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The reversibility of cardiac damage after transcatheter aortic valve implantation and short-term outcomes

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Background

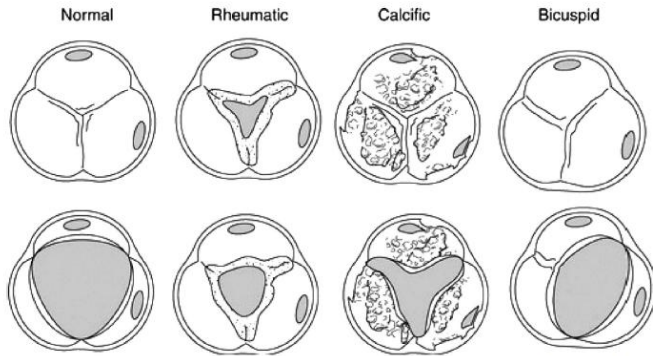
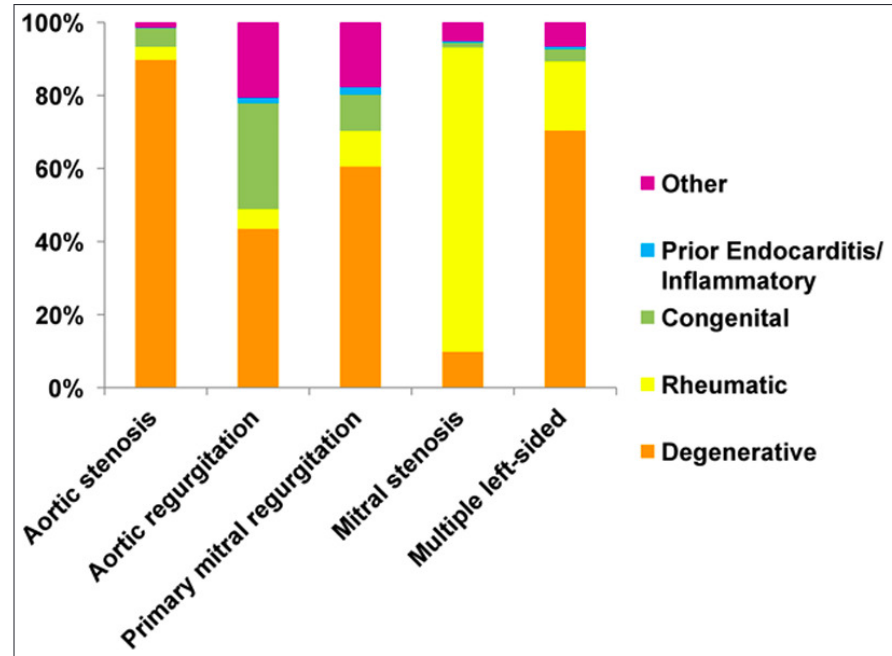


Figure 1 Aortic stenosis aetiology: morphology of calcific AS, bicuspid valve, and rheumatic AS. (Adapted from C. Otto, Principles of Echocardiography, 2007).

Aortic stenosis (AS) is the abnormal narrowing, thickening and stiffening of the aortic valve, which restricts the blood flow from left ventricle into the aorta.

Table 3 Recommendations for grading of AS severity

	Aortic sclerosis	Mild	Moderate	Severe
Peak velocity (m/s)	≤2.5 m/s	2.6–2.9	3.0–4.0	≥4.0
Mean gradient (mmHg)	–	<20	20–40	≥40
AVA (cm ²)	–	> 1.5	1.0–1.5	<1.0
Indexed AVA (cm ² /m ²)	–	>0.85	0.60–0.85	<0.6
Velocity ratio	–	> 0.50	0.25–0.50	<0.25



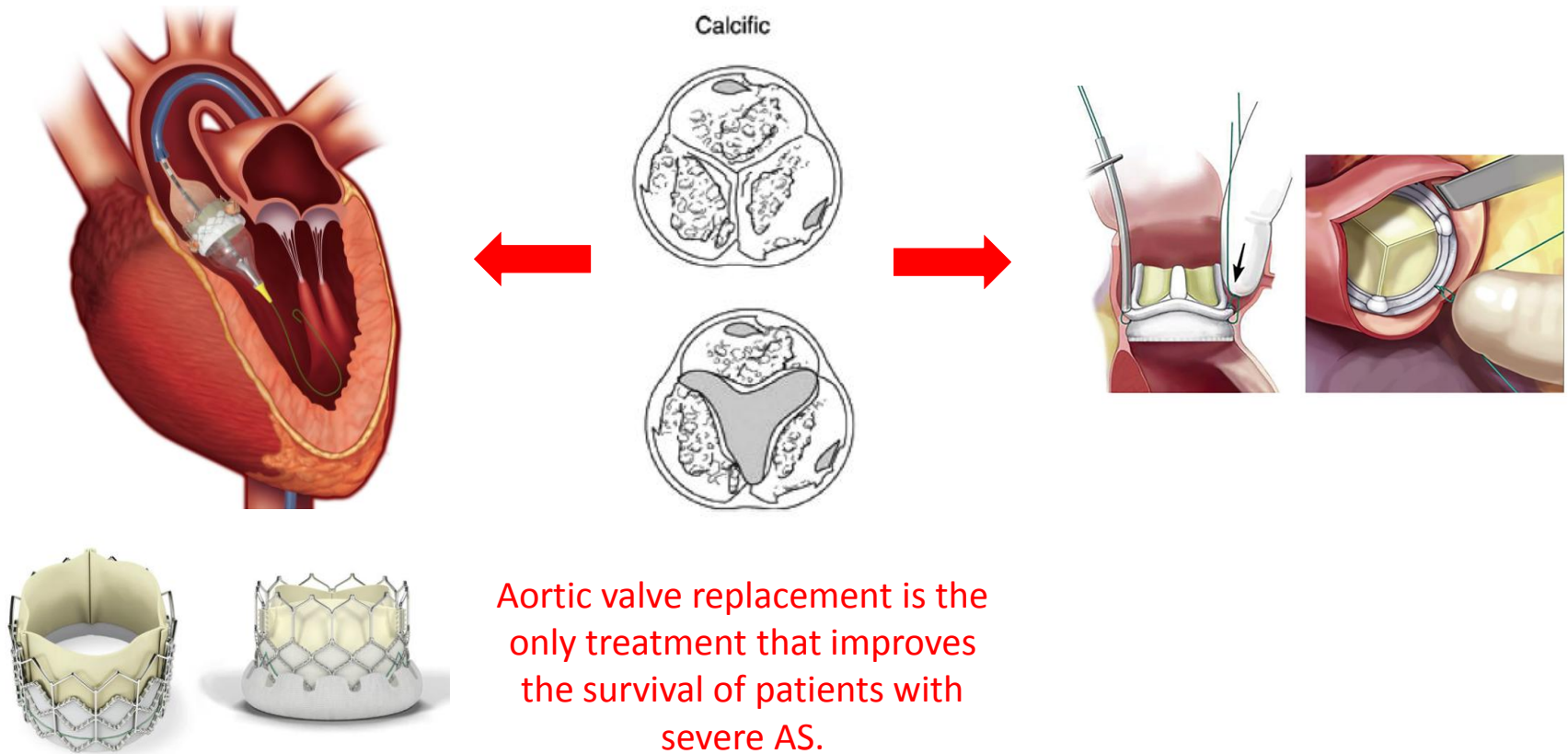
	AS (n=2152), n (%)	AR (n=279), n (%)	MS (n=234), n (%)	Primary MR (n=746), n (%)
Intervention performed	866/2149 (40.3)	93 (33.3)	109 (46.6)	277 (37.1)
Intervention scheduled but not performed	724/2149 (33.7)	77 (27.6)	41 (17.5)	191 (25.6)
No indication for intervention according to the investigator	559/2149 (26.0)	109 (39.1)	84 (35.9)	278 (37.3)

Calcific aortic stenosis (AS) is the most common valvular heart disease in aging population of western world.

Background

Transcatheter aortic valve implantation (TAVI)

Surgical aortic valve replacement



Aortic valve replacement is the only treatment that improves the survival of patients with severe AS.

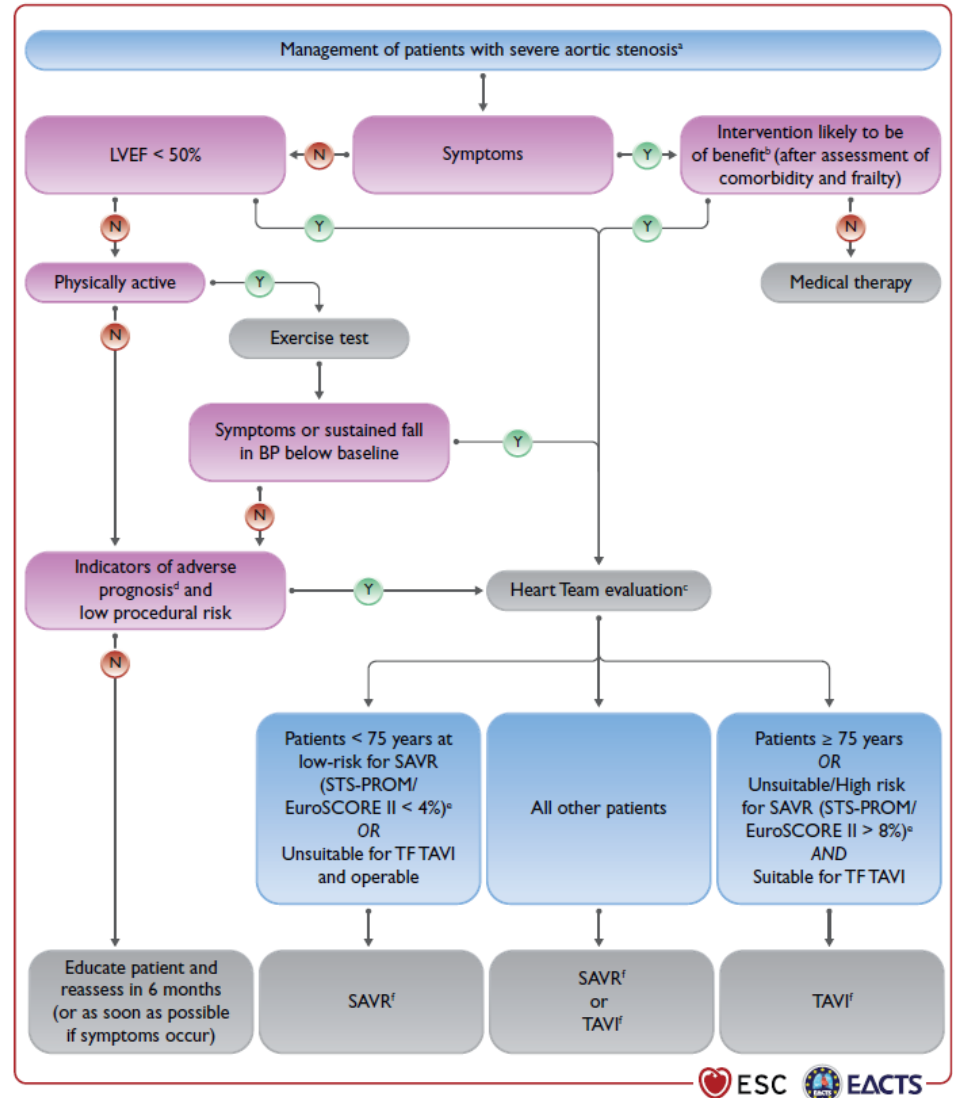
Background

2021 ESC/EACTS Guidelines for the management of valvular heart disease

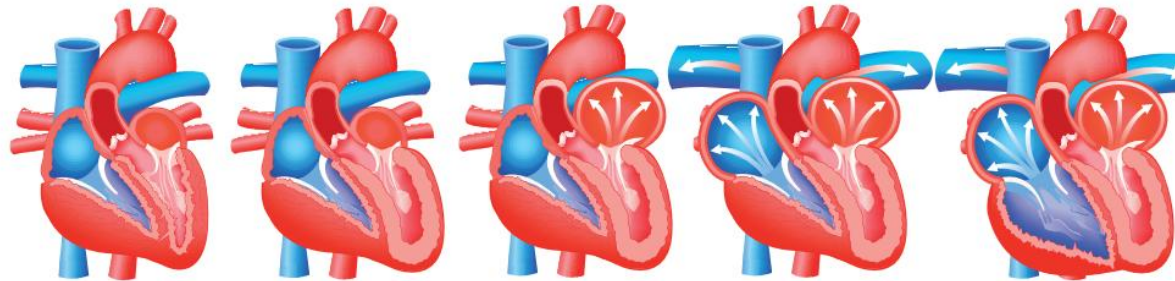
Developed by the Task Force for the management of valvular heart disease of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery (EACTS)

Current criteria:

- i) Valvular criteria (Vmax, mean TV grad, AVAi)
- ii) Presence of AS symptoms (dyspnea, heart failure, angina, or syncope)



Background

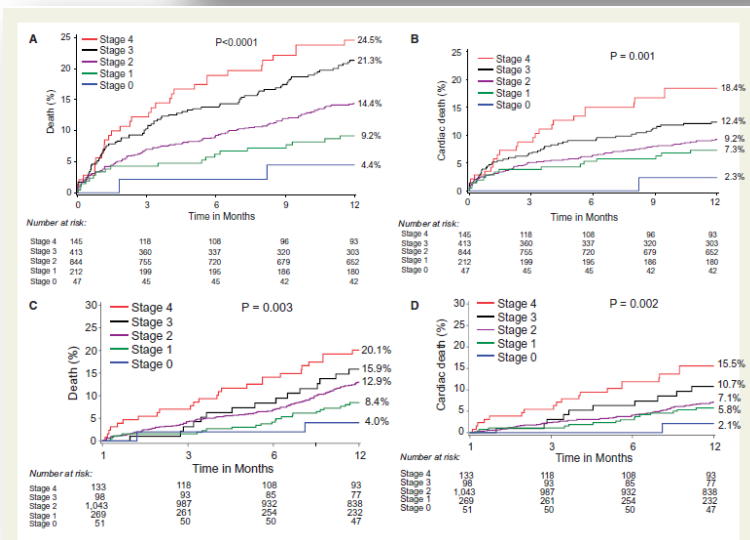


Stages/Criteria	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
	No Cardiac Damage	LV Damage	LA or Mitral Damage	Pulmonary Vasculature or Tricuspid Damage	RV Damage
Echocardiogram		Increased LV Mass Index >115 g/m ² (Male) >95 g/m ² (Female)	Indexed left atrial volume >34mL/m ²	Systolic Pulmonary hypertension ≥60 mmhg	Moderate-Severe right ventricular dysfunction
		E/e' >14	Moderate-Severe mitral regurgitation	Moderate-Severe tricuspid regurgitation	
		LV Ejection Fraction <50%	Atrial Fibrillation		

AS staging based on concomitant cardiac damage

Cardiac damage: LV dysfunction, LA enlargement, PH, RVD
 Aims: Prevalence, categorization & impact on survival and adverse outcome

Included: Severe AS from PARTNER 2A (N= 2032, 57 centers) & PARTNER 2B (N= 671, 28 sites)

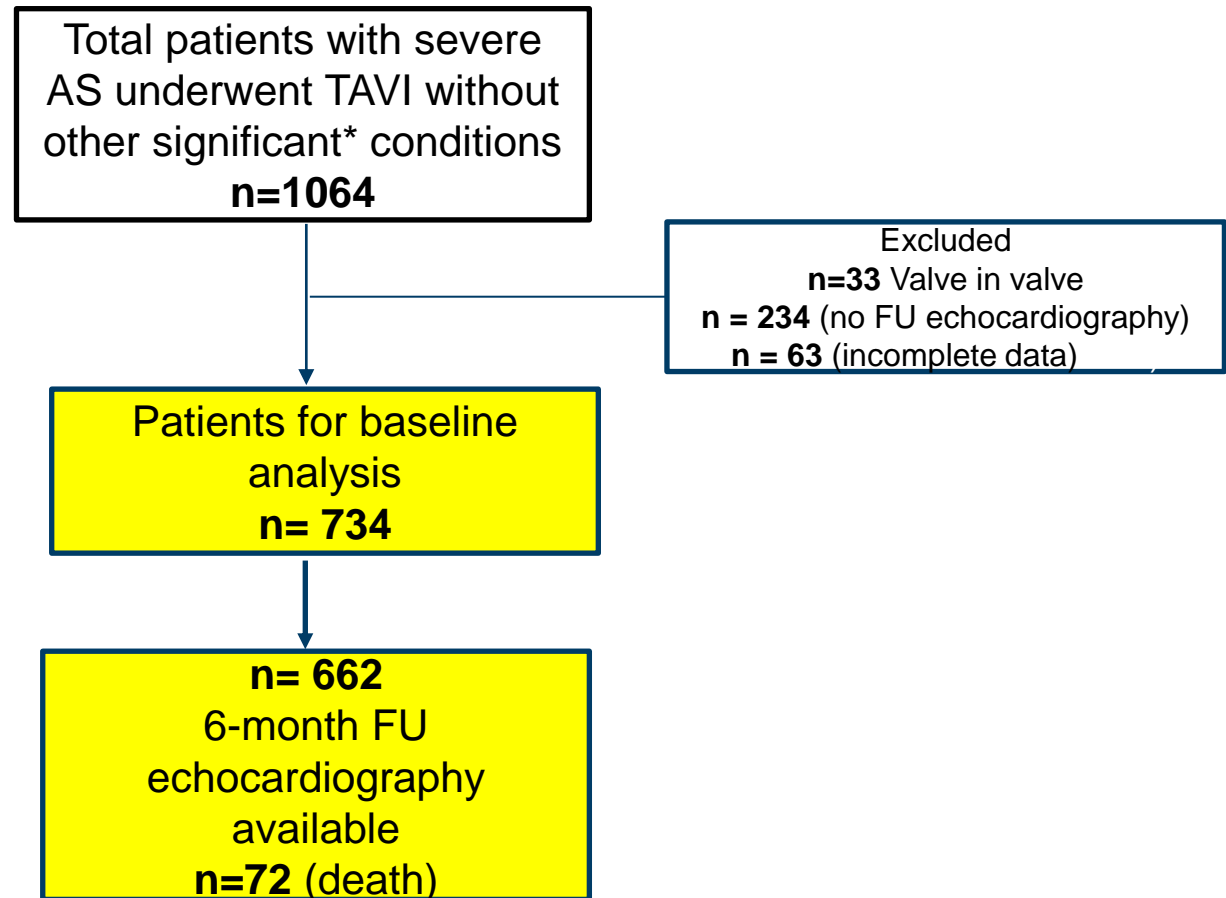


Aims

1. To evaluate cardiac damage at baseline and 6-month after transcatheter aortic valve replacement (TAVI);
2. To propose a prognosis at 2-year follow-up based on cardiac damage staging at baseline and 6 months after TAVI;
3. To determine the evolution staging and its main **predictors in a real-world population** (validate the reproducibility).

Methodology

Figure 1. Patient Inclusion Flow-Chart.



*Congenital heart disease, heart transplantation, supra or subvalvular AS, dynamic LVOT obstruction, infectious endocarditis

Methodology

- Patients with severe AS undergoing TAVI were included.
- Echocardiographic data before and 6 months after TAVI were collected and **hierarchically classified** in proposed staging.
- The primary endpoint was all-cause mortality at 2-year.
- The evolution in the extent of cardiac damage at follow-up was assessed.

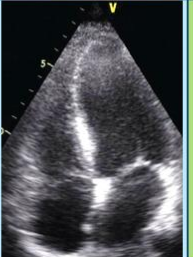


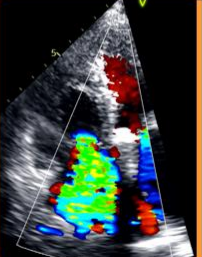
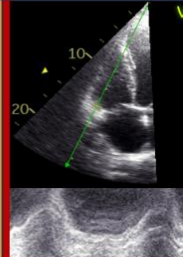
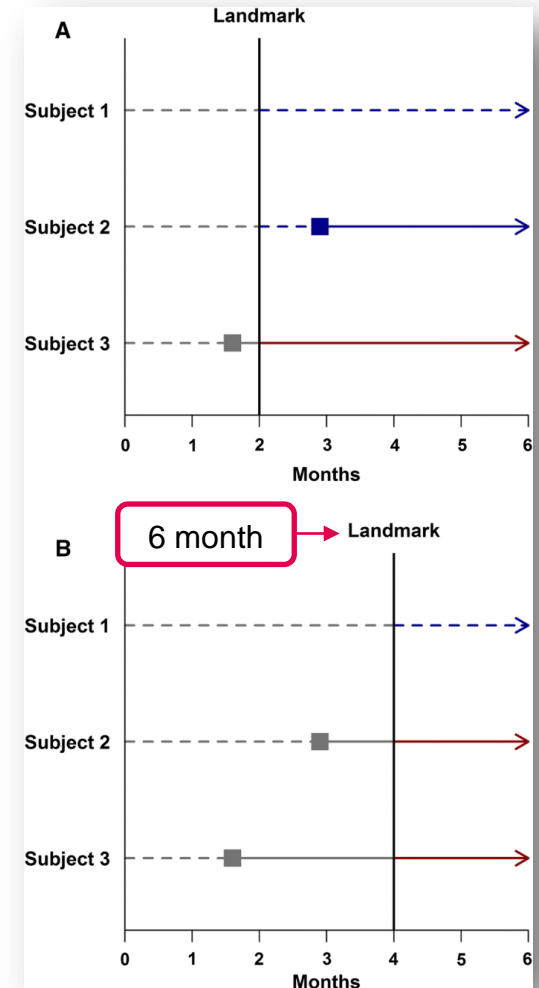
	Stage 0	Stage 1	Stage 2	Stage 3	Stage 4
	No cardiac damage	LV damage	Left atrial or Mitral damage	Pulmonary vasculature or tricuspid damage	Right ventricular damage
Echocardiographic criteria	-	<ul style="list-style-type: none"> • LV mass index $\sigma > 115 \text{ g/m}^2$ $\rho > 95 \text{ g/m}^2$ • LV ejection fraction $< 50\%$ • E/e' ratio > 14 	<ul style="list-style-type: none"> • Left atrial volume index $> 34 \text{ ml/m}^2$ • Moderate/severe mitral regurgitation 	<ul style="list-style-type: none"> • Pulmonary arterial systolic pressure $\geq 60 \text{ mmHg}$ • Moderate/severe tricuspid regurgitation 	TAPSE $< 16 \text{ mm}$
					

Figure 2. Stages of Cardiac damage in Severe AS

Methodology

- Categorical variables - using the chi-square test.
- Kolmogorov-Smirnov test and visual assessment – normality
- Continuous data - one-way ANOVA and Bonferroni's post hoc analysis for normally distributed variables, whereas the Kruskal-Wallis test was used for variables with a non-normal distribution.
- Survival analysis:
 - Kaplan-Meier method & Cox proportional hazards analysis
 - Onset of follow-up – using Landmark analysis:
 - date of AVR (for baseline staging)
 - date of follow-up TTE (for follow-up staging) at 6 month after TAVI
 - For the analysis of the association between cardiac damage stage at follow-up and 2-year outcomes.



Morgan, C.J. Landmark analysis: A primer. *J. Nucl. Cardiol* 2019.

Results: Clinical characteristics of total study population according to cardiac damage staging

	Total population (n=734)	Baseline					p-value*
		Stage 0 (n=32)	Stage 1 (n=85)	Stage 2 (n=220)	Stage 3 (n=227)	Stage 4 (n=170)	
Age years	79.8 ± 7.4	78.7±7.8	78.0 ± 8.4	80.0 ± 5.9	81.0 ±7.0	79.0 ± 8.6	0.008
Male gender, n (%)	400 (55)	17 (53)	53 (62)	121 (55)	107 (47)	102 (60)	0.056
Body mass index (kg/m ²)	26.6 ± 4.5	26.4 ± 3.9	27.2 ± 6.2	27.3 ± 4.4	25.7 ± 4.2	26.4 ± 3.7	0.001
Body surface area (m ²)	1.9 ± 0.2	1.9 ± 0.2	1.9 ±0.2	1.9± 0.2	1.8 ± 0.2	1.9 ±0.2	0.006
Hypertension, n (%)	548 (76)	21 (68)	68 (81)	166 (77)	167 (75)	126 (75)	0.593
Diabetes Mellitus, n (%)	211 (29)	6 (19)	29 (35)	74 (34.3)	48 (22)	54 (32.0)	0.016
Atrial fibrillation, n (%)	138 (19)	1 (3)	3 (4)	25 (11)	45 (20)	64 (38)	<0.0001
Pacemaker, n (%)	89 (12)	3 (9)	5 (6)	21 (10)	32 (14)	28 (17)	0.072
Hyperlipidemia, n (%)	469 (65)	21 (68)	48 (57)	141 (65)	149 (67)	110 (65)	0.609
Coronary artery disease, n (%)	440 (60)	15 (48)	51 (60)	126 (58)	130 (58)	118 (69)	0.067
Previous cardiac surgery, n (%)	150 (20)	3 (9)	13 (15)	40 (18)	32 (14)	62 (37)	<0.0001
Previous myocardial infarction, n (%)	162 (22)	4 (13)	21 (25)	38 (18)	50 (22)	49 (29)	0.063
History of smoking, n (%)	148 (21)	5 (18)	26 (31)	47 (23)	47 (23)	35 (22)	0.081
Chronic obstructive pulmonary disease, n (%)	142 (22)	10 (33)	18 (26)	45 (23)	33 (18)	36 (23)	0.318
Peripheral artery disease, n (%)	207 (29)	10 (32)	26 (31)	61 (28)	54 (24)	56 (33)	0.374
EuroSCORE II, n (%)	3.3 (2.1-5.3)	1.9 (1.5-3.5)	2.7 (1.7-4.4)	3.0 (1.9-4.8)	3.0 (2.1-4.6)	4.6 (2.8-8.4)	<0.0001
NYHA class III or IV, n (%)	415 (58.4)	16 (53)	40 (49)	115 (54)	136 (62)	108 (65)	0.064
Hemoglobin (g/dL)	12.5 ± 1.7	13.1 ± 1.5	12.8 ± 1.6	12.4 ± 1.9	12.3 ± 1.9	12.3 ± 1.7	0.025
Creatinine (mg/dl)	1.0 (0.8-1.3)	1.0 (0.9-1.2)	1.0 (0.8-1.4)	1.0 (0.9-1.3)	1.0 (0.8-1.2)	1.1 (0.9-1.5)	<0.0001
Systolic blood pressure (mmHg)	137.9 ± 22.6	141.6 ± 20.5	141.0 ± 21.7	141.4 ± 22.7	137.5 ± 22.5	131.7 ± 22.5	0.001
Diastolic blood pressure (mmHg)	68.3 ± 12.7	68.7 ±10.1	68.7 ± 13.1	66.9 ±12.3	68.6 ±13.8	69.4 ± 11.8	0.439
Medication							
Beta-blocker, n (%)	433 (60.5)	17 (55)	49 (59)	122 (57)	130 (59)	115 (69)	0.145
ACEi/ARB, n (%)	394 (55.0)	19 (61)	44 (53)	119 (55)	112 (51)	100 (60)	0.443
Calcium antagonist, n (%)	186 (26.0)	6 (19)	22 (27)	61 (28)	46 (21)	51 (31)	0.191
Diuretics, n (%)	407 (56.8)	16 (52)	36 (43)	113 (53)	130 (59)	112 (67)	0.004
Aspirin, n (%)	335 (47.6)	20 (67)	48 (59)	112 (53)	94 (43.3)	61 (37.2)	0.001
OAC/NOAC, n (%)	273 (38.8)	4 (13)	20 (25)	56 (26)	96 (44)	97 (59)	<0.0001
Statin, n (%)	468 (65.4)	21 (68)	49 (59)	149 (69)	141 (64)	108 (65)	0.523

Results: Baseline echocardiographic characteristics based on cardiac damage staging

	Total population (n=734)	Baseline					p-value
		Stage 0 (n=32)	Stage 1 (n=85)	Stage 2 (n=220)	Stage 3 (n=227)	Stage 4 (n=170)	
Heart rate (beats per minute)	70.9 ± 13.4	70.0 ± 10.5	69.3 ± 10.1	68.2 ± 12.0	70.5 ± 13.9	75.9 ± 15.2†‡§	<0.0001
Valve morphology							
Tricuspid	658 (96)	29 (94)	77 (98)	195 (96)	203 (97)	154 (95)	0.816
Bicuspid	27 (4)	2 (6)	2 (2)	8 (4)	7 (3)	8 (5)	
LV end-diastolic diameter indexed (mm/m ²)	25.2 ± 4.5	21.9 ± 3.6†‡§*	25.4 ± 4.0	25.0 ± 4.1	25.3 ± 4.5	25.9 ± 5.1	<0.0001
LV end-systolic diameter indexed (mm/m ²)	18.2 ± 5.3	15.3 ± 4.1*	18.3 ± 4.6	17.7 ± 5.1	18.1 ± 5.2	19.4 ± 6.1‡	<0.0001
Septal wall thickness (mm)	13.3 ± 2.8	11.8 ± 2.2‡§	13.1 ± 2.5	13.5 ± 2.9	13.6 ± 2.8	13.0 ± 2.7	0.004
Posterior wall thickness, mm	12.3 ± 2.3	10.9 ± 2.0‡§*	11.9 ± 1.9†	12.8 ± 2.5†§	12.1 ± 2.1	12.4 ± 2.4	<0.0001
Relative wall thickness (mm)	0.6 ± 0.2	0.6 ± 0.2	0.5 ± 0.1	0.6 ± 0.2	0.6 ± 0.2	0.5 ± 0.2	0.246
LV end-diastolic volume (ml/m ²)	47.9 (37.6-64.1)	37.1 (29.7-43.3)‡§*	45.0 (35.9-56.2)*	48.2 (37.9 – 63.0)	49.2 (38.7-64.3)	51.2 (37.5-74.1)	<0.0001
LV end-systolic volume (ml/m ²)	20.1 (13.3-32.2)	12.0 (8.8-15.3)‡§*	18.4 (12.1-26.1)	19.8 (13.6-30.7)	20.5 (13.7-31.9)	26.1 (15.1-46.2)†‡§	<0.0001
LV mass index (g/m ²)	126.3 ± 38.7	83.6 ± 16.8†‡§*	124.1 ± 34.9	130.1 ± 38.3	127.2 ± 39.5	128.9 ± 38.4	<0.0001
LV ejection fraction, %	58.0 (46.0-65.0)	66.0 (60.5-71.0)†‡§*	60.1 (50.2-66.5)	60 (52.0-66.3)	58.0 (47.0-65.0)	48.0 (37.0-60.0) †‡§	<0.0001
E/e' ratio	16.6 (12.0-24.2)	9.9 (8.5-12.0)†‡§*	15.8 (11.5-20.8)§	17.0 (12.5-24.9)	16.8 (12.4-25.0)	17.5 (12.8-25.6)	<0.0001
Left atrial volume index (ml/m ²)	44.4 ± 16.5	24.7 ± 4.5‡§*	27.3 ± 4.5‡§*	47.0 ± 11.4	47.9 ± 18.4	49.2 ± 16.3	<0.0001
Significant mitral regurgitation, n (%)	155 (22)	-	-	37 (17)	68 (31)	50 (30)	<0.0001
Systolic pulmonary arterial pressure (mmHg)	34.1 ± 15.1	26.7 ± 11.3§*	26.2 ± 14.2§*	28.8 ± 13.4§*	40.7 ± 13.4	37.6 ± 15.7	<0.0001
Significant tricuspid regurgitation, n (%)	322 (44)	-	-	-	220 (97)	102 (60)	<0.0001
Tricuspid annular plane systolic excursion (mm)	18.7 ± 4.5	19.6 ± 2.5	20.5 ± 4.0	21.0 ± 3.6§*	20.1 ± 3.1‡*	13.1 ± 2.0†‡§	<0.0001
Stroke volume index, ml/m ²	39.0 ± 12.5	40.3 ± 10.9*	39.3 ± 12.0	41.3 ± 12.9	40.6 ± 12.9	33.4 ± 10.2†‡§	<0.0001
Mean aortic valve gradient (mmHg)	41.1 ± 17.4	44.1 ± 14.3*	43.8 ± 18.6	45.3 ± 17.8	40.9 ± 17.0	34.3 ± 15.1†‡§	<0.0001
Peak aortic jet velocity (m/s)	3.9 ± 0.8	4.1 ± 0.6*	4.0 ± 0.8	4.1 ± 0.8§	3.9 ± 0.8‡	3.6 ± 0.8†‡§	<0.0001
Indexed Aortic valve area (cm ²)	0.4 ± 0.2	0.4 ± 0.1	0.5 ± 0.2	0.4 ± 0.2	0.5 ± 0.2	0.4 ± 0.2	0.623

†P-value <0.05 vs. Stage 1 with Bonferroni's post hoc analysis. ‡P-value <0.05 vs. Stage 2 with Bonferroni's post hoc analysis. §P-value <0.05 vs. Stage 3 with Bonferroni's post hoc analysis. *P-value <0.05 vs. Stage 4 with Bonferroni's post hoc analysis.

Results: Components in each cardiac damage stages at baseline and follow-up with evolution percentages

	Baseline (n=734)	6-month after TAVR (n=662)*	Baseline staging components by evolution groups			p-value
			Improved (at least 1 stage) 277/734 (37.7%)	Stabilized 290/734 (39.5%)	Worsened (at least 1 stage) 95/734 (12.9%)	
Stage 0	32 (4)	23 (3)	-	10/290 (3)	21/95 (22)	
Stage 1	85 (12)	129 (19)	5/277 (2)	35/290 (12)	42/95 (44)	
Increased LV mass index*	497 (69)	405 (66)	187/272 (69)	200/288 (69)	52/94 (55)	0.031
E/e' >14	447 (64)	489 (75)	182/265 (69)	165/276 (60)	46/90 (51)	0.006
LV ejection fraction <50%	222 (30)	122 (20)	100/276 (36)	71/289 (25)	19/95 (20)	0.001
Stage 2	220 (30)	324 (49)	54/277 (19)	127/290 (44)	23/95 (24)	
LA volume index >34 mL/m²	532 (73)	434 (67)	228/275 (83)	218/288 (76)	31/95 (33)	<0.0001
Moderate/severe MR	155 (22)	180 (28)	70/275 (26)	51/286 (18)	10/94 (11)	0.004
Stage 3	227 (31)	130 (20)	116/277 (42)	80/290 (28)	9/95 (10)	
PASP ≥60 mm Hg	37 (5)	20 (3)	16/277 (6)	14/290 (5)	1/95 (1)	0.169
Moderate/severe TR	323 (44)	145 (22)	169/277 (61)	107/290 (37)	9/95 (10)	<0.0001
Stage 4	170 (23)	56 (9)	102/ (37)	38/290 (13)	-	
Moderate/severe RV dysfunction	170 (23)	56 (9)	102/277 (37)	38/290 (13)	-	<0.0001

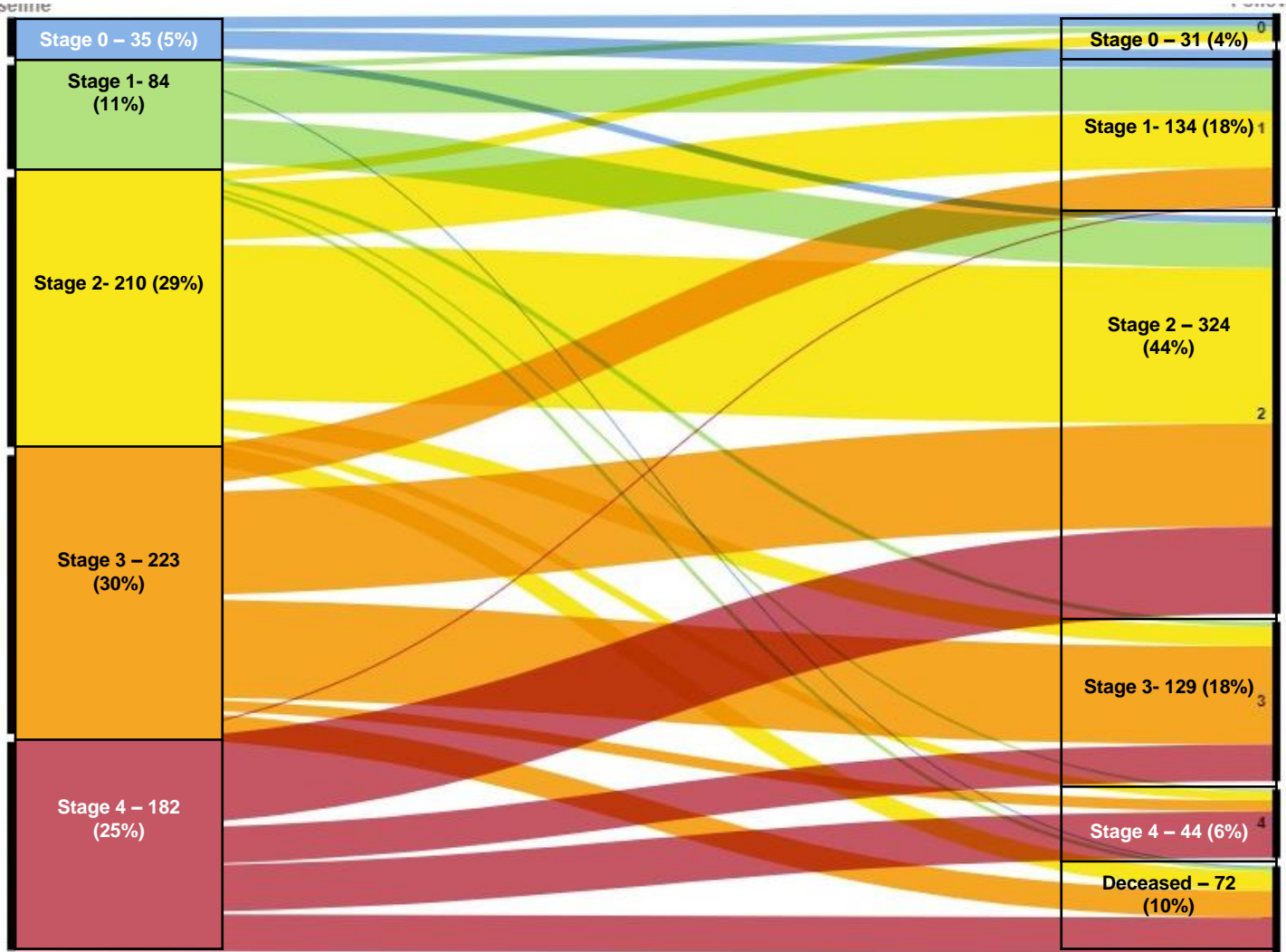
*72 patients died at 6-month follow-up.

Results:

Staging dynamic at 6 months after TAVI (n=734)

Baseline staging

Staging at follow-up



Results: Evolution of cardiac damage at 6-month follow-up by each stage (color-coded)

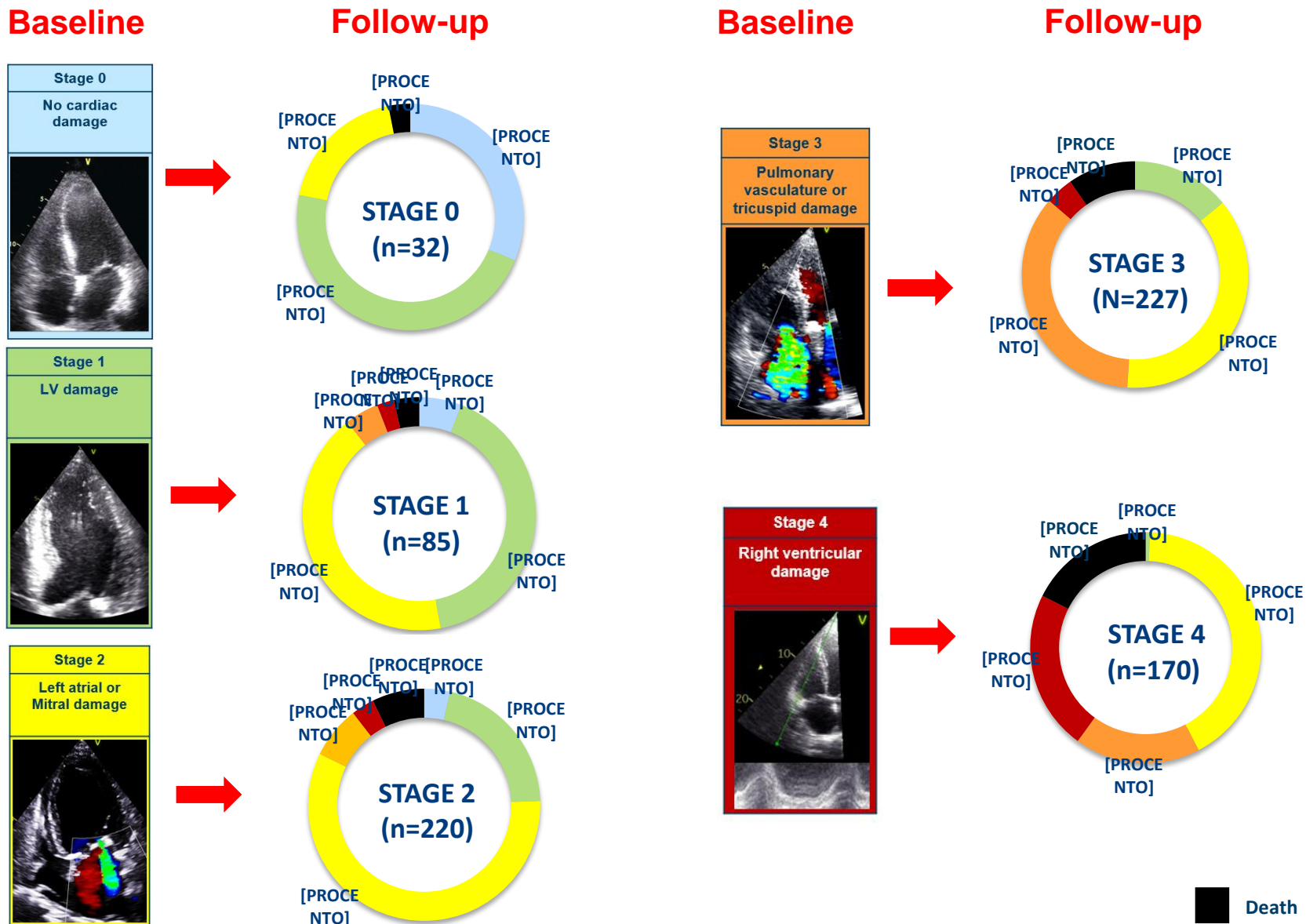


Figure 4. Evolution of cardiac damage at 6-month follow-up by each stage

Results: KM curve for all-cause death based on baseline and at follow-up staging at 2-year

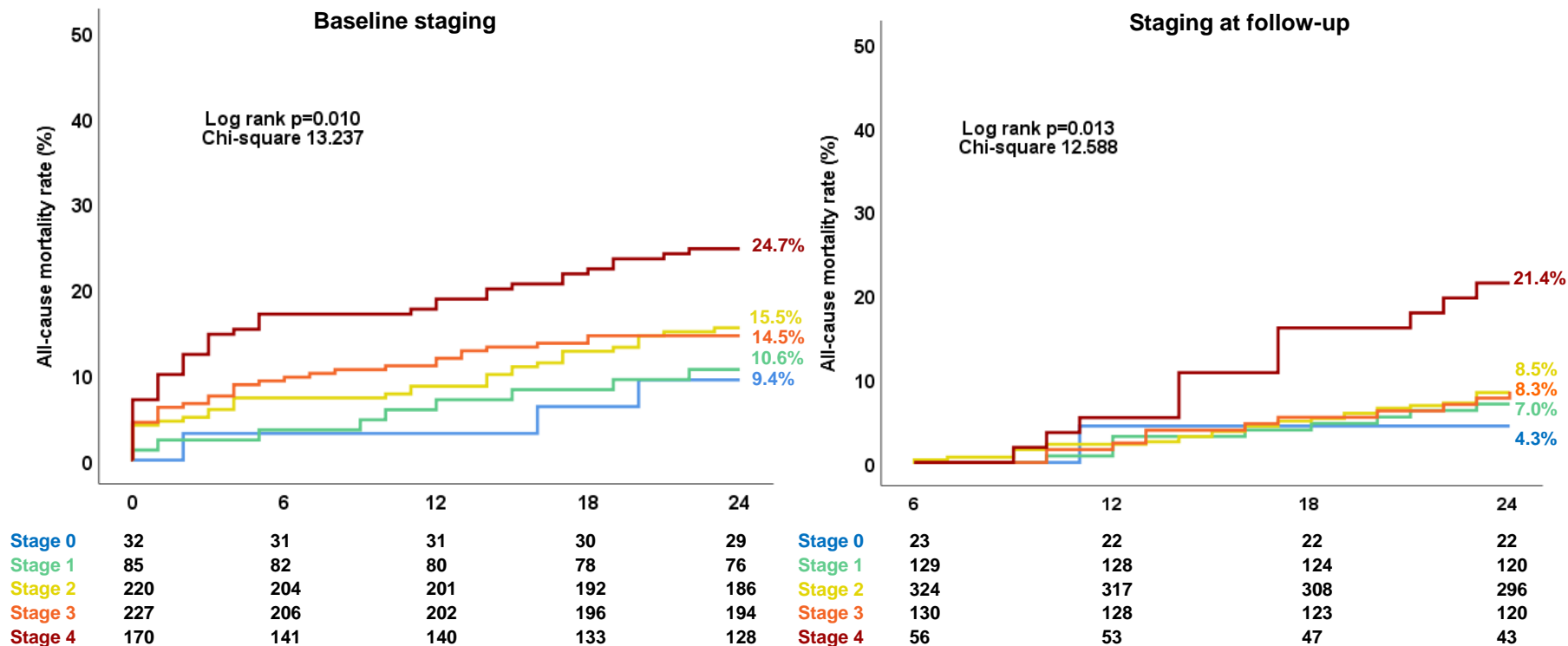


Figure 3. Kaplan-Meier survival curves for all-cause death according to cardiac damage assessed at baseline (A) and follow-up (B).

Results: Independent Predictors of 2-Year Mortality at 2-year FU (from date of follow-up to 2 year)

Parameters	HR (95% CI)	p-value
Model 1.		
Euroscore II, per 1% increase	1.035 (0.982-1.090)	0.196
Staging at baseline (per 1 stage increase)	0.934 (0.706-1.237)	0.636
Staging at 6-month (per 1 stage increase)	1.422 (1.038-1.948)	0.029
Model 2.		
Euroscore II, per 1% increase	1.035 (0.982-1.090)	0.198
Staging at baseline (per 1 stage increase)	1.406 (1.039-1.903)	0.027
Staging evolution at 6-month		0.013
Stabilized	ref	ref
Improved	0.526 (0.285-0.969)	0.039
Worsened	2.021 (0.946-4.318)	0.069

Conclusion

- The extra-valvular cardiac damage was prevalent among patients before and 6-month after TAVI.
- More than one third of patients reversed at least one stage in terms of cardiac damage at 6-month after TAVI.
- The extra-valvular cardiac damage staging may further improve risk stratification in patients undergoing TAVI.

Thank you for your attention!

