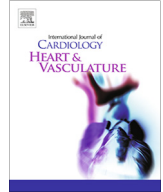




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## Patients younger than 70 undergoing transcatheter aortic valve implantation: Procedural outcomes and mid-term survival

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### ABSTRACT

**Introduction:** Based on recent data, the indication for transcatheter aortic valve implantation (TAVI) is expanding to individuals at lower surgical risk, who are generally younger than subjects historically treated for severe aortic stenosis. Indeed, younger patients have traditionally been under-represented in current TAVI literature. The aim of the present study is to report about clinical features, procedural outcomes and mid-term outcomes of patients younger than 70 who underwent TAVI in a single high-volume center.

**Materials and methods:** Consecutive patients younger than 70 years of age who underwent TAVI for severe, symptomatic aortic stenosis between 2007 and 2019 at a single, tertiary referral center have been included in this retrospective study. Procedural and mid-term outcomes were analyzed, comparing 1st generation with 2nd generation devices.

**Results:** Between 2007 and 2019, 1740 TAVI procedures were performed in our center. Among these, one hundred twenty-nine (7.4%) patients were younger than 70 years at the time of the intervention and were included in the present analysis. Fifty-eight patients (45%) were implanted with a 1st generation prosthesis while seventy-one patients (55%) were implanted with a 2nd generation device. Reasons which lead to a transcatheter approach in this population were: previous CABG (27.9%); porcelain aorta (24%); severe left ventricular systolic dysfunction (21.7%); prior chest radiation (19.4%); severe lung disease (8.5%); hemodynamic instability (7.0%); advanced liver disease (4.6%) and active cancer (3.9%). Overall device success rate was 89%, with no differences among 1st and 2nd generation devices. Threeyears all-cause mortality was 34%, with no difference among the two groups. Low incidence of aortic-valve re-intervention was observed at mid-term follow-up (late valve re-intervention = 2.3%).

**Conclusions:** TAVI in young patient with appropriate indication for intervention is a safe procedure, associated with low rate of in hospital mortality and low rate of severe complications both with 1st and with 2nd generation devices. When considering long term durability, more data are needed; in our case series long-term follow up shows a good survival and also an extremely low rate of valve re-intervention.

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**Abbreviations:** BEV, balloon expandable valve; CABG, coronary artery bypass graft; SAVR, surgical aortic valve replacement; SEV, self expandable valve; TAVI, transcatheter aortic valve implantation; THV, transcatheter heart valve.

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### 1. Introduction

Aortic stenosis (AS) is the most common valve disease in Europe and North America and it is increasing in prevalence due to the ageing population [1].

Nowadays, transcatheter aortic valve implantation (TAVI) is deemed a safe and effective procedure for the treatment of severe

symptomatic AS in patients at prohibitive [2,3] or high surgical risk [4].

In the last few years TAVI indication moved to the intermediate [5,6] and low-risk population [7–9,10]. However, since AS in its most common etiology is a degenerative senile, the majority of patients undergoing TAVI in the recent past was represented by elderly (mostly over 75 years old) both in clinical trials and in real world scenarios [11–14].

Instead, patients younger than 70 with severe AS usually presented low surgical risk and were so far referred for surgical aortic valve replacement (SAVR) [15]. However, this population sometimes has significantly increased surgical risk or contraindications for surgery (porcelain aorta, prior chest radiation, prior cardiac surgery, active cancer, advanced lung or liver disease, etc). In this particular setting, TAVI should be the treatment of choice despite the young age [16].

There is little available data about procedural and mid-term outcomes of young patients treated with TAVI [17,18].

Aim of the present study was to investigate clinical features, procedural outcomes and mid-term survival of patients younger than 70 who underwent TAVI at a single, high-volume, tertiary referral center.

## 2. Materials and methods

This is a single-center retrospective study including all patients younger than 70 who underwent TAVI for severe, symptomatic aortic stenosis at San Raffaele Scientific Institute, Milan, Italy, between 2007 and 2019.

Baseline clinical and echocardiographic characteristics were collected for each patient. Diagnosis of severe AS was defined as one or more of the following findings: an aortic valve area (AVA) < 1 cm<sup>2</sup>, an indexed AVA < 0.6 cm<sup>2</sup>/m<sup>2</sup>, a maximum jet velocity (Vmax) > 4 m/s, or a mean transvalvular gradient > 40 mmHg at transthoracic echocardiography [19]. Pulmonary hypertension was defined as systolic pulmonary artery pressure (PAPs) > 40 mmHg [20]. Aortic regurgitation, mitral regurgitation and grading of paravalvular leaks [21] (PVL) were defined according to current guidelines [22]. Functional status was evaluated according to New York Heart Association (NYHA) classification. Hemodynamic instability was defined as need for intravenous inotropes, mechanical circulatory support or invasive ventilation. Patients with bioprosthetic aortic valve degeneration (i.e. valve-in-valve procedures) were excluded from the present study.

All patients were evaluated by a multidisciplinary Heart Team comprising of cardiologists, interventional cardiologists, cardiothoracic surgeons, and cardiac anesthetists. The decision to perform TAVI was based on severity of symptoms, risk evaluation and contraindications to surgery, as expressed by the Heart Team.

TAVI was performed through transfemoral, *trans*-axillary, transapical or transaortic approach according to clinical judgment and after multimodality imaging evaluation, as already described [23]. The choice of prosthesis type was left to the operator's discretion. Trans-axillary, transapical or transaortic procedures were performed under general anesthesia; transfemoral procedures were performed under general anesthesia or conscious sedation. The decision to perform pre-dilation or post-dilation was left to operator's discretion. Valve deployment was performed according to manufacturer's instruction.

Patients included in the study were treated with different transcatheter heart valve (THV) devices: Edwards Sapien, Edwards Sapien XT and Edwards Sapien 3 (Edwards Lifesciences, Irvine, CA, USA); CoreValve and CoreValve Evolut R (Medtronic, Minneapolis, MN, USA); Portico (Abbot, Chicago, IL, USA); Lotus and Acurate Neo (Boston Scientific, Marlborough, MA, USA); NVT

Allegra (New Valve Technology, Hechingen, Germany); Direct Flow (Direct Flow Medical, Santa Rosa, CA, USA), Myval (Meril Life Sciences Pvt. Ltd., Vapi, Gujarat, India).

Balloon expandable prosthesis were all the Edwards and the Myval; self-expanding prosthesis were CoreValve, Evolut R, Portico, Acurate Neo, Allegra and Direct Flow; mechanically expandable prosthesis was the Lotus.

Data were prospectively recorded but retrospectively analyzed. All subjects gave informed consent for data collection and analysis by signing TAVI consent.

All outcomes were defined according to Valve Academic Research Consortium (VARC)-2 criteria [24]. The primary endpoint of the study was the VARC-2 defined device success (absence of procedural mortality, correct positioning of a single valve in the correct anatomic position, the absence of prosthesis-patient mismatch as well as of moderate or greater aortic regurgitation and mean aortic gradient < 20 mmHg). Secondary endpoints were *peri*-procedural efficacy outcomes (prosthesis embolization, second valve implantation, coronary obstruction, final paravalvular leak less than moderate) and *peri*-procedural safety outcomes (major vascular complications, stroke, major or life-threatening bleeding). Rate of new permanent pacemaker (PM) implantation and development of post-procedural left bundle branch block (LBBB) were also collected.

All-cause mortality and need for valve re-intervention (SAVR or TAVI-in-TAVI) were evaluated in-hospital and at follow up, through clinical visits or telephone calls.

### 2.1. Subgroup analysis

In order to identify a potential role of THV generation on procedural, in-hospital and mid-term outcomes, we divided overall population in two subgroups: 1st generation THV (Edwards Sapien, Edwards Sapien XT and CoreValve from 2007 to 2014) and 2nd generation THV (Edwards Sapien 3, CoreValve Evolut R, Allegra, Portico, Lotus, AcurateNeo, Directflow, Myval from 2014 to 2019). THV were also classified in self-expandable (SEV), balloon-expandable (BEV) or mechanically expandable (MEV). Both primary and secondary endpoints were assessed for each subgroup and compared in the statistical analysis.

### 2.2. Statistical analysis

Statistical analyses were performed using SPSS (IBM, Armonk, NY) software. Data were reported as mean ± standard deviation for continuous variables, and absolute numbers (percentages), for qualitative variables. Chi square test was performed for categorical to test categorical variables association; t-student test was performed for continuous group differences in continuous variables. Time to event outcomes was analyzed using Kaplan Mayer Survival estimate and logistic regression analyses to obtain death hazard ratio according to different THV generation, baseline characteristics and procedural outcomes. Statistical significance was established for p value < 0.05.

## 3. Results

Between 2007 and 2019, 1740 TAVI patients underwent TAVI at San Raffaele Scientific Institute; among these, one hundred twenty-nine (7.4%) patients were younger than 70 years at the time of the intervention and were included in the present analysis. Fifty-eight patients (45%) were implanted with a 1st generation prosthesis while seventy-one patients (55%) received a 2nd generation device. Baseline characteristics are reported in Table 1.

**Table 1**  
Baseline Clinical Characteristics.

	Overall study population (n = 129)	1st generation THV (n = 58)	2nd generation THV (n = 71)	p value
Age (years)	63.6 ± 6	64.4 ± 6	63 ± 6	0.25
Female sex	58 (45)	25 (43.1)	33 (46.5)	0.71
Previous MI	29 (22.5)	11 (19)	18 (25.4)	0.38
Previous PCI	41 (31.8)	16 (27.6)	25 (35.2)	0.35
Previous CABG	36 (27.9)	20 (34.5)	16 (22.5)	0.13
Previous Cardiac Surgery	47 (36.4)	25 (43.1)	22 (31.4)	0.17
Coronary Artery Disease	64 (49.6)	29 (50)	35 (49.3)	0.94
Diabetes	52 (40.3)	27 (46.6)	25 (35.2)	0.19
Insulin-dependent diabetes	32 (24.8)	20 (34.5)	12 (16.9)	0.02
Hypertension	92 (71.3)	46 (79.3)	46 (64.8)	0.07
Prior stroke or TIA	10 (7.8)	4 (6.9)	6 (8.5)	0.74
COPD	33 (25.6)	15 (25.9)	18 (25.4)	0.94
Peripheral Artery Disease	40 (31)	20 (34.5)	20 (28.2)	0.44
GFR (ml/min)	64 ± 35	60.4 ± 53	67.7 ± 35	0.24
GFR < 60 ml/min	55 (42.6)	28 (48.3)	27 (38)	0.24
Renal Replacement Therapy	18 (14)	9 (15.5)	9 (12.7)	0.47
BMI (kg/m <sup>2</sup> )	26.5 ± 6	25.9 ± 5	26.6 ± 5	0.47

Values are mean ± SD or n (%).

MI: Myocardial infarction. PCI: percutaneous coronary intervention. CABG: coronary artery bypass graft. TIA: transient ischemic attack. COPD: chronic obstructive pulmonary disease. GFR: glomerular filtration rate. RRT: renal replacement therapy.

Mean age was 63.6 ± 6 years, 45% were female. Cardiovascular risk factors were highly prevalent: 40.3% of patients were diabetic, 71.3% had hypertension and 42.6% of patients had an estimated Glomerular Filtration Rate (eGFR) < 60 ml/min/1.73 m<sup>2</sup>. Mean eGFR was 64 ± 35 ml/min, with 14% of patients being on chronic renal replacement therapy. Half of the patients (49.6%) had history of coronary artery disease (CAD), 22.5% of patients had a history of prior myocardial infarction (MI), 31.8% of patients had history of prior percutaneous coronary intervention (PCI), 36.4% of patients had history of previous cardiac surgery and 27.9% of patients had history of prior coronary artery by-pass graft (CABG).

Echocardiographic characteristics are shown in [table 2](#). Ten patients had a bicuspid aortic valve (7.7%). Mean aortic gradient was 44.9 ± 14 mmHg, 30.2% of patients had low-flow low-gradient aortic stenosis. Mean left ventricle ejection fraction (EF) was 48.6 ± 14%, 21.7% of patients had severe left ventricle systolic dysfunction (EF ≤ 35%). More than half of patients (57.4%) were in NYHA functional class 3 or 4. Nine patients (7%) were hemodynamically unstable at the time of intervention. Baseline echocardiographic characteristics and NYHA functional class were similar between subgroups.

**Table 2**  
Baseline echocardiographic characteristics and symptoms. [Table 2](#): Baseline echocardiographic characteristics and symptoms.

	Overall Study population (n = 129)	1st generation THV (n = 58)	2nd generation THV (n = 71)	p value
Ejection Fraction (%)	48.6 ± 14	49.2 ± 16	48.1 ± 14	0.68
Ejection Fraction ≤ 35%	28 (21.7)	13 (22.4)	15 (19.7)	0.86
Mean aortic gradient (mmHg)	44.9 ± 14	48 ± 16	42.3 ± 14	0.16
LF-LG Aortic Stenosis	39 (30.2)	15 (25.9)	24 (33.8)	0.32
Bicuspid aortic valve	10 (7.7)	6 (10.3)	4 (5.6)	0.32
Porcelain Aorta	31 (24)	16 (27.6)	15 (21.1)	0.39
sPAP (mmHg)	41 ± 15	42.6 ± 15	41.1 ± 15	0.58
Pulmonary Hypertension	70 (54.3)	37 (63.8)	33 (46.5)	0.11
Aortic regurgitation > moderate	20 (15.5)	8 (14)	12 (17)	0.14
Mitral regurgitation > moderate	15 (11.6)	4 (7)	11 (15)	0.08
NYHA class				
NYHA class II	55 (42.6)	25 (43.1)	30 (42.3)	0.21
NYHA class III	60 (46.5)	26 (44.8)	34 (47.9)	0.98
NYHA class IV	14 (10.9)	7 (12.1)	7 (9.9)	0.88
Hemodynamic instability	9 (7.0)	5 (8.6)	4 (5.6)	0.51
STS-M (mean)	7.35 ± 12	10.5 ± 14	5.2 ± 8	0.02
STS-M > 8%	23 (18)	16 (27.6)	7 (9.9)	0.03

Values are mean ± SD or n (%).

LF-LG-Aortic Stenosis: low-flow low-gradient aortic stenosis. NYHA: New York Heart Association. sPAP: systolic pulmonary artery pressure. STS-M: society of thoracic surgeon's mortality risk.

The Society of Thoracic Surgeons -mortality (STS-M) score in the overall population was 7.35%: it was significantly higher in the 1st THV generation group than in the 2nd one (10.5% vs 5.2%, p = 0.02). Furthermore, 18% of patients in the overall population presented an STS score > 8%: this rate was again significantly higher in the 1st generation group (p = 0.03).

### 3.1. TAVI indication

Reasons which lead to a transcatheter approach in this population were as follow: 27.9% of patients had already undergone coronary artery bypass graft (CABG) with patency of retrosternal grafts; 24% of patient had porcelain aorta; 21.7% of patients had severe left ventricular systolic dysfunction; 19.4% of patients had a history of prior chest radiation (as part of malignancy treatment, mostly Hodgkin lymphoma or breast cancer); 8.5% of patients had severe lung disease; 7.0% were hemodynamically unstable, 4.6% of patients had advanced liver disease (mostly hepatic cirrhosis), and 3.9% had active cancer. Moreover, 21% of patients had more than one risk factor/contra-indication for cardiac surgery (see [Table 3](#) and [Fig. 1](#)).

**Table 3**  
TAVI indication.

	Overall study population (n = 129)
Prior CABG	36 (27.9)
Porcelain Aorta	31 (24)
Severe LV systolic dysfunction	28 (21.7)
Prior chest radiation	25 (19.4)
Severe lung disease	11 (8.5)
Hemodynamic instability	9 (7.0)
Advanced liver disease	6 (4.6)
Active cancer	5 (3.9)
> 1 risk factor for cardiac surgery	27 (21)

CABG: coronary artery bypass graft. LV: left ventricle.

**3.2. Procedural details**

Access site was transfemoral (TF) in 78.5% of cases (67.2% in the 1st generation vs 87.3 in the 2nd generation, p = 0.006) and transapical in 13.5%.

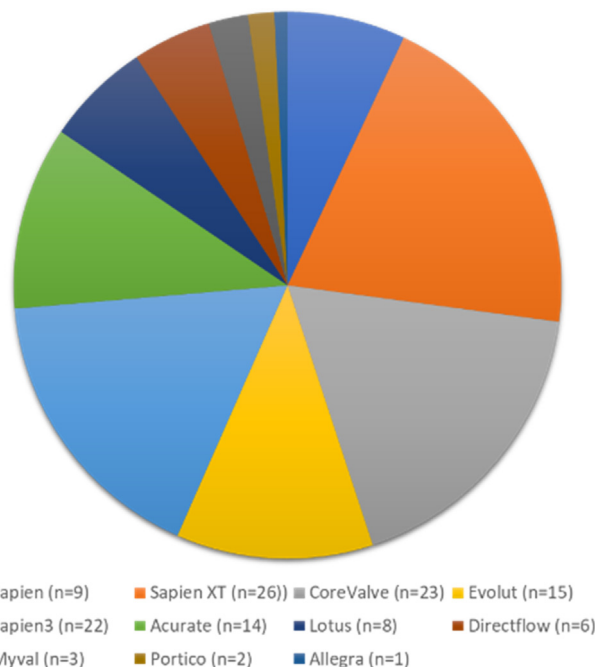
Compared to 1st generation group, significantly less individuals receiving a 2nd generation prosthesis received a BEV (60.3% vs 35.2%, p = 0.004) in this subgroup. Implanted TAVI devices are reported in Fig. 2.

Aortic valve pre-dilation was performed in 60.5% of cases and prosthesis post-dilation was performed in 21.7% of cases. In case of transfemoral access, percutaneous closure device was implanted in 99% of cases, mostly Prostar™ in the 1st generation and Proglide™ in the 2nd generation.

**3.3. Procedural and in-hospital outcomes**

VARC-2 device success was achieved in 89% of cases, with no differences among the two groups; prosthesis embolization occurred in 5 cases, all of them requiring a second valve implantation and one case resulting in fatal coronary obstruction. Rate of major vascular complications (according to VARC-2 definition) was 5.4% (8.6% in the 1st generation vs 2.8% in the 2nd generation, p = 0.15) (Tables 4–5).

The rate of stroke was 2.3% in the overall population (1.7% in the 1st generation vs 2.8% in the 2nd generation, p = 0.68).

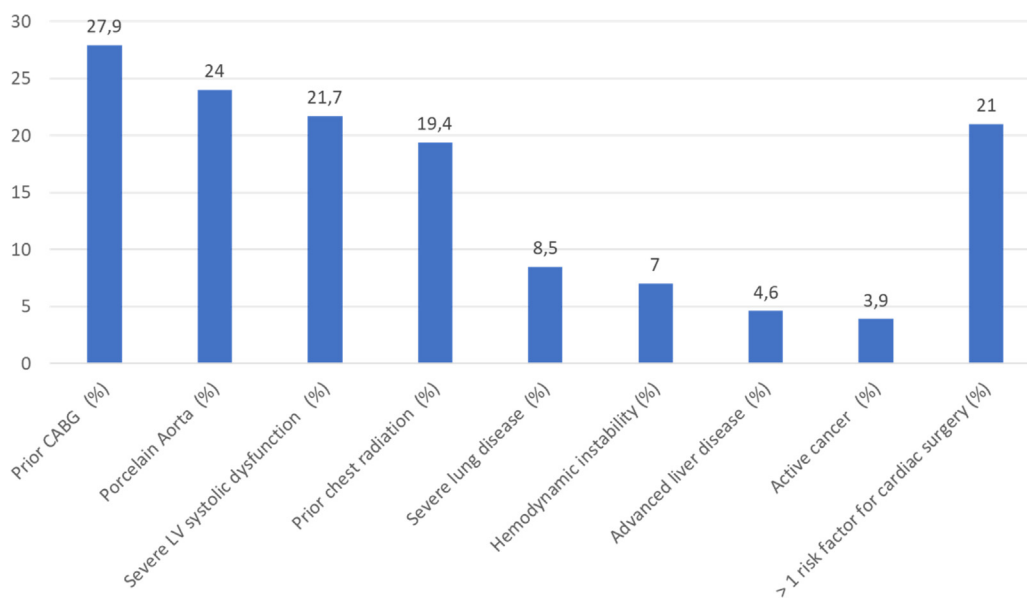


**Fig. 2.** TAVI devices.

The overall rate of major or life-threatening bleeding was 25.6%; it was significantly higher in the 1st generation than in the 2nd generation group (44.8% vs 9.8%, p < 0.001).

In hospital mortality was similar between subgroups: 6.2% in the overall population, 3.4% in the 1st generation vs 8.5% in the 2nd generation, p = 0.24). Among the 8 patients who died in hospital, 6 were receiving an emergent procedure due to hemodynamic instability, one died as consequence to prosthesis embolization and fatal left coronary ostium occlusion, one died because of limb ischemia after prolonged mechanical circulatory.

Paravalvular leak was less than moderate in 95.3% of procedures, 93.1% in the 1st generation vs 97.2% in the 2nd generation (p = 0.27).



**Fig. 1.** TAVI indication.

**Table 4**  
Procedural Details.

	Overall study Population (n = 129)	1st generation THV (n = 58)	2nd generation THV (n = 71)	p value
General Anesthesia	35 (27.1)	24 (41.4)	11 (15.5)	0.001*
Transfemoral	101 (78.5)	39 (67.2)	62 (87.3)	0.006*
Transapical	17 (13.5)	11 (19)	6 (8.5)	0.79
Transaortic	4 (3.1)	4 (6.9)	0	0.025*
Transaxillary	6 (5.4)	4 (6.9)	3 (4.2)	0.51
BEV	60 (46.5)	35 (60.3)	25 (35.2)	0.004*
SEV	61 (47.3)	23 (39.7)	38 (53.5)	0.117
MEV	8 (6.2)	0	8 (11.3)	0.008*
Percutaneous closure device, when transfemoral (%)	100/101 (99)	38/39 (97.4)	62/62 (100)	0.95
Prostar™ n(%)	70 (69)	35 (89.7)	35 (56.5)	0.001*
Proglide™ n(%)	26 (26)	2 (5.1)	24 (39)	0.001*
Aortic valve Predilation	78 (60.5)	43 (74.1)	35 (49.3)	0.04*
Prosthesis Postdilation	28 (21.7)	11 (19)	17 (23.9)	0.49

BEV: balloon expandable valve. MEV: mechanically expandable valve. SEV: self-expanding valve.

**Table 5**  
Procedural Outcomes.

	Overall study population (n = 129)	1st generation THV (n = 58)	2nd generation THV (n = 71)	p value
Device success (%)	115 (89)	53 (91.4)	62 (87.3)	0.97
Prosthesis embolization	5 (3.9)	1 (1.7)	4 (5.6)	0.25
Second valve implantation	5 (3.9)	1 (1.7)	4 (5.6)	0.25
Coronary obstruction	1 (0.7)	0	1 (1.4)	0.36
Major vascular complications	7 (5.4)	5 (8.6)	2 (2.8)	0.15
Stroke	3 (2.3)	1 (1.7)	2 (2.8)	0.68
Major or life-threatening bleeding	33 (25.6)	26 (44.8)	7 (9.8)	<0.001*
Paravalvular leak less than moderate	122 (95.3)	54 (93.1)	68 (97.2)	0.27
New Permanent Pacemaker implantation *	6 (5.4)	1 (1.9)	5 (8.4)	0.13
New-LBBB	15 (11.6)	3 (5.2)	12 (16.9)	0.039*
In Hospital death	8 (6.2)	2 (3.4)	6 (8.5)	0.24

**Table 5 TAVI outcomes.** LBBB: left bundle branch block.

\* patients with pre-procedural permanent Pacemaker have been excluded from the analysis.

Eighteen patients (14% of overall population) had already been implanted an ICD or permanent PM before TAVI procedure. Among the remaining patients, the rate of new permanent PM implantation after TAVI was 5.4%, with no difference between 1st and 2nd generation devices (1.9% vs 8.4%,  $p = 0.12$ ).

The rate of new LBBB was significantly lower in the 1st than in the 2nd generation group (5.2% vs 16.9%,  $p = 0.03$ ).

### 3.4. Follow-up

The median follow-up period was 1195 days (interquartile range 208–1755).

Overall 3-years all-cause mortality rate was 34% and did not differ between patients receiving 1st and 2nd generation prosthesis ( $p = 0.574$ ) (Fig. 3).

Logistic regression analysis was performed to analyze the predictors of 3 years all-cause mortality (Table 6).

Among baseline characteristic, diabetes, CKD and STS-score above 8% resulted as predictors of 3 years all-cause mortality on univariate analysis. Moreover, on univariate analysis, post-procedural major bleeding resulted as significant predictors of 3 years all-cause mortality.

On multivariate analysis, only diabetes, CKD and STS-score above 8% resulted as statistically significant independent predictors of 3 years all-cause mortality.

Low incidence of aortic-valve re-intervention was observed at follow-up: two patients underwent SAVR < 30 days after TAVI because of PVL causing severe aortic regurgitation (early valve re-intervention, 1.5%). At long-term follow up, 3 patients underwent TAVI-in-TAVI for THV degeneration (late valve re-intervention, 2.3%).

## 4. Discussion

The main results of the present study are as follows:

- On a large single-center retrospective study, one hundred twenty-nine patients younger than 70 years (7.4% of the overall TAVI population) were treated with TAVI because deemed at increased surgical risk
- Most frequent reasons which lead to TAVI were previous CABG, porcelain aorta, severe left ventricular systolic dysfunction and previous chest radiation
- In-hospital outcomes were good, with no difference among 1st and 2nd generation THV groups in terms of efficacy end-points, while among safety end-points major bleeding resulted significantly lower with current generation devices
- Mid-term all-cause mortality rate was not negligible, likely because of the significant comorbidities of the study population; however, no differences were documented among 1st and 2nd generation THV groups on multivariate logistic regression analysis.

During the last decade, TAVI has completely changed the treatment of severe aortic stenosis. When comparing 1 year all-cause mortality, TAVI was initially proven to be superior to medical therapy in patients who were not deemed surgical candidates[2]; then TAVI was shown to be non-inferior to surgery in high[25] and intermediate risk[5,6] population. Low risk population was also tested for comparison, and results confirmed the non-inferiority of TAVI when compared to SAVR[7–9].

However, data about mid-term outcome of young patient (i.e. younger than 70) treated with TAVI are lacking.



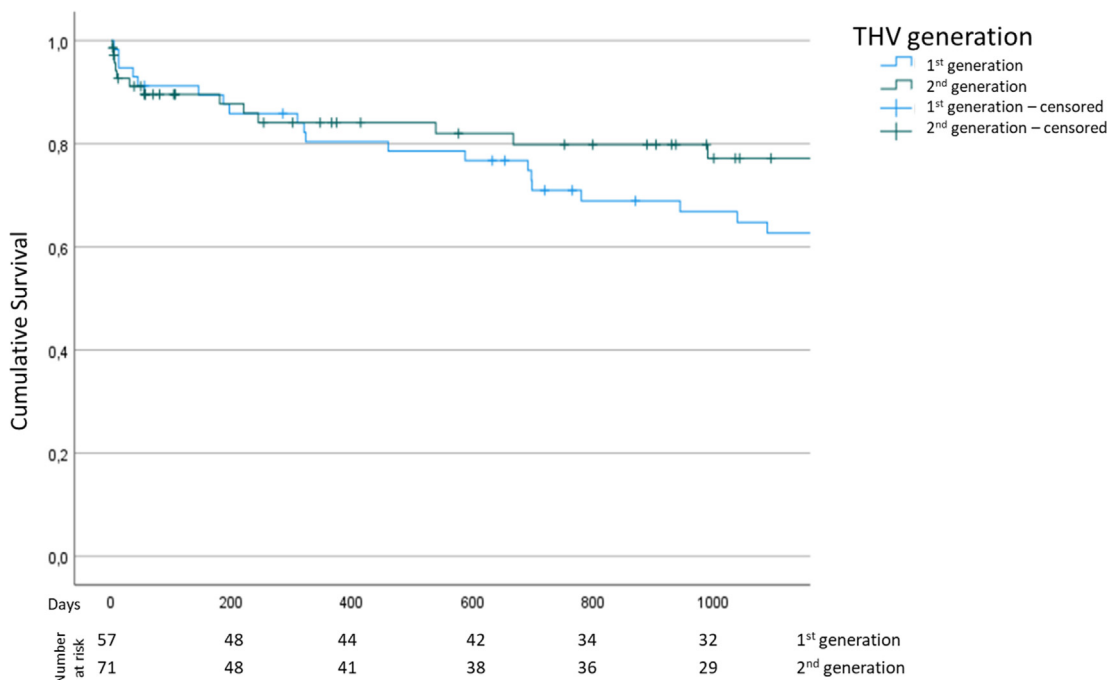


Fig. 3. Kaplan-Meier survival analysis, p = 0.574.

Table 6

Logistic regression analysis, univariate and multivariate. \*p < 0.005.

Variable	HR (univariate)	p value	HR (multivariate)	p value
CAD	1.75 (0.75–4.1)	0.193	1.5 (0.53–4.21)	0.441
Diabetes	5.61 (2.2–14.3)	<0.001*	4.69 (1.72–12.8)	0.003*
CKD	3.35 (1.38–8.18)	0.008*	2.91 (1.08–7.85)	0.035*
STS-M > 8%	4.64 (1.41–15.2)	0.011*	3.81 (1.06–13.7)	0.040*
2nd generation THV	0.56 (0.24–1.31)	0.185	0.82 (0.28–2.38)	0.718
BEV	1.04 (0.45–2.41)	0.921	–	–
Paravalvular leak less than moderate	0.42 (0.024–4.21)	0.462	–	–
Permanent pacemaker implantation	0.78 (0.05–12.8)	0.859	–	–
LBBB post TAVI	0.55 (0.12–2.6)	0.448	–	–
Major bleeding	3.0 (1.06–8.5)	0.039*	1.49 (0.41–5.44)	0.548

The population in this series, in fact, differs from ‘conventional’ young patients, because it involves patients deemed at increased surgical risk.

Our study shows that TAVI in this setting is a safe procedure, with low in-hospital mortality. Furthermore, procedural outcomes improved with technology evolution, with 2nd generation THV having better procedural outcomes when compared to 1st generation.

Low rate of stroke was observed in this population, probably due to the younger age and lowest rate of prior cerebrovascular disease. Moreover, rate of PM implantation was extremely low in this population, compared to those reported in clinical trials and registries[26]: this can be explained by the low prevalence of the commonly recognized risk factors for permanent PM implantation (advanced age and pre-existing conduction disturbance) [27,28] in our population.

New onset LBBB was significantly higher in the second-generation group than in the first one. This can be explained by the increased use of SEVs and MEVs in second generation subgroup.

When considering long term survival, crude rate of all-cause mortality is very high in this population and this observation can possibly be explained considering the high prevalence of severe comorbidities (cancer, CKD, diabetes).

Moreover, none of the valve-related factors (THV generation, THV type, PM implantation, LBBB post TAVI, major bleeding) resulted as significant independent predictor of mortality on multivariate analysis. According to that, it can be postulated that once resolved the valvular disease, long term prognosis becomes totally related to patient’s comorbidities.

### 5. Conclusions

TAVI in young patient with appropriate indication for intervention is a safe procedure, associated with low rate of in hospital mortality and low rate of severe complications.

Current generation devices are associated with lower rate of major or life-threatening bleeding, with a very high rate of device success.

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