Rapid deployment aortic valve replacement versus trans-catheter aortic valve replacement in intermediate-risk patients: a propensity score analysis

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Abstract

Background: There is insufficient evidence regarding the comparison of Rapid Deployment aortic valve replacement(RDAVR) to TAVR in intermediate-risk patients with severe symptomatic aortic stenosis(AS) Aims: We compare the 2-years outcomes between RDAVR with INTUITY and TAVR with SAPIEN 3 in intermediate-risk patients with AS. Methods: Inclusion criteria: severe AS implanted with RDAVR or TAVR; EUROSCORE II [?] 4% and clinical evaluation by Heart Team. Regression adjustment for the propensity score was used to compare RDAVR with TAVR(1:1). Primary endpoint: composite criterion of death, disabling stroke or rehospitalization. Secondary endpoints: occurrence of major bleeding post-operative complications, paravalvular regurgitation (PVR)[?]2 and patient-prosthesis mismatch(PPM) at 1 month and pacemaker implantation at 2 years. Results: A total of 152 patients were included from 2012 to 2018: 48 in the RDAVR group and 104 in the TAVR group. Mean age was 82.7±6, 51.3% were female, mean Euroscore II was 6.03±1.6% and mean baseline LVEF was 56±13%,mean indexed iEOA was 0.41±0.1cm/m2, mean gradient was 51.7±14.7mmHg. Patients with RDAVR were younger(79.5±6vs82.6±6,p=0.01), at higher risk (EUROSCORE2 6,61±1,8%vs5,63±1,5%, p=0.005), combined surgery was performed in 28 patients(58.3%). Twenty-two patients(45.99%) met the primary outcome in the RDAVR group and 32 patients(66.67%) in the TAVR group. By 1:1propensity score matching analysis, there was a significant difference between both groups in favor of RDAVR(HR=0.58[95%CI:0.34;1.00],p=0.04). No difference were observed in PPM occurrence(0.83;[0.35-1.94];p=0.67),major bleeding events(1.33;[0.47-3.93];p=0.59),PVR[?]2(0.33[0-6.28],p=0.46), and pacemaker implantation (0.84[0.25-2.84],p=0.77).Conclusion: RDAVR is associated with better 2-years outcomes than TAVR in intermediate-risk patients with severe symptomatic AS.

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Abstract

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ABBREVIATIONS

AS: aortic stenosis**AVR:** aortic valve replacement **BMI:** body mass index**BSA:** body surface area**CAD:** Coronary Artery Disease**CHF:** Congestive Heart Failure**CPBT:** cardiopulmonary bypass time**EOA:** effective orifice area**FU:** Follow-Up**LVEF:** Left Ventricular Ejection Fraction**LVOT:** Left ventricular Outflow Tract

MR: Mitral regurgitation

NYHA: New York Heart Association

PCI: Percutaneous Coronary Intervention**PM:** Pace maker**PPM:** patient-prosthesis mismatch**PVR:** paravalvular regurgitation**RDAVR:** rapid deployment aortic valve replacement**S3-THV:** Sapien 3 transcatheter heart valves**sPAP:** systolic Pulmonary Artery Pression**SVD:** Structural Valve Degeneration**TAVR:** transcatheter aortic valve replacement

TTE: Transthoracic Echocardiography

INTRODUCTION

Aortic stenosis(AS) is considered the most common valvular heart disease with a prevalence of 2.8% in patients aged 75 years and over [1]. Its natural history has been well known for several years with a slow and benign evolution when asymptomatic but a high mortality rate when symptoms begin manifesting [2]. Since 1960, surgical aortic valve replacement (AVR) has remained the gold standard treatment for AS, promoting both survival and quality of life.

Since 2008, Transcathether Aortic Valve Replacement (TAVR) has proved a reliable alternative to conventional surgery in non-operable patients, in high-risk patients, more recently so in patients at intermediate and low-risk groups [3–6].

The expandable Sapien 3 transcatheter heart valve (S3-THV; Edwards Lifesciences, Irvine,CA,USA) has replaced the previous generation of XT-THV, which was associated with a high prevalence of paravalvular regurgitation (PVR). S3-THV provides a novel outer annular sealing skirt that functions as a blood-soaked sponge and limits the risk of PVR [7–9]. However, the protrusion of this skirt within the aortic annulus combined with the proximity to the normal conduction pathways have been shown to increase the risks of patient-prosthesis mismatch (PPM) [10] and the implantation of pacemakers (PM) [9,11,12].

In the meantime, Rapid Deployment Aortic Valve Replacement (RDAVR) with EDWARDS INTUITY Valve System (Edwards Lifesciences LLC, Irvine, California) has been introduced as a hybrid option between conventional and THV offering the benefits of both procedures. When compared to conventional surgery, this allows reduction in cardiopulmonary bypass time (CPBT) [13]. Moreover, the presence of a sub-annular balloon-expandable stent frame, which functionally widens the left ventricular outflow tract (LVOT), may ensure improved hemodynamic performance and a larger effective orifice area (EOA) [14,15].

Even though previous prospective studies have already demonstrated the non-inferiority of TAVR in intermediate-risk patients with symptomatic severe AS when compared to conventional AVR, there has been no specific validated study that exclusively compares RDAVR to TAVR.

The aim of the present study was therefore to retrospectively compare the mid-term outcomes of intermediate risk patients with severe symptomatic AS implanted with RDAVR or TAVR.

METHODS

Study population and design

This was a single-center retrospective study conducted from 2012 to 2018 at the La Timone Hospital, Marseille, France. The study included consecutive patients at intermediate-risk treated for severe symptomatic AS. All patients have been subjected to a pre-operative multi-disciplinary "Heart Team" evaluation to validate the indication of either TAVR with S3-THV or RDAVR with INTUITY. Based on the 2017 European Society of Cardiology and European Association for Cardio-Thoracic surgery (ESC/EACTS) guidelines, intermediate surgical risk was defined by EUROSCORE II[?]4% [16] and clinical evaluation by "Heart Team". The study was approved by the La Timone Hospital review Board (protocol number RGPD/AP-HM 2019-48) with written informed consent obtained from each participant.

Procedural characteristics

Depending on the vascular routes evaluated by computed tomography (CT) , TAVR was performed via trans-femoral, trans-subclavian, trans-aortic or trans-apical approach. The size of the prosthesis was selected by a multidisciplinary team, based on the CT scanned aortic annulus size. The procedure was performed under general or local anesthesia. Fluoroscopic guidance was used to guide prosthesis positioning and deployment. Prosthesis position and function were evaluated with angiography and transthoracic echocardiography (TTE).

For RDAVR, after standard aortotomy, the aortic valve leaflets were removed concomitant with calcium debridement. Three equidistant guiding sutures were placed through the nadir of the annulus and then

placed in corresponding positions through the sewing ring of the prosthesis. Using the guiding sutures, the valve and attached delivery system were lowered onto the annulus and secured into position under direct vision. The balloon catheter was then inflated to deploy the stent frame in a controlled fashion. On deployment, the prosthesis was fixed in a supra-annular position with the 3 guiding sutures and the aortotomy was closed. Prosthesis position and function were evaluated with per-operative trans-esophageal echocardiography.

Endpoints

Based on the recent PARTNER 3 study, the primary endpoint was a composite criterion comprising all-cause mortality, disabling stroke and hospitalization at two years. Rehospitalization was defined as any hospitalization related to the procedure, the valve, or congestive heart failure (CHF).

The secondary endpoints included : 1/ life-threatening and major bleeding, defined as a drop in the haemoglobin level of at least 3.0 g/dl or requiring transfusion of more than two units of red blood cells, or causing hospitalization or permanent injury, or requiring surgery 2/ moderate or severe PPM at one month follow-up (FU), defined by an iEOA[?]0,85cm^2/m^2 and iEOA<0,65cm^2/m^{2}respectively; 3/ PVR[?]2/4 at one-month FU; 4/ PM implantation at two-years. All outcomes were defined according to the Valve Aortic Research Consortium-2 definitions [17].

Follow-up assessments

All patients had a clinical examination, neurological examination, 12-lead electrocardiogram and TTE at discharge, thirty days, one year and two years. Patients who had suspected stroke after the procedure underwent serial neurologic examinations by physician specialist.

Statistical analysis

The initial clinical and echographic characteristics were first described and compared according to both groups. Quantitative variables are presented as means (+-SD) and compared using Student t-test when appropriate. Categorical variables are presented as numbers (percentages) and compared using chi-squared test when appropriate (Fisher test otherwise).

To reduce confounding by indication, analysis of the endpoints was based on a propensity score matching. The propensity score model was built using a logistic regression model including all variables known to be related to the endpoints and/or to the type of procedure (TAVR or RDAVR) regardless of their statistical significance. **Appendix**

This model allowed to calculate for each patient the probability of RDAVR procedure. Using the propensity score, RDAVR patients were matched to TAVR patients. An optimal 1:1 matching algorithm on the basis of the propensity score was applied. Analyses of all outcomes were then performed on the matched population.

The analysis of the occurrence of the primary composite endpoint and of all-cause death was performed using time-to-event approach. Univariate Cox models were built to estimate hazard ratios with their 95% confidence intervals. The analysis of the occurrence of secondary outcomes was performed using time-to-event approach taking into account the competing risk of death. Univariate Fine and Gray model were built to estimate cause-specific hazard ratios with 95% confidence intervals. Analysis of the occurrence of early outcomes (major bleeding, PPM and PVR) was performed by using univariate logistic regression models, allowing estimation of odds ratios with 95% confidence intervals. All tests were two-sided, and P values less than 0.05 were considered to indicate statistical significance. Statistical analyses were performed using R software, version 3.4.1.

RESULTS

Baseline characteristics

A total of 152 consecutive intermediate-risk patients were included between 2012 and 2018: 104 patients belonged to the TAVR subgroup and 48 patients belonged to the RDAVR subgroup. Clinical FU at two-

years was completed for the entire population. Mean age was 82.74+-6.36 years and female gender was predominant (n=78, 51.32%). Mean body surface area (BSA) was 1.74+-0.2 m2 and mean Body Mass Index (BMI) was 25.41+-4.45 kg/m2. Mean EUROSCORE II was 6.03 +-1.64%. Patients belonging to the RDAVR subgroup were significantly younger (79.54+-5.95 years versus 82.60+-6.02 years, p=0.01) and their EUROSCORE 2 was significantly higher (6.61+-1.82 versus 5.63+-1.54, p=0.005). One hundred and nineteen patients had hypertension (78.29%) and 35 patients (23.03%) had severe renal insufficiency. One hundred and nine patients (71.71%) were class 3 or 4 NYHA at inclusion. *Table 1.*

Mean left ventricular ejection fraction (LVEF) was 56.01+-13.03%. All patients had a severe AS, with a mean indexed aortic valve area of 0.41+-0.1cm2/m2 and a mean trans-aortic gradient of 51.68mmHg+-14.69mmHg. Eleven patients (7.24%) had a bicuspid aortic valve. Systolic pulmonary artery pressure (sPAP) was similar between both groups. The baseline echo parameters were comparable between both subgroups. *Table 2.*

Procedural characteristics

The main procedural characteristics are listed in *Table 3*.

In the TAVR subgroup, the majority of patients (81.73%) were treated by trans-femoral approach. Forty-nine patients had a 23mm TAVR (47.12%), 39 patients had a 26mm TAVR(37.50%) and 16 patients had a 29mm TAVR (15.38%). Two immediate post-operative deaths (1.92%) occurred from an aortic annulus rupture for the first patient and acute renal failure for the second patient.

In the RDAVR group, conventional full sternotomy was used in all patients. Fourteen patients had a 19mm INTUITY (29.17%), 14 patients had a 21mm INTUITY (29.17%), 11 patients had a 23mm INTUITY (22.92%), 8 patients had a 25mm INTUITY (16.67%) and 1 patient had a 27mm INTUITY (2.08%). Twenty-eight patients (58.33%) had combined procedures with a majority of CABG (43.75%). One death (2.08%) occurred from a septic shock in the immediate post-operative period. Mean duration of cross clamp time was 47.8+-13.2min. The duration of hospitalization was 15.78+-10.44days; 8.81+-3.93 in the TAVR group and 16.08+-13.61 in the RDAVR group(p<0,001).

End points

1/ Primary outcome at two years FU. *Table 4.*

Twenty-two patients (45.99%) met the primary outcome in the RDAVR group and 32 patients (66.67%) in the TAVR group. By propensity score matching analysis, there was a significant difference between both groups in favor of RDAVR (HR=0.58[95%CI:0.34;1.00], p=0.04).

Figure 1A

Five patients died in the RDAVR group, exclusively from non-cardiovascular causes. In the TAVR group, 13 patients died, mainly from a cardiovascular causes including CHF (n=6), myocardial infarction (n=1), sudden cardiac death (n=1) and infective endocarditis (n=1). By propensity score matching analysis, there was a trend in favor of RDAVR concerning all-cause mortality without reaching statistical significance (HR = 0.40[95%CI:0.12,1.14], p=0.08). *Figure 1B*

Five patients were hospitalized in the RDAVR group, exclusively due to congestive heart failure (CHF). In the TAVR, 10 patients were hospitalized, mainly due to CHF (80%). The rate of re-hospitalization related to the procedure, the valve, or heart failure at two-years FU was 39.58% in the RDAVR group and 60.42% in the TAVR group. By propensity score matching analysis, there was a significant difference between both groups in favor of RDAVR (HR=0.56[95%CI 0.32,1.0], p=0.04). *Figure 1C*

No disabling stroke occurred in the RDAVR group and one (2.08%) occurred in TAVR group.

2/ Secondary endpoints. *Table 5.*

a. *Life-threatening or major bleeding*

Nine RDAVR patients underwent reoperation for post-operative bleeding. One TAVR patients had life threatening bleeding and eleven TAVR patients had major bleeding mainly due to vascular complications. By propensity score matching analysis, the rate of life-threatening or major bleeding was similar between both groups (HR=1.33[95% CI: 0.47,3.93], p=0.59).

b. Occurrence of moderate or severe PPM

At one-month FU, echo data were available for 143 patients (97 for the TAVR group, 46 for the RDAVR group). LVEF was 61.33+-9.09% in RDAVR group and 60.39+-13.67% in TAVR group(p=0.67). Indexed EOA was 1.02+-0.28cm2/m2 in the RDAVR group and 0.97+-0.23cm2/m2 in the TAVR group(p=0.31). Mean gradient was 10.33+-3.42mmHg in the RDAVR group and 12.84+-3.81mmHg in the TAVR group (p<0.001). The rate of Mitral regurgitation (MR) [?] grade 2 was 11.54% in TAVR group in 2.22% in RDAVR group (p=0.14). Systolic pulmonary artery pressure (sPAP) was 33.53+-9.40mmHg in RDAVR group and 41.52+-14.28mmHg in TAVR group (p=0.009). Fifteen patients (32.61%) had PPM in RDAVR group, including 13 moderate PPM (86.66%) and 2 severe PPM (13.34%). Seventeen patients (36.96%) had PPM in TAVR group, including 15 moderate PPM(88.23%) and 2 severe PPM(11.77%). By propensity score matching analysis, the rate of moderate/severe PPM was similar between both groups (HR=0.83[95%CI: 0.35,1.94],p=0.66).

c. Occurrence of PVR **[?] 2**

At one-month FU, echo data were available for 144 patients (98 for the TAVR group, 46 for the RDAVR group). None of patients had PVR [?] 2 in RDAVR group. One patient (2.17%) had PVR [?] 2 in TAVR group without significant difference between both groups (HR=0.33[95% CI:0.01, 6.28], p=0.46). *Table 5.*

d. Pacemaker implantation

The rate of PM implantation at discharge was 8.55% including 2 patients (4,17%) in the RDAVR group and 11 patients (10,58%) in the TAVR group (p=0.14).

At two-years FU, the rate of PM implantation was 11.11% in the RDVAR group and 12.50% in the TAVR group with no significant difference between both groups (HR=0.84[95% CI:0.25,2.84], p=0.77).

Table 5.

DISCUSSION

The aim of this study was to compare the mid-term outcomes of intermediate-risk patients operated on for severe AS with RDAVR with INTUITY, or TAVR with Sapien 3 valve. The main findings were: (1) At two years, there was a significantly lower occurrence of the composite criterion (death from any cause, disabling stroke and/or rehospitalization) in RDAVR group. (2) This result was mainly driven by less rehospitalization related to CHF in RDAVR group (3) Both valves provide a similar rate of PPM, PVR[?] 2 and PM implantation.

The recent progress in new generation THV urges surgeons to rethink surgical techniques. The INTUITY Valve is a hybrid option between conventional AVR and TAVR. RDAVR allows removal of the native leaflets as would a surgical procedure and is balloon-expanded as for TAVR. This enable to reduce CPBT by nearly 20 minutes compared to conventional AVR [18]. However, the clear benefit of this reduction on morbidity and mortality has not been demonstrated so far [19]. Thus, authors propose to limit its implantation to elderly patients in need of a combined surgery or in case of a complex aortic valve reoperation [20]. Meanwhile, indications for TAVR in patients with severe, symptomatic AS have been widely extended to younger patients since recent data showed that TAVR is non-inferior to surgery in intermediate and low risk patients [5,6].

While several studies have compared RDAVR with conventional AVR[13–15] and TAVR with conventional AVR[4–6], literature is poor on the direct comparison of RDAVR with INTUITY to TAVR with Sapien 3.

In this study, RDVAR with INTUITY provides better outcomes than TAVR with Sapien 3 at two-years FU. Based on the same composite criterion used in PARTNER 3, we showed a significantly lower rate of death

from any cause, disabling stroke and/or rehospitalization in RDAVR group when compared to TAVR group. This was mainly driven by a lower rate of rehospitalization related to CHF in RDAVR group.

The ultimate goal of AVR is to decrease left ventricular (LV) afterload to allow LV mass regression and improve LV compliance and myocardial perfusion. This enhances survival and quality of life and decreases the risk for CHF.

CHF after TAVR is already known as a powerful predictor of mortality and multiple CHF readmissions predicted the highest mortality rates [21]. CHF symptoms develop usually in case of incomplete LV afterload relief, untreated mitral regurgitation or residual myocardial ischemia leading to increase in left atrial pressure and sPAP [22–24]. Interestingly, sPAP was significantly higher in TAVR group at one-month FU when compared to RDAVR group. Moreover, LVEF was similar in both groups as well as the rate of MR[?] 2. This suggests that other mechanisms could be involved in the increased risk of CHF in TAVR group.

Most TAVR patients had a history of coronary artery disease (CAD) but no standardized revascularization strategy was endorsed in the absence of guidelines [25]. Hence, the timing to perform percutaneous coronary intervention (PCI) before or after TAVR was at the discretion of the heart team. We assume that postponing PCI could have increase the risk of ischemic myocardial injury after the TAVR procedure. Conversely, most RDAVR patients had combined procedures with coronary artery bypass grafting (CABG), limiting the risk of residual myocardial ischemia, LV diastolic or systolic dysfunction and CHF.

Another explanation to understand the higher rate of CHF after TAVR could be an increased incidence of significant PVR. PVR is known as a powerful predictor of mortality and CHF after TAVR [26]. PVR could limit LV hypertrophy regression by exposing patients to a residual LV afterload, diastolic dysfunction and impaired coronary flow reserve. However, we didn't find any difference regarding the occurrence of PVR[?] 2 in both groups. The rate of PVR[?] 2 was low in TAVR group(2,17%) in accordance with previous results reported in the literature [27].

The occurrence of PPM can also promote CHF after TAVR [28]. PPM leads to a lesser LV mass regression owing to the persistence of a residual LV afterload. However, the rate of moderate/severe PPM was similar between both RDAVR and TAVR groups in our study and could not explain a significantly higher rate of CHF in TAVR group.

Strengths and limitations

There were several limitations to this study, the most important one being its retrospective, single-center, non-randomized design.

There was also a significant bias due to the "associated procedures" in the RD-AVR group. In our center, TAVR is indicated in intermediate-risk patients older than 75 years while RD-AVR is actually indicated in patients older than 70 years with more comorbidities needing AVR + CABG. This explains why both subgroups were not similar before matching. However, our aim was to analyze the impact of each heart valve prosthesis on outcomes. To this end, we performed a 1:1 propensity-score matched comparison that allowed us to avoid differences between both groups at the expense of a decrease in the size of the populations being compared. The variables used for matching were the subject of lengthy reflection. Euroscore 2 cannot be used in the propensity score analysis since it includes several variables already used in the model.

We cannot exclude that subclinical leaflet thrombosis(SLT) could have promoted CHF in the TAVR group since CT scans were not routinely performed to confirm the diagnosis [29]. However, all TTE were performed by experienced cardiologists and CT scans were performed if there was any doubt of SLT on TTE.

Finally, our current results reflect only two-year outcomes and do not address the problem of long-term structural valve deterioration (SVD). An extended FU with a larger number of patients would highlight the occurrence and the impact of SVD on a long-term prognosis.

CONCLUSION

In this single-center, retrospective, propensity score-matched study conducted among intermediate-risk patients with severe AS, RDAVR showed a lower rate of the composite criterion of death, stroke or rehospitalization at two years than TAVR.

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Data available on request due to privacy/ethical restrictions

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	Unmatched cohort	**Unmatched cohort**	**Unmatched cohort**	**Matched cohort**	**Matched cohort**	**Matched cohort**
	RDAVR n = 48	TAVR n = 104	p value	RDAVR n = 48	TAVR n = 48	p value
Age - years	79.54±5.95	84.21±6.02	<0.001	79.54±5.95	82.60±5.75	0.01
Male gender - no./total no.(%)	27/48 (56.25%)	47/104 (45.19%)	0.20	27/48 (56.25%)	24/48 (50%)	0.54
Body surface - m^2	1.76±0.22	1.73±0.19	0.54	1.76±0.22	1.77±0.18	0.71

	Unmatched cohort	**Unmatched cohort**	**Unmatched cohort**	**Matched cohort**	**Matched cohort**	**Matched cohort**
Body-Mass Index - kg/m^2	24.92±3.76	25.64±4.74	0.35	24.92±3.76	26.06±4.69	0.19
EuroSCORE II - %	6.61±1.82	5.76±1.48	0.002	6.61±1.82	5.63±1.54	0.005
Diabetes - no./total no.(%)	9/48 (18.75%)	35/104 (33.6%)	0.02	9/48 (18.75%)	15/48 (31.25%)	0.16
Hypertension - no./total no.(%)	41/48 (85.42%)	78/104 (75%)	0.14	41/48 (85.42%)	38/48 (79.17%)	0.42
Dyslipidemia - no./total no.(%)	24/48 (50%)	56/104 (53.85%)	0.65	24/48 (50%)	27/48 (56.25%)	0.54
Severe renal insufficiency - no./total no.(%)	1/48 (2.08%)	34/104 (32.69%)	<0.001	1/48 (2.08%)	1/48 (2.08%)	1.0
Creatinine clearance - mL/min	52.51±15.92	36.69±15.33	<0.001	52.51±15.92	43.48±14.76	0.005
COPD - no./total no.(%)	8/48 (16.67%)	12/104 (11.54%)	0.38	8/48 (16.67%)	6/48 (12.50%)	0.56
Smoke - no./total no.(%)	15/48 (31.25%)	31/104 (29.81%)	0.85	15/48 (31.25%)	18/48 (37.50%)	0.52
Coronary artery disease - no./total no.(%)	8/48 (16.67%)	51/104 (49.04%)	<0.001	8/48 (16.67%)	17/48 (35.42%)	0.04
Atrial fibrillation - no./total no.(%)	15/48 (31.25%)	53/104 (50.96%)	0.02	15/48 (31.25%)	21/48 (43.75%)	0.21
Previous stroke - no./total no.(%)	2/48 (4.17%)	14/104 (13.46%)	0.08	2/48 (4.17%)	4/48 (8.33%)	0.68
Previous cardiac surgery - no./total no.(%)	6/48 (12.5%)	6/104 (5.77%)	0.19	6/48 (12.5%)	5/48 (10.42%)	0.74
Permanent pacemaker - no./total no.(%)	4/48 (8.33%)	18/104 (17.31%)	0.14	4/48 (8.33%)	8/48 (16.67%)	0.22

	Unmatched cohort	**Unmatched cohort**	**Unmatched cohort**	**Matched cohort**	**Matched cohort**	**Matched cohort**
NYHA			0.002			0.39
I	3/48 (6.25%)	4/104 (3.85%)		3/48 (6.25%)	2/48 (4.17%)	
II	18/48 (37.50%)	18/104 (17.31%)		18/48 (37.50%)	11/48 (22.92%)	
III	26/48 (54.17%)	62/104 (59.62%)		26/48 (54.17%)	33/48 (68.75%)	
IV	1/48 (2.08%)	20/104 (19.23%)		1/48 (2.08%)	2/48 (4.17%)	
Syncope - no./total no.(%)	1/48 (2.08%)	3/104 (2.88%)	0.99	1/48 (2.08%)	1/48 (2.08%)	1.0
Vitamin K antagonists - no./total no.(%)	11/48 (22.92%)	38/104 (36.54%)	0.13	11/48 (22.92%)	15/48 (31.25%)	0.36
Direct oral anticoagulants - no./total no.(%)	3/48 (6.25%)	11/104 (10.58%)	0.55	3/48 (6.25%)	7/48 (14.58%)	0.18
Mono-antiplatelet therapy - no./total no.(%)	29/48 (60.42%)	43/104 (41.34%)	0.05	29/48 (60.42%)	16/48 (33.33%)	0.007
Dual-antiplatelet therapy - no./total no.(%)	7/48 (14.58%)	24/104 (23.08%)	0.28	7/48 (14.58%)	10/48 (20.83%)	0.42

Table 1. Clinical Characteristics of the overall population at baseline.

NYHA : New York Heart Association, COPD : chronic obstructive pulmonary disease

	Unmatched cohort	Unmatched cohort	Unmatched cohort	Matched cohort	Matched cohort	Matched cohort
	RDAVR n = 48	TAVR n = 104	P value	RDAVR n = 48	TAVR n = 48	P value
LVEF - %	58.75±10.49	54.74±13.92	0.07	58.75±10.49	56.60±13.49	0.39
LV diastolic volume - ml	123.1±57.58	122.33±48.69	0.94	123.1±57.58	116.66±46.47	0.61
LV systolic volume - ml	51.98±35.44	57.17±37.47	0.47	51.98±35.44	52.53±35.76	0.94
LV septum diameter - mm	14.28±2.14	14.60±2.33	0.44	14.28±2.14	14.73±2.31	0.37

	Unmatched cohort	Unmatched cohort	Unmatched cohort	Matched cohort	Matched cohort	Matched cohort
sPAP - mmHg	35.62±14.43	39.00±15.26	0.21	35.62±14.43	35.28±12.64	0.91
Aortic regurgitation[?]2/4 - no./total no.(%)	12/48 (25%)	17/104 (17%)	0.25	12/48 (25%)	10/48 (21.74%)	0.71
Mitral regurgitation[?]2/4 - no./total no.(%)	6/48 (12.5%)	21/104 (20.19%)	0.24	6/48 (12.50%)	7/48 (14.58%)	0.77
Tricuspid regurgication[?]2/4 - no./total no.(%)	7/48 (14.58%)	7/104 (6.80%)	0.14	7/48 (14.58%)	5/48 (10.42%)	0.54
Bicuspid aortic valve - no./total no.(%)	8/48 (16.67%)	3/104 (2.8%)	0.005	8/48 (16.67%)	2/48 (4.35%)	0.09
Mean gradient – mmHg	51.04±17.20	51.97±13.46	0.71	51.04±17.20	51.92±10.89	0.77
EOA - cm2	0.74±0.20	0.68±0.17	0.04	0.74±0.20	0.72±0.18	0.47
iEOA - cm^2/m^2	0.43±0.11	0.40±0.09	0.05	0.43±0.11	0.40±0.10	0.22
Indexed SV - ml/m2	44.29±10.20	43.12±13.39	0.50	44.29±10.20	41.92±10.26	0.27
LA volume - ml/m2	58.27±41.05	57.51±28.18	0.53	58.27±41.05	56.90±30.21	0.75

Table 2. Echo data at baseline

LVEF : left ventricular ejection fraction, LV : left ventricle, sPAP : Systolic pressure of pulmonary artery EOA : effective orifice area, iEOA : indexed effective orifice are, LA : left atrial

	RDAVR N = 48	**TAVR N = 104**
Valve size - no./total no.(%)		
19mm	14/48 (29,17%)	0/104 (0%)
21mm	14/48 (29,17%)	0/104 (0%)
23mm	11/48 (22,92%)	49/104 (47,12%)
25mm	8/48 (16,67%)	0/104 (0%)
26mm	0/48 (0%)	39/104 (37,50%)
27mm	1/48 (2,08%)	0/104 (0%)
29mm	0/48 (0%)	16/104 (15,38%)
Access - no./total no.(%)		
Median sternotomy	48/48 (100%)	0/104 (0%)

	RDAVR N = 48	**TAVR N = 104**
Transfemoral	0/48 (0%)	85/104 (81,73%)
Transcarotid	0/48 (0%)	2/104 (1,92%)
Subclavian	0/48 (0%)	6/104 (5,77%)
Transaortic	0/48 (0%)	8/104 (7,69%)
Transapical	0/48 (0%)	3/104 (2,88%)
Combined procedure - no./total no.(%)	28/48 (58,33%)	0/104 (0%)
Coronary bypass	21/48 (43,75%)	0/104 (0%)
Other valves	8/48 (16,67%)	0/104 (0%)
Aortic surgery	1/48 (2,08%)	0/104 (0%)

Table 3. Procedure characteristics

	Unmatched cohort	**Unmatched cohort**	**Unmatched cohort**	**Unmatched cohort**	**Matched cohort**	**Matched cohort**	**Matched cohort**	**Matched cohort**
	RDAVR N = 48	TAVR N = 104	TAVR vs RDAVR HR(95%CI)	P value	RDAVR N = 48	TAVR N = 48	TAVR vs RDAVR HR(95%CI)	P value
Composite criterion - %	**45.99%**	**57.69%**	**0.74 (0.45 to 1.19)**	**0.22**	**45.99%**	**66.67%**	**0.34 (0.34 to 1.00)**	**0.04**
Overall mortality - %	8.38%	16.35%	0.53 (0.16 to 1.37)	0.20	8.38%	20.83%	0.40 (0.12 to 1.14)	0.08
Rehospitalization - %	39.58%	52.88%	0.70 (0.41 to 1.18)	0.17	39.58%	60.42%	0.56 (0.32 to 1.00)	0.04
Disabing Stroke - %	0%	3.85%	<0.01 (<0.01 to <0.01)	<0.001	0%	2.08%	<0.01 (<0.01 to <0.01)	<0.001

Table 4. Primary end point

	Unmatched cohort	**Unmatched cohort**	**Unmatched cohort**	**Unmatched cohort**	**Matched cohort**	**Matched cohort**	**Matched cohort**	**Matched cohort**
	RDAVR N = 48	TAVR N = 104	TAVR vs RDAVR HR(95%CI)	P value	RDAVR N = 48	TAVR N = 48	TAVR vs RDAVR HR(95%CI)	P value

	Unmatched cohort	Unmatched cohort	Unmatched cohort	Unmatched cohort	Matched cohort	Matched cohort	Matched cohort	Matched cohort
Life-threatening or major bleeding compli-cations - no./total no.(%)	9/48 (18.75%)	13/104 (12.50%)	1.63 (0.64 to 4.03)	0.29	9/48 (18.75%)	7/48 (14.58%)	1.33 (0.47 to 3.93)	0.59
PPM at 1 month - no./total no.(%)	15/46 (32.61%)	37/97 (38.14%)	0.79 (0.38 to 1.64)	0.53	15/46 (32.61%)	17/46 (36.96%)	0.83 (0.35 to 1.94)	0.66
PVR [?] 2/4 at 1 month - no./total no.(%)	0/46 (0.00%)	6/98 (6.12%)	0.15 (0.00 to 1.34)	0.10	0/46 (0.00%)	1/46 (2.17%)	0.33 (0.00 to 6.28)	0.46
PM implan-tation at 2years - no./total no.(%)	11.11%	16.28%	0.64 (0.24 to 1.73)	0.37	11.11%	12.50%	0.84 (0.25 to 2.84)	0.77

Table 5. Secondary endpoints

Figures

Figure 1

Kaplan-Meier freedom from composite of death, stroke or rehospitalization(A), death from any cause(B) and rehospitalization(C) in consecutive patients operated on severe AS with INTUITY (blue curve) and TAVR(red curve).

Figure 1