The heart rate of ventricular tachycardia following an old myocardial infarction is inversely related to the size of scarring

Leik Woie1*, Trygve Eftestøl2, Kjersti Engan2, Jan Terje Kvaløy3, Dennis W.T. Nilsen1,4, and Stein Ørn1

1Department of Cardiology, Stavanger University Hospital, 4011 Stavanger, Norway; 2Department of Electrical and Computer Engineering, University of Stavanger, 4036 Stavanger, Norway; 3Department of Mathematics and Natural Sciences, University of Stavanger, 4036 Stavanger, Norway; and 4Institute of Medicine, University of Bergen, Bergen, Norway

Received 27 October 2010; accepted after revision 27 November 2010; online publish-ahead-of-print 11 January 2011

Aims
The purpose of the study was to examine the relationship between the initial cycle length (CL) of ventricular tachycardia (VT) and the size of the myocardial scar and its border zone in patients with old myocardial infarction (MI).

Methods and results
Late gadolinium-enhancement cardiac magnetic resonance was performed prior to implantable cardioverter-defibrillator (ICD) implantation in 24 patients. The size of non-scared myocardium, scar, scar core, and border zone were measured as voxel numbers. The number of core islands, contour-regularity of scar and left-ventricular ejection fraction were also calculated. During the first year after ICD implantation, VT was recorded in 20 patients. With univariate regression analysis, the number of core islands had the highest correlation with the CL of VT ($R = 0.614$, adjusted $R^2 = 0.342$, $P = 0.004$). By multiple regression analyses, the highest correlation was found by the use of scar core and core islands ($R = 0.721$, adjusted $R^2 = 0.464$, $P = 0.002$).

Conclusion
The heart rate of VT (bpm) in patients with old MI is inversely related to the properties of the densest parts of the myocardial scar.

Keywords
Late gadolinium-enhancement cardiac magnetic resonance • Myocardial scar • Rate of ventricular tachycardia

Introduction
It is generally agreed that sustained monomorphic ventricular tachycardia (VT) is due to re-entry mechanisms, mainly caused by scarred tissue following a myocardial infarction (MI). The heart rate of VT is dependent on the time it takes for the circulating excitation wave to propagate once around the circuit. The excitation wave front may travel through normal tissue along the border of the scar or through the infarct region, and is dependent on conduction velocity, dispersion of refractoriness, and cellular uncoupling in various parts of the substrate.1 Despite numerous studies of the electrophysiological properties of a re-entrant circuit, no studies have examined the relationship between the rate of sustained VT and the size of the myocardial scar or its border zone. In this study, we investigate whether such a relationship can be found.

Methods
In this study, we have analysed late gadolinium-enhancement cardiac magnetic resonance (LGE-CMR) images obtained before implantation of implantable cardioverter-defibrillator (ICD) and all VT stored in the ICD during a follow-up period of 1 year.

Study population
Twenty-four patients with scars following old MIs and an ICD indication were included. For recording and definition of VT, we used the same ICD device (Vitality 2 DR®, model T165 and T167, Guidant Corp.). The ICD device was implanted for secondary prevention in 18 patients (nine survivors of sudden cardiac death and nine symptomatic VT), and for primary prevention in six patients with left-ventricular ejection fraction (LVEF) of <30% and non-sustained VT (NSVT). All patients were examined by coronary angiography, and four had non-ST-elevation MI in need of percutaneous coronary
intervention and one patient underwent coronary artery bypass graft surgery prior to ICD implantation. All patients had stable sinus rhythm and were examined by LGE-CMR within a few days (5.9 ± 5.5) prior to ICD implantation.

The patients were controlled every 3 months during the first year after ICD implantation. The detection zones of VT were set at RR intervals between 500 and 353 ms (120–170 bpm). Ventricular tachycardia was recorded when 8 of 10 cycle lengths (CLs) were below the detection zone and with a duration of at least 2.5 s. The measured CL of VT was calculated as the mean value of eight RR intervals before and six RR intervals after detection, i.e. a total of 13 intervals. Only the first VT during the observation period is used for the regression analyses, and was recorded in 20 of the 24 patients, in the 9 subjects with VT indication, in 6 of 9 with cardiac arrest indication, and in 5 of 6 with NSVT indication. The VTs recorded had a median CL of 325 ms (range 239–438) and a median variance of 303 ms² (range 36–14242).

The study was approved by the Regional Ethics Committee, and informed consent was obtained from all patients.

LGE-CMR protocol

Cardiac magnetic resonance was performed with a 1.5 T Philips Intera R 8.3. Functional assessment of LVEF, volumes, and mass were performed according to the current recommended standards with the use of steady-state, free precession sequence covering the whole LV with 8-mm thick short-axis slices, and an inter-slice gap of 2 mm. After functional assessment, a gadolinium-based contrast agent was administered intravenously at a dosage of 0.25 mmol/kg. Late gadolinium-enhancement images were acquired 10–15 min later, using an inversion recovery-prepared T1-weighted gradient-echo sequence with a pixel size of 0.82 × 0.82 mm², covering the whole ventricle with short-axis slices of 10 mm thickness, without inter-slice gaps. Inversion recovery sequences were performed with individually adapted infrared times of 200–300 ms aiming to nullify normal myocardium.

All post-processing was performed using the View Forum™ software (Philips Medical Systems, Best, The Netherlands). Assessment of LV volumes and mass, as well as scar characteristics, were performed on both full short-axis data sets in a random, blinded fashion. Indexes for LV mass and volumes were obtained by division of body surface area. Scar size was assessed manually with planimetry on each short-axis slice, delineating the hyperenhanced area, and adding all slices to generate scar volume. The same density (1.05 g/cm³) was assumed for both hyperenhanced (scanned) and non-hyperenhanced (non-scarred) myocardium.

Myocardial segments

The myocardial segment analyses were performed on stored DICOM (Digital Imaging and Communications in Medicine) images with a pixel resolution of 512 × 512. The images were segmented as illustrated in Figure 1. The left ventricular area and the scar area were assessed interactively on each short-axis slice, delineating the left ventricle and the hyperenhanced area. An optional number of coordinates, marked as grey dots on the figure, is set by an experienced CMR cardiologist (S.O.) using the mouse pointer. The contours are generated as cubic spline interpolations of these coordinates. The yellow contours mark the inner and outer boundary of the myocardium. The red line marks the contour of the scar area. In this work, we define two other areas, the scar core and the border zone. The scar core is, as the name suggests, a part of the scarred area. We want to define the part(s) of the scar that are mostly damaged, i.e. with highest intensity in the LGE-CMR images. The definition needs to be image dependent since a global threshold strategy would fail due to large patient-to-patient (and image-to-image) variations. First, the max-level (ML) is found as the highest intensity level, i.e. what appears as the brightest pixel (picture element), in the scarred area.

Secondly, the standard deviation, SD, of the intensity values of all the pixels in the scarred area is calculated. Then, the scar core is defined as follows: an image-dependent threshold, decided as Ti = ML − 2 × SD. For every pixel in the scar area, if the intensity level is larger than the threshold, Ti, that pixel belongs to the scar core group. With this definition the scar core does not need to be one continuous area, but can consist of a image-by-image variable number of islands (‘core islands’ is a feature used later in the experiments and corresponds to this number for each image) strictly within the scarred area. The scar core of the example is depicted in Figure 2G and I, and here it consists of four islands.

The motivation for defining a border zone is that the border between what is considered to be scar and healthy myocardium can be hard to decide accurately and objectively, and that the part of the myocardium that is a little bit damaged but not heavily damaged can be an important area regarding how the heart muscle will behave later. Thus, we want the border zone to include a part outside but near the border defined by the scar segmentation.

The border zone is defined by several operations. First, we consider the scar area as (manually) segmented, and the convex hull (CH) of this area is found. This can be explained as placing an imaginary rubber-band around the area. The scar segment is shown alone in Figure 2C, and the CH area in Figure 2E. The CH area is enlarged by a morphological image processing operation, called dilation. The dilation is performed using a diamond-shaped structure element (SE) with the distance from the SE origin to the points of the diamond is 4 pixels. The dilation can be pictured as moving the SE element around the area. The dilation can be an important area regarding how the heart muscle will behave later. Thus, we want the border zone to include a part outside but near the border defined by the scar segmentation.

The border zone is defined by several operations. First, we consider the scar area as (manually) segmented, and the convex hull (CH) of this area is found. This can be explained as placing an imaginary rubber-band around the area. The scar segment is shown alone in Figure 2C, and the CH area in Figure 2E. The CH area is enlarged by a morphological image processing operation, called dilation. The dilation is performed using a diamond-shaped structure element (SE) with the distance from the SE origin to the points of the diamond is 4 pixels. The dilation can be pictured as moving the SE element around the area. The dilation can be an important area regarding how the heart muscle will behave later. Thus, we want the border zone to include a part outside but near the border defined by the scar segmentation.

The border zone is defined by several operations. First, we consider the scar area as (manually) segmented, and the convex hull (CH) of this area is found. This can be explained as placing an imaginary rubber-band around the area. The scar segment is shown alone in Figure 2C, and the CH area in Figure 2E. The CH area is enlarged by a morphological image processing operation, called dilation. The dilation is performed using a diamond-shaped structure element (SE) with the distance from the SE origin to the points of the diamond is 4 pixels. The dilation can be pictured as moving the SE element around the area. The dilation can be an important area regarding how the heart muscle will behave later. Thus, we want the border zone to include a part outside but near the border defined by the scar segmentation.

The border zone is defined by several operations. First, we consider the scar area as (manually) segmented, and the convex hull (CH) of this area is found. This can be explained as placing an imaginary rubber-band around the area. The scar segment is shown alone in Figure 2C, and the CH area in Figure 2E. The CH area is enlarged by a morphological image processing operation, called dilation. The dilation is performed using a diamond-shaped structure element (SE) with the distance from the SE origin to the points of the diamond is 4 pixels. The dilation can be pictured as moving the SE element around the area. The dilation can be an important area regarding how the heart muscle will behave later. Thus, we want the border zone to include a part outside but near the border defined by the scar segmentation.
within the myocardium area, subtracting the scar core area. It is illustrated in Figure 2F and I.

The scar area divided by the CH area is called the contour-regularity of the scar, and if close to 1, the contour of the scar area is quite regular. From Figure 2E, this can be seen as the number of pixels in the blue area divided by the number of pixels in the blue + orange segments. The size of cardiac segments is defined as the numbers of voxels in: non-scarred myocardium, scar, scar core, and border zone. In addition, LVEF, contour-regularity of scar, and the numbers of core islands were also used for analysis. Complete details of the method have been described elsewhere.3

General statistical methods

Simple linear regression and ordinary Pearson correlation are calculated for the relationship between the CL of VT and cardiac segments, contour-regularity of scar, numbers of core islands, and LVEF.

Results

Characteristics of the study population with 24 patients are given in Tables 1 and 2. It was impossible to determine the time of the first MI in three patients. The medications are at the time of the first VT or at the end of the first year for the four patients without VT.

With univariate regression analysis, scar, border zone, and the numbers of core islands were significantly (P < 0.014) correlated with the RR interval of the VT, Table 3. The numbers of core islands had the highest correlation with the RR interval of the VT, Table 3. The numbers of core islands had the highest correlation with the RR interval of the VT, Table 3. The numbers of core islands had the highest correlation with the RR interval of the VT, Table 3.

Discussion

The main result of this study is the correlation of numbers of core islands after MI and the heart rate of patients with sustained VT. The highest correlation is achieved by a combination of numbers of core islands and scar core. Islands of core are the parts of the scar with the highest hyperenhancement. The histopathological
Heart rate of VT following an old MI

Table 3 Correlations of RR interval of ventricular tachycardia and sizes of cardiac segments quantified as mean number of voxels, left-ventricular ejection fraction, contour regularity of scar or numbers of core islands in 20 patients with ventricular tachycardia

<table>
<thead>
<tr>
<th></th>
<th>R</th>
<th>R^2</th>
<th>Adjusted R^2</th>
<th>Sig.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scar</td>
<td>0.603</td>
<td>0.364</td>
<td>0.329</td>
<td>0.005</td>
</tr>
<tr>
<td>Border zone</td>
<td>0.539</td>
<td>0.291</td>
<td>0.252</td>
<td>0.014</td>
</tr>
<tr>
<td>Scar core</td>
<td>0.430</td>
<td>0.185</td>
<td>0.140</td>
<td>0.058</td>
</tr>
<tr>
<td>Non-scarred-myocardium</td>
<td>0.108</td>
<td>0.012</td>
<td>0.043</td>
<td>0.651</td>
</tr>
<tr>
<td>LVEF</td>
<td>0.292</td>
<td>0.085</td>
<td>0.034</td>
<td>0.212</td>
</tr>
<tr>
<td>Contour-regularity of scar</td>
<td>0.121</td>
<td>0.015</td>
<td>0.040</td>
<td>0.611</td>
</tr>
<tr>
<td>Numbers of core islands</td>
<td>0.614</td>
<td>0.377</td>
<td>0.342</td>
<td>0.004</td>
</tr>
<tr>
<td>Best multiple model found by stepwise selection</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Numbers of core islands + core</td>
<td>0.721</td>
<td>0.520</td>
<td>0.464</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Limitation

This is an observational study of only 24 patients, with primary ICD indication in 6 patients and secondary indication in 18 patients. During the first year after ICD implantation, 20 had VT according to the ICD interpretation. Since we have performed large numbers of hypothesis tests, some low P-values may have been obtained by chance.

Conclusion and clinical implications

The heart rate of VT (bpm) in patients with old Mls is inversely related to the size of dense myocardial scar. When the tachycardia detection rate of VT is programmed in an ICD, the size of the myocardial scar should be considered, since large scars often have lower heart rates of VT. Left-ventricular ejection fraction is not correlated with the heart rate of VT, and patients with low LVEF do not tolerate prolonged VT.

Acknowledgements

We acknowledge Fredrikke Wick, RT, Bent Erdal, RT, Kurt Tjelta, RN, and Torbjørn Aarsland, RN, for important contributions.

Conflict of interest: none declared.
References


