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Original article

Noninvasive estimation of pulmonary capillary wedge pressure in patients with mitral regurgitation: A speckle tracking echocardiography study

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ABSTRACT

Background: Echocardiographic parameters to predict pulmonary capillary wedge pressure (PCWP) in mitral regurgitation (MR) are not yet elucidated. We reported that PCWP could be accurately estimated by novel KT index which is defined as $\log_{10}$ [left atrial (LA) emptying function (EF)/LA volume]. We examined the usefulness of the KT index as a predictor of PCWP in primary and secondary MR with sinus rhythm and also MR with atrial fibrillation.

Methods: LA dimension, strain, volume, EF, and E/e' were measured in moderate to severe MR with sinus rhythm ($n = 58$, age: 67 ± 8 years) and MR with atrial fibrillation ($n = 24$, age: 69 ± 11 years) just before catheterization and in normal subjects ($n = 26$, age: 67 ± 11 years) using speckle tracking echocardiography. MR with sinus rhythm was divided into primary MR ($n = 27$) and secondary MR ($n = 31$). The estimated PCWP (ePCWP) was calculated as $10.8–12.4 \times$ KT index.

Results: There was a correlation between PCWP and LA dimension, E/e', minimum LA volume index, active LAEF, total LAEF, or LA strain ($r = 0.32$, $r = 0.31$, $r = 0.55$, $r = -0.61$, $r = -0.51$, and $r = -0.50$, respectively, $p < 0.05$). The better correlation was found between PCWP and ePCWP in MR including both primary and secondary MR and also MR with atrial fibrillation ($r = 0.70$, $r = 0.67$, and $r = 0.58$, respectively, $p < 0.01$). Multiple regression analysis revealed that ePCWP was an independent predictor of PCWP in MR. The ePCWP demonstrated good diagnostic accuracy (area under the curve of 0.86) and sensitivity (81%) and specificity (71%) to predict elevated PCWP >15 mmHg using a cut-off of 16 mmHg.

Conclusion: The ePCWP was the reliable echocardiographic parameter to predict PCWP in primary and secondary MR and might also be useful in MR with atrial fibrillation. The ePCWP may have an incremental value in a clinical setting.

Introduction

Echocardiography, especially Doppler echocardiography plays an important role in the diagnosis and treatment of patients with mitral valve regurgitation (MR). It is practical to estimate pulmonary capillary wedge pressure (PCWP) by measuring transmitral inflow velocity by Doppler echocardiography for treatment in those patients, but this method is influenced by factors such as age, heart rate, preload, and afterload [1–3].

It was demonstrated that the ratio of early transmitral inflow velocity to mitral annulus early diastolic tissue Doppler velocity (E/e') correlates with the left ventricular filling pressure (LVFP) measured invasively in patients without MR [4] and E/e' is widely

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used as a non-invasive tool to estimate LVFP. However, existing Doppler and two-dimensional methods including left atrial volume (LAV), mitral inflow pattern, pulmonary vein flow pattern, and E/e' have several limitations when they are applied to the estimation of LVFP in patients with MR [1,5]. There was conflict in the use of E/e' to estimate LV end-diastolic pressure (LVEDP) in MR [1,5]. It was reported that the e' would be increased in patients with MR and preserved LV ejection fraction because of the increased LV stroke volume [1].

In the absence of severe MR, LV pressure at the mitral valve opening (LVFP) correlates closely to mean LA pressure that can be approximated by PCWP [6,7]. The increase in LVFP in patients with heart failure is the primary mechanism responsible for symptoms such as dyspnea. Thus, it is of exceeding importance to estimate LVFP or PCWP in patients with MR to decipher the cause of dyspnea and determine the therapeutic strategy. However, echocardiographic parameters to predict LVFP or PCWP in MR have not been elucidated.

We recently reported that PCWP estimated by the combination of LAV and LA function (ePCWP) using speckle tracking echocardiography (STE) is a strong predictor of PCWP measured by cardiac catheterization [8]. Moreover, LA strain assessed by STE was reported to be a powerful predictor of LVFP in heart failure [9]. Thus, the aim of this study is to examine the most useful and reliable echocardiographic parameter including E/e', ePCWP, and LA strain to predict PCWP in patients with moderate to severe MR dividing MR into primary and secondary using STE.

Materials and methods

Study population and protocol

The study population consisted of 62 consecutive patients with moderate to severe MR and sinus rhythm (SR) and an additional 25 patients with moderate to severe MR and chronic atrial fibrillation (AF) who were referred for clinically indicated cardiac catheterization. We also included 26 age-matched controls for the comparison of echocardiographic parameters. The controls had symptoms such as chest pain and discomfort and underwent electrocardiography and echocardiography. The controls had no abnormal findings on electrocardiography and echocardiography, and did not take any medication. Exclusion criteria in MR patients were the presence of mitral stenosis, moderate to severe aortic valve regurgitation or stenosis, past history of surgery for structural heart disease, and poor echocardiographic recording. Therefore, those who had mitral stenosis ($n = 1$), moderate to severe aortic valve disease ($n = 2$), and poor echocardiographic window ($n = 2$) were excluded. Accordingly, 58 MR patients with SR, 24 MR patients with AF and 26 controls without cardiovascular disease were enrolled in our study. Transthoracic echocardiography including the measurement of LA strain and LAV and LA function using two-dimensional STE (2D-STE) was performed in our echo laboratory by two experienced sonographers just prior to pressure measurements by right heart catheterization. The MR was graduated at first semi-quantitatively and then quantitatively using color flow imaging and the Doppler quantitative method such as regurgitant fraction (RF) according to the American Society of Echocardiography criteria [10]. The MR was defined as mild (mitral RF <30%), moderate (mitral RF; 30–49%), and severe (mitral RF ≥50%). Only moderate and severe MR patients were enrolled to our study. MR patients with SR ($n = 58$) were divided into two groups; primary MR group [MR due to change of mitral valve itself such as prolapse ($n = 21$) and flail leaflet ($n = 6$)] and secondary MR group [MR due to the tethering of the mitral valve leaflet because of LV remodeling such as LV dilation due to ischemia ($n = 25$) and dilated cardiomyopathy ($n = 6$)]. The present study was approved by the ethics committee of our institution and all patients gave written informed consent before participation. The reliability of STE method for the quantification of phasic LAV and LA function has been well established in our previous studies [8,11].

Echocardiography

Echocardiographic studies were performed using a commercially available ultrasound system (iE33, Philips Medical Systems, Best, The Netherlands) that was equipped with a broadband (1–5 MHz) S5-1 probe. All echocardiographic measurements were made according to criteria of the American Society of Echocardiography [12] and were averaged from three heartbeats in MR patients with SR and averaged from five heartbeats in MR patients with AF.

Just before catheterization, LV ejection fraction, LV mass, LA dimension (LAD), and E/e' were measured. LV ejection fraction was measured by bi-plane modified Simpson's method. LV mass was calculated at end diastole using the two-dimensional area-length method: LV mass = 0.8 × 1.04 × [(LV dimension + LV posterior wall thickness + LV septal wall thickness)^3 − LV dimension^3] + 0.6*g*. Volume and mass were indexed for body surface area. Doppler measurements of mitral inflow E-wave and A-wave velocity were obtained from the apical four-chamber view and tissue Doppler measurement of mitral e' wave velocity was made at the septal mitral annulus.

Speckle tracking analysis

After measurements of the standard echocardiographic parameters, three cardiac cycles were recorded in an apical four-chamber view using gray-scale acquisition to obtain a time–LA strain curve and a time–LAV curve by STE in MR with SR and five cardiac cycles were recorded in MR with AF. To optimize STE, images were obtained at a frame rate of 70–100 frames/s. The off-line time–longitudinal LA strain data analysis and time–LAV curve analysis were performed with QLAB 9.0 software (Philips Medical Systems, Andover, MA, USA) to evaluate LA strain and phasic LAV and LA emptying function (EF). To assess LA strain, LAV and EF, the focus was set at the level of LA and three tracking points were manually placed on an end-diastolic frame on LA endocardial layer (two points at medial and lateral mitral annulus and one point at apex of LA in Fig. 1). The LA was then automatically traced during one cardiac cycle, for regions of interest with a thickness of 3 mm between endocardial and epicardial layer (Fig. 1). The user can optimize both contours globally or regionally. Once completed, the user verifies the tracking based on how well it follows the endocardial and epicardial contours of the left atrium. Maximum, pre-atrial contraction and minimum LAV, and active and total LAEF were measured in sinus rhythm. Active LAEF that reflects LA pump function was defined as (pre-atrial contraction LAV − minimum LAV)/pre-atrial contraction LAV. Total LAEF that reflects LA reservoir function was defined as (maximum LAV − minimum LAV)/maximum LAV as we previously described [8,11]. The ePCWP was calculated as 10.8–12.4 × KT index. KT index was defined as $\log_{10}$ (active LAEF/minimum LAV index) as we reported [8]. In MR patients with AF, total LAEF was substituted for active LAEF because pre-atrial LAV was not present [8].

Invasive measurements of pulmonary capillary wedge pressure

Mean PCWP was measured with a pulmonary artery balloon-occlusion catheter, and the wedge portion was verified fluoroscopically and by changes in the pressure waveform. Fluid-filled transducers were balanced before the study with zero obtained at the mid-axillary line. The pressure measurements were performed