



## Clinical Paper

# Ventricular fibrillation waveform characteristics differ according to the presence of a previous myocardial infarction: A surface ECG study in ICD-patients<sup>☆</sup>



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## ARTICLE INFO

## Article history:

Received 11 June 2015

Received in revised form 22 July 2015

Accepted 20 August 2015

## Keywords:

Ventricular fibrillation

Fourier analysis

Myocardial infarction

Implantable cardioverter defibrillator

Electrocardiography

## ABSTRACT

**Background:** Characteristics of the ventricular fibrillation (VF) waveform reflect arrest duration and have been incorporated in studies on algorithms to guide resuscitative interventions. Findings in animals indicate that VF characteristics are also affected by the presence of a previous myocardial infarction (MI). As studies in humans are scarce, we assessed the impact of a previous MI on VF characteristics in ICD-patients.

**Methods:** Prospective cohort of ICD-patients ( $n=190$ ) with defibrillation testing at the Radboudumc (2010–2013). VF characteristics of the 12-lead surface ECG were compared between three groups: patients without a history of MI ( $n=88$ ), with a previous anterior ( $n=47$ ) and a previous inferior MI ( $n=55$ ).

**Results:** As compared to each of the other groups, the mean amplitude and amplitude spectrum area were lower, for an anterior MI in lead V3 and for an inferior MI in leads II and aVF. Across the three groups, the bandwidth was broader in the leads corresponding with the infarct localisation. In contrast, the dominant and median frequencies only differed between previous anterior MI and no history of MI, being lower in the former.

**Conclusions:** The VF waveform is affected by the presence of a previous MI. Amplitude-related measures were lower and VF was less organised in the ECG-lead(s) adjacent to the area of infarction. Although VF characteristics of the surface ECG have so far primarily been considered a proxy for arrest duration and metabolic state, our findings question this paradigm and may provide additional insights into the future potential of VF-guided resuscitative interventions.

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## Introduction

Ventricular fibrillation (VF) is the first observed cardiac rhythm in about 30% of out-of-hospital cardiac arrests (OHCAs).<sup>1</sup> As a

potential strategy to improve the rather poor outcomes, the VF signal itself has become subject of study.<sup>2–4</sup>

It has been demonstrated that the VF waveform can be related to survival and favourable neurological outcome.<sup>5–7</sup> Given that the VF waveform reflects arrest duration and myocardial metabolic state, VF characteristics have also been studied to predict shock success, and may be used to guide the decision whether to opt for a strategy of immediate defibrillation or CPR-first.<sup>2–5</sup> Based on this idea, a randomised trial was designed in which first shock delivery was guided by a VF-based algorithm incorporated into an automatic external defibrillator.<sup>8</sup> This strategy did not result in improved outcomes. The basis for this study was derived from the many observational studies that suggested a positive association between VF waveform

<sup>☆</sup> A Spanish translated version of the abstract of this article appears as Appendix in the final online version at <http://dx.doi.org/10.1016/j.resuscitation.2015.08.014>.

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characteristics and shock success, albeit generally with modest predictive values.<sup>2–5,9,10</sup>

In view of the above, there is room for improvement. The observed results may be explained by the fact that the appearance of the VF waveform does not merely reflect time delay or metabolic state, but is influenced by other factors as well. Observations in animals indicate that the presence of a myocardial infarction (MI) is associated with less coarse VF.<sup>11,12</sup> Accordingly, it may be difficult to differentiate whether fine VF reflects a longer arrest duration – with a lower chance of successful defibrillation – or is related to a short arrest duration in an animal with an MI. Evidence on this topic in humans is scarce, although there are studies using intracardiac recordings that demonstrate that the VF waveform is affected by the presence of a previous MI.<sup>13,14</sup>

Therefore, we studied a large series of patients who underwent defibrillation testing after implantable cardioverter defibrillator (ICD) implantation and assessed the impact of a previous MI and its localisation on VF waveform characteristics of the surface electrocardiogram (ECG).

## Methods

### Patient population

We identified all first ICD implantations with defibrillation testing at the Radboud University Medical Center from June 2010 till December 2013. For the present analysis, we studied patients with a previous anterior MI, a previous inferior MI and those without a history of MI. Exclusion criteria were the following: age <18 years, congenital heart disease, right-sided ICD implants, no analysable 12-lead ECG-recording of the induced VF. In addition, patients were excluded in case of a history of MI that did not involve the anterior or inferior wall. Patients with both anterior and inferior wall infarctions were excluded as well. Given the observational design of the study, written informed consent was not necessary to obtain according to the Dutch Act on Medical Research involving Human Subjects.

### ICD implantation and testing

The devices implanted were Medtronic® (Minneapolis, MN, USA), St Jude Medical® (St. Paul, MN, USA) or Biotronik® (Berlin, Germany) ICD or cardiac resynchronisation therapy-defibrillator systems with transvenous single coil leads. Routine defibrillation testing was performed after ICD implantation to test the ability of the implanted device to sense, detect and terminate VF appropriately. After sedation with propofol, VF was induced using T-wave shock, direct current pulses or 50 Hz burst pacing. The presence of VF, defined as a rapid (around 300 bpm) grossly irregular ventricular rhythm with marked variability in QRS cycle length, morphology, and amplitude, was confirmed on surface ECG-recordings.<sup>15</sup> Sequential shocks were delivered (15–25–35 joule) until VF was terminated. In case of persisting VF after the third shock, an external defibrillation shock was delivered.

### Data acquisition

Demographic, clinical and echocardiographic parameters were collected from patient records.

During defibrillation testing, a standard 12-lead ECG of the induced VF was recorded (sampling frequency 1000 Hz; 16-bit A/D converter) with BARD® LabSystem (Lowell, MA, USA). Lead I, II, aVF, V1, V3 and V6 were selected for VF analysis, as these represent the main electrical vectors and include uni- and bipolar leads.

### VF waveform analysis

VF waveform characteristics were determined using a time segment of 4.1 s prior to first shock delivery (4096 time-points). The signal was pre-processed with a 2 Hz high-pass filter and a 20 Hz low-pass filter. To study different aspects of the VF waveform, we analysed several previously studied VF characteristics.<sup>4,16,17</sup> From the ECG-signal in the time domain, we determined the mean absolute amplitude. Subsequently, the signal was converted to the frequency domain by using a fast Fourier transform to visualise the frequencies and corresponding amplitudes which the sampled VF signal contains.<sup>4</sup> From the amplitude frequency spectrum, the amplitude spectrum area (AMSA) was calculated as the summed product of individual frequencies and their corresponding amplitudes over an interval of 2–20 Hz.<sup>16,17</sup> From the power spectrum, we determined the dominant frequency, which is the frequency where the power spectrum attains its maximum.<sup>4</sup> In addition, we determined the median frequency, i.e. the frequency for which the integrated signal power was one half of the total integrated power. Finally, we calculated the bandwidth, which is the difference in frequency corresponding to the first and third quartile of the total power, providing a measure of the spread in frequencies.<sup>17</sup> Definitions of the analysed VF characteristics are described in detail in the [Appendix](#). Calculations were performed using Matlab (version 2011a, Mathworks, Natick, MA, USA).

### Outcome measures and study groups

The outcome measures are the ECG-characteristics of the VF waveform as described above. These were compared between three study groups: patients with a previous anterior MI, a previous inferior MI and without a history of MI. Evidence for the presence or absence of a previous MI was based on reports in the medical charts. MI was defined according to the ESC criteria.<sup>18</sup> Infarct localisation was based on a combination of information obtained from ECGs (e.g. area with ST-elevation or pathological Q waves) and coronary angiographies, and was confirmed by imaging reports.<sup>18,19</sup> Imaging was performed and analysed as part of daily clinical practice following the recommendations of the ACC/AHA/ESC guidelines for ICD therapy and was not part of a particular study protocol.<sup>18,20</sup> In short, for MRI the presence of delayed enhancement, regional wall motion abnormalities and information on myocardial thickness and thickening were used in the diagnosis and localisation of the MI. In case of echocardiography, information on regional differences in wall motion, myocardial thickness and thickening were used. For nuclear imaging, the combination of a persistent perfusion defect and wall motion abnormalities were used as indicators. For all modalities, wall motion abnormalities had to be present in at least two corresponding segments.

### Statistical analysis

Statistical analysis was performed with IBM SPSS statistics software version 20 (IBM Corp., Armonk, NY, USA). Baseline variables and the VF waveform characteristics were compared between the three study groups. Categorical data were expressed as frequencies (percentages) and analysed using the Chi square test. Continuous baseline variables were reported as means ± standard deviations and compared using the analysis of variance analysis (ANOVA). The VF waveform characteristics were reported as medians (interquartile ranges) and compared between the three study groups with the Kruskal–Wallis test. Post hoc pairwise comparisons were performed using Mann–Whitney *U* with Bonferroni correction. A *p*-value of <0.05 was considered statistically significant.

**Table 1**  
Baseline characteristics of the study population.

	No previous MI n = 88	Previous anterior MI n = 47	Previous inferior MI n = 55	p-Value
Age (years)	58 ± 14	64 ± 12	68 ± 9	<0.001
Male gender	57 (65)	35 (75)	51 (93)	0.001
Hypertension	30 (34)	18 (38)	23 (43)	0.59
Diabetes	17 (19)	13 (28)	13 (24)	0.53
Atrial fibrillation	26 (30)	11 (23)	20 (36)	0.36
Secondary prevention	24 (27)	16 (34)	27 (49)	0.03
CRT-D	33 (38)	14 (30)	12 (22)	0.14
BMI (kg/m <sup>2</sup> )	26 ± 4	27 ± 4	28 ± 4	0.13
LVEF (%)	37 ± 16	31 ± 11	38 ± 14	0.09
LVIDd-index (cm/m <sup>2</sup> )	3.1 ± 0.6	3.2 ± 0.4	3.0 ± 0.4	0.52
QRS duration (ms)	126 ± 31	116 ± 25	125 ± 28	0.16
Creatinine (μmol/l)	109 ± 151	99 ± 66	100 ± 35	0.85
Beta blocker	76 (86)	45 (96)	48 (89)	0.24
ACE inhibitor/ARB	73 (83)	41 (87)	49 (91)	0.41
Aldosterone blocker	31 (35)	28 (60)	15 (28)	0.003
Diuretics	41 (47)	29 (62)	21 (39)	0.07
Antiplatelet	33 (38)	34 (72)	44 (82)	<0.001
Anticoagulation	35 (40)	21 (45)	20 (37)	0.73
Cholesterol reducer	35 (40)	41 (87)	48 (89)	<0.001
Amiodarone	9 (10)	5 (11)	9 (17)	0.49

Values are n (%) or means ± standard deviations. ACE inhibitor: angiotensin converting enzyme inhibitor, ARB: angiotensin receptor blocker, BMI: body mass index, CRT-D: cardiac resynchronisation therapy-defibrillator, LVEF: left ventricular ejection fraction, LVIDd: left ventricular internal diastolic diameter, MI: myocardial infarction.

## Results

### Study group

In total, 337 eligible patients underwent a first ICD implantation with defibrillation testing. Twelve-lead ECG-recordings of VF inductions were available in 214 patients; the ECG could not be analysed in 8 patients due to artefacts. Sixteen patients with a previous MI were excluded, because they had evidence of infarction of (1) both the anterior and the inferior wall (n = 15) or (2) the posterior wall only (n = 1). Accordingly, a total of 190 patients were included in the present analysis. Baseline characteristics did not differ between the in- and excluded patient groups (Supplementary Table 1).

### Patient characteristics

The mean age was 63 years ± 13 and 75% (143/190) were male. In 35% (67/190) of patients, ICDs were implanted for secondary prevention. The mean left ventricular ejection fraction (LVEF) was 36% ± 14. In 46% (88/190) of patients, there was no evidence of a previous MI. A previous anterior MI was present in 25% (47/190) and a previous inferior MI in 29% (55/190). Of the subset without a history of MI, left ventricular dysfunction was caused by cardiomyopathies, hypertensive or valvular heart diseases in 88% (77/88), while 5% (4/88) had a cardiac channelopathy and in 8% (7/88) the cause of the ventricular arrhythmias was unknown. Baseline characteristics of the study groups are presented in Table 1.

### VF waveform characteristics

**Study groups:** In Figs. 1 and 2, we present the medians with interquartile ranges of the analysed VF characteristics for the study groups. The only lead without between-group differences in VF characteristics was V1. The exact numerical values can be found in Supplementary Table 2.

**Previous anterior MI:** We observed a lower mean amplitude and AMSA and a broader bandwidth for patients with a previous anterior MI in lead V3 than for patients with a previous inferior MI and those without a history of MI, respectively. When compared to the latter, the mean amplitude and AMSA were lower in lead V6 for a previous anterior MI. The dominant and median frequencies were

lower for patients with an anterior MI in leads V3, I and V6 when compared to those without a history of MI. The adjusted p-values of pairwise comparisons are presented in Supplementary Table 3.

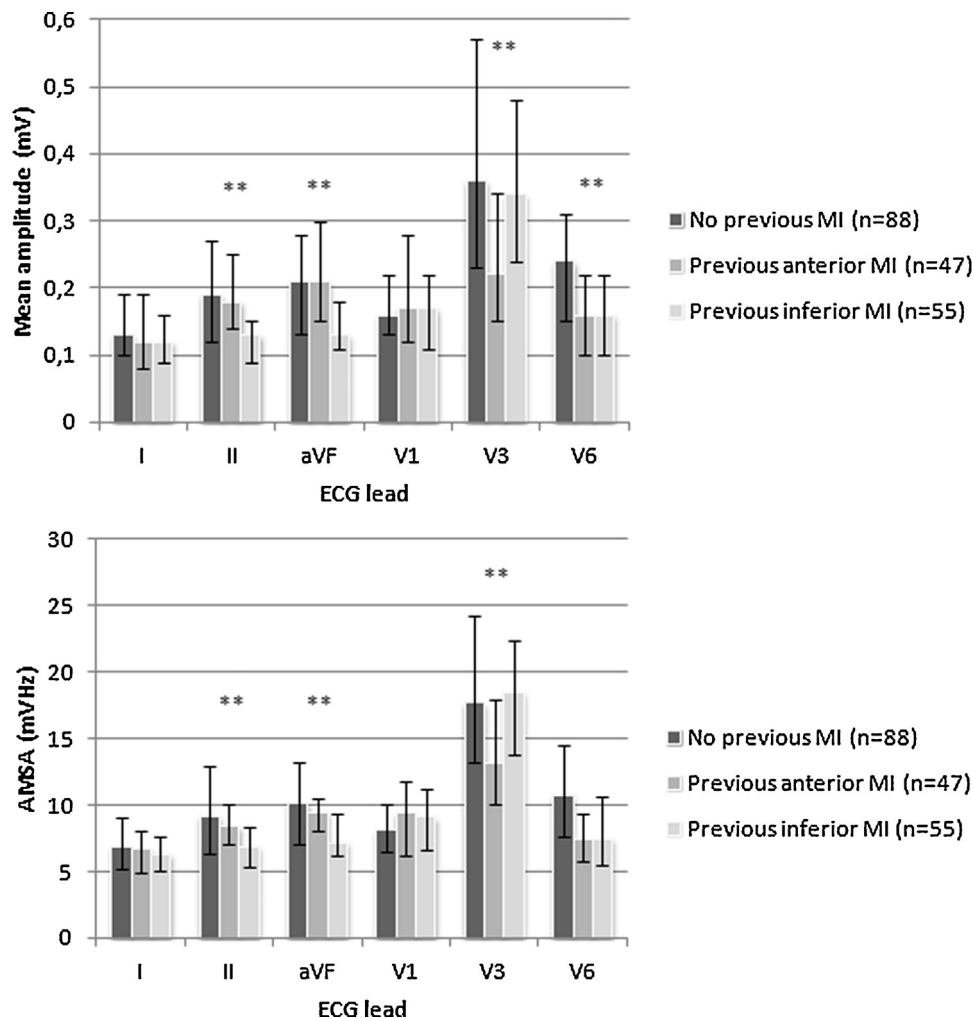
**Previous inferior MI:** We observed a lower mean amplitude and AMSA and a broader bandwidth for patients with a previous inferior MI in leads II and aVF than for patients with a previous anterior MI or those without a history of MI, respectively. When compared to the latter, the mean amplitude and AMSA were lower and the bandwidth was broader in lead V6. The dominant and median frequencies did not differ from those of the other study groups in all leads. The adjusted p-values of the pairwise comparisons can be found in Supplementary Table 3.

## Discussion

To our knowledge, this is the largest surface ECG study in humans analysing the impact of the presence of a previous MI and its localisation on characteristics of the VF waveform. Amplitude-related characteristics of the induced VF waveform were markedly lower in the leads adjacent to the area of infarction, i.e. in lead V3 for an anterior MI, and in leads II and aVF for an inferior MI. In the leads corresponding with the infarct localisation, the bandwidth was broader as well, indicating less organised VF. The dominant and median frequencies of VF were affected in case of an anterior MI only. Our observations challenge the currently used concept that fine VF is a mere proxy for a longer arrest duration and myocardial metabolic state and indicate that the underlying aetiology also plays an important role in the appearance of the VF waveform on the surface ECG.

### Animal studies

Animal studies primarily investigated the impact of a previous anterior wall infarction, induced by ligation of the left anterior descending artery and reported lower VF frequency characteristics for this subset when compared to controls.<sup>21,22</sup> We observed lower dominant and median frequencies in patients with a previous anterior MI as well, but not in case of a previous inferior MI. While we focused on early, short-duration, induced VF, animal studies analysed the VF signal at different time points during the arrest.<sup>21–23</sup> In these studies, it has also been demonstrated that – when compared to arrests in animals with a previous MI – VF in the



**Fig. 1.** Amplitude-related VF waveform characteristics in the analysed surface ECG-leads. VF waveform characteristics are presented as medians with interquartile ranges. \*\**p*-Value < 0.001 for comparisons between the three study groups. AMSA: amplitude spectrum area, Hz: hertz, MI: myocardial infarction, mV: millivolt. Pairwise comparisons showed significant differences between the following study groups: *Mean amplitude*: Lead II: inferior vs. anterior MI ( $p < 0.001$ ); inferior vs. no MI ( $p < 0.001$ ). Lead aVF: inferior vs. anterior MI ( $p < 0.001$ ); inferior vs. no MI ( $p < 0.001$ ). Lead V3: anterior vs. inferior MI ( $p = 0.001$ ); anterior vs. no MI ( $p < 0.001$ ). Lead V6: anterior vs. no MI ( $p = 0.001$ ); inferior vs. no MI ( $p < 0.001$ ). *AMSA*: Lead II: inferior vs. anterior MI ( $p = 0.001$ ); inferior vs. no MI ( $p < 0.001$ ). Lead aVF: inferior vs. anterior MI ( $p = 0.001$ ); inferior vs. no MI ( $p < 0.001$ ). Lead V3: anterior vs. inferior MI ( $p < 0.001$ ); anterior vs. no MI ( $p < 0.001$ ). Lead V6: anterior vs. no MI ( $p = 0.001$ ); inferior vs. no MI ( $p = 0.001$ ).

setting of an acute, ongoing MI seems to have even lower frequency characteristics.<sup>21,23</sup> Mapping studies in animals provided insight into the potential electrophysiological background of the observed lower frequency characteristics. In dog hearts with a previous MI, it was observed that during VF the mean size of activation wavefronts was larger than in controls. Larger wavefronts have been associated with lower dominant frequencies on the ECG.<sup>24,25</sup>

With regard to the amplitude-related VF characteristics, observations in animals were less uniform.<sup>11,12,21,22,26</sup> This may be related to the fact that some studies analysed paddle ECGs or recordings from needle electrodes (*y*-axis) – more or less corresponding to lead II of the surface ECG – while the localisation of the (previous) MI was not in the inferior but in the anterior wall.<sup>12,21,26</sup> Hypothetically, an effect on amplitude-related characteristics may have gone undetected in these studies due to the lack of chest leads.

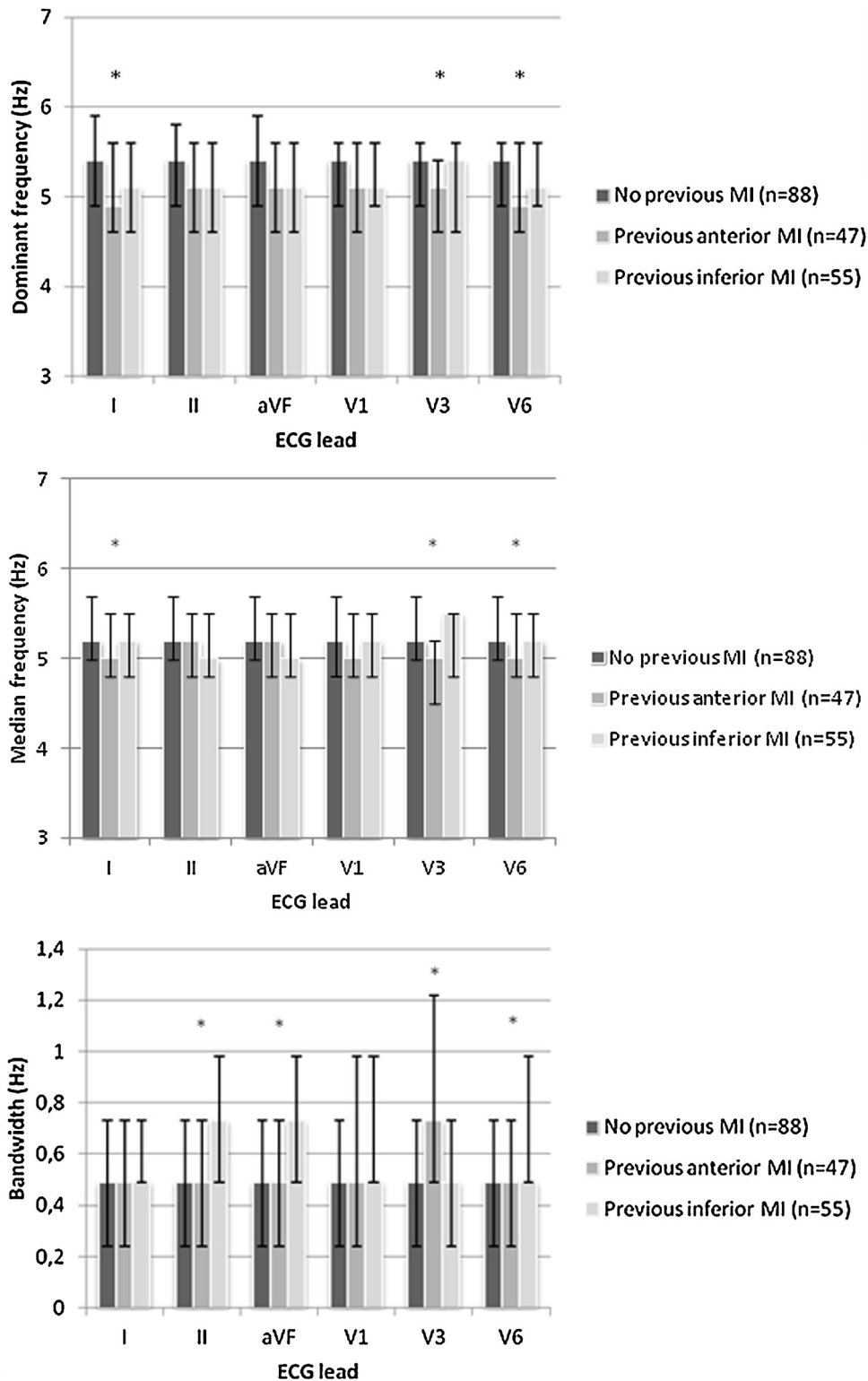
#### Human studies

**OHCA-setting:** Studies on the impact of an MI on VF characteristics in OHCA-patients are hampered by a lack of information on the exact underlying aetiology, especially in the non-surviving patients. Nonetheless, for patients with VF in the setting of a

suspected acute MI, the waveform showed significant differences when compared to patients without acute MI, including lower AMSA values.<sup>27</sup> In a study on shock success prediction, it was described that patients with a prior MI demonstrated a lower median frequency, but not a lower AMSA.<sup>5</sup> However, in the absence of data on the actual arrest aetiology, it remains uncertain to what extent the baseline characteristics, on the one hand, and the actual underlying aetiology, on the other, were the primary drivers behind the observed differences in the VF waveform.

**Defibrillation testing:** In the above-described context, VF induction during defibrillation testing provides a unique setting to study the VF waveform under controlled conditions.<sup>13,14,17</sup> As for the impact of a previous MI, a small study analysing limb leads reported a trend towards lower VF frequencies in ischaemic than in non-ischaemic heart disease.<sup>17</sup> With regard to infarct localisation, a study of intracardiac recorded VF reported a higher fraction of energy in the low frequency region for patients with a previous inferior MI than for an anterior MI.<sup>13</sup>

In follow-up of our previous intracardiac ECG study that demonstrated differences in the VF waveform related to the history of a previous MI, we now conducted a comprehensive 12-lead surface ECG study to expand the current knowledge on the impact of an MI



**Fig. 2.** Frequency-related characteristics of the VF waveform in the analysed surface ECG-leads. VF waveform characteristics are presented as medians with interquartile ranges. \*p-Value <0.05 for comparisons between the three study groups. Hz: hertz, MI: myocardial infarction. Pairwise comparisons showed significant differences between the following study groups: *Dominant frequency*: Lead I: anterior vs. no MI ( $p = 0.026$ ). Lead V3: anterior vs. no MI ( $p = 0.015$ ). Lead V6: anterior vs. no MI ( $p = 0.009$ ). *Median frequency*: Lead I: anterior vs. no MI ( $p = 0.019$ ). Lead V3: anterior vs. no MI ( $p = 0.013$ ). Lead V6: anterior vs. no MI ( $p = 0.021$ ). *Bandwidth*: Lead II: inferior vs. anterior MI ( $p = 0.054$ ); inferior vs. no MI ( $p = 0.012$ ). Lead aVF: inferior vs. anterior MI ( $p = 0.063$ ); inferior vs. no MI ( $p = 0.017$ ). Lead V3: anterior vs. inferior MI ( $p = 0.017$ ); anterior vs. no MI ( $p = 0.001$ ). Lead V6: inferior vs. no MI ( $p = 0.031$ ).

and its localisation on the VF waveform.<sup>14</sup> We found that amplitude characteristics were lower in V3 for an anterior MI and in II and aVF for an inferior MI, i.e. in the leads adjacent to the area of infarction. In contrast, the dominant and median frequencies were lower only

in the presence of a previous anterior MI (I, V3, V6). An explanation for this finding could be that the patients with anterior MIs had larger infarctions, which may have affected the VF waveform to a greater extent than the smaller inferior infarctions. This hypothesis

is supported by fact that the LVEF was slightly lower in the subset with a previous anterior MI than in the other study groups. In lead V6, we observed lower amplitudes and less organised VF both for patients with a previous anterior and inferior MI when compared to the subset without an MI. This may indicate that involvement of the lateral wall occurred in both groups with a previous MI.

### Implications

Our findings that both amplitude and frequency characteristics of early VF are affected by a prior MI and its localisation warrant a more comprehensive concept of the VF waveform that goes beyond an indicator of arrest duration. In addition, previous studies have shown that the VF waveform has promising predictive value for longer-term clinical outcomes.<sup>5–7</sup>

The first implication of our findings is that fine VF during OHCA does not necessarily reflect longer arrest duration, with a low chance of successful defibrillation, but may be influenced by the underlying aetiology as well. For example, in patients with a previous inferior MI, a low AMSA at the paddle ECG (corresponding to limb lead II) may be the result of the previous MI rather than a long arrest duration. The issue may be overcome with the use of multiple leads, reflecting different recording directions, but the potential benefit of such an approach needs further study. As lead V1 does not seem to be influenced by the presence of a prior MI, one might hypothesise that VF characteristics in that lead are more reliable indicators of arrest duration and less affected by left ventricular disease. In the context that the number and choice of leads affects study findings, the use of only one lead during OHCA seems a complicating factor.

Further study is warranted to see whether our findings on short-duration, electrically induced VF apply to the OHCA-setting. Signal differences between spontaneous and induced VF have been described, but animal studies and an OHCA cohort have reported that a previous MI affects the VF waveform in the acute setting as well.<sup>11,12,21,22,27–29</sup>

Appreciating that other factors than time affect the VF waveform, the modest prediction in earlier OHCA studies on shock success could possibly be optimised. More comprehensive studies on VF characteristics are warranted to unravel the future potential of VF-guided resuscitative interventions.

### Limitations

This study describes the impact of a previous infarction in patients with short-duration, electrically induced VF. This may limit inferences to the OHCA-setting with spontaneous VF of longer duration. Second, about a third of patients was excluded, as digital 12-lead ECG-recordings were not available. Given the similar baseline characteristics (Supplementary Table 1), it is unlikely that this selection has affected our findings. Third, for an even more academic approach, the use of a single imaging technique (MRI), including systematic quantification of infarct extent, would have been preferable.

### Conclusions

In the present study on VF characteristics in a large series of patients undergoing ICD testing, we observed that a previous MI and its localisation affect the VF waveform on the surface ECG. Amplitude-related characteristics were significantly lower and VF was less organised in the leads adjacent to the area of infarction, i.e. in lead V3 for an anterior MI and in leads II and aVF for an inferior MI. Frequency characteristics were lower in case of an anterior MI only. Although VF characteristics have so far primarily been

considered a proxy for arrest duration and myocardial metabolic state, our findings warrant more comprehensive studies on VF to re-evaluate this paradigm and to study the future potential of VF-guided resuscitative interventions.

### Funding

None.

### Conflict of interest statement

Prof. De Boer is a member of the European advisory board on interventional cardiology of Medtronic. J.L. Bonnes, J. Thannhauser, M.C. Hermans, S.W. Westra, T.F. Oostendorp, G. Meinsma, M.A. Brouwer and J.L.R.M. Smeets have no conflicts of interest to declare.

### Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.resuscitation.2015.08.014>.

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