Utility of tissue Doppler imaging of systolic function to diagnose diastolic dysfunction in critically ill patients

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Abstract

Background: Diastolic dysfunction might be associated with increased mortality in severe sepsis and septic shock. In 2016 new American Society of Echocardiography (ASE)/European Association of Cardiovascular Imaging (EACVI) guidelines were published. They simplify our approach to diastolic dysfunction recognition, but they were not validated in critical care settings. The aim of the study was to assess the applicability of systolic tissue Doppler imaging of left ventricle in patients with and without diastolic dysfunction classified on the basis of the new guidelines.

Methods: Two echocardiographers analyzed transthoracic echocardiography (TTE) examinations and assigned patients according to ASE/EASCVI guidelines to three groups: patients with systolic dysfunction and diastolic dysfunction, patients with normal systolic function and diastolic dysfunction, and patients with normal systolic and diastolic function.

Results: We performed 593 examinations in 320 patients and 390 examinations in 200 patients were included in the study. In 264 examinations with ejection fraction (EF) < 55% systolic and diastolic dysfunction was diagnosed (group 1). In 114 examinations with EF ≥ 55% normal systolic and diastolic function was diagnosed (group 2). In 12 examinations with EF ≥ 55% normal systolic and abnormal diastolic dysfunction was diagnosed (group 3). After analyzing mean systolic tissue Doppler of the mitral annulus we found a statistically significant difference between group 1 and 2 ($P < 0.0001$) and between group 2 and 3 ($P < 0.0001$). The difference in values of means in group 1 vs. 3 was not statistically significant ($P = 0.853$).

Conclusions: Systolic tissue Doppler analysis of mitral annulus might help to diagnose diastolic dysfunction especially in patients with preserved ejection fraction.

Key words: diastolic dysfunction, tissue Doppler imaging, point of care ultrasound, TTE.

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Diastolic dysfunction in critically ill patients can seriously impede the treatment process. It might be associated with increased mortality in severe sepsis and septic shock and might be associated with prolonged weaning from mechanical ventilation [1–3]. The incidence of diastolic dysfunction in critical care ranges from 20% to 67% and thus proper recognition is very important [4–16]. The latest recommendations from the American Society of Echocardiography (ASE) and the European Association of Cardiovascular Imaging (EASCVI) published in 2016 simplified the method of diastolic dysfunction recognition and grading [17]. Moreover, they recognize that patients with abnormal systolic function or structural abnormalities must automatically have a degree of impaired diastolic function [17, 18]. This means that all patients with systolic dysfunction have diastolic dysfunction. But what about patients with preserved systolic function? There are four equal criteria of diastolic dysfunction in patients with normal left ventricular ejection fraction (LVEF): average E/e' > 14, septal e' velocity < 7 cm s^{-1} or lateral e' velocity < 10 cm s^{-1}, TR velocity > 2.8 m s^{-1}, LA volume index > 34 mL m^{-2}. To recognize diastolic dysfunction one needs > 50% of positive criteria. If 2 criteria are met it is not possible to determine

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whether the patient has diastolic dysfunction or not [17, 18]. One of the methods that might be used in difficult situations is strain echocardiography, but this technique is not cheap and it is not available in every intensive care unit (ICU) [19]. In our study we decided to analyze the utility of systolic tissue Doppler imaging in patients with and without diastolic dysfunction.

METHODS

Study design

We conducted an observational study at the 4th Military Hospital in Wroclaw and the District Hospital in Rawicz, Poland, from May 2014 to July 2017. As transthoracic echocardiography has become a standard procedure in the ICU, consent was waived. Inclusion criteria were: all adult patients with at least one complete transthoracic echocardiography (TTE) examination in the course of treatment. Patients with more than one examination were also included. Repeated examination was performed when the clinical condition of the patient changed and thorough examination was deemed necessary. Exclusion criteria included: artificial valve prosthesis and severe mitral pathology. Two echocardiographers analyzed TTE examinations and assigned patients to three groups: patients with systolic dysfunction and diastolic dysfunction, patients with normal systolic dysfunction and diastolic dysfunction, and patients with normal systolic function and normal diastolic function. After assigning patients to groups according to 2016 ASE/EACVI (Figure 1), tissue Doppler of systolic function of the mitral annulus was assessed in all three groups.

Patient data collected included demographic and physiological data, the Simplified Acute Physiology Score (SAPS II), the Sequential Organ Failure Assessment (SOFA) score, the Charlson comorbidity index, and the diagnosis at the time of examination.

Echocardiography

Transthoracic echocardiography was routinely performed in all our ICU patients. It has become our main method of hemodynamic assessment due to its non-invasiveness and diversity of information it provides. The parameters measured included left ventricular (LV) function, mitral inflow velocity, septal and lateral tissue Doppler of mitral annulus, tricuspid regurgitation, left atrium volume, and septal and lateral systolic tissue Doppler of the mitral annulus. Ejection fraction was estimated by "eyeballing", and left atrial volume was measured with Simpson's biplane technique. Tissue Doppler measurements were taken from the peak intensity of the Doppler signal in the mitral annulus and averaged from 3 cardiac cycles if the patient was in sinus rhythm or at least 5 cycles when the rhythm was not sinus in origin.

Systolic dysfunction was diagnosed when EF estimated by "eyeballing" was below 55%. Abnormal systolic function measured by tissue Doppler was diagnosed based on the average of septals' and medials'. The cut-off value of < 10 cm s^{-1} was established for systolic dysfunction. Diastolic dysfunction

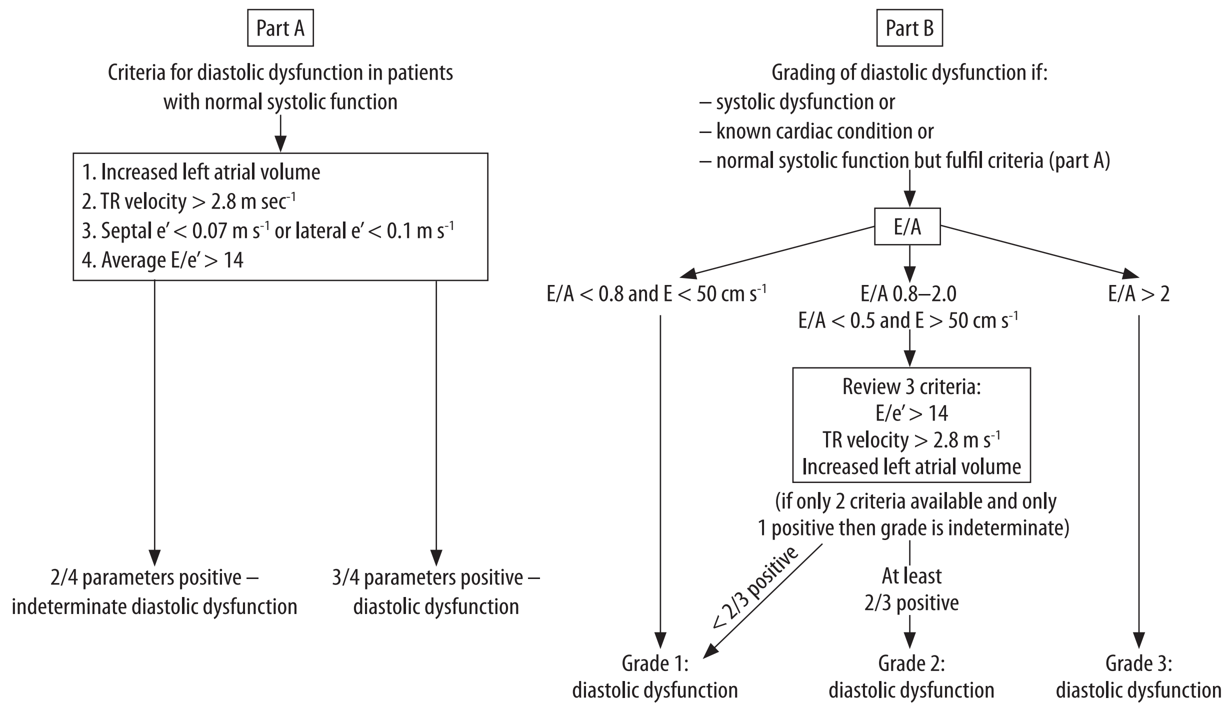

FIGURE 1. 2016 ASE/EACVI (American Society of Echocardiography/European Association of Cardiovascular Imaging) algorithms for diagnosis of diastolic dysfunction

TABLE 1. Patients' characteristics

Factor	
Gender (M/F)	M : F = 120 : 80
Age	18–97 years (median = 67)
ICU admission	
SAPS II	12–98 (median = 52)
Charlson Comorbidity Index	0–13 (median = 2)
Admission category	
Sepsis	60 (30%)
Respiratory failure	50 (25%)
Heart failure	43 (21.5%)
Liver failure	10 (5%)
Trauma	7 (3.5%)
Acute pancreatitis	7 (3.5%)
Neurological disorders	5 (2.5%)
Diabetic ketoacidosis	2 (1%)
Acute renal failure	1 (0.5%)
Gastrointestinal bleeding	1 (0.5%)

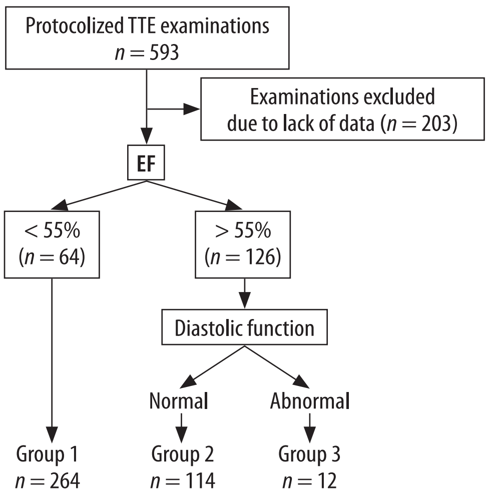

FIGURE 2. Diagram of protocalized transthoracic echocardiography examinations

was diagnosed according to 2016 ASE/EACVI guidelines. Left atrial volume was considered abnormal if > 34 mL m^{-2} (indexed for body surface area) or if > 52 mL for females and > 58 mL for males (not indexed for body surface area). Patients with normal systolic function had different criteria of diastolic dysfunction compared to patients with abnormal systolic function assessed by "eyeballing". The patients with systolic dysfunction did not proceed to grading of diastolic dysfunction. The assumption was made that they all had diastolic dysfunction.

Statistical analysis

The difference in means' value between defined groups was assessed using the Kruskal-Wallis test. Post-hoc analysis was done using the Conover method with Holm correction. Analysis was performed using R for Windows (version 3.4.4) [20].

RESULTS

We performed 593 TTE protocolized examinations in 320 patients between May 2014 and July 2017. 200 patients were included in the study. There were 390 TTE examinations approved for analysis. 203 examinations were excluded from the analysis due to lack of data regarding LVEF, systolic tissue Doppler measurement from either the medial or lateral annulus, or when it was not possible to determine diastolic function. Baseline demographics of the patients are included in Table 1. 390 TTE examinations were performed on day 0–63 (median 3) of ICU admission, SOFA score on the examination day was 0–18 (median 7), mean arterial pressure was 39–137 mm Hg (median 82 mm Hg), heart rate was 39–155 beats min^{-1} (median 89 beats min^{-1}), PEEP 3–20 cm H_2O (median 8 cm H_2O). 293 examinations were performed in sinus rhythm.

In 264 examinations we assessed EF below 55% and systolic and diastolic dysfunction was diagnosed (group 1). In 114 examinations we assessed EF ≥ 55% and normal systolic and normal diastolic function was diagnosed (group 2). In 12 examinations we assessed EF ≥ 55% and normal systolic and abnormal diastolic function was diagnosed (group 3) (Figure 2).

After qualifying examinations into 3 groups we analyzed mean velocity of lateral and medial tissue Doppler of the mitral annulus in all groups and the results are presented in Table 2. A statistically significant difference between groups 1 and 2 (P < 0.0001) and between groups 2 and 3 (P < 0.0001) was observed. The values of mean s' in groups 1 and 3 were not determined to be statistically significant (P = 0.853). Velocity of systolic tissue Doppler was significantly higher in examinations with good systolic and diastolic function as compared to groups with diastolic dysfunction.

TABLE 2. S' value analysis in defined groups of patients

Group	*n*	Mean	SD	Min	Q1	Median	Q3	Max
1	264	0.1071	0.2045	0.03	0.07	0.08	0.1	2.9
2	114	0.1419	0.3088	0.05	0.1	0.11	0.13	3.4
3	12	0.08333	0.0123	0.07	0.07	0.08	0.092	0.1

DISCUSSION

The publications of the 2016 ASE/EACVI guidelines simplified the method of diastolic dysfunction recognition in ICU patients although they were not validated in the critical care setting [18]. The new guidelines clearly state that one cannot separate diastolic dysfunction from systolic dysfunction and all patients with systolic dysfunction have abnormal diastolic function [17]. The guidelines also state that patients with preserved ejection fraction should have 4 elements of diastolic function assessed: left atrial volume, TR velocity, septal e' or lateral e' and averaged E/e' [17]. But patients in the ICU are not that easy to visualize and measure. Performing Simpson biplane evaluation of ejection fraction in ventilated patients is time consuming and it is often difficult to visualize a clear outline of the endocardium. We usually perform visual assessment of left ventricle ejection fraction because it is easy to perform and is reliable [21]. Reliability of "eyeballing" usually is restricted to determining whether the systolic function is good, moderate or severely impaired. It does not provide precise information about EF and thus diastolic dysfunction. To complement our systolic function assessment we performed tissue Doppler in the mitral annulus. We chose the mean velocity of < 10 cm s^{-1} as a cut-off value for impaired systolic function [22].

In our study we tried to analyze the utility of systolic tissue Doppler in patients with and without diastolic dysfunction. We wanted to find out whether tissue Doppler could help in determining diastolic function especially in patients with preserved ejection fraction. We analyzed 390 TTE examinations performed in 200 patients. We divided the examinations into three groups: group 1 – abnormal systolic and diastolic function, group 2 – normal systolic and diastolic function, group 3 – normal systolic and abnormal diastolic function. Our results show that the velocity of systolic tissue Doppler was significantly higher in group 2 with normal systolic and diastolic function as compared to groups with abnormal diastolic function (1 and 3).

In our opinion tissue Doppler plays a very important role in echocardiographic assessment of ICU patients especially when strain echocardiography is not available [19, 23]. It can help especially in situations when we cannot measure all parameters necessary to diagnose diastolic dysfunction according to the newest guidelines. When we classify a patient with preserved systolic function in the intermediate group – 2 parameters positive and 2 parameters negative – systolic tissue Doppler analysis might be decisive.

But why is there so much interest in diastolic dysfunction in the ICU population? We think it might be influenced by studies identifying diastolic dysfunction as a predictor of mortality especially in the septic population [1, 2, 4, 6–8]. The 2016 ASE/EACVI guidelines simplify our approach to diastolic dysfunction but they do not solve all diagnostic problems in critically ill and mechanically ventilated patients. We need clear definitions and simple tools to diagnose diastolic dysfunction in the ICU. Sturgess *et al*. [24] proposed brain natriuretic peptide (BNP) as a marker of diastolic dysfunction. They suggest a cut-off value of 43 pg mL^{-1} (sensitivity 80% and specificity of 59%) for diagnosing diastolic dysfunction. However, elevated B-type natriuretic peptide (BNP) appears to lack validity as a biomarker of myocardial dysfunction in sepsis and cannot be used solely to diagnose diastolic dysfunction [8]. Can speckle tracking echocardiography help in difficult patients? Orde *et al*. [25] performed speckle tracking echocardiography in adult patients with early severe sepsis/septic shock. The incidence of RV and LV dysfunction was approximately twice as high based on strain analysis when compared to assessment by conventional echocardiography, suggesting that speckle tracking echocardiography is more sensitive than the conventional technique [19, 25]. Unfortunately, speckle tracking echocardiography is not available in most Polish intensive care units, so we try to apply tissue Doppler in many clinical scenarios. A very interesting application of tissue Doppler was proposed by Clancy *et al*. [26]. They proposed a novel parameter (septal e'/s') to identify diastolic dysfunction in patients with severe sepsis and septic shock who had normal systolic function. They concluded that a reduction in septal e'/s' may indicate diastolic dysfunction and might be applicable even in hyperdynamic systolic function. Our study strengthens the role of tissue Doppler in diagnosing diastolic dysfunction and remains in accordance with the newest guidelines. It has some important limitations. First of all, the cut-off value of < 55% was proposed as a marker of systolic dysfunction, which is slightly higher than the reference value for males (< 52%) and females (< 54%). It is difficult to be precise when performing "eyeball" estimation, and physicians tend to quantify EF every 5%, for example 45%, 50%, 55%, etc. Also the cut-off value of mean velocity of systolic tissue Doppler is oversimplified, but it was useful in our analysis. We did not perform grading of diastolic dysfunction as it was not our goal. Grading of diastolic dysfunction would be necessary to guide the treatment and to determine the mortality. As this study was performed only in two hospitals, the number of examinations was limited by the number of sonographers available. A significant number of examinations were lost due to discordance with

2016 ASE/EACVI guidelines and lack of necessary data. Further research of tissue Doppler and its application in diastolic dysfunction is needed with efforts to find novel and easy parameters applicable in the ICU population.

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REFERENCES

1. Sanfilippo F, Corredor C, Fletcher N, et al. Diastolic dysfunction and mortality in septic patients: a systematic review and meta-analysis. Intensive Care Med 2015; 41: 1004-1013. doi: 10.1007/s00134-015-3748-7.
2. Gonzalez C, Begot E, Dalmay F, et al. Prognostic impact of left ventricular diastolic function in patients with septic shock. Ann Intensive Care 2016; 6: 36. doi: 10.1186/s13613-016-0136-6.
3. Roche-Campo F, Bedet A, Vivier E, Brochard L, Mekontso Dessap A. Cardiac function during weaning failure: the role of diastolic dysfunction. Ann Intensive Care 2018; 8: 2. doi: 10.1186/s13613-017-0348-4.
4. Lanspa MJ, Gutsche AR, Wilson EL, et al. Application of a simplified definition of diastolic function in severe sepsis and septic shock. Crit Care 2016; 20: 243. doi: 10.1186/s13054-016-1421-3.
5. Brown SM, Pittman JE, Hirshberg EL, et al. Diastolic dysfunction and mortality in early severe sepsis and septic shock: a prospective, observational echocardiography study. Crit Ultrasound J 2012; 4: 8. doi: 10.1186/2036-7902-4-8.
6. Landesberg G, Jaffe AS, Gilon D, et al. Troponin elevation in severe sepsis and septic shock: the role of left ventricular diastolic dysfunction and right ventricular dilatation. Crit Care Med 2014; 42: 790-800. doi: 10.1097/CCM.0000000000000107.
7. Landesberg G, Gilon D, Meroz Y, et al. Diastolic dysfunction and mortality in severe sepsis and septic shock. Eur Heart J 2012; 33: 895-903. doi: 10.1093/eurheartj/ehr351.
8. Sturgess DJ, Marwick TH, Joyce C, et al. Prediction of hospital outcome in septic shock: a prospective comparison of tissue Doppler and cardiac biomarkers. Crit Care 2010; 14: R44. doi: 10.1186/cc8931.
9. Bouhemad B, Nicolas-Robin A, Arbelot C, Arthaud M, Féger F, Rouby JJ. Isolated and reversible impairment of ventricular relaxation in patients with septic shock. Crit Care Med 2008; 36: 766-774. doi: 10.1097/CCM.0B013E31816596BC.
10. Jafri SM, Lavine S, Field BE, Ahorozian M, Carlson R. Left ventricular diastolic function in sepsis. Crit Care Med 1990; 18: 709-714.
11. Poelaert J, Declerck C, Vogelaers D, Colardyn F, Visser CA. Left ventricular systolic and diastolic function in septic shock. Intensive Care Med 1997; 23: 553-560.
12. Sturgess DJ, Marwick TH, Joyce CJ, Jones M, Venkatesh B. Tissue Doppler in critical illness: a retrospective cohort study. Crit Care 2007; 11: R97. doi: 10.1186/cc6114.
13. Munt B, Jue J, Gin K, Fenwick J, Tweeddale M. Diastolic filling in human severe sepsis: an echocardiographic study. Crit Care Med 1998; 26: 1829-1833. doi: 10.1097/00003246-199811000-00023.
14. McLean AS, Huang SJ, Hyams S, et al. Prognostic values of B-type natriuretic peptide in severe sepsis and septic shock. Crit Care Med 2007; 35: 1019-1026. doi: 10.1097/01.CCM.0000259469.24364.31.
15. Pulido JN, Afessa B, Masaki M, et al. Clinical spectrum, frequency, and significance of myocardial dysfunction in severe sepsis and septic shock. Mayo Clin Proc 2012; 87: 620-628. doi: 10.1016/j.mayocp.2012.01.018.
16. Micek ST, McEvoy C, McKenzie M, Hampton N, Doherty JA, Kollef MH. Fluid balance and cardiac function in septic shock as predictors of hospital mortality. Crit Care 2013; 17: R246. doi: 10.1186/cc13072.
17. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. Eur Heart J Cardiovasc Imaging 2016; 17: 1321-1360. doi: 10.1093/ehjci/jew082
18. Clancy DJ, Scully T, Slama M, Huang S, McLean AS, Orde SR. Application of updated guidelines on diastolic dysfunction in patients with severe sepsis and septic shock. Ann Intensive Care 2017; 7: 121. doi: 10.1186/s13613-017-0342-x.
19. Dalla K, Hallman C, Bech-Hanssen O, Haney M, Ricksten SE. Strain echocardiography identifies impaired longitudinal systolic function in patients with septic shock and preserved ejection fraction. Cardiovasc Ultrasound 2015; 13: 30. doi: 10.1186/s12947-015-0025-4.
20. R Core Team. R: a language and environment for statistical computing. R Foundation for Statistical Computing, Vienna 2015.
21. Bergenzaun L1, Gudmundsson P, Öhlin H, et al. Assessing left ventricular systolic function in shock: evaluation of echocardiographic parameters in intensive care. Crit Care 2011; 15: R200. doi: 10.1186/cc10368.
22. Chahal NS, Lim TK, Jain P, Chambers JC, Kooner JS, Senior R. Normative reference values for the tissue Doppler imaging parameters of left ventricular function: a population-based study. Eur J Echocardiogr 2010; 11: 51-56. doi: 10.1093/ejechocard/jep164.
23. De Geer L, Engvall J, Oscarsson A. Strain echocardiography in septic shock – a comparison with systolic and diastolic function parameters, cardiac biomarkers and outcome. Crit Care 2015; 19: 122. doi: 10.1186/s13054-015-0857-1.
24. Sturgess DJ, Parmar D, Dulhunty JM, Hedge R, Jarrett P, Udy A. A preliminary evaluation of plasma b-type natriuretic peptide as a screening test for left ventricular diastolic dysfunction in non-cardiac intensive care. Anaesth Intensive Care 2013; 41: 591-595. doi: 10.1177/0310057X1304100503
25. Orde SR, Pulido JN, Masaki M, et al. Outcome prediction in sepsis: speckle tracking echocardiography based assessment of myocardial function. Crit Care 2014; 18: R149. doi: 10.1186/cc13987.
26. Clancy DJ, Slama M, Huang S, et al. Detecting impaired myocardial relaxation in sepsis with a novel tissue Doppler parameter (septal e'/s'). Crit Care 2017; 21: 175. doi: 10.1186/s13054-017-1727-9.