



A new electrocardiogram algorithm for diagnosing loss of ventricular capture during cardiac resynchronisation therapy

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Received 7 July 2012; accepted after revision 4 September 2012

Aims

The prerequisite for cardiac resynchronization therapy (CRT) is ventricular capture, which may be verified by analysis of the surface electrocardiogram (ECG). Few algorithms exist to diagnose loss of ventricular capture.

Methods and results

Electrocardiograms from 126 CRT patients were analysed during biventricular (BV), right ventricular (RV), and left ventricular (LV) pacing. An algorithm evaluating QRS narrowing in the limb leads and increasing negativity in lead I to diagnose changes in ventricular capture was devised, prospectively validated, and compared with two existing algorithms. Performance of the algorithm according to ventricular lead position was also assessed.

Results

Our algorithm had an accuracy of 88% to correctly identify the changes in ventricular capture (either loss or gain of RV or LV capture). The algorithm had a sensitivity of 94% and a specificity of 96% with an accuracy of 96% for identifying loss of LV capture (the most clinically relevant change), and compared favourably with the existing algorithms. Performance of the algorithms was not significantly affected by RV or LV lead position.

Conclusion

A simple two-step algorithm evaluating QRS width in the limb leads and changes in negativity in lead I can accurately diagnose the lead responsible for intermittent loss of ventricular capture in CRT. This simple tool may be of particular use outside the setting of specialized device clinics.

Keywords

Cardiac resynchronization therapy • Electrocardiogram • Ventricular capture • Algorithm • Sensitivity • Specificity

Introduction

Cardiac resynchronization therapy (CRT) is indicated in selected patients with systolic heart failure to reduce mortality and morbidity.¹ The prerequisite for CRT efficacy is ventricular capture. Outside specialized device clinics, the electrocardiogram (ECG) is the only easily available tool to identify left ventricular (LV), right ventricular (RV) or biventricular (BV) capture. Even with a device programmer, the ECG is useful for troubleshooting issues such as anodal capture and pseudofusion.

Few algorithms are published to confirm LV capture on a standard ECG. Ammann *et al.*² described an algorithm (*Figure 1*) whereby loss of LV capture is diagnosed in case of an R/S ratio

<1 in V1 and >1 in lead I. The sensitivity of this algorithm to correctly identify loss of LV capture was 94% and the specificity was 93%. This algorithm was evaluated in a monocentric cohort of 54 patients, all of whom had an RV lead located at the apex (and not the interventricular septum, which is the preferred site of many operators). The algorithm requires recording lead V1, which may not always be available.

Another ECG algorithm (*Figure 1*) was developed by Yong and DUBY³ for use during threshold tests in the era of CRT devices that had a single ventricular channel with an internal Y-connector to the RV and LV (as opposed to current devices that have separate ventricular channels that allow measurement of RV and LV

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What's new

- A simple and intuitive algorithm using only limb leads based on change of QRS width and negativity in lead I can accurately identify the lead responsible for intermittent loss of biventricular capture, and compares favourably with previously described algorithms.
- The accuracy of the algorithm is independent of right or left ventricular lead position
- This simple tool may be of particular use outside of specialized device clinics

thresholds individually). The threshold test is initiated with a high-voltage output that results in BV capture, with gradual reduction in amplitude until one of the ventricles fails to be entrained, resulting in a change in QRS morphology. The algorithm was designed to identify the ventricle which had lost capture by evaluating changes in QRS axis. Loss of LV capture is indicated by increasing QRS positivity in lead I, and loss of RV capture by increasing positivity in lead III. The algorithm had a sensitivity of 97–100% and a specificity of 92–97%, but presumes that BV capture is present initially (which may not always be the case with intermittent ventricular capture), and like the Ammann algorithm, was validated only for RV leads positioned at the apex.

Our aims were (i) to devise a new ECG algorithm using only limb leads that may be used in the case of intermittent loss of capture during CRT (i.e. does not presume that BV capture is present initially) and (ii) to evaluate whether lead position affects the accuracy of the ECG algorithms (including those described by Ammann and Yong).

Methods

The study was conducted in two phases. The first exploratory phase consisted of systematically analysing a number of ECG parameters recorded in the six limb leads, and thereby devising an algorithm to differentiate BV capture from either LV or RV univentricular capture. The second validation phase prospectively tested the algorithm in a separate population and also evaluated the algorithms described by Yong and by Amman. For the exploratory phase, files of patients followed up at the device clinic of the University Hospital of Geneva, Switzerland were randomly selected. For the validation phase, consecutive patients followed up at the device clinic of the University Hospital of

Grenoble, France were studied. The study was approved by the institutional ethics committees.

Data acquisition

When performing the threshold tests during routine follow-up, standard ECGs were recorded in intrinsic rhythm and during BV, RV, and LV pacing. Pacing mode was DDD for BV pacing in patients in sinus rhythm, and VVI for patients in AF and during univentricular pacing. Tracings were recorded on millimeter grid paper, at 25 mm/s paper speed. Data were acquired retrospectively during the exploratory phase, and prospectively during the validation phase. Cases with evidence of RV anodal capture during LV pacing (resulting in BV capture), or poor quality tracings, were excluded. The position of the ventricular leads was assessed by analysis of biplane chest X-rays.

Measurements

For the exploratory phase, ECGs during BV, RV, and LV pacing were analyzed for QRS width (in the limb lead with the widest complex) and for amplitudes of Q, R, and S waves in leads I and aVF. The net QRS amplitude was calculated as $R - (Q + S)$. All measurements were performed manually by a medical student and verified by an electrophysiologist. QRS axis was calculated by an Excel spreadsheet using the net QRS amplitudes in leads I and aVF with the following formula we have previously published:⁴ $\text{axis} = 57.3 \times \text{ATAN}(\text{AVF/I})$, expressed from 0° to 360° . The amplitude of the QRS vector was calculated using Pythagoras' theorem and QRS amplitudes in leads I and aVF.

For the validation phase, the ECGs were analysed by two trained cardiologists who were blinded to the mode of stimulation (BV, RV, or LV pacing). The Geneva algorithm devised in the exploratory phase was evaluated by pairs of ECGs showing the six limb leads with BV pacing and univentricular pacing, in random order. The process was repeated showing only lead I. The algorithm described by Yong was evaluated by displaying pairs of ECGs starting with BV pacing followed by either RV or LV pacing. The algorithm described by Ammann was evaluated on 12-lead ECGs during all three modes of pacing to assess for the presence or absence of LV capture. The evaluation of QRS width and amplitudes was performed using the eyeball method, without use of callipers.

Statistical analysis

As angles have a circular distribution (i.e. boundaries of the distribution such as 359° and 1° are in fact adjacent, making usual calculation of means nonsensical), descriptive statistics and differences between groups using Moore's paired test were computed by dedicated software (Oriana v. 4.01). Distribution of the ECG data was non-Gaussian according to histogram analysis and the K-S and Shapiro-Wilk tests. For numerical data, Friedman's test was performed followed by the Wilcoxon test in case of a P value of <0.05 . For categorical data, Fisher's exact test and the Mc Nemar test were used as appropriate. Spearman's test was used for correlating data. Data are expressed as median \pm interquartile range unless specified otherwise. IBM SPSS statistics v19 was used for analysis. A two-tailed P value <0.05 was considered statistically significant.

Results

Exploratory phase

Datasets from 51 patients (Table 1) were analysed and the results are shown in Table 2. We observed significant changes in QRS

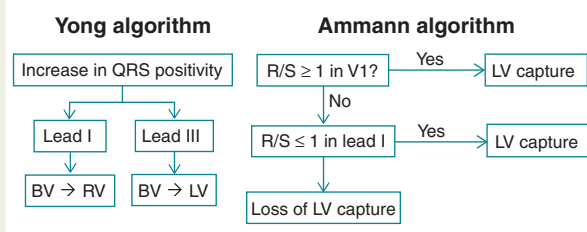


Figure 1 Electrocardiogram algorithms described by Yong and Duby³ and by Ammann et al.²

duration between BV and univentricular pacing, as well as significant differences in QRS amplitude in lead I that resulted both from changes in QRS axis as well as in the QRS vector amplitude (Figure 2). Following these observations, we devised a two-step

Table 1 Patient demographics of the exploratory and validation cohorts

	Exploratory cohort (n = 51)	Validation cohort (n = 75)
Age (years, mean \pm SD)	70 \pm 11	71 \pm 10
Sex (M/F)	40/11	58/17
Aetiology of heart failure		
Ischaemic	32	42
Non-ischaemic	19	33
Intrinsic QRS		
Duration (ms)	160 (140–180)	140 (120–180)
LBBB/NIVCD/RBBB/paced	35/8/2/5	40/18/11/7
Chronic AF	14	14
LVEF (%; mean \pm SD)	26 \pm 9	30 \pm 7
RV lead position		
Apex	17	32
Septum	34	22
LV lead position		
(postero)-lateral	45	46
Antero-lateral	5	5
Anterior	1	3

Lead position is reported for patients with available biplane chest X-rays (all patients of the exploratory cohort and 54 patients of the validation cohort). AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LBBB, left bundle branch block; NIVCD, non-specific intra-ventricular conduction delay; RBBB, right bundle branch block; LV, left ventricle; RV, right ventricle.

algorithm (Figure 3) to identify changes in ventricular capture between two ECGs (presented in any order), assuming that BV capture was present in one of the two tracings, with loss of either RV or LV capture. The overall accuracy of the algorithm for diagnosing the correct sequence from 204 combinations of ECGs was 84%. The number of sequences correctly diagnosed were for LV \rightarrow BV: 43/51 (84%); RV \rightarrow BV: 41/51 (80%); BV \rightarrow RV: 45/51 (88%); and BV \rightarrow LV: 43/51 (84%). The difference in accuracy for diagnosing RV \rightarrow BV and BV \rightarrow RV was due to four patients in whom no change in net QRS amplitude in lead I was observed between the two pacing modes (and were therefore counted as not having increased negativity in both instances). Absence of change in QRS width was observed in 28/204 (14%) ECG pairs.

There were no significant difference in accuracy of the algorithm in patients with an apical compared with a septal RV lead (79 vs. 87%, $P = 0.22$) or between those with a (post)-lateral compared with an anterior/antero-lateral lead (92 vs. 83%, $P = 0.38$). Absence of fusion with intrinsic atrioventricular conduction during BV pacing was observed in 25/51 patients due to atrial fibrillation (with consistent paced QRS morphology) or to atrioventricular block. Accuracy of the algorithm was comparable in patients with possible fusion pacing compared with those without fusion (85 vs. 84%, $P = 1.00$).

Validation phase

A separate population of 75 patients was studied. Our algorithm yielded an overall accuracy of 88% (132/150 ECG pairs were correctly diagnosed) when using the limb leads for measuring QRS width (as initially performed in the exploratory phase for deriving the algorithm). The accuracy fell slightly to 84% when only lead I was used throughout the entire process ($P = 0.039$ compared with using all limb leads), due to underestimation of QRS width because of an initial or terminal isoelectric segment in lead I in six patients (during RV pacing in five and LV pacing in one) that confounded the first step of the algorithm.

Table 2 Electrocardiogram data from the exploratory phase (n = 51) during different pacing configurations (data shown as median \pm interquartile range except for QRS axes which are expressed as mean \pm 95th confidence interval)

	BV pacing	LV pacing	P (LV vs. BV)	RV pacing	P (RV vs. BV)
QRS axis (degree)	−125 (−153 to −99)	171 (158 to −177)	0.001	−59 (−47 to −71)	<0.001
QRS duration (ms)	160 (140 to 180)	200 (200 to 220)	<0.001	180 (160 to 200)	<0.001
QRS amplitude in lead I (mV)	−0.2 (−0.5 to −0.2)	−0.6 (−0.9 to −0.1)	<0.001	0.4 (0 to 0.6)	<0.001
QRS mean vector amplitude (mV)	0.58 (0.45 to 0.89)	0.78 (0.63 to 1.12)	0.008	0.94 (0.52 to 1.30)	<0.001
Presence of q-wave in lead I	30/51 (59%)	43/51 (84%)	0.25	14/51 (27%)	0.025
Negative or isoelectric QRS in lead I	34/51 (67%)	49/51 (96%)	<0.001	9/51 (18%)	<0.001

BV, biventricular; LV, left ventricular; RV, right ventricular.

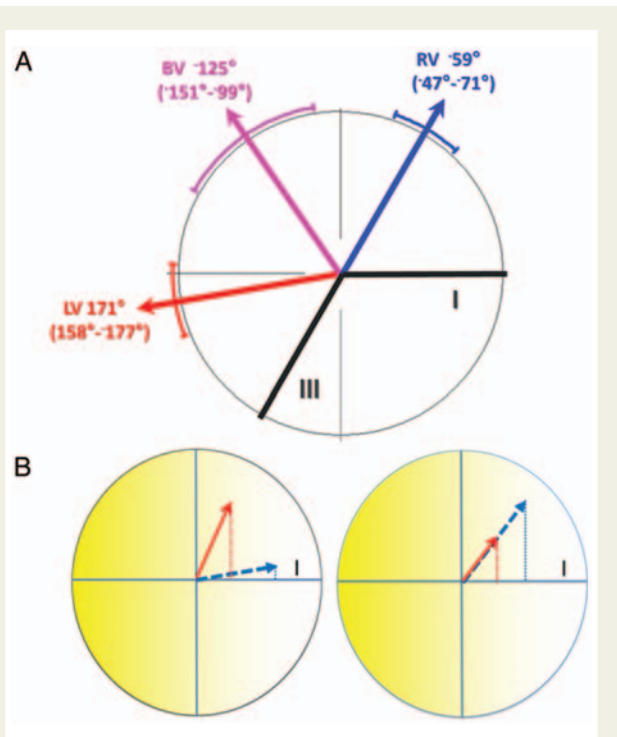


Figure 2 (A) Frontal QRS axes during different ventricular pacing configurations (data shown as mean \pm 95th confidence interval). (B) Changes in QRS amplitude in lead I due to changes in axis (with same vector amplitude) on the left, or due to changes in vector amplitude (with same QRS axis) on the right. BV, biventricular capture; LV, left univentricular capture; RV, right univentricular capture.

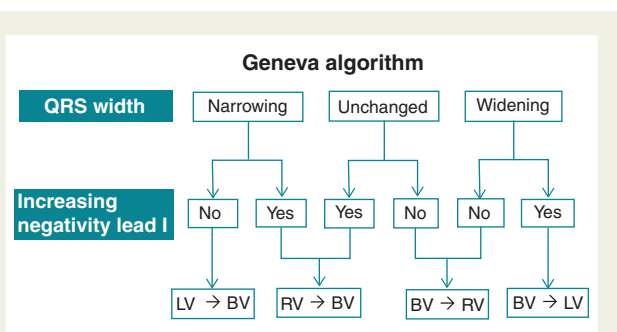


Figure 3 Two-phase Geneva algorithm designed to identify changes in ventricular capture between two ECGs (e.g. BV \rightarrow RV indicates initial biventricular capture with subsequent loss of left ventricular capture). The first step involves change in QRS width measured in the limb leads, followed by presence or absence of increasing net QRS negativity in lead I. BV, biventricular capture; LV, left univentricular capture; RV, right univentricular capture.

The algorithm by Yong correctly diagnosed 126/150 (84%) ECG pairs. A diagnosis was impossible to determine using the algorithm in 14/150 (9%) pairs of tracings due to ambiguous findings (e.g. increasing negativity in both leads I and III).

Table 3 Performance of different algorithms in the validation cohort (n = 75) for diagnosing loss of left ventricular capture (right ventricular pacing for the Ammann algorithm, BV \rightarrow RV pacing for the Yong and Geneva algorithms)

	Sensitivity (%)	Specificity (%)	Accuracy (%)
Ammann	71	97	88
Yong	89	79	84
Geneva	96	96	95
Geneva (lead I only)	95	96	94

The performance of our algorithm was evaluated along with the algorithms of Amman and of Yong for diagnosing loss of LV capture (see Table 3). The relatively low sensitivity of the algorithm of Amman *et al.* was due to erroneous diagnosis of LV capture (false positivity) during RV pacing in 22/75 (29%) patients. This was due to $R/S \geq 1$ in V1 in 15 patients (an example is shown in Figure 4) and an $R/S \leq 1$ in lead I in 7 patients during RV pacing. In all but one case of $R/S \geq 1$ in V1 [with a pseudo-right bundle branch block (pseudo-RBBB) aspect] during RV pacing, QRS transition occurred before V4. False negativity for LV capture ($R/S < 1$ in V1 and $R/S > 1$ in lead I) was less frequent and was observed during BV pacing in five patients and during LV pacing in one patient.

Performance of the algorithms according to ventricular lead position

Biplane chest X-rays allowing evaluation of lead position were available in a subset of 54 patients. During RV pacing, patients with an apical RV lead tended to have more frequently an $R/S \geq 1$ in V1 than those with a septal lead: 9/32 (28%) vs. 4/22 (18%), $P = 0.52$. Conversely, patients with a septal lead had more often an $R/S \leq 1$ in lead I: 7/22 (32%) vs. 2/32 (6%), $P = 0.023$. There were no significant differences in accuracy of the algorithms with respect to RV lead position for all the algorithms ($P > 0.1$ for all comparisons).

None of the eight patients with an anterior or antero-lateral LV lead had erroneous diagnosis of LV non-capture during LV or BV pacing with the algorithms. However, all three patients who had the LV positioned in the anterior cardiac vein had greater negativity of the QRS complex in V1 (decreasing R/S ratios) with increasing LV participation (RV \rightarrow BV and BV \rightarrow LV ECG pairs), whereas increasing positivity in V1 was observed in 89% of the total population. These patients nevertheless had correct diagnosis of LV capture with the algorithm by Amman *et al.* due to an $R/S \leq 1$ in lead I during LV and BV pacing.

Discussion

Beyond measurement of QRS width as an indication criterion for CRT, more detailed ECG analysis could be used to predict response to therapy,^{5,6} to optimize device settings,^{7,8} and to assist

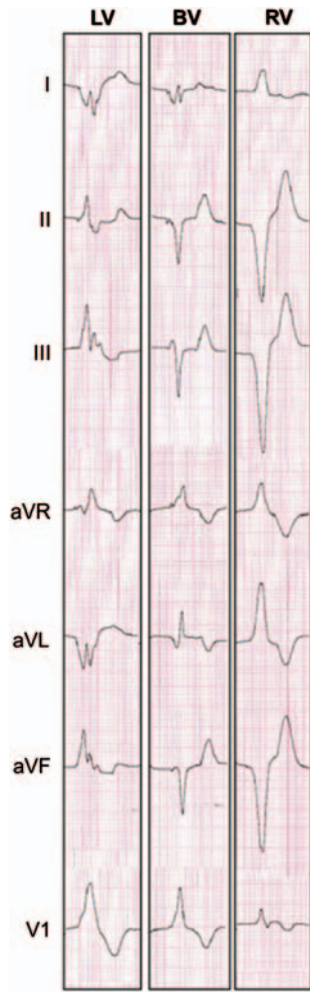


Figure 4 QRS morphology during left univentricular, biventricular, and right univentricular capture. Note increasing QRS duration in the limb leads with left univentricular and right univentricular pacing compared with biventricular pacing, and increasing negativity in lead I from RV→BV→LV pacing, consistent with the Geneva algorithm. The algorithm described by Yong also yields correct results (BV→LV pacing with increasing QRS positivity in lead III, and BV→RV pacing with increasing QRS positivity in lead I). The algorithm described by Amman correctly identifies left univentricular capture during left univentricular and biventricular pacing but incorrectly indicates left univentricular capture during right univentricular pacing ($R/S > 1$ in lead V1 with pseudo-right bundle branch block pattern).

in device troubleshooting for diagnoses such as of loss of ventricular capture.⁹ Our report describes a simple and intuitive algorithm that accurately identifies the lead responsible for intermittent loss of ventricular capture. Accuracy of the algorithm was initially 84% in the exploratory phase, and was then confirmed to be 88% in a separate validation population. The first step of the algorithm evaluates QRS width in the limb leads, whose widening points to a change from BV capture to univentricular (LV or RV) capture and vice versa. Absence of change in QRS width indicates

Table 4 Comparison of the three existing algorithms for evaluating ventricular capture during cardiac resynchronization therapy

	Ammann algorithm	Yong algorithm	Geneva algorithm
Diagnosis	Presence or absence of LV capture	Loss of RV or of LV capture	Loss or gain of LV or RV capture
Number of tracings	1	2	2
Leads analysed	I and V1	I and III	I (alone, or in combination with other limb leads for measuring QRS width)
Comments	Does not distinguish between LV and BV pacing	Assumes that BV capture is present initially (was designed for threshold testing)	Diagnoses loss or gain of RV or LV capture in any order (but assumes that BV capture is present on one of the tracings).

alternation between BV and RV capture (intermittent loss of LV capture). The second step evaluates net QRS amplitude in lead I, with greater negativity indicating increasing participation of LV capture (i.e. RV→BV or BV→LV capture). The algorithm was also tested using only lead I for the two steps, with slightly lower accuracy (84%) due to underestimation of QRS duration in patients with an initial or terminal isoelectric QRS complex in lead I. Another clue that indicates increasing participation of LV capture is increasing positivity in V1 that was observed in 89% of cases. As the LV lead is usually positioned in a posterior position in the thorax, the electrical forces are directed anteriorly (hence with greater positivity in V1). As an exception to this rule, patients with LV leads placed in the anterior cardiac vein have electrical forces directed posteriorly, with increasing negativity in V1 with LV capture. Right ventricular and LV lead position did not otherwise significantly affect the performance of the algorithms tested.

The main advantage of the Geneva algorithm over that described by Yong (designed for threshold tests) is that there is no assumption that BV capture is present initially (comparison between algorithms are summarized in Table 4). Also, we found that 9% of the tracings showed ambiguous results with the algorithm by Yong and that the 84% accuracy of this algorithm in our population was considerably lower than the 97% reported originally.³ These differences are difficult to explain, especially as the QRS axes observed during RV, LV, and BV pacing are almost identical in the two reports.

We found that the algorithm described by Ammann *et al.*² had good specificity (97%) but relatively poor sensitivity (71%, compared with 94% in the original publication) for diagnosing loss of LV capture. This was essentially due to a high prevalence of an $R/S \geq 1$ in V1 (the first step of the algorithm that diagnoses LV

capture) during RV pacing. As many as 20% of the patients showed a 'pseudo-RBBB' ECG pattern during RV pacing. This finding has been previously described, with a prevalence of 8–18% of patients.^{10–12} Electrode malposition may in part explain the high prevalence, as it has been shown that placing the V1–V2 electrodes in the third instead of the fourth intercostal space accentuates the phenomenon.¹¹ Nevertheless, this issue may often be encountered in general clinical practice, and remains a pitfall when applying the Amman algorithm. Another cause for erroneous diagnosis according to the Ammann algorithm is the presence of a negative QRS in lead I during RV pacing, which may falsely indicate LV capture. We have previously described that this is encountered in 29% of patients when pacing from the anterior RV,⁴ where the lead is often inadvertently placed while aiming at the interventricular septum.¹³

Study limitations

Net QRS amplitudes during the exploratory phase were measured by maximal values of the deflections, and not by area under the curve (which may have increased accuracy, but is impractical to measure precisely). This may explain why the accuracy of the Geneva algorithm had an even better performance in the validation phase, when the 'eyeball' analysis could have assessed better the true net QRS amplitude. Ventricular scar may have affected electrical propagation wavefronts and may also have confounded results due to latency;¹⁴ this was not evaluated in our study. Intermittent RV anodal capture during BiV pacing may lead to small changes in QRS morphology (that are considerably less than during loss of either RV or LV capture). It is unlikely that this would confound the algorithm, although we did not specifically evaluate this.

Acknowledgements

We wish to thank Mrs Carine Stettler (University Hospital of Geneva), Mrs Charlotte Vandeneynde, and Mrs Natacha Pellet (University Hospital of Grenoble) for their technical assistance in performing this study. Haran Burri MD is funded in part by a research grant from the Fondation de recherche de la Tour. Carine Stettler and Vincent Ganière were funded by research grants from Medtronic Switzerland.

Conflict of interest: none declared.

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