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Review

New horizon for infection prevention technology and implantable device

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ABSTRACT

There has been a significant increase in the number of patients receiving cardiovascular implantable electronic devices (CIED) over the last two decades. CIED infection represents a serious complication after CIED implantation and is associated with significant morbidity and mortality. Recently, newly advanced technologies have offered attractive and suitable therapeutic alternatives. Notably, the leadless pacemaker and anti-bacterial envelope decrease the potential risk of CIED infection and the resulting mortality, when it does occur. A completely subcutaneous implantable cardioverter defibrillator is also an alternative to the transvenous implantable cardioverter defibrillator (ICD), as it does not require implantation of any transvenous or epicardial leads. Among the patients who require ICD removal and subsequent antibiotics secondary to infection, the wearable cardioverter defibrillator represents an alternative approach to inpatient monitoring for the prevention of sudden cardiac death. In this review paper, we aimed to introduce the advanced technologies and devices for prevention of CIED infection.

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1. Introduction

There has been a significant increase in the number of patients receiving cardiovascular implantable electronic devices (CIED) over the last two decades [1,2]. This is largely owing to the expanding indications of CIED based on technological improvements and new evidence demonstrating improved survival and quality of life among certain groups of patients having structural heart diseases [3,4]. However, the advantage of these devices is limited by associated adverse events and complications. CIED infection represents a serious complication of cardiac device therapy and is associated with significant morbidity and mortality. Despite appropriate care, in-hospital

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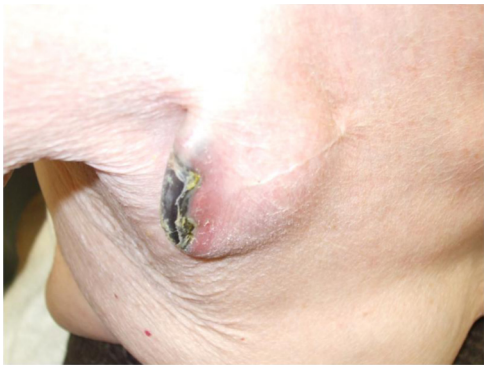

Fig. 1. A case of cardiac implantable electronic device infection.

mortality among patients admitted because of CIED infection ranges from 4% to 10% and one-year mortality from 15% to 20% [5–11].

The majority of patients with CIED infection have pocket and/or endovascular lesions (Fig. 1). If aggressive antibiotic therapy fails to control CIED infection, then complete removal of the device is recommended in many instances [2,6]. The timing of re-implantation is another critical issue. An early re-implantation should be performed in patients who are solely dependent on the CIED; however, at least one week is required to control local or systemic bacterial infections [12]. Currently, the advanced technologies may contribute to a decrease in infection risk and mortality and may bridge the critical period between device removal and re-implantation.

2. New technologies to reduce the risk of CIED infection

In the USA and Europe, some new alternatives to prevent CIED infection are available. The leadless pacemaker and antibacterial envelope represent attractive and suitable therapeutic options to minimize the risk of CIED infection.

2.1. Leadless pacemaker

To reduce the complications associated with the standard transvenous electrode lead of the pacemaker, a leadless pacemaker has been invented. The concept of a completely self-contained VVIR intracardiac pacemaker, first explored about 45 years ago by Spickler JW et al., has finally become a reality with the development of the Nanostim™ Leadless Pacemaker (St Jude Medical, Inc., St. Paul, MN, USA) and the Micra™ Transcatheter Pacing System (Medtronic plc) for use in humans [13–16]. Technological advances in electronics miniaturization and battery chemistries have enabled creation of a device small enough to be implanted within the heart via a percutaneous, transvenous approach, while still providing similar battery longevity without leads. The leadless pacemaker has been expected to reduce CIED infections, because this system has no physical connection between the endocardium and the subcutaneous pocket, which are the most likely source and channel of bacterial infection, respectively. Furthermore the leadless standalone system never produces subclavian or supra vena-cava occlusions. Both systems have received the CE Mark in Europe, but are not approved in the USA.

The Nanostim system is delivered to the implant site at the lower septum of the right ventricle (RV) via a transfemoral route and allows for bradycardia pacing via a miniature pulse generator with a built-in battery and electrodes that can be entirely and permanently implanted (Fig. 2). The first successful Nanostim implantation in humans took place in December 2012 in Prague, Czech Republic. Recently, a nonrandomized first-in-human study

Fig. 2. The Nanostim™ Leadless Pacemaker (St Jude Medical, Inc., St. Paul, MN, USA) Reprinted with permission from St Jude Medical, Inc.

Fig. 3. The Micra™ Transcatheter Pacing System (Medtronic plc). Reprinted with permission from Medtronic plc.

demonstrated this system to be safe and feasible over a 90-day period [15]. This preclinical study expanded on the previous study by demonstrating that the pacing and sensing properties remain adequate for up to 18 months. In addition, the histological analyses at the 90-day mark revealed a limited local response to the implanted device at the RV apex. Furthermore, there were no significant adhesions between the device and the RV walls. These pathological features may have important implications related to the long-term efficacy and safety of this system, as well as for designing approaches to extract the device.

The Micra system, similar to the Nanostim system, is an investigational device and is being assessed in a pivotal global clinical trial. The miniaturized device is only one-tenth the size of a conventional pacemaker (Fig. 3). The Micra system is also delivered directly into the heart through a catheter inserted in the femoral vein. Once positioned, the pacemaker is securely attached to the heart wall in the RV and can be repositioned or retrieved during implantation if needed (Fig. 4). The device does not require the use of leads and is attached via small tines securing it to the heart wall. The first successful in-human Micra implantation occurred in December 2013 in Linz, Austria. It is currently being evaluated in the Medtronic Micra Transcatheter Pacing System (TPS) Global Clinical Trial, which is a single-arm, multicenter study that will enroll up to 780 patients at approximately 50 centers [16].

Both systems allow for retrievability, if needed; however, there are significant differences in the designs that are worth noting: (i) the Micra device has an active fixation mechanism consisting of four electrically-inactive extendable and retractable tines to anchor it to the cardiac tissue, whereas the Nanostim device uses an electrically active fixed helix, (ii) the Micra device is wider (20 Fr) and shorter (25.9 mm) than the Nanostim pacemaker (18 Fr and 41.4 mm), (iii) the Micra pacemaker's communication between the device and programmer is established using a standard programming head, whereas the Nanostim pacemaker communicates with the St. Jude Medical Merlin™ Patient Care System using a programmer link and surface electrocardiographic electrodes, and (iv) the Micra device