms
- Grade 3: Reversible restrictive pattern E:A ratio >2 and DT is <150
- Grade 4: Irreversible restrictive pattern (ratio E:A ratio >2 and DT is <150 not reversed after Valsalva)

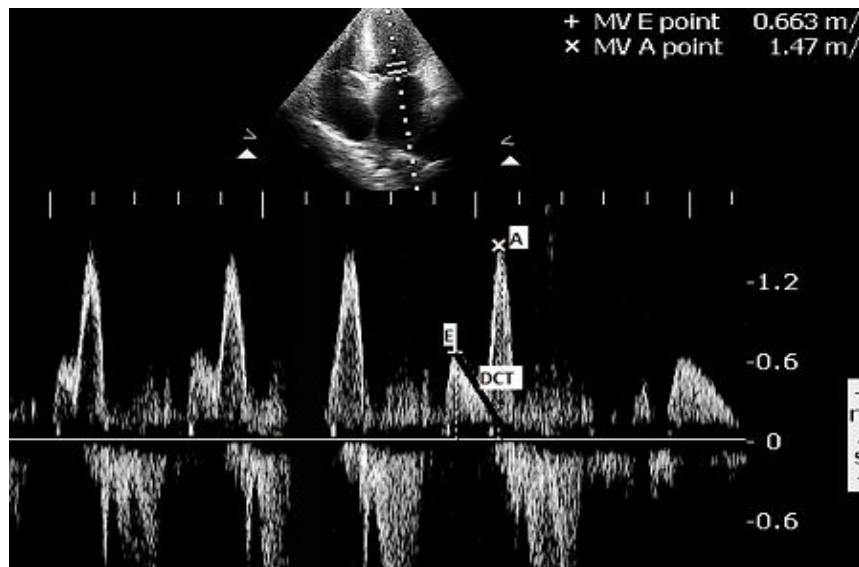


Fig. 1. Pulse wave Doppler with mitral inflow pattern

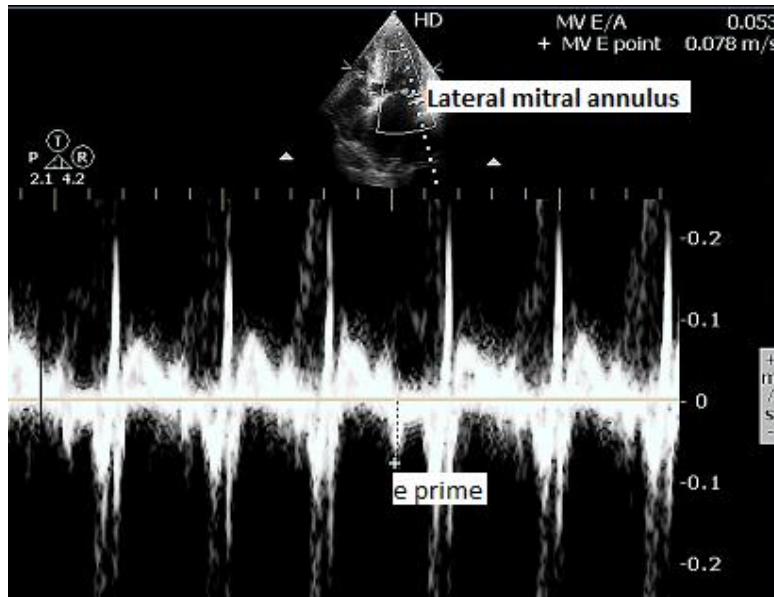


Fig. 2. Tissue Doppler at lateral mitral annulus

e prime (e') peak velocities at septal and lateral mitral annulus (cm/s) ,E= peak velocity of mitral inflow early wave (cm/s), average E/e1(mean of septal and lateral E/e¹)

All measurements were stored in the computer of the ultrasonic unit for interpretation. Hard copies of the echocardiographic data was be interpreted by a cardiologist who was masked to clinical data.

2.3 Sample Size Determination

Sample size was calculated using open epi version 3 based on the study done by Redfield [11] with prevalence of 20% sample size was calculated as 260 for confidence level of 95 %.

2.4 Methods of Statistical Analysis

Data Analysis was done using SPSS version 19.0. Continuous variables was expressed as mean+/- SD or median with IQR as wherever required. Normally distributed data was compared using t test as a test of significance for the difference of mean and categorical variables were analysed using chi-square test for

difference in proportion .Analysis was done with two-tailed at $p < 0.05$ as statistically significant.

3. RESULTS

Diastolic function between healthy subjects in different age group A (50 -60) years old, group B (60 -70) years old, and C ≥ 70 years old) was recorded (Table 1).

In the group A normal profile of mitral inflow was observed in 85 patients, two patients had pseudonormalized pattern with normal DT, whereas in group B, 58 subjects presented with normal filling and 29 with delayed relaxation. In the oldest group 71 patients had delayed relaxation profile with deceleration time less than 150 millisecond. Statistically significant differences were observed in mitral inflow parameters.

Table 1. Comparison of demographic profile between groups

Parameter	Group A	Group B	Group C	P-value A Vs B	P-value B Vs C	P-value A Vs C
Number	87	87	86	ns	ns	ns
Age	54±5	63±6	76±4	<0.001	<0.001	<0.001
Sex Male	43	45	48	=0.67	=0.64	=0.75
Female	44	42	38	=0.71	=0.73	=.67
Weight	58.5±6	54.8±4	51.6±8.5	ns	ns	ns

Table 2. Pulse wave Doppler Mitral inflow patterns between groups

Parameter	Group A 50-60 years	Group B 60-70 years	Group C 70-80 years	P-value A Vs B	P-value B Vs C	P-value A Vs C
E(cm/s)	72.5±18	68.6±18	56.7±26	ns	ns	0.03
A(cm/s)	51.3±11	64.3±14	93±23	<0.001	<0.001	<0.001
E/A	1.4±0.6	1±0.3	0.7±0.1	<0.001	=0.003	<0.001
DCT(msec)	204±16	198±22	170±24	ns	=0.003	<0.001
LAVI (mL/m ²)	23 ± 5	28 ± 11	32 ± 7	ns	ns	=0.04
EF%	65%	63%	62%	ns	ns	ns

E = peak velocity of mitral inflow early wave (cm/s); A = peak velocity of mitral inflow atrial wave (cm/s) E/A=ratio of peak velocity of early wave to peak velocity of atrial wave; DCT=deceleration time of mitral inflow early wave (ms); LAV=left atrial volume index(mL/m²).EF ejection fraction

Table 3. Comparison of tissue doppler variables

Parameter	Group A 50-60 years	Group B 60-70 years	Group C 70-80 years	P-value A Vs B	P-value B Vs C	P-value A Vs C
Septal e ¹ cm/s	10.5±4.3	10.31±3.3	9.11±5.3	ns	=.05	=.03
Lateral e ¹ cm/s	12.1±5.2	11±2.6	9.4±1.83	ns	<0.01	<0.01
Septal E/ e ¹	5.2±1.4	5.5±1.8	6.8±3.5	ns	=.05	=.05
Lateral E/e ¹	7.8±4.5	8.2±4.1	10.7±5.4	ns	<0.01	<0.01
Average E/e ¹	9.45±1.7	9.8±1.9	13.2±1.1	ns	=0.014	<0.001

4. DISCUSSION

DD increases perioperative risk in asymptomatic patients over a wide range of non-cardiac specialities. Perioperative diagnosis of DD has been facilitated by the increasing use of tissue doppler imaging echocardiography.

It is important to distinguish the difference between diastolic dysfunction and diastolic heart failure. Diastolic dysfunction is a physiologic or preclinical state in which abnormal relaxation or increased LV stiffness is compensated for by increasing LA pressure so that LV preload remains adequate. Progression to diastolic heart failure, is characterized by signs and symptoms of HF with normal ejection fraction (>50%), the absence of valvular disease, and echocardiographic evidence of diastolic dysfunction.

Phillip et al. [10] and Redfield et al. [11] have reported that more than 50% of geriatric patients undergoing cardiac and non-cardiac surgery had preoperative diastolic dysfunction with normal LVEF.

The index most commonly used to describe LV diastolic function is the ratio between the early rapid filling and the atrial filling phases, the E/A ratio. In our study there was a significant decrease in E/A ratio between groups.(P-value A

vs B, B vs C, A Vs C =<0.001, 0.003, <0.001) (Table 2).

In healthy young subjects, this ratio well exceeds 1.0, but it declines with age as the compliance of the LV diminishes. Regression analysis based on healthy subjects of different ages has shown that this decline in the E/A ratio falls below 1.0 at an age of about 65 years [12]. Thus, when evaluating LV diastolic function, the powerful effect of age has to be taken into account.

In the present study, deceleration time was normal in group A, but decreased in group B and C and the change was significant. This was concordant with study of Marui et al. [13] and Flu W-J et al. [7]

LV inflow Doppler is the most commonly used measurement in the echocardiographic examination of diastolic function because transmitral flow patterns and associated deceleration times represent increasing degrees of LV diastolic impairment [14]. These measurements change rapidly with preload variations, heart rate and rhythm disturbances so we incorporated tissue doppler imaging a more sensitive tool in the assessment of diastolic function in our study. Tissue Doppler imaging is a powerful tool for identifying whether mitral valve inflow velocity patterns represent pseudonormalization and elevated filling pressures.

A major advantage of TDI is its high feasibility, high reproducibility, and ease of application in the clinical setting.

A robust quantification of elevated left ventricular filling pressures in diastolic dysfunction is the ratio of trans-mitral E wave velocity to mitral annular velocity (E/e'). This ratio normalizes early transmitral left ventricular filling to mitral annular motion and is used to estimate mean left atrial pressure (with values >15 representing elevated filling pressures, and <8 reflecting normal filling pressures). Moreover, accuracy of this measurement has been shown to be relatively independent of LV systolic function, rhythm abnormalities LV hypertrophy, and functional mitral regurgitation [15].

TDI of mitral annulus was significantly higher in the group C (13.2 ± 1.1 in C and 9.8 ± 1.9 in B vs 9.4 ± 1.7 in A; $P < 0.05$) (Table 3). Maria Krzemi et al reported TDI of mitral annulus E/e' increases progressively with age [16,17]. Tissue Doppler index E/e' represents the relationship between LV pressure and volume change known as elastance, with its reciprocal being compliance. E/e' is used clinically and in multidisciplinary research for estimation of left ventricular filling pressure (LVFP) and diastolic dysfunction (DD)/heart failure with preserved ejection fraction (HFpEF) [18].

Left atrial volume index progressively increased with age in our study as DD causes left atrial remodelling. Pritchett, Allison Mahoney et al. [19]. and El Aouar LM [20] concluded the left atrial volume index (LAVi) increased with worsening DD, and they have graded DD based on LAVi as absent (21 ± 4 mL/m²), grade I (26 ± 7 mL/m²), grade II (33 ± 5 mL/m²), grade III (50 ± 5 mL/m²).

The combination of tissue Doppler imaging of the mitral annulus and mitral inflow velocity curves provides better estimates of LV filling pressures than other methods [21].

In patients with preserved systolic function measurement of transmitral flow in combination with mitral annular TDI velocities provides efficient means of assessing LV diastolic function and filling pressure [22].

Our study emphasis TDI based diastolic variables e', a', and E/e' should be incorporated with traditional transmitral flow velocities in assessing DD. The anesthesiologist should be knowledgeable about the age-related

cardiovascular changes, be prepared to modify the anaesthetic plan and care accordingly.

Limitations our study are first, the doppler blood flow measurements and the TDI velocities are prone to measurement error. Doppler measurement of pulmonary flow and Brain natriuretic peptide (BNP) and N-terminal proBNP (NT proBNP) were not included in our study. We did not look into the symptoms and signs of heart failure.

5. CONCLUSION

Our study demonstrates as patients age increases, they might frequently have diastolic filling abnormalities with normal LVEF and preoperative evaluation of LV diastolic function in geriatric surgical patients should be adequately evaluated.

CONSENT

As per international standard or university standard, patient's written consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard or university standard, written approval of Ethics committee has been collected and preserved by the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
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