Characteristics of VT Ablation in Patients with Continuous Flow Left Ventricular Assist Devices

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Abstract:

Background - Left ventricular assist devices (LVADs) are increasingly used as a bridge to cardiac transplantation or as destination therapy. Patients with LVADs are at high risk for ventricular arrhythmias (VA). This study describes VA characteristics and ablation in patients implanted with a Heart Mate 2 (HM2) device.

Methods and Results - All patients with a HM2 device who underwent VA catheter ablation at 9 tertiary centers were included. Thirty-four patients (30 male, age 58 ±10 years) underwent 39 ablation procedures. The underlying cardiomyopathy etiology was ischemic in 21 and non-ischemic in 13 patients with a mean left ventricular ejection fraction of 17±5% before LVAD implantation. One hundred and ten ventricular tachycardias (VTs) (cycle lengths: 230-740ms, arrhythmic storm n=28) and 2 ventricular fibrillation triggers were targeted (25 transseptal, 14 retrograde aortic approaches). Nine patients required VT ablation <1 month after LVAD implantation due to intractable VT. Only 10/110 (9%) of the targeted VTs were related to the HM2 cannula. During follow-up, 7 patients were transplanted and 10 died. Of the remaining 17 patients, 13 were arrhythmia-free at 25 ±15 months. In 1 patient with VT recurrence, change of turbine speed from 9400 to 9000 rpm extinguished VT.

Conclusions - Catheter ablation of VT among LVAD recipients is feasible and reasonably safe even soon after LVAD implantation. Intrinsic myocardial scar, rather than the apical cannula, appears to be the dominant substrate.

Key words: ablation, ventricular arrhythmia, ventricular assist device, ventricular tachycardia
Introduction

Left ventricular assist device (LVAD) therapy has extended the survival of patients with advanced heart failure as a bridge to transplantation\textsuperscript{1} or as destination therapy\textsuperscript{2} with improved quality of life. In the LVAD experience, postoperative ventricular arrhythmias (VA) occur in up to 35% of the patients within 30 days\textsuperscript{3,4}. Despite the long-held belief that recipients of LVADs are unaffected by VA, the crude mortality rate is as high as 52% for patients with VA occurring within 1 week postoperatively\textsuperscript{5}. However the benefit of implantable cardioverter-defibrillators (ICDs) in patients with LVADs remains controversial\textsuperscript{6,7}. Although they are associated with a mortality reduction in some studies, ICD therapies (eg shocks) that occur in up to 30% of patients, are a common complaint\textsuperscript{8}. Catheter ablation offers an opportunity to reduce or eliminate these events and has been shown to be feasible in single center studies\textsuperscript{9-11}. However, the electrophysiologic (EP) characteristics and outcomes associated with catheter ablation for VAs in patients with Heart Mate II (HM2) device (Thoratec) have not yet been evaluated in a multicenter series.

Methods

Patients were recruited from 9 tertiary electrophysiology centers. All patients with ventricular tachycardia/fibrillation (VT/VF) ablation after LVAD implantation (Heart Mate 2, Thoratec) (Figure 1) were included in this retrospective study. The HM2 LVAD is a continuous flow rotary pump that provides continuous unloading of the left ventricle throughout the cardiac cycle. The pump is axially-configured, where the path of blood flow through the rotor is parallel to the pump’s axis\textsuperscript{12}(Figure 1). Data were collected from the medical chart, electrophysiological procedure report, 3D mapping system, ICD and LVAD log. Study was approved by the institutional review committee and patients gave informed consent.
Ablation procedure

Patients were referred for ablation because of refractory recurrent VAs. Transesophageal and/or intracardiac echocardiography was performed if a retrograde aortic approach was planned to rule out thrombus in the aortic root or in patients with AF to rule out left atrial appendage thrombus. The procedure was performed in patients fully anticoagulated either having a therapeutic INR (between 2 and 3) or receiving unfractionated heparin with an ACT >250/300 depending on centers. Femoral venous and arterial access was obtained for vascular access and hemodynamic monitoring (Figure 2). A 3D electro-anatomic mapping system (Carto 3, Biosense Webster or Velocity, St Jude Medical) was used to perform substrate mapping and to annotate points of interest. Endocardial voltage maps were created and scar was defined as an area with voltage <1.5mV. Except in cases of incessant arrhythmias, programmed stimulation was performed to induce and map VT. A macro-reentrant mechanism was diagnosed based on activation pattern and entrainment mapping, whereas a VT was considered focal or due to micro-reentry when activation was concentric. VT was defined as related to the cannula when activation showed either an origin in the vicinity of the cannula with centrifugal activation or an activation consistent with a circuit turning around the cannula.

The ablation strategy was primarily targeting the clinical/induced arrhythmia via activation and entrainment mapping. Whether additional substrate modification was performed was dependent on the preference of the individual operators.

Irrigated tip ablation catheters were used for all procedures.

Statistical analysis

Categorical variables were described as numbers with corresponding percentages and compared by using the chi-square test. Continuous variables were described as mean ± SD or median [25th,
75th percentile] when not normally distributed. Comparisons were performed using the Student's t-test or the Wilcoxon rank test when not normally distributed. Statistical analyses were performed by using SPSS Software. All p values were 2-tailed with statistical significance set at 0.05. All confidence intervals were calculated at the 95% confidence interval.

Results

Population

Thirty-four patients (30 male, mean age 58 ±10 years old) with HM2 LVAD underwent VT/VF ablation in 9 EP centers between 2009 and 2014 (Table). The indication for LVAD implantation was progressive heart failure (n=21, 62%) or acute cardiogenic shock (n=13, 38%) with the underlying etiologies for the cardiomyopathy either ischemic (n=21, 62%) or non-ischemic (n=13, 38%). In 25 (74%) patients, the LVAD implantation was considered as a bridge to cardiac transplant. Mean turbine speed was 8968 ±491 rpm (range: 7800-9800).

An ICD was present in 32 patients (94%) including 2 which were implanted after LVAD placement. ICDs were implanted for secondary prevention in 13 (41%). Patients were implanted with a single chamber (n=11), a dual chamber (n=4) or a cardiac resynchronization therapy (CRT) (n=17) device. Two patients did not have an ICD at the time of their ablation. Of note, 3 patients required ICD replacement (Atlas, St Jude Medical n=1; Paradym, Sorin Group n=2) after LVAD implantation because of interference that prevented device interrogation.

The mean left ventricular ejection fraction (LVEF) was 17 ± 5% with a mean LV end diastolic diameter (LVEED) before LVAD of 71 ± 9 mm that shortened to 57 ± 11mm (p<0.001) at least 1 month after LVAD implantation.

Ventricular Arrhythmia Characteristics in Patients Undergoing Catheter Ablation

Prior to LVAD implantation, 8 patients had experienced arrhythmic storm and 19 patients had at
least one VT/VF episode while 7 had no prior history of VA. After LVAD implantation, VA occurred in all 34 patients after a median of 11 [2-58] days (min-max: 0 days to 510 days); twenty-three patients experienced arrhythmic storm post LVAD implantation. All of them had at least one VA episode before LVAD implantation. Nine patients required VT ablation < 1 month after LVAD implantation due to intractable VT. These patients more often had arrhythmic storm episodes before LVAD implantation (5/9; 56%). On the contrary, patients without VA before LVAD implantation experienced VA later after implantation (60 days [27-210] vs 7 days [2-25]; p= 0.02). Symptoms during VA were mainly related to ICD shocks (n=19) and, less commonly, syncope/lightheadedness (n=7) or asthenia/palpitation (n=8).

**Mapping and Ablation**

Five patients had a history of VT ablation before LVAD implantation. After implantation, the 34 patients underwent 39 new ablation procedures. A transseptal approach was used in 25 procedures (74%) and a retrograde-aortic approach in the remaining 14 (36%). Pericardial access was not attempted in any patient. An electro-anatomic mapping system (CARTO 3, Biosense Webster n= 37, or Velocity, St Jude Medical n=1) was used in all but one case (Figure 3) to perform a substrate map in baseline rhythm. In 2 other patients, interference between LVAD and the CARTO system prevented mapping the entire LV (transient loss of catheter visualization in some areas). In 6 patients, no endocardial scar could be identified. In the remainder, the mean scar surface was 65±50 cm² (median: 57 cm² [23-72]) with a maximum of 239 cm² (93% of the LV surface –Figure 3A) and a mean total LV surface of 202 ±39 cm². Scar locations were limited to the basal area in 4 (all patients with non-ischemic CMP) but involving the apex (insertion site of the cannula) in 11. They were also located at the anterior n=13, septal n=10, inferior n=8 and/or lateral n=7 LV wall. Of note, more than one segment was involved in
some patients.

One hundred and ten VTs (median 2 [1 - 4.5] per procedure) with a cycle length from 230 to 740ms and 2 VF triggers were targeted during these 39 procedures. Of note, in 2 patients referred for VT ablation, no VA could be induced during the procedure.

The suspected VT mechanisms based on the electrophysiology study were macro-reentry (n=105, 95%), focal or micro-reentry (n=4, 4%) and bundle branch reentry (n=1, 1%). A possible epicardial VT origin was suspected for 6 VTs (5 patients with non-ischemic CMP and one with ischemic CMP). Only 10/110 (9%) of the targeted VAs were related to the HM2 cannula site based on activation and entrainment mapping (Figure 4). In 9 of these patients, the VT mechanism was macro-reentry around the cannula insertion site. The pre-existing substrate was anterior scar through which the cannula had been inserted. In the remaining patient, the VT was related directly to the cannula which touched the LV endocardium.

In these 10 patients in whom VT was related to the cannula, the first episode of VT occurred a median of 38 days [3.5-187] after HM2 placement. In 5 of these patients with VT related to the cannula, VT occurred within one month of LVAD placement, in one at 2 months and in the remaining 4, after 5 months. No particular 12-lead ECG VT morphology could be identified for VTs that were related to the cannula.

In the remaining 24 patients in whom VA was not related to the cannula, the first episode of VA occurred a median of 8 days [2-30] after LVAD placement (p=0.07 compared to VT related to the cannula). VA started mainly during the first month (n=19), but continued to appear regularly thereafter. For 5 of the 7 patients without any VA episodes prior to HM2 implantation, VT began to occur > 1.5 months after LVAD implantation.

Acute success (absence of VT inducibility at the end of the case or successful elimination
of a culprit PVC in the case of a VF trigger) was present in 30/39 procedures (77%). Median RF duration was 24 min [10-35.5] ranging from 2 to 118 min. In 14 procedures, only VT/VF triggers were targeted whereas additional substrate ablation was performed in the remaining 25 ablations.

Complications
One patient with VT ablation for arrhythmic storm developed cardiogenic shock with acidosis. One patient experienced a transient ischemic attack and another, a stroke 8 days after ablation. Red blood cell transfusion (2 units) was required following groin hematoma in 1.

Outcome
During follow-up, 7 patients underwent cardiac transplantation including one with VT recurrence before transplant and 10 patients died (septic shock n=2, massive stroke n=2, intracranial hemorrhage n=1, hemolysis n=1, LVAD deactivation n=1, terminal heart failure n=1, sudden death n=1 and during redo emergency surgery due to cable failure n=1). Of the remaining 17 patients, 13 were arrhythmia-free at 25 ±15 months (median 24 months) after their last ablation procedure. In 1 patient with VT recurrence, a change of turbine speed from 9400 to 9000 rpm extinguished VT.

Discussion
The predominant substrate for VA in patients referred for ablation after HM2 implantation in our series is their underlying ventricular scar with a macro-reentrant mechanism rather than mechanical induction from the left ventricular cannula. Whereas some studies speculated that VT in LVAD patients could be linked to the cannula\(^3,13\) others have reported findings similar to ours\(^10,11\). Cantillon et al.\(^10\) found that 75% of VTs originated from the intrinsic scar versus 14% from the cannula area. They also found some VTs due to micro-reentrant mechanisms (7%) and bundle branch reentry (3.5%). In our study, all patients with VT originating from the cannula
area had the cannula inserted within an antero-apical scar and 9/10 had macro-reentrant VT.

Patients having VA early after LVAD implantation (<1 month) all had a history of VA before LVAD implantation. It has been reported previously that the risk of VA after LVAD was extremely low in the absence of VA before LVAD implantation (4% vs. 46%)\textsuperscript{14}. In our series, 7/34(21\%) did not have VA before LVAD implantation. In these patients, VA occurred later compared to patients with a history of VA (60 days [27-210] vs 7 days [2-25]; p= 0.02).

Interestingly, in patients with VT originating near the cannula, only half experienced VT within one month after LVAD implantation. Even if VT seems to occur later in this population (median: 38 days) compared to patients with VT from other locations (median: 8 days), this difference was not statistically significant (p=0.07). However very early VT occurrence (<48 hours after LVAD placement) was more frequent for VT not related to the cannula. Mechanisms of early appearance of VT post LVAD implantation are not fully understood. Fluid and electrolyte shifts as well as autonomic nervous system imbalance may certainly play a role in the arrhythmia onset especially as beta-blockers are often withheld during the post-operative period. Further, LVAD implantation leads to more specific changes such as ventricular unloading with changes in parietal stretch that may alter the electrical properties of the tissue (refractory periods or conduction times), particularly in the scar area. However no significant difference was observed in our study in terms of LV end-diastolic diameter reduction in patients with early vs. late occurrence of ventricular arrhythmia after LVAD implantation.

Another possible mechanism is suction applied to an adjacent ventricular wall from the cannula\textsuperscript{15}, which occurred in at least one of our patients in whom a change of turbine speed from 9400 to 9000 rpm extinguished VT. The surgeon should be aware of this complication in order to prevent it. It is probably important to orient the cannula towards the infero-lateral part of the LV
because in the closed chest the diaphragm will push on the device and may orient it towards the septum.

In patients undergoing LVAD implantation with a history of VA, the optimal VA management is unknown. Occurrence of VA post LVAD implantation, particularly in the early phase, is deleterious by increasing ICU length of stay and drug requirement. In the patients with a high risk of developing VA post LVAD implantation, prophylactic ablation may be an option but the risk to benefit ratio of this approach is unknown. Based on the data from our series and others, performing ablation before LVAD implantation will likely result in overtreatment with associated procedural risk in this very sick population. Another option is to perform substrate ablation during LVAD implantation as proposed by Mulloy et al.16 This approach requires precise knowledge of the area of scar, potentially obtained pre-operatively by cardiac magnetic resonance imaging or CT scan, for example, to plan the approach and minimize the cross-clamp and perfusion times. In their experience, cryoablation at the time of LVAD implantation resulted in a dramatically shorter ICU length of stay (165 vs. 441 hours; \( p=0.01 \)) and postoperative hospital length of stay (26 vs. 57 days; \( p=0.03 \)). The final option is to perform only catheter ablation in the case of recurrent VA post LVAD implantation, as was the case in our series.

Patients generally received an HM device because they could not be immediately transplanted due to clinical status or absence of a donor heart or that they received the LVAD as destination therapy due to contraindication to transplantation. When feasible, cardiac transplantation is likely a better strategy than catheter ablation of VT because it eliminates the substrate both for the VT and end-stage heart failure. Catheter ablation may not improve survival but improves quality of life by reducing ICD therapies.
Practical consideration for VT ablation in LVAD patients

Given the absence of a pulsatile peripheral pulse with a continuous flow device (Figure 2), the automatic sphygmomanometer may be misleading. It is crucial to invasively monitor arterial blood pressure. In the case of retrograde aortic access, it is important to recognize that there is no or little flow going across the aortic valve and it may then be difficult to cross the valve with the ablation catheter because of the absence of aortic valve opening. This can be facilitated by transiently decreasing the LVAD flow. Moreover there is risk of dislodging any thrombus that can formed in the aortic root even in patients who are fully anticoagulated; therefore it is reasonable to perform transesophageal echocardiography before attempting retrograde aortic access to the LV. For transseptal access, a steerable sheath is extremely helpful.

The risk of catheter entrapment in the cannula is extremely low. Several times during these procedures, catheters went into the initial part of the cannula without any adverse event. The catheters were never aspirated by the cannula. However they should not be advanced too far in, particularly never beyond the initial portion of the cannula where the turbine is located.

As previously reported, 3 patients had LVAD interference that prevented ICD interrogation and programming (Atlas, St Jude Medical n=1; Paradym, Sorin Group n=2). LVADs can also produce interference with the 3D electro-anatomic mapping systems, which we did encounter in 2 patients resulting in areas (inferior apical LV wall close to the turbine) where the ablation catheter could not be visualized during mapping.

Limitations

This is an observational study with a limited number of patients included because of the very specific entity studied. Due to the study design (observational and multicenter), ablation strategy was not uniform in all patients but reflects current strategies in different centers.
Conclusions

In this study, all patients developing intractable VT soon after LVAD implantation have a history of VT before HM II implantation. Despite a high mortality rate among LVAD recipients, catheter ablation of VT is effective and relatively safe even within 1 month post implantation. Intrinsic myocardial scar, rather than the apical cannula, appears to be the dominant substrate.

Conflict of Interest Disclosures: Frederic Sacher has received lecture honorarium from Biosense Webster and is consultant from St Jude Medical and Sorin Group. Kenneth Ellenbogen is consultant and received research grant and fellowship support from Biosense Webster. Josef Kautzner is a member of Scientific Advisory Board of Boston Scientific, Biosense Webster, Medtronic and St Jude Medical. He received lecture honoraria from Biosense Webster, Biotronik, Boston Scientific, Medtronic and St Jude Medical. Jayanthi Koneru received fellowship support and research grant from Biosense Webster. Richard Shepard received fellowship support and research grant from Biosense Webster. James Coffey has received consulting fees from Biosense Webster. Michel Haissaguerre has received lecture honorarium and is part of the Scientific Advisory Board of Biosense Webster. William Stevenson is co-holder of a patent for needle ablation (Biosense Webster) that is consigned to Brigham and Women's Hospital. Francis Marchlinski has received lecture honorarium and is part of the Scientific Advisory Board of Biosense Webster. Pierre Jais has received lecture honorarium and is part of the Scientific Advisory Board of Biosense Webster and St Jude Medical.

References:


**Table:** Clinical characteristics of the population at LVAD implantation

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
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<tbody>
<tr>
<td>n = 34</td>
<td></td>
</tr>
<tr>
<td><strong>Sex, male (n, %)</strong></td>
<td>30 (88%)</td>
</tr>
<tr>
<td><strong>Age, y</strong></td>
<td>58 ±10</td>
</tr>
<tr>
<td><strong>Ischemic CMP</strong></td>
<td>21 (62%)</td>
</tr>
<tr>
<td><strong>VT/VF pre LVAD</strong></td>
<td>27 (79%)</td>
</tr>
<tr>
<td><strong>Arrhythmic Storm pre LVAD</strong></td>
<td>8 (24%)</td>
</tr>
<tr>
<td><strong>Atrial Arrhythmia</strong></td>
<td>14 (41%)</td>
</tr>
<tr>
<td><strong>Beta-blocker therapy</strong></td>
<td>24 (71%)</td>
</tr>
<tr>
<td><strong>Amiodarone</strong></td>
<td>28 (82%)</td>
</tr>
<tr>
<td><strong>LVEF pre LVAD</strong></td>
<td>17 ±5%</td>
</tr>
<tr>
<td><strong>LVEDD (mm) pre LVAD</strong></td>
<td>71 ±9 mm</td>
</tr>
<tr>
<td><strong>Normal RV function</strong></td>
<td>21 (62%)</td>
</tr>
<tr>
<td><strong>ICD</strong></td>
<td>32 (94%)</td>
</tr>
<tr>
<td><strong>CRT</strong></td>
<td>17/32 (53%)</td>
</tr>
</tbody>
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CMP: cardiomyopathy, VT: ventricular tachycardia, VF: ventricular fibrillation, LVAD: left ventricular assist device, LVEF: left ventricular ejection fraction, LVEDD: left ventricular end diastolic diameter, RV: right ventricle, ICD: implantable cardioverter-defibrillator, CRT: cardiac resynchronization therapy.
Figure Legends:

Figure 1: A) Heart Mate II device (Thoratec Corporation, CA, USA ). B) Chest X-Ray showing the cannula and the turbine. C) Implantation of a Heart Mate II device.

Figure 2: Programmed ventricular stimulation in a patient with LVAD and dilated CMP. Arterial Pressure line is displayed (BP4). Note the low pulsatility during baseline rhythm. When a fast VT is induced (cycle length 280ms) the pulse pressure disappears but mean arterial pressure remains around 70 mmHg and the patient is asymptomatic which allows for safe VT mapping.

Figure 3: Bipolar voltage map (Carto 3) of the left ventricle in a patient implanted with a Heart Mate II device (Green) for progressive heart failure due to ischemic CMP (panel A). Scar area (voltage <1.5mV) represents 93% of the LV surface. Panel B: Unipolar voltage map of left ventricle in a patient with dilated CMP. The Heart Mate II device image (green) is imported into Carto 3 from the CT scan after processing and transformation to a vtk format with the MUSIC platform.

Figure 4: Left ventricle activation map (Carto 3) of a VT that was anchored near the cannula in a 55 year old woman with a prior anterior myocardial infarction. The orange dot represents the site of ablation that terminated VT.
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Circ Arrhythm Electrophysiol. published online April 13, 2015;
Circulation: Arrhythmia and Electrophysiology is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 1941-3149. Online ISSN: 1941-3084

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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