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Temporal changes of new-onset atrial fibrillation in patients randomized to surgical or transcatheter aortic valve replacement☆

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ABSTRACT

Background: Temporal development of new-onset atrial fibrillation (NOAF) after aortic valve replacement is unclear, and opportunistic screening has limited diagnostic accuracy. This is the first study to investigate the incidence and temporal development of NOAF detected by implantable loop recorder (ILR) in patients with aortic stenosis, randomized to surgical aortic valve replacement (SAVR) or transcatheter aortic valve replacement (TAVR).

Method: An ILR was implanted in a subgroup of patients without pre-procedural atrial fibrillation (AF), randomized to SAVR or TAVR in the NOTION trial. Data from the ILR were transmitted in intervals of 2 weeks for 12 weeks post-procedurally and analyzed.

Results: The study included 25 and 27 patients who underwent SAVR and TAVR, respectively. The cumulative rate of NOAF was 100% and 81.5% for patients undergoing SAVR and TAVR, respectively ($P = 0.06$). TAVR patients without NOAF 6 weeks post-procedurally remained free from NOAF. The prevalence of AF after SAVR decreased significantly after 8 weeks when compared with the first 2 weeks (50.0% vs. 84.0%, respectively; $P < 0.05$). The prevalence of AF after TAVR did not change significantly during follow-up. The median AF burden (percentage of time with AF) was 2.8% and 0.04% during the first 2 weeks after SAVR and TAVR, respectively ($P = 0.01$) and it decreased significantly over time after SAVR but not after TAVR.

Conclusion: NOAF subsided 6 weeks after TAVR. AF prevalence and burden decreased significantly over time after SAVR, but remained stable after TAVR. These findings may be considered for post-procedural anti-coagulation strategy.

1. Introduction

Aortic stenosis is a common valvular heart disease occurring in 3% of individuals older than 75 years of age [1]. Once the symptoms of aortic stenosis develop the average remaining life expectancy is approximately 3 years [2]. Surgical aortic valve replacement (SAVR), or the more recently introduced transcatheter aortic valve replacement (TAVR) procedure, can alleviate symptoms and increase life expectancy, compared with the life expectancy of patients with untreated severe aortic stenosis [3–5]. Both SAVR and TAVR are associated with the risk of severe complications including bleeding, stroke or the development of arrhythmias such as new-onset atrial fibrillation (NOAF). After SAVR and TAVR both the mortality and risk of stroke are increased in patients with NOAF when compared to patients without atrial fibrillation (AF) [6–9]. NOAF has been found to develop not only during the procedure, but also during the following post-procedural weeks, when rhythm monitoring is usually discontinued [6,10].

The current study is the first to describe the incidence and temporal development of NOAF, and AF burden after aortic valve replacement via continuous monitoring using an implantable loop recorder (ILR) (Reveal XT 9529™ ILR [Medtronic Inc., Minneapolis, MN, USA]), in a patient population randomized to either SAVR or TAVR.

2. Methods

2.1. Patient population

All consecutive patients from the final phase of the enrolment period in the NOTION trial were considered eligible for inclusion in this substudy. The design of the multi-

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center 1:1 randomized clinical NOTION trial comparing SAVR versus TAVR in all-comers patients with severe aortic stenosis has previously been described in detail [11]. The current study was developed after the initiation of the NOTION trial. Patients eligible for analysis in this study had no pre-procedural AF, as verified by pre-procedural 24-hour Holter monitoring and 12 lead ECG, or history of AF. The regional ethics committee approved the trial protocol. All patients provided written informed consent before implantation of ILR and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki.

2.2. Procedure

All TAVR procedures were performed using the third generation of the self-expanding CoreValve bioprosthesis (Medtronic Inc., Minneapolis, MN, US) of sizes 23, 26, 29 or 31 mm under general anaesthesia. The predominant access route was the common femoral artery, while the alternative route was the left axillary artery. Patients randomized to SAVR underwent conventional open heart surgery, with the use of cardiopulmonary bypass. No patients underwent any surgical anti-arrhythmic procedure. Post-procedure, all SAVR and TAVR patients were prescribed 75 mg of oral acetylsalicylic acid (ASA) for lifelong use, combined with 75 mg of oral clopidogrel for 3 months. If anti-coagulation was indicated, warfarin for lifelong use combined with 75 mg of oral clopidogrel for 3 months followed by 75 mg oral ASA for lifelong use was administered.

2.3. Reveal XT ILR device and implantation

At the end of the SAVR or TAVR procedure, the Reveal XT 9529™ ILR was implanted subcutaneously in the left pectoral region and programmed to nominal settings. By sensing R-waves the ILR continuously detects AF by a pre-programmed algorithm based on pattern recognition of beat-to-beat variation in time windows of 2 min. The Reveal XT 9529™ ILR have previously been validated by comparing the ILR on nominal settings with concomitant Holter monitoring, and were found to have a sensitivity, specificity, positive predictive value, and negative predictive value of 96.1%, 85.4%, 79.3%, and 97.4%, respectively [12].

2.4. Data collection

Patients were instructed to transmit data every second week via remote monitoring. The date and time of each transmission, arrhythmias since last transmission, and AF burden, defined as the duration of detected AF relative to the total duration between transmissions, were recorded. Owing to the varying intervals between transmissions, the AF burden was recalculated giving the mean AF burden for every patient in intervals of 2 weeks. The duration of AF episodes was pre-defined in time intervals by the manufacturer: 2–10 min; 10 min–1 h; 1–4 h; 4–12 h; 12–24 h; 24–48 h; 48–72 h and >72 h. NOAF was defined as any AF recorded by the ILR within 12 weeks after the procedure. Clinical follow-up was performed before discharge, and at one and 3 months after the procedure.

2.5. Statistical analysis

Continuous variables were expressed as mean (±standard deviations [SD]) or median (interquartile range [IQR]), according to variable distribution. Categorical variables were expressed as percentages. Intergroup and intragroup comparisons of continuous variables were analyzed using Student's *t*-test, Wilcoxon rank-sum, or Wilcoxon signed rank test, as appropriate. Intergroup and intragroup comparisons of categorical variables were analyzed using Chi-square test, Fisher's exact test, or McNemar's test, as appropriate. The rate of NOAF was analyzed using the Kaplan-Meier method. Data were censored at the time of death, or if the ILR was explanted, or upon completion of 12 weeks of follow-up. The log-rank test was used for comparisons. Data were analyzed using SAS Base 9.3. (SAS software, Cary, NC).

3. Results

3.1. Patient population

From February 2012 to May 2013, 74 patients undergoing SAVR or TAVR underwent concomitant implantation of a Medtronic Reveal XT 9529™ ILR. A total of 52 patients assigned to SAVR (n = 25) and TAVR (n = 27) were included in the analysis (Fig. 1). Of the 52 included patients, one patient died owing to pericardial effusion leading to cardiac arrest, and had the last transmission 58 days after SAVR; one patient had the ILR explanted owing to infection, with last transmission 43 days after TAVR. Both patients developed NOAF before the last transmission. One patient kept in the TAVR group for analysis was converted peri-procedurally to SAVR owing to complications. In 2 patients undergoing SAVR the ILR started recording 7 and 21 days after the procedure and in 3 patients undergoing TAVR, the ILR started recording 5, 6 and 16 days after the procedure.

3.2. Baseline and follow-up characteristics

The baseline characteristics are shown in Table 1 and baseline echocardiographic and procedural characteristics are shown in Table 2. The procedure time was longer for SAVR patients, use of inotropics was more frequent during the TAVR procedure, and more patients undergoing TAVR were treated with pre-procedural ASA. The anti-thrombotic and anti-arrhythmic therapy administered to patients at discharge, and at one and 3 months of follow-up is shown in Supplementary Appendix Table 1. Significantly more patients undergoing SAVR received anti-coagulants, beta-blockers, and amiodarone at discharge and at the one-month follow-up, as well as anti-coagulants and beta-blockers at the three-month follow-up when compared with patients undergoing TAVR. The 4 patients undergoing SAVR who were treated with amiodarone at the one-month follow-up were among the 6 patients undergoing SAVR who received amiodarone at discharge. More patients undergoing TAVR received ASA at discharge, and at the one-month and three-month follow-up, as well as clopidogrel at the one-month follow-up.

3.3. Development of atrial fibrillation

Fig. 2 shows the prevalence of AF in intervals of 2 weeks, describing the relative number of patients with AF detected by the ILR in the denoted interval. During the first 2 weeks after intervention, AF

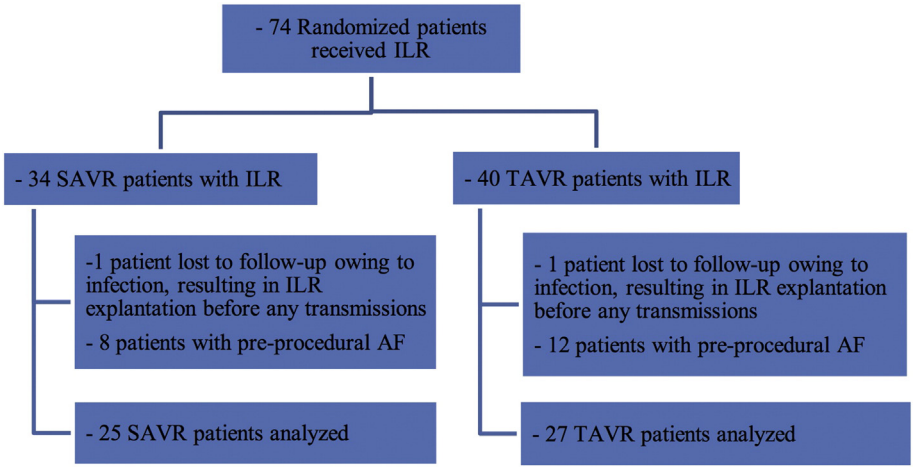

Fig. 1. Trial profile. AF: Atrial fibrillation; ILR: Implantable loop recorder; SAVR: Surgical aortic valve replacement; TAVR: Transcatheter aortic valve replacement.

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