The \( E/e \) filling index and right ventricular pressure in relation to applied international Doppler recommendations of left ventricular filling assessment

Cecilia Wallentin Gurona\(^a,\ast\), Odd Bech-Hanssen\(^b\), Ronny Wikh\(^b\), Annika Rosengren\(^c\), Marianne Hartford\(^d\), Kenneth Caidahl\(^b,e\)

\(^a\) Department of Clinical Physiology, Sahlgrenska University Hospital, SE 416 85 Göteborg, Sweden
\(^b\) Department of Clinical Physiology, Sahlgrenska University Hospital, SE 413 45 Göteborg, Sweden
\(^c\) Department of Internal Medicine, Sahlgrenska University Hospital, SE 416 85 Göteborg, Sweden
\(^d\) Department of Cardiology, Sahlgrenska University Hospital, SE 413 45 Göteborg, Sweden
\(^e\) Department of Clinical Physiology, Karolinska Institute, SE 171 76 Stockholm, Sweden

Received 15 September 2004; received in revised form 3 January 2005; accepted 15 January 2005
Available online 31 March 2005

**KEYWORDS**

Left ventricular filling; Diastolic function; Left ventricular filling pressure; Doppler; Tissue Doppler; Right ventricular pressure

**Abstract**

**Aim:** A ratio > 15 between the early diastolic pulsed Doppler velocities of the mitral inflow (E) and the basal left ventricular (LV) tissue (e) has been demonstrated to predict an elevated LV filling pressure (FP). An elevated LVFP implies an elevated right ventricular pressure (RVp). In order to investigate the sensitivity of the \( E/e \) filling index, we compared \( E/e \) and RVp, in their ability to identify a Doppler-assumed elevation of LVFP.

**Methods and results:** Application of pulsed Doppler international recommendations grouped 134 patients with acute coronary syndromes (ACS) and 50 age- and sex-matched controls, according to LV filling: normal; delayed relaxation; an isolated pathological mitral–pulmonary venous-A-wave-duration difference; pseudo normal; or a restrictive filling pattern. An \( E/e \geq 15 \) and an RVp > 30 mmHg showed the following (%): sensitivity (32/94), specificity (95/76), positive (68/59), and negative (80/97) predictive values of a Doppler-assumed elevation of LVFP, in terms of either a pseudo normal or a restrictive filling pattern.

**Conclusion:** The low sensitivity of \( E/e \) to detect a Doppler-assumed elevation of LVFP could limit its clinical usefulness as a single variable, in ACS. The high

\* Corresponding author. Tel.: +46 703 127772; fax: +46 31 7780551. E-mail address: c.wallentin@home.se (C. Wallentin Guron).

1525-2167/530 © 2005 The European Society of Cardiology. Published by Elsevier Ltd. All rights reserved.
doi:10.1016/j.euje.2005.01.005
Introduction

Tissue Doppler has opened new possibilities to study left ventricular (LV) diastolic both function and filling. The ratio between the early diastolic pulsed Doppler velocities of the mitral inflow (E) and the basal left ventricular (LV) tissue (e) is suggested as new tool in the identification of an elevated LV filling pressure (FP). Among non-invasive filling variables, the E/e index > 15 was shown by Ommen et al., to be the single best predictor of an invasively confirmed elevation of LVFP, to have high specificity, and also to point to an adverse outcome. Its clinical value over traditional pulsed Doppler in LV filling assessment, however, is not established.

Even though pulsed Doppler echocardiography cannot measure LVFP, it can describe the degree of LV filling dysfunction, of which the most severe forms, i.e. the pseudo normal and the restrictive filling pattern, include an assumed elevated LVFP. Since Doppler variables pseudo normalize, combining them enhances diagnostic accuracy. To our knowledge, E/e has not been viewed in relation to a semi-quantitative LV filling assessment, based on internationally recommended combinations of Doppler variables.

When LVFP is elevated, the pressure difference, physiologically required for blood flow, is maintained by increased pressure generated from the right ventricle. Pulmonary capillary wedge pressure and pulsed Doppler determinants both correlate to an invasively measured pulmonary artery pressure, clinically exemplified by secondary pulmonary artery hypertension in LV heart failure. Still, right ventricular pressure (RVp) is not routinely considered when estimating LV filling.

The clinical usefulness of the E/e filling index would depend also on its sensitivity — in relation to currently recommended non-invasive technique — to detect an elevation of LVFP. We hypothesized that the sensitivity of E/e might be lower than previously evident (from E/e set against Doppler variables one by one). As an elevated RVp is a prerequisite for an elevated LVFP, we aimed to compare the sensitivity of the E/e filling index to that of RVp, in predicting an assumed elevation of LVFP, as semi-quantitatively determined from an internationally recommended combined Doppler assessment, in patients with acute coronary syndromes (ACS).

Methods

Study population

We studied 160 consecutive patients with ACS admitted to the coronary care unit at Sahlgrenska University Hospital, Göteborg, Sweden, who were echocardiographically examined, with tissue Doppler recordings, in sinus rhythm and without any hemodynamically significant valvular disease. The echocardiogram was performed in the early stable phase (approximately three days from admission) using an ultrasonic machine (Acuson XP, Acuson/Siemens Mountain View, California) with a 2.5–4 MHz transducer.

We defined ACS as an ST-elevation or a non-ST-elevation acute myocardial infarction (AMI) or unstable angina pectoris, the latter with typical chest pain and either ECG signs of myocardial ischemia (ST depression of ≥0.1 mV or T-wave inversion in at least two adjacent leads), a minor increase in biochemical markers (CK-MB 5–10 μg/l or troponin T 0.05–0.19 μg/l) or previously diagnosed ischemic heart disease. Spirometry-verified chronic obstructive pulmonary disease in association with an RVp exceeding 30 mmHg (n = 4) resulted in exclusion, as did poor image quality or inadequate recordings of the pulsed Doppler (n = 6) or the tricuspid regurgitation velocity gradient (n = 16), leaving a total of 134 patients.

The patients were clinically categorized as having an ST-elevation AMI in 41% (n = 55), a non-ST-elevation AMI in 46% (n = 61) or unstable angina pectoris in 13% (n = 18). Prior to admission, 19% of the patients had a previous myocardial infarction, 45% had angina pectoris, 46% had systemic hypertension, 8% had symptoms LV heart failure, 20% had diabetes mellitus and 10% had undergone coronary artery by-pass surgery and/or percutaneous coronary intervention therapy.

Fifty healthy individuals, age- and sex-matched to the cases (Table 1) and selected from a randomly sampled population within the County Census base, served as controls. They were all free of sensitivity and negative predictive value of RVp support its use as an additional LV filling variable in these patients.

© 2005 The European Society of Cardiology. Published by Elsevier Ltd. All rights reserved.
cardiovascular, pulmonary, other systemic disease or chest pain, had no medication and a normal ECG. Their measured cardiovascular risk related variables were; serum-cholesterol 5.3 ± 0.7 mmol/l, serum-triglycerides 1.0 ± 0.4 mmol/l, blood pressure after 1 h rest; 129 ± 16/73 ± 6 mmHg, body mass index 23.6 ± 3.8 and 60% had never smoked.

Patients and controls underwent an identical echocardiographic examination. All enrolled participants gave their informed consent and the regional scientific ethics committee (Göteborg University) approved the protocol.

**Echocardiography and Doppler**

The examination was carried out in accordance with the recommendations of the American Society of Echocardiography. In addition, in order to optimize image quality, the subjects were, from the left recumbent position, facing the examiner, who had an extra monitor opposite and two hands free for the transducer, as an assisting technician mastered the ultrasonic machine. Registrations were made, whenever possible, in relaxed end expiratory apnoea at a sweep rate of 100 mm/s. A cut-out in the mattress facilitated a proper access to the apical LV views. We applied pulsed tissue Doppler to the septal, lateral, inferior and anterior LV basal walls. Pulsed blood pool Doppler from between the mitral tips, the upper right pulmonary vein and the LV outflow tract were recorded. Care was taken to register any tricuspid regurgitation with a small single continuous wave transducer, and in case of a non-definable pressure gradient in a patient, the signal was enhanced by transvenous contrast (agitated Haemaccel). Central venous pressure was semi-quantitatively assessed, as is routine in our laboratory, as normal, presumably 0–5 mmHg; suspected or mildly elevated, 5–10 mmHg; moderately elevated, 10–15 mmHg; or, severely elevated, 15–20 mmHg, from the dimension and breathing variation of the inferior vena cava. Central venous pressure (for calculation purposes set to 2.5, 7.5, 12.5 and 17.5 mmHg, respectively) was added to the right ventricular–right atrial pressure gradient for an estimation of systolic RVp. A normal RVp was defined as ≤30 mmHg. Ejection fraction was measured online using the biplanar disc sum method (Simpson’s rule), or (in 11%) visually estimated.

**Analyses**

Each measurement and evaluation was performed blinded to all other information. All Doppler curves were digitized for off-line analyses in a computer program, developed by our group. The pulsed aortic, mitral and pulmonary venous Doppler signals were manually outlined around their outer envelope and vertical lines were set to further define events. The blood pool peak mitral early diastolic velocity, E, and velocity at atrial contraction, A, were measured to calculate the E/A ratio. The isovolumic relaxation time (IVRT) and the deceleration time (DT) were defined. The systolic, S, and diastolic, D, pulmonary venous peak flow velocities were likewise measured to render the

**Table 1** Descriptive data, including pulsed Doppler absolute values and ratios

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>All</td>
<td>0</td>
</tr>
<tr>
<td>n (%)</td>
<td>50</td>
<td>134</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>65 ± 10</td>
<td>64 ± 10</td>
</tr>
<tr>
<td>Sex, F/M (%)</td>
<td>26/74</td>
<td>30/70</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>60 ± 8</td>
<td>66 ± 12</td>
</tr>
<tr>
<td>EF (%)</td>
<td>62 ± 4</td>
<td>53 ± 11</td>
</tr>
<tr>
<td>Volume, D (ml)</td>
<td>101 ± 25</td>
<td>109 ± 42</td>
</tr>
<tr>
<td>E/A</td>
<td>1.3 ± 0.4</td>
<td>1.2 ± 0.5</td>
</tr>
<tr>
<td>IVRT (ms)</td>
<td>89 ± 17</td>
<td>86 ± 25</td>
</tr>
<tr>
<td>DT (ms)</td>
<td>188 ± 33</td>
<td>185 ± 55</td>
</tr>
<tr>
<td>S/D</td>
<td>1.4 ± 0.4</td>
<td>1.3 ± 0.4</td>
</tr>
<tr>
<td>ΔA-waves (ms)</td>
<td>29 ± 16</td>
<td>–23 ± 37</td>
</tr>
</tbody>
</table>

0 = Normal; 1 = delayed relaxation; 2 = an isolated pathological A-wave-duration difference; 3 = pseudo normal; 4 = a restrictive filling pattern. HR = heart rate, EF = (left ventricular) ejection fraction, Volume, D = (left ventricular) diastolic volume, E/A = ratio between the early and atrial peak pulsed mitral Doppler velocities, IVRT = isovolumic relaxation time, DT = deceleration time, S/D = ratio between the systolic and diastolic peak pulsed pulmonary venous Doppler velocities, ΔA-waves = difference in the mitral and pulmonary venous-A-wave terminations, yrs = years, F/M = Females/males, bpm = beats per minute, ml = millilitre, ms = milliseconds.
S/D ratio. The temporal difference between the mitral and pulmonary venous A-waves at their point of cessation, with the nearest ECG R-wave as a reference, was established, diagnostically equivalent to the difference in mitral—pulmonary venous-a-wave duration.8

In accordance with international recommendations,7–9 we used all pulsed Doppler variables to semi-quantitatively classify each individual, with increasing degree of impaired LV filling:

**Group 0, normal**, a normal S/D ratio, a normal mitral—pulmonary venous-A-wave-duration difference, a normal E/A ratio, a normal DT and IVRT,

**Group 1, delayed relaxation**, a normal/increased S/D ratio, a normal mitral—pulmonary venous-A-wave-duration difference, a decreased E/A ratio, an increased DT and IVRT,

**Group 2, an isolated pathological A-wave-duration difference**, a pathological mitral—pulmonary venous-A-wave-duration difference, a normal/increased S/D ratio, a normal/decreased E/A ratio, a normal/increased DT and IVRT,

**Group 3, pseudo normal**, a decreased S/D ratio, a pathological mitral—pulmonary venous-A-wave-duration difference, a normal E/A and a normal DT and IVRT,

**Group 4, a restrictive filling pattern**, a decreased S/D ratio, a pathological mitral—pulmonary venous-A-wave-duration difference, an increased E/A ratio, a decreased DT and IVRT.

A mitral—pulmonary venous-A-wave-duration difference of >20 ms was regarded as abnormal.21 Reference values of E/A, DT, IVRT and S/D were defined from the control group, considering age and heart rate in regression models (see Results). Hence, prior to the LV filling classification, control correlations were used to adjust the patient variables in order to identify them as normal (within 2 SDs), increased or decreased. The most compatible diastolic filling group was then chosen, but with three of five fulfilled criteria as a minimum. Mandatory, however, for group 3, was either a 2 SD decrease in S/D ratio, or a pathological mitral—pulmonary venous-A-wave-duration difference in combination with at least 1 SD decrease in either the S/D or E/A ratio or the DT. The consensus of two doctors with long echocardiographical experience was entered.

We further merged the study population into four classes: (I) controls, and (II) patients with a presumed normal LVFP (groups 0 and 1), (III) patients with presumed normal mean LVFP but signs of an elevated end-diastolic pressure (group 2), and (IV) patients with a presumed elevated mean LVFP (groups 3 and 4).

The E/e filling index was calculated as the ratio between the peak early mitral inflow (E) and the maximal basal septal velocity (e).

**Reproducibility**

Two doctors initially independently performed a semi-quantitative LV filling assessment in all patients before their consensus decision on LV filling group. Intra observer Doppler measurement variability was investigated in 10% (14/134) of the patients.

**Statistics**

Values are presented as mean and SD, when not stated otherwise. Mann–Whitney U test investigated differences between patients and controls. Relations to diastolic groups of LV filling were evaluated by Spearman’s rank correlation. We applied logistic regression to compare the relation of E/e and RVp to Doppler-estimated LV filling.

**Results**

**Descriptive data**

Among the controls there was an age correlation for the pulsed mitral Doppler E/A ratio (r = −0.46, p = 0.0009), and the pulmonary venous S/D ratio correlated both with age (r = 0.36, p = 0.012) and heart rate (r = 0.35, p = 0.014). These relationships, which were used to define the adjusted Doppler reference limits, could be expressed as ‘E/A = 2.464 – (0.018 × age)’ and ‘S/D = −0.219 + (0.011 × age) + (0.015 × heart rate)’.

Absolute values and ratios of pulsed Doppler are presented in Table 1, and values of RVp and E/e in Table 2. Three controls (6%) were diagnosed as group 1 and the remaining as group 0. Examples of pulsed Doppler combinations for the five LV filling groups, as well as of the E/e measurement, are shown in Fig. 1.

**Reproducibility**

The inter observer concordance in semi-quantitative LV filling grading was 97% (as 130/134 patients
were identically graded). Repeated measurements in 10% of the patients revealed a coefficient of variation of: 4% for the E/A ratio, IVRT 4%, DT 5%, S/D ratio 2%, delta A-wave duration 4%, E velocity 2%, septal e velocity 5%, the E/e filling index 5% and the tricuspid velocity gradient 3%.

### Analyses of E/e and RVp

The proportion with an RVp exceeding 30 mmHg of controls (class I) and patients with a Doppler-assumed: normal LVFP (class II), elevated pressure at end-diastole only (class III) and elevated mean LVFP (class IV), are shown in Fig. 2A. Correspondingly, the proportion of subjects with an E/e > 15, 8–15, and < 8 are presented in Fig. 2B. Conversely, the patient class distribution for an RVp > 30 mmHg (n = 75) versus that of ≤30 mmHg (n = 59) is shown in Fig. 3A and likewise for an E/e > 15 (n = 22), 8–15 (n = 77) and < 8 (n = 35) in Fig. 3B.

An E/e > 15 and an RVp > 30 mmHg had the following (%): sensitivity (32/94), specificity (95/76), positive (68/59), and negative (80/97) predictive values of a Doppler-assumed elevated LVFP (class IV). Table 3. For E/e < 8 to predict an assumed normal LVFP (class I and II) these values were 46, 81, 76 and 53%, Table 4.

Systolic RVp for patients differed significantly from controls (34 ± 11 versus 21 ± 3 mmHg, p < 0.0001), as did E/e (11.2 ± 4.4 versus 7.5 ± 1.3 mmHg, p < 0.0001). Both RVp and E/e related to Doppler-assessed LV filling, for patients (r_s = 0.63 and r_s = 0.40, respectively, p < 0.0001) as well as for all individuals (r_s = 0.71 and

### Table 2  Variables related to the assessment of RVp and the E/e filling index

| Variables related to the assessment of RVp and the E/e filling index |
|----------------------------------|----------------------------------|----------------------------------|
| Controls                        | Patients                        | All                             |
| RVp (mmHg)                      | 19 ± 3                          | 29 ± 9                          |
| CVT (mmHg)                      | 3 ± 0                           | 5 ± 5                           |
| RVp (mmHg)                      | 21 ± 3                          | 34 ± 11                         |
| E (cm/s)                        | 66 ± 11                         | 64 ± 16                         |
| e Range (cm/s)                  | 3.2 ± 1.8                       | 2.7 ± 1.6                       |
| e Mean (cm/s)                   | 10.1 ± 1.8                      | 6.8 ± 1.8                       |
| e Lateral (cm/s)                | 10.9 ± 2.8                      | 8.0 ± 5.5                       |
| e Septal (cm/s)                 | 8.8 ± 1.5                       | 6.2 ± 1.8                       |
| E/e Mean                        | 6.6 ± 1.2                       | 10.1 ± 3.3                      |
| E/e Lateral                     | 6.5 ± 1.8                       | 9.2 ± 3.5                       |
| E/e Septal                      | 7.5 ± 1.3                       | 11.2 ± 4.4                      |

0 = Normal; 1 = delayed relaxation; 2 = an isolated pathological A-wave-duration difference; 3 = pseudo normal; 4 = a restrictive filling pattern. RV—RA gradient = pressure gradient between the right ventricle and right atrium. CVT = right atrial/central venous pressure. RVp = systolic right ventricular pressure. E = peak early diastolic Doppler velocity. e = maximal tissue velocity of a basal left ventricular wall. e range = the intra individual range of maximal tissue velocities of the four left ventricular basal walls, e mean = the intra individual mean of maximal tissue velocities of the four left ventricular basal walls, E/e = the E/e filling index, mmHg = millimetre Mercury, cm/s = centimetre per second.

#### Success rate

After having excluded 4% (6/156) due to inadequate Doppler recordings for the LV filling assessment, the success rates for the finally included 134 patients (and 50 controls) were: for E/A ratio: 100% (98%), IVRT: 99% (100%), DT: 100% (100%), S/D ratio 100% (98%), Delta A-wave duration 78% (96%) and E/e 100% (98%). An RVp was obtained in 89% (134/150) of the patients and 84% (42/50) of the controls.

### Discussion

We have in this study visualized the E/e filling index in relation to the combined contents of pulsed Doppler, in comparison with RVp. Our approach revealed that E/e > 15 may have a
Figure 1  Top image: examples of mitral (left) and pulmonary venous Doppler (right) constellations for the five left ventricular filling groups; 0, normal; 1, delayed relaxation; 2, an isolated pathological A-wave-duration difference; 3, pseudo normal; and 4, a restrictive filling pattern. Bottom image: example of $E$ and $e$ ($e$ from the basal septal LV wall), which constitute the $E/e$ filling index.
limited sensitivity to predict an elevated LVFP. This might not be apparent from comparisons to Doppler variables one by one. Moreover, the previously suggested cut off value for normality, $E/e < 8$, may not exclude an elevated pressure. In our study, 20% of these patients showed Doppler signs of an elevated mean LVFP, and an additional 20% at atrial contraction only.

The difficulties of LV filling assessment allow no single Doppler variable to be sufficient in itself. As a consequence, it is internationally recommended that variables are interpreted in combination. LV filling assessment includes the analysis of the biphasic, pseudo normalizable, courses for several variables, which render them different informative weight depending on the situation. A longer pulmonary venous than mitral A-wave duration, for instance, is an informative sign when present, as healthy individuals do not display it. However, the difference in A-wave duration can be difficult to register, and may also disappear as the left atrial contraction weakens, a not uncommon finding in a seriously dysfunctional left ventricle. The mitral DT, on the other hand, possesses great predictive value, for pulmonary capillary artery wedge pressure and prognosis, when registered short, but the identification of an elevated LVFP should preferably precede that stage. These well-known conditions can explain why $E/e$ was the single best non-invasive predictor of an elevated LVFP.

A moderate specificity in detecting an elevated LVFP is an expected clinical feature for RVp, as there are alternative reasons for RVp to be elevated (pulmonary disease or embolism etc.). The LV filling history of the patient (i.e., the variations in pressure over time, for instance with physical activity, intermittent ischemia, medications etc.) may also interfere, since longstanding pulmonary hypertension can lead to persistently increased resistance in the pulmonary circulation. Pulmonary artery pressure, as well as its relation to pulmonary capillary wedge pressure, varies considerably between patients. RVp can therefore not be used as a direct measurement of LV filling. Nevertheless, it has been shown to decrease if heart failure is treated, with concomitant

Figure 2 The percentage individuals of class I, controls; class II, patients with an assumed normal LVFP; class III, patients with signs of an elevated end-diastolic pressure; and class IV, patients with an assumed elevated mean LVFP, who display (A) an estimated $RVp > 30$ mmHg (black bars), (B) $E/e > 15$, 8–15 and <8 (black, grey and white bars).

Figure 3 The distribution of class II, patients with assumed normal LVFP (white bar area); class III, patients with signs of an elevated end-diastolic pressure (grey bar area); and class IV, patients with an assumed elevated LVFP (black bar area), in percentages of all patients with (A) an estimated $RVp > 30$ mmHg (left bar) and $\leq 30$ mm Hg (right bar), (B) $E/e > 15$ (left bar), 8–15 (middle bar) and <8 (right bar).
improvement of the non-invasive LV filling variables.\textsuperscript{24,25}

In the present study, intensified pharmacological treatment — according to the clinical condition on and after admission — could hence have contributed to reduce the specificity of RVp. Even though medications can influence both the Doppler signals and RVp through altered loading conditions, variables may not be equally affected,\textsuperscript{25} for instance due to the less reversible changes in the pulmonary vasculature. However, in our study, the high sensitivity of RVp strongly supported the accuracy of our combined Doppler assessment. In the clinical setting, a reliably registered low RVp should rule out a currently elevated LVFP. If considered with care, RVp could also add information when estimating LV filling. In heart failure patients with a restrictive LV filling pattern and secondary pulmonary hypertension, one mechanism through which the LV function may be influenced is by ventricular interaction,\textsuperscript{16} but whether this has played a role for any of our patients can only be speculated upon.

Our study population — patients with ACS — is not identical to that of previous studies exploring the E/e filling index,\textsuperscript{27–29} even though coronary artery disease has been represented.\textsuperscript{2,3} Clinically, patients with ACS form an important subset of patients with LV filling dysfunction. Methodologically, differences in study populations might account for differences in results, as ACS/coronary artery disease usually affect the left ventricle asymmetrically. There is not, to our knowledge, a consensus with respect to which LV wall to calculate E/e from. Some investigators have, when using the septum, excluded individuals with septal wall motion abnormalities.\textsuperscript{2} In our population, that would have excluded the majority of the patients. It should be noted, however, that when using the septum, information is gathered also from the right ventricle. If we had applied the present E/e values to calculations based on the lateral wall,\textsuperscript{12,27,28} E/e would have recognized even fewer patients, since lateral tissue velocities tend to be higher, unless the lateral wall is exclusively affected. Also a mean value of all the four LV wall velocities would require lower upper limits for the E/e filling index.

Our data do not restrain the E/e filling index from being of possible greater value in sub groups of patients, where ordinary Doppler variables are less easily achieved and/or correlate less well with LVFP, such as in patients with atrial fibrillation\textsuperscript{29} or hypertrophic cardiomyopathy.\textsuperscript{27} This, however, goes beyond the scope of our study, as we can make no conclusion concerning patient groups other than those included here.

All in all, we do not find our results contradictory of those of Ommen et al., who registered scattering for E/e 8–15, where traditional Doppler variables are less easily achieved and/or correlate less well with LVFP, such as in patients with atrial fibrillation\textsuperscript{29} or hypertrophic cardiomyopathy.\textsuperscript{27} This, however, goes beyond the scope of our study, as we can make no conclusion concerning patient groups other than those included here.

### Study limitations/concerns

Without access to invasively measured LV pressures we obviously cannot, for each individual, guarantee our combined Doppler assessment to have predicted or excluded an elevation of LVFP correctly. Some error of assessment is inevitable and possibly also accounts for the failure of RVp to have identified all patients with a presumed elevation of LVFP. One advantage of the E/e index is its applicability, also when acoustic windows are poor. Thus, patients excluded due to lack of a measurable RVp may have had adequate signals for the E/e calculation.

---

**Table 3** Class I, II, III versus IV distribution with E/e ≤ or >15 and RVp ≤ or >30 mmHg

<table>
<thead>
<tr>
<th></th>
<th>Class I, II, III (n)</th>
<th>Class IV (n)</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E/e ≤ 15</td>
<td>129</td>
<td>32</td>
<td>161</td>
</tr>
<tr>
<td>E/e &gt; 15</td>
<td>7</td>
<td>15</td>
<td>22</td>
</tr>
<tr>
<td>Total</td>
<td>136</td>
<td>47</td>
<td>183</td>
</tr>
<tr>
<td>RVp ≤ 30 mmHg</td>
<td>98</td>
<td>3</td>
<td>101</td>
</tr>
<tr>
<td>RVp &gt; 30 mmHg</td>
<td>31</td>
<td>44</td>
<td>75</td>
</tr>
<tr>
<td>Total</td>
<td>129</td>
<td>47</td>
<td>176</td>
</tr>
</tbody>
</table>

Class I = controls; Class II = patients with a Doppler-assumed normal mean left ventricular filling pressure (LVFP); Class III = patients with Doppler signs of an elevated end-diastolic pressure but normal mean LVFP; Class IV = patients with a Doppler-assumed elevated mean LVFP. RVp = systolic right ventricular pressure, E/e = the E/e filling index, mmHg = millimetre Mercury.

**Table 4** Class I, II versus III, IV distribution with E/e < or ≥ 8

<table>
<thead>
<tr>
<th></th>
<th>Class I, II (n)</th>
<th>Class III, IV (n)</th>
<th>Total (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>E/e &lt; 8</td>
<td>48</td>
<td>15</td>
<td>63</td>
</tr>
<tr>
<td>E/e ≥ 8</td>
<td>57</td>
<td>63</td>
<td>120</td>
</tr>
<tr>
<td>Total</td>
<td>105</td>
<td>78</td>
<td>183</td>
</tr>
</tbody>
</table>

See Table 3 for legend.
Conclusions

The sensitivity of $E/e > 15$ to detect a Doppler- 
assumed elevated LVFP was only one third of that 
of $RVp > 30$ mmHg. Moreover, $E/e < 8$ could co- 
effect with Doppler signs of affected LV pressures. 
Our findings indicate a limitation in the clinical 
usefulness for $E/e$, as a single variable, to predict 
or exclude an elevation of LVFP in patients with 
ACS. Furthermore, our data allow us to suggest 
that RVp is included in the LV filling assessment of 
these patients, especially as a negative predictor 
of an elevated LVFP, if RVp is reliably registered as 
being normal, $\leq 30$ mmHg.

Acknowledgements

The authors are grateful to the staff at the 
Departments of Clinical Physiology and Cardiology 
for their valuable assistance with the patient 
investigations. We also thank Ingemar Wallentin, 
M.D., Ph.D., for consult work as the second LV 
investigations. We also thank Ingemar Wallentin, 
Departments of Clinical Physiology and Cardiology 
Go¨taland Region, the Vardal Foundation, Go¨teborg 
University and the Go¨teborg Medical Society sup-
ported this study.

References

1. Nagues SF, Middleton KJ, Kopele HA, Zoghbi WA, 
Quinones MA. Doppler tissue imaging: a noninvasive tech-
nique for evaluation of left ventricular relaxation and 
estimation of filling pressures. J Am Coll Cardiol 1997;30: 
1527–33.
2. Kim YJ, Sohn DW. Mitral annulus velocity in the estimation 
of left ventricular filling pressure: prospective study in 200 
3. Ommen SR, Nishimura RA, Appleton CP, Miller FA, Oh JK, 
Redfield MM, et al. Clinical utility of Doppler echocardiog-
raphy and tissue Doppler imaging in the estimation of 
left ventricular filling pressures: a comparative simulta-
neous Doppler-catherization study. Circulation 2000;102: 
1788–94.
4. Hills GS, Moller JE, Pelikika PA, Gersh BJ, Wright RS, 
Ommen SR, et al. Noninvasive estimation of left ventricular 
filling pressure by $E/e$ is a powerful predictor of survival 
after acute myocardial infarction. J Am Coll Cardiol 2004; 
5. Appleton CP, Hatle LK, Popp RL. Relation of transmural flow 
velocity patterns to left ventricular diastolic function: new 
insights from a combined hemodynamic and Doppler echo-
6. Rossvoll O, Hatle LK. Pulmonary venous flow velocities 
recorded by transthoracic Doppler ultrasound: relation to 
left ventricular diastolic pressures. J Am Coll Cardiol 1993; 
7. Appleton CP, Jensen JL, Hatle LK, Oh JK. Doppler 
evaluation of left and right ventricular diastolic function: 
a technical guide for obtaining optimal flow velocity 
8. Oh JK, Appleton CP, Hatle LK, Nishimura RA, Seward JB, 
Tajik AJ. The noninvasive assessment of left ventricular 
diastolic function with two-dimensional and Doppler echo-
Jue J, et al. Canadian consensus recommendations for the 
measurement and reporting of diastolic dysfunction by 
echocardiography: from the Investigators of Consensus on 
Diastolic Dysfunction by Echocardiography. J Am Soc 
Riccardi G, et al. Invasive and non-invasive determinants of 
pulmonary hypertension in patients with chronic heart 
Determinants of pulmonary hypertension in left ventricular 
12. Khouri SJ, Maly GT, Suh DD, Walsh TE. A practical approach 
to the echocardiographic evaluation of diastolic function. 
Spectral pulsed tissue Doppler imaging in diastole: a tool 
to increase our insight in and assessment of diastolic 
Thelle D, Caidahl K. Timing of regional left ventricular 
lengthening by pulsed tissue Doppler. J Am Soc Echocar-
diogr 2004;17:307–12.
15. Schiller NB, Shah PM, Crawford M, DeMaria A, Devereux R, 
Feigenbaum H, et al. Recommendations for quantitation of 
the left ventricle by two-dimensional echocardiography. 
American Society of Echocardiography Committee on Stan-
dards, Subcommittee on Quantitation of Two-Dimensional 
A new formula for echo-Doppler estimation of right ventricu-
17. Yock PG, Popp RL. Noninvasive estimation of right ventricu-
lar systolic pressure by Doppler ultrasound in patients with 
18. Skjaerpe T, Hatle L. Noninvasive estimation of systolic 
pressure in the right ventricle in patients with tricuspid 
In: Braunwald E, editor. Heart disease. A textbook of 
cardiovascular medicine. 5th ed. Philadelphia: WB Saunders; 
20. Caidahl K, Kazzam E, Lidberg J, Neumann Andersen G, 
Nordanstig J, Rantapaa Dahlqvist S, et al. New concept in 
echocardiography: harmonic imaging of tissue without use 
21. Appleton CP, Galloway JM, Gonzalez MS, Gaballa M, 
Basnight MA. Estimation of left ventricular filling pressures 
using two-dimensional and Doppler echocardiography in 
adult patients with cardiac disease. Additional value of 
analyzing left atrial size, left atrial ejection fraction and 
the difference in duration of pulmonary venous and mitral 
flow velocity at atrial contraction. J Am Coll Cardiol 1993; 
22. Giannuzzi P, Imparato A, Temporelli PL, de Vito F, Silva PL, 
Scappellato F, et al. Doppler-derived mitral deceleration 
time of early filling as a strong predictor of pulmonary 
capillary wedge pressure in postinfarction patients with left 
ventricular systolic dysfunction. J Am Coll Cardiol 1994;23: 
1630–7.


