European Journal of Echocardiography (2010) **11**, 703–710
doi:10.1093/ejechocard/jeq047

Validation of an echo-Doppler decision model to predict left ventricular filling pressure in patients with heart failure independently of ejection fraction

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Received 11 January 2010; accepted after revision 10 March 2010; online publish-ahead-of-print 17 April 2010

Aims To test a decision model for non-invasive estimation of left ventricular filling pressure (LVFP) in patients with left ventricular (LV) dysfunction and a wide range of ejection fractions (EF).

Methods and results In patients with LV dysfunction ($n = 270$; EF = 42 ± 16%), classification and regression tree (CART) analysis was used to generate a model for the prediction of elevated LVFP, defined as pulmonary capillary wedge pressure (PCWP) >15 mmHg, in a derivation cohort ($n = 178$). At each step of the decision tree, nodes including single or multiple criteria connected by Boolean operators were tested to achieve the best information entropy gain. Averaged mitral-to-myocardial early velocities ratio (E/e') ≥13 OR E-wave deceleration time <150 ms was closely associated with elevated LVFP. Alternatively, prediction of PCWP >15 mmHg needed the following criteria to be satisfied: (i) intermediate E/e' ($13 > E/e' > 8$); (ii) left atrial volume index >40 mL/m^2 OR ratio of mitral E-wave and colour M-mode propagation velocity >2 OR difference in duration of pulmonary vein and mitral flow at atrial contraction >30 ms; (iii) estimated pulmonary artery systolic pressure >35 mmHg. Patients were correctly allocated according to PCWP with an 87% sensitivity and a 90% specificity. Compared with the best single parameter estimating LVFP, a 17% relative increase in accuracy was achieved in patients with EF >50%. The model was prospectively validated in a testing group ($n = 92$): 80% sensitivity, 78% specificity.

Conclusion This sequential testing is useful to non-invasively predict LVFP in patients with LV dysfunction, especially in those with preserved EF.

Keywords Echocardiography • Diastole • Heart failure

Introduction

Non-invasive estimation of left ventricular filling pressure (LVFP) is paramount in the evaluation and treatment of patients with left ventricular (LV) dysfunction and heart failure (HF). Several echo-Doppler parameters have been reported to provide non-invasive means for estimating LVFP.[1,2] However, their widespread clinical use has been affected by feasibility,[3] need for off-line calculations,[4] and lack of applicability to patients irrespective of LV size and ejection fraction (LVEF).[5] It has been recently suggested that the

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diagnostic flowcharts based on multiple echocardiographic and Doppler parameters may be particularly helpful for diagnosing elevated LVFP. It is important, though, that these algorithms should be statistically derived and validated with the use of variables that are not affected by changes with age.[2,6] Among statistical methods, the classification and regression tree (CART) analysis may be useful to design models for the estimation of LVFP that include combinations of echo-Doppler parameters.[7] In an attempt to investigate whether a decision model based on CART analysis was valuable to obtain a non-invasive estimate of LVFP independently of LVEF, a study was performed in patients with LV dysfunction and preserved or reduced LVEF undergoing both Doppler echocardiographic examination and haemodynamic measurement of pulmonary capillary wedge pressure (PCWP).

Methods

Study patients

Two-hundred and seventy consecutive patients with LV dysfunction and a wide range of LVEF identified on the echocardiogram were prospectively enrolled and underwent diagnostic right-heart catheterization at a tertiary cardiovascular centre. An echo-Doppler examination was performed within 1 h of cardiac catheterization. Patients with inadequate acoustic window ($n = 12$), atrial fibrillation or flutter ($n = 41$), mitral stenosis ($n = 43$), organic or severe mitral regurgitation ($n = 57$), previous mitral valvuloplasty ($n = 1$), moderate-to-severe aortic regurgitation ($n = 35$), mechanical valve prosthesis ($n = 1$), and permanent pacemaker ($n = 3$) were excluded. Elevated LVFP was defined by a PCWP >15 mmHg.[8] All patients were studied while haemodynamically stable and on medical therapy. Patients receiving infusion therapy with inotropic agents and diuretics were also excluded. The research protocol was approved by the internal review board, and all patients gave written informed consent.

Doppler echocardiography

Transthoracic two-dimensional and Doppler echocardiography was performed with an Acuson Sequoia C256 ultrasound instrument (Mountain View, CA, USA) with second-harmonic imaging and a 3.5 MHz transducer. M-mode and two-dimensional measurements, including LV mass and volumes and biplane left atrial volume index, were measured according to recent recommendations.[9] From the pulsed-Doppler mitral velocity tracings, the following measurements were made: peak E diastolic wave velocity, peak A wave velocity, and E-wave deceleration time (EDT). From mitral and pulmonary vein flow recordings, the difference in duration of pulmonary vein flow and mitral flow velocity at atrial contraction was measured (AR dur − A dur). Doppler tissue-imaging (DTI) longitudinal velocities were recorded with the sample volume placed at the junction between the septal and lateral LV wall and the mitral annulus in the four-chamber view, and peak early myocardial wave (e') velocities were measured. The ratio of mitral E peak velocity and averaged e' velocity (E/e') was calculated. Measures of colour M-mode Doppler flow propagation velocity (V_p) as the slope of the first aliasing velocity were achieved during early filling as described previously.[10] Mitral regurgitation severity was graded according to the vena contracta method.[11] Doppler-derived pulmonary artery systolic pressure (PAP_s) was estimated from tricuspid regurgitation velocity according to a previously described method, and a cut-off value of 35 mmHg was set to identify patients with pulmonary hypertension.[12] In case of weak or poor velocity signals, a saline medium for contrast-enhancement was utilized.[13] All measurements were averaged over three consecutive beats.

Cardiac catheterization

Right-heart catheterization was carried out using a 7 F MPA1 catheter (Cordis, Miami, FL, USA). Mean PCWP was determined automatically by the monitoring system (Horizon 9000 WS, Mennen Medical Ltd, Israel). The true pulmonary wedge position in a distal pulmonary artery was verified radiologically and by the typical phasic pressure waveforms. Cardiac output was assessed by the Fick technique. Haemodynamic measurements were obtained before any injection of the contrast medium.

Statistical analysis

Comparisons between Doppler echocardiographic variables and haemodynamic measures were analysed by the standard parametric methods. Sensitivity, specificity, positive predictive value, and negative predictive value were calculated by standard formulas. CART analysis was used to generate the best decision tree starting from a group of pre-definite attributes. The following predictors of PCWP >15 mmHg were considered in the analysis: EDT <150 ms; AR dur − A dur >30 ms; $E/e' \geq 13$; $13 > E/e' > 8$; left atrial volume index >40 mL/m^2; ratio of mitral E-wave and colour M-mode flow propagation velocity (E/V_p) >2, and abnormal LV mass (defined as LV wall mass index >122 g/m^2 in women and >149 g/m^2 in men).[10,14] The diagnostic accuracy of the CART algorithm was compared with that of every single parameter using the exact binomial test. The relative increases in accuracy observed in patients with LVEF >50 and ≤50% were compared using the Fisher exact test. The sample size for this study was calculated under the hypothesis that the best algorithm generated by CART analysis would have provided a significant increase in the overall accuracy for the prediction of normal or raised LVFP in comparison with the best single criterion. Assuming that the best single predictor variable of increased LVFP would have correctly identified 80% of subjects in the entire study population, a sample size of 173 or more subjects would have achieved 80% power in detecting a relative increase of ≥10% in the overall accuracy (corresponding to an effect size of 0.19, i.e. a small effect) using a two-sided binomial test at a 0.05 significance level. The first 178 patients in the study population (derivation cohort; September 2002–June 2005) were analysed to develop the model for predicting PCWP >15 mmHg. Then, the validity of the model was prospectively tested using data from 92 additional patients (validation cohort; June 2005–August 2008).

Results

Patient characteristics

Mean age of the study population was 67 years (range 27–87, males 169). Mean LVEF was 42 ± 16%. Twenty-nine per cent of patients were in stage B HF, 67% in stage C, and 4% in stage D, according to the staging system proposed in the guidelines of the American College of Cardiology/American Heart Association for the Diagnosis and Management of Chronic Heart Failure in the Adult.[15] Significant coronary narrowings were observed in 49% of patients. Thirty-two per cent of patients had a history of acute myocardial infarction. Idiopathic dilated cardiomyopathy, as defined as LV systolic dysfunction and dilation in the absence of significant coronary artery disease on coronary angiography, was

Table 1 Demographic, clinical, haemodynamic, and Doppler echocardiographic variables in patients of the derivation cohort and in patients of the validation cohort

Variable	Derivation cohort (n = 178)	Validation cohort (n = 92)	P-value
Age (years)	68 ± 11	67 ± 12	NS
Percentage of women	39	35	NS
HR (beats/min)	76 ± 13	72 ± 13	NS
LBBB >150 ms (%)	11	10	NS
LBBB 120–150 ms (%)	9	11	NS
NYHA class >2 (%)	44	37	NS
Therapy			
Diuretics (%)	72	66	NS
ACE-inhibitors (%)	75	67	NS
Nitrates (%)	30	16	0.012
Anti-aldosterone drugs (%)	44	43	NS
Digoxin (%)	15	10	NS
Beta-blockers (%)	62	53	NS
Haemodynamics			
PCWP (mmHg)	18 ± 7	18 ± 8	NS
CO (L/min)	4.3 ± 1.2	4.4 ± 1.1	NS
CI (L/min/m^2)	2.3 ± 0.6	2.4 ± 0.5	NS
Echocardiography			
LV EDV$_i$ (mL/m^2)	107 ± 42	94 ± 33	0.011
LV ESV$_i$ (mL/m^2)	68 ± 40	57 ± 33	0.025
LVEF (%)	41 ± 16	44 ± 15	NS
Mitral regurgitation[a] (%)	56	40	0.013
VCW ≥0.5 cm (%)	14	10	NS
LV mass index (g/m^2)	140 ± 42	136 ± 44	NS
LA volume index (mL/m^2)	44 ± 10	41 ± 12	NS
E/A	1.4 ± 1.3	1.3 ± 0.9	NS
EDT (ms)	175 ± 61	175 ± 60	NS
AR dur − A dur (ms)	37 ± 26	31 ± 28	NS
E' septal (cm/s)	8 ± 4	8 ± 3	NS
E' lateral (cm/s)	9 ± 3	8 ± 2	NS
E/e' septal	13 ± 7	12 ± 7	NS
E/e' lateral	11 ± 5	11 ± 5	NS
E/e' mean	12 ± 6	12 ± 6	NS
V_p (cm/s^2)	45 ± 18	42 ± 13	NS
E/V_p	2.1 ± 0.8	2.2 ± 0.8	NS
PAP$_s$ (mmHg)	41 ± 11	40 ± 14	NS

HR, heart rate; LBBB, left bundle branch block; PCWP, pulmonary capillary wedge pressure; CO, cardiac output; CI, cardiac index; LV, left ventricular; EDV$_i$, end-diastolic volume index; ESV$_i$, end-systolic volume index; EF, ejection fraction; VCW, vena contracta width; LA, left atrial; EDT, E-wave deceleration time; AR dur − A dur, difference in duration of pulmonary vein flow and mitral flow velocity at atrial contraction; e′, early mitral annular diastolic velocity; E/e', ratio of mitral to myocardial early velocities; V_p, colour M-mode flow propagation velocity; E/V_p ratio of mitral E-wave and colour M-mode flow propagation velocity; PAP$_s$, pulmonary artery systolic pressure.
[a]More than trivial.

present in 30% of patients. Mitral regurgitation was present in 50% of patients, and aortic valve disease in 39%. The characteristics of the study patients (derivation cohort and validation cohort) are listed in *Table 1*. *Table 2* shows clinical and Doppler echocardiographic variables of patients of the derivation cohort divided according to LVEF ≤50% or >50%. PCWP >15 mmHg was present in 56% of the study patients, 101 in the derivation cohort (75 among patients with LVEF ≤50% and 26 among patients with LVEF >50%) and 51 in the validation cohort.

Feasibility of acquisition of echo-Doppler parameters

Left atrial volume measurement and mitral flow recordings were obtained in 100% of study patients. DTI and colour M-mode signals were recorded in 99 and 90%, respectively. Pulmonary vein flow retrograde velocity wave signals were obtained in 91%. Estimates of PAP$_s$ from tricuspid peak regurgitation velocity were obtained in 76% of patients at baseline, whereas after saline enhancement they were determined in 94%.

Table 2 Demographic, clinical, haemodynamic, and Doppler echocardiographic variables in patients grouped according to left ventricular ejection fraction

Variable	EF ≤50% (*n* = 123)	EF >50% (*n* = 55)	*P*-value
Age (years)	66 ± 11	71 ± 12	0.0045
Percentage of women	30	58	0.0004
HR (beats/min)	76 ± 13	77 ± 13	NS
LBBB >150 ms (%)	14	5	NS
LBBB 120–150 ms (%)	9	9	NS
NYHA class >2 (%)	52	27	0.0021
Therapy			
Diuretics (%)	81	49	<0.0001
ACE-inhibitors (%)	81	60	0.0025
Nitrates (%)	29	31	NS
Anti-aldosterone drugs (%)	53	20	<0.0001
Digoxin (%)	20	4	0.0041
Beta-blockers (%)	72	38	<0.0001
Haemodynamics			
PCWP (mmHg)	19 ± 8	16 ± 6	0.0045
CO (L/min)	4.1 ± 1.1	4.6 ± 1.6	0.017
CI (L/min/m^2)	2.2 ± 0.5	2.6 ± 0.7	<0.0001
Echocardiography			
LV EDV$_i$ (mL/m^2)	124 ± 38	68 ± 19	<0.0001
LV ESV$_i$ (mL/m^2)	85 ± 35	27 ± 9	<0.0001
LVEF (%)	32 ± 9	61 ± 6	<0.0001
Mitral regurgitation[a] (%)	64	36	0.0005
VCW ≥0.5 cm (%)	18	5	0.0027
LV mass index (g/m^2)	158 ± 37	101 ± 22	<0.0001
LA volume index (mL/m^2)	46 ± 11	40 ± 8	0.0005
E/A	1.6 ± 1.5	1.0 ± 0.7	0.0023
EDT (ms)	160 ± 54	210 ± 61	<0.0001
AR dur − A dur (ms)	41 ± 28	28 ± 19	0.0022
E′ septal (cm/s)	7 ± 3	10 ± 5	0.0002
E′ lateral (cm/s)	8 ± 3	10 ± 3	0.0043
E/e′ septal	14 ± 7	11 ± 6	0.0086
E/e′ lateral	12 ± 6	10 ± 3	0.0102
E/e′ mean	13 ± 6	10 ± 4	0.0028
V_p (cm/s^2)	42 ± 13	52 ± 24	0.0002
E/V_p	2.2 ± 0.9	1.9 ± 0.7	0.033
PAP$_S$ (mmHg)	43 ± 12	37 ± 10	0.0021

For abbreviations, see *Table 1*.
[a]More than trivial.

Classification and regression tree analyses

The rank order of single or combined echo-Doppler parameters to predict elevated LVFP was derived using the statistical method. The algorithm identified *E*/e′ ≥13 OR EDT <150 ms (logical OR, that means at least one) as the root node. Patients who fulfilled the first node were categorized as having raised PCWP, and no further criteria were needed. For the remaining patients, 13 > *E*/e′ > 8 was generated by CART analysis as the second decision node. Patients who did not fulfil this criterion were considered as having normal LVFP, and no further criteria were needed. For the remaining patients, CART analysis generated a third complex node that comprised AR dur − A dur >30 ms OR left atrial volume index >40 mL/m^2 OR E/V_p >2. If none of the criteria of the third node was present, a normal LVFP was definitely attributed. Finally, for patients showing at least one positive criterion of the third node, the acquisition of PAP$_s$ was deemed necessary to discern those with the higher probability of elevated LVFP.

The rank-based CART model exhibited a 9.8% ($P = 0.0071$) relative increase in accuracy with respect to the best single performing parameter, i.e. EDT. *Table 3* illustrates the predictive accuracies of echocardiographic and Doppler parameters for estimating LVFP. *Figure 1A* depicts the final tree generated by CART analysis for the prediction of PCWP >15 or ≤15 mmHg. In *Figure 2A*,

Table 3 Sensitivity, specificity, positive predictive value, and negative predictive value of Doppler and echocardiographic variables in predicting pulmonary capillary wedge pressure >15 mmHg in the 178 patients of the derivation cohort

	Accuracy	Sensitivity	Specificity	PPV	NPV
EDT <150 ms	80	67	97	97	69
AR dur − A dur >30 ms	76	73	80	83	70
$E/e' \geq 13$	74	59	95	94	64
LA volume index >40 mL/m^2	70	71	68	74	64
$E/V_p > 2$	65	55	78	76	58
CART model	88	87	90	92	84

PPV, positive predictive value; NPV, negative predictive value. For other abbreviations see *Table 1*.

the comparative accuracies of echo-Doppler parameters and the CART model are presented. As far as the ability of the CART model to predict LVFP in patients with more than mild mitral regurgitation, a similar degree of accuracy in the estimation of LVFP was achieved in patients with a vena contracta width >0.5 cm.

The CART model developed from the derivation cohort was tested for its ability to detect increased LVFP in the validation cohort. Correct identification of raised or normal PCWP was achieved in 79% of patients (sensitivity 80%, specificity 78%, positive predictive value 82%, negative predictive value 76%). *Table 4* shows the percentages of patients with Doppler and echocardiographic parameters suggestive of elevated LVFP in the two cohorts.

Subgroup analysis

CART analysis was also carried out in patients of the derivation cohort divided according to the presence of reduced or preserved LVEF (*Figure 1B* and *C*). In patients with LVEF ≤50% ($n = 123$), the first node including $E/e' \geq 13$ or EDT <150 ms correctly identified 65 out of 75 patients with PCWP >15 mmHg. The whole CART model allowed correct detection of increased LVFP in further six patients with PCWP >15 mmHg, and correctly categorized 43 out of 48 patients with PCPW ≤15 mmHg (*Figure 2B*).

In patients with LVEF >50% ($n = 55$), $E/e' \geq 13$ or EDT <150 ms identified only 11 out of 26 patients with PCWP >15 mmHg at the first decision node. However, application of the whole CART model allowed correct diagnosis of raised LVFP in further six patients, and correctly categorized as normal 26 out of 29 patients with PCWP ≤15 mmHg (*Figure 2C*; *Table 5*). When the diagnostic accuracy provided by CART analysis was compared with that obtained using the best single echo-Doppler predictor in the two subgroups, the relative increase in accuracy was higher in patients with LVEF >50% (17.2%) than that with LVEF ≤50% (4.6%; $P = 0.034$).

Discussion

The main finding of this study is that the sequential testing by CART analysis of multiple echocardiographic and Doppler parameters has superior sensitivity and specificity compared with the standard approach in identifying an increased LVFP in patients with a wide range of LVEF. This grading system seems particularly helpful in patients with LVEF >50%, whereas its contribution could be less important in patients with LVEF ≤50%.

Development of the model

CART analysis is a tree-building statistical method that employs Boolean logic and allows generation of predictive models based on sequential decision rules. This analysis is particularly valuable when there are many variables to choose from (connectable by AND or OR Boolean operators), as it can select those that are the most important in predicting the target variable in terms of Shannon entropic information. It generates a final decision tree characterized by the highest entropy gain.[16]

In this study, a number of Doppler and echocardiographic variables, single or in combination, that have been associated with increased LVFP were tested to build the best predictive model. As a result, a decision tree was obtained by ranking Doppler and echocardiographic variables according to their ability to predict a PCWP >15 mmHg. The dichotomization of estimated PCWP at a single cut-off of 15 mmHg followed the findings of Stevenson *et al.*,[17] who demonstrated that the outcome of HF patients can be considerably improved if a PCWP ≤15 mmHg was achieved as a result of optimized medical therapy, although it was generally unfavourable when PCWP was persistently above 15 mmHg.

Comparison with literature algorithms

The estimation of LVFP in patients with normal LVEF is more challenging than in patients with depressed LVEF.[18] In this group, several algorithms of different Doppler and echocardiographic parameters have been proposed.[2,6,14,19,20] We found that the application of CART analysis to patients with preserved LVEF was associated with a 17% increment in predicting elevated LVFP, which is likely to have significance in the clinical setting.

The results of our study confirm the value of the sequential diagnostic approach recently proposed by the consensus statement of the European Society of Cardiology in order to diagnose diastolic HF.[6] This flowchart to predict LVFP is centred around the E/e' ratio, which is widely recognized as one of the cornerstone for the evaluation of diastolic dysfunction, especially because of its easy acquisition and reproducibility.[21] In the recent recommendations of the European Association of Echocardiography for the

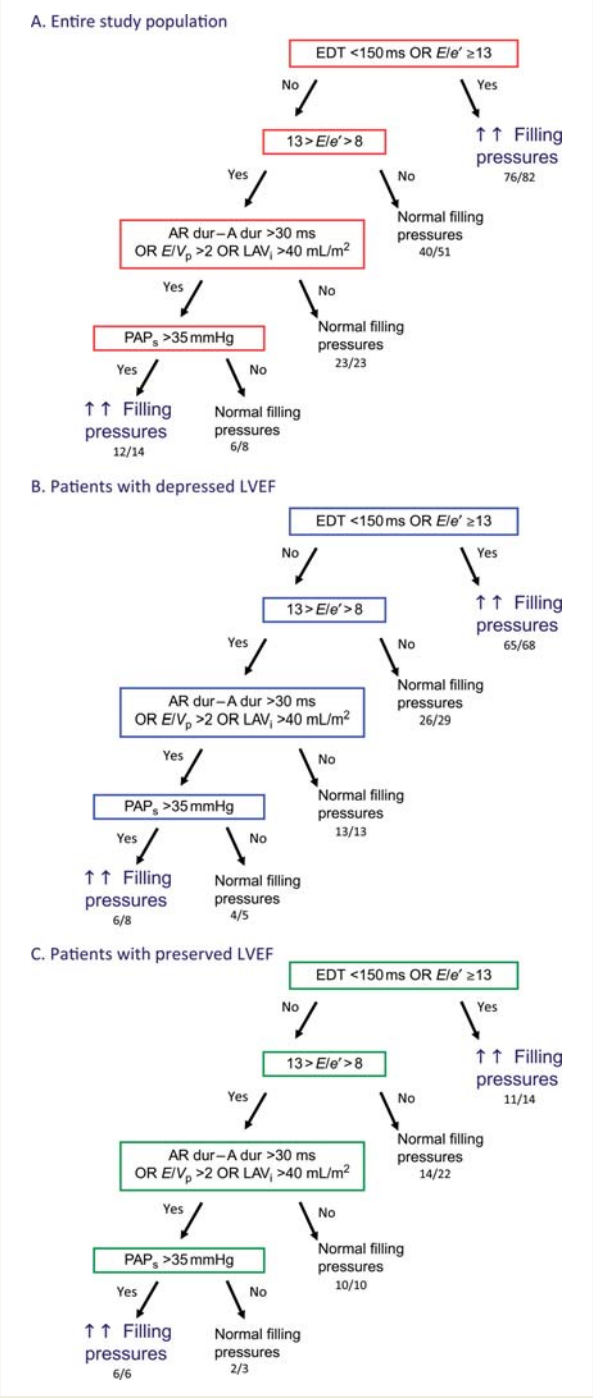

Figure 1 CART-based predictive model of elevated pulmonary capillary wedge pressure constructed with Doppler and echocardiographic variables. (*A*) Entire study population. (*B*) Patients with depressed left ventricular ejection fraction. (*C*) Patients with preserved left ventricular ejection fraction. Variables are connected by OR Boolean operators so that the whole box response is positive if at least one criterion is satisfied, and negative if all criteria are not satisfied. EDT, E-wave deceleration time; *E*/*e*′, ratio of mitral to myocardial early velocities; AR dur − A dur, difference in duration of pulmonary venous and mitral flow at atrial contraction; LAV_i, left atrial volume index; E/V_p, ratio of mitral E-wave and Colour M-mode flow propagation velocity; PAP_s, pulmonary artery systolic pressure.

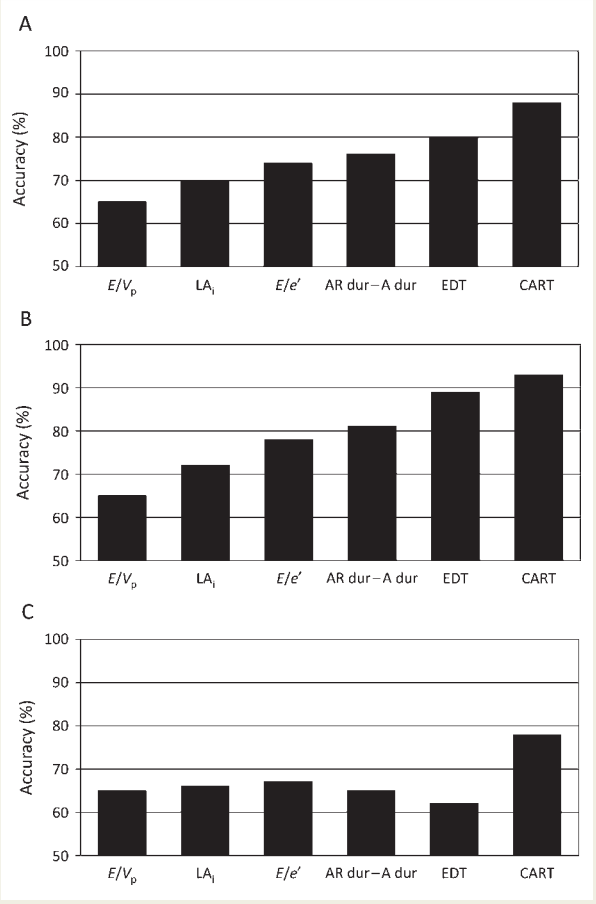

Figure 2 Comparative accuracies of Doppler and echocardiographic variables in predicting pulmonary capillary wedge pressure >15 mmHg. CART analysis, including mitral and pulmonary vein flow variables, tissue Doppler, colour M-mode flow propagation velocity, and left atrial volume index, was better than any single-parameter LVFP estimate at identifying patients with elevated pulmonary capillary wedge pressure in the entire study population (*A*), in patients with depressed ejection fraction (*B*), and in those with preserved ejection fraction (*C*). For abbreviations, see *Figure 1*.

evaluation of LV diastolic function by echocardiography,[2] an algorithm has been proposed in patients with preserved LVEF. This emphasized that an averaged *E*/*e*′ ratio ≥13 is almost invariably associated with an increased LVFP, whereas confirmation of the diagnosis in the presence of an *E*/*e*′ ratio ranging from 9 and 12 needs other non-invasive investigations, including AR dur − A dur >30 ms, left atrial enlargement, positive response to the Valsalva manoeuvre and PAP_s >35 mmHg.

In the CART model, the combination of *E*/*e*′ ≥13 OR EDT <150 ms was selected first because of the highest entropy gain for the prediction of increased LVFP. The next steps almost followed the algorithm proposed by the European Association of Echocardiography. A normal LVFP was attributed with *E*/*e*′ ≤8, whereas diagnostic evidence of increased LVFP with an intermediate *E*/*e*′ ratio required the implementation of other criteria. Patients were classified as having normal LVFP if AR dur − A

Table 4 Percentages of patients with Doppler and echocardiographic parameters suggestive of elevated left ventricular filling pressure

Variable	Derivation cohort ($n = 178$)	Validation cohort ($n = 92$)	*P*-value	EF ≤50% ($n = 123$)	EF >50% ($n = 55$)	*P*-value
$E/e' \geq 13$	35	32	NS	41	20	0.006
EDT <150 ms	39	36	NS	51	13	<0.0001
LA volume index >40 mL/m^2	54	45	NS	62	38	0.003
AR dur − A dur >30 ms	49	54	NS	57	33	0.005
$E/V_p > 2$	41	44	NS	42	37	NS

For abbreviations, see *Table 1*.

Table 5 Sensitivity, specificity, positive predictive value, and negative predictive value of Doppler and echocardiographic variables in predicting pulmonary capillary wedge pressure >15 mmHg in the 178 patients of the derivation cohort, categorized according to left ventricular ejection fraction

	EF ≤50%				EF >50%			
	Sensitivity	Specificity	PPV	NPV	Sensitivity	Specificity	PPV	NPV
EDT <150 ms	83	98	98	78	23	97	86	58
AR dur − A dur >30 ms	81	80	86	73	48	81	69	64
$E/e' \geq 13$	66	96	96	65	36	93	82	63
LA volume index >40 mL/m^2	77	63	76	64	54	76	67	65
$E/V_p > 2$	56	79	80	54	52	77	67	65
CART model	95	90	93	91	65	90	85	74

For abbreviations, see *Tables 1 and 2*.

dur, left atrial volume index, and E/V_p fell in the normal range; the response was otherwise positive if at least one criterion was satisfied. The rationale behind this is related to limitations of these criteria to reach the conclusion of increased LVFP. For instance, E/V_p performs particularly well in dilated ventricles and, although a close correlation with LVFP has been found also in patients with normal LVEF,[18] is limited in the presence of concentric hypertrophy and small hyperdynamic ventricles with little space of flow propagation to occur. As far as the combined mitral and pulmonary vein flow assessment is concerned, our data indicate that when used in a setting with a >90% success rate, as in the present study and differently from other investigators,[22] this approach may still be considered a first line technique in the evaluation of LVFP. A PAP_s >35 mmHg as a parameter to predict elevated LVFP was selected by the CART model as the final step of the decision tree. Doppler echocardiography has made the measurement of PAP_s easy and accurate. The estimation of PAP_s is a valuable adjunct to assess LVFP since it can reflect the retrograde transmission of elevated left-side filling pressures.[23]

Strengths and limitations

The strengths of the study is a large sample size for this type of studies and the fact that it tries to overcome the inaccuracies of previous single-parameter LVFP estimates by combining them into a single decision tree.[24,25] Moreover, differently from recent empirical algorithms,[2,6,19,20] our strategy was to try to objectively derive and validate the model based on actual data and not on a consensus of expert opinions. We specifically paid attention to use variables that were easy to record and reproducible even during standard examination and that were not affected by ageing, like E/V_p, E/e'[26], or AR dur − A dur.[27] Other variables, i.e. non-restrictive mitral flow or pulmonary venous flow systolic-to-diastolic forward wave velocity ratio, whose value for the assessment of LVFP is limited by changes occurring with ageing were not considered. Nevertheless, although the application of the model may increase our confidence in diagnosing elevated LVFP, some cautions should be reminded. As a matter of fact, no echo-Doppler parameters, method, or algorithm can guarantee about normal or abnormal LVFP, and, more importantly, it is impossible to give non-invasively a quantitative information about the filling pressures. There are other limitations that should be taken into account. First, not all parameters could be obtained in all patients, thus reducing the discriminant ability of the algorithm especially in patients with an intermediate E/e'. Second, invasive and non-invasive studies were not carried out simultaneously, and this might have introduced some discrepancies between invasive and non-invasive estimation of LVFP. Third, in patients with diastolic HF, elevated LVFP may be intermittent and will

only be detected when they are challenged by increased venous return or by low-grade exercise. Finally, introduction of newer imaging technologies might have improved the value of this CART-based approach for the evaluation of LVFP.[28,29]

Conclusion

In patients with LV dysfunction and a wide range of LVEF submitted to near-simultaneous echocardiographic and haemodynamic assessments, CART analysis was applied to discern which combination of echo-Doppler parameters best predicts elevated LVFP. This approach may be implemented in clinical practice and may improve the detection of raised LVFP with the inherent therapeutic implications in a variety of cardiac disorders, especially in patients with signs and symptoms of HF and preserved LVEF.

Conflict of interest: none declared.

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