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Outcomes of RDAVR with Coronary Revascularization: 3-year Results from the German INCA Registry

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Abstract

Background The long-term outcomes of combined rapid-deployment aortic valve replacement (RDAVR) with coronary artery bypass graft surgery (CABG) are not well explored. We report 3-year results from the INCA registry on combined RDAVR with CABG.

Methods INCA is a prospective, multicenter registry that enrolled 224 patients undergoing RDAVR with CABG at 10 cardiac institutions in Germany. Prosthetic valve hemodynamics, clinical outcomes, and quality of life (QoL) up to 3 years were assessed.

Results The mean age of patients was 73.6 ± 6.1 years, and the mean logistic EuroSCORE was $7.8 \pm 6.0\%$. The mean number of distal arterial and venous anastomoses was 3.13 ± 1.56, aortic cross-clamp time was 79.4 ± 24.1 minutes, cardiopulmonary bypass time was 109.6 ± 34.5 minutes, and operation time was 224.2 ± 62.7 minutes. The majority of implanted valve size was 25 mm. At baseline, 11 patients (4.9.%) had a permanent pacemaker. Postoperatively, 17 patients (7.6%) required a new pacemaker implantation (5.4% valve-related). All-cause mortality at 30 days was 2.2%, and 11.2% at 3 years. Patient QoL (SF-12v2) was significantly restored and maintained for up to 3 years ($p < 0.001$). Five patients (0.9%) underwent reoperation related to endocarditis. The postimplant mean gradient was 9.2 ± 3.7 at discharge and 8.9 ± 4.6 mm Hg at 3 years.

Conclusion Combined RDAVR with CABG procedure is safe and effective over time. It offers stable and low transvalvular gradients with satisfactory clinical outcomes at 3 years. The pacemaker rate appears to be slightly increased, with no significant clinical effect at 3 years.

Keywords
- rapid-deployment aortic valve replacement
- structural valve degeneration
- valve durability

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Introduction

Rapid-deployment aortic valves (RDAVs) are known for ease of implantation, as only a few sutures are required to secure the device efficiently compared with conventional sutured bioprosthesis.[1] In cardiac surgery, prolonged cardiopulmonary bypass (CPB) time and aortic cross-clamp time are strong independent risk factors for postoperative mortality and morbidity, particularly in older patients with serious comorbidities.[2,3] Rapid-deployment aortic valve replacement (RDAVR) procedures have demonstrated a significant reduction in the operation time by minimizing CPB and aortic cross-clamp durations achieved by eliminating the passage and tying of sutures, resulting in fewer complications and improved outcomes in low and high-risk patients.[4–6] Moreover, several studies have indicated that isolated RDAVR enhances hemodynamic profile, reduces myocardial ischemia, decreases patient–prosthesis mismatch, and facilitates other minimally invasive approaches compared with conventional bioprosthesis implantation.[6–11]

Aortic stenosis (AS) is highly prevalent among patients with coronary artery disease (CAD). In such patients, surgical interventions often involve aortic valve replacement (AVR) combined with coronary artery bypass graft (CABG) procedures to treat both conditions.[12,13] Given the encouraging outcomes and hemodynamic benefits associated with RDAVR, the integration of RDAVR with CABG would be advantageous in managing severe AS and significant CAD.[10,13] Gonzalez-Barbeito et al reported an appreciable midterm outcome for combined RDAVR using the Edwards INTUITY valve system with other cardiac procedures and supported the utility of RDAVR in concomitant surgeries including CABG where surgical time is expected to prolong.[5]

To our knowledge, robust evidence-based data on the efficiency and performance of RDAVR combined with CABG are scarce. Consequently, follow-up studies and registry data are necessary to adequately assess the safety, durability, and long-term outcomes of this combined approach. Therefore, in this study, we present the 3-year findings from the prospective INCA German registry, explicitly focusing on the clinical outcomes of combined RDAVR with CABG procedures.

Method/Design

INCA is a prospective, non-randomized multicenter registry that included data from the patients who underwent RDAVR with concomitant CABG across 10 high-volume cardiac institutions in Germany between 2017 and January 2020.

Patient Population

The study included consecutive patients (≥18 years of age) with aortic valve disease and CAD indicated for a combined RDAVR using Edwards INTUITY Elite aortic valve and CABG willing to provide informed consent before enrollment.

The study excluded patients with emergency indications for surgery, required reoperation, have other cardiac diseases requiring additional cardiac surgery, have acute endocarditis or other systemic infections, and required mechanical prosthesis. Additionally, patients with anatomical contraindications to the Edwards INTUITY Elite valve system were excluded from the study.

Data Documentation

Baseline clinical parameters, as well as patient-specific data such as established risk scores (Logistic EuroSCORE I & EuroSCORE II, STS score, and Syntax score I) to estimate the perioperative risk, were collected and documented during screening. The local cardiac surgical team at each center evaluated patients according to the inclusion and exclusion criteria and determined the number of necessary coronary bypasses based on the morphology and location of the coronary stenoses.

Further, the intraoperative parameters and discharge information were appropriately collected and documented. Post-surgery follow-up data were collected at 30 days, 1 year, and 3 years through a telephone interview with the patient. Additionally, at 3 years, a follow-up examination at the center was conducted. All patient data were anonymized and captured using a specifically designed electronic case report form (eCRF) within a secure, password-protected, web-based electronic database.

Objectives

The primary objective was to determine all-cause mortality after 30 days in patients undergoing combined RDAVR with CABG. The secondary objective was to assess the hemodynamic performance of the Edwards INTUITY Elite bioprosthesis and further durability parameters, early (≤30 days) and late (>30 days to 3 years) clinical outcomes, and quality of life (QoL). Clinical outcomes of interest were all-cause, cardiovascular, and valve-related mortality, structural valve deterioration (SVD) according to VARC-2 criteria, reoperation related to valve or CABG or bleeding/tamponade, permanent pacemaker implantation (PPI), unplanned percutaneous coronary intervention (PCI), myocardial infarction (MI), and bypass obstruction. In addition, we compared the New York Heart Association (NYHA) functional class at 3 years post-surgery. QoL was assessed using the Short Form-12 Health Survey Version 2 (SF-12v2) questionnaire.

Statistical Analysis

Data were analyzed using descriptive statistics, with categorical variables presented as absolute values and frequencies (%) and the continuous variables presented as means (standard deviation [SD]) and median (interquartile range [IQR]). Test for normal distribution was performed using Kolmogorov-Smirnov test. Wilcoxon signed ranks test for paired data was used to compare QoL scores between baseline and follow-up visits. A p-value of <0.05 was considered statistically significant. Statistical analysis was performed using SPSS Version 28.0 (Armonk, NY, IBM Corp.).[14]

Results

A total of 224 patients undergoing RDAVR with concomitant CABG receiving Edwards INTUITY Elite aortic valve meeting the inclusion criteria were included in the present analysis.

Patient Characteristics

Patients had a mean age of 73.6 ± 6.1 years, primarily males (80.4%), had a BMI of 28.3 ± 4.1 kg/m^2, and mean systolic blood pressure of 138.4 ± 19.0 mm Hg and diastolic blood pressure of 75.0 ± 9.7 mm Hg (►**Table 1**). The mean logistic EuroSCORE I and EuroSCORE II of the patients were 7.8 ± 6.0 and 3.5 ± 2.9%, respectively, with an STS Risk Score of 3.8 ± 3.8 and Syntax score I of 13.0 ± 8.6. Furthermore, 139 patients (62.1%) had NYHA class III/IV symptoms, and 45 patients (26.9%) had angina Canadian Cardiovascular Society (CCS) III/IV symptoms. Common comorbidities included arterial hypertension, CAD with left anterior descending artery abnormality, myocardial infarction, type II diabetes, and peripheral vascular disease. Moreover, 57 patients (25.4%) had a history of previous PCI, and 11 patients (4.9%) had a history of previous permanent pacemakers.

Procedural Details

Among the total population ($n = 224$), 198 patients (88.4%) had tricuspid valve morphology (►**Table 2**). The left internal mammary artery (IMA) was used for revascularization in 146 patients (65.2%), the right IMA in 3 patients (1.3%), and both IMAs were used in 25 patients (11.2%), and the radial artery was used in only 4 patients (1.8%). The number of distal arterial anastomoses was one in 134 patients (59.8%), two in 33 patients (14.7%), three in 7 patients (3.1%), and four in 2 patients (0.9%). The venous graft was performed in 170 patients (75.9%), with the majority receiving one anastomosis (distal in 96 patients [56.5%] or proximal in 98 patients [57.6%]). However, the mean number of distal arterial and venous anastomoses was 3.13 ± 1.56.

Regarding the type of CABG performed, one patient (0.4%) underwent off-pump CABG, and eight patients (3.6%) had beating-heart CABG, whereas the majority (96%; 215 patients) underwent on-pump CABG. The mean duration of operation (skin-to-skin) was 224.2 ± 62.7 minutes, with a mean cross-clamp time of 79.4 ± 24.1 and cardiopulmonary bypass (CBP) time of 109.6 ± 34.5.

The first valve implantation was successful in 221 patients (98.7%) with a mean valve implantation time of 14.1 ± 7.4 minutes. The mean valve size utilized was 23.8 ± 2.1 mm, as most patients (36.2%) received 25-mm size valve. Notably, there were no (0%) intraoperative complications such as aortic rupture/dissection, annulus rupture, coronary artery obstruction, or prosthesis dislocation reported in any case. However, a visual paravalvular leak was noted in only one patient (0.4%).

Hospital Stays and Discharge

The overall mean duration of hospital stay was 12.0 ± 6.7 days, with a mean intensive care unit (ICU) stay of 3.4 ± 4.8 days and a mean duration of mechanical ventilation of 17.5 ± 34.3 hours (►**Table 3**).

After the procedure, most patients were discharged to the standard cardiac rehabilitation unit (48.7%), followed by other hospitals (26.8%) and home (22.3%). Among all patients, five patients (2.2%) died after surgery due to

Table 1 Patient characteristics

	Mean ± SD or *n* (%) *N* = 224
Age (years)	73.6 ± 6.1
Female gender	44 (19.6)
Height (cm)	171.3 ± 8.7
Weight (kg)	83.2 ± 14.3
Body mass index (k/m^2)	28.3 ± 4.1
Systolic blood pressure (mmHg)	138.4 ± 19.0
Diastolic blood pressure (mmHg)	75.0 ± 9.7
Heart rate (bpm)	73.4 ± 11.5
NYHA class III or IV	139 (62.1)
Angina CCS class 3 or 4	45 (26.9)
Logistic EuroSCORE I	7.8 ± 6.0
EuroSCORE II (%)	3.5 ± 2.9
STS Risk Score	3.8 ± 3.8
Syntax Score I	13.0 ± 8.6
Medical history	
Coronary artery disease	
RCA affected	161 (71.9)
LCA/LM affected	45 (20.1)
LAD affected	183 (81.7)
LCX affected	121 (54.0)
Recent myocardial infarction	44 (19.6)
Previous percutaneous interventions	57 (25.4)
Permanent pacemaker	11 (4.9)
Diabetes Type I	3 (1.3)
Diabetes Type II	81 (36.2)
Peripheral vascular disease	37 (16.5)
Transient ischemic attack/Stroke	20 (8.9)
Chronic obstructive coronary disease	19 (8.5)
Arterial hypertension	175 (78.1)
Pulmonary hypertension	19 (8.5)
Dialysis	3 (1.3)
Laboratory	
Creatinine >2.3 mg/dL	4 (1.8)
Creatinine (mg/dL)	1.08 ± 0.48
Dialysis	3 (1.3)
Lactate dehydrogenase (U/L)	212.9 ± 52.6
S-Bilirubin (mg/dL)	0.62 ± 0.35

Abbreviations: CCS, Canadian Cardiovascular Society; EuroSCORE, European System for Cardiac Operative Risk Estimation; IQR, interquartile range, LAD; left anterior descending artery; LCA, left coronary artery; LCX, left circumflex coronary artery; LM, left main artery; NYHA, New York Heart Association; RCA, right coronary artery; SD, standard deviation; STS, Society of Thoracic Surgeon.

Table 2 Interventional details

	Mean ± SD, Median (IQR) or *n* (%) *N* = 224
Aortic valve morphology	
Tricuspid	198 (88.4)
Bicuspid	12 (5.4)
Functional bicuspid	14 (6.3)
Annulus size (Edwards INTUITY sizer) (mm)	23.9 ± 2.1
Annulus diameter (Hegar sizer) (mm)	23.5 ± 2.0
Internal mammary artery	
No	50 (22.3)
Left	146 (65.2)
Right	3 (1.3)
Both	25 (11.2)
Radial artery	4 (1.8)
Number of distal arterial anastomoses	
0	48 (21.4)
1	134 (59.8)
2	33 (14.7)
3	7 (3.1)
4	2 (0.9)
Venous grafts	170 (75.9)
Number of distal venous anastomoses	
0	2 (1.2)
1	96 (56.5)
2	57 (33.5)
3	13 (7.6)
4	2 (1.2)
Number of proximal venous anastomoses	
0	17 (10.0)
1	98 (57.6)
2	49 (28.8)
3	6 (3.5)
4	0 (0)
Number of distal arterial and venous anastomoses	3.13 ± 1.56
Intraoperative complications	
Aortic rupture/dissection	0 (0)
Annulus rupture	0 (0)
Coronary artery obstruction	0 (0)
Prosthesis dislocation	0 (0)
Off-pump CABG	1 (0.4)
On-pump beating-heart CABG	8 (3.6)
Duration of intervention	
Aortic cross-clamp time (min)	79.4 ± 24.1 73.5 (IQR 60.8; 95.3)
Cardiopulmonary bypass time (min)	109.6 ± 34.5 104.5 (IQR 83.0; 134.0)
Operation time (skin-to-skin) (min)	224.2 ± 62.7 211 (IQR 178; 261.5)
Implantation 1st attempt	
INTUITY Elite valve size (mm)	23.8 ± 2.1 25 (IQR 23; 25)
19	10 (4.5)
21	32 (14.3)
23	69 (30.8)
25	81 (36.2)
27	32 (14.3)
Paravalvular leak (visually)	10 (4.5)
Extra stitch(es) placed	6 (2.7)
Valve implant time (min)	14.1 ± 7.4 12 (IQR 8; 19) 12 (8; 19)
Attempt successful	221 (98.7)
Implantation 2nd attempt	
2nd attempt performed	2 (0.9)
Paravalvular leak (visually)	1 (0.4)
Extra stitch(es) placed	0
Valve implant time (min)	12
Second cross-clamp needed	1 (0.4)
Attempt successful	2 (0.9)

Abbreviations: CABG, coronary artery bypass graft; IQR, interquartile range; SD, standard deviation.

electromechanical decoupling ($n = 1$), ventricular fibrillation ($n = 1$), multi-organ failure ($n = 2$), and myocardial infarction ($n = 1$).

Post-surgery, 31 patients (13.8%) experienced delirium, and 6 patients (2.7%) had a cerebrovascular accident/stroke, which was unrelated to the Edwards INTUITY Elite aortic valve. Notably, 17 patients (7.6%) required reoperation due to bleeding or tamponade, 1 patient (0.4%) reoperated due to INTUITY Elite valve issue (0.4%), and 1 patient (0.4%) reoperated due to CABG. Furthermore, four patients (1.8%) had post-surgical deep sternal wound infection, two patients (0.9%) had vascular complications due to peripheral obstruction, and one patient (0.4%) had MI unrelated to valve implantation. Notably, 17 patients (7.6%) required new PPI in which 12 patients (5.4%) required pacemakers due to valve implantation. Five patients (2.2%) required post-AVR dialysis (new onset).

Table 3 Hospital stay and discharge

	Mean ± SD, Median (IQR) or *n* (%) *N* = 224
Length of hospital stay (days)	12.0 ± 6.7 2 (IQR 1; 4)
ICU length of stay (days)	3.4 ± 4.8 10 (IQR 8;14)
Duration of mechanical ventilation (h)	17.5 ± 34.3
Discharged to	
Home	50 (22.3)
Standard rehabilitation	109 (48.7)
Other hospital	60 (26.8)
Death	5 (2.2)
Complications after surgery	
Transient ischemic attack/stroke	6 (2.7)
INTUITY Elite related	0 (0)
Delirium	31 (13.8)
Reoperations due to:	
Bleeding/tamponade	17 (7.6)
Other than bleeding	2 (0.9)
INTUITY Elite valve	1 (0.4)
CABG	1 (0.4)
Platelet concentrates used	60 (26.8)
Deep sternal wound infection	4 (1.8)
Unplanned PCI	0 (0)
Myocardial infarction	1 (0.4)
MI related to INTUITY Elite valve	0 (0)
New PPI	17 (7.6)
PPI valve-related	12 (5.4)
Vascular complication	2 (0.9)
Peripheral obstruction	2 (0.9)
Aortic dissection	0 (0)
Related to INTUITY Elite valve	0 (0)
Laboratory parameters	
Dialysis (new onset post AVR)	5 (2.2)
Creatinine	1.12 ± 0.49
Creatinine >2.3 mg/dL	6 (2.7)
Glomerular filtration rate	
>85	65 (29.0)
50–85	117 (52.2)
<50	42 (18.8)
Lactate dehydrogenase (U/L)	328.2 ± 136.1
S-Bilirubin	0.74 ± 0.51
Haptoglobin	64.1 ± 74.5

Abbreviations: AVR, aortic valve replacement; CABG, coronary artery bypass graft; ICU, intensive care unit; IQR, interquartile range; MI, myocardial infarction; PCI, percutaneous coronary intervention; PPI, permanent pacemaker implantation; SD, standard deviation.

ECG and Echocardiography Up to 3 Years

After the procedure, atrial fibrillation (AF) was noted in 32 patients (14.5%) upon discharge (19 patients had a new onset of AF), 9 patients (10.8%) exhibited AF at 1 year, and 12 patients (9.3%) at 3-year follow-up (►**Table 4**). Echocardiography revealed a consistent decrease in mean aortic valve pressure gradient (AV PG) at discharge (9.2 ± 3.7 mmHg), at 1 year (8.6 ± 3.1 mmHg), and 3 years (8.9 ± 4.6 mmHg) post-surgery compared with baseline (39.4 ± 13.4 mmHg). Conversely, the mean effective orifice area (EOA; 0.81 ± 0.23 cm^2) increased after surgery, measuring 1.90 ± 0.55 cm^2 at discharge, 2.1 ± 0.5 cm^2 at 1 year, and 2.0 ± 0.5 cm^2 at 3-year follow-up, compared with baseline EOA (0.81 ± 0.23 cm^2). In addition, the mean pulmonary arterial pressure-systolic (PAP sys) was decreased from 34.2 ± 11.6 mmHg (baseline) to 25.7 ± 10.2 mmHg at 1 year and 27.7 ± 8.5 mmHg at 3 years follow-up.

Furthermore, hemodynamic by valve size indicates a low mean AV PG (mmHg) with an increased EOA (cm^2) after the procedure across all valve sizes stable for up to 3 years (►**Fig. 1**). Compared with other sizes, ≤21 mm valves had a slightly higher transvalvular gradient and lower EOA at discharge, and 1- and 3-year follow-up.

Quality of Life and Functional Status

In the present analysis, the SF-12v2 questionnaire was used to assess the patient's QoL after surgery (►**Supplementary Table S1**, available in the online version). At 1 year after surgery, the mean SF-12v2 physical summary score was significantly increased to 44.1 ± 9.9 points ($p < 0.001$) compared with baseline and further remained stable at 3-year follow-up (44.2 ± 9.8 points; $p < 0.001$; ►**Fig. 2**). Similarly, the mean SF-12v2 mental summary score significantly increased to 52.3 ± 11.6 points ($p < 0.001$) at 1 year and remained stable at 3-year follow-up (52.5 ± 8.6 points; $p < 0.001$). The physical summary scores at 1 and 3 years were as expected for the general population mean (50.0 points), and mental summary scores were above 50.0 points, indicating a favorable QoL in patients.

Assessment of the functional status of the patients showed significant improvement after surgery. At 1 and 3 years, 66.0 and 59.2% of patients had NYHA class I symptoms, respectively, compared with baseline (►**Fig. 3**). There was a significant reduction in the proportion of patients belonging to the NYHA III/IV class at 1 year (4.5%) and 3 years (5.1%) compared with baseline (62.1%; ►**Supplementary Table S2**, available in the online version).

At baseline, 27% (45 patients) experienced angina CCS III/IV symptoms, which decreased to 0.6% (one patient) at 1 year after surgery. Notably, at 3 years, no patients (0%) had angina CCS III/IV symptoms (►**Supplementary Table S2**, available in the online version).

Anticoagulation/Antiplatelet Therapy

Compared with baseline (19.2%), the use of post-surgical anticoagulation therapy with various pharmacological agents increased at discharge (58.9%), 1 year (24.9%), and 3 years (24.7%) (►**Table 5**). Non-vitamin K oral

Table 4 Electrocardiography and echocardiography baseline up to 3 years

Mean ± SD or *n* (%)	Baseline	Discharge	1 year	3 years
Electrocardiogram				
Paced	6 (2.7)	23 (10.4)	11 (13.3)	16 (12.4)
Sinus rhythm	189 (85.5)	175 (79.2)	63 (75.9)	110 (85.3)
Atrial fibrillation	26	32 (14.5)	9 (10.8)	12 (9.3)
Atrial fibrillation (new onset)		19 (8.6)		
Atrial flutter	0 (0)	2 (0.9)	0	0
Atrioventricular block				
1st degree	16 (7.2)	26 (11.8)	7 (8.4)	17 (13.2)
2nd degree	3 (1.4)	1 (0.5)	0	0
3rd degree	0 (0)	5 (2.3)	3 (3.6)	3 (2.3)
LBBB complete	5 (2.3)	43 (19.7)	16 (19.5)	21 (16.4)
RBBB complete	3 (1.4)	2 (0.9)	1 (1.2)	4 (3.1)
Ventricular tachycardia	0	2 (0.9)	0	2 (1.6)
Unknown	1 (0.5)	1 (0.5)	0	0
Echocardiography				
Peak AV PG (mmHg)	64.9 ± 20.8	17.3 ± 6.6	15.6 ± 5.8	15.6 ± 6.7
Mean AV PG (mmHg)	39.4 ± 13.4	9.2 ± 3.7	8.6 ± 3.1	8.9 ± 4.6
LVOT VTI (cm)	20.8 ± 9.3	19.1 ± 8.2	24.7 ± 14.8	20.7 ± 5.4
LVOT Diameter (mm)	21.2 ± 7.4	–	17.0 ± 14.5	21.9 ± 6.3
LVEDD (mm)	52.5 ± 36.2	47.7 ± 7.3	49.1 ± 5.4	48.9 ± 5.7
EOA (cm^2)	0.81 ± 0.23	1.90 ± 0.55	2.1 ± 0.5	2.0 ± 0.5
EOA indexed (cm^2/m^2)	0.42 ± 0.12	0.96 ± 0.28	1.1 ± 0.2	1.0 ± 0.3
LVEF (%)	55.9 ± 9.8	54.0 ± 9.0	55.4 ± 10.5	54.9 ± 8.1
Aortic valve insufficiency ≥ moderate	18 (8.6)	1 (0.5)	0	1 (0.7)
Mitral valve stenosis ≥ moderate	0	0	0	0
Mitral valve insufficiency ≥ moderate	6 (2.9)	5 (2.6)	3 (4.1)	7 (5.3)
Tricuspid valve insufficiency	1 (0.5)	7 (3.6)	0	2 (1.5)
Pulmonary arterial pressure—systolic (mmHg)	34.2 ± 11.6		25.7 ± 10.2	27.7 ± 8.5

Abbreviations: AV PG, aortic valve pressure gradient; EOA, effective orifice area; LBBB, left bundle branch block; LVEDD, left ventricular end-diastolic diameter; LVEF; left ventricular ejection fraction; LVOT, left ventricular outflow tract; RBBB, right bundle branch block; VTI, velocity time integral.

anticoagulants were commonly used in these patients. Conversely, there was a decrease in patients using antiplatelet drugs at 1 year (69.2%) and 3 years (67.7%) compared with baseline (79.0%) and discharge (88.8%).

Clinical Outcomes at 1 Year and 3 Years

Post-surgery outcomes within 30 days (early outcomes) included death of five patients (2.2%), all attributed to cardiovascular causes (►**Table 6**). Beyond 30 days up to 3 years outcomes (late outcomes) showed death of 25 patients (4.6%/valve years [vy]), with 2 patients (0.2%/vy) dying of valve-related reasons, 8 patients (1.5%/vy) dying due to cardiovascular reasons, and 1 patient (0.2%/vy) dying of unknown reasons. Freedom from all-cause mortality at 1 and 3 years was 93.0% (95% confidence interval [CI] 89.6; 96.4) and 84.6% (95%CI 79.5; 89.7), respectively, while freedom from valve-related mortality was 99.5% at both time points.

Two patients (0.4%/vy) had SVD as a late outcome with freedom from events (FFE) 98.9% (95%CI 97.4; 100) at 3 years. Five patients (0.9%/vy) developed endocarditis at 3 years (FFE 97.4% [95%CI 95.0; 99.7]). No cases (0%/vy) of valve thrombosis were reported at 3 years. Furthermore, three patients (0.6%/vy) were reoperated due to AVR-related causes (FFE 96.9 [95%CI 94.5; 99.4]). Notably, after surgery, 17 patients (7.6%) required new PPI within 30 days, of which 12 patients (5.4%) had valve-related PPI and 7 patients (1.3%/vy) required PPI at 3 years with FFE 90.3% (95%CI 86.4; 94.3) and 88.5% (95%CI 84.1; 92.9) at 1 and 3 years, respectively. There were no instances (0%) of unplanned PCI and bypass obstruction within 30 days. However, eight patients (1.5%/vy) underwent unplanned

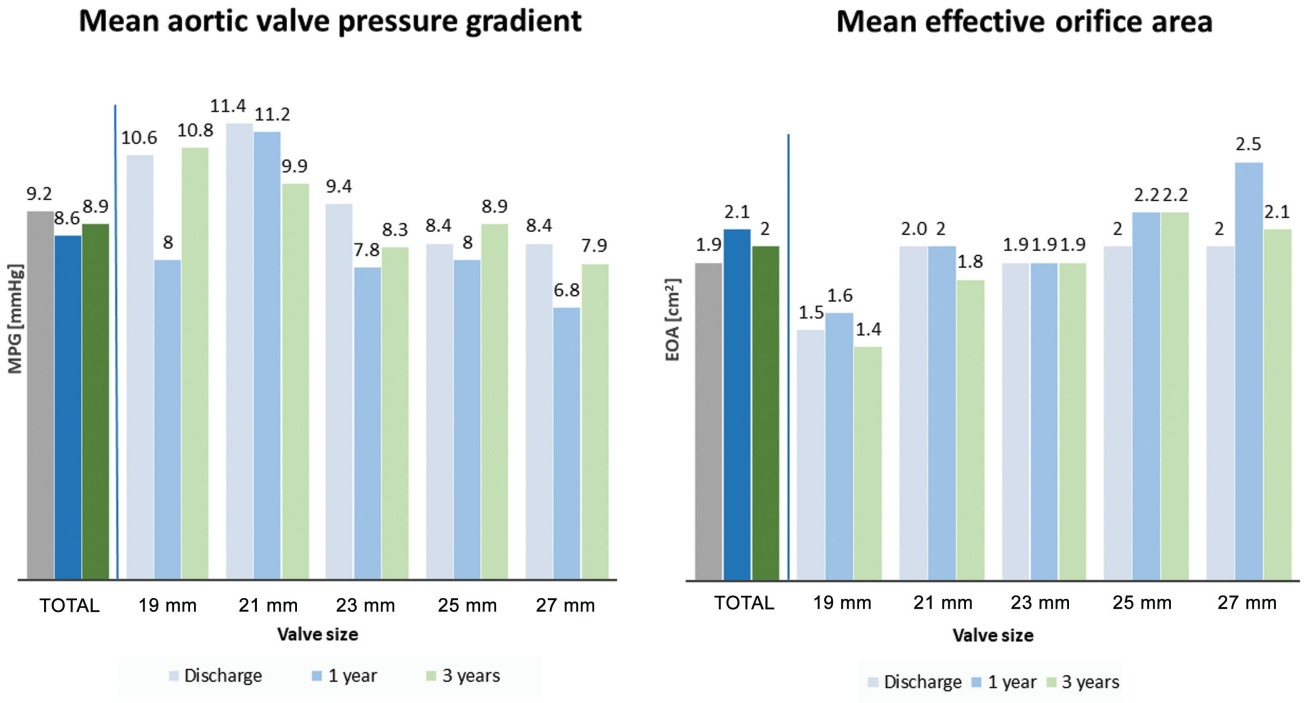

Fig. 1 Hemodynamic by valve size. EOA, effective orifice area; MPG, mean pressure gradient.

PCI, and three patients (0.6%/vy) developed bypass obstruction at 3 years. Additionally, within 30 days, one patient (0.4) had MI, and six patients (2.7%) had a stroke. At 3 years, three patients (0.6%/vy) developed MI, and five patients (0.9%/vy) developed a stroke.

Discussion

The 3-year results of combined RDVAR with CABG using Edwards INTUITY Elite aortic valve from the INCA registry demonstrated: (1) a good clinical outcome at 3 years with

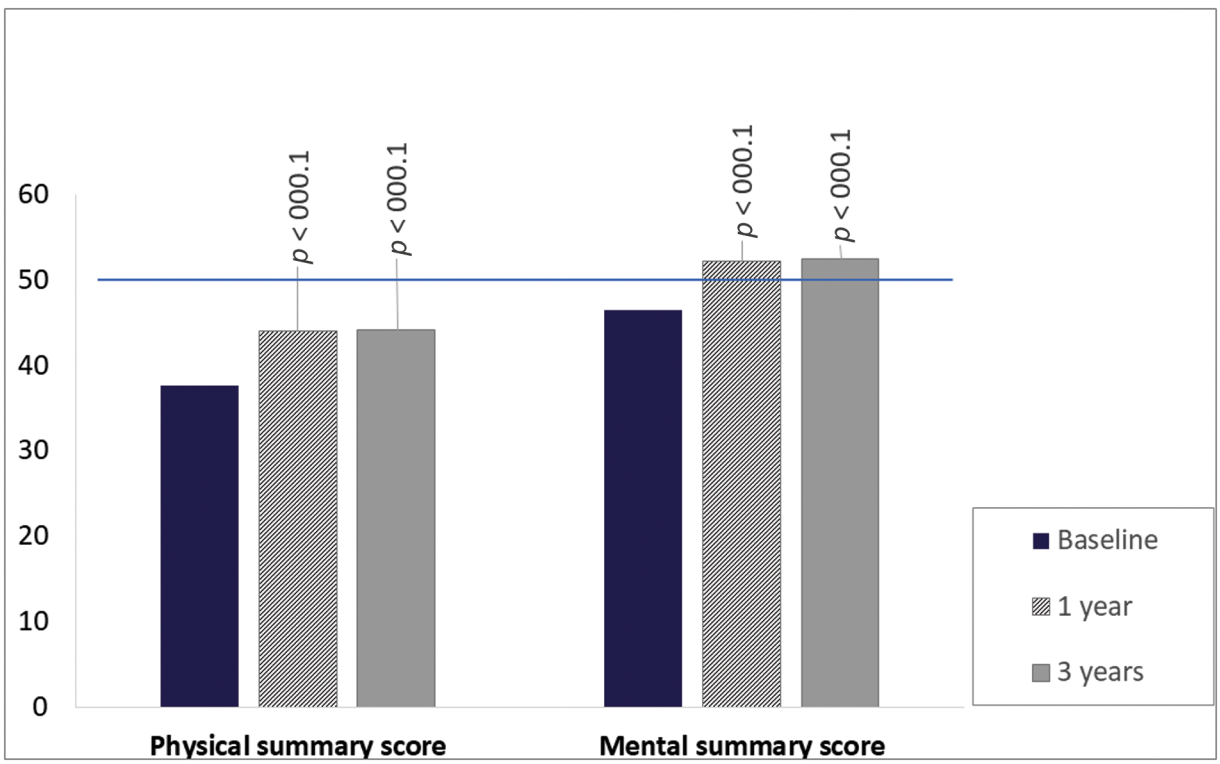

Fig. 2 Quality of life by SF-12v2 questionnaire. SF-12v2, the 12-item short-form survey version 2.

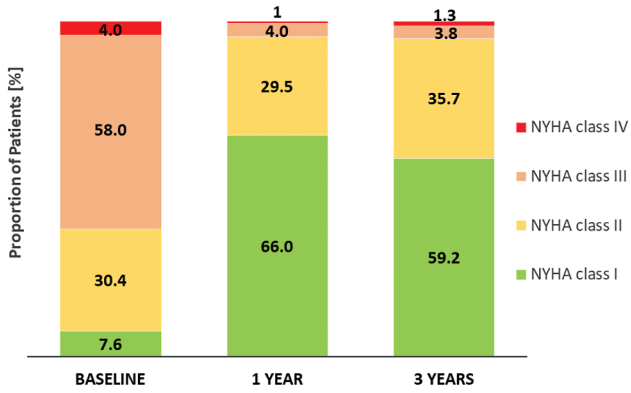

Fig. 3 NYHA functional status up to 3 years. NYHA, New York Heart Association.

99.5% (95%CI 98.6; 100) freedom from valve-related mortality and 98.9% (95%CI 97.4; 100) freedom from SVD; (2) a stable postoperative hemodynamic performance up to 3 years; (3) a significant improvement in the patient's QoL at 1 year ($p < 0.001$) and maintained up to 3 years ($p < 0.001$); and (4) a significant improvement in NYHA functional status up to 3 years ($p < 0.001$).

Clinical Outcomes Up to 3 Years

In our analysis, the patients had high surgical risk as predicted by logistic EuroSCORE I (7.8) and Euro SCORE II (3.5%). However, 30-day observed mortality (2.2%) of combined RDAVR/CABG was lower than predicted, with good clinical outcomes for up to 3 years after the procedure. Notably, there were no instances (0%) of in-hospital mortality related to

Table 5 Anticoagulation/antiplatelet therapy up to 3 years

n (%)	Baseline *N* = 224	Discharge *N* = 224	1 year *N* = 221	3 years *N* = 158
Anticoagulants	43 (19.2)	132 (58.9)	50 (24.9)	39 (24.7)
Vitamin K antagonists	8 (3.6)	92 (41.1)	17 (8.5)	13 (8.2)
Non-vitamin K oral anticoagulants	22 (9.8)	21 (9.4)	31 (15.4)	24 (15.2)
Low molecular weight heparin	11 (4.9)	34 (15.2)	1 (0.5)	2 (1.3)
Unfractionated heparin	4 (1.8)	16 (7.1)	0	1 (0.6)
Antiplatelet drugs	177 (79.0)	199 (88.8)	139 (69.2)	107 (67.7)
Acetylsalicylic acid	167 (74.6)	187 (83.5)	154 (76.6)	112 (70.9)
Other than acetylsalicylic acid	30 (13.4)	26 (11.6)	18 (9.0)	14 (8.9)

Table 6 Outcomes up to 3-year follow-up

	Early (≤30 days) *n* (%)	Late (>30 days to 3 years) *n* (%/vy)[a]	Freedom from event 1 year % (95%CI)	Freedom from event 3 years % (95%CI)
All-cause mortality	5 (2.2)	25 (4.6)	93.0 (89.6; 96.4)	84.6 (79.5; 89.7)
Cardiovascular	5 (2.2)	8 (1.5)	96.3 (93.8; 98.8)	93.3 (89.8; 96.9)
Valve-related	0 (0)	1 (0.2)	99.5 (98.6; 100)	99.5 (98.6; 100)
Unknown	0 (0)	1 (0.2)	100	99.3 (98.2; 100)
Structural valve deterioration	0 (0)	2 (0.4)	99.5 (98.5; 100)	98.9 (97.4; 100)
Prosthetic valve endocarditis	0 (0)	5 (0.9)	98.1 (96.2; 100)	97.4 (95.0; 99.7)
Prosthetic valve thrombosis	1 (0.4)	0	99.5 (98.6; 100)	99.5 (98.6; 100)
Reoperation valve- or CABG-related	3 (1.3)	3 (0.6)	97.7 (95.6; 99.7)	96.9 (94.5; 99.4)
Due to CABG	2 (0.9)	0	99.1 (97.8; 100)	99.1 (97.8; 100)
Due to aortic valve replacement	1 (0.4)	3 (0.6)	98.6 (97.0; 100)	97.8 (95.7; 100)
Reoperation due to bleeding/ tamponade	17 (7.6)	–	–	–
Unplanned percutaneous coronary intervention	0 (0)	8 (1.5)	98.5 (96.8; 100)	95.3 (92.1; 98.6)
Myocardial infarction	1 (0.4)	3 (0.6)	99.0 (97.7; 100)	97.9 (95.8; 99.9)
Bypass obstruction	0	3 (0.6)	99.5 (98.5; 100)	98.3 (96.4; 100)
Stroke	6 (2.7)	5 (0.9)	95.8 (93.2; 98.5)	94.7 (91.6; 97.8)
Permanent pacemaker implantation	17 (7.6)	7 (1.3)	90.3 (86.4; 94.3)	88.5 (84.1; 92.9)

Abbreviations: CABG, coronary artery bypass graft; CI, confidence interval.
Note: [a]$n = 224$ patients with 540 valve-years; mean follow-up 2.4 ± 1.1 years.

valve implantation in our study, while 2.2% all-cause mortality was observed, which is comparable to 2.5% recorded by Taghiyev et al[12] for RDAVR using the Edwards INTUITY valve system and higher than 1.8% of in-hospital mortality reported by Rahmanian et al[10] in their respective studies.

Moreover, after surgery, none of the patients (0%) experienced early prosthetic valve endocarditis in our study, while five patients (0.9%/vy) developed late endocarditis, yielding freedom from event rates of 98.1% (95% CI 96.2; 100) at 1 year and 97.4% (95% CI 95.0; 99.7) at 3 years, respectively. Similarly, Laufer et al[15] reported a low incidence of early or late prosthetic endocarditis for combined procedures, highlighting it as an additional advantage of rapid-deployment valves.

In our study, there was a slightly higher incidence (7.6%) of postoperative PPI within 30 days compared with 4.2% reported by Rahmanian et al for combined AVR using conventional valves and CABG[10] and lower than reported in other publications on rapid-deployment sutureless valves.[16–18] However, Rahmanian et al's study also revealed a higher PPI rate (12.5%) in combined RDAVR/CABG procedures, with lower rates observed in isolated RDAVR (4.5%), thus underscoring the heightened risk of PPI in combined RDAVR/CABG procedures.[10] Romano et al[18] and Matthews et al[19] identified conducting system diseases such as right bundle branch block (BBB), left BBB, first-degree atrioventricular block, left anterior hemiblock, and female gender, as well as larger valve size, as significant contributors to postoperative PPI following RDAVR. However, in our study, we were unable to establish a clear association between PPI and any of the aforementioned risk factors. Although reduced operative, CPB, and cross-clamp times are beneficial, these advantages must be weighed against the increased rates of associated PPI as studies have noted (in the case of isolated AVR) that the reduction in operative, CPB, and cross-clamp times does not obviously translate into a better clinical outcome and must therefore be weighed against the higher PPI rate which may increase the risk of endocarditis in the long term.[20,21] In our study, we did not explore such an association.

Surgical Outcomes and Hemodynamic Performance

The first attempt for valve implantation was successful in 221 patients (98.7%), and only 2 patients (0.9%) required a second implantation attempt (successful). There were no intraoperative complications recorded in our analysis. This high level of technical success aligns with findings from other published literature.[8,22] The mean aortic cross-clamp time in our study was 79.4 ± 24.1 minutes (median 73.5 minutes), and CPB time was 109.6 ± 34.5 minutes (median 104.5 minutes), which was higher compared with the cross-clamp (67.0 minutes) and CPB time (103.2 minutes) reported by Rahmanian et al for combined RDAVR (Edwards INTUITY Valve System) and CABG procedure.[10] Also, in their study, the mean number of arterial and venous anastomoses was 2.08 ± 1.0, which is lower than the 3.13 ± 1.56 anastomoses required in our study. However, Gonzalez-Barbeito et al noted in their study that 5% of patients undergoing RDAVR received one or two grafts, while 25% received three or more grafts, which is consistent with our findings.[5]

Furthermore, in our study, the mean implanted valve size was 23.8 ± 2.1 mm (median 25mm), which was comparable to the mean valve size of 23.3 ± 1.8 mm (median 25 mm) reported by Rahmanian et al.[10] In our analysis, combined RDAVR with CABG has demonstrated a stable hemodynamic status over the course of 3 years. Postoperatively, the mean AV PG was reduced to 9.2 ± 3.7 mmHg at discharge, further decreasing to 8.6 ± 3.1 mmHg at 1 year and stabilizing at 8.9 ± 4.6 mmHg by 3-year mark, compared with baseline mean AV PG (39.4 ± 13.4 mmHg). Similarly, EOA has significantly increased to 1.90 ± 0.55 cm^2 at discharge, maintained at 2.1 ± 0.5 cm^2 at 1 year and 2.0 ± 0.5 cm^2 at 3 years, compared with baseline EOA (0.81 ± 0.23 cm^2). A similar trend of improved hemodynamic performance within 30 days and 1 year after RDAVR was reported by several studies.[6–8,10,17] Moreover, the 3-year results from the TRITON trial demonstrated a significant decrease in mean AV PG at 1 year (9.0 ± 3.6 mmHg) and 3 years (8.7 ± 4.1 mmHg) compared with discharge (10.7 ± 4.2 mmHg), indicating sustained hemodynamic stability after combined RAVR/CABG procedure.[8]

Along with hemodynamic benefits in our study, a noteworthy reduction in the proportion of patients having NYHA class III/IV symptoms at 1 year (4.5%) and 3 years (5.1%) was observed compared with baseline (62.1%). Similar improvement was also confirmed in 3-year results of the TRITON trial, showing 53% of patients in NYHA class III or IV at baseline, and improvement in functional class was observed in 90% of these patients during the follow-up period,[8] indicating a consistent trend toward enhanced functional status over time.

Quality of Life

In this study, we evaluated the health-related QoL using the SF-12v2 questionnaire, revealing a significant improvement in QoL compared with baseline in both physical and mental health dimensions at 1 year ($p < 0.001$) post-surgery with further improvement at 3 years ($p < 0.001$). To our knowledge, this is the first report of QoL measurement based on SF-12v2 for a combined RDAVR/CABG procedure over a 3-year period. However, findings from the TRANSFORM US clinical trial also reported a significant improvement in QoL, with physical health scores increasing from 41.8 ± 10.2 to 47.6 ± 9.7 ($p < 0.0001$) and mental health scores increasing from 51.3 ± 9.9 to 54.3 ± 8.6 ($p < 0.0001$) at 1 year from baseline.[17] Furthermore, a study by Borger et al compared the QoL using EQ-5D between patients undergoing minimally invasive surgery RDAVR (Edwards INTUITY Elite bioprosthesis) and conventional full sternotomy AVR revealing consistent EQ-5D scores from baseline to 3 months with no difference in both groups: baseline EQ-5D scores were 0.9 ± 0.1 and 0.9 ± 0.1, and 3-month EQ-5D scores were 0.9 ± 0.1 and 0.9 ± 0.1, respectively ($p = 0.630$).[23]

Since it is an industry-funded registry to evaluate the performance of Edwards INTUITY valve system, the second commercial sutureless valve, PERCEVAL, was not considered.

Limitation

This study has some obvious limitations. First, the data was based on the prospective, small cohort from the INCA Germany registry applicable to clinical practice in Germany. Additionally, there was no active comparator group with other valve generation or conventional bioprosthesis in our study. Furthermore, we did not compare valve data with the outcomes and performance of conventional sutured bioprosthesis in combined surgery.

Conclusion

The 3-year results from the INCA registry showed very satisfactory valve performance with a stable hemodynamic profile, improved QoL, and good safety outcomes in patients undergoing combined RDAVR with CABG using using Edwards INTUITY Elite aortic valve.

Ethical Approval Statement

The study documents were submitted to the ethics committees responsible for each site and there were no objections to conducting the study. Formal written informed consent was obtained from every patient before enrolment.

Authors' Contribution

A.D., J.S., M.S., F.F., and A.L. were involved in the conception and design of the study. The idea was discussed and refined by the rest of the authors. D.M.V., J.G., R.G., P.M., M.K., R.M., G.W., T.W., and J.G. contributed significantly to study execution, acquisition of data, analysis, and interpretation. P.B. drafted the manuscript and all the other authors revised the article for important intellectual content. All the authors gave approval for the final version.

Data Availability Statement

All relevant data within this manuscript will be shared upon reasonable request to the corresponding author.

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Conflict of Interest

None declared.

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