Mobile Thrombus on Device Leads in Patients Undergoing Ablation
Identification, Incidence, Location, and Association With Increased Pulmonary Artery Systolic Pressure

Gregory E. Supple, MD; Jian-Fang Ren, MD; Erica S. Zado, PA-C; Francis E. Marchlinski, MD

Background—Mobile thrombi, not routinely recognized on transthoracic echocardiography, are frequently identified on cardiovascular implantable electronic device leads with intracardiac echocardiography (ICE) during ablation procedures. Their incidence, characteristics, and consequences have not yet been defined.

Methods and Results—We used ICE to examine leads for thrombi and to measure the pulmonary artery systolic pressure in patients with a cardiovascular implantable electronic device presenting for ablation. Patient clinical characteristics, device type, and lead characteristics were correlated with presence of thrombi. Most patients had congestive heart failure (84%), with an average left ventricular ejection fraction of 40%. Thrombi were seen with ICE in 26 of 86 patients (30%) but were seen on transthoracic echocardiography in only 1 of the 26 patients. Thrombi on ICE were mobile, averaged 18±5.9 mm long by 4.4±2.3 mm wide, and were more commonly identified in the right atrium (n=25) than in the right ventricle (n=5). Thrombi were associated with higher pulmonary artery systolic pressure: 39±9 mm Hg with thrombi versus 33±7 mm Hg without thrombi (odds ratio, 1.11; 95% confidence interval, 1.03 to 1.20; P=0.01). No other characteristic assessed was associated with a significant difference in the presence of lead thrombi.

Conclusions—Mobile thrombi on cardiovascular implantable electronic device leads are present in 30% of patients undergoing ablation and are readily identified with ICE despite being underrecognized with transthoracic echocardiography. Further study is warranted to determine whether lead thrombi are a clinically relevant source of pulmonary emboli in some patients with cardiovascular implantable electronic devices. (Circulation. 2011;124:00-00.)

Key Words: cardiac implantable electronic device ■ implantable cardioverter-defibrillator ■ intracardiac echocardiography ■ pacemakers ■ thrombus

The venous approach to implanting endocardial leads for permanent pacemaker systems has been practiced since 1965 because of its relative ease and safety. However, patients who have a cardiovascular implantable electronic device (CIED) such as a pacemaker or implantable cardioverter-defibrillator (ICD) are at risk for developing venous complications. Venous thrombosis is relatively common and can result in venous stenosis and occlusion or even pulmonary embolism. Many studies have evaluated the incidence of venous abnormalities after CIED implantation with venous angiography or Doppler ultrasonography, with abnormal findings in 23% to 64% of patients after implantation, depending on the imaging methods used and the duration of follow-up after implantation. The clinical impact of such findings is not clear.

Clinical Perspective on p ●●●

Venous thrombosis can lead to symptomatic upper-extremity deep venous thrombosis or superior vena cava syndrome; however, the incidence of symptomatic complications is much less common, seen in only 0% to 6% of patients. Similarly, symptomatic pulmonary embolism after pacemaker/ICD implantation is relatively rare, seen in 0% to 5% of patients. However, the incidence of asymptomatic pulmonary embolism has been found to be much more common: One study demonstrated pulmonary embolism in 15% of patients on ventilation/perfusion scans done 14 days after pacemaker implantation. A more recent autopsy series of patients with pacemakers or ICDs identified pulmonary emboli in 21% of patients. Despite this relative frequency, the etiology and potential long-term implications of subclinical pulmonary emboli still remain poorly understood.

The aforementioned studies have used a variety of imaging modalities to evaluate thrombosis in the upper extremity and great veins and their potential downstream emboli to the lungs but have not evaluated the presence of thrombi on the intracardiac segment of the leads. Intracardiac thrombi are
sometimes seen on transthoracic echocardiography (TTE), but given the limited resolution of TTE, the presence of intracardiac lead thrombi may be underrecognized.

We have frequently identified mobile thrombi with intracardiac echocardiography (ICE) on sheaths and catheters placed at the time of ablation in patients undergoing ventricular tachycardia or atrial fibrillation/atrial flutter ablation.\textsuperscript{16,17} The incidental finding of thrombus on CIED leads has also been recognized occasionally but not evaluated systematically. The aim of this study was to systematically evaluate the incidence and location of intracardiac lead thrombi on patients undergoing ablation procedures and to evaluate their clinical associations and potential clinical impact.

**Methods**

A cohort of consecutive patients with prior pacemaker or ICD who presented to our center for ventricular tachycardia or atrial fibrillation/atrial flutter ablation with the use of ICE to guide the ablation was evaluated retrospectively for this study. At the beginning of each case before any ablation, ICE was used to examine the pacemaker and ICD leads for the presence, location, and size of thrombus. Continuous-wave Doppler recording of tricuspid regurgitation was used to calculate the right atrial–right ventricular (RV) systolic pressure difference from the modified Bernoulli equation ($P_{r} - P_{a} = 4V^{2}$) with the use of the peak velocity of the regurgitant jet. Pulmonary artery systolic pressure (PASP) was calculated as the sum of this transtricuspid pressure gradient and the estimated right atrial pressure (10 mm Hg for a normal right atrium, 14 mm Hg if abnormally dilated). We also evaluated the following patient characteristics: age, gender, type of ablation, left ventricular ejection fraction (assessed qualitatively with TTE), type of cardiomyopathy, number and age of intracardiac leads, presence of a superior vena cava coil on the lead, type of device (ICD versus pacemaker), and treatment with warfarin, aspirin, or clopidogrel before ablation.

Routine TTE was obtained in all patients and was performed within 3 days of the ICE imaging in the majority of these patients (77 of 86 patients). We reviewed the TTE reports for these patients to determine whether lead thrombus was otherwise identified during that admission. We subsequently reviewed the TTE images in a blinded fashion to determine whether a thrombus was identifiable on detailed follow-up review. When available, transesophageal echocardiographic (TEE) reports and images were also reviewed for the presence of lead-associated thrombus.

**Statistical Analysis**

Fisher exact tests, Student t tests with unequal sample size and unequal variance analysis, Mann-Whitney U tests (for nonnormally distributed data [patient age and CIED lead age]), and $\chi^{2}$ tests were performed to determine whether there was a statistically significant difference in the clinical characteristics assessed between the group that demonstrated lead thrombus and the group that did not. Statistical analysis was performed on Microsoft Excel with XLSTAT 2010 (www.xlstat.com). Results are expressed as the median (Q1, Q3) or mean ± SD where applicable. A P value of <0.05 was considered statistically significant.

Nineteen of the 86 patients evaluated did not have sufficient tricuspid valve regurgitation to allow calculation of their PASP. These patients were excluded from the analysis of the correlation between PASP and the presence of mobile lead thrombus.

**Results**

Between February 2007 and November 2009, 86 patients with a prior CIED presenting for ablation with ICE guidance were evaluated. The patients were predominantly male (84%) with a median age of 59.5 years. The majority of patients had a cardiomyopathy with an average left ventricular ejection fraction of 40±19% (with ischemic cardiomyopathy being the most frequent type); most of the patients had an ICD (93%), and patients were most commonly undergoing ventricular tachycardia ablation (85%). See Table 1 for a summary of the baseline characteristics of these patients.

<table>
<thead>
<tr>
<th>Patient Characteristics</th>
<th>Total (n=86)</th>
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<tbody>
<tr>
<td>Male, n (%)</td>
<td>72 (84)</td>
</tr>
<tr>
<td>Age, y (quartiles)</td>
<td>59.5 (53, 71)</td>
</tr>
<tr>
<td>No. with ICD (%)</td>
<td>80 (93)</td>
</tr>
<tr>
<td>VT/AF ablation</td>
<td>73/13</td>
</tr>
<tr>
<td>History of MI, n (%)</td>
<td>40 (47)</td>
</tr>
<tr>
<td>Diabetes mellitus, n (%)</td>
<td>15 (17)</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>40±19</td>
</tr>
<tr>
<td>Cardiomyopathy, n (%)</td>
<td>72 (84)</td>
</tr>
<tr>
<td>Ischemic</td>
<td>39 (45)</td>
</tr>
<tr>
<td>ARVD</td>
<td>9 (10)</td>
</tr>
<tr>
<td>HOCM</td>
<td>6 (7)</td>
</tr>
<tr>
<td>Idiopathic DCM</td>
<td>18 (21)</td>
</tr>
<tr>
<td>Mobile thrombus</td>
<td>26 (30)</td>
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</tbody>
</table>

ICD indicates implantable cardioverter-defibrillator; VT, ventricular tachycardia; AF, atrial fibrillation; MI, myocardial infarction; LVEF, left ventricular ejection fraction; ARVD, arrhythmogenic right ventricular dysplasia; HOCM, hypertrophic obstructive cardiomyopathy; and DCM, dilated cardiomyopathy.

Twenty-six of 86 patients (30%) had 30 lead thrombi identified with ICE. The thrombi were mobile and averaged 18±5.9 mm long (range, 1 to 45 mm) by 4.4±2.3 mm wide (range, 0.3 to 30 mm). Four patients had thrombi over 30 mm in length (Movie I in the online-only Data Supplement for an example of a large thrombus). Thrombi were more commonly identified on the lead in the right atrium (n=25) than in the right ventricle (n=5). Twenty-five of these were identified at the beginning of the case before ablation; however, 1 patient who did not have a thrombus seen on initial imaging had a large thrombus (43×4.5 mm) on the RV portion of the lead noted during ICE imaging in the middle of the case.

Thrombus was not reported on the routine TTEs in any of the 26 patients despite being easily identified with ICE (Figures 1 and 2). Our blinded review of the TTE images identified only 1 patient with a lead thrombus in the right atrium that had not been noted in the clinical report. This thrombus was also identified with ICE.

One patient had a large (2.6 cm in length) mobile thrombus seen on routine TTE performed the day after the ablation procedure (Figure 3). No thrombus had been seen on ICE during the procedure in this patient. In addition, 5 patients had routine TEE studies done. No lead thrombi were noted in the TEE reports, but, on blinded review, in 2 of these 5 patients we identified mobile lead thrombi. Interestingly, no thrombus was seen on ICE during the ablation procedures in these patients.

Table 2 displays the clinical characteristics that were assessed to evaluate a possible correlation with mobile thrombi. Mobile lead thrombi were associated with a significantly higher PASP: 39±9 mm Hg (range, 26 to 52 mm Hg)
in the group with thrombi versus 33±7 mm Hg (range, 23 to 48 mm Hg) in the group without thrombi (odds ratio [OR], 1.11; 95% confidence interval [CI], 1.03 to 1.20; $P=0.01$). No other clinical characteristic was associated with a significant difference in the presence of lead thrombi. However, there were nonsignificant associations between the presence of lead thrombus and an increased number of endocardial leads (OR, 1.84; 95% CI, 0.74 to 4.6; $P=0.19$), as well as increased lead age (OR, 1.09; 95% CI, 0.94 to 1.26; $P=0.69$).

Similarly, there was a nonsignificant association between warfarin use and the absence of lead thrombus (OR, 0.36; 95% CI, 0.08 to 1.53; $P=0.17$). Because warfarin is frequently stopped periprocedurally, we also assessed for the presence of consistent therapeutic anticoagulation on admission and up to the time of the procedure (international normalized ratio or partial thromboplastin time consistently in a therapeutic range). There was no significant difference between the 2 groups (OR, 1.28; 95% CI, 0.28 to 5.87; $P=0.75$).

**Discussion**

We have demonstrated that mobile thrombi are seen on device leads in 30% of patients with CIED presenting for ablation procedures when evaluated with ICE. These thrombi are typically of modest size but occasionally can be $\geq$3 cm in length. Of note, the thrombi are rarely identified with routine TTE. However, because a high proportion of this population had cardiomyopathy and congestive heart failure, this may not be representative of the incidence of lead thrombi in all patients with CIEDs.

Despite the frequency of thrombi in these patients, none of them demonstrated a history of clinically recognized pulmonary embolism, and the implications of these thrombi are unclear. We did not perform ventilation/perfusion scans or computed tomographic angiography to assess for pulmonary embolism in our study and therefore cannot comment specifically on the embolic risk of the observed thrombi; however, our observations in individual patients raise concern for a process of repeated formation and embolization. One of our patients had a large lead thrombus seen in the middle of an ablation procedure (Figure 4), which had not been seen on detailed ICE imaging at the beginning of the procedure. This patient had not been anticoagulated initially because it was a right heart procedure, but after the thrombus was identified, he was treated with argatroban, and at the end of the case the thrombus was no longer seen. The patient did not develop any symptoms or signs of pulmonary embolism during the case. In several other cases, thrombi were seen on TEE or subsequent TTE, despite not being identified on ICE. Although these thrombi may have been missed during ICE imaging, it is also possible that these thrombi developed in the intervening time between the 2 echocardiograms. We have demonstrated previously that thrombi can form rapidly on sheaths and catheters during ablation, and all of these findings...
therefore raise the possibility that thrombi can form and perhaps resolve, or more likely dislodge, over a short time frame, even on leads that have been chronically implanted. These observations may explain why many thrombi were seen in patients despite the use of chronic warfarin and why we did not demonstrate a statistically significant difference in warfarin use between the 2 groups. Warfarin was frequently stopped periprocedurally (only 23 of 41 patients on chronic warfarin had consistently therapeutic anticoagulation in the days leading up to the procedure), and perhaps even transient periods of subtherapeutic anticoagulation allow for the formation of thrombi in some patients.

We also found that patients with mobile lead thrombi have a significantly increased pulmonary artery pressure, which has not been reported previously. At the same time, however, we did not find a significant difference in RV function (as assessed qualitatively by TTE) between the 2 groups. The clinical significance of the increased PASP therefore remains to be defined and should be verified with a larger prospective study, but it raises concern about a persistent thromboembolic risk of endocardial leads. If lead thrombi are repeatedly forming and embolizing, they may contribute to worsening pulmonary hypertension. This would be of particular concern in patients with underlying RV dysfunction such as those

Figure 2. Example of patient with thrombus seen on intracardiac echocardiography (A) but not seen on parasternal short-axis or apical 4-chamber transthoracic echocardiographic images (B). RA indicates right atrium; Ao, aorta; LV, left ventricle; AV, aortic valve; TV, tricuspid valve; and RV, right ventricle.

Figure 3. Two-centimeter lead thrombus that was visible on transthoracic echocardiographic images (off-axis parasternal short-axis and apical 4-chamber views). RV indicates right ventricle; LV, left ventricle; and RA, right atrium.
with arrhythmogenic RV dysplasia/cardiomyopathy. The potential of accelerating RV dysfunction with elevations in PASP may lead to a more rapid deterioration of the underlying disease process and even a further risk of recurrent emboli if the thrombus formation is potentiated by low-flow states. Previous studies have demonstrated an incidence of pulmonary embolism in patients with CIED5–13 similar to the incidence of lead thrombi we demonstrate here, making it possible that chronic pulmonary embolism is causing increased pulmonary pressures.

Our study failed to identify other factors that were significantly associated with the presence of lead thrombi other than the elevation in PASP and precluded our ability to define specific high-risk groups. Notably, the use of warfarin or antiplatelet medications was not significantly different between the 2 groups, although there was a nonsignificant trend toward higher chronic use of warfarin in the group without thrombi. Treatment with prophylactic low-dose warfarin has been shown to reduce the incidence of venous thrombosis in oncology patients receiving central venous catheters.19 Similarly, prophylactic treatment with low-dose heparin after pacemaker implantation has been shown to prevent the development of pulmonary embolism on follow-up ventilation/perfusion scanning.12 However, despite these small prospective studies of anticoagulation, most larger observational studies have not demonstrated a difference in the incidence of venous thrombosis in anticoagulated patients.8,15 It may be that even brief periods of subtherapeutic anticoagulation are sufficient to allow lead thrombi to form.

Our study did not demonstrate a significant correlation between the number of leads and the presence of thrombus, although there was a nonsignificant trend toward a higher number of leads in the thrombus group. One previous study has shown an association of number of leads and venous thrombosis10; however, most previous work has not demonstrated an association.5,6,8,9,11,14

Of note, thrombi were more commonly seen on atrial rather than ventricular leads. This observation begs the question of whether thrombus formation is due to a combination of the lead being present and low flow. It is possible that the elevated PASP is not a consequence of lead thrombus but rather contributes to a low-flow state and actually potentiates thrombus formation and identifies a clinical factor that puts patients at an even greater risk.

Table 2. Thrombus and Clinical Characteristics

<table>
<thead>
<tr>
<th></th>
<th>With Thrombus (n=26)</th>
<th>Without Thrombus (n=60)</th>
<th>P (Univariate)</th>
<th>OR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median patient age, y</td>
<td>58 (53, 68)</td>
<td>61.5 (52, 71)</td>
<td>0.97</td>
<td>1.00</td>
<td>0.95–1.05</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>22 (84)</td>
<td>50 (83)</td>
<td>0.88</td>
<td>0.85</td>
<td>0.14–4.5</td>
</tr>
<tr>
<td>Ablation: VT/AF</td>
<td>22/4</td>
<td>51/9</td>
<td>0.96</td>
<td>0.47</td>
<td>0.08–4.6</td>
</tr>
<tr>
<td>LVEF, %</td>
<td>40±18</td>
<td>41±20</td>
<td>0.75</td>
<td>3.30</td>
<td>0.05–200.7</td>
</tr>
<tr>
<td>Myocardial infarction, n (%)</td>
<td>13 (54)</td>
<td>20 (47)</td>
<td>0.38</td>
<td>1.47</td>
<td>0.36–5.93</td>
</tr>
<tr>
<td>Heart failure, n (%)</td>
<td>23 (88)</td>
<td>49 (82)</td>
<td>0.41</td>
<td>1.48</td>
<td>0.13–16.77</td>
</tr>
<tr>
<td>Decreased RV function, n (%)</td>
<td>6 (26)</td>
<td>13 (22)</td>
<td>0.85</td>
<td>2.16</td>
<td>0.45–10.32</td>
</tr>
<tr>
<td>No. of leads</td>
<td>2.2±0.8</td>
<td>2.0±0.7</td>
<td>0.20</td>
<td>1.84</td>
<td>0.74–4.6</td>
</tr>
<tr>
<td>SVC coil, n (%)</td>
<td>21 (84)</td>
<td>51 (85)</td>
<td>0.46</td>
<td>0.38</td>
<td>0.06–2.34</td>
</tr>
<tr>
<td>Median lead age, y (quartiles)</td>
<td>5 (2.5, 7)</td>
<td>5 (1.75, 7)</td>
<td>0.69</td>
<td>1.09</td>
<td>0.94–1.26</td>
</tr>
<tr>
<td>Device: ICD/pacemaker</td>
<td>24/2</td>
<td>56/4</td>
<td>0.87</td>
<td>0.14</td>
<td>0.01–4.19</td>
</tr>
<tr>
<td>Warfarin use, n (%)</td>
<td>10 (38)</td>
<td>31 (52)</td>
<td>0.26</td>
<td>0.36</td>
<td>0.08–1.53</td>
</tr>
<tr>
<td>Consistent anticoagulation, n (%)</td>
<td>6 (23)</td>
<td>14 (23)</td>
<td>0.98</td>
<td>1.28</td>
<td>0.28–5.87</td>
</tr>
<tr>
<td>Aspirin/clopidogrel (%)</td>
<td>19 (73)</td>
<td>42 (60)</td>
<td>0.77</td>
<td>0.7</td>
<td>0.01–40.12</td>
</tr>
<tr>
<td>PASP, mm Hg</td>
<td>39±9</td>
<td>33±7</td>
<td>0.01</td>
<td>1.11</td>
<td>1.03–1.20</td>
</tr>
</tbody>
</table>

OR indicates odds ratio; CI, confidence interval; VT, ventricular tachycardia; AF, atrial fibrillation; LVEF, left ventricular ejection fraction; RV, right ventricular; SVC, superior vena cava; ICD, implantable cardioverter-defibrillator; and PASP, pulmonary artery systolic pressure.

Figure 4. A 4.5-cm-long thrombus attached to the atrial portion of the right ventricular (RV) lead, noted in the middle of the case but not seen on initial intracardiac echocardiographic images. The patient was started on argatroban, and the thrombus was not seen at the end of the case. RV indicates right ventricle. See Movie I in the online-only Data Supplement.
Future Directions

None of our patients had clinical evidence of pulmonary embolism, and the clinical relevance of these lead thrombi is unclear. We are concerned, however, that the increased PASP in the group with thrombi puts these patients at risk for clinically significant pulmonary hypertension or RV dysfunction. The potential causal relationship of lead thrombosis and increased PASP warrants further investigation with prospective study and evaluation for subclinical pulmonary emboli. Additionally, we should seek to identify additional hematologic and physiological factors that may predict the risk of forming thrombi and how rapidly they can form and dislodge and to determine prospectively whether anticoagulation or other therapies can prevent the formation or embolization of lead thrombi.

In our study, we used ICE to assess for the presence of thrombus, which afforded a reliable way to identify such thrombi and did not appear to contribute to thrombus dislodgement. TEE may also allow evaluation for lead thrombus in patients with CIED,15,20 and using echocardiography to screen patients at risk for having lead thrombi may help to guide the decision to stop anticoagulation therapy periprocedurally. Determining whether ICE or TEE is superior for this will require further study with direct comparison of the 2 modalities.

Limitations

Our study was an observational cohort study and as such has the limitation that potential unknown confounders are present. We have also only demonstrated a correlation between lead thrombus and increased PASP, but, as indicated, we do not know whether lead thrombi is a causative factor. We used echocardiography to measure pulmonary artery pressure, which limited our assessment to patients with sufficient tricuspid valve regurgitation to allow the estimation of PASP. This method may be less accurate than invasive catheter-based measurement of pulmonary artery pressure but has been validated as the principal technique for measuring PASP in cases in which invasive measurement is impractical.21 Furthermore, several studies have shown that there is not a significant difference in PASP between patients with and without a measurable tricuspid valve gradient.22,23 We did not routinely perform TEE in this study to provide a reference test for the accuracy of ICE in detecting lead thrombi; thus, we could not determine whether the true incidence of lead thrombi was even higher. A systematic head-to-head comparison of ICE with TEE will be required to determine the gold standard modality for detecting lead thrombi.

In addition, we selected patients with CIED undergoing ablation, which may not be representative of the general population of all patients with CIED. Many of the patients had significant structural heart disease and congestive heart failure, and low-flow states in such patients may contribute to increased thrombus formation. Patients undergoing procedures such as ventricular tachycardia ablation typically have anticoagulation interrupted, and this may have affected our observed relationship between thrombus and the use of anticoagulation.

Our study may have been underpowered to detect an association between the use of chronic anticoagulation or number of leads and the presence of thrombus. Prior studies have also been equivocal on an association between these factors and venous thrombosis, raising the possibility that there is a small effect that is difficult to demonstrate with small studies.5,10,14

Conclusion

Mobile thrombi on CIED leads are present in 30% of patients undergoing ablation procedures, are readily identified with ICE, and are seen more frequently in the right atrium than in the RV. We have demonstrated that patients with mobile lead thrombi have a significantly higher PASP than those without thrombi. Further study is warranted to confirm the increased pulmonary pressure, to determine whether lead thrombi are causing worsening PASP and RV dysfunction, and, if so, to identify strategies to prevent lead thrombi from developing.

Sources of Funding

This study was supported by the Harlan Batrus Research Fund.

Disclosures

None.

References


CLINICAL PERSPECTIVE

This article describes the frequent (30% of patients) presence of sizable mobile thrombus on pacemaker and defibrillator leads identified with careful intracardiac echocardiographic assessment during ablation procedures for atrial fibrillation and ventricular tachycardia. These thrombi were more frequently seen on the atrial portion of the leads. Prior use of oral anticoagulants or antiplatelet agents, the number and age of leads, and presence of a superior vena cava coil were not specifically associated with lead thrombi during the procedure. The group with thrombus had a higher pulmonary artery pressure, suggesting the possibility that patients with lead thrombi may have subclinical pulmonary emboli elevating the pressure and/or that higher pulmonary artery pressure predisposes to thrombus formation in right-sided cardiac chambers. Further study is warranted to identify hematologic or other clinical factors that may increase patients’ risk of forming device lead thrombi and to assess the potential clinical impact of these thrombi.