Device-Related Endocarditis and Infected Leads Extraction: The Dark Side of The Moon

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1. Introduction

Cardiac rhythm management devices are being increasingly implanted worldwide not only for symptomatic bradycardia, but also for the management of arrhythmia and heart failure (Adabag et al. 2011; COMPANION Investigators 2004; Multicenter Automatic Defibrillator Implantation Trial Investigators 1996; Sudden Cardiac Death in Heart Failure Trial Investigators 2005). The benefit of cardiac resynchronization therapy (CRT) with permanent pacemakers (PPM) as first invasive step to treat the failing heart (Adabag et al. 2011; COMPANION Investigators 2004) and the survival advantage of internal cardiac defibrillator (ICD) in patients with end stage heart failure compared with medical therapy alone (Multicenter Automatic Defibrillator Implantation Trial Investigators 1996; Sudden Cardiac Death in Heart Failure Trial Investigators 2005), have supported a more liberal implantation policy of these devices. Moreover the widespread use of the trans-catheter aortic valve implantation (TAVI) for the percutaneous treatment of severe aortic stenosis, in high risk patients that would, otherwise, deemed inoperable by conventional surgery, has carried along a high post procedural implantation rate of PPMs in this elderly subgroup of patients (Bates et al. 2011; D’Ancona et al. 2011). It seems logical to expect an increased rate of device related infections to follow the boom of PPMs and ICDs implantation in the last two decades (Voigt et al. 2006). Of the 400,000 -500,000 permanent pacemaker leads implanted worldwide each year, around 10% may eventually fail or become infected, becoming potential candidates for removal (Byrd et al. 1999). Device infections can be local, involving the insertion site of PPM or ICD box, or systemic because of the spreading along the PPM leads and, in worst case scenario, lead to septic shock and device-related endocarditis. Device-related endocarditis has been reported in 23% of infected PPMs, the remainder being pocket infections (Sohail et al. 2007). The infection can spread over the cardiac structures and typically involves the tricuspid valve. Right-sided endocarditis accounts for only 5–10 % of cases of infective
endocarditis (Chan et al. 1989) and occurs predominantly in selected patient’s subgroup, such as: intravenous drug users, patients with pacemakers, ICD or central venous lines and with congenital heart diseases (Robbins et al. 1986). The tricuspid valve can show massive vegetations with or without valve regurgitation (figure 1).

LA: left atrium; LV: left ventricle; RA: right atrium; RV: right ventricle.

Figure 1. Transesophageal echocardiography –four chamber view - shows multiple vegetations on the tricuspid valve (long arrow) and pacing leads (short arrow).

This chapter will focus on the presentation, diagnosis and management of device-related endocarditis and explore different extraction techniques - both percutaneous and surgical.

2. Device-related endocarditis

Mortality rates for infected PPM devices range from 31% to 66% when the device is not explanted (Cacoub et al. 1998). Better outcomes, with mortality rates of 18% or less, have been reported when a combined management with device removal and antimicrobial therapy is adopted (Klug et al. 1997). Pacemaker related sepsis or endocarditis is a class I

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indication for lead extraction, according to the recently updated device infection guidelines (Baddour et al. 2010). Standard treatment includes removal of infected PPM device combined with six weeks of antimicrobial therapy. Management of device-related endocarditis is challenging and requires collaborative efforts between cardiologists, surgeons, and infective disease specialists.

2.1. Clinical presentation

The presentation can be acute, with onset of symptoms in the first 6 weeks after the last procedure on the implant site, or chronic, with >6 weeks from the last procedure on the implant site to the onset of symptoms. In the acute form, the short time elapsed between PM implantation and the occurrence of infection facilitates the diagnosis. The vast majority of patients will have systemic symptoms from septic shock to fever, pneumonia, pulmonary embolism, associated with local signs of infection at the PM site. In the chronic form, the delay between the onset of symptoms and the implant time makes it difficult to diagnose PM-lead infection. Often delays in diagnosis of chronic device-related endocarditis are related to the fact that PM-lead infection was not considered in the differential diagnosis or because, possible clues were ignored: for example, blood cultures positive for S. epidermidis were erroneously considered contamination of the specimens (Klug et al. 1997). The most common chronic presentation would be fever or chills with asthenia, and wasting, sometimes associated with symptoms and signs of low tract respiratory infection (cough, expectoration, bronchitis, pneumonia, pulmonary abscess, pleural effusion). History of pulmonary embolism, arthralgia, spondylitis or signs of local infection at the PM site could be present. The diagnosis of systemic infection related to PM-lead infection must be systematically considered in the presence of chronic fever, recurrent bronchitis, or pulmonary infection or in case of recurrent or persistent evidence of infection at the implant site (Klug et al. 1997). More over endocarditis of the right heart should be specifically excluded, regardless the presence or absence of tricuspid regurgitation (Love et al. 2000).

2.2. Diagnosis

Patients will have elevated markers of inflammation. Erythrocyte sedimentation rate (ESR) and CRP will be elevated, often along with high white cell count (WCC) due to an increase in polymorphonuclear cells. Positive blood cultures will confirm the diagnosis. Blood cultures should be taken on 3 consecutive days and integrated with cultures at the site of battery pocket if appropriate (wounds, local infection, or PM exteriorization). The Duke criteria are useful to define systemic infection related to PM-lead infection (tab.1), but as suggested by Klug et al (1997), the importance of some clinical criteria, should, probably, be highlighted, such as, local symptoms of infection at the PM site and pulmonary infections, to facilitate the diagnosis (tab.2).

Chest roentgenogram will often show signs of pulmonary infection or pleural effusion. Echocardiography is essential to confirm the diagnosis and to clarify whether treatment will require removal of the infected pacing system. However, a single negative transthoracic
Echochardiogram (TTE) is not enough to exclude the diagnosis of lead-related endocarditis. Although TTE has about 80% sensitivity in the detection of vegetations in the right heart (Love et al. 2000), often patients present with PM-lead–related endocarditis with intact tricuspid leaflets (Klug et al. 1997). This is the reason why a transoesophageal echocardiogram (TOE) should always be performed in the diagnostic algorithm when device-related endocarditis is suspected. Ventilation perfusion pulmonary scintigraphy can corroborate the diagnosis showing multiple septic lung embolisms. It is wise to perform also a wider range of investigations to exclude other sources of infection. These will normally include a dental pantomogram, sinus radiographs and abdominal ultrasound.

<table>
<thead>
<tr>
<th>Definite infective endocarditis</th>
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<tr>
<td>Pathological criteria</td>
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<td>Microorganisms: demonstrated by culture or histology in vegetation, in a vegetation that has embolized, or in intracardiac abscess, or</td>
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<tr>
<td>Microorganisms demonstrated by culture of the lead</td>
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<td>Clinical criteria (as listed in Table 2)</td>
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<td>Two major criteria, or</td>
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<td>One major and three minor criteria, or</td>
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<td>Five minor criteria</td>
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<th>Possible infective endocarditis</th>
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<td>Findings consistent with infective endocarditis that fall short of &quot;definite&quot; but not &quot;rejected&quot;</td>
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<th>Rejected</th>
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<td>Firm alternate diagnosis explaining evidence of infective endocarditis, or</td>
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<td>Resolution of infective endocarditis syndrome, with antibiotic therapy for ≤4 days, or</td>
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<tr>
<td>No pathological evidence of infective endocarditis at surgery or autopsy, with antibiotic therapy for ≤4 days</td>
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**Table 1.** Modified Duke Criteria for Diagnosis of Infective Endocarditis on PM Leads

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2From Klug et al. with permission
Major criteria

Positive blood culture for infective endocarditis

Typical microorganisms for infective endocarditis from two separate blood cultures

*Streptococcus viridans, Streptococcus bovis, HACEK group*, or

Community-acquired *Staphylococcus aureus* or enterococci, in the absence of a primary focus, or

Persistently positive blood culture, defined as microorganism consistent with infective endocarditis from Blood cultures drawn >12 hours apart, or

All of three or a majority of four or more separate blood cultures, with first and last drawn at least 1 hour apart

Evidence of endocardial involvement:

Positive echocardiogram for infective endocarditis:

Oscillating intracardiac mass on PM leads or on the endocardial structure in contact with PM leads

Abscess in contact with PM leads

Minor criteria

Fever >38°C

Vascular phenomena: arterial embolism, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, Janeway lesions

Immunologic phenomena: glomerulonephritis, Osler nodes, Roth spots

Echocardiogram: consistent with infective endocarditis but not meeting major criterion as noted previously (sleevelike appearance)

Microbiological evidence: positive blood culture but not meeting major criterion as noted previously.

| Table 2. | Definition of Terms Used in the Proposed Modified Diagnostic Criteria |

2.3. Pathophysiology

It is commonly accepted that the most common portal of entry to develop device-related endocarditis is the subcutaneous site of insertion of the pacing system. Extension along the lead into the vascular system is the usual explanation for the localization of the infection to the lead. Bacterial colonization of the lead during the course of bacteremia whose origin is not related to the pacing system might be possible but has been less well documented. Staphylococci are responsible for the vast majority of these infections, especially *S. epidermidis* in the chronic group and *S. aureus* in the acute group. A fungal infection is rare and more subtle to indentify. Fungal endocarditis is associated with high mortality and usually presents with scant growth of the microorganism in blood cultures (Figure 2). A

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*From Klug et al. with permission*
high index of suspicion for fungal endocarditis should be maintained in individuals with implantable pacemakers and fever of an uncertain source, especially in the context of negative blood cultures (Leong 2006). However, there is a 20-30% of device-related endocarditis with negative BC (Klug et al. 1997).

**Figure 2.** A: Transthoracic echocardiogram of the right atrium (RA), tricuspid valve (TV) and right ventricle (RV) demonstrating a pacemaker lead (P) and no valvular vegetations. B: Second transthoracic echocardiogram of the right heart, seven weeks after the initial echocardiogram, demonstrating a right ventricular pacemaker lead thrombus (Th)

### 2.4. Management

The removal of the entire pacing system should be performed immediately rather than attempting prolonged antibiotic therapy alone. As in the study by Camus et al, the high rate of uncontrolled infection or relapse among patients with septicemia in relation to PM-material infection confirms the need for (Camus et al. 1993). Moreover immediate removal of the entire pacing system should be performed in all cases both for systemic infection related to PM-lead contamination and for infection of the PM pocket or the subcutaneous part of the lead (Panidis et al. 1984). Cultures of the leads and of the PM should be done after the extraction. Complete PPM or ICD removal should be performed when patients undergo valve replacement or repair for infective endocarditis, because the pacing system could serve as a nidus for relapsing infection and subsequent seeding of the surgically treated heart valve. Hardware removal is not required for superficial or incisional infection at the pocket site if there is no involvement of the device, 7-10 days of antibiotic therapy with an oral agent with activity against staphylococci is reasonable (Baddour 2010).

*From Leong et al. with permission.*
3. Technique of extraction: Surgical or percutaneous?

After implantation, transvenous device leads usually undergo fibrotic encapsulation by activation of different cellular and humoral mechanisms (Esposito et al. 2002). The ensuing fibrotic lead adhesions tend to increase over time. Young patients, however, usually develop fibrotic adhesions earlier than elderly. On the contrary, systemic lead infection seems to counteract or dissolve fibrotic adherences. Current literature suggests that, the best outcome is achieved with percutaneous removal of infected devices by applying external traction on the leads (Sohail et al. 2007; Ruttmann et al. 2006). However, while simple traction is often successful in newly placed leads, it can be problematic with chronic leads and cause catastrophic complications, ranging from septic embolic phenomena to tricuspid valve injury, subclavian vein laceration, hemothorax, pocket hematoma, massive hemorrhage, and lead fracture requiring urgent surgical intervention (Sohail et al. 2007; Ruttmann et al. 2006; Panidis et al. 1984). Damage to the left sided cardiac structures is rare but may be a complication of an infected lead extraction, manifesting as iatrogenic ventricular septum disruption with consequent aortic valve leaflet prolapse and massive acute aortic regurgitation (fig.3)(Rossi et al. 2011).

Chronically implanted leads are fixed to the myocardium by fibrous tissue. Fibrous scar tissue may also encase the lead along its course. Furthermore, fragility of the lead and its tendency to break when extraction force is applied to overcome resistance imparted by the scar tissue add to the challenge of lead extraction. Thus, selecting the appropriate extraction procedure for chronically implanted leads is an important issue.

3.1. Percutaneous extraction

The removal of the entire pacing system should be performed in one session. Newpercutaneous PM and ICD lead extraction techniques have been developed to overcome the problem of a difficult extraction with the aim to reduce damage to the cardiac structures produced by the simple counter traction. Telescoping mechanical sheaths and locking stylets were introduced during the late 1980s and early 1990s. Special tools for femoral lead extraction soon followed. They can be used though a superior approach (jugular or subclavian vein) using locking stylet; or via a femoral vein approach using double lasso catheters (Needle’s eye snare) (Byrd et al. 1999; Bracke et al. 2001; Fearnott et al. 1990). In the superior vena cava approach, a locking stylet is introduced into the lead and locked close to the distal electrode in order to apply traction directly to the tip. If gentle traction is not successful, telescoping sheaths can be advanced over the lead to disrupt fibrous binding of the lead to veins or myocardium. When necessary, the tip of the lead is freed by countertraction, the sheath being positioned against the myocardium to prevent inversion during traction on the lead. In the transfemoral approach, the pacing lead is grabbed with a deflecting guide wire or retriever through a long sheath inserted from the femoral vein. The proximal end of the lead is pulled down from the subclavian vein. Then the outer sheath is advanced over the lead to disrupt the scar tissue, as with the superior approach. When the myocardium is reached countertraction is applied.
AV: aortic valve; MV: mitral valve; PV: pulmonary valve; TV: tricuspid valve.

**Figure 3.** Four-valve view of the fibrous skeleton of the heart showing disruption of the tricuspid valve (long black arrow), ventricular septal defect (white arrow), and prolapse of the noncoronary cusp of the aortic valve (short black arrow).

### 3.1.1. Laser extraction

Progress has also been made in developing other systems for lead extraction powered with laser energy. The first laser-assisted lead extraction performed in 1994 was a major breakthrough. The laser extraction sheath offers a method for removal by "cutting" through scar tissue, without excessive use of force (such as with purely mechanical systems). It appears to be an efficient tool for removal of chronic implanted infected leads but its use is

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Intraoperative cultures of the aortic valve and ventricular septal defect edges did not show any significant growth, supporting the hypothesis that the prolapse of the noncoronary cusp was due to lack of support on the valve structure.
associated with a high number of bleeding complications often requiring surgical revision (see section 3.3).

3.2. Surgical extraction

Surgical removal has a higher complication rate and worse outcome compared with percutaneous techniques (Klug et al. 1997). Although, in concept, the surgical approach is the cleanest way to extract an infected lead together with its vegetation without risks of pulmonary or systemic septic embolism, it is generally accepted both by surgeon and cardiologist to prefer the percutaneous extraction as first attempt. However we should not forget that the surgical population is highly selected, i.e. made of cases not suitable for percutaneous extraction or with heart damage after percutaneous attempt or with severe tricuspid valve involvement. Moreover, the presence of intracardiac vegetations alone, identifies a subset of patients at increased risk for complications and early mortality from systemic infection regardless the technique of extraction (percutaneous or surgical) and appropriate antimicrobial therapy (Grammes et al. 2010). From a review of the current literature, it appears that the indication for surgical removal is mainly limited as rescue intervention to fix complicated or failed percutaneous extraction. Surgical removal generally requires median sternotomy or thoracotomy and sometimes cardiopulmonary bypass (CBP). Nevertheless there are still patients that will benefit from a surgical removal as a first attempt rather than later, especially those with large vegetations that might obstruct the main pulmonary artery or those who need the implantation of an epicardial pacing system.

A primary surgical approach to lead removal in patients with PPM/ICD infection is recommended by the current guidelines for implantable electronic device infections and management in patients who have significant retained hardware after attempts at percutaneous removal or in patients with lead vegetations > 2 cm in diameter, because of concerns about the risk of pulmonary embolism with percutaneous lead extraction (Baddour et al. 2010). In fact, it is useful to reconsider the indication for pacing after successful extraction of the infected pacing system. Discontinuation of pacemaker treatment after lead extraction has been reported in 13–52% of patients (Bracke et al. 2001). However when permanent pacing is a must, an epicardial system is the recommended choice especially after valve surgery with initial hardware removal (Baddour et al. 2010). With the surgical approach, the epicardial permanent system can be easily placed at the same time of the extraction and offers the advantage of eliminating the contact between leads and systemic circulation taking the chances of infection of the new system to the ground.

3.3. Evidence-based discussion

Wilkoff et al, in a randomized control trial of 465 chronically implanted leads, achieved 94% complete removal with a laser sheath against 64% with conventional sheaths, but with a higher rate of potentially life-threatening complications (Wilkoff et al. 1999). In a multicenter study over 2338 patients, Byrd et al, reported an increased risk of failed or partial extraction with increasing implant duration, doubling every three years (Byrd et al. 1999). Kennergren
et al, in a retrospective analysis of their activity on 647 lead extractions, surprisingly showed that the implantation time was not associated with extraction failure neither there was an association between implantation time and the incidence of serious complications. Actually they showed that leads can often be extracted by a superior transvenous approach with simple traction; Laser-assisted lead extraction appeared to be a useful technique to extract leads that could not be removed by manual traction but at the cost of a higher rate of bleeding complications requiring open-chest surgical revision (Kennergren et al. 2009). Alt et al, achieved total removal of 81% of 150 leads, without major complications with the use of only locking stylets (Alt et al. 1996). Tokunaga et al, performed a surgical removal without CBP after a failed extraction using the Excimer Laser Sheath Extraction System (Tokunaga et al. 2011). The authors highlight the potential risk of perforation and lethal bleeding complications using this tool and suggest a close backup by a cardiovascular surgeon. Neuzi et al, in a randomized control trial (RCT) compared the safety and efficacy of transvenous pacemaker and implantable cardioverter-defibrillator (ICD) lead extraction, with an electrosurgical dissection sheath (EDS) system using radiofrequency (RF) current or standard countertraction lead removal in 120 consecutive patients (Neuzi et al. 2007). Although the EDS extraction system appeared quicker and more effective in complete removal of leads, they could not demonstrate a significant superiority versus the standard counter-traction method. Buongiorni et al, in a retrospective analysis of 1330 leads extraction, concluded that transvenous lead extraction is an effective and safe procedure. They showed how the use of the jugular approach, in the presence of free-floating or difficult exposed leads, increases both safety and success rate (Buongiorni et al. 2005). Kratz et al, in a retrospective analysis of 365 patients who underwent PPM or ICD lead removal, showed that performing a lead extraction in a protected environment, such as an operating room, allowed rapid and effective treatment of potential procedure-related complications. Actually, the use of several extraction tools, arterial line monitoring, transesophageal echocardiography, general anesthesia, and an experienced team, yielded complete extraction in more than 90% of patients, with a low complication rate and no procedurally related deaths (Kratz et al. 2010). Grammes et al, reported their experience using percutaneous leads extraction by simple traction of 1,838 infected leads with echocardiographic evidence of intracardiac vegetations. Post-operative 30-day mortality was 10%; no deaths were related directly to the extraction procedure (Grammes et al. 2010). The common message that comes from the literature is that extraction of infected PM-leads is not just a “pull and go” procedure and should be performed by expert physicians, in tertiary centres, with a cardiac surgery back up to best manage their complications.

3.3.1. Septic embolism

There is also a concern in pacemaker related endocarditis over embolisation of vegetations adhering to the lead when endovascular extraction is attempted. Klug et al, in their series of 52 patients with device-related endocarditis, suggested to chose the technique of removal (surgical versus percutaneous) on the size of the vegetations: percutaneous when vegetation size was ≤10 mm and surgical if > 10mm at transesophageal echocardiogram (Klug et al.
1997). This policy was based on previous observations by Mugge et al and by Robbins et al, who found that embolism was more frequent with vegetation size was >10 mm in endocarditis related to valve infection (Mugge et al. 1989; Robbins et al. 1986). More recently Ruttmann et al, showed that transvenous lead removal is a safe and effective even in patients with large vegetations. Embolism to the lung happens but tends to proceed mainly without complications. However there are still cases where surgical approach is preferred, such as, in presence of large vegetations that might occlude the main pulmonary artery(Ruttmann et al. 2006) or with vegetations > 2 cm in diameter (Baddour et al. 2010).

4. Conclusion

The diagnosis of endocarditis related to PM-lead infection should be systematically considered in patients with fever, history of local complications, or pulmonary pathology after PM insertion. There are two different clinical presentations: the acute form, that presents early with sepsis, often in conjunction with local signs of infection, and a chronic form, beginning several months later. The presentation may be atypical and the symptoms may occur late after the last intervention at the PM site. CRP, ESR, scintigraphy or chest CT angiogram may be of diagnostic value. TTE and TOE must be performed in search of vegetations. Immediate removal of the entire pacing system is paramount, in addition to prolonged antimicrobial therapy. We believe that multidisciplinary approach is the key to manage device-related endocarditis and good professional relationships are essential between cardiologists, surgeons, and infective disease specialists to make the appropriate decisions to best treat these complex patients. Our recommendation, in the patients’ best interest, is not to embark on extracting infected leads without doing a serious ongoing individual risk–benefit analysis. Finally a word of wisdom to the future generations: even if we are moving faster towards new innovative ways to pace the heart, we will always be dealing with their complications, therefore, is worth to create a network of professionals to address them in the best possible way.

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5. References


