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Electrocardiographic changes after implantation of a left ventricular assist device – Potential implications for subcutaneous defibrillator therapy

Christos Zormpas [a], Johanna Mueller-Leisse [a], Thorben Koenig [a], Jan D. Schmitto [b], Christian Veltmann [a], David Duncker [a,*]

[a] Rhythmology and Electrophysiology, Department of Cardiology and Angiology, Hannover Medical School, Hannover, Germany
[b] Department of Cardiac, Thoracic, Transplant and Vascular Surgery, Hannover Medical School, Hannover, Germany

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ABSTRACT

Background: Implantation of a left ventricular assist device (LVAD) leads to a diverse spectrum of changes on the twelve-lead surface electrocardiogram (ECG). We aimed to elucidate the changes of the surface ECG in patients after LVAD implantation potentially impacting ECG based screening tests of subcutaneous implantable cardioverter-defibrillators (S-ICD).

Methods: Patients from 2005 until 2017 with a documented twelve-lead ECG before and after LVAD implantation were included. Baseline parameters were obtained through hospital records. The twelve-lead ECGs registered before and after LVAD implantation were analyzed.

Results: From 415 patients undergoing an LVAD implantation, complete datasets were available for 253 patients. 216 patients (85%) were male. Mean age at time of LVAD implantation was 54.7 ± 12.4 years. The underlying etiology was ischemic cardiomyopathy in 119 (47%), dilated cardiomyopathy in 112 (44%), myocarditis in 8 (3%) and other in 14 (6%). We observed a reduction in the amplitude of the R wave in lead I ($p < 0.0001$), lead II ($p < 0.0001$), lead III ($p < 0.004$), lead aVL ($p < 0.001$) and lead aVF ($p < 0.0001$) as well as of the S wave in lead III ($p < 0.001$) and lead aVR ($p < 0.0001$) after LVAD implantation. We also noticed a reduction of the R:T ratio in lead I ($p < 0.0001$) as well as in lead II ($p = 0.100$) and lead aVF ($p = 0.292$) although statistically non-significant.

Conclusion: LVAD implantation leads to significant alterations of the surface ECG, especially the R:T ratio in leads I, II and aVF. These leads correlate with the vectors of the ECG based S-ICD screening test. Thus, these ECG changes may impact the continuous eligibility for subcutaneous ICD therapy in patients after LVAD implantation.

Introduction

Heart failure (HF) accounts for significant morbidity and mortality worldwide [1–3]. Left ventricular assist devices (LVADs) have evolved to an important bridging therapy to heart transplantation, to recovery or as destination therapy [4]. LVAD implantation leads to a significant improvement of overall prognosis as well as HF symptoms [5–9] Patients undergoing LVAD implantation show a reduction of the amplitude in the limb leads of the twelve-lead surface electrocardiogram (ECG) as well as changes of the QRS complex after implantation [10,11]. Likewise, patients with implantable cardioverter/defibrillators (ICD) show a significant reduction of intracardiac R wave sensing [12,13]. Subcutaneous ICD (S-ICD) represents a reliable alternative to transvenous ICD systems. Avoiding transvenous devices might be beneficial in patients with LVAD who may be candidates for heart transplant. Nevertheless, surface ECG quality and evolution is of major importance in S-ICD since S-ICD detection algorithms are solely based on surface ECG analysis. Therefore, the aim of the present study was to perform a systematic analysis of ECG changes after implantation of an LVAD.

Methods

All patients who underwent LVAD implantation at Hannover Medical School between November 2005 and June 2017 were analyzed retrospectively. Baseline parameters and medical history were retrieved through hospital records. Patients having received a twelve-lead ECG in our hospital before and after LVAD were included in the study. ECG paper speed was 50 mm/s with an amplitude scale of 10 mm/mV. All patients with available ECGs were included, though those with a paced QRS complex were analyzed separately. Detailed ECG parameters

* Corresponding author at: Department of Cardiology and Angiology, Hannover Medical School, Carl-Neuberg-Strasse 1, 30625 Hannover, Germany.
E-mail address: duncker.david@mh-hannover.de (D. Duncker).

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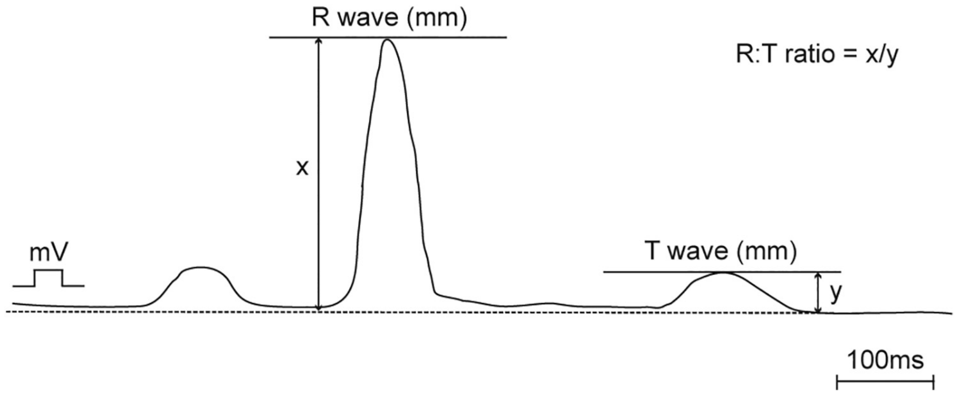

Fig. 1. Representative for R:T ratio calculation in twelve-lead surface ECG.

including rhythm, intervals, amplitudes and morphology were recorded. R:T ratio was calculated for all leads as shown in Fig. 1.

Categorical variables were expressed as numbers and percentages and continuous variables as mean ± standard deviation (SD). ECG parameters before and after LVAD implantation were compared using paired *t*-test. For the analysis of amplitude changes in the different limb leads two-way analysis of variances (ANOVA) was performed. Values of $p < 0.05$ were considered statistically significant. Statistical analysis was conducted using GraphPad PRISM 6 software (GraphPad Software, Inc., California, CA, USA).

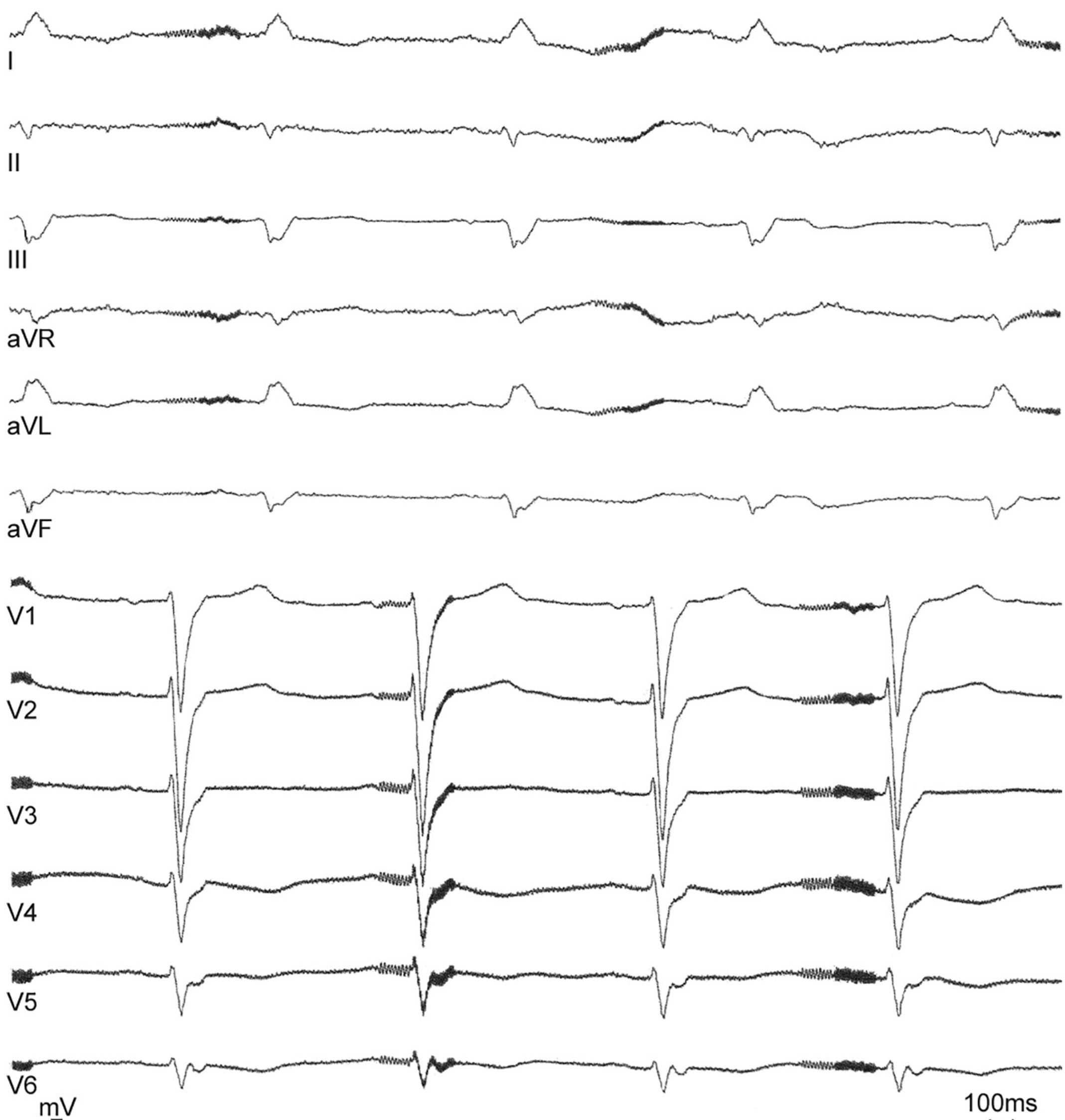

Fig. 2. Example of a twelve-lead surface ECG from a patient implanted with an LVAD. ECG analysis is challenging due to the pronounced artifacts provoked by the LVAD.

Table 1
Baseline patient characteristics.

Parameter	n = 253
Age at time of implantation (years)	54.7 ± 12.4
Male (n, %)	216 (85%)
Underlying cardiomyopathy (n, %)	
• Ischemic cardiomyopathy	119 (47.1%)
• Dilated cardiomyopathy	112 (44.2%)
• Myocarditis	8 (3.2%)
• Other	14 (5.5%)
LVAD type (n, %)	
• HeartMate II	60 (23.7%)
• HeartMate 3	21 (8.3%)
• HVAD	162 (64.1%)
• Other (aVAD, HeartAssist5, MVAD, SunshineHeart)	10 (3.9%)
Minimally invasive operation technique (n, %)	116 (46%)
Urgent LVAD implantation (n, %)	71 (28%)

Results

415 patients underwent LVAD implantation between 2005 and 2017. Twelve-lead ECGs of suitable quality before and after LVAD implantation were available for 253 patients. ECGs with relevant artifacts were excluded, an example of representative artifacts after LVAD implantation is shown in Fig. 2. The ECG before LVAD was performed 43 ± 180 days prior to LVAD implantation. The ECG after LVAD was obtained 209 ± 318 days after LVAD implantation. 216 (85%) patients were male. 71 (28%) patients underwent LVAD implantation under emergency conditions and 5 patients (2%) received a biventricular assist device (BiVAD). 162 (64%) patients were implanted with the third generation HVAD (Medtronic, Dublin, Ireland), 60 (24%) patients received the second-generation HeartMate II (Thoratec Corp., Pleasanton, PL, USA). Baseline parameters are shown in Table 1.

ECG findings

ECG parameters analyzed are shown in Table 2. The cardiac axis showed a slight deviation to the left although statistically non-significant (−17.6 ± 87.3° before LVAD, −29.5 ± 98.6° after LVAD; $p = 0.098$).

Intervals

PR interval remained unaffected from LVAD implantation (171.5 ± 39.4 ms before LVAD, 170.5 ± 36.5 ms after LVAD; $p = 0.382$) as well as the QTc interval (471.7 ± 48.6 ms before LVAD, 468.5 ± 52.1 ms after LVAD; $p = 0.372$). Heart rate increased significantly after LVAD implantation (82 ± 19 bpm before LVAD, 87 ± 18 bpm after LVAD; $p < 0.001$). A significant decrease in QRS duration was observed (128.8 ± 32.8 ms before LVAD, 124.1 ± 32.8 ms after LVAD; $p = 0.009$).

Table 2
ECG parameters before and after LVAD implantation (n = 253).

	Before LVAD	After LVAD	*p*-Value
Atrial rhythm (n, %)			
• Sinus rhythm	179 (71%)	177 (70%)	0.895
• Atrial fibrillation	72 (28%)	71 (28%)	0.982
• Other	2 (1%)	5 (2%)	0.755
QRS morphology (n, %)			
• No block	128 (50%)	129 (51%)	0.999
• Left bundle branch block	35 (14%)	30 (12%)	0.952
• Right bundle branch block	12 (5%)	15 (6%)	0.994
• Interventricular conduction delay	10 (4%)	18 (7%)	0.776
• Paced	68 (27%)	61 (24%)	0.848
Cardiac axis (°)	−17.6 ± 87.3	−29.5 ± 98.6	0.098
Heart rate (bpm)	82 ± 19	87 ± 18	<0.001
PR interval (ms)	171.5 ± 39.4	170.5 ± 36.5	0.382
QRS duration (ms)	128.8 ± 32.8	124.1 ± 32.8	0.009
QTc interval (ms)	471.7 ± 48.6	468.5 ± 52.1	0.372

Table 3
R wave, S wave and T wave amplitudes (mean ± SD) before and after LVAD implantation (n = 253).

	Before LVAD	After LVAD	*p*-Value
R wave (mV)			
• Lead I	0.3 ± 0.33	0.19 ± 0.22	<0.0001
• Lead II	0.27 ± 0.36	0.16 ± 0.24	<0.0001
• Lead III	0.27 ± 0.36	0.21 ± 0.29	0.004
• Lead aVR	0.21 ± 0.24	0.22 ± 0.21	0.988
• Lead aVL	0.34 ± 0.32	0.26 ± 0.26	<0.001
• Lead aVF	0.25 ± 0.31	0.16 ± 0.23	<0.0001
S wave (mV)			
• Lead I	0.19 ± 0.28	0.18 ± 0.24	0.999
• Lead II	0.35 ± 0.34	0.33 ± 0.31	0.949
• Lead III	0.45 ± 0.41	0.38 ± 0.35	<0.001
• Lead aVR	0.21 ± 0.3	0.11 ± 0.17	<0.0001
• Lead aVL	0.19 ± 0.29	0.17 ± 0.23	0.711
• Lead aVF	0.13 ± 0.12	0.11 ± 0.13	0.977
T wave (mV)			
• Lead I	0.08 ± 0.1	0.07 ± 0.08	0.857
• Lead II	0.13 ± 0.12	0.11 ± 0.12	0.301
• Lead III	0.15 ± 0.14	0.12 ± 0.14	0.032
• Lead aVR	0.07 ± 0.09	0.07 ± 0.08	0.999
• Lead aVL	0.09 ± 0.11	0.08 ± 0.1	0.486
• Lead aVF	0.13 ± 0.12	0.11 ± 0.13	0.365

Amplitudes

R wave amplitude was significantly reduced after LVAD implantation in leads I ($p < 0.0001$), II ($p < 0.0001$), III ($p = 0.004$), aVL ($p < 0.001$) and aVF ($p < 0.0001$). S wave amplitude was significantly reduced in leads III ($p < 0.001$) and aVR ($p < 0.0001$). T waves did not show a relevant reduction after LVAD implantation except for lead III, in which a statistically significant amplitude reduction was observed (0.15 ± 0.14 mV before LVAD, 0.12 ± 0.14 mV after LVAD; $p = 0.032$). Table 3 provides a detailed analysis of R, S and T waves before and after LVAD implantation.

R:T ratio

Fig. 3 provides an overview of electrocardiographic changes observed after implantation of the different LVAD types. After LVAD implantation, R:T ratio was reduced in leads I, II, aVL and aVF. This reduction was statistically significant for lead I ($p < 0.0001$). In lead aVR an increase of the R:T ratio was observed, although not statistically significant ($p = 0.292$). Table 4 shows detailed analysis of R:T ratios in the different limb leads. Fig. 4 presents the R:T ratio delta in the analyzed leads. Neither implantation technique (conventional versus minimally-invasive) nor LVAD type influenced the changes in amplitude of R:T ratios.

Discussion

The aim of the present study was to analyze ECG changes after implantation of an LVAD in the perspective of potential changes in ECG-based screening tests, such as the S-ICD screening test. With 253 patients the present study is the largest detailed electrocardiographic analysis elucidating ECG changes in patients after LVAD implantation.

The main findings of the present study are (1) significant changes of the R:T ratio in leads I, II, aVR and aVF, (2) a reduction of R waves in leads I, II, III, aVL, and aVF and (3) a reduction of the S wave in leads III and aVR.

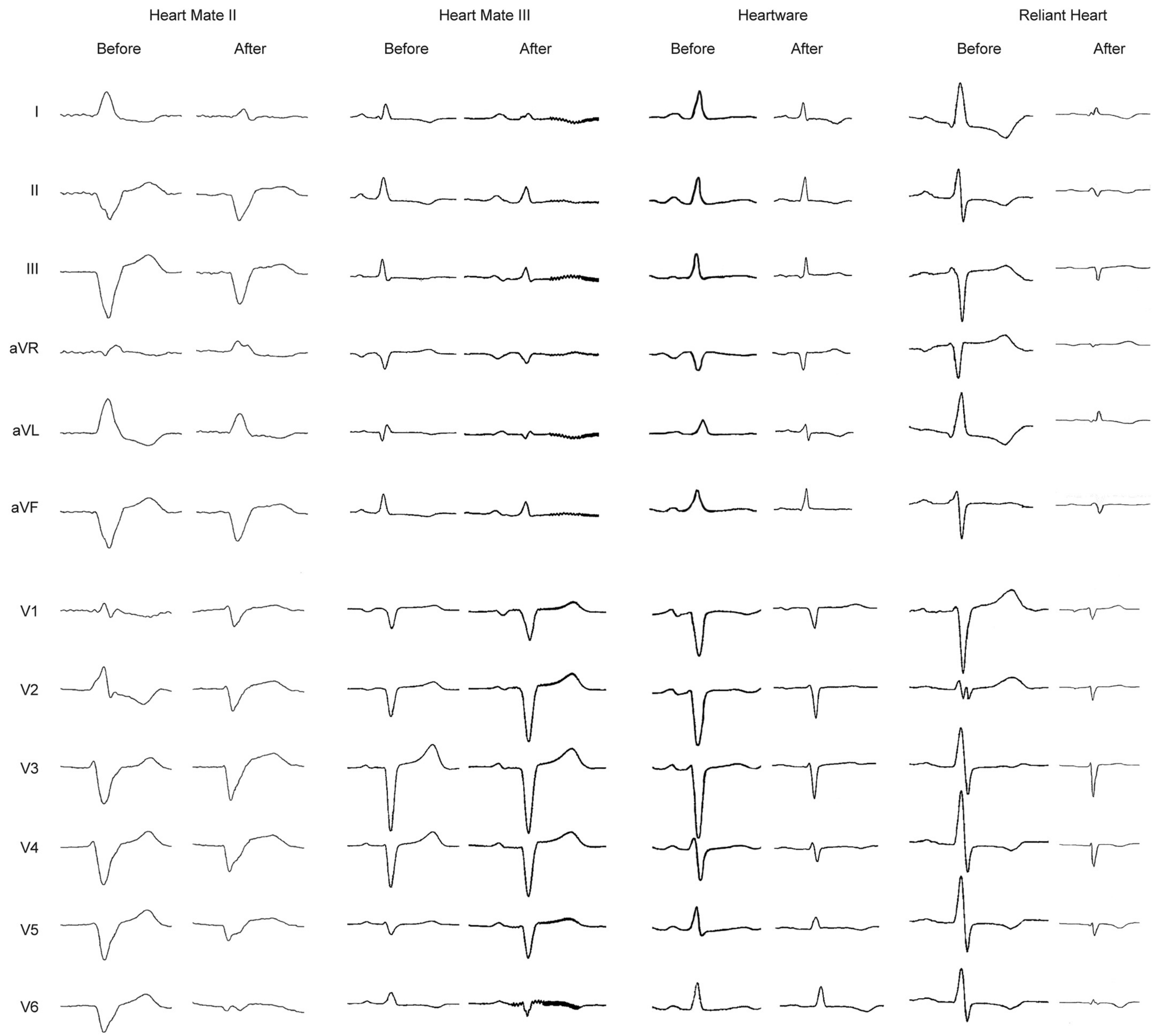

Fig. 3. Illustrative twelve-lead surface ECGs before and after LVAD implantation according to LVAD type. In all different LVAD types the same tendency towards a reduction of the R wave and S wave amplitudes was observed.

LVAD implantation leads to hemodynamic and anatomic alterations in the heart, which can impact the surface ECG. Thus, these electrocardiographic changes could lead to clinically important complications for the patients, especially considering the increasing use of S-ICD.

Table 4
R:T ratio before and after LVAD implantation (n = 253).

	Before LVAD (mean ± SD)	After LVAD (mean ± SD)	*p*-Value
R:T ratio			
• Lead I	12.1 ± 18	7.4 ± 12.1	<0.0001
• Lead II	7.3 ± 13.7	4.8 ± 8.4	0.100
• Lead III	6.1 ± 13.4	6 ± 10.6	0.999
• Lead aVR	6.1 ± 10.5	8.2 ± 12.3	0.260
• Lead aVL	9.8 ± 15.1	9 ± 13.9	0.974
• Lead aVF	6.8 ± 16.3	4.8 ± 9.4	0.292

Numerous studies have shown that ECG abnormalities including low voltage in the limb leads and T wave alterations can be observed in the presence of heart failure (HF) even before the onset of symptoms [14–18]. Some studies have focused on specific ECG abnormalities in HF patients concentrating on the QRS morphology, T wave alterations as well as the QRS/T ratio, which are associated with an elevated mortality or morbidity [19–21]. To date there have been only few studies focusing on ECG changes after LVAD implantation [10,11]. In the present study, we observed no significant changes in PR and QTc intervals. QRS duration and morphology also did not change after LVAD implantation, a finding concordant with the data of Thomas et al. [11]. In this study aiming to address the clinical relevance of a fragmented QRS complex in 98 patients with HF undergoing LVAD implantation focusing on mortality there was no difference in QRS morphology regarding bundle branch block or QRS < 120 ms. Nevertheless, other important ECG parameters like R, S and T wave amplitudes as well as R:T ratios have not been analyzed in this study.

Furthermore, our findings showed a significant reduction of R wave and S wave amplitudes in the limb leads. This finding was also reported in the study of Martinez et al., which concentrated on ECG changes after implantation of a HeartMate II in 43 patients aiming to identify ECG characteristics associated with the presence of an LVAD [10]. On the other hand, Fresiello et al. studied ECG changes in a pig model with a continuous-flow LVAD according to different levels of ventricular support [22]. Changes of flow power and ventricular volumes correlated with the R wave amplitude. Lower ventricular volumes led to a reduction of R wave amplitude whilst not affecting QRS morphology. The implantation of an LVAD leads to a reduction of the intraventricular volumes [23], which could be an explanation for the amplitude reduction observed in our study.

Discrimination of QRS complex and T wave is crucial for appropriate ECG analysis within the S-ICD sensing algorithm [24]. The rationale to investigate R:T ratio in our study was based on case reports on S-ICD and LVAD interferences resulting in inappropriate S-ICD therapy delivery [25–27]. In the present study, we observed changes in surface ECG after LVAD implantation regarding the R:T ratio, which could impact ECG-based S-ICD sensing vectors. To our knowledge, this is the first study addressing this clinical issue in this special population of patients with an LVAD. Studies have tried to correlate QRS and T wave morphology variants in surface ECG with candidacy for S-ICD implantation according to the ECG-based S-ICD screening test [28–30]. Nordkamp et al. described S-ICD screening tests in 230 patients with an ICD. Their results showed increased test failure when the R:T ratio was below 3 in the lead with the highest T wave in twelve-lead ECG [28]. This finding highlights the importance of R:T ratio for the ECG-based S-ICD screening test. Using the ECG-based screening test, Groh et al. showed the importance of T wave inversion, specifically in leads I, II, and aVF since in these patients S-ICD screening test is 23 times more likely to fail [29]. In line with these findings, our data showed significant changes of the R:T ratio in lead I (statistically significant) as well as leads II and aVF, changes which may impact the ECG-based S-ICD screening test. Campbell et al. reported a higher S-ICD screening failure incidence in children compared to adults [30]. Predictors for test failure were longer QTc intervals, wider QRS and a low R:T ratio in aVF.

We can hypothesize that the observed ECG changes in our study could lead to alterations of the ECG-based S-ICD screening test after LVAD implantation mainly due to changes of the R:T ratio. Thus, these changes may lead to undersensing or oversensing in the S-ICD vectors bearing a high risk for inappropriate S-ICD therapies.

Limitations

Due to the retrospective study design, we could not retrieve ECG data from all patients undergoing LVAD implantation in our institution. This was in many cases due to the high percentage (28%) of LVAD implantations performed under emergency conditions, since patients with a documented ECG before LVAD performed in another medical center were excluded. A small amount of patients suffered severe intra- or perioperative complications hampering a surface ECG after LVAD.

Conclusion

After LVAD implantation, patients show a reduction of both R and S wave amplitudes without relevant change of the T wave amplitudes in surface ECG. There is a significant reduction of R:T ratio in lead I as well as leads II and aVF. These changes may impact the ECG-based S-ICD screening test bearing a risk for inappropriate ICD therapy delivery. Further studies investigating S-ICD eligibility in patients with LVAD as well as prospective analyses of the ECG-based S-ICD screening test in patients undergoing LVAD implantation should be performed.

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Disclosures

CZ received travel grants and a fellowship grant from Biotronik, JML received travel grants and a fellowship grant from Boston Scientific and Medtronic, DD received lecture honorary, travel grants and/or a fellowship grant from Biotronik, Boston Scientific, Medtronic, Sorin/LivaNova, St. Jude Medical/Abbott, Zoll. CV received lecture honorary, travel grants and/or a fellowship grant from Biotronik, Boston Scientific, Medtronic, Sorin/LivaNova, St. Jude Medical/Abbott, Zoll. TK received lecture

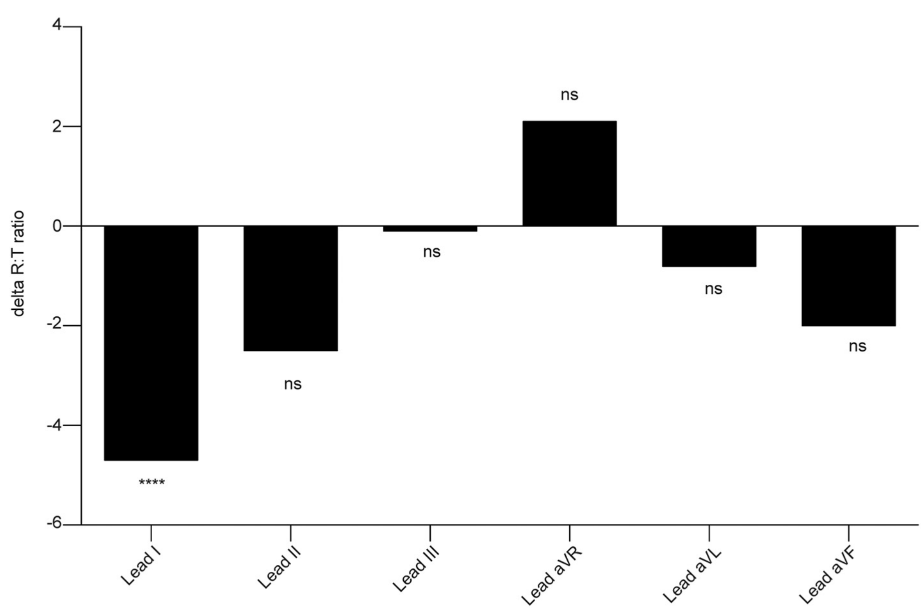

Fig. 4. R:T ratio delta in the different limb leads. Reduction of the R:T ratio in lead I was statistically significant. In leads II, aVL and aVF a reduction was also observed, although statistically non-significant.

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