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# Chapter 18

## **Value of the surface electrocardiogram in detecting right ventricular dilatation in the presence of left bundle branch block**

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## ABSTRACT

**Background:** Approximately 20% of patients with heart failure have left bundle branch block (LBBB) on the surface ECG. In this group of patients, detection of right ventricular (RV) dilatation using a standard ECG can be of clinical relevance, since RV enlargement is an important prognostic marker. Consequently, aim of this study was to evaluate the diagnostic accuracy for several ECG criteria in determining significant RV dilatation in these patients.

**Methods:** Standard 12-lead ECGs were obtained in 173 heart failure patients with known LBBB. From the ECG, 3 criteria for RV dilatation were defined; presence of terminal positivity in lead aVR (late R wave in lead aVR), low voltage ( $<0.6$  mV) in all extremity leads and an R/S ratio  $<1$  in lead V5. Additionally, all patients underwent comprehensive echocardiographic evaluation, including assessment of RV dimensions. Measurements were performed blinded to ECG results. Significant RV dilatation was defined as either an RV base-to-apex length  $\geq 86$  mm, or an RV diastolic area  $\geq 33$  cm<sup>2</sup>.

**Results:** Eighty-six patients (50%) had a late R wave in lead aVR, 36 patients (21%) had low voltage in the extremity leads and 67 patients (39%) had an R/S ratio  $<1$  in lead V5. An RV base-to-apex length  $\geq 86$  mm was present in 67 patients (39%), while 62 patients (36%) had an RV diastolic area  $\geq 33$  cm<sup>2</sup>. Any combination of 2-3 positive criteria could predict an RV base-to-apex length  $\geq 86$  mm with a positive predictive value (PPV) of 89% and a negative predictive value (NPV) of 88%. Similarly, an RV diastolic area  $\geq 33$  cm<sup>2</sup> was predicted with a PPV of 80% and a NPV of 88%.

**Conclusions:** Combining 2-3 distinct ECG criteria allows for accurate detection of RV dilatation in heart failure patients with LBBB.

## INTRODUCTION

Approximately 20% of patients with heart failure have left bundle branch block (LBBB) on the surface electrocardiogram (ECG).<sup>1,2</sup> In patients with LBBB, ventricular activation occurs abnormally affecting the application of the conventional ECG rules for diagnosing abnormalities in blood supply, scar location and ventricular hypertrophy, as these are based upon normal conduction over the bundle branch system. Attempts have been made to recognize those abnormalities in the presence of LBBB. More specifically, the possibility of detecting right ventricular (RV) dilatation using a standard ECG can be of clinical relevance, since RV enlargement is a prognostic marker in these patients.<sup>3</sup> Consequently, aim of this study was to evaluate the diagnostic accuracy for several ECG criteria in determining RV dilatation in heart failure patients with LBBB.

## METHODS

### Patient population and protocol

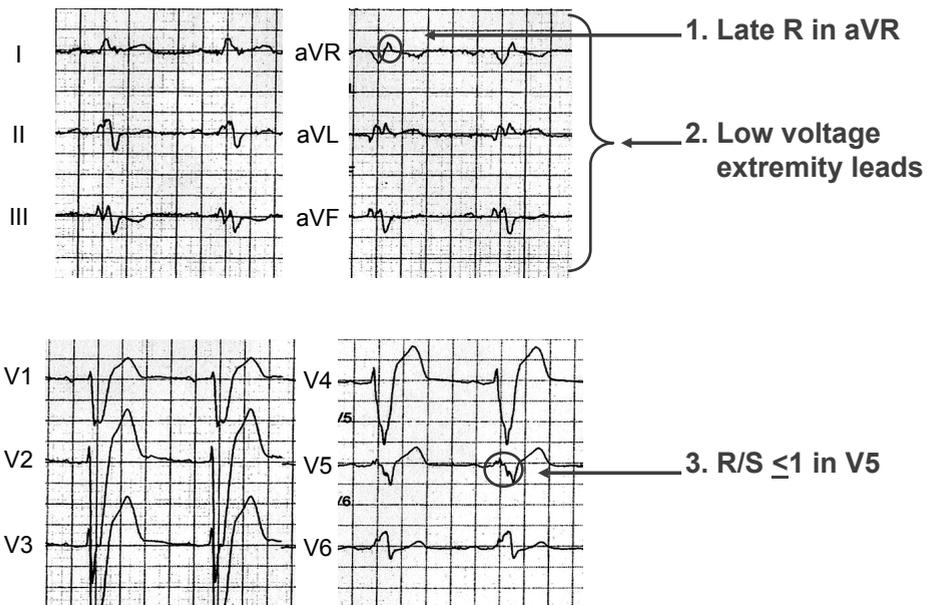
A total of 173 heart failure patients were selected, according to the following criteria: New York Heart Association (NYHA) functional class III and IV and a LBBB configuration on the surface ECG. Etiology of heart failure was considered ischemic in the presence of significant coronary artery disease ( $\geq 50\%$  stenosis in 1 or more of the major coronary arteries) and/or a history of myocardial infarction or prior revascularization. In all patients a 12-lead ECG was obtained and extensive echocardiographic evaluation, including assessment of RV size and function was performed. All echocardiographic measurements were performed blinded to ECG results. From the 12-lead ECG, 3 criteria for RV dilatation were defined. Finally, the diagnostic accuracy of these ECG criteria for detecting RV dilatation was evaluated.

### ECG analysis

A standard supine artifact free 12-lead ECG (filter range, 0,15 to 100 Hz; AC filter, 60 Hz, 25mm/sec, 10mm/mV) showing a supraventricular rhythm (sinus or atrial fibrillation) with a LBBB pattern was available for analysis. The time interval between the ECG and the echocardiogram was  $< 10$  days in all patients.

The ECG was analyzed manually, and the following ECG parameters were obtained: frontal plane axis, ventricular rate, QRS width, the frontal plane axis of the full and the second half of the QRS complex, voltage of the extremity and precordial leads, the T wave axis in the frontal

plane, the QRS-T angle in the frontal plane, presence of terminal positivity in lead aVR, presence of an R/S ratio,  $<1$  in lead V5, presence of a low QRS voltage ( $<0.6$  mV) in all 6 extremity leads with a normal or increased voltage in the precordial leads. For reasons outlined in the discussion, 3 ECG criteria were selected as indicators for RV dilatation; presence of terminal positivity in lead aVR, a low QRS voltage ( $<0.6$  mV) in all extremity leads and an R/S ratio  $<1$  in lead V5 (Figure 1).



**Figure 1.** A 12-lead ECG showing the 3 ECG criteria evaluated to detect RV dilatation.

## Echocardiography

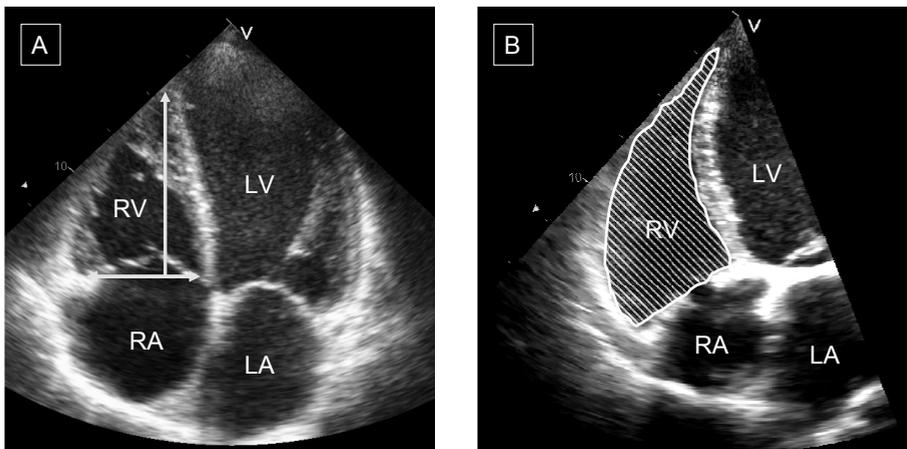
All patients underwent echocardiography in the left lateral decubitus position. Imaging was performed using a commercially available echocardiographic system (VIVID 7, General Electric Vingmed Ultrasound, Milwaukee, USA). Images were obtained using a 3.5 MHz transducer, at a depth of 16 cm in the parasternal and apical (2-, and 4-chamber) views. Standard 2D and color Doppler data, triggered to the QRS complex, were saved in cineloop format and analyzed offline with commercial software (EchoPac 108.1.5, General Electric Vingmed Ultrasound, Milwaukee, USA). Left ventricular (LV) end-diastolic (LVEDV) and LV end-systolic (LVESV) volumes were determined from the conventional apical 2- and 4-chamber views and LV ejection fraction (LVEF) was calculated using the biplane Simpson's technique.<sup>4</sup> Severity

of tricuspid regurgitation (TR) and mitral regurgitation (MR) was assessed according to the current guidelines.<sup>5,6</sup>

### Assessment of RV size and function

For quantification of RV size, the apical 4-chamber view was used. Special care was taken to obtain a true non-foreshortened apical 4-chamber view, oriented to obtain the maximum RV dimension. The RV base-to-apex length (Figure 2A) and the RV diastolic area (Figure 2B) were assessed as described previously.<sup>7</sup> Significant RV dilatation was defined in as either an RV base-to-apex length  $\geq 86$  mm, or an RV diastolic area  $\geq 33$  cm<sup>2</sup> (moderate to severe RV dilatation).<sup>7,8</sup> These specific measures were selected as they were expected to best identify RV dilatation defined by the chosen ECG criteria.

For assessment of RV function, the tricuspid annular plane systolic excursion (TAPSE) was measured.<sup>9</sup> Finally, pulmonary artery systolic pressure (PASP) was derived from the right ventricular to right atrial pressure gradient or TR jet gradient and calculated with the modified Bernoulli equation.<sup>10</sup>



**Figure 2.** Examples of echocardiographic measurements to evaluate RV dilatation Panel A displays the measurement of the RV base-to-apex length (87 mm in this example), while Panel B displays the measurement of the RV diastolic area (34.2 cm<sup>2</sup> in this example).

## Statistical analysis

Continuous data are presented as mean $\pm$ SD, and dichotomous data are presented as numbers and percentages. Comparison of data between patient groups was performed using the independent-samples t test for continuous data. Fisher's exact tests or  $\chi^2$  tests were used as appropriate to compare dichotomous data. Comparisons between more than 2 patient groups were performed using one-way analysis of variance (ANOVA) with Bonferroni post-hoc testing. All analyses were performed with SPSS for Windows, version 16.0 (SPSS, Chicago, IL). All statistical tests were 2-sided. A p-value <0.05 was considered statistically significant.

## RESULTS

### Patient characteristics

Baseline characteristics of the patient population are presented in Table 1. The majority of patients were male (64%) and the cause of heart failure was ischemic cardiomyopathy in 83 (48%) patients. No differences were observed between ischemic heart failure patients and non-ischemic heart failure patients, except that ischemic patients were older (68 $\pm$ 9 years vs. 63 $\pm$ 10 years,  $p$ <0.001) and more frequently male (76% vs. 53%,  $p$  = 0.002).

### Electrocardiographic parameters

Mean heart rate during ECG registration was 71 $\pm$ 13 beats per minute and the mean QRS duration was 178 $\pm$ 16 ms. Other ECG parameters are displayed in Table 1. When assessing the predefined ECG criteria, the following observations were made: 1) eighty-six (50%) patients had a late R wave in lead aVR, 2) 36 (21%) patients had low voltage in the extremity leads and 3) 67 (39%) patients had an R/S ratio <1 in lead V5. There were 51 (29%) patients without any positive criterion for RV dilatation, 61 (35%) patients had 1 positive criterion, 55 (32%) patients had 2 positive criteria, and finally, 6 (3%) had all 3 positive criteria.

**Table 1.** Patient characteristics (n = 173)

<i>Clinical parameters</i>	
Age (years)	65 ± 10
Men / Women	111 / 62
New York Heart Association functional class	
III	162 (94%)
IV	11 (6%)
Etiology of heart failure	
Ischemic	83 (48%)
Non-ischemic	90 (52%)
Medications	
Angiotensin-converting enzyme inhibitors	151 (87%)
Diuretics	158 (91%)
Beta-blockers	123 (71%)
Spironolactone	83 (48%)
Digoxine	25 (14%)
<i>Electrocardiographic parameters</i>	
Heart rate (beats / minute)	71 ± 13
QRS duration (ms)	178 ± 16
QRS axis (degrees)	-22 ± 39
QRS axis 2 <sup>nd</sup> half (degrees)	-50 ± 43
QRS-T angle (degrees)	136 ± 43
<i>Echocardiographic parameters</i>	
Left ventricular end-diastolic volume (ml)	234 ± 88
Left ventricular end-systolic volume (ml)	180 ± 77
Left ventricular ejection fraction (%)	24 ± 8
Mitral regurgitation (grade)	1.7 ± 1.0
Right ventricular base-to-apex length (mm)	82 ± 8
Right ventricular diastolic area (cm <sup>2</sup> )	28 ± 7
Tricuspid annular plane systolic excursion (mm)	18 ± 3
Pulmonary artery systolic pressure (mmHg)	34 ± 9
Tricuspid regurgitation (grade)	1.5 ± 1.0

## Echocardiographic parameters

Mean values for all echocardiographic findings are displayed in Table 1. Significant RV dilatation defined as an RV base-to-apex length  $\geq 86$  mm was present in 67 (39%) patients, while an RV diastolic area  $\geq 33$  cm<sup>2</sup> was noted in 62 (36%) patients. Of note, a concordance between both definitions was found in 160 (92%) patients.

## RV size and function measurements vs. ECG criteria

Mean values of RV size and function measurements among patients with 0, 1, 2 or 3 positive ECG criteria are displayed in Table 2. There were significant differences between groups in all tested RV size and RV function measurements. In particular, after post-hoc testing, patients with either 2 or 3 positive ECG criteria had a larger RV base-to-apex length, larger RV diastolic area, higher TR grade and higher PASP ( $p < 0.05$  for all tests) as compared to patients with 0 positive ECG criteria (Table 2).

Subsequently, the diagnostic accuracy of the 3 ECG criteria for detecting RV dilatation was tested. An RV base-to-apex length  $\geq 86$  mm was observed in 62% of patients with a late R wave in lead aVR (Table 3A), while an RV diastolic area  $\geq 33$  cm<sup>2</sup> was observed in 57% of these patients (Table 3B). Conversely, an RV base-to-apex length  $\geq 86$  mm was observed in 61% of patients with a low voltage in all extremity leads (Table 3A), while an RV diastolic area  $\geq 33$  cm<sup>2</sup> was observed in 56% of patients with low voltage in all extremity leads (Table 3B). Finally, an RV base-to-apex length  $\geq 86$  mm was observed in 69% of patients with an R/S ratio  $\leq 1$  in lead V5 (Table 3A), while an RV diastolic area  $\geq 33$  cm<sup>2</sup> was observed in 63% of these patients (Table 3B). As no single ECG criterion could predict significant RV dilatation defined as either an RV base-to-apex length  $\geq 86$  mm or an RV diastolic area  $\geq 33$  cm<sup>2</sup> with a PPV  $> 69\%$ , and patients with either 2 or 3 positive criteria had both a larger RV base-to-apex length and larger RV diastolic area than patients with either 0 or 1 positive criteria (Table 2), separate ECG criteria were combined and 2 sub-groups were constituted: patients with 0-1 positive ECG criteria and patients with 2-3 positive criteria. An RV base-to-apex length  $\geq 86$  mm was observed in only 13 out of 112 (12%) patients with 0-1 positive criteria, and an RV diastolic area  $\geq 33$  cm<sup>2</sup> was present in 13 out of 112 (12%) patients with 0-1 positive criteria. Consequently, any combination of 2-3 positive criteria was able to predict an RV base-to-apex length  $\geq 86$  mm with a PPV of 89% and a NPV of 88% (Table 3A). Similarly, an RV diastolic area  $\geq 33$  cm<sup>2</sup> could be predicted with a PPV of 80% and a NPV of 88% (Table 3B).

**Table 2.** Differences in right ventricular dimensions and function between patients with 0, 1, 2 or 3 positive electrocardiographic criteria

	0 positive (n = 51)	1 positive (n = 61)	2 positive (n = 55)	3 positive (n = 6)	p-value
Right ventricular base-to-apex length (mm)	78 ± 6	78 ± 6	90 ± 5*	92 ± 6*	<b>&lt;0.001</b>
Right ventricular diastolic area (cm <sup>2</sup> )	25 ± 6	25 ± 7	34 ± 5*	36 ± 3*	<b>&lt;0.001</b>
Tricuspid annular plane systolic excursion (mm)	18 ± 3	19 ± 2	18 ± 4	16 ± 4	<b>0.034</b>
Pulmonary artery systolic pressure (mmHg)	30 ± 8	30 ± 9	38 ± 7*	46 ± 2*	<b>&lt;0.001</b>
Tricuspid regurgitation (grade)	1.1 ± 0.8	1.4 ± 0.9	2.0 ± 0.9*	2.2 ± 1.3*	<b>0.002</b>

Provided p-values are for trend (least squares regression) between sub-groups.

\*  $p < 0.05$  vs. 0 positive electrocardiographic criteria

**Table 3A.** Diagnostic accuracy of the presence (or combination) of electrocardiographic criteria to detect a right ventricular base-to-apex length  $\geq 86$  mm

	PPV	NPV	Sensitivity	Specificity
late R wave in lead aVR	62%	84%	79%	69%
low voltage in all extremity leads	61%	67%	33%	87%
R/S ratio $<1$ in lead V5	69%	80%	69%	80%
2-3 positive criteria	89%	88%	81%	93%

NPV = negative predictive value; PPV = positive predictive value

**Table 3B.** Diagnostic accuracy of the presence (or combination) of electrocardiographic criteria to detect a right ventricular diastolic area  $\geq 33$  cm<sup>2</sup>

	PPV	NPV	Sensitivity	Specificity
late R wave in lead aVR	57%	85%	79%	67%
low voltage in all extremity leads	56%	69%	33%	86%
R/S ratio $<1$ in lead V5	63%	81%	68%	78%
2-3 positive criteria	80%	88%	79%	89%

NPV = negative predictive value; PPV = positive predictive value

## DISCUSSION

Current experience with cardiac resynchronization therapy (CRT) in heart failure patients indicates that the best results are obtained in patients with left bundle branch block with a QRS width  $>140$  ms.<sup>11</sup> This ECG pattern is found in approximately 20 % of heart failure patients.<sup>1,2</sup> Still, about 30-40 % of those patients do not respond favorably to CRT. Several patient and device related factors play a role in the non-responders.<sup>12</sup> Lack of improvement can be related to patient and/or pacing characteristics. Examples of patient related causes are a too large LV or too much scar, class IV heart failure, renal dysfunction and (supra-) ventricular arrhythmias. Pacing related causes include: suboptimal LV pacing site, pacing in a scarred area of the LV, suboptimal RV pacing site, no optimal LV-RV activation interval, and no optimal A-V activation interval. In heart failure patients with LBBB, the value of the ECG has been studied in relation to outcome of CRT. The baseline QRS duration was found to be helpful in several, but not all, of the reported studies.<sup>13-16</sup> Recently, Sweeney et al, when analyzing LV activation on the baseline 12-lead ECG, described 2 findings able to predict CRT outcome.<sup>17</sup> A favorable one, related to the LV activation time and an unfavorable one when LV scar was present, as determined by the Selvester LV scar score.<sup>18</sup> It is well known that in the heart failure patient with LV disease, additional RV dysfunction worsens prognosis.<sup>3</sup> The aim of our study therefore was to investigate the possibility of using the standard 12-lead ECG to detect RV dilatation in heart failure patients with LV systolic dysfunction and complete LBBB. Three ECG findings were considered to be of possible value. 1) Terminal positivity of the QRS

in lead aVR; 2) An R/S ratio of  $<1$  in lead V5; and 3) A low QRS voltage in the extremity leads, with a normal or increased QRS voltage in the precordial leads. Positivity in the terminal portion of the QRS in lead aVR suggests that the last part of ventricular activation occurs in the direction of the right shoulder, suggesting a greater delay in activation of the basal part of the right than of the left ventricle. Clockwise rotation in the precordial leads as manifested by an R/S  $<1$  in lead V5 suggests that the right ventricle extends further to the left in the horizontal plane. And lastly, as pointed out by Goldberger many years ago, the voltage in the bipolar extremity leads decreases when the intra-cardiac fluid volume increases.<sup>19</sup> This is not the case with unipolar precordial leads. When the value of the 3 criteria was examined separately, none reached a high predictive value for RV enlargement. However, the presence of any combination of 2-3 positive criteria could predict an RV base-to-apex length  $\geq 86$  mm, and an RV diastolic area  $\geq 33$  cm<sup>2</sup> with satisfactory predictive values.

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