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Predictors of Poor Clinical Improvement After Transcatheter Aortic Valve Implantation: To TAV or not to TAV

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ABSTRACT

Background: Transcatheter aortic valve implantation (TAVI) has become an appealing option in managing patients with severe aortic stenosis (AS) after demonstrating better survival rates, reduction in symptom burden, and improvement in the quality of life (QOL). However, some patients fail to demonstrate benefits after TAVI, whether in terms of survival or QOL.

Objective: This study opted to investigate the predictors of poor clinical outcomes following TAVI from a real-world national registry

Patients and Methods: This prospective observational study was derived from an Egyptian single-center registry through the duration from November 2022 to May 2023. It included 122 patients who were treated with TAVI. The participants' QOL was evaluated using the EuroQol 5-Dimension 5-Level (EQ-5D-5L) questionnaire at baseline and 6 months follow-up after TAVI. Participants were subdivided into two groups: Group A (good improvement) reported survival and >20% improvement from baseline and group B (poor improvement) reported mortality or ≤ 20% improvement.

Results: The mean age of our patients was 73.67 ± 7.04 years, 47.5% were males. A total of 106 patients (86.9%) showed good outcomes in the form of survival and QOL improvement >20%. Three patients (2.5%) experienced periprocedural mortality and 13 patients (10.6%) did not show an improvement in QOL of >20%. The independent predictors correlated to poor outcomes were: DM (*P*=0.028), creatinine clearance ≤ 46 ml/min (*P*=0.002), and pre-existing intraventricular conduction delay (IVCD) (*P*=0.017) and post-procedural CrCl ≤ 49ml/min (*P*= 0.011).

Conclusions: Our study concluded that certain preoperative risk factors and postoperative complications can predict patients' outcomes after TAVI. The independent predictors of poor outcomes were pre-procedural factors (pre-existing DM, chronic kidney disease (CKD) with CrCl ≤ 46 ml/min, and pre-existing IVCD) and a post-procedural factor which was CrCl ≤ 49 ml/min.

Keywords: Aortic stenosis, TAVI, VARC-3, QOL, Predictors of outcome.

INTRODUCTION

TAVI provides an acceptable alternative to surgery for many high-risk individuals [(1)]. It has proven non-inferiority to surgical aortic valve replacement (SAVR) in patients with intermediate risk. And, in low-risk trials such as the PARTNER 3, Nordic NOTION 2, and the Medtronic TAVR low-risk trial. TAVI was able to show either non-inferiority or superiority when compared to SAVR in terms of efficacy and safety [(2-4)].

Compared to medical therapy, TAVI significantly improved QOL, symptom burden reduction, and better rates of survival. However, it is now obvious that TAVI does not benefit all patients in terms of enhanced functional capacity, QOL, or mortality [(5-6)].

It's unlikely that extended survival on its own - without better QOL- would be considered a desirable result. Thus, both survival and QOL must be taken into account when defining a good -or bad- outcome for TAVI. Therefore, the most logical definition of poor outcome after TAVI should include the combination of death and poor improvement or worsened QOL [(7)].

Patient-reported outcome assessments (PROs) e.g., EQ-5D-5L and KCC questionnaires offer prognostic significance in addition to chances for better patient-centered treatment [(8)]. Clinically, significant changes in health status over time were more likely to be identified by evaluation utilizing PROs, and these changes demonstrated greater prognostic significance than changes in symptom burden and NYHA class [(9)].

Although the prediction of poor outcomes after TAVI is still imprecise, a better basis for informed consent can be provided for patients by identifying predictors of bad outcomes, and the increasing trend of treating low-risk patients has highlighted the significance of lowering the risk of complications that may have an impact on long-term prognosis. Registries are great resources that offer valuable information into outcomes and can be used to assess how cost-effectively different interventions work [(10)].

This study opted to investigate the predictors of poor clinical outcomes following TAVI from a real-world national registry.

PATIENTS AND METHODS

This was a prospective observational study derived from an Egyptian single-center registry. It was from November 2022 to May 2023. The study included 122 patients who suffered from severe aortic stenosis and were treated with TAVI after a decision from our conjoint heart team including cardiologists, cardiothoracic surgeons and anaesthesiologists following the latest ESC guidelines for the

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management of valvular heart diseases [11]. All patients underwent close follow-ups at 1,3, and 6 months. Failure to gain informed consent and failure of follow-up were excluded.

All patients involved in the study were subjected to the following (at baseline and 6 months follow-up):

A. Preprocedural and procedural data: Thorough history taking including symptomatology with emphasis on NYHA score, local examination, ECG, echocardiography, Pre-TAVI CT aortography, and procedural data collection.

B. Patient-reported outcomes (PROs) [12]:

- ***EQ-5D-5L questionnaire: (Euro quality of life 5 dimensions 5 levels)***

The EuroQol Group created the EQ-5D-5L, a standardized health status measure, to offer an easy, general-purpose indicator of health for clinical and financial evaluation. The following five categories make up the descriptive system: mobility, self-care, ordinary activities, pain or discomfort, and anxiety or depression. There are five levels for each dimension: none, minor, moderate, severe, and extreme difficulties.

The participant was requested to check (or place a cross) the box next to the statement that best fit each of the five dimensions to represent his or her current state of health.

-The EQ VAS score: (Euro- quality of life visual analogue scale)

A visual analogue scale that is 20 cm vertical and has endpoints labeled "the best health you can imagine" and "the worst health you can imagine," measuring the participant's total self-rated health state. The respondents' subjective assessments of their own health are quantified using this data.

Participants were subdivided into two groups: Group A (good improvement) reported survival and > 20% improvement from baseline and group B (poor improvement) reported mortality or ≤ 20% improvement from baseline at follow-up based on the EQ-5D-5L questionnaire and overall EQ-VAS score.

C. Procedural outcomes:

The procedural outcomes were studied according to the Valve Academic Research Consortium-3 (VARC-3) definitions of complications following TAVI including conduction disturbances or the need for permanent pacemaker implantation, bleeding, vascular complications, acute kidney injury (AKI), stroke, and mortality [13].

Ethical approval: The study protocol was approved by The Local Ethical Committee, Ain Shams University. After gathering all of the information, the participants gave their signed permissions. All the patients were coded by numbers to preserve their confidentiality. The study adhered to the Helsinki Declaration throughout its execution.

Statistical analysis:

The data were entered, coded, and modified using IBM SPSS, version 23.0. When it was discovered that the quantitative data were not parametric, they were given as the median, IQR, mean ± SD, and ranges. Numbers and percentages were also used to illustrate qualitative aspects. The qualitative data was compared between groups using the X^2-test and/or Fisher exact test when the expected count in any cell was found to be less than 5. When comparing two independent groups with quantitative data and a parametric distribution, the independent t-test was employed. For non-parametric distributions, the Mann-Whitney test was utilized. The quantitative data from two paired groups with a non-parametric distribution were compared using the Wilcoxon Rank test, while the parametric data from two groups were compared using the Paired t-test. The factors linked to inadequate progress were assessed using univariate and multivariate logistic regression analysis in the study. To evaluate the variability between two qualitative variables, use kappa agreement. Using the Log Rank Test, Kaplan Meier analysis was utilized to assess the relationship between overall survival and the other factors under investigation. The confidence interval was 95%, and the accepted error margin was 5%. Thus, the following p-value was deemed significant: P-values greater than 0.05 indicate non-significates (NS), 0.05 indicates significance (S), and 0.01 indicates high significance (HS).

RESULTS

The present study included 122 patients, with a mean age of 73.67 ± 7.04 years, 47.5% were males. The comparison between group A (Good outcome) and group B (Poor outcome) as regards demographic and clinical parameters revealed that BSA was significantly lower in group B (P=0.047), Euro Score II was significantly higher in group B (P=0.008), DM was higher in group B (P=0.012), and creatinine clearance (CrCl) was significantly lower in group B (P=0.016). As regards NYHA classification, group A showed a significantly larger percentage in NYHA class III and IV (P=0.016) (Table 1).

Table (1): Baseline demographic data, clinical parameters, and laboratory investigations

Parameters		**Total number = 122 patients**				
Age (years)		Mean ± SD (Range)		73.67 ± 7.04 (55 – 90)		
Sex		Female /Male		64 (52.5%) /58 (47.5%)		
BMI (kg/m^2)		Mean ± SD(Range)		30.32 ± 6.35 (18.31 – 50.52)		
BSA (m^2)		Mean ± SD(Range)		1.89 ± 0.21(1.35 – 2.47)		
Comparison between demographic parameters among the two study groups						
Parameters		**Good outcome(A)**	**Poor outcome(B)**	**Test value**	**P-value**	**Sig.**
		No. = 106	**No. = 16**			
Sex	**Female**	55 (51.9%)	9 (56.2%)	0.106*	0.745	NS
	Male	51 (48.1%)	7 (43.8%)			
Age	**Mean ± SD**	73.25 ± 6.90	76.50 ± 7.49	-1.738•	0.085	NS
Body mass index	**Mean ± SD**	30.61 ± 5.90	28.39 ± 8.81	1.309•	0.193	NS
Body surface area	**Mean ± SD**	1.90 ± 0.20	1.79 ± 0.22	2.009•	0.047	S
Euro Score II	**Median (IQR)**	3.26 (1.85 – 5.6)	7.31 (2.59 – 13.19)	-2.272≠	0.023	S
Euro Score II	**< 4%**	65 (61.3%)	7 (43.8%)	9.626*	0.008	HS
	(4% - 8%)	31 (29.2%)	3 (18.8%)			
	>8%	10 (9.4%)	6 (37.5%)			
STS PROM	**Median (IQR)**	2.51 (1.72 – 4.3)	3.76 (2.11 – 7.67)	-1.832≠	0.067	NS
Previous CABG		10 (9.4%)	2 (12.5%)	0.147*	0.701	NS
Valve in Valve		1 (0.9%)	0 (0.0%)	0.152*	0.696	NS
Smoking	**Current smoker**	8 (7.5%)	1 (6.2%)	0.721*	0.697	NS
	Ex-smoker	7 (6.6%)	2 (12.5%)			
Diabetes mellitus		38 (35.8%)	11 (68.8%)	6.262*	0.012	S
Hypertension		81 (76.4%)	13 (81.2%)	0.184*	0.668	NS
Ischemic heart disease		44 (41.5%)	9 (56.2%)	1.229*	0.268	NS
Cerebrovascular stroke		6 (5.7%)	3 (18.8%)	3.486*	0.062	NS
Chronic liver disease		11 (10.4%)	2 (12.5%)	0.066*	0.798	NS
Rheumatic heart disease		5 (4.7%)	0 (0.0%)	0.787*	0.375	NS
Bicuspid aortic valve		5 (4.7%)	0 (0.0%)	0.787*	0.375	NS
NYHA baseline	**I**	0 (0.0%)	1 (6.2%)	6.680*	0.035	S
	II	0 (0.0%)	0 (0.0%)			
	III	78 (73.6%)	11 (68.8%)			
	IV	28 (26.4%)	4 (25.0%)			
Hemoglobin baseline	**Mean ± SD**	11.46 ± 1.08	10.84 ± 0.84	-0.955•	0.342	NS
Creatinine clearance	**Median (IQR)**	62.5 (48 – 80)	41.5 (35 – 62)	-2.408≠	0.016	S

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test

BMI: body mass index, BSA: body surface area, STS score: Society of Thoracic Surgeons.

According to the EQ-5D-5L questionnaire and overall EQ-VAS score, we divided our patients into two groups: Group A (Good outcome group) with an improvement of > 20% and no mortality, and group B (Poor outcome group) mortality or improvement < 20%. Group A consisted of 106 patients (86.9%), and Group B consisted of 16 patients (13.1%) as shown in table (2).

Table (2): EQ-5D-5L questionnaire and EQ-VAS score at baseline and 6 months follow up

		Baseline	Follow-up	Test value	P-value	Significance
		No. (%)	No. (%)			
Mobility/ Independence	**No problem**	0 (0.0%)	84 (68.9%)	225.564*	<0.001	HS
	Slight	0 (0.0%)	33 (27.0%)			
	Moderate	13 (10.7%)	2 (1.6%)			
	Severe	75 (61.5%)	1 (0.8%)			
	Extreme	34 (27.9%)	2 (1.6%)			
Ordinary activities	**No problem**	0 (0.0%)	91 (74.6%)	225.018*	<0.001	HS
	Slight	1 (0.8%)	27 (22.1%)			
	Moderate	32 (26.2%)	1 (0.8%)			
	Severe	68 (55.7%)	1 (0.8%)			
	Extreme	21 (17.2%)	2 (1.6%)			
Self-care	**No problem**	0 (0.0%)	103 (84.4%)	212.243*	<0.001	HS
	Slight	9 (7.4%)	16 (13.1%)			
	Moderate	63 (51.6%)	0 (0.0%)			
	Severe	47 (38.5%)	1 (0.8%)			
	Extreme	3 (2.5%)	2 (1.6%)			
Pain or Discomfort	**No problem**	0 (0.0%)	96 (78.7%)	202.878*	<0.001	HS
	Slight	13 (10.7%)	23 (18.9%)			
	Moderate	68 (55.7%)	0 (0.0%)			
	Severe	39 (32.0%)	1 (0.8%)			
	Extreme	2 (1.6%)	2 (1.6%)			
Anxiety or Depression	**No problem**	2 (1.6%)	91 (74.6%)	167.253*	<0.001	HS
	Slight	34 (27.9%)	28 (23.0%)			
	Moderate	64 (52.5%)	0 (0.0%)			
	Severe	17 (13.9%)	0 (0.0%)			
	Extreme	5 (4.1%)	3 (2.5%)			
EQ-VAS Score	**Mean ± SD**	62.48 ± 4.99	84.92 ± 7.33	-29.663•	<0.001	HS
Outcome	**Good improvement (Group A)**		**Poor improvement (Group B)**			
	106 (86.9%)		16 (13.1%)			

*: Chi-square test. •: Paired t-test
EQ-5D -5L(euro-quality of life – 5 dimensions- 5 levels), EQ-VAS (euro-quality of life visual analogue scale)

As regards baseline ECG and echocardiographic data, group B had a significantly higher percentage of patients with IVCD (P=0.006). Group B had a significantly higher percentage of patients with reduced EF (P= 0.002). Moreover, group B showed a significantly thinner SWT (P < 0.001), larger left ventricular end-systolic diameter (P=0.007), and lower PPG (P< 0.001). There were no statistically significant differences between the two groups as regards CT parameters as shown in table (3).

Table (3): Baseline ECG, TEE, and CT data of the studied patients comparing good Vs. poor outcomes

Parameters		Good outcome(A) No. = 106	Poor outcome(B) No. = 16	Test value	P-value	Sig.
Baseline ECG parameters						
Atrial Fibrillation	Permanent	11 (10.4%)	0 (0.0%)	3.597*	0.166	NS
	Paroxysmal	8 (7.5%)	3 (18.8%)			
BBB	LBBB	10 (9.4%)	1 (6.2%)	0.172*	0.678	NS
	RBBB	8 (7.5%)	2 (12.5%)	0.453*	0.501	NS
	IVCD	3 (2.8%)	3 (18.8%)	7.534*	0.006	HS
PR	Mean ± SD	177.79 ± 38.57	173.75 ± 39.81	1.697•	0.092	NS
QRS	Mean ± SD	102.36 ± 26.42	109.38 ± 29.32	0.386•	0.700	NS
Baseline Echocardiographic parameters						
Ejection fraction	Reduced function	17 (16.0%)	8 (50.0%)	9.842*	0.002	HS
	Normal function	89 (84.0%)	8 (50.0%)			
SWT	Mean ± SD	12.78 ± 1.92	11.78 ± 1.71	4.288•	< 0.001	HS
	Range	8 – 20.1	8 – 15			
LVEDD	Mean ± SD	50.12 ± 7.04	53.38 ± 6.60	-0.122•	0.903	NS
LVESD	Mean ± SD	32.87 ± 7.89	39.69 ± 8.11	-2.744•	0.007	HS
PPG	Mean ± SD	81.66 ± 21.25	75.94 ± 23.24	-3.721•	<0.001	HS
MPG	Mean ± SD	50.50 ± 13.78	47.56 ± 15.56	0.991•	0.323	NS
AVA	Mean ± SD	0.70 ± 0.20	0.70 ± 0.20	0.782•	0.436	NS
RVSP	Mean ± SD	42.90 ± 11.65	45.31 ± 15.01	-0.750•	0.455	NS
Baseline CT parameters						
Annulus Diameter	Mean ± SD	23.88 ± 2.18	23.03 ± 1.66	-0.743•	0.459	NS
Annulus Perimeter	Mean ± SD	76.99 ± 6.77	74.52 ± 5.58	-0.756•	0.451	NS
MS Length	Mean ± SD	8.41 ± 1.88	9.26 ± 2.62	0.026•	0.979	NS
Grade of Calcification	0	1 (0.9%)	0 (0.0%)	3.025*	0.554	NS
	I	21 (19.8%)	3 (18.8%)			
	II	38 (35.8%)	8 (50.0%)			
	III	33 (31.1%)	2 (12.5%)			
	IV	13 (12.3%)	3 (18.8%)			
BSC	Yes	12 (11.3%)	2 (12.5%)	0.019*	0.890	NS

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test

IVCD: Intraventricular conduction delay, LBBB: Left bundle branch block, RBBB: Right bundle branch block, SWT: septal wall thickness, LVEDD: left ventricular end-diastolic diameter, LVESD: left ventricular end-systolic diameter, AV: aortic valve, PPG: peak pressure gradient, MPG: mean pressure gradient, RVSP: right ventricular systolic pressure, MS: membranous septum, BSC: basal septal calcification

There were no statistically significant differences between the two groups as regards procedural parameters except for the percentage of depth of implantation to the membranous septum (DIMS), which was significantly higher in group B (P=0.027) as shown in tables (4).

Table (4): Baseline procedural data of the studied patients comparing good Vs. poor outcomes

Procedural data		Good outcome(A)	Poor outcome(B)	Test value	P-value	Sig.
		No. = 106	No. = 16			
THV type	Evolut R *(96 valves, 78.6%)*	88 (83%)	8 (50%%)	2.393*	0.495	NS
	Acurate neo 2 *(12 valves, 9.8%)*	8 (7.5%)	4 (25%)			
	Sapien 3 *(14 valves, 11.4%)*	10 (9.4%)	4 (25%))			
THV size	Mean ± SD	29.59 ± 2.67	29.50 ± 2.61	0.132•	0.895	NS
	Range	23 – 34	26 – 34			
DI (mm)	Mean ± SD	3.78 ± 1.94	4.79 ± 3.50	1.144•	0.255	NS
DIi (mm/m^2)	Mean ± SD	1.98 ± 1.03	2.67 ± 1.76	-1.716•	0.089	NS
Pre-Dilatation	Yes	21 (19.8%)	4 (25.0%)	0.230*	0.632	NS
Post-Dilatation	Yes	19 (17.9%)	2 (12.5%)	0.287*	0.592	NS
DIMS	Mean ± SD	46.64 ± 23.97	59.20 ± 45.33	-2.244•	0.027	S
Approach	Percutaneous	102 (96.2%)	13 (81.2%)	1.116*	0.572	NS
	Surgical	2 (1.9%)	2 (12.5%)			
	Percutaneous then Surgical	2 (1.89%)	1 (6.2%)			

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test
THV: Transcatheter heart valve, DI: depth of implantation, DIMS: Percentage of depth of implantation to membranous septum length

Follow-up of laboratory, ECG, and echocardiography, data of the studied patients revealed statistically significant differences between the two groups regarding haemoglobin and creatinine clearance levels in which both were lower in group B (P=0.03, and P= 0.024, respectively). Permanent CHB was higher in group B (P< 0.001), and mean pressure gradient (MPG) was also higher in group B (P=0.009). As regards Post-TAVI clinical outcomes, there were statistically significant differences between the two groups regarding total mortality, stroke, hospitalization, and permanent pacemaker implantation (PPM) with P value < 0.001. Moreover, the NYHA classification was worse in group B (P=0.005). Other clinical outcome parameters can be seen in table (5).

Table (5): Follow-up laboratory, ECG, and echocardiography data of the studied patients comparing good Vs. poor outcomes

		Good outcome(A)	Poor outcome(B)	Test value	P-value	Sig.
		No. = 106	No. = 16			
Laboratory parameters at follow-up						
Hemoglobin (gm/dl)	**Mean ± SD**	11.52 ± 1.19	10.84 ± 0.92	2.163•	0.033	S
	Range	8.8 – 14.4	9.2 – 12.2			
Creatinine clearance (ml/min)	**Median (IQR)**	67 (55 – 84)	51.5 (37 – 71)	-2.253≠	0.024	S
	Range	15 – 120	15 – 103			
ECG at follow up	**Cond. Disturbances**	37 (34.9%)	9 (56.3%)	2.696*	0.101	NS
	New LBBB	19 (17.9%)	2 (12.5%)	0.287*	0.592	NS
	Permanent CHB	4 (3.8%)	5 (31.3%)	15.360*	< 0.001	HS
Echocardiographic parameters at follow-up						
EF	**Mean ± SD**	64.25 ± 10.35	52.44 ± 15.29	0.083•	0.934	NS
	Range	32 – 84	32 – 70			
MPG	**Mean ± SD**	6.08 ± 1.54	6.48 ± 1.82	-2.638•	0.009	HS
PVL	**No**	94 (88.7%)	11 (68.8%)	5.411*	0.067	NS
	Mild	11 (10.4%)	5 (31.2%)			
	Moderate	1 (0.9%)	0 (0.0%)			
	Severe	0 (0.0%)	0 (0.0%)			
Post-TAVI outcomes according to VARC-3 and follow-up of the NYHA classification						
Total Mortality	**Cardiac**	0 (0.0%)	3 (18.8%)	20.482*	<0.001	HS
	Non-cardiac	1 (0.9%)	0 (0.0%)			
Total stroke	**Yes**	0 (0.0%)	2 (12.5%)	13.471*	<0.001	HS
Hospitalization (days)	**Cardiac**	6 (5.7%)	9 (56.2%)	34.210*	<0.001	HS
	Non-cardiac	10 (9.4%)	2 (12.5%)			
PPM implantation	**Yes**	4 (3.8%)	5 (31.2%)	15.360*	<0.001	HS
AKI	**Yes**	1 (0.9%)	0 (0.0%)	0.152*	0.696	NS
Bleeding	**Minor**	6 (5.7%)	2 (12.5%)	1.195*	0.550	NS
	Major	1 (0.9%)	0 (0.0%)			
Vascular complications	**Pseudoaneurysm**	1 (0.9%)	0 (0.0%)	0.307*	0.858	NS
	Infection	1 (0.9%)	0 (0.0%)			
NYHA	**I**	100 (94.3%)	12 (75.0%)	10.420*	0.005	HS
	II	6 (5.7%)	3 (18.8%)			
	III	0 (0.0%)	0 (0.0%)			
	IV	0 (0.0%)	1 (6.2%)			

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test
EF: Ejection fraction, MPG: mean pressure gradient, PVL: paravalvular leak, PPM: Permanent pacemaker, AKI: Acute kidney injury

ROC curves were done to obtain cut-off values of some of the significant predictors as shown in figures (1 and 2) and table (6). Univariate analysis revealed multiple predictors of poor improvement, these predictors are Euro Score II > 7.96, history of DM, baseline creatinine clearance ≤ 46 ml/min, pre-existing IVCD, LVESD > 32 mm, and indexed LVESD > 17.61. On the other hand, pre-existing normal LV systolic functions in TTE showed a protective effect with an Odds ratio (OR) of 0.191. Post-procedural and follow-up parameters that showed significance were hemoglobin <11.9 gm/dl, creatinine clearance ≤ 49 ml/min, permanent CHB, cardiac hospitalization, and NYHA > II. When applying multivariate logistic regression analysis, there were 4 independent predictors of poor outcome; 3 pre-existing factors: DM, CKD (CrCl ≤ 46 ml/min), and baseline IVCD in ECG, and 1 factor at follow-up: CrCl ≤ 49ml/min as shown in table (7).

Table (6): Best cut-off point, AUC, sensitivity, and specificity for predictors of poor improvement at baseline and follow up

	Cut off point	AUC	Sensitivity	Specificity	PPV	NPV
Euro Score II	>7.96	0.677	50.00	88.68	40.0	92.2
Creatinine clearance (baseline)	≤ 46	0.687	68.75	79.25	33.3	94.4
LVESD (mm) (baseline)	>32	0.746	87.50	58.49	24.1	96.9
LVESDi (mm/m^2) (baseline)	>17.61	0.779	81.25	63.21	25.0	95.7
Hemoglobin (gm/dl) (follow-up)	≤ 11.9	0.677	87.50	46.23	19.7	96.1
Creatinine clearance (follow-up)	≤ 49	0.675	50.00	83.96	32.0	91.8
MPG (mmHg) (follow-up)	≥ 5	0.550	87.50	27.36	15.4	93.5

AUC: area under curve, ROC: receiver operating characteristic curve, PPV: positive predictive value, NPV: negative predictive value, LVESD: left ventricular end-systolic diameter, MPG: mean pressure gradients

Table (7): Univariate and Multivariate logistic regression analysis for factors associated with poor outcome

		Univariate				Multivariate			
		P-value	Odds ratio (OR)	95% C.I. for OR		P-value	Odds ratio (OR)	95% C.I. for OR	
				Lower	Upper			Lower	Upper
Body surface area ≤ 1.9 m^2		0.087	2.833	0.858	9.356	–	–	–	–
Euro Score II >7.96		**< 0.001**	7.833	2.482	24.727	0.680	0.980	0.888	1.080
Diabetes mellitus		**0.017**	3.937	1.273	12.177	**0.028**	5.028	1.190	21.236
Creatinine clearance at baseline ≤46		**< 0.001**	8.400	2.642	26.706	**0.002**	14.248	2.725	74.498
NYHA at baseline		0.288	0.548	0.180	1.663	–	–	–	–
IVCD at baseline		**0.017**	7.923	1.446	43.419	**0.017**	18.437	1.687	201.510
EF at baseline (Normal function)		**0.003**	0.191	0.063	0.579	0.795	0.776	0.114	5.276
ECHO at baseline	**LVESD >32**	**0.003**	9.864	2.133	45.604	0.083	8.430	0.757	93.891
	LVESDi >17.61	**0.003**	7.150	1.919	26.642	0.834	0.776	0.073	8.294
	PPG <=73	0.061	2.786	0.955	8.129	–	–	–	–
DIMS ≥ 70.42		0.102	2.550	0.829	7.841	–	–	–	–
Follow-up data									
Hemoglobin ≤ 11.9 mg/dl		**0.022**	6.018	1.303	27.790	–	–	–	–
CrCl at follow-up ≤ 49		**0.003**	5.235	1.727	15.867	**0.011**	6.324	1.538	26.004
Permanent CHB		**0.001**	11.591	2.707	49.636	–	–	–	–
MPG ≥ 5 mmHg		0.218	2.636	0.564	12.321	–	–	–	–
Cardiac hospitalization		**0.040**	7.071	1.098	45.536	–	–	–	–
NYHA ≥ II		**0.016**	5.556	1.370	22.522	–	–	–	–

*: Chi-square test; •: Independent t-test; ≠: Mann-Whitney test
CI: confidence interval, OR: odds ratio, IVCD: intraventricular conduction delay, DIMS: depth of implantation/membranous septum, CHB: complete heart block, MPG: mean pressure gradient

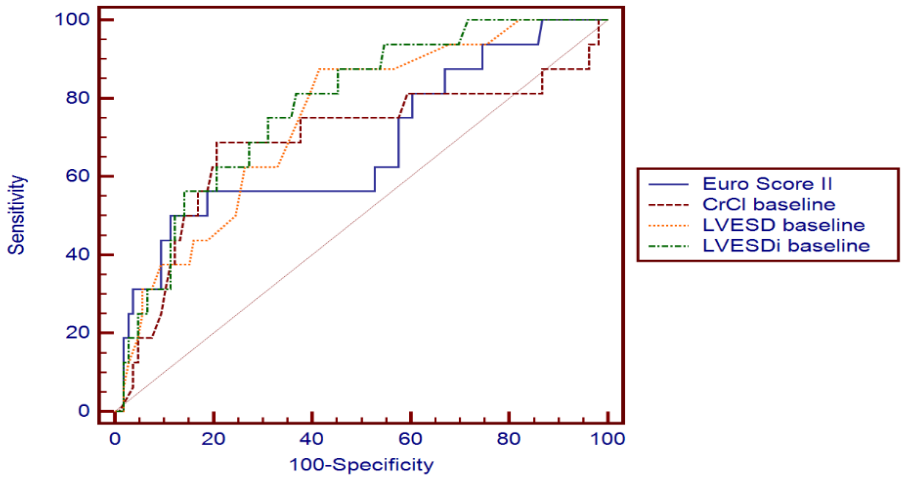

Figure (1): ROC curves for significant baseline predictors of poor improvement

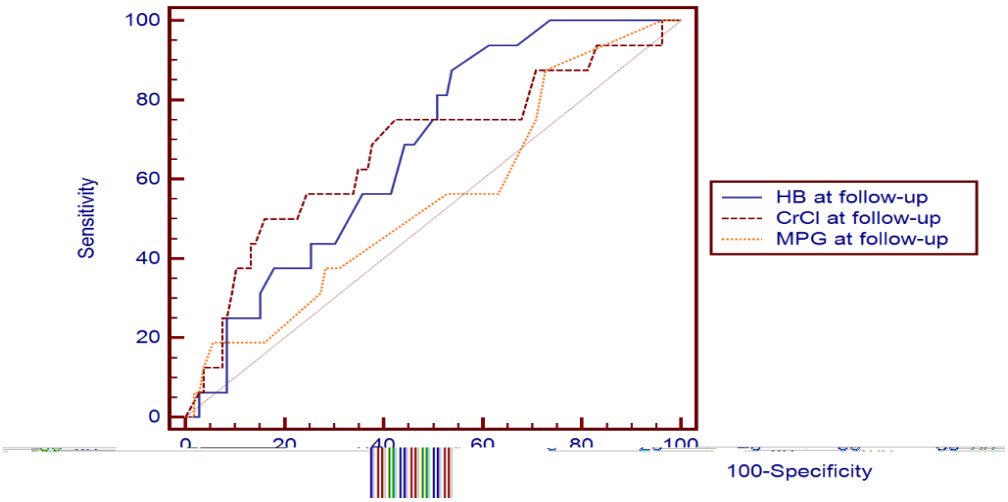

Figure (2): ROC curves for significant follow-up predictors of poor improvement.

DISCUSSION

In our study, we opted to study predictors of poor clinical outcomes after TAVI based on VARC-3 definitions and the Euro-QOL questionnaire. It is well known that the ultimate goal of TAVI is not only to add years to patients' lives by reducing mortality but also to add life to their years by improving quality of life. That is why the most logical definition of a poor outcome following TAVI should include both mortality and QOL components.

Our study demonstrated that 106 patients (86.9%) had good outcomes in the form of survival and QOL improvement > 20%; 3 patients (2.5%) died and 13 patients (10.6%) did not have a significant improvement in QOL. The France TAVI registry [14], also studied outcomes based on the Euro-QOL questionnaire and showed that 18.9% of patients died and 14.5% showed a significant decline in QOL. The outcome sub-study from the PARTNER trial [15], revealed overall poor outcome (32.9%). This may be attributed to a large number of participants and higher risk scores in the France registry and the PARTNER trial. When compared to another national TAVI study, **Ghanem *et al.*** [16] showed 11.1% mortality, which is close to our results.

In our study we found multiple significant predictors of poor outcome after TAVI, these predictors are Euro Score II >7.96 (P <0.001), History of DM (P= 0.017), chronic kidney disease (CKD) with CrCl < 46 ml/min (P<0.001), IVCD at baseline (P = 0.017), LVESD > 32 mm (P= 0.003). When applying multivariate logistic regression analysis, DM (P= 0.028), Baseline CrCl ≤ 46 ml/min) (P= 0.002), and pre-existing IVCD (P=0.017), were the most significant independent predictors of poor outcome. This goes in concordance with the France TAVI registry [14], which concluded that DM (P=0.001), CKD (P<0.001), supraventricular arrhythmia (P <0.001), and anticoagulation therapy at discharge (P=0.01) as independent factors were associated with procedure futility. On the other hand, **Auffret *et al.*** [17] revealed that RV dysfunction, significant baseline pulmonary hypertension, and AF are the indicators of poor 6-month outcomes.

A multicentre Canadian study [18] showed that atrial fibrillation (AF) and CKD were correlated with reduced survival after TAVI. A multicentre Brazilian study [19] showed that chronic obstructive pulmonary disease (COPD), stroke, AKI, and moderate to severe paravalvular leakage (PVL) were correlated with overall mortality after TAVI. In another multicentre Spanish study [20], predictors of mortality were renal failure, atrial fibrillation, peripheral vascular disease, and moderate to severe postoperative PVL. A single-center Canadian

study [21] showed that male sex, CLD, and the 6-minute walk test distance were correlated with 1-year mortality after TAVI. Another single-center German study [22] showed that older age, lower BMI, NYHA class IV, depressed LV ejection fraction, and higher calculated surgical risk scores were all correlated with 1-year mortality.

Different predictors of poor outcomes reported by different studies may be attributed to differences in the study populations (numbers, comorbidities and overall mortality risk score), team experience and immediate complications, follow-up periods, assessment tools, cut-off points, and standardized definitions of poor outcomes.

CONCLUSIONS

Our study concluded that certain preoperative risk factors and postoperative complications can predict patients' outcomes after TAVI. The independent predictors of poor outcomes were pre-procedural factors (pre-existing DM, CKD with CrCl ≤ 46 ml/min, and pre-existing IVCD) and a post-procedural factor, which was CrCl ≤ 49 ml/min. These findings should be validated on a larger scale and in multiple centers and may assist physicians in obtaining the best possible results with such a promising technique if these factors have been taken into consideration when evaluating patients for TAVI.

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