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Complications after implantation of a new-generation insertable cardiac monitor: Results from the LOOP study

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ABSTRACT

Background: Insertable cardiac monitors (ICM) are leadless devices utilized in long-term monitoring of the heart rhythm. The implantation procedure of the new-generation ICMs is minimally invasive, but little experience exists regarding complications. We thus aimed to investigate adverse events (AE) according to procedure-related characteristics after implantation of a large number of new-generation ICMs.
Methods: The study population consisted of participants randomized to receive ICM in a multi-center trial. The Reveal LINQ™ ICM was implanted using provided insertion tools, either in an electrophysiology laboratory or outpatient procedure room. If device sensing was insufficient in the first subcutaneous position, one or more repositions were performed. Patients were urged to make contact if they suspected any AE. Furthermore, follow-up for safety endpoints consisted of evaluation of medical records and planned study visits.
Results: 1420 patients received an ICM, 753 (53%) in a procedure room and 667 (47%) in an electrophysiology laboratory. During a median follow-up of 499 days, 9 (0.63%) and 15 (1.13%) patients experienced AEs with and without need for device explantation, respectively. In the 38 patients requiring device repositioning, more AEs requiring explantation were seen (3 (7.9%) vs. 6 (0.4%), $p = 0.001$). Patients undergoing implantation in a procedure room had more infections (12 (1.6%) vs. 1 (0.1%), $p = 0.004$), though no significant difference was reached in AEs requiring explantation (7 (0.9%) vs. 2 (0.3%), $p = 0.19$).
Conclusion: The Reveal LINQ™ ICM can be inserted with a very low risk of complications, both in the traditional electrophysiology laboratory setting and in an outpatient procedure room.

1. Introduction

Insertable cardiac monitors (ICM), also known as implantable loop recorders, are leadless devices implanted subcutaneously to perform long-term heart rhythm monitoring. ICMs are important tools in patients with unexplained syncope [1], and more recently, guidelines commenced to recommend consideration of ICM in patients with cryptogenic stroke to detect atrial fibrillation (AF) [2]. An increasing number of patients receive these devices, and new clinical indications are emerging, such as in AF monitoring post-ablation or after transcatheter aortic valve implantation [3,4]. Currently, we are conducting a large randomized clinical trial to evaluate ICMs in screening for AF to prevent stroke (ClinicalTrials.gov: NCT02036450).

Since the first ICMs reached the market in the late 1990s, substantial improvements have been achieved with regard to data storage, transmission capabilities and automated arrhythmia detection algorithms [5]. The physical design is trending towards miniaturization [6,7]. The

Abbreviations: AE, adverse event; AF, atrial fibrillation; BMI, body mass index; CI, confidence interval; CIED, cardiac implantable electronic device; EP Lab, electrophysiology laboratory facility; HR, hazard ratio; ICM, insertable cardiac monitor; Q1;Q3, 1st and 3rd quartile.

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new generation of ICMs emerged in 2014, when Medtronic released the Reveal LINQ™. Later, Biotronik followed with the Biomonitor 2™, while St. Jude Medical recently registered a trademark for the upcoming device, Confirm Rx™. These ICMs have different technological features, but notably, manufacturers are designing device-specific insertion tools to promote the least invasive implantation procedure, i.e. subcutaneous injection through a minimal skin incision without suturing of the device to the underlying tissue. This development possibly decreases the rates of complications after implantation, and indeed, initial experiences indicate that implantation is safe [8–10]. These first reports comprise only few complications and are thus limited by small sample sizes, keeping in mind the large number of patients that will possibly undergo ICM implantation in the future.

We investigated rates of all types of adverse events (AEs) after implantation of a large number of Reveal LINQ™ devices in a real-world setting. Furthermore, we sought to investigate AEs according to procedure-related characteristics.

2. Methods

2.1. Study population

The current study is a sub-study of the LOOP study, an ongoing large multi-centre randomized clinical trial investigating stroke prevention in individuals at risk using ICM to detect AF [11]. In brief, participants were 70 years or older and diagnosed with at least one disease increasing the risk of stroke; hypertension, diabetes mellitus, heart failure or previous stroke. Exclusion criteria included history of AF, treatment with oral anticoagulation therapy and implanted cardiac implantable electronic device (CIED; pacemakers, cardiac resynchronization therapy or implantable cardioverter-defibrillators). Eligible subjects were randomized 3:1 to a control arm or to receiving an ICM with continuous ECG monitoring and subsequent treatment according to study guidelines. For the current study, we prospectively followed all participants undergoing insertion of an ICM in the LOOP study.

2.2. Device

The Medtronic Reveal LINQ™ ICM was used. It has a size of 1.19 cm^3 and enables fully automated daily remote transmissions. The device is delivered in a sterile pack along with tools to perform the implantation; an incision tool (two-edged arrow-shaped scalpel 10 mm wide), an insertion tool to create the subcutaneous device pocket, pre-loaded with the device, and an injector tool to slide the device from the insertion tool into the subcutaneous pocket.

2.3. Insertion procedure

The implanting physician was a senior cardiologist, or a medical doctor under supervision by the cardiologist, and the surgical environment was either an electrophysiology laboratory facility (EP Lab), or an outpatient procedure room, at the discretion of the local centre. Patients in antiplatelet therapy were not recommended to discontinue the treatment upon implantation. To reflect a real-world setting, implantation procedures were performed according to the discretion of the physician, assisted by a nurse, however meeting the standard recognized requirements for a surgical procedure: Approximately 1 h prior to implantation, a single dose of oral dicloxacillin 1 g was planned, or in case of suspected intolerance to the antibiotic, either intravenous antibiotics or no antibiotics were given. The surgical field was prepared with chlorhexidine preceded by shaving if needed. Standard sterile technique was applied, including 85% ethanol 0.5% chlorhexidine scrub, sterile gown, gloves and drape. Infiltration with lidocaine was used as local anaesthetic. An incision over the fourth intercostal space on the left hemi-thorax was utilized, with subcutaneous device insertion 45° relative to the sternal border, according to the manufacturer's suggestion [6]. Before wound closure, the device-recorded QRS amplitude was tested, and if sensing was insufficient (<0.2 mV), one or more device repositions were performed. Wound closure was performed with suture, glue or adhesive strips. A sterile pad was applied as wound dressing, and the patient was discharged home to resume normal activity, instructed to remove the dressing after minimum 24 h.

2.4. Definition of procedure-related adverse events

An AE was defined as an event taking place after discharge, and could be; bleeding from the incision, haematoma related to the device pocket, pain, infection, or pocket erosion, as diagnosed by the attending physician. AEs were registered in case report forms and medical records and reported to the core laboratory. AEs were grouped according to if device explantation was required or not. If a device was explanted without the presence of bleeding, haematoma, pain, infection, or pocket erosion, it was not categorized as an AE. Thus, explantations performed due to patient request; impracticality, anxiety or sensation of the device without soreness, were registered as device explantation for other reasons.

2.5. Follow-up

By written and oral information, participants were urged to make telephone contact with the local centre promptly if they suspected any AE. In-hospital study visits were performed after 12 and 24 months. Furthermore, if the daily transmissions were not received, participants were contacted. Finally, data collection was accomplished by a physician evaluating all medical records from hospital or outpatient visits from the time of implantation to the end of follow-up, whereas details about the implantation procedure were obtained correspondingly.

2.6. Ethical considerations

The study complies with the Declaration of Helsinki. All participants signed informed consent documents upon inclusion in the LOOP study. The LOOP study has been approved by the Ethics Committee of the Capital Region of Denmark (H-4-2013-025). The trial is registered at ClinicalTrials.gov (NCT02036450).

2.7. Data handling and statistics

One centre acted as core laboratory for study procedures and follow-up. All data was handled in a centralized online encrypted system, the case report forms. The exact binomial procedure was utilized to calculate 95% confidence intervals (CI) for AE rates. Comparisons between groups were performed by Fischer's exact test or *t*-test where appropriate, with a two-sided *p*-value of 5% for significance. To supplement our analyses, possible explanatory factors for AE requiring explantation or infection were analysed in binary logistic regression with age, gender, body mass index, surgical environment (procedure room vs. EP Lab), periprocedural antibiotics (yes vs. no), repositioning (0 vs. >0 attempts), type of wound closure (suture vs. suture + adhesive strips vs. adhesive strips vs. glue + adhesive strips), type of physician (physician in training vs. senior cardiologist), and platelet inhibitors (yes vs. no) as independent variables in univariate models, after which backwards selection with all these variables and significance level of 5% was performed to create the final model. Analyses were performed with SAS 9.4 (SAS Institute, Cary, NC, USA) and IBM SPSS Statistics 22 (IBM, Armonk, NY, USA).

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