ECG Identification of Scar-Related Ventricular Tachycardia with a Left Bundle Branch Block Configuration

Running title: Wijnmaalen et al.; ECG identification of scar-related LBBB VT

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Abstract:

**Background** - A left bundle branch block-like (LBBB) pattern with a dominant S-wave in V1 is common in idiopathic ventricular arrhythmias (VA). Discrimination between idiopathic and scar-related LBBB pattern VA has important clinical implications. We hypothesized that the VA QRS morphology is influenced by the presence of ventricular scar allowing electrocardiographic discrimination of VA arising from structurally normal versus scarred myocardium.

**Methods and Results** - Twelve-lead ECGs of 297 LBBB pattern monomorphic VA were recorded during catheter ablation procedures. QRS morphology characteristics associated with scar-related VA were identified in retrospective analysis of 118 LBBB pattern VA (95 scar-related, 23 idiopathic) to develop a stepwise algorithm, that was prospectively tested in 179 LBBB pattern VA (120 scar-related, 59 idiopathic). The diagnosis of scar was based on sinus rhythm surface ECG, cardiovascular imaging and electroanatomical catheter mapping. A precordial transition beyond V4, notching of the S-wave downstroke in lead V1 or V2 and a duration from the onset of QRS to the S-nadir in V1>90ms were independent predictors for scar-related VA. The proposed algorithm classified a VA as scar-related if any of these criteria was met. If none of the criteria was present a VA was classified as idiopathic. In prospective validation the algorithm was highly sensitive (96%) and specific (83%) for the identification of scar-related LBBB pattern VA.

**Conclusions** - The QRS morphology of VA is different between scar-related and idiopathic VA. A simple ECG algorithm is sensitive for identifying scar-related LBBB VA, which could be helpful in guiding further evaluation of these patients.

**Key words:** cardiomyopathy, ECG criteria, imaging, mapping, ventricular arrhythmia.
INTRODUCTION

Monomorphic ventricular arrhythmias (VA) in patients without structural heart disease referred to as ‘idiopathic’ VA are considered benign in the majority of cases.\(^1\,^2\) In contrast patients with scar-related monomorphic VA may be at risk for sudden cardiac death (SCD).\(^3\,^4\) Discrimination between idiopathic and scar-related VA therefore has important prognostic and therapeutic implications.

Most idiopathic VA have a left bundle branch block (LBBB) like morphology in lead V1.\(^5\) LBBB pattern VA however can also arise from right ventricular (RV) and septal myocardial scars due to cardiomyopathies including arrhythmogenic RV cardiomyopathy and sarcoidosis.

The QRS morphology of a VA is determined by the location of the site from which a focal VA arises or from the location of the reentry circuit exit from which the excitation wavefront emerges to depolarize the surrounding myocardium, but may also be influenced by the presence and extend of myocardial scar.

We hypothesized that the VA QRS morphology may be influenced by the presence of ventricular scar allowing electrocardiographic discrimination of VA arising from structurally normal versus scarred myocardium.

METHODS

Data was analyzed from 213 patients with LBBB pattern VA who were referred to Brigham and Women’s hospital, Boston, MA, USA and The Leiden University Medical Center, Leiden, The Netherlands for catheter ablation of VA. Twelve-lead ECGs of 297 LBBB pattern monomorphic VA were documented and stored during radiofrequency catheter
ablation (RFCA). The ECG algorithm was developed from retrospective analysis of 118 LBBB pattern VA from 81 consecutive patients (65 male, age 53±16 years) studied between November 2002 and July 2006. The ECG algorithm was then prospectively validated in 179 LBBB pattern VA registered during RFCA in 132 patients (94 male, age 53±17 years) between July 2006 and April 2009.

Algorithm development

All patient records were reviewed to establish or rule out the presence of myocardial scar. Scar was diagnosed by any of the following: (1) The presence of pathologic Q-waves in ≥2/12 leads of the baseline surface ECG), (2) akinetic or dyskinetic wall motion abnormalities and/or (3) global ventricular dilatation with dysfunction on echocardiography, ventricular angiography or MRI and/or (4) areas of delayed enhancement on contrast enhanced MRI (5) fixed perfusion defects on nuclear imaging; or (6) regions with adjacent, fragmented, prolonged (≥3 positive deflections, ≥40ms signal duration) and low amplitude bipolar electrograms (≤1.5mV) on contact electroanatomical voltage mapping (EAM).

Electrophysiology study and Electroanatomic Mapping

Electrophysiological evaluation included electrical programmed stimulation (EPS) and EAM. Studies were performed in the post absorptive, non-sedated state. Antiarrhythmic drugs were discontinued for 5 half-lives, with the exception of amiodarone. The EPS-protocol consisted of 2 or 3 drive-cycle lengths (600, 500 and 400ms) and up to 3 ventricular extrastimuli from 2 right ventricular sites and burst pacing. Burst pacing and programmed stimulation during intravenous infusion of isoproterenol (2-8μg/min) were used if the VA was not inducible at baseline. Twelve-lead ECGs and intracardiac electrograms were recorded simultaneously (Cardio-Lab 4.1; Prucka Engineering, Houston, TX, USA) and stored in digital format for
off-line analysis. More than three monomorphic, consecutive beats were classified as ventricular tachycardia (VT) and ≤3 consecutive monomorphic beats as premature ventricular contractions (PVCs). Bipolar EAM of the RV and/or LV was performed in all patients, facilitated by a 3D EA mapping system (CARTO XP EP system Biosense Webster Inc, Diamond Bar, CA, USA) during sinus rhythm in 193(91%) patients and paced rhythm in 20(9%). A 4mm or 3.5mm tip, irrigated quadripolar mapping catheter (NaviStar or Navistar ThermoCool, Biosense Webster Inc, Diamond Bar, CA, USA) was used inserted via a transvenous or retrograde aortic approach. In the algorithm development group mapping was restricted to the RV in 35(43%), to the LV in 35(43%), both ventricles were mapped in 11(14%) and epicardial voltage mapping through a subxyphoid puncture was performed in 4 patients.

A VA exit site was determined based on activation and entrainment mapping for mappable VA and based on pace-mapping for unmappable VA. During activation mapping VA exit sites were defined as sites with the earliest ventricular activation and a local unipolar QS-pattern for focal VA and/or sites where pacing entrained the VT with concealed fusion and a postpacing interval within 30ms of the VT cycle length and a S-QRS of ≤30% of VT cycle length for reentry tachycardia. During pace-mapping VA exit sites were defined as sites with a paced QRS morphology that matches the VA QRS morphology (≥11/12 lead QRS pace-match). VA were considered scar-related if a VA exit site was located in or near an area of scar.

**ECG analysis**

All 12-lead surface ECGs of spontaneous or induced VA were analyzed by two independent observers blinded to the findings of imaging and EAM. In case of discrepancy agreement was reached by consensus. Measurements were performed on the digitally recorded electrograms
at a sweep speed of 100mm/s (Cardio-Lab 4.1; Prucka Engineering, Houston, TX, USA) using electronic callipers.

Based on previous literature and theoretical considerations analysis included:

1. QRS duration (QRSd) measured from the QRS onset, defined as the earliest deflection from the isoelectric line in any ECG lead to the QRS offset, defined as the latest intercept of the S or R-wave with the isoelectric line in any ECG lead.

2. Frontal plane axis categorized as inferior (≥0° and <180°) or superior (≥180° and <0°).

3. Precordial transition defined as the first precordial lead with an R/S ratio of >1. An R wave transition beyond V4 (e.g. V5, V6, or negative concordance) was considered ‘late’ (transition>V4).

4. QRS-S (QRS-SV1) interval in precordial lead V1 defined as the interval from QRS onset in any lead to the nadir of the S wave in V1.

5. Total amplitude of the QRS complex (QRSa) in precordial lead V2

6. The total number of notched QRS complexes in all leads (notch total)

7. The presence of a notch in the downstroke of the S-wave in precordial lead V1 and V2 (Notch S downstroke V1/2).

**Statistical analysis**

Continuous variables are expressed as mean±SD, and categorical variables as frequency (%) or percentage (95% confidence interval). Differences between scar-related and non-scar-related VA were assessed using the unpaired student t-test. Dichotomous variables were compared using chi-square test. Since the exit site and the propagation wavefront which determine the surface ECG characteristics of a VA differ between VA in one patient, multiple VA in the same patient were regarded as independent for the primary analysis. Variables where the means or frequencies were significantly different between groups were considered
for further analysis. Cutoffs were based on choosing the value where the sensitivity and specificity were the same for the prediction of scar. Sensitivity and specificity for each individual value were calculated based on the cut point chosen by the ROC curve.

Variables were categorized accordingly. Next, these variables were analyzed in univariate and multivariable binary logistic regression. Multivariable analysis was performed in a backward stepwise fashion excluding the variable that was the least significant with for each consecutive step until all remaining variables in the model had a p-value lower than 0.25.

These variables were incorporated in a stepwise algorithm. If any of the algorithm variable criteria for scar was met, outcome was considered positive for scar. If none of the variable criteria for scar was met, the outcome was considered idiopathic.

All statistical analyses were performed with SPSS software (version 16 SPSS Inc., Chicago, Illinois). For all tests a p-value ≤ 0.05 was considered significant.

**Algorithm validation**

The algorithm was then prospectively evaluated in 179 LBBB type VA recorded and stored during RFCA in 132 patients. All 12-lead surface ECGs of the VA were analyzed by two independent observers blinded to the results of scar detection. Each algorithm criterion was separately classified as positive or negative. In case of discrepancy agreement was reached by consensus. A VA was defined as scar-related if ≥1 out of the variables selected for the algorithm were positive, a VA was classified as idiopathic if all criteria were negative.

These results were compared to the results of scar detection based on baseline ECG, imaging and EAM according to the defined criteria for scar. All patients underwent 12-lead ECG recording, 2-dimensional echocardiography and endocardial EAM as described. In the algorithm development group only the RV was mapped in 76(58%) patients, only the LV in 37(28%), both ventricles in 19(14%) and epicardial voltage mapping was performed in
24(18%). To rule out scar-related VA further analysis was performed including coronary angiography, MRI/contrast enhanced-MRI, nuclear imaging and biopsy if appropriate. Seven VA in 6 patients with evidence of scar on baseline ECG, imaging or EAM but with a VA exit mapped to an area of normal myocardium and remote from scar areas were excluded from the analysis.

Follow-up
Data regarding survival was collected for all patients (from the social security death index for the US patients and from long-term follow-up visits for the Netherlands patients). The date of last contact, heart transplantation or death was considered the date of last follow-up.

RESULTS
Algorithm development
One hundred-eighteen LBBB type VA were analyzed. A total of 95 VA were scar-related and 23 arose from normal myocardium. The etiology of scar and the modality of scar detection are summarized in table 1.

ECG analysis
Scar-related VA had a longer QRSd, a longer QRS-S duration in V1, and a smaller QRS amplitude in V2 as compared to non scar-related VA. In addition, a superior axis, a notch in the downstroke of the S-wave in lead V1 or V2 and a late precordial transition were more frequent in VA that arose from scar areas. The total number of notched QRS complexes was higher in scar-related VA, the difference however did not reach statistical significance between both groups (p=0.055).
The best cutoff values to discriminate between scar-related and non-scar-related VA were a QRSd of >155ms, a QRS-S interval of >90ms and a QRS amplitude in V2 >1.55mV (Table 2).

In multivariable analysis a late transition, a notch in the S downstroke of V1 or V2 and a QRS-S interval of >90ms were independently predictive for the presence of scar and therefore selected for the algorithm (table 3, figure 1).

**Prospective validation**

The developed algorithm was validated in 179 VA collected prospectively in 132 patients during consecutive RFCA procedures. In 31 patients >1 LBBB pattern VA was recorded. Scar was detected by ECG, imaging and/or EAM in 76 patients with a total of 120 documented VA. The remaining 59 VA recorded in 56 patients were considered to be non scar-related. The results of scar detection and the etiology of scar in scar-related VA are summarized in table 1. The outcome of the algorithm was positive for scar in 125(70%) VA and negative for scar in 54(30%) VA (table 4). Based on scar detection the outcome of the algorithm was considered true positive in 115 VA, true negative in 49 VA, false positive in 10 VA and false negative in 5 VA. This results in a sensitivity of 96%(90-98) and specificity of 83%(71-91) to discriminate between scar-related and non-scar-related VA (Figure 2). The values for each algorithm component are provided in table 4.

Since sustained VT was more common in patients with scar (116(85%) scar-related sustained VT) as compared to patients without scar (20(34%) non scar-related sustained VT) the algorithm was separately evaluated for the prediction of scar in VT and PVC subgroups. Sensitivity and specificity were found to be high for the prediction of scar in VT (sensitivity 96%(90-98) and specificity 70%(46-87)) and PVCs (sensitivity 100%(40-100) and specificity...
90%(75-97)). Likely attributable to the different prevalence of PVCs and VT in scar-related and non scar-related groups the positive predictive value (PPV) for scar-related VA was low for PVCs (PPV 50%(17-83)) with a negative predictive value (NPV) of 100%(88-100). For VT the PPV was 95%(89-98) and the NPV 74%(49-90).

As most idiopathic VTs arise from the outflow tract region, the algorithm was separately evaluated for 105 VA with an inferior axis. Among these VA the algorithm correctly identified 46 out of 51 scar-related VA and 47 out of 54 non scar-related VA. This resulted in a sensitivity of 90%(78-96) and specificity of 87%(75-94).

In patients with known heart disease, VA should be presumed to be related to the underlying disease unless proven otherwise. We therefore assessed the algorithm excluding patients with ischemic heart disease or congenital heart disease, in whom prior knowledge of heart disease may be most likely. In the remaining 101 patients with 134 VA the sensitivity of the algorithm to predict scar was 93% (84-97) with a specificity of 83%(71-91).

Analysis of misclassified VA

Ten VA recorded in 9 patients were classified as scar-related based on the ECG algorithm without scar detection on ECG, imaging or EAM (table 5). Two VA were recorded in one patient in whom mapping revealed a focal endocardial exit of presystolic activity, but where ablation was unsuccessful; no epicardial mapping was performed. We can not exclude the possibility that epicardial EAM would have revealed scar, improving the algorithm performance. Four VA were mapped to the aortic cusp or epicardial LVOT, two arose from the tricuspid annulus and two from the RVOT (figure 3).

Five VA in 4 patients were misclassified as non scar-related. Three were related to a small epicardial scar area not detected by endocardial voltage mapping or imaging, one to a small
posterior RVOT scar detected by EAM and one to a basal septal scar in a patient with dilated cardiomyopathy.

Interestingly in patients 4, 11 and 13 (table 5) ≥1 other VA were correctly classified as non scar or scar-related.

First induced VA

To adjust for the possible unequal representation of individual patients due to multiple inducible VA an additional analysis was performed testing the algorithm for only the first VA that was induced or recorded spontaneously in each of the 132 patients. When only these VA were taken into consideration the algorithm correctly identified 73 of 76 scar-related and 49 of 56 non scar-related VA. This resulted in a similar sensitivity (96%(88-99)) and specificity of (88%(79-95)) as in the analysis of all VA.

Amiodarone

In the algorithm validation group 22 patients with 34 VA were treated with amiodarone, the dosage was 324±247mg daily. The VA QRSd in patients on amiodarone was 218±50ms as compared to 170±121ms(p=0.03) in patients not on amiodarone. Since the use of Amiodarone may influence conduction properties an additional analysis excluding all patients using amiodarone was performed to determine whether the use of amiodarone affected the outcome of the algorithm. In the remaining 145 VA the sensitivity of the algorithm was 94%(86-98) and specificity 83%(71-91) to identify scar-related VA.

Mortality

Patients in whom the algorithm was developed were followed for 42±21months. During follow-up 13(16%) patients with scar-related VA classified by the ECG algorithm died and
2(2%) patients underwent cardiac transplantation. In contrast, all patients who were classified as having non-scar VA survived. The follow-up duration in the prospective analysis group was 14±11 months (median 10, range 0-34 months). Eleven (6%) patients with algorithm based scar-related VA died whereas all patients who were classified as having non scar-related VA survived.

**DISCUSSION**

Scar-related reentry is the most common cause of sustained monomorphic VT in patients with structural heart disease, and usually warrants implantation of a defibrillator for protection from sudden cardiac death.\(^7\) In contrast, most idiopathic VA have a focal origin not associated with detectable scar, and a benign prognosis. Most have a LBBB pattern morphology and originate in the outflow tract of the RV or LV.\(^5\) LBBB pattern VA however can also be due to scar-related reentry, arising from RV and septal scars.\(^1-4\) A correct diagnosis of scar-related and idiopathic VA is important for long-term prognosis and therapeutic considerations. Diagnosis of idiopathic VA is still one of exclusion and may therefore require extensive non-invasive and invasive assessment.\(^8\)

The current study evaluated the affect of ventricular scar assessed by sinus rhythm ECG, cardiovascular imaging and electroanatomical voltage mapping on QRS morphology characteristics of LBBB pattern VA on 12-lead ECG.

A simple stepwise algorithm of 3 ECG criteria was developed based on 118 retrospectively collected VA ECGs and prospectively tested in 179 LBBB pattern VA allowing for discrimination of VA originating from scarred or structurally normal myocardium with a high sensitivity and specificity.
**Ventricular Scar**

In the current study only VA ECGs from patients referred for RFCA were included. These patients underwent extensive evaluation including evaluation of the baseline ECG for the presence of Q-waves, cardiac catheterization and cardiovascular imaging. In addition, EAM was performed during RFCA in all patients to diagnose or confirm the presence of scar at the VT exit. The latter is of importance because EAM has been shown to be highly sensitive to detect scars that may escape detection by imaging. Accordingly, scar associated with VA was diagnosed only by EAM in 5(4%) VA evaluated retrospectively and in 22(12%) VA evaluated prospectively. In the latter group epicardial EAM was applied more frequently. Only patients in whom no scar was detected by any modality were considered to have idiopathic VA. That none of these patients died during follow-up, further suggests that important structural heart disease was unlikely to escape detection in our cohort.

**12-lead ECG of the VA and Site of Origin**

ECG analysis of the VA included morphology characteristics related to the site of origin, QRS amplitude, duration and notching with special emphasis on the precordial leads V1 and V2.

A superior axis is consistent with a more inferior and apical exit which is frequently observed in patients with ARVD/C but rare in idiopathic VA. An inferior axis with a late transition beyond V4 is consistent with a more inferior and anterior exit below the pulmonary valve and is therefore also not frequently found in idiopathic VA. However, a superior axis or inferior axis with a late precordial transition may occur in VA that arise from the tricuspid annulus region accounting for <5% of idiopathic VA. Of interest, in one series patients with idiopathic VA arising from the tricuspid annulus were older and experienced more often ablation failure than patients with idiopathic VA originating from the RVOT. Although
structural abnormalities were excluded by imaging perivalvular fibrosis as observed in other non-ischemic cardiomyopathies can not be fully excluded as a cause of this type of VA.\textsuperscript{14}

Accordingly, the majority of idiopathic VA in the current study had a transition before or at V4. A transition beyond V4 was only observed in 4 of the VA that were classified as idiopathic. Two arose from the tricuspid annulus, both with a superior axis, one arose from the mid to apical septal region and one occurred in a patient with an epicardial circuit.

A broadly notched QRS(\textgreater 160ms) of PVCs has been associated with a dilated and hypokinetic left ventricle.\textsuperscript{15} In a study by Ainsworth the mean VA QRSd for all 12 leads was longer in ARVD/C patients (135.1±8.5ms) as compared to patients with idiopathic VA (126.5±13ms) measured on ECG paper copies recorded at 25mm/s. We found longer QRS durations in scar-related (184±43ms) and idiopathic (147±15ms) VA likely due to measurement of QRS duration from simultaneous recordings of all leads, which likely avoids errors introduced due to isoelectric components in some leads.

QRS duration was significantly longer in scar-related VT as compared to idiopathic VA and a QRSd>155ms argues for a scar-related VA. However, scar-related VA that arise from or near the septum might have a short QRS duration. In contrast, idiopathic VA that arise from the free wall of the RV may exhibit a longer QRS duration.\textsuperscript{16}

The presence of notches might reflect disturbed conduction and may therefore be a sign of scar tissue but has also been demonstrated in idiopathic VA that arise from the RV free wall in up to 86\% of patients.\textsuperscript{15} Although, we found a slightly higher number of total notches in the 12 leads, the difference as compared to idiopathic VA were not significant.

The QRS morphology of VA is determined by the location at which the activation wavefront emerges to activate the ventricles. Areas of delayed conduction at this site, as typically found in scar-related reentry, may contribute to the QRS characteristics by prolongation and notching of its initial portion. In contrast in patients with structurally normal hearts, the
spread of activation from the site of origin is rapid. The interval from the QRS onset in any lead to the nadir of the S in V1 was significantly prolonged in scar-related VA and notching of the S-downstroke in V1 or V2 was associated with the presence of ventricular scar. This is in line with the assumption that activation delay due to RV and septal fibrosis translates into a prolonged and notched initial portion of the VA QRS in lead V1 and V2.

Interestingly, longer QRS onset to S nadir in V1 (>60ms) and notching in the S-wave downstroke of V1 or V2 have previously been identified by Kindwell and used by Brugada for the discrimination between supraventricular and ventricular origin of broad complex LBBB type tachycardias. Ninety-five percent of the VTs studied by Kindwell however were originating from structurally abnormal hearts, the majority being related to infarct scar.

**Algorithm development and validation**

In multivariable analysis a late precordial R-wave transition, notching of the S downstroke in V1 or V2 and the QRS to S duration in V1 were shown to be independently associated with scar-related VA, but individually have a high specificity, but low sensitivity. Combining the three criteria improved sensitivity to 96% with a specificity of 83%. In subgroup analysis the algorithm was sensitive and specific to predict scar in patients with PVCs and with sustained VT. Furthermore if only VA with an inferior axis were taken into consideration, the most frequently observed axis in idiopathic VA, the sensitivity was still 90% and the specificity 88%. Despite the high sensitivity in identifying scar-related VA the algorithm misclassified 10 VA as scar-related. In half of those the origin of the VA was considered to be epicardial or found in the aortic cusps.

Idiopathic VA with an epicardial or aortic cusp origin may have a prolonged QRS duration due to the time needed for the activation wavefront to traverse the myocardial wall and reach
and could be falsely classified as scar-related by our algorithm based on prolonged initial QRS duration. This QRS prolongation can be present or absent according to the epicardial location or origin of VA. Similarly idiopathic LBBB type VA that originate from the TA may be misclassified due to the late precordial R-wave transition associated with this site of origin. Five VA were misclassified as idiopathic. In three patients small scar areas were only detected by epicardial voltage mapping and in one by endocardial EAM underlying the importance of EAM to differentiate between idiopathic and scar-related VA.

Limitations

In addition to the caveats discussed above there are other limitations to this study. As in previous studies the diagnosis of idiopathic VA was made when evaluation excluded the presence of scar. Even though the extensive evaluation including EAM is a strength of this study the lack of a currently available gold-standard for the diagnosis of idiopathic VA may allow misclassification of patients with a currently undetectable substrate for VA. The studied population did not include patients with known channelopathies, such as Brugada syndrome or long QT syndrome. Commenting on the VA QRS morphology in these patients who may be at risk for sudden death despite the absence of structural heart disease is therefore beyond the scope of this study.

ECG measurements were performed during electrophysiological study at a sweep speed of 100mm/s, standard ECGs in clinical practice however are often printed at 25mm/s. It is possible that some of the observations, such as the QRS-Sd in V1, may be more difficult in standard ECGs recorded at speed of 25mm/s.

Finally although the absence of mortality in the idiopathic group is reassuring and further supports the diagnosis of idiopathic VT, we can not exclude the possibility of small regions
of ventricular scar that escape detection with present methods are present in some patients and that could lead to later development of other VA.

**Clinical implications**

The proposed algorithm detects scar-related VA with high specificity. Although it is not a substitute for imaging to define ventricular function and structural disease, it does provide an immediate electrocardiographic indication of the likelihood of whether ventricular scar is likely to be present, that can inform further evaluation. Furthermore, patients with algorithm positive VA ECG who do not have evidence of structural heart disease on initial clinical assessment may be considered for more detailed imaging, such as MRI.

**Conflict of Interest Disclosures:** Lawrence Epstein received grants from Boston Scientific, Medtronic & St. Jude Medical. Usha Tedrow received research grants from St. Jude Medical and Biosense Webster.

**References:**


### Table 1. Baseline characteristics

<table>
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<th></th>
<th>Algorithm development</th>
<th>Algorithm validation</th>
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<tbody>
<tr>
<td></td>
<td>n=118 VA</td>
<td>n=179 VA</td>
</tr>
<tr>
<td>Scar-related</td>
<td>95(81)</td>
<td>120(67)</td>
</tr>
<tr>
<td>Underlying disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ischemic cardiomyopathy</td>
<td>48(41)</td>
<td>40(22)</td>
</tr>
<tr>
<td>Dilated cardiomyopathy</td>
<td>18(15)</td>
<td>31(17)</td>
</tr>
<tr>
<td>ARVC/D</td>
<td>13(11)</td>
<td>20(11)</td>
</tr>
<tr>
<td>Congenital</td>
<td>6(5)</td>
<td>5(3)</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td>4(3)</td>
<td></td>
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<tr>
<td>Valvular</td>
<td>6(5)</td>
<td>2(1)</td>
</tr>
<tr>
<td>Hypertrophic</td>
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<td>1(1)</td>
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<tr>
<td>Cardiomyopathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scar of unknown etiology</td>
<td>0</td>
<td>21(12)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>23(19)</td>
<td>59(33)</td>
</tr>
<tr>
<td>Scar detected by</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ECG + imaging + EAM</td>
<td>36(31)</td>
<td>30(17)</td>
</tr>
<tr>
<td>Imaging + EAM</td>
<td>51(43)</td>
<td>62(35)</td>
</tr>
<tr>
<td>Only ECG</td>
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<td>0</td>
</tr>
<tr>
<td>Only imaging</td>
<td>3(3)</td>
<td>6(3)</td>
</tr>
<tr>
<td>Only EAM</td>
<td>5(4)</td>
<td>22(12)</td>
</tr>
<tr>
<td>VT/PVCs</td>
<td>107/11</td>
<td>136/43</td>
</tr>
</tbody>
</table>

ARVC/D indicates arrhythmogenic right ventricular cardiomyopathy/dysplasia; ECG, electrocardiogram; EAM, electroanatomical mapping; VT, ventricular tachycardia; PVC, premature ventricular contraction; VA, ventricular arrhythmia. Values are displayed as frequency(%) or mean±SD.
Table 2. VT QRS variables and test variables in the 118 algorithm development VA

<table>
<thead>
<tr>
<th>Scar n=95</th>
<th>Non scar n=23</th>
<th>p=</th>
<th>Test Variable</th>
<th>Test variable positive n=</th>
</tr>
</thead>
<tbody>
<tr>
<td>QRSd (ms)</td>
<td>184±43</td>
<td>147±15</td>
<td>&lt;0.001</td>
<td>QRSd &gt;155ms</td>
</tr>
<tr>
<td>Superior Axis</td>
<td>35(37)</td>
<td>3(13)</td>
<td>0.028</td>
<td>Axis 180°≥ and &lt;0°</td>
</tr>
<tr>
<td>Transition &gt;V4</td>
<td>50(53)</td>
<td>1(4)</td>
<td>&lt;0.001</td>
<td>Transition &gt;V4</td>
</tr>
<tr>
<td>QRS-S interval V1 (ms)</td>
<td>107±29</td>
<td>83±18</td>
<td>&lt;0.001</td>
<td>QRS-SV1 &gt;90ms</td>
</tr>
<tr>
<td>QRS amplitude V2</td>
<td>1.5±0.7</td>
<td>2.1±1.2</td>
<td>0.005</td>
<td>QRSa V2 &gt;1.55</td>
</tr>
<tr>
<td>Notch total</td>
<td>3.0±2.4</td>
<td>1.9±2.0</td>
<td>0.055</td>
<td></td>
</tr>
<tr>
<td>Notch S downstroke V1/2</td>
<td>35(37)</td>
<td>3(13)</td>
<td>0.028</td>
<td>NotchS downstroke V1/2</td>
</tr>
</tbody>
</table>

QRSd indicates QRS duration. Variables are displayed as frequency(%) or mean±SD.

Table 3. Univariable and multivariable logistic regression of test variables in the algorithm development VA

<table>
<thead>
<tr>
<th></th>
<th>Univariate</th>
<th>Multivariate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>OR (95% CI)</td>
<td>p=</td>
</tr>
<tr>
<td>QRSd &gt;155ms</td>
<td>3.7 (1.4–9.5)</td>
<td>0.006</td>
</tr>
<tr>
<td>Superior Axis</td>
<td>3.9 (1.1–14.0)</td>
<td>0.038</td>
</tr>
<tr>
<td>Transition &gt;V4</td>
<td>24.4 (3.2–188.8)</td>
<td>0.006</td>
</tr>
<tr>
<td>QRS-S nadir V1 &gt;90ms</td>
<td>6.4 (2.4–17.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>QRS amplitude V2 &gt;1.55</td>
<td>0.6 (0.2–1.5)</td>
<td>0.291</td>
</tr>
<tr>
<td>Notch S downstroke V1/2</td>
<td>3.9 (1.1–14.0)</td>
<td>0.038</td>
</tr>
</tbody>
</table>

OR indicates Odds ratio; QRSd, QRS duration. Variables are displayed as frequency(%) or mean±SD.
Table 4. Outcome of the algorithm in 179 validation VA

<table>
<thead>
<tr>
<th></th>
<th>Transition &gt;V4</th>
<th>Notch d V1/2</th>
<th>QRS-Sd V1 &gt;90ms</th>
<th>Algorithm</th>
</tr>
</thead>
<tbody>
<tr>
<td>True Positive</td>
<td>83(46)</td>
<td>42(23)</td>
<td>86(48)</td>
<td>115(64)</td>
</tr>
<tr>
<td>False Positive</td>
<td>3(2)</td>
<td>5(3)</td>
<td>7(4)</td>
<td>10(6)</td>
</tr>
<tr>
<td>True Negative</td>
<td>56(31)</td>
<td>54(30)</td>
<td>52(29)</td>
<td>49(27)</td>
</tr>
<tr>
<td>False Negative</td>
<td>37(21)</td>
<td>78(44)</td>
<td>34(19)</td>
<td>5(3)</td>
</tr>
<tr>
<td>Sensitivity (%)</td>
<td>69(60-77)</td>
<td>35(27-44)</td>
<td>72(63-79)</td>
<td>96(90-98)</td>
</tr>
<tr>
<td>Specificity (%)</td>
<td>95(85-99)</td>
<td>92(81-97)</td>
<td>88(76-95)</td>
<td>83(71-91)</td>
</tr>
<tr>
<td>PPV (%)</td>
<td>97(89-99)</td>
<td>89(76-96)</td>
<td>93(85-97)</td>
<td>92(85-96)</td>
</tr>
<tr>
<td>NPV (%)</td>
<td>60(50-70)</td>
<td>41(33-50)</td>
<td>61(49-71)</td>
<td>91(79-97)</td>
</tr>
</tbody>
</table>

VA indicates ventricular arrhythmia; PPV, positive predictive value; NPV, negative predictive value. Values are displayed as frequency(%) or percentage(95% confidence interval).
### Table 5. Misclassified VA according to the ECG algorithm

<table>
<thead>
<tr>
<th>Patient</th>
<th>VA</th>
<th>Scar</th>
<th>Axis</th>
<th>Transition &gt;V4</th>
<th>Notching V1/V2</th>
<th>QRSs V1&gt;90ms</th>
<th>Site of origin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
<td>1</td>
<td>non-scar</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>2</td>
<td>non-scar</td>
<td>Sup</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>3</td>
<td>non-scar</td>
<td>Sup</td>
<td>1</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>4</td>
<td>non-scar</td>
<td>Inf</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>5</td>
<td>non-scar</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>6</td>
<td>6</td>
<td>non-scar</td>
<td>Sup</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>7</td>
<td>non-scar</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>8</td>
<td>non-scar</td>
<td>Inf</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>9</td>
<td>9</td>
<td>non-scar</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>1 Small epicardial scar on EAM</td>
<td>Inf</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>2 Small epicardial scar on EAM</td>
<td>Inf</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>3 DCM</td>
<td>Inf</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>4 Posterior RVOT, endocardial scar</td>
<td>Inf</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>5 Epicardial scar RV inferior and RVOT</td>
<td>Inf</td>
<td>Inf</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

DCM indicates dilated cardiomyopathy; EAM, electroanatomical mapping; RV, right ventricle; RVOT, right ventricular outflow tract; VA, ventricular arrhythmia.
Figure Legends:

Figure 1. Representative examples of the variables that were used in the algorithm. The first 3 panels show scar-related VT morphologies, the most right panel shows a non scar-related VT.

Figure 2. The step by step flow chart of the algorithm for the 179 validation VA. VA indicates ventricular arrhythmia; TP, true positive; FP, false positive; TN, true negative and FN, false negative.

Figure 3. Examples of three QRS morphologies of false positive VA. These VA were originating from the epicardium, aortic cusp and tricuspid annulus (table 5 patient 2, 4 and 5) respectively. Notches in lead V1/2, a late transition and QRS S V1>90ms are indicated.
Precordial transition > V4

- no
  - 93
  - Notch downstroke V1/2
    - no
    - 78
    - QRS-Sd V1 > 90ms
      - no
      - 54 non scar-related
        - TN=49, FN=5
    - yes
      - 24 scar-related
        - TP=20, FP=4

- yes
  - 86 scar-related
    - TP=83, FP=3

125 scar-related
  TP=115, FP=10
ECG Identification of Scar-Related Ventricular Tachycardia with a Left Bundle Branch Block Configuration
Adrianus P. Wijnmaalen, William G. Stevenson, Martin J. Schalij, Michael E. Field, Kent Stephenson, Usha B. Tedrow, Bruce A. Koplan, Hein Putter, Lawrence M. Epstein and Katja Zeppenfeld

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