Autopsy and clinical context in deceased patients with implanted pacemakers and defibrillators: intracardiac findings near their leads and electrodes

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Aims
To evaluate intracardiac findings near leads and causes of death in pacemaker/defibrillator patients.

Methods and results
Special autopsy was performed on 78 patients deceased in a hospital. Age at death was 77.9 ± 10.0, implantation-death interval 4.0 ± 3.3 years, ventricular leads n = 78, and atrial leads n = 21. Thrombi along leads in brachiocephalic vein/upper caval vein (BV/UCV) were found in 22 (7%), in right atrium (RA) in 11 (8), and in right ventricle (RV) in 11 cases. Bipolar lead rings were fixed by fibrous tissue in 43 (44) cases. Connective tissue bridges and tunnels were found in BV/UCV in 44 (13), in RA in 17 (15), and in RV in 68 cases, with a length of 0.2–12.0 cm. Right ventricular leads in tricuspidal orifice were fixed by fibrous tissue in 11 and penetrating chordae in 25 cases. Main causes of death were: heart failure in 35, pulmonary embolism in 9, and myocardial infarction in 11 cases.

Conclusion
We have found (i) thrombi on ventricular/atrial leads in 33/48%, (ii) bipolar lead rings fixed by fibrous tissue in 68/22%, (iii) connective tissue bridges or tunnels in ventricle/atrium in 87/71%, and (iv) ventricular leads fixed to valve or penetrating chordae in 46% of patients. We do recommend caution when extracting leads.

Keywords
Pacemaker/defibrillator leads • Autopsy • Thrombi • Connective tissue bridges • Extraction

Introduction
A number of studies have analysed the cause of death in patients with implanted pacemakers (PM) and defibrillators (ICD). Potential relationship between the death and PM or ICD malfunction, including lead problems, has been described. Moreover, the encapsulation of leads by connective tissue, adhesion at the tricuspid valve apparatus, and difficulties during leads extraction have been encountered. Data on thrombi forming on the leads are relatively scarce.

Endocardial leads represent a foreign body in the bloodstream. Thrombi form a sheath along the leads (covering 30–80% of its length) within 12 h after implantation. Then, they undergo organization over several months forming a fibrous sheath around the leads (via growth of fibroblasts and formation of connective tissue). This extends from the site of electrode contact with endocardium of the right ventricle (RV) across the tricuspid valve into the right atrium (RA).11

Transvenous extraction of PM and ICD leads is associated with possible risks and complications. The predominant indication for the extraction of PM or ICD leads is local or systemic infection often with endocarditis. Vegetations on valves or leads are established echocardiographically. Treating the infection by means of antibiotics and pocket drainage is usually of little help and relapses are frequent. Extraction can also be performed surgically, which brings a substantial risk of complications.

Another indication for lead extraction is a damaged lead such as insulation defect, infraction, or fracture, most frequently seen in the subclavian crush syndrome. In these cases, the ‘sterile’ lead can be left in situ and its connector must be capped and fixed to
the subcutaneous connective tissue to prevent its migration. Significant tricuspid regurgitation, which is more frequent in the presence of several leads, can also be an indication for extraction. Another reason for lead extraction may be the case of manufacturer recall (recommended extraction because of technical failure).

The aim of our study was to assess intracardiac findings in deceased PM and ICD patients. We focused on thrombus formation and connective tissue encapsulation around the leads in the heart. We also analysed the causes of death and potential relation to implanted PM and ICD leads. We evaluated the thrombo-embolic complications too.

Methods

Patient population and material

In the period between February 2005 and June 2008, 124 deceased patients with implanted PM or ICD were transferred from two Brno hospitals to the Department of Pathology. Standard autopsy was performed on 12 and special autopsy on 78 patients. Autopsy was not carried out in 34 patients, either due to the wish of the relatives or for technical reasons.

All PM/ICD leads were insulated with silicon-rubber or polyurethane.

Autopsy

In the standard autopsy, the PM or ICD was removed from the subclavian area. In the evisceration of cervical and thorax organs, the leads were cut off in the area of brachiocephalic or subclavian vein. The intracardiac parts of leads with electrodes were left in the heart, which was autopsied using the standard technique.

The special autopsy (n = 78) consisted in: (i) localizing precisely the electrode tip, (ii) assessing the total length of thrombi on leads, (iii) evaluating the connective tissue covering of bipolar electrode rings, (iv) location and total length of connective tissue bridges (<1 cm) or tunnels (>1 cm), (v) assessing the fixation or penetration of the leads into the tricuspid valve apparatus, and (vi) examining the occurrence of thrombi on the walls of both atria and both ventricles.

The number of explanted PM/ICD and the causes of death given in the clinical reports and pathological–anatomical conclusions were evaluated for all the autopsied persons (n = 90).

Results

The average age of the deceased patients was 77.9 ± 10.0 years. The interval between the first implantation and death was 4.0 ± 3.3 years.

Pathological findings in hearts were as follows: heart weight ranged between 300 and 980 g (543.6 ± 157.3). Hypertrophy and macroscopically assessed dilatation of left and right ventricles were present in 90% deceased.

In the autopsies, 90 implants were taken out. In the case of pacemakers, they were ventricular VVI (49), dual-chamber VDD (7), DDD (20), and biventricular devices (3). In the case of defibrillators, they were ventricular VVI (seven), dual-chamber DDD (two), and biventricular devices (two).

After performing the special autopsy (n = 78), we established the following findings.

Table 1 Position of electrode tip

<table>
<thead>
<tr>
<th>Ventricular leads, single leads included</th>
<th>Atrial leads n = 21</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apex</td>
<td>27</td>
</tr>
<tr>
<td>Posterior wall</td>
<td>34</td>
</tr>
<tr>
<td>Anterior wall</td>
<td>5</td>
</tr>
<tr>
<td>Septum</td>
<td>10</td>
</tr>
<tr>
<td>Non-anchored*</td>
<td>2</td>
</tr>
</tbody>
</table>

*Probably unintentional pull-up during autopsy.

Table 2 Thrombi along the leads

<table>
<thead>
<tr>
<th>Leads</th>
<th>Ventricular (n = 78)</th>
<th>Atrial (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachiocephalic vein</td>
<td>22</td>
<td>7</td>
</tr>
<tr>
<td>Right atrium</td>
<td>11</td>
<td>8</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>11</td>
<td>–</td>
</tr>
</tbody>
</table>

‘Ventricular leads’ (n = 78) were bipolar in 58 (74.4%), unipolar in 15 (19.2%), and bipolar single-pass leads (VDD leads) in 5 (6.4%) cases. There were 16 (20.5%) leads with active fixation and 62 (79.5%) leads with passive fixation. Steroid-eluting electrodes were used in 30%.

‘The electrode tip was fixed’ (Table 1) in the apex of the RV in 27 cases, in the posterior wall in 34, in the anterior wall in 5, in the septum in 10, and non-anchored in 2 cases (probably unintentional pull-up during autopsy). The electrode tips were grown into the endocardium or myocardium of the RV usually linked up with a connective tissue bridge or tunnel.

‘Thrombi’ along the lead were evident in 26 patients (33%), 22 patients in brachiocephalic vein and/or in upper caval vein, 11 patients in the RA, and 11 patients in the RV (Table 2). Twelve patients exhibited simultaneously thrombi on the leads in the large veins and in RA or RV (Figures 1 and 2).

‘Rings of bipolar electrodes, single-pass leads included’ (n = 63), were fixed by fibrous tissue in 43 (68%) and free in 20 (32%) cases (Table 3).

‘Connective tissue bridges and/or tunnels’ were found in 68 patients (87%), 44 in brachiocephalic vein and/or the upper caval vein, 17 in the RA, and 68 patients in the RV, their total length ranging from 0.2 to 12 cm (Table 4). A large number of leads (42) exhibited simultaneously connective tissue bridges or tunnels in the large veins and in the RA or RV (Figures 1 and 2).

In ‘tricuspid orifice’, the leads were free in 42 (54%), fixed by fibrous tissue in 11 (14%), and penetrating the chordae tendineae of tricuspid valve in 25 (32%) cases (Table 5, Figures 3–5).

‘Defibrillator leads’ (n = 10) were examined. In two cases, a small thrombus was found on the defibrillation coil in the RV.
On each defibrillator coil, 1–2 bridges or tunnels were found, with a length ranging from 0.5 to 6.8 cm.

There were only three ventricular leads abandoned and unconnected because of their malfunction or deterioration.

‘Atrial leads’ (n = 21) were unipolar in 3 (14.3%) cases and bipolar in 18 (85.7%) cases. There were 11 (52%) leads with active and 10 (48%) with passive fixations, steroid-eluting electrodes were used in 9 (43%).

‘The tip of atrial electrode’ was found in the RA appendage in 18 (Figure 2) and on the atrial septum in 3 patients (Table 1).

‘Thrombi’ were formed on the leads in 10 (48%) patients, in brachiocephalic vein and/or in upper caval vein in 7, and in the RA in 8 cases (Table 2). Five patients had thrombi on the leads in the large veins as well as in the RA (Figure 2).

Among 18 bipolar electrodes, the ring was fixed by fibrous tissue in 4 (22%) and free in 14 (78%) cases (Table 3).

‘Connective tissue bridges and/or tunnels’ were present in 15 (71%) patients, in brachiocephalic vein and/or in upper caval vein in 13 (Figure 2), and in the RA in 15 cases, their total length ranging from 0.2 to 12 cm (Table 4). Thirteen leads exhibited simultaneously connective tissue bridges or tunnels in the large veins as well as in the RA.

### Table 3 Ring of bipolar electrodes

<table>
<thead>
<tr>
<th></th>
<th>Ventricular leads (n = 63) (single leads included)</th>
<th>Atrial leads (n = 18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free</td>
<td>20</td>
<td>14</td>
</tr>
<tr>
<td>Covered with</td>
<td>43</td>
<td>4</td>
</tr>
<tr>
<td>connective</td>
<td></td>
<td></td>
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<tr>
<td>tissue</td>
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</table>

### Table 4 Connective tissue bridges/tunnels

<table>
<thead>
<tr>
<th>Leads</th>
<th>Ventricular (n = 78) (single leads included)</th>
<th>Atrial (n = 21)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brachiocephalic vein and/or upper</td>
<td>44</td>
<td>13</td>
</tr>
<tr>
<td>caval vein</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Right atrium</td>
<td>17</td>
<td>15</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>68</td>
<td>–</td>
</tr>
</tbody>
</table>

### Table 5 Ventricular leads (single leads included) in tricuspidal orifice (n = 78)

<table>
<thead>
<tr>
<th>Insertion features</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free</td>
<td>42</td>
</tr>
<tr>
<td>Fixed by fibrous tissue</td>
<td>11</td>
</tr>
<tr>
<td>Penetrating chordae tendineae</td>
<td>25</td>
</tr>
</tbody>
</table>

Figure 1 Brachiocephalic vein dextra et sinistra (BCV dx., BCV sin.), upper caval vein (superior vena cava, SVC), right atrium (RA), and tricuspid valve (TV). Single lead for VDD pacing. (1) Connective tissue tunnel covering the lead in the right brachiocephalic vein, (2) thrombus on atrial dipole, (3) fibrosed in the middle, and (4) wall thrombus in the RA.

Figure 2 Upper caval vein (superior vena cava, SVC), right atrium (RA), right atrium auricle (RAA), tricuspid valve (TV), and right ventricle (RV). Three leads for biventricular pacing. RVL, right ventricle lead; RAL, right atrium lead; LVL, left ventricle lead. (1) Shared connective tissue tunnel on the leads in the upper caval vein, thrombus on the lead (2) in the upper caval vein and (3) in the RA. Transition between thrombi and connective tissue tunnel should be taken notice of.
The continuous transition between thrombi and connective tissue bridges/tunnels was observed in several cases (Figures 1 and 2).

‘Left ventricle leads’ (n = 3). The tip of left ventricle lead was found in posterior vein of the left ventricle in two patients and in the lateral vein branch in one case.

Thrombi were found on two leads, in the first case in brachioccephalic vein, in upper caval vein, in the RA, and in coronary sinus and in the second case in brachioccephalic vein, in upper caval vein, and in the posterior vein of left ventricle.

One to two tunnels were present in the large veins in all cases, in the RA in one, in the coronary sinus in one, and in posterior vein of left ventricle in two cases, once with partial obliteration of the vein.

‘Wall thrombi’ (n = 78) were found in the RA in five cases (Figure 1), in the RV in two, in the left atrium in one, in the left ventricle in two, and on the artificial mitral valve in one case (Table 6). Two of these patients were had anticoagulation treatment with warfarin, the rest had antiplatelet treatment. Two pulmonary thromboembolisms were found, these two patients were had antiplatelet therapy (see ‘the direct causes of death’, pt no. 2 and 3 below).

Looking through the medical notes (n = 90), we found that 43 patients had atrial fibrillation, 34 patients did not have it, and in 13 patients this information was lacking. Antiplatelet treatment was prescribed in 49 patients, anti-coagulation treatment with warfarin in 17 patients, 11 patients were on neither treatment, and in 13 patients this information was absent.

‘The direct causes of death’ (n = 90) were as follows: heart failure in 35 cases, pulmonary embolism in 9 (extra-cardiac origin in 5, cardiac origin in 4), acute myocardial infarction in 11, pneumonia in 17, tumour in 6, sepsis in 6 (with bacterial myocarditis in one), brain attack in 5 (haemorrhage in 3, non-haemorrhage in 2), and thrombosis of arteria mesenterica in 1 case.
As regards four fatal cases of pulmonary thromboemboli of possible cardiac origin, the autopsy findings were as follows. In patient (pt) no. 1, thrombus on the lead in the RA 10.5 × 0.4 cm and a recent thromboembolus in the pulmonary artery bifurcation. Mostly, older thromboemboli in the two main and more peripheral branches too. In pt no. 2, wall thrombus in the auricle of the RA and thromboemboli in the right main branch and in the left lower lobar branch. In pt no. 3, wall thrombi in the RA, RV, and left atrium. Thromboemboli in the two lower lobes with pulmonary infarctions formed. In pt no. 4, thrombus on the lead in the RA, 1 cm long, and thrombi in vena femoralis profunda. Multiple bilateral thromboemboli were found in the main branches of pulmonary arteries. All these patients except no. 2 suffered with atrial fibrillation. In patients 1, 2, and 3, antiplatelet therapy with acetylsalicylic acid (ASA) was used; in pt no. 4, warfarin therapy was discontinued because of multi-organ failure 1 week before death.

Another five pulmonary thromboembolisms of extracardiac origin were caused probably by thrombi from pelvic venous plexi, deep femoral veins, and in one case from upper caval vein.

In addition to the nine pulmonary embolisms given above, minor pulmonary thrombi were found in another eight deceased patients.

The link between pre-mortem anticoagulation therapy and the presence of thrombus on the lead is unclear. Anticoagulation medical therapy effectiveness or antiplatelet agents regular taking could not be verified in this study.

**Discussion**

In our population sample, the time elapsed between implantation and death was relatively short (4.0 ± 3.3 years). Survival of patients with implanted devices is probably longer. But the patients involved in this study were admitted to hospital due to a non-cardiac condition such as acute abdominal event requiring laparotomy, dissemination of malignant tumour, sepsis, etc.

Flaker monitored a population sample of 2010 patients with a median age of 74 years, with sick sinus syndrome and implanted PM. After a median follow-up of 33 months, there were 404 cases (20%) of death. There were 198 cases (49%) of non-cardiac cause, 143 (35%) of cardiac cause, and 63 (16%) of unknown cause.

In our study group, quite a high occurrence is evident of ‘thrombi forming on leads’ along large veins, the RA, and RV: in ventricular leads, this was the case in 33% and 48% in atrial leads. These findings support the possibility of pulmonary thromboembolism being the immediate cause of death in four patients. In addition, in eight deceased patients minor pulmonary thromboembolizations were found. According to pre-mortem documentation, they were probably asymptomatic or oligosymptomatic. Singer reports asymptomatic pulmonary embolism in 8% of a group of autopsied ICD patients.

Alizadeh in a transoesophageal echocardiography study confirmed thrombus formation on PM leads in 23% of patients with the AV sequential pacing mode and in 39% of patients in the VVI mode, in average 6 years after implantation. The left atrial appendage flow velocity was significantly higher in patients with the AV sequential pacing vs. patients in the VVI mode.

Moreover, in patients with implanted PM or ICD, it is in the case of atrial fibrillation necessary to resort to anticoagulation treatment using warfarin, or at least to anti-aggregation treatment with ASA, as recommended in currently valid guidelines to prevent the appearance of a thrombo-embolic disease.

In our population sample, ‘connective (fibrous) tissue bridges and/or tunnels’ are found in atrial leads in 71% and ventricular leads in 87%. Connective tissue bridges and tunnels originate from organized thrombi as described by Wilson.

Electrode rings were found to be fixed by fibrous tissue: 68% in ventricular bipolar leads and 22% in atrial leads. Depending on their location, all these connective tissue surrounding the leads may further increase the risk during lead extraction. Extraction itself presents the risk of pericardiac tamponade, upper caval vein syndrome, arteriovenous fistula, and other kinds of vein injury.

Ventricular leads in our population sample were fixed by fibrous tissue to ‘the tricuspid valve apparatus’ (14%) and sometimes they penetrated through the chordae tendineae of tricuspid valve (32%). Candinas found adhesion at the tricuspid valve apparatus in 7 of 11 deceased persons. Sakai reported on a group of 18 patients with RV stimulation without clinical signs of right heart insufficiency. He diagnosed evident tricuspid insufficiency via a positive finding in contrast and pulsed Doppler echocardiography in 28%, probable tricuspid insufficiency (only one method is positive) in 17%, and none in 55% of patients.

In the extraction of ventricular lead in patients with the lead fixed to or penetrating the tricuspid valve apparatus, there is the danger that the valve will be damaged, entailing subsequent regurgitation and potential manifestation of right heart insufficiency. During or after the lead extraction, an obstruction of the upper caval vein may occur, requiring a surgical or other intravenous intervention.

In view of the potential complications in extracting the leads, it is usual to indicate this intervention especially for infected or otherwise problematic leads. If in the case of ICD lead, the failure of sensing is only involved, it is of greater advantage to introduce an additional pacemaker lead and leave the ICD lead for defibrillation only. Moreover, from the frequent occurrence of thrombi on leads, it can be expected that in the course of lead extraction the thrombi may get released and minor or major pulmonary thromboembolisms may occur.

When ‘bacterial endocarditis’ is suspected in patients with implanted devices, transoesophageal echocardiography is usually helpful to confirm the diagnosis. In a retrospective study, Lo found an echogenic mass associated with RV lead in 15 of 125 PM patients. Endocarditis was suspected in nine cases, and the mass was felt to be vegetation. Six of these patients were treated with antibiotics alone (one patient died of pulmonary embolism), and in three patients, the lead extraction was performed. Sohail describes uncomplicated extractions of leads with vegetation exceeding 10 mm in 15 patients. Calton reports successful laser-assisted extraction of ICD leads with vegetation larger than 41 × 12 mm. Long-term treatment with antibiotics is recommended; in Sohail group the treatment took 28 days on average.
Several ‘extraction techniques’ are currently used: mechanical traction and counter-traction, and extraction using stylet and dilatation sheath under fluoroscopy (Cook Medical).

More sophisticated methods consist in extraction using rotational pistol dissection sheath (Evolution, Cook Medical), extraction using radiofrequency (RF) energy—electrosurgical dissection sheath (EDS, Perfecta, Cook Medical)—and extraction using laser-assisted extraction dilator (Spectranetics). In the case of extracting damaged or abandoned leads present in the body for several years, extraction can be difficult because of the presence of fibrous adhesions to blood vessel endothelium or endocardium, i.e. bridges and tunnels, and may require the application of some of the newer techniques. In a randomized study of 120 patients, Neuzil23 reports reduced intervention time and higher success rate when using RF current supported extraction, in comparison with standard counter-traction lead removal. Gula24 reports greater necessity of using laser-assisted extraction in the case of ICD leads and longer time after implantation.

Releasing and extracting the atrial lead can cause a higher risk of atrium laceration and cardiac tamponade because of the RA wall thinness. The damage of the veins (inclusive of the coronary sinus branches), RA, or RV together with the development of cardiac tamponade belongs to the main complications of transvenous extraction. For a group of 212 consecutive patients, Agarwal25 reports 26 (11.8%) complications, inclusive of 9 (4.2%) major complications (1 death, 4 haemothorax, 2 pneumothorax, 1 tamponade, and 1 stroke). Predictors of complication were: higher number of extracted leads and presence of ICD as opposed to PM leads. Embolization of vegetation is reported by Rizello.26

Intravenous extraction of leads can, with caution indication, be considered relatively safe and in most cases successful. Interventions must be performed in erudite cardiology centres in an operating theatre that is properly equipped for immediate cardio-thoracic surgical intervention if massive bleeding occurs.27

Limitations
Clinical data obtained via the retrospective study of documentation were not always complete or they were not available at all and therefore they could not be evaluated.

The pathologists have respected the family members’ wish not to perform autopsy. Therefore, it was not possible to include all the PM/ICD patients who died in hospital in the study.

Conclusions
(i) Relatively frequent thrombi on ventricular (V) leads in 33% and on atrial (A) leads in 48%. (ii) Very frequent rings of BP leads covered with connective tissue (V: 68%; A: 22%). (iii) Connective tissue bridges and tunnels in large number of leads (V: 87%; A: 71%). (iv) Ventricular leads frequently fixed to the apparatus of tricuspid valve (14%), and penetrating the chordae tendineae (32%). (v) Connective tissue bridges and tunnels and, in particular, leads fixed to the apparatus of tricuspid valve or penetrating the chordae tendineae need to be taken into consideration when extracting leads in vivo. (vi) We recommend anticoagulation/anti-aggregation treatment according to the guidelines every time when indicated. (vii) We do recommend caution when extracting leads.

Conflict of interest: none declared.

References


