Infections of Permanent Transvenous Pacemakers - Etiology, Medical Treatment and Optimal Surgical Techniques

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1. Introduction

Intracardiac electrostimulation devices have achieved remarkable progresses in the treatment of patients with heart disorders, with an increasing number of implants in recent years. One of the most relevant complications are device-related infections that are increasing significantly; what is more, the rate of increase in device-related infections per year has been disproportionally higher than the rate of newly implanted devices. Such infections are caused mainly by *staphylococci* and are associated with the formation of biofilms on the device. Diagnosis requires both a well-defined etiology, with the obtainment of appropriate samples, and a well-established location (catheter lead and/or endocardium) in order to carry out the most appropriate therapeutic strategy, which usually requires both a complete device withdrawal and a correct antibiotic treatment. But there is still no consensus about the most appropriate antibiotic pattern, particularly in relation to its duration, and the best time to reintroduce a new device.

2. Epidemiology and incidence

Pacemaker infections are infrequent but there has been an increase over last years, with an older population associated to an increment in morbidity and mortality rates and in financial cost. In a retrospective analysis of the National Hospital Discharge Survey database (Voigt et al., 2010) from 1996 through 2006, a 57% increment in cardiac device-related infections was registered. A population-based study in Olmsted County Minnesota calculated an incidence of permanent pacemaker and implantable cardioverter defibrillator infection of 1.9 per 1000 device-years (95% confidence interval (CI) 1.1-3.1). The incidence of pocket infection was 1.37 per 1000 device-years (95% CI 0.62 - 3.05) and pocket infection with bacteremia or device-related endocarditis occurred in 1.14 per 1000 devices-year (95% CI 0.47 - 2.74) (Uslam et al, 2007). Another prospective multicenter study in France observed an incidence of pacemaker related infective endocarditis of 0.39 cases per 1000 devices-year (Duval et al, 2004).

Nowadays, the estimated average cost of medical and surgical treatment of this kind of infections is $25,000 (Daouriche, 2004). Treatment of pacemaker-related infections typically requires a two-stage surgical approach, with complete removal of the implanted system

followed by insertion of a new one; so major costs are derived from hospitalization, diagnostic procedures, intravenous antibiotics and commonly two surgical procedures with a new device.

3. Pathogenesis

Staphylococci are the mean etiological agents (60-80%) and include *Staphylococcus aureus* and coagulase-negative *staphylococci* with meticillin-resistant strains in some institutions. Gram negative bacilli represent 5-10% of cases and another 10% are negatives cultures (Table 1). Rarely fungi or mycobacteria are etiological agents.

Early infections are acquired by contamination of cutaneous microbiota when pacemaker is implanted or generator is revised (Da Costa et al., 1998). When microorganisms adhere to device's surface, biofilms are formed (Daouriche, 2001). The biofilm is an extraordinarily complex structure formed by a community of microorganisms, involved in a molecular matrix. Their training begins with the adhesion of the microorganisms to the surface of the biomaterial through nonspecific physicochemical forces and bacterial structures called adhesins, which are different depending on the microbial agent involved. The bacterial inoculum needed to cause infection is several thousand times lower in the presence of prosthetic material. Once the organism is attached to the surface it produces a matrix, which in the case of *Staphylococcus epidermidis* is composed of a gelatinous substance called slime, which consists mostly of polysaccharides (polysaccharide intercellular adhesion). Subsequently, depending on the interaction between the microorganisms and the host defense systems, there will be or not a progression in the formation of a mature biofilm. Periodically shedding fragments of the biofilm with the more superficially located organisms liberated in the cardiovascular system will result in symptoms (Vila et al., 2008).

The microorganisms located within biofilms are protected from host defense mechanisms and are resistant to the action of antimicrobials. This resistance is determined by different mechanisms such as reduced diffusion of drugs, altered growth rate of microorganisms, resistance mechanisms expressed in planktonic bacteria, genetic elements transfer and biomaterial own action. In these circumstances it is common that the antimicrobial minimum inhibitory concentration for the organisms inside the biofilm is thousands times higher than for the microorganisms located on the surface (Rodríguez-Martínez & Pascual, 2008).

If pocket infections persist they may progress by catheter leads to a systemic infection with bloodstream and/or endocardium affectation. In other cases, this systemic involvement is caused by a different focus bacteremia that colonizes the leads, as can occur in health-care related procedures like vascular catheter related bacteremia (Uslan et al., 2009; Chamis et al., 2001).

There are many risk factors for pacemaker devices infection. One retrospective study observed that long-term corticoid use (OR: 13.9; 95%CI 1.44-20.29) and the presence of more than two pacing leads (OR: 5.41; 95%CI: 1.44-20.29) were independent risk factors for pacemakers infections; in contrast, antimicrobial prophylaxis prior to implantation was a protective one (OR: 0.087; 95%CI: 0.016-0.48) (Sohail et al., 2006). Another prospective multicenter study observed that the occurrence of infection was positively correlated with fever within 24 hours before the implantation procedure (OR: 5.83; 95%CI, 2.00-16.98), use of temporary pacing before the implantation procedure (OR: 2.46; 95%CI: 1.09-5.13) and early reinterventions (OR: 15.04; 95%CI: 6.7-33.73); however, implantation of a new system (OR: 0.46; 95%CI 0.24-0.87) and antibiotic prophylaxis (OR: 0.4; 95%CI: 0.18-0.86) were negatively correlated with risk of infection (Klug et al., 2006).

Microorganism	Sohail et al N=189	Alarcón et al N=243	Catanchin et al N=39	Chua et al N=123
Staphylococcus aureus	29%	20%	60%	24%
Coagulase-negative *staphylococci*	42%	42%	32%	68%
Other Gram positive cocci	4%	3%	4%	NR
Gram negative bacilli	9%	9%	4%	17%
Fungal	2%	1%	-	NR
Polymicrobial	7%	9%	-	13%
Culture negative	7%	13%	36%	NR

Table 1. Etiology of intracardiac electronic devices infections in clinical series.

4. Clinical manifestations

There are local and systemic infections. Local infections affect only generator's pocket and are expressed by local inflammatory symptoms like pain, tenderness, erythema and purulent drainage. In another cases exteriorization of the device material could be the only manifestation. Some patients with localized pocket infection have bacteremia without lead affectation. One study observed that local manifestations at the site of pacemaker implantation are associated with infection of the intravascular part of the leads in 79% of patients, and no clinical observations or laboratory investigations permitted identification of these patients with negative lead cultures (Klug et al., 2004).

Systemic infections affect the intravascular catheter lead and/or endocardium; they are manifested by fever, pulmonary embolism, severe sepsis and metastatic infections (Table 2). In many cases, local and systemic symptoms coexist, but there can also exist a systemic infection without any local symptomatology; which is more frequent in late infections. Sometimes, the diagnosis of recurrent pneumonia is made due to recurrent embolisms from catheter's tip or tricuspid vegetations. Since this is a bacteriemic infection, metastatic infections are frequent such as septic arthritis, osteomyelitis or endophthalmitis. In a recent international cohort of 2781 episodes of infective endocarditis, 10% of them were device-related endocarditis (Murdoch et al., 2009). When endocarditis is present, it is right-sided with tricuspid valve or

Clinical variable	Range %
Fever	80-100
Murmur on examination	20-43
Local findings	45
Pulmonary embolism	29-33
Anemia	66
Leukocytosis	59
High erythrocyte sedimentation rate	59
Positive blood cultures	77-95
Positive swab cultures from generator-pocket	61
Lead vegetation	85-92
Valve vegetation	90-100

Table 2. Clinical features in intracardiac device-related endocarditis in different series (N=180) (Sohail et al., 2008; Massoure et al., 2006; Duval et al., 2004; Del Río et al., 2003)

mural endocardium affected. Only in exceptional cases mitral and/or aortic valves are affected. In left-sided endocarditis systemic embolism, stroke, congestive heart-failure and metastatic infections are more frequent and have a more severe prognosis.

Leukocytosis with neutrophilia, elevation of the C-reactive protein or another acute phase reactant are the main altered laboratory parameters.

5. Diagnosis

The diagnostic must be microbiological and anatomical. The main procedures are blood cultures and culture of exudates of the pocket. Any purulent drainage should be properly processed for staining and suitable cultures. Bacteremia is present in many patients with systemic infections and sometimes in local infections too, so blood cultures are crucial for diagnostic, perhaps previous to any antimicrobial treatment. Bacteremia can be detected even in patients without fever. The sonication of extracted device can be a useful method that allows the recovering of microorganisms that cannot be isolated by conventional methods. Despite this, the results obtained with these methods must be interpreted with caution in the appropriate clinical context, because they can have an uncertain clinical significance or can be the result of a contamination (Mason et al., 2011; Rohacek et al., 2010).

Transesophageal echocardiography is a good diagnostic procedure to detect leads involvement because it has a higher sensibility to detect vegetations than transthoracic echocardiography. These vegetations are usually located on the distal extreme of the lead, and/or the endocardium, generally at the level of the tricuspid valve, but in some patients they may also exist in the endocardial wall and the mitral or aortic valves (Victor et al., 1999). The vegetations may be single or multiple and often easily distinguishable from the strands that are filamentous structures attached to the electrodes without clinical relevance (Kerut et al., 2007). In other occasions the affectation of the lead adopts an aspect of thickening or sleeve (Klug et al., 2007). In patients with cardiac prosthetic valves, the involvement of the same should be ruled out by transesophageal echocardiography, especially when the causative agent is *S aureus* (Habib et al., 2010).

6. Medical treatment

Antimicrobial agents are one of the main elements of treatment, along with early and complete withdrawal of the device. Antibiotic regimen depends on the location of the infection and its severity. In local infections may be sufficient to use oral antibiotics for several days, while severe and/or systemic infections, as those with bacteremia or endocarditis, require intravenous antibiotics for several weeks.

In critically ill patients empirical use of these drugs is justified, especially in systemic infections, in patients with significant comorbidities and when a high risk of complication development exists. In these cases antibiotics associations directed against the main organisms should be used. Since *Staphylococcus aureus* and coagulase-negative *Staphylococci* are the main microorganisms involved and, depending on each institution, the number of meticillin-resistant strains may be high, it is recommended the use of glycopeptides such as vancomycin or teicoplanin associated with a drug active against gram-negative bacilli, which depends on the epidemiology of each institution and include cefazidime, cefepime, piperacillin + tazobactam or carbapenems (Mermel et al., 2009).

Vancomycin should be used according to current recommendations, which means that there should be given an initial loading dose adjusted to patient's weight in seriously ill patients (25-30 mg/Kg) and continue with the following doses adjusted to renal function and serum trough levels (15-20 µg/ml) (Ryback et al., 2009).

The association of aminoglycosides is not well established, since we only have evidence of a decrease in bacteremia duration in some cases, but it is also associated with more adverse effects, especially nephrotoxicity (Cosgrove et al., 2009).

Once culture results are obtained, treatment should be adjusted depending on the isolated organisms and their antimicrobial susceptibility. Thus, in the case of methicillin-sensitive *Staphylococcus aureus* (MSSA) the drug of choice should be cloxacillin or nafcillin in appropriate doses. In methicillin-resistant *Staphylococcus aureus* (MRSA), drug selection depends on the minimum inhibitory concentration (MIC) against vancomycin: strains with MIC ≤ 1 µg/ml should continue with vancomycin at appropriate doses, whereas strains with MIC ≥ 1 µg/ml require an alternative to vancomycin (Soriano et al., 2008). In these cases, the most employed drugs are daptomycin and linezolid. Daptomycin is a lipopeptide antibiotic rapidly bactericidal on most of gram-positive cocci, including drug-resistant strains; a recent clinical trial demonstrated it is not inferior to antistaphylococal penicillin or vancomycin in patients with bacteremia and right-sided endocarditis by MSSA and MRSA, using a dose of 6 mg/Kg/day (Fowler et al., 2006). However, some therapeutic failures on this drug at low doses advise for the use of greater doses between 8 and 10 mg/Kg/day. Linezolid an oxazolidinone antibiotics exhibit bacteriostatic activity against many Gram-positive cocci and provide the advantage of having a high bioavailability which permits an oral administration and do not require dose adjustment for renal insufficiency; although prolonged treatment may have more side effects such as myelosuppression or neuropathy. For patients allergic to beta-lactam antibiotics glycopeptides are the drugs of choice. There are other alternatives as dalbavancin, telavancin, ceftobiprole or trimethoprim-sufametoxazole but the experience is limited.

Infections caused by coagulase-negative staphylococci should follow a similar attitude. In methicillin-sensitive strains, oxacillin or nafcillin are the drugs of choice; whereas in strains resistant to methicillin, use of vancomycin is preferred, although it is still not clear which role do new drugs play in these cases. New drugs such as daptomycin or linezolid are of great interest due to the activity of some of these drugs in bacterial biofilms, and maybe the need for device removal could be avoided in the future, at least in selected cases (Parra et al., 2010).

The use of rifampicin is controversial since it has not been proven to increase its clinical efficacy and, in turn, it is associated with an increased number of adverse reactions and interactions with other drugs such as oral anticoagulants, used regularly in this population. On the other hand, there is a theoretical advantage in its use when a more intense action on microorganisms located inside the biofilm is required. However, device removal is necessary in most cases to eradicate the infection and after its extraction, rifampicin benefits do not appear to outweigh risks, so its use is discouraged (Perlroth et al., 2008).

Directed treatment for gram negative microorganisms depends on the characteristics of each center. In general quinolones, cotrimoxazole, amoxicilin + clavulanate or cephalosporins, could be useful. However there is a gradual increase in infections caused by multidrug resistant pathogens as gram-negative bacilli-producing β-lactamases by different mechanisms, so it may be necessary to employ more complex treatments (Table 3). Once again, the complete removal of the device facilitates eradication (Rodríguez-Baño et al., 2010).

There is no consensus on the optimal duration of medical treatment. It is possible that in infections involving only the generator pocket, several days treatment duration may be sufficient. In systemic infections the antimicrobial regimen depends on the type of organism, site of infection (pacemaker lead versus endocardium) and the effective withdrawal of the infected device. In the published series, the average treatment duration was of 4-6 weeks, although in the series of Dumont et al., they describe 8 patients treated during 8.2 ± 5.4 days without recurrence (Dumont et al., 2003). Commonly, 2 weeks of parenteral therapy after device removal may be enough if there are no septic complications, whereas when there is device-related endocarditis or a complicated *Staphylococcus aureus* bacteremia, it is necessary to prolong this treatment for 4 weeks. In patients who can not remove the system completely due to their comorbidity and/or technical difficulties, they may require prolonged treatment with antibiotics for several months or even a lifetime (chronic suppressive therapy); in these cases the objective would be to keep localized the infection in the system, avoiding a possible dissemination. This should be exceptional and restricted to selected patients, but is expected to increase in coming years (Baddour, 2001; Baddour et al., 2010).

Microorganism	Antibiotic
Staphylococcus aureus and Coagulase negative Staphylococci Meticillin sensible	Cloxacillin or nafcillin
Staphylococcus aureus meticillin resistant MIC vancomycin > 1 μg/ml MIC vancomycin < 1 μg/ml	Daptomycin. Linezolid Vancomycin
Coagulase negative *Staphylococii* meticilin resistant	Vancomycin
Enterococcus faecalis	Penicillin, Ampicillin
Enterobacter sp, *Serratia* sp, *Citrobacter freundii*, *Morganella* sp	Cefepime, carbapenems Fluorquinolones
Pseudomonas aeruginosa	Cefepime, Ceftazidime, aztreonam Piperacillin+tazobactam, carbapenems (except ertapenem) Fluorquinolones

Table 3. Directed antimicrobial therapy for systemic infections. Abbreviations: MSSA, meticillin-sensible Staphylococcus aureus; MRSA, meticillin-resistant Staphylococcus aureus; MIC, minimal inhibitory concentration.

7. Surgical techniques

Although randomized trials comparing lead extraction to conservative management are lacking, observational studies have clearly demonstrated the role of extraction in case of infections of pacemakers; because mortality rates of device-related endocarditis treated only with antibiotics are very high, as much as 66% in some series.
Like in any other surgical procedure, the best way of treating an infectious complication is avoiding it with a good prevention, consisting in a strict aseptic manipulation of a patient without signs of infection anywhere and employing periprocedural prophylactic antibiotics. A standard regimen includes administration of 2 g of cefazolin intravenously one hour before the procedure, or vancomycin, 90 to 120 minutes before surgery, if the patient is

penicillin allergic or in centers where oxacillin resistance among staphylococci is high (Bertaglia et al., 2006).

Superficial wound infections that do not involve the device do not require extraction and can be managed with oral antibiotherapy; but, in general, foreign body infection requires removal of the entire system to ensure a complete eradication and to prevent the recurrence of infection. When there is a localized pocket infection, there is still controversy with which is the best way to approach. The NASPE 2000 guidelines accept a conservative treatment consistent in device removal cutting the exposed parts of the leads; an attitude that is proving to be unsuccessful and increases the risk of recurrence or spreading of the infection and patient's mortality (Chua et al., 2000). What is more, the recent AHA scientific statement and update (Baddour et al., 2010) does not include this approach.

The first techniques employed for extraction of a transvenous lead were external traction with counter weights or open cardiac surgery with inflow occlusion or cardiopulmonary bypass. In 1988 Byrd and his colleagues (Smith et al., 1994) incorporated a percutaneous technique for lead extraction attempted via the implant vein using locking stylets and dilator sheaths or via the femoral vein using snares, retrieval baskets, and sheaths. After this introduction, cardiac pacemaker lead extraction techniques have improved and there are currently many options to select.

7.1 Direct traction

Direct traction techniques consist in lead traction with standard or locking stylets without countertraction. Care must be taken not to compromise the integrity of the lead, because this difficult the removal and increases the risk of complications or incomplete extraction. To avoid this risk, forceful traction is contraindicated and any lead that cannot be freed from tissue without distortion or stretching should be extracted with countertraction techniques.

7.1.1 Simple traction

Simple traction is the first employed and most basic lead extraction technique. The lead exits via the implant vein using standard non-locking stylets and fixation screw retraction clips. A modification consists on prolonged graded traction with increasing weights that are connected to the proximal end of the lead. Although it can be performed in any case, best results are obtained when used with recently implanted leads (less than one or two years).

When removing older leads, excessive traction may result in coil rupture, leaving fragments in the cardiovascular system with subsequent thrombotic or infectious complications. Unopposed traction can also lead to invagination of the myocardium, myocardial rupture, arrhythmia, hypotension or acute severe tricuspid regurgitation secondary to valve leaflet avulsion (Farooqi et al., 2010).

Rosenheck et al. (2002) employed lead rotation during simple traction technique in 89 patients with 113 lead extractions. Removal was fully completed in 97 (85.8%) leads with a 6.9% of partial and an 8% of unsuccessful removal rate. The only predictor of successful removal was lead age and there was only a small asymptomatic pericardial effusion in one patient.

7.1.2 Locking stylet

This technique uses a special traction device to assist in the removal of cardiac leads. This specialized stylet wire can be inserted through a cardiac lead's conductor lumen once the

proximal connector has been removed. The stylet can then be locked into position, firmly grasping the distal end of the lead or anywhere along the conductor coil. This technique prevents the risk of elongation of the lead body and coil during exertion, ensuring that the entire lead is removed. Compared to simple traction, the use of a locking stylet results in extraction of greater number of intact leads (Kennergren et al., 2000) and a reduced risk of rupture.

The use of a locking stylet is limited when the conductor is broken or central lumen distorted, and has similar complications than simple traction such as myocardial invagination or rupture.

Alt et al. (1996) described the experience gathered between 1990 and 1994 by seven European centers regarding a locking stylet for removal of 150 leads. Complete removal was possible in 122 cases (81%) and in 18 cases (12%) a partial removal was obtained. Failure to remove the lead with the extraction stylet was experienced in 10 cases (7%). There were no major complications or deaths.

7.2 Lead extraction sheaths
7.2.1 Telescoping sheaths

The function of telescoping sheaths is to mechanically disrupt the fibrosis and provide a passage to remove a lead. The use of a sheath is a two-staged process: counterpressure and countertraction (Byrd & Wilkoff, 2000). In the first stage, the sheath is pushed along the lead while a similar traction is applied to the locking stylet to avoid a tear through the vascular wall. The second stage is initiated when the sheath has been advanced to the lead tip-myocardial interface and countertraction is employed. In this stage, traction is placed on the lead while countertraction is utilized in the sheath to minimize the risk of myocardial invagination or rupture. Care must be taken to maintain the sheath angle in parallel with the lead to minimize the risk of vascular lesion. Although counter traction prevents invagination of the myocardium, perforation of the myocardium is still possible. Major risks associated with this technique involve vascular lesion and myocardial perforation.

Results using conventional sheaths are reported in the U.S. Lead Extraction Database (Smith et al., 1994; and Byrd et al., 1999), with a complete removal rate of 86.8% and partial removal rate of 7.5%. Major complications occurred in 2.5% (haemopericardium, tamponade, haemothorax and one death).

7.2.2 Electrosurgical sheaths

The electrosurgical sheath (fig. 1) uses radiofrequency energy, similarly to a surgical cautery tool. It consists on two electrodes settled on the beveled tip of a sheath and the radiofrequency energy is conducted between the bipolar electrodes. It is used to locally dissect the binding tissue that surrounds and anchors transvenous leads. The tapered distal end of the sheath can also be used to mechanically disrupt these adhesions, like a conventional one; and dislocation of the tip is achieved with countertraction.

In the Excl trial (Farooqi et al., 2010) 287 leads in 166 patients were extracted with bipolar electrosurgical sheaths; 96% of leads were completely removed, 4% partially removed and only one lead could not be removed (laser sheath as an adjunct was used in 2% of cases). Major complications included three cardiac tamponade, one haemothorax and an arteriovenous fistula.
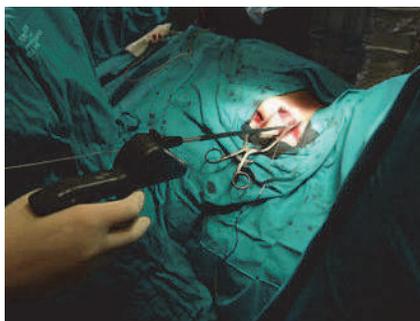
Fig. 1. Intraoperative image of a lead extraction with an electrosurgical sheath.

Compared to laser ablation, electrosurgical sheaths are designed to be more supple so that may be easier to maneuver. The radiofrequency energy is confined to less than one fourth of the circumference of the sheath allowing a directed and careful dissection of the tissue and reducing the chance of vascular damage; but in the other hand this directional control reduces the cutting efficacy through the fibrosis (Verma & Wilkoff, 2004).

7.2.3 Laser ablation

The Excimer laser sheath consists on a circumferential thin layer of optical fibers that run along the sheath and finish at the distal tip producing a ring of laser light in pulses to a tissue depth of 100 μm, dissolving the nearest fibrous tissue adherent to leads. Thus, fibrous tissue encapsulating the lead body is removed in a controlled manner and occluded vasculature can be re-canalised (Farooqi et al., 2010).

The outer layer of the sheath is made of plastic and acts as a support for maneuvering the laser but for mechanical countertraction too. Compared to electrosurgical sheaths, the circumferencial cutting is more powerful for extraction of multiple leads or with older implantation date, and in veins occluded by clot and fibrosis too. On the other hand, this circumferential cutting increases the risk of venous laceration, especially at the superior vena cava.

Appropriate sizing of the laser sheath and a proper traction/countertraction technique are crucial to prevent complications. A coaxial orientation of the sheath and lead, with the leading edge of the sheath oriented away from the wall of the vessel decreases the risk of vascular injury; and we must be careful not to advance the outer sheath more deeply than the laser sheath to avoid pinching the vascular wall (Henrikson & Brinker, 2008).

Major complications associated with laser-assisted lead extraction include: major venous injury, arrhythmia, myocardial tear, pneumothorax, hemothorax, arteriovenous fistula, tricuspid valve injury and pulmonary embolus (Lawton et al., 2006).

The total initial experience of laser lead extraction in the U.S. (Byrd et al., 2002) was reported on 2561 pacing and defibrillator leads from 1684 patients at 89 sites, with a procedural success rate of 90%, a major complication rate (tamponade, hemothorax, pulmonary embolism, lead migration, and death) of 1.9% and an in-hospital death rate of 0.8%. The latest report about laser lead extraction is the LExICon study (Wazni et al., 2010), an observational retrospective study of 2405 consecutive laser-assisted lead extractions in 13 sites in the U.S. and Canada. In this study, the most common indication

for extraction was infection and a 96.5% of leads were completely removed, with a procedural failure rate that statistically increased when leads were implanted for more than 10 years. The clinical success rate was of 97.7% (resolution of clinical goals associated with the indication for lead removal), and failure to achieve it was associated with body mass index <25 kg/m² and low extraction volume centers. Major adverse events (any complication related to the procedure that required procedural intervention or transfusion to prevent death, threat to life, or any complication related to the procedure that resulted in death or serious harm to bodily function or structure) occurred in 1.4% of procedures, with a death rate of 0.28%; and were associated with body mass index <25 kg/m². Indicators of all-cause in-hospital mortality were pocket infections, device-related endocarditis, diabetes and creatinine ≥ 2.0; with an overall in-hospital mortality of 1.86%, a higher rate than the one presented by Byrd et al in 2002 and that reflects the complex comorbid condition of this patient population, especially device-related endocarditis. In this study, the all-cause in-hospital mortality rate for the device-related endocarditis population was 4.3%, 1.7% for pocket infection and 0.3% for all noninfected patients, proving the seriousness of deep advanced and pocket infections.

Moon et al. (2002), found three independent predictors of the need for laser-assist during lead extractions: prolonged implant duration, nonseptic leads and necessary or discretionary versus mandatory indications.

7.3 Femoral and transjugular extraction techniques

The preferred via for lead extraction is the same transvenous access by which they were implanted, usually subclavian, cephalic or axillary veins. However, when removing broken or cut leads with free ends and when the primary approach via the implant vein fails, a femoral or transjugular access is the procedure of choice.

The internal jugular transvenous access was described by Mazetti et al. (2008), and, although their experience was based only on 18 patients and 22 leads, they achieved a high success rate with very few complications.

Lead extraction using the femoral vein is called "the inferior approach" and probably it is the most versatile approach for lead removal. There are two fundamental snaring techniques (Belott, 2007): a direct approach in which, once the lead is grabbed with a snare, an attempt is made to remove the lead by traction; and a two-step process, by first pulling either the proximal or distal end of the lead into the inferior vena cava and secondly, snaring the free end and pulling it for its removal. There are many tools for femoral lead extraction; the more advanced one is the Byrd Femoral Work Station (Cook Vascular Inc., Leechburg, PA).

Recently (Fischer et al., 2009), it has been described a simple and safe technique of transfemoral lead snaring to assist lead extraction and maintain vascular access in the setting of venous occlusion, when the distal lead tip pulls free of the myocardium before an extraction sheath is passed beyond the point of venous obstruction.

Finally, both the transjugular and transfemoral approaches have the same potential complications of cardiac or vascular perforations.

7.4 Surgical lead removal and other techniques

An open heart surgical approach for lead removal should be limited to two scenarios:
1.   Patients with significant retained hardware after percutaneous removal failure.

2. Lead vegetations greater than 2 cm in diameter, because of concern of pulmonary embolism with percutaneous procedures. This is not a definitive indication because there is some experience in transvenous lead extraction with large vegetations without precipitating a pulmonary embolism or, even having evidence of it, neither survival nor length of hospital stay has been affected by this complication (Meier-Ewert et al., 2003).

In some cases, a combined technique is the best treatment option. Removal of the distal end of the lead by sternotomy and cardiopulmonary bypass due to the presence of large vegetations; and a simultaneous percutaneous procedure for extraction of the proximal end, due to severe fibrosis around the lead at the venous system, that precluded its traction from the atrium.

Although the currently recommended treatment for pacemaker infection is complete removal, both surgery and percutaneous techniques are complex and of very high risk in some patients with many comorbidities, in these cases, less invasive techniques have been applied at some centers:

-   Closed irrigation system (Hurst et al., 1986), they treated 19 patients for infected or eroded permanent pacemaker pockets with local debridement and insertion of a closed irrigation system using a solution of tyloxapol and tobramycin. Successful eradication of the infection, without complete replacement of the pacemaker system, was achieved in all cases.
-   Placement of an antibiotic-releasing envelope to treat an infected pacemaker pocket: only one case report has been described in the literature (Lopez, 2010), with good results.
-   Vacuum-assisted system for pacemaker infection: Satsu & Onoe (2010) describe the application of vacuum-assisted therapy for treating four patients with infected permanent pacemaker with good results.

7.5 Selection of percutaneous lead extraction technique in permanent transvenous pacemaker infections

Extraction of recently implanted cardiac rhythm devices (less than one year) is commonly a safe and easy procedure which consists in pulse generator removal and direct lead traction. However, chronically implanted leads become encapsulated by fibrotic attachments along any length of the lead where there is contact with the vein, valve or endocardial structures. In these cases, percutaneous lead extraction has become the preferred method to remove leads with a rate of success in centers with a high-volume case load of 95-97% and high rates of resolution of infection. On the other side, these procedures are associated with complications rates between 0 and 11% and involve significant risks such as cardiac tamponade, hemothorax, pulmonary embolism, lead migration, pneumonia and death.

Every of these previous described techniques remain useful and its employment depends on the indication and the experience of each center, but there are some recent reviews that may be of interest in selecting one or another technique. They are summarized in next table (Table 4). Anyway, it is important to emphasize that operator experience is vital in determining success as familiarity of a wide array of techniques will increase the likelihood of uncomplicated extraction.

Mathur et al. (2003), made a retrospective analysis of various conventional techniques for lead extraction, obtaining good results and a low complication rate. They conclude that the only independent predictor associated with successful lead extraction with these techniques was a shorter dwell time. Success rates for leads in situ for greater than six years considerably decreased in their study.

Reference	Techniques	Results	Complications
Mathur et al Retrospective analysis hospital database 1986-1999	158 leads extracted in 80 patients: - Simple traction 16.4% - Locking stylet 6.1% - Telescoping sheath 67.3% - Transfemoral approach 6.1% - Thoracotomy 4.8%	Success at 1st procedure 87.7% - Cephalic approach 90% - Transfemoral approach 56% - Thoracotomy 75% Complete lead removal 86.7% Lead remnants 7.3% Complete lead remaining 6.1%	Deaths - 0 Tamponade - 1 Stroke - 1 Pulmonary embolism - 1 Significant bleeding 12%
Centella et al Retrospective analysis of their experience 1989-2006	314 leads extracted in 187 patients: -Symple traction 44 leads -Telescoping sheath 34 patients -Electrosurgical sheath 80 patients	Complete extraction 96.8% 48 patients required a second technique for lead remnant removal	Deaths - 1 Tamponade - 1 Sepsis - 1 Pulmonary embolism – 1 Severe tricuspid insufficiency – 1
Rusanov et al Retrospective analysis of a single operator experience 1993-2008	Percutaneous techniques 88.8% - Simple traction - Locking stylet - Telescoping sheath Open surgical approach 11.2% - No CPB 4.2% - CPB 6.3%	Complete extraction 86.2% Partial success (<4cm retained) 9.2% Failure to extract (>4cm retained) 4.6%	Pneumothorax – 2 (surgical approach) Persistent infection – 1 (percutaneous) Tamponade – 1 (surgical approach) No procedure-related deaths
Neuzil et al Prospective randomized study 2.5 years	161 leads implanted for at least 6 months in 120 patients: - 84 leads extracted with radiofrequency sheaths - 77 leads extracted with telescoping sheaths	Radiofrequency extraction: - Complete success 93% - Partial success 7% Standard extraction: - Complete success 73% - Partial success 14%	Pulmonary embolism – 2 Sepsis – 3 Blood transfusion requirement – 3 No procedure-related deaths
Wilkoff et al Randomized trial (PLEXES) 1995-1996	301 patients with 465 leads: - laser extraction: 244 leads - non-laser: 221 leads	Complete extraction: - laser 94% - non-laser 64% Partial extraction: - laser 2.5% - non-laser 1.8% Failure: - laser 3.3% - non-laser 34% Clinical success: - laser 94.8% - non-laser 95.9%	Tamponade – 2 (laser) Hemothorax – 1 (laser) Valve damage – 1 (laser) Procedure-related death – 1 (laser)
Verma & Wilkoff Retrospective study 1998-2001	450 consecutive lead extractions: - 354 laser-assisted - 96 radiofrequency-assisted	Procedure time lower in radiofrequency group Fluoroscopy time reduced in radiofrequency group	No complications in radiofrequency group Two deaths in laser group Success rates comparables in both groups

Table 4. Contemporary reviews of different transvenous lead extraction techniques.

In the same manner, Centella et al. (2007) revised their experience with percutaneous lead extraction between 1989-2006, using conventional techniques and electrosurgical sheaths. A statistically significant relation is observed between younger patients and major complication development, as well as with endocarditis being the indication for lead removal.

Rusanov et al. (2010), describe a single operator experience with percutaneous and open surgical techniques for lead removal in 143 endocardial leads. Complete radiographic success was achieved for 131 leads with a low rate of major complications. They also describe an interesting multistage procedure for patients with purulent wounds: first they exteriorize the generator and irrigate and débride the pocket while initiate or continue antibiotherapy. In a second stage, when wound cultures are negative, they perform lead extraction with a caudal approach. They refer an accelerated wound healing with this technique.

Neuzil et al. (2010) performed a prospective randomized study comparing conventional telescoping sheaths lead extraction results with electrosurgical sheaths one. They obtained statistically significant differences in success rates between both techniques, in favour of the electrosurgical system. They also observed a significant reduction in the time of traction with this technique.

Another prospective randomized study is the PLEXES study (Wilkoff et al., 1999), which compares lead extraction results using conventional or laser techniques. Extraction efficacy was significantly higher in patients randomized to laser-assisted removal, with shorter mean procedure duration. Complication rates were not significantly different between both groups, with an incidence in the laser group below 2%.

Verma & Wilkoff (2004) performed a retrospective review of 450 lead extractions in their institution and concluded that electrosurgical sheath appeared to have success rates comparable to laser sheath; although there was a selection bias because laser had been selected for more challenging lead extraction cases. Based on their experience, they recommend the use of radiofrequency sheaths, especially in patients at higher risk of complications; and they employ laser techniques as first option for cases requiring extraction of multiple leads, defibrillator leads, older implantation date ones and in occluded veins.

Regarding to the removal of infected leads, there are some data suggesting that leads associated with systemic sepsis may be easier to extract with little effort (Moon et al., 2002) and that infected leads that are difficult to remove and require electrosurgical or laser sheaths, are unlikely to be infected at their endocardial tip with some reported data suggesting that tip-only retentions at incomplete extractions do not develop recurrence of infection and do well without another intervention requirement (Kratz & Toole, 2010).

Finally, there is a short experience in relation to coronary sinus lead extraction. In many cases, this leads are extracted with simple traction but there are some reports of laser sheath employment for coronary sinus lead removal.

8. Conclusion

According to the increasing use of cardiac implantable electrophysiological devices, associated infectious complications are increasing, so that the most common essential indication for lead extraction remains infected systems. This can be a life-threatening complication associated with significant morbidity and mortality and its management

represents a difficult challenge for cardiology, cardiac surgery and infectious diseases specialists.

Although we dispose of a wide range of antibiotics to face pacemaker infections, the treatment of choice in device-related infections requires its complete removal. Considering that are healthcare-related infections, an increasing number of episodes caused by multiresistant microorganism strains is expected, so a better knowledge of the role of new antimicrobials is mandatory. We also need to investigate which is the appropriate duration of antibiotic therapy as well as the optimal time for a new device implantation.

Nowadays, there are many surgical tools to remove infected leads with high success rates. This sort of techniques must be performed at tertiary referral centers with a high volume demand on these procedures and with a cardiac surgeon as the primary operator or aware of the procedure at least. With a well-structured team and the availability of different surgical lead extraction techniques, the rate of major complications is very low.

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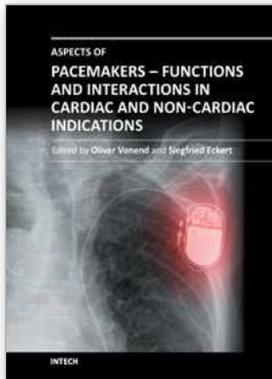
Aspects of Pacemakers - Functions and Interactions in Cardiac and Non-Cardiac Indications
Edited by Dr. Oliver Vonend

Outstanding steps forward were made in the last decades in terms of identification of endogenous pacemakers and the exploration of their controllability. New â€œartificalâ€ devices were developed and are now able to do much more than solely pacemaking of the heart. In this book different aspects of pacemaker â€" functions and interactions, in various organ systems were examined. In addition, various areas of application and the potential side effects and complications of the devices were discussed.

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