

Significant beat-to-beat variability of E/e' irrespective of respiration

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Abstract

The E/e' ratio is commonly used in Doppler echocardiographic examinations to estimate the pulmonary capillary wedge pressure. The rationale of using this ratio is to combine left ventricular (LV) filling (E) and relaxation (e') velocities to indirectly assess left atrial pressure. However, the accuracy of this index has recently been questioned, particularly in patients with controlled heart failure¹. Likewise, the potential beat-to-beat variability of such measurements remains undetermined.

The cardiovascular system is subject to several oscillations with the potential of influencing LV function and its intra-cavitary pressures, hence measurements of its filling and relaxation velocities. The aim of this pilot study was to assess the beat-to-beat variability of the E/e' ratio in one minute long examination in healthy subjects, and patients with various severity of amyloid heart disease.

The results show that despite critical application of the standard echocardiographic recording recommendations, E/e' beat-to-beat variability was 36 % (22 to 50%) in healthy subjects and 17 % (11-26%) in patients, and where the most severe amyloid heart disease had the least variability. Thus, clinical use of a single or few cardiac beats might not necessarily reflect an accurate ratio between the two velocities, and hence casts doubt over their diagnostic value.

Key words: Echocardiography, E/e', variability, Amyloid, color Doppler

Introduction

One of the main objectives of echocardiographic examinations is the assessment of intracardiac pressures. In particular, the ratio between early diastolic blood flow velocity and early diastolic myocardial velocity (E/e') is often used to assess pulmonary capillary wedge pressure (PCWP) (Nagueh S page 2). Typically, a few cardiac cycles are recorded and the average reading is calculated. The cardiovascular system comprises several oscillating components, including physiological transients, respiration, loading conditions, heart rate variability, blood pressure variability, etc which may potentially influence the E and e' velocities³. In particular, the influence of respiration on LV function has been shown to be related to age and heart disease^{4,5}. Although standard echocardiography guidelines recommend acquiring images and Doppler recordings at end-expiration⁶, significant velocity variability might remain within the expiratory phase⁷. The aim of this pilot study was to assess the beat-to-beat variability of the E/e' ratio within a minute of continuous recording in healthy young and old subjects, and patients with varying severity of amyloid heart disease.

Methods

Subjects

Seven subjects participated in this study: two young (20-30y), two middle aged (50-60y) healthy subjects, and three patients (65-72y). The patients had fat biopsy proven ATTR (amyloid transthyretin type) amyloid disease with increased septal wall thickness (>20 mm) who had clearly defined different patterns of

LV filling and diastolic dysfunction: type 1, abnormal relaxation (E/A < 1); type 2, pseudo-normalization (E/A >1<2); and type 3, restrictive (E/A >2) pattern. All subjects gave informed consent to participate in the study which conformed to the declaration of Helsinki and was approved by the Regional ethics committee of Umeå.

Echocardiographic examination

A 60 seconds long Doppler echocardiographic examination was acquired using a Vivid E9 ultrasound scanner with a M5S cardiac probe (GE Medical, Horten, Norway) in color Doppler imaging mode (CDI). Subjects were examined in the semi-left lateral position. The imaging sector depth, width and location were optimized for maximal frame rate, allowing simultaneous registration of septal axial myocardial motion (B-mode) and blood flow velocity (CDI) across the mitral annulus. A two-chamber view with 45 degrees field-of-view was used for the B-mode sequence, and a 10 deg field-of-view was used for the CDI sequence to cover the tip of the mitral valve. Respiration and ECG were simultaneously recorded by the ultrasound system. The frame rates of the CDI and B-mode image sequences were 100 Hz and 33 Hz, respectively. Image sequences were exported in hdf5 format for offline processing, with the CDI and B-modes as separate image sequences.

Simultaneous mitral (E) and septal myocardial (e') velocities were measured for each heart beat by validated in house software⁸. Myocardial velocity curves were obtained by a speckle-tracking technique from a ROI at the proximal septum of the B-mode sequence, and mitral flow velocity curves was measured from the CDI sequence.

Table 1: E/e' beat-to-beat variability. Values in italics are coefficient of variation (CV).

	Young 1	Young 2	Middle aged 1	Middle aged 2	Patient 1 (Relax)	Patient 2 (Pseudo)	Patient 3 (Restrict)
Without guideline procedure							
Beat-to-beat	4,2 (4,0)	6,0 (6,0)	9,1 (10,4)	10,1 (12,0)	15,9 (12,8)	12,1 (7,5)	11,4 (3,7)
CV, %	48,1	50,5	57,0	58,2	40,3	31,0	16,2
Using guideline procedure							
End expiration	4,9 (2,2)	6,4 (5,3)	10,2 (7,9)	10,5 (10,6)	16,3 (5,5)	12,0 (6,2)	11,4 (2,5)
Difference	1,4 (0,5)	0,8 (0,3)	2,3 (2,6)	0,8 (0,4)	-0,35 (-0,6)	-0,46 (0,41)	-0,22 (-0,82)
CV (end-expiration), %	22,4	35,6	38,7	50,5	16,9	25,8	11,0

Variability in E/e' was quantified separately on a beat-to-beat, end-inspiration, and end-expiration basis using the coefficient of variation (CV) calculated as range divided by mean.

Results

The Figure illustrates the beat-to-beat variability over one minute long acquisition for healthy subjects and patients. The results of the E/e' variability of all subjects are summarised in the Table.

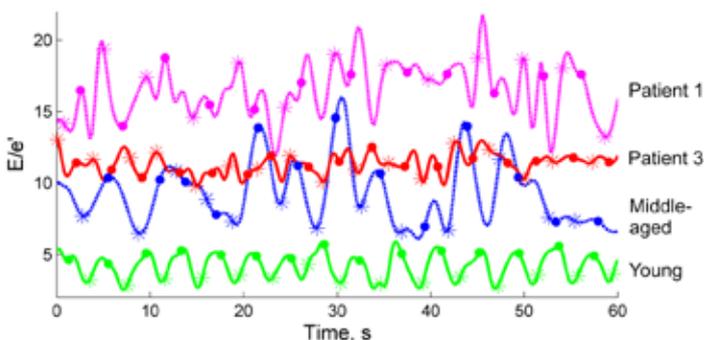


Figure: Beat-to-beat variability of E/e'. The phases of the respiration are indicated by (·) = end-expiration and (*) = end-inspiration.

Beat-to-beat variability was higher in healthy subjects compared to patients (50-60% vs 16-40%), and variability decreased according to disease severity (relaxation abnormality to restrictive). The respiratory phase was relatively coherent with the E/e' signal in healthy subjects but not in patients. Mean and range of variability of E velocity was 7.2 (3.1), 5.0 (2.5) and 3.0 (1.0) %, for the young, old and patient groups and corresponding values of e' were 20.2 (16.3), 15.7 (4.9), and 8.0 (3.2) %.

In healthy individuals E/e' was higher at end-expiration compared to end-inspiration but there was no difference in the patients, irrespective of disease severity. Also, variability with expiration was higher in the healthy compared to patients (23-50% vs 11-26%).

Discussion

In this pilot study continuous and simultaneous recordings of LV filling and myocardial velocities varied between consecutive beats, resulting in significant E/e' variability. The variation was

50-60 % in healthy subjects but to a significantly lesser extent in patients with heart failure. The least variability was in the patient with restrictive LV filling. Furthermore, such variability remained consistent during end-expiration, even when using standard guidelines for Doppler echocardiographic acquisition.

Although our findings are based on individuals rather than a cohort they seem to draw a pattern of interaction between cardiac function and intra-thoracic pressure changes. In young normals with compliant cardiovascular and respiratory systems even minor alterations in venous return result in significant beat to beat variability, a picture that is compromised in older people without cardiac disease. This highlights the effect of age on the systemic and pulmonary circulations as well as respiratory system. As for heart failure and progressive increase in left atrial pressure and intra-thoracic pressure, the normal variability drops to the minimum suggesting that the raised filling pressures take the upper hand in dictating the pattern of LV filling and myocardial lengthening. These findings propose that considering E/e' as a simplified marker of raised left atrial pressure may only apply to patients with end stage heart failure rather than all comers with different disease severity and pathologies.

This study presents for the first time beat-to-beat information on simultaneously recorded myocardial and blood flow velocities. A potential limitation of this study is that the blood flow velocity was quantified using color Doppler mode, thus giving lower peak velocities as compared to pulsed wave Doppler therefore not comparable in absolute values. However, since the study assesses the variability in peak velocities, the normalized values of the CV should minimize this limitation.

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