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Acute and long-term (2-years) clinical outcomes of the CoreValve 31 mm in large aortic annuli: A multicenter study☆

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ABSTRACT

Introduction: Little is known about the early and late performance of the 31 mm CoreValve Revalving System (CRS, Medtronic Inc., Galway, Ireland). Our aim was to compare acute and long-term results of the 31 mm CRS with other valve sizes.

Methods: Consecutive patients undergoing transcatheter aortic valve implantation (TAVI) with CRS in nine Italian centers were prospectively included and dichotomized according to prosthesis size in two different groups, as follows: 31 mm and other valve sizes (i.e., 23, 26, and 29 mm combined). End points were defined according to Valve Academic Research Consortium definitions. Propensity score matching was performed.

Results: In total, 2069 patients (n = 169 [8%] in the 31 mm group and n = 1900 [92%] in the other valve sizes group) were included. After propensity matching, the implantation of the 31 mm valve was associated with lower rates of procedural- (91.3% vs. 98.1%, p = 0.030) and device-success (88.5% vs. 97.1%, p = 0.016), longer procedural time (120 [80–180] min. vs. 90 [60–120] min., p < 0.001), and higher rates of implantation of a second valve (10.6% vs. 2.9%, respectively, p = 0.027). The rates of permanent pacemaker implantation in the 31 mm group were higher but not statistically different from other valve sizes (41.7% vs. 30.9%, respectively, p = 0.149). Significant improvement, without between-group differences, was observed in NYHA functional class. Cardiovascular death was lower in the 31 mm valve group through 2-years (3.8% vs. 13.5%, respectively, p = 0.014).

Conclusions: The acute performance of the 31 mm CRS was worse than other valve sizes but no negative impact was observed in long-term outcomes.

1. Introduction

Transcatheter aortic valve implantation (TAVI) is the gold standard treatment for inoperable patients with severe symptomatic aortic stenosis (AS) and a potential alternative to surgical aortic valve replacement (SAVR) for high surgical risk patients [1–3]; in fact, a recent study demonstrated that TAVI outcomes were improved compared with SAVR in this clinical setting [4]. The CoreValve Revalving System (CRS) (Medtronic Inc., Galway, Ireland) is available in four different sizes, labeled according to the inflow portion of the valve, as follows: 23-, 26-, 29-, and 31-mm. While the largest (i.e., 31 mm) CRS enables

Abbreviations: TAVI, Transcatheter aortic valve implantation; SAVR, Surgical aortic valve replacement; CRS, CoreValve revalving system; AS, Aortic stenosis; NYHA, New York Hear Association; AKI, Acute kidney injury; STS, Society of thoracic surgeons; TIA, Transient ischemic attack.

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the treatment of larger aortic annuli and more complex anatomical scenarios, it has been consistently observed among operators the higher level of difficulty to implant this device compared with the smaller CRS sizes. In particular, the design of the 31 mm valve with a larger inflow portion that when exteriorized from the capsule releases significant stored tension makes it more prone to dive into the left ventricle. Nonetheless, the lack of a comprehensive study that assessed the acute and long-term performance of this device compared with the smaller CRS sizes has impaired our understanding in this setting.

We, therefore, aimed at evaluating the acute and long-term (2-year) clinical outcomes associated with the 31 mm CRS and compare with the other sizes utilizing multicenter data from consecutive patients.

2. Methods

Starting from June 2007, all consecutive patients with degenerative severe AS undergoing TAVI with the third-generation 18 Fr CRS in nine Italian centers were prospectively included in the ClinicalService® Project [http://clinicaltrials.gov/ct2/show/NCT01007474]. This is a nation-based clinical data repository and medical care project aimed at describing and improving the use of implantable devices in Italian clinical practice. The project was approved by each site's Institutional Review Board or medical director and conforms to the principles outlined in the Declaration of Helsinki. Each patient signed an informed consent for data collection and analysis. Clinical and echocardiographic follow-up were performed at 30 days, 1 year, and then yearly with visits or telephone contacts according to each centre's clinical practice. Herewith, we report two-year follow-up data. All events were site reported. All data provided by each interventional site were anonymized, centrally collected, and assessed for quality. In particular, all outcome data were confirmed by source documentation collected from each participating center. TAVI program in all the participating sites was supported by a local heart team [1]. For the purpose of the current study, patients with tricuspid aortic valves who underwent TAVI with CRS from September 2007 to August 2015 were dichotomized according to the prosthesis size in two different groups, as follows: 31 mm valve size and other valve sizes (i.e., 23, 26, and 29 mm combined). End points were defined according to Valve Academic Research Consortium definitions [5].

Design features of the CRS and technical details of the procedures have been previously described [6–8]. The CRS, initially available in 26 mm and 29 mm sizes and, starting from September 2011 and August 2012 respectively, also in the 31 mm and 23 mm sizes, was implanted using the transfemoral, subclavian, and transaortic approaches with an 18 Fr delivery catheter, later improved by an AccuTrak Stability Layer (Medtronic Inc.). All procedures were performed under local anesthesia (with or without additional sedation and/or analgesia) or general anesthesia and endotracheal intubation (i.e., decided by the heart team during pre-operative meetings), under angiography associated with transesophageal echo guidance or exclusive angiography guidance in a standard cardiac catheterization laboratory with surgical back-up or in a hybrid operating room. Post valve deployment, the angiographic assessment of aortic regurgitation (AR) severity was performed utilizing previously described methodology [9,10]. Evaluation was initially performed by 2 treating physicians and discrepancies in the measured degree of post-TAVI aortic regurgitation were resolved by consensus. After the procedure, most patients were managed in an intensive care unit or coronary care unit for at least a day, and a temporary pacemaker was left in place for at least 48 h. All patients received acetylsalicylic acid (at least 100 mg before the procedure and lifelong) and clopidogrel (300–600 mg loading dose plus 75 mg daily for 3 to 6 months unless prolonged administration was required for previous coronary intervention with drug-eluting stents). During the intervention, unfractionated heparin 70–100 IU/kg was administered to achieve an activated clotting time of 200 to 250 s for the duration of the procedure.

2.1. Statistical analysis

Consecutive patients from the Italian ClinicalService® who underwent TAVI with Medtronic CoreValve prosthesis were classified according to prosthesis size. Continuous variables are presented as mean and standard deviation or as median and interquartile range, depending on the distribution. Categorical variables are presented as frequencies and percentages. Baseline, pre-procedural and follow-up data were compared between groups. The non-parametric Wilcoxon test was used to compare continuous variables. A chi-square test was used to compare categorical variables when no cells had an expected count less than 5, whereas the Fisher exact test was performed when at least 1 cell had an expected count less than 5. The Kaplan Meier method was used to estimate the cumulative rates of major adverse events in the groups, such as death, cardiovascular death and stroke; groups were compared using the log rank test.

A 2-way analysis of variance or analysis of covariance for repeated measures was used to evaluate the effects of time (baseline vs. discharge vs. follow-up) and group on echocardiographic variables and New York Heart Association (NYHA) class. Aiming at balancing groups, propensity score matching was performed using a greedy algorithm. Variables used to balance groups were those that were different at baseline. A logistic regression model has been fitted with these covariates to calculate the propensity scores for each observation. Finally, a total number of 208 patients were selected in a 1:1 manner.

3. Results

In total, 2069 consecutive patients (n = 169 [8%] in the 31 mm group and n = 1900 [92%], in the other valves size group) were included. Baseline characteristics demonstrated that patients included in the 31 mm valve group were younger with a major prevalence of male gender; moreover, a trend towards lower STS score but significantly worse ejection fraction and higher rates of previous aortic regurgitation ≥ moderate was observed in the 31 mm vs. the other valve size group (Table 1). Procedural characteristics are shown in (Table 2). The 31 mm valve was more frequently implanted utilizing an alternative access, therefore, leading to higher rates of general anesthesia compared with smaller valve sizes; furthermore, significantly longer procedural times with higher rates of implantation of a second valve (11.2% vs. 4.1%, $p < 0.001$) and post-dilation (36.9% vs. 22.2%, $p < 0.001$), as well as lower rates of device- (87% vs. 93.5%, $p = 0.001$) and procedural-success (89.3% vs. 95.1%, respectively, $p = 0.002$) were observed with the 31 mm valve compared with the other valve sizes. Any vascular complication (9% vs. 17.5%, $p = 0.005$) and major bleeding (6.3% vs. 17%, $p = 0.012$) were less frequent whereas permanent pacemaker implantation rates were significantly higher in the 31 mm group (36% vs. 23.7%, respectively, $p = 0.001$). Furthermore, acute kidney injury (AKI) rates were comparable between groups, while a trend towards lower rates of stroke/transient ischemic attack (TIA) was observed in the 31 mm valve group (0% vs. 2.1%, $p = 0.057$) (Table 3).

4. 30-day follow-up clinical outcomes

Data were available in 100% of patients at 30-day. Comparable rates of death, cardiovascular death and myocardial infarction were revealed but lower stroke/TIA rates were demonstrated in the 31 mm- compared with other valve sizes group (0% vs. 2.6%, respectively, $p = 0.035$) (Table 3).

5. 2-year clinical outcomes

Data were available in 100% of patients through 2-year follow-up. While marked improvement in NYHA functional class, compared with pre-procedure, was observed over time in both groups, these benefits were significantly less pronounced in the 31 mm valve group (Supplementary Fig. 1). Likewise, a trend towards worse degrees of aortic regurgitation was demonstrated in the 31 mm valve group (Supplementary Fig. 2). Nevertheless, rates of death (20.1% vs. 19.8%, $p = 0.918$), cardiovascular death (7.7% vs. 9.2%, $p = 0.511$), and myocardial infarction (2.4% vs. 1.7%, $p = 0.554$) were comparable between groups while stroke/TIA rates were consistently lower in the 31 mm prosthesis group, compared with other valve sizes group (0.6% vs. 4.5%, respectively, $p = 0.015$).

6. Propensity matching

Aiming at providing more robust results and minimizing potential bias, we performed propensity matching analysis including 208 patients (104 patients in each group, Table 1). Importantly, the differences observed between groups in procedural- (91.3% vs. 98.1%, respectively for 31 mm valve- and other valve sizes- group, $p = 0.030$) and device-success (88.5% vs. 97.1%, $p = 0.016$) rates, as well as procedural time (120 [80–180] min. vs. 90 [60–120] min., $p < 0.001$) and the need for the implantation of a second valve (10.6% vs. 2.9%, respectively, $p = 0.027$) were sustained (Table 2). Major bleeding was consistently less frequent in the 31 mm valve group (6.3% vs. 19.1%, $p = 0.058$), while vascular complications rates were also lower but not statistically significant (7.7% vs. 14.6%, respectively, $p = 0.116$) compared with other valve sizes group. While the rates of permanent pacemaker implantation were numerically higher in the 31 mm valve group, this difference was not statistically significant (41.7% vs. 30.9%, $p = 0.149$).

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