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Association of Acute Improvement in Left Ventricular Longitudinal Function After Transcatheter Aortic Valve Implantation with Outcomes for Severe Aortic Stenosis and Preserved Ejection Fraction

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Key words; echocardiography; global longitudinal strain; aortic stenosis; transcatheter aortic valve implantation

Word Counts: 3,491

Abstract

Background: Global longitudinal strain (GLS) is reportedly a sensitive marker for early subtle abnormalities in left ventricular (LV) performance of asymptomatic patients with severe aortic stenosis (AS) and preserved LV ejection fraction (LVEF). For symptomatic patients with severe AS and preserved LVEF, however, the association of immediate improvement in GLS after transcatheter aortic valve implantation (TAVI) with long-term outcomes remains uncertain.

Methods: This study concerned 157 symptomatic patients with severe AS and preserved LVEF who had undergone TAVI. Echocardiography was performed before TAVI and 7 (7-9) days after TAVI. GLS was determined by means of a two-dimensional speckle-tracking strain using current guidelines. The primary endpoint was defined as a composite endpoint comprising cardiovascular death or re-hospitalization for HF after TAVI over a median follow-up period of 27.7 (11.9-51.4) months.

Results: Mean LVEF and GLS were 65 ± 7% and 12.8 ± 3.4%, respectively. The Kaplan-Meier curve indicated that patients with acute improvement in GLS after TAVI experienced fewer cardiovascular events than those without such improvement (log-rank P=0.02). Multivariate analysis showed that non-acute improvement in GLS after TAVI was independently associated with worse outcomes as well as deterioration of the mean transaortic pressure gradient.

Conclusion: Assessment of GLS immediately after TAVI is a valuable additional parameter for better management of symptomatic patients with severe AS and preserved LVEF who are scheduled for TAVI.

Introduction

Since the primary etiology of aortic stenosis (AS) is age-related degeneration of the aortic valve, the frequency of AS increases with age. The incidence of severe AS for patients aged < 70 years is reportedly < 1%, and approximately 7% for those ≥ 80 years[1-3]. AS as a cause of heart failure (HF), especially for the elderly, therefore also increases with age. This accounts for the fact that transcatheter aortic valve implantation (TAVI) has become vital treatment option for the growing number of elderly patients with severe AS because medical treatment only for AS cannot result in improved outcomes.

Left ventricular (LV) systolic dysfunction with LV ejection fraction (LVEF) < 50% occurs late in the course of AS, because LVEF may be maintained despite reduced myocardial contractility and potentially irreversible alterations in myocardial function. These changes result from myocardial fibrosis caused by the use of preload reserve, which leads to diastolic dysfunction or changes in LV geometry including LV concentric hypertrophy and remodeling[4-7]. It has been found that speckle-tracking echocardiographic parameters are useful for the detection of early LV functional abnormalities in patients with AS. In particular, global longitudinal strain (GLS) assessed by two-dimensional speckle-tracking echocardiography is reportedly a sensitive marker for early subtle abnormalities of LV myocardial performance. This marker is thus helpful for the prediction of outcomes for asymptomatic patients with severe AS and preserved LVEF, and superior to conventional echocardiographic indices[8-11]. Previous studies focused on the association of GLS with outcomes for patients with severe AS and preserved LVEF, especially asymptomatic patients. As for symptomatic patients with severe AS and preserved LVEF, it was also reported that GLS significantly improved 3 months after TAVI [12], but the association of immediate improvement in GLS after TAVI with long-term outcome remains uncertain. The objectives of this study were therefore to investigate the association of acute

improvement in GLS after TAVI with long-term outcome for symptomatic patients with severe AS and preserved LVEF.

Materials and Methods

Patient population

This study concerned 217 consecutive symptomatic patients with severe AS who had undergone TAVI between October 2015 and September 2020 at Kobe University Hospital. Severe AS was defined as an aortic valve area ≤ 1.0 cm^2 (and/or ≤ 0.6 cm^2/m^2) measured by means of transthoracic echocardiography. After the exclusion of 61 patients with reduced LVEF of < 50% and 5 with insufficient data for analysis, the 151 remaining symptomatic patients, who had severe AS and preserved LVEF of ≥ 50% and had undergone TAVI, formed the final study group (Figure 1). The indication for TAVI for an individual patient was decided upon by consensus of a multidisciplinary heart team at our institution, consisting of clinical cardiologists, interventional cardiologists, cardiac surgeons, imaging specialists with expertise in interventional imaging, cardiovascular anesthesiologists, and physical therapists. The team used current guidelines to reach their consensus[13]. This study was approved by the local ethics committee of our institution (No. B220060) and was conducted in accordance with the Declaration of Helsinki.

Echocardiographic examination

All patients had undergone transthoracic echocardiography before and 7 (7-9) days after TAVI, while echocardiographic data were obtained with a commercially available echocardiographic system. Digital routine grayscale two-dimensional cine loops from three consecutive heartbeats were obtained at end-expiratory apnea from standard parasternal and apical views. The sector width was optimized to allow for complete myocardial visualization while maximizing the frame rate. Standard

echocardiographic measurements were obtained in accordance with the current guidelines of the American Society of Echocardiography/European Association of Cardiovascular Imaging[13]. Specifically, the aortic valve area was calculated with the continuity equation using velocity-time integrals of the aortic valve and LV outflow tract and was indexed for the body surface area, while peak and mean aortic transvalvular gradients were calculated with the modified Bernoulli equation[14].

Speckle-tracking strain analysis was performed for each patient with the aid of a single dedicated software to evaluate GLS (AutoSTRAIN; TOMTEC-ARENA, TOMTEC Imaging Systems GmbH, Munich, Germany). Briefly, apical 4-, 2- and long-axis views, obtained as Digital Imaging and Communications in Medicine (DICOM) formatted file images, were uploaded onto a personal computer for subsequent off-line GLS analysis. Longitudinal speckle-tracking strain was calculated by means of an automated contouring detection algorithm, and manual adjustments of regions of interest were performed if necessary. Longitudinal strain results were visualized as color-coded in individual clips and combined in a bull's eye plot. GLS was then determined as the averaged peak longitudinal strain of 18 LV segments, and, in accordance with current guidelines, was expressed as an absolute value [13]. Patients whose GLS increased after TAVI were defined as those with acute improvement in GLS after TAVI, and patients who showed a reduction in GLS after TAVI were defined as those with non-acute improvement in GLS after TAVI.

Definition of primary endpoint

The primary endpoint was defined as a composite endpoint including cardiovascular death and re-hospitalization for HF after TAVI over a median follow-up period of 27.7 (11.9-51.4) months.

Statistical analysis

Continuous variables were expressed as mean values with their standard deviations for normal distributed data and as medians with their interquartile range for non-normal distributed data.

Categorical variables were expressed as frequencies and percentages. Survival curves of freedom from cardiovascular death and re-hospitalization for HF were determined with the Kaplan-Meier method, and cumulative event rates were compared by using the log-rank test. The initial univariate associated parameters of cardiovascular death and re-hospitalization for HF were identified by means of a Cox proportional hazards model and were followed by a multivariate Cox proportional hazards analysis using the enter method Variables with a univariate value of $P < 0.05$ were incorporated into multivariate analysis. The intraclass correlation coefficient was used to determine inter- and intra-observer reproducibility for GLS from 78 randomly selected patients using an identical cine-loop for each view. For all steps, a P-value of <0.05 was considered statistically significant. All analyses were performed using commercially available software (MedCalc software version 20.106; MedCalc Software, Mariakerke, Belgium).

Results

Baseline characteristics

The baseline clinical and echocardiographic characteristics of the 151 symptomatic patients with severe AS and preserved LVEF are summarized in Table 1. Their mean age was 85.3 ± 4.2 years and 41 patients (27%) were male. The median aortic valve area was 0.625 (0.530-0.780) cm^2 [0.438 (0.359-0.526) cm^2/m^2], mean LVEF was 65 ± 7%, and mean GLS was 12.8 ± 3.4%. The intraclass correlation coefficient for inter- and intra-observer reproducibility of GLS were 0.984 (95 % confidence interval 0.975 - 0.990) and 0.942 (95 % confidence interval 0.911 - 0.963), respectively.

Associations with outcomes of acute improvement in GLS after TAVI

During the median follow-up period of 27.7 (11.9-51.4) months, 11 (7.3%) patients reached primary endpoint, with 7 patients dying of cardiovascular death, and the remaining 4 being hospitalized

due to worsening HF. In overall patients, changes in heart rate, LVEF and GLS between before and 7 days after TAVI were small (heart rate: from 67.0 (60.0 - 70.3) bpm to 68.0 (60.0 - 73.3) bpm, P = 0.03; LVEF: from 67.1 ± 2.7% to 65.3 ± 1.4%, P = 0.53; GLS: from 12.8 ± 0.5% to 13.3 ± 0.6%, P = 0.13).

Ninety-two patients showed acute improvement in GLS after TAVI, and the remaining 59 patients did not. The baseline clinical and echocardiographic characteristics of the patients with acute improvement and non-acute improvement in GLS after TAVI are summarized in Table 2. The baseline clinical and echocardiographic characteristics between both groups were similar except for that patients with acute improvement in GLS after TAVI had lower GLS and more prevalence of coronary artery disease. The Kaplan-Meier curve indicated that the former 92 patients experienced fewer cardiovascular events than the latter 59 (log-rank P=0.02, Figure 2). Furthermore, there were 12 patients (7.9%) with preserved baseline GLS (≥ 16%) and acute improvement in GLS after TAVI. This pattern was associated with favorable outcomes with an evet-free rate of 100% (Figure 3). Patients with impaired baseline GLS (< 16%) and non-acute improvement in GLS after TAVI, on the other hand, was associated with unfavorable outcomes with an evet-free rate of 84.4% (Figure 3). The hazard ratio and 95% confidence interval for each of the variables of the univariate and multivariate Cox proportional hazards analyses are shown in Table 3. An important finding of the multivariate analysis showed that non-acute improvement in GLS after TAVI, as well as mean transaortic pressure gradient, was independently associated with cardiovascular events.

Figure 4 shows representative cases of polar plot longitudinal strain mapping before and after TAVI for patients with and without cardiovascular events.

Discussion

The findings of this study demonstrate that acute improvement in GLS after TAVI may be

associated with favorable long-term outcomes for symptomatic patients with severe AS and preserved LVEF. Moreover, results of multivariate Cox proportional hazards analyses indicate that non-acute improvement in GLS after TAVI was an independent parameter for the development of cardiovascular events.

LV longitudinal myocardial function for patients with AS and preserved LVEF

Echocardiography is the most useful and widely available examination for the quantification and early detection of LV functional and morphological abnormalities in HF patients. However, these indices have limited power to detect subtle LV myocardial performance abnormalities. However, LV longitudinal myocardial function assessed by means of GLS has recently been found to be a more sensitive marker of LV functional abnormalities, and thus more helpful than conventional indices such as LVEF for the prediction of outcomes for various cardiac diseases. Furthermore, GLS is now well validated and has been shown to be robust and easily performed on most modern echocardiography machines. In short, GLS can detect LV dysfunction more effectively than LVEF and has been found to reveal additional pathological features of various cardiovascular diseases.

Similar to other cardiovascular diseases, GLS is reportedly a sensitive marker for early subtle abnormalities of LV myocardial performance, and superior to conventional echocardiographic indices for patients with AS, especially asymptomatic patients with severe AS and preserved LVEF[8-11]. The impairment of LV longitudinal myocardial function is also associated with myocardial fibrosis[15, 16], which in turn is a potential prognostic marker of patients with AS[17, 18]. The changes in LV longitudinal myocardial function correspond to changes in AS severity and in LV morphology, LV myocardial damage, and fibrosis proliferation[15, 19, 20]. In addition, the presence of LV myocardial fibrosis may be a predictor of the risk of no LV function recovery following aortic valve replacement and no favorable outcome[17, 18]. Therefore, the development of LV fibrosis is the main

pathophysiologic mechanism involved in the reduction in LV longitudinal myocardial function of patients with AS. In a recent individual participant data meta-analysis using 10 studies involving 1,067 asymptomatic patients with severe AS and preserved LVEF from Magne et al., GLS was found to be strongly associated with mortality, with a >2.5-fold increase in the risk of death of patients with impaired GLS defined as GLS < 14.7%[21].

The findings of the current study showed that acute improvement in GLS was associated with favorable long-term outcome, but baseline GLS was not. It has been reported that myocardial strain-derived parameters are directly related to LV contractility[22], and was associated with prognosis. However, patients with preserved baseline GLS and acute improvement in GLS after TAVI was associated with favorable outcomes, whereas, those with impaired baseline GLS and non-acute improvement in GLS after TAVI was associated with unfavorable outcomes in this study. Thus, baseline GLS alone was not a predictor of long-term outcome in this study, but it may be relevant. In addition, previous studies regarding the utility of baseline GLS focused on asymptomatic patients with severe AS and preserved LVEF, but all patients in this study were symptomatic. Attias et al. reported that GLS of symptomatic patients with severe AS and preserved LVEF was significantly lower than that of asymptomatic patients with severe AS and preserved LVEF (17.5 ± 6 3% vs. 19.0 ± 3.7%, P < 0.001)[23]. In fact, mean GLS before TAVI in this study was as low as 12.8% ± 3.4% regardless of preserved LVEF due to symptomatic status. Therefore, baseline GLS may be less useful as a marker of subclinical LV dysfunction or as a prognostic marker of symptomatic patients with severe AS, even those with preserved LVEF. Thus, reverse remodeling of GLS one week after TAVI may be more useful than baseline GLS.

Clinical implications

Severe AS occurs in 12.4% of people over 75 years of age and represents a substantial burden on health services[24]. TAVI has been established as a treatment option for HF patients with severe AS considered to be at intermediate to high surgical risk or deemed inoperable. However, HF develops in a certain number of patients with AS even those who have undergone a TAVI[25]. The clinical course of HF is generally chronic and progressive. Patients with established HF show chronic progression and may experience repeated episodes of acute decompensated HF while repeated acute exacerbations can lead to the gradual development of more severe HF, from Stage C HF to Stage D HF. This means that attending physicians need to prevent repeated acute exacerbations for HF patients. The findings of this study demonstrated that early evaluation of LV longitudinal myocardial function by means of GLS one week after TAVI is useful for avoiding HF re-hospitalization and having a positive impact on outcome after TAVI. However, careful attention is needed for patients who have been discharged but do not show acute improvement GLS after TAVI. Moreover, it has been reported that the GLS after TAVI can change over time[12, 26]. Though not part of this study, the measurement of GLS over time may be a more accurate predictor of outcomes than the measurement of GLS only in the one week after TAVI.

Study limitations

This study covered a small number of patients in a retrospective single-center study, so that further studies with larger patient populations will be needed to validate our findings. Moreover, the amount of change in GLS before and after TAVI was small, so the definition of acute improvement in GLS after TAVI may be difficult. However, reproducibility of GLS in this study was acceptable.

Conclusion

Acute improvement in GLS after TAVI was found to be associated with favorable long-term outcomes for symptomatic patients with severe AS and preserved LVEF. Assessment of GLS one week

after TAVI is thus a valuable additional parameter for better management of symptomatic patients with severe AS after TAVI.

Conflict of interest

H.T. is a consultant for AstraZeneca plc, Ono Pharmaceutical Company, Limited. Pfizer Inc, Otsuka Pharmaceutical Co., Ltd., Daiichi Sankyo Company, Limited, and Novartis International AG.

H.O is a consultant for Abbott Vascular Japan and Terumo Co.

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The remaining authors have no conflicts of interest to declare.

References

1. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M Burden of valvular heart diseases: a population-based study. Lancet 2006; 368 9540:1005-11.
2. Danielsen R, Aspelund T, Harris TB, Gudnason V The prevalence of aortic stenosis in the elderly in Iceland and predictions for the coming decades: the AGES-Reykjavik study. Int J Cardiol 2014; 176 3:916-22.
3. Eveborn GW, Schirmer H, Heggelund G, Lunde P, Rasmussen K The evolving epidemiology of valvular aortic stenosis. the Tromso study. Heart 2013; 99 6:396-400.
4. Tanaka H Efficacy of echocardiography for differential diagnosis of left ventricular hypertrophy: special focus on speckle-tracking longitudinal strain. J Echocardiogr 2021; 19 2:71-9.
5. Aurigemma GP, Silver KH, Priest MA, Gaasch WH Geometric changes allow normal ejection fraction despite depressed myocardial shortening in hypertensive left ventricular hypertrophy. J Am Coll Cardiol 1995; 26 1:195-202.
6. Krayenbuehl HP, Hess OM, Ritter M, Monrad ES, Hoppeler H Left ventricular systolic function in aortic stenosis. Eur Heart J 1988; 9 Suppl E 19-23.
7. Abe Y Screening for aortic stenosis using physical examination and echocardiography. J Echocardiogr 2021; 19 2:80-5.
8. Vollema EM, Sugimoto T, Shen M, Tastet L, Ng ACT, Abou R *et al* Association of Left Ventricular Global Longitudinal Strain With Asymptomatic Severe Aortic Stenosis: Natural Course and Prognostic Value. JAMA Cardiol 2018; 3 9:839-47.
9. Dahl JS, Magne J, Pellikka PA, Donal E, Marwick TH Assessment of Subclinical Left Ventricular Dysfunction in Aortic Stenosis. JACC Cardiovasc Imaging 2019; 12 1:163-71.
10. Nagata Y, Takeuchi M, Wu VC, Izumo M, Suzuki K, Sato K *et al* Prognostic value of LV

deformation parameters using 2D and 3D speckle-tracking echocardiography in asymptomatic patients with severe aortic stenosis and preserved LV ejection fraction. JACC Cardiovasc Imaging 2015; 8 3:235-45.

11. Sato K, Seo Y, Ishizu T, Takeuchi M, Izumo M, Suzuki K *et al* Prognostic value of global longitudinal strain in paradoxical low-flow, low-gradient severe aortic stenosis with preserved ejection fraction. Circ J 2014; 78 11:2750-9.
12. Al-Rashid F, Totzeck M, Saur N, Janosi RA, Lind A, Mahabadi AA *et al* Global longitudinal strain is associated with better outcomes in transcatheter aortic valve replacement. BMC Cardiovasc Disord 2020; 20 1:267.
13. Lang RM, Badano LP, Mor-Avi V, Afilalo J, Armstrong A, Ernande L *et al* Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr 2015; 28 1:1-39 e14.
14. Vahanian A, Beyersdorf F, Praz F, Milojevic M, Baldus S, Bauersachs J *et al* 2021 ESC/EACTS Guidelines for the management of valvular heart disease. Eur Heart J 2022; 43 7:561-632.
15. Weidemann F, Herrmann S, Stork S, Niemann M, Frantz S, Lange V *et al* Impact of myocardial fibrosis in patients with symptomatic severe aortic stenosis. Circulation 2009; 120 7:577-84.
16. Mele D, Censi S, La Corte R, Merli E, Lo Monaco A, Locaputo A *et al* Abnormalities of left ventricular function in asymptomatic patients with systemic sclerosis using Doppler measures of myocardial strain. J Am Soc Echocardiogr 2008; 21 11:1257-64.
17. Barone-Rochette G, Pierard S, De Meester de Ravenstein C, Seldrum S, Melchior J, Maes F *et al* Prognostic significance of LGE by CMR in aortic stenosis patients undergoing valve replacement. J Am Coll Cardiol 2014; 64 2:144-54.

18. Azevedo CF, Nigri M, Higuchi ML, Pomerantzeff PM, Spina GS, Sampaio RO *et al* Prognostic significance of myocardial fibrosis quantification by histopathology and magnetic resonance imaging in patients with severe aortic valve disease. J Am Coll Cardiol 2010; 56 4:278-87.

19. Ng AC, Delgado V, Bertini M, Antoni ML, van Bommel RJ, van Rijnsoever EP *et al* Alterations in multidirectional myocardial functions in patients with aortic stenosis and preserved ejection fraction: a two-dimensional speckle tracking analysis. Eur Heart J 2011; 32 12:1542-50.

20. Takeda S, Rimington H, Smeeton N, Chambers J Long axis excursion in aortic stenosis. Heart 2001; 86 1:52-6.

21. Magne J, Cosyns B, Popescu BA, Carstensen HG, Dahl J, Desai MY *et al* Distribution and Prognostic Significance of Left Ventricular Global Longitudinal Strain in Asymptomatic Significant Aortic Stenosis: An Individual Participant Data Meta-Analysis. JACC Cardiovasc Imaging 2019; 12 1:84-92.

22. Greenberg NL, Firstenberg MS, Castro PL, Main M, Travaglini A, Odabashian JA *et al* Doppler-derived myocardial systolic strain rate is a strong index of left ventricular contractility. Circulation 2002; 105 1:99-105.

23. Attias D, Macron L, Dreyfus J, Monin JL, Brochet E, Lepage L *et al* Relationship between longitudinal strain and symptomatic status in aortic stenosis. J Am Soc Echocardiogr 2013; 26 8:868-74.

24. Osnabrugge RL, Mylotte D, Head SJ, Van Mieghem NM, Nkomo VT, LeReun CM *et al* Aortic stenosis in the elderly: disease prevalence and number of candidates for transcatheter aortic valve replacement: a meta-analysis and modeling study. J Am Coll Cardiol 2013; 62 11:1002-12.

25. Spitzer E, Hahn RT, Pibarot P, de Vries T, Bax JJ, Leon MB *et al* Aortic Stenosis and Heart Failure: Disease Ascertainment and Statistical Considerations for Clinical Trials. Card Fail Rev

2019; 5 2:99-105.

26. D'Ascenzi F, Cameli M, Iadanza A, Lisi M, Zaca V, Reccia R *et al* Improvement of left ventricular longitudinal systolic function after transcatheter aortic valve implantation: a speckle-tracking prospective study. Int J Cardiovasc Imaging 2013; 29 5:1007-15.

Figure Legends

Figure 1: Flowchart of patients recruited for this study.

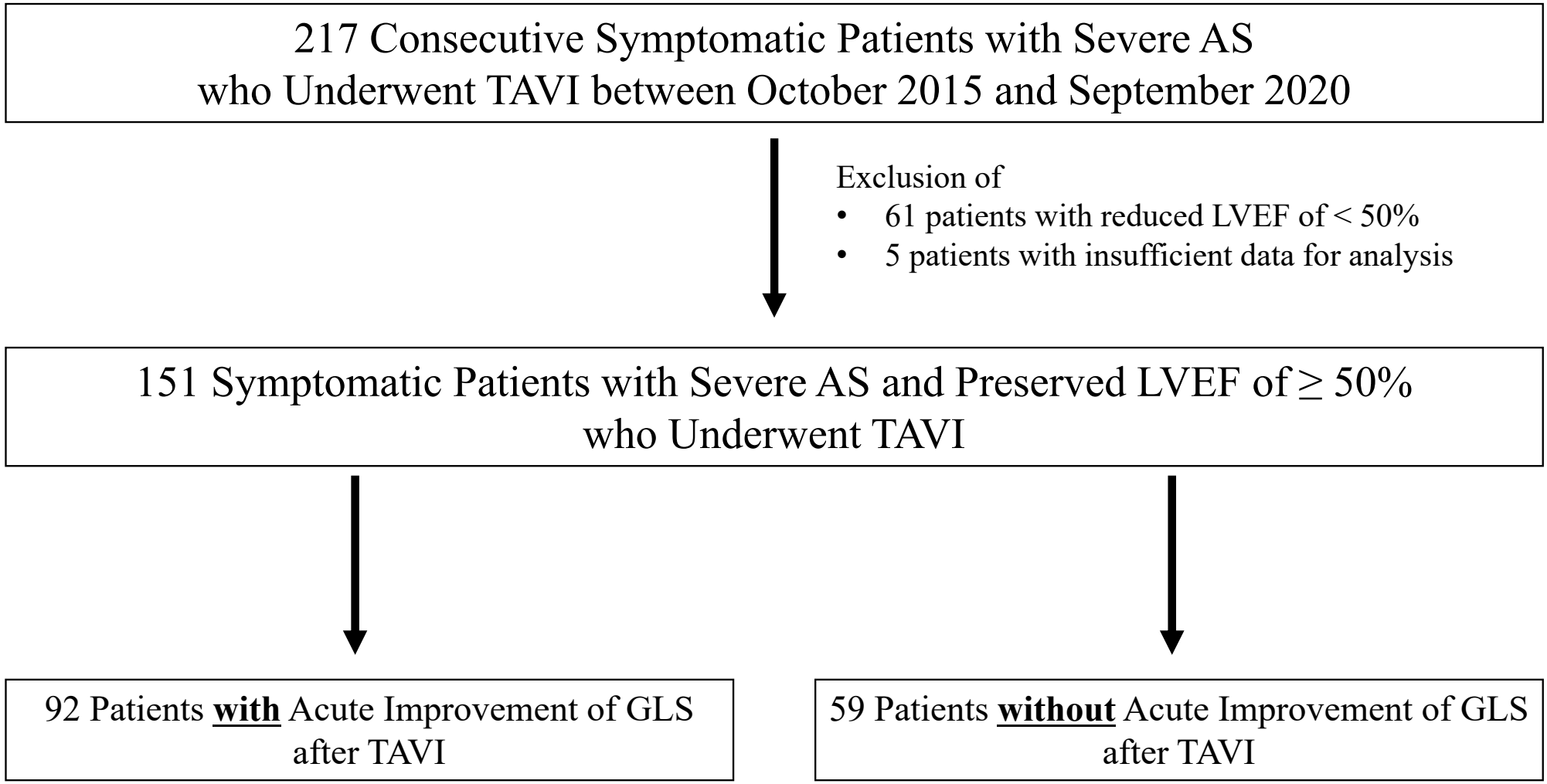
AS, aortic stenosis; TAVI, transcatheter aortic valve implantation; LVEF, left ventricular ejection fraction; GLS, global longitudinal strain

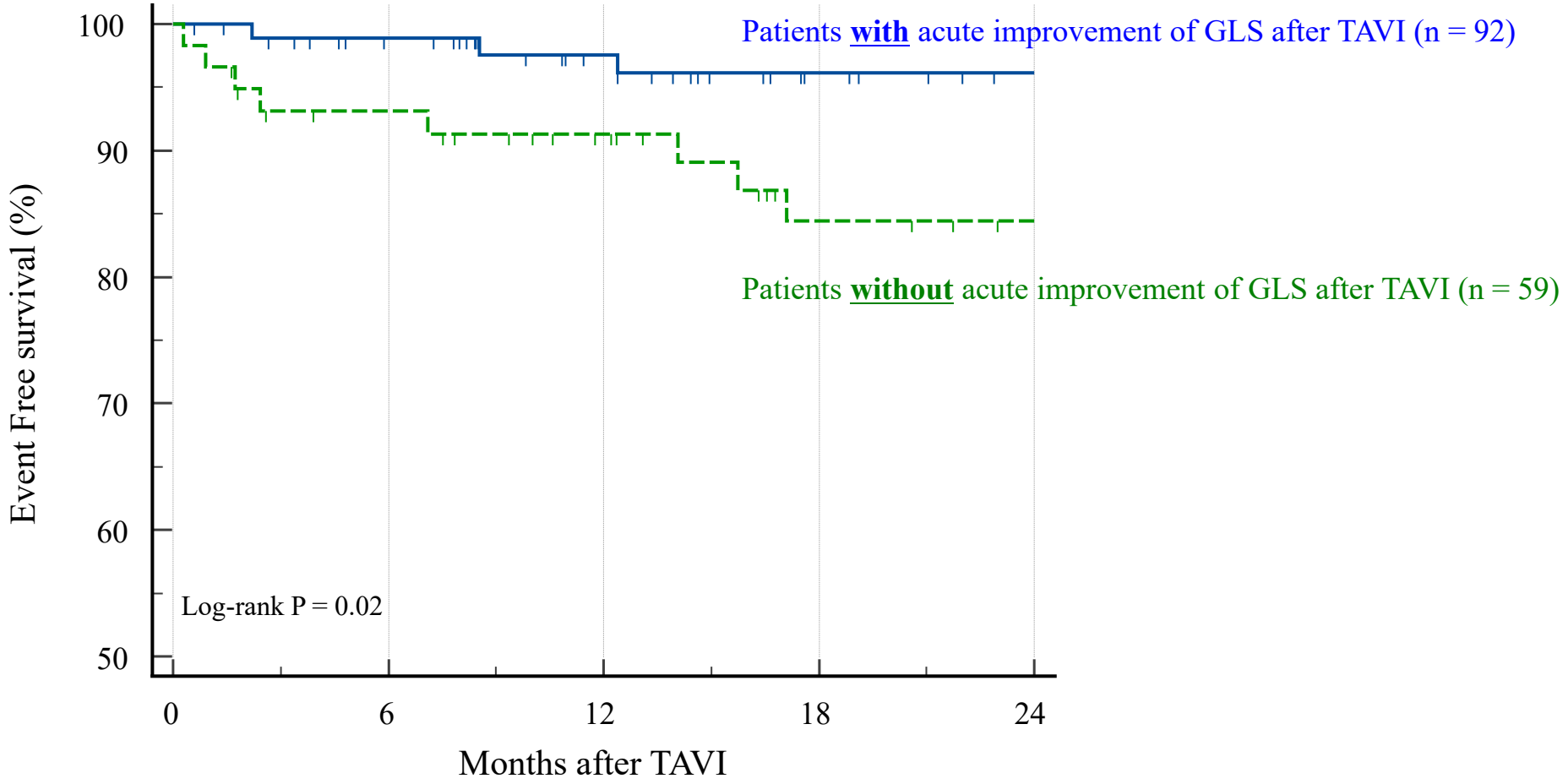
Figure 2: Kaplan-Meier curve representing the primary endpoint, showing that patients who showed acute improvement in global longitudinal strain (GLS) after transcatheter aortic valve implantation (TAVI) experienced fewer cardiovascular events than patients who did not.

Figure 3: Kaplan-Meier curve representing the primary endpoint, showing that patients with preserved baseline global longitudinal strain (GLS) (≥ 16%) who showed acute improvement in GLS after transcatheter aortic valve implantation (TAVI) was associated with favorable outcomes. Patients with impaired baseline GLS (< 16%) and non-acute improvement in GLS after TAVI, on the other hand, was associated with unfavorable outcomes.

Figure 4: Representative cases of polar plot longitudinal strain mapping for one patient with and one without cardiovascular events.

LVEF, left ventricular ejection fraction; AVAi, indexed aortic valve area; TAVI, transcatheter aortic valve implantation; GLS, global longitudinal strain


217 Consecutive Symptomatic Patients with Severe AS
who Underwent TAVI between October 2015 and September 2020
Exclusion of
• 61 patients with reduced LVEF of < 50%
• 5 patients with insufficient data for analysis
151 Symptomatic Patients with Severe AS and Preserved LVEF of ≥ 50%
who Underwent TAVI
92 Patients with Acute Improvement of GLS after TAVI
59 Patients without Acute Improvement of GLS after TAVI



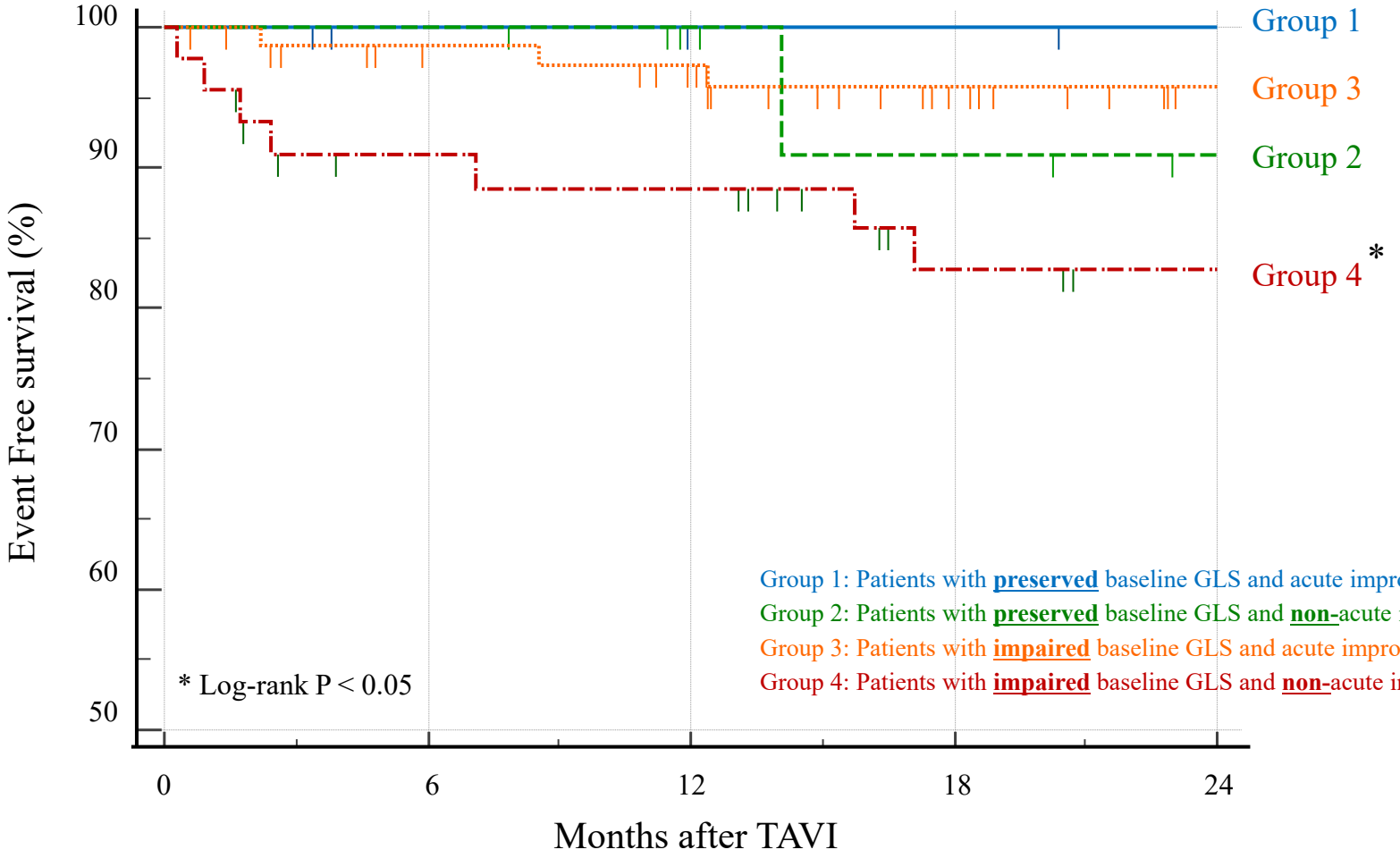
Number at risk

Patients **with** acute improvement of GLS after TAVI

92	82	69	58	53

Patients **without** acute improvement of GLS after TAVI

59	51	44	35	32



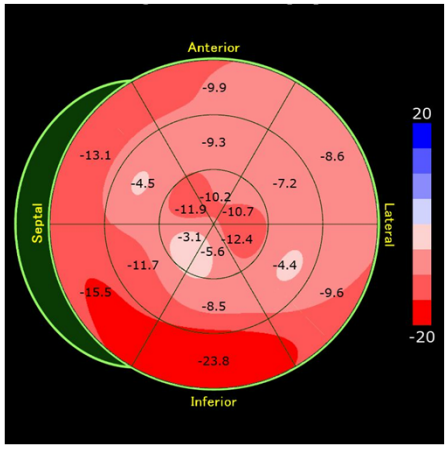
Number at risk

Group 1	12	10	9	9	8
Group 2	15	15	12	10	8
Group 3	79	70	66	54	46
Group 4	45	37	36	28	26

Patient **with** Cardiovascular Event

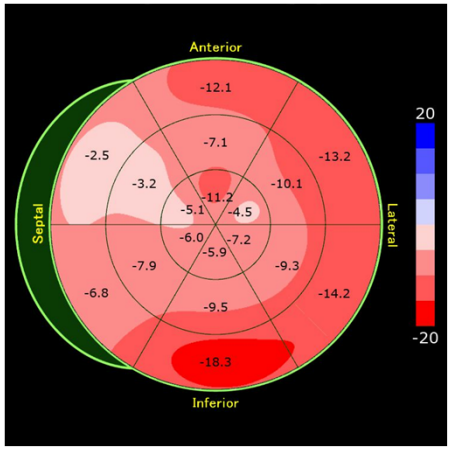
- ✓ 88-year-old female
- ✓ LVEF = 77.2%
- ✓ Peak Transaortic Velocity = 5.09 m/s
- ✓ Mean Pressure Gradient = 64 mmHg
- ✓ AVAi = 0.33 cm^2/m^2

Before TAVI



GLS=10.2%

7 Days After TAVI



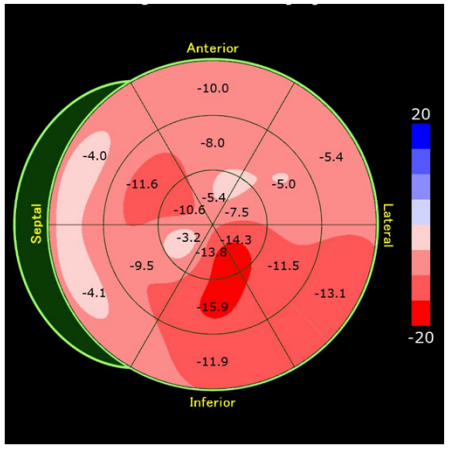
GLS=8.5%

ΔGLS = -1.4%

Patient **without** Cardiovascular Event

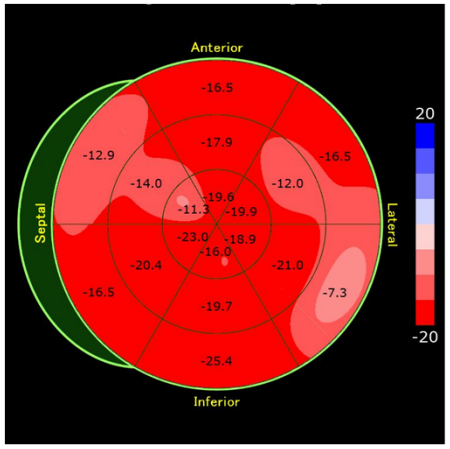
- ✓ 89-year-old male
- ✓ LVEF = 56.5%
- ✓ Peak Transaortic Velocity = 4.45 m/s
- ✓ Mean Pressure Gradient = 48 mmHg
- ✓ AVAi = 0.45 cm^2/m^2

Before TAVI



GLS=8.7%

7 Days After TAVI



GLS=14.4%

ΔGLS = 5.7%

Table 1

Baseline clinical and echocardiographic characteristics of the patients

Variables	Value
Clinical Data	
Age, year	85.3 ± 4.2
Gender (men), n (%)	41 (27 %)
Body surface area, m^2	1.46 ± 0.17
Systolic blood pressure, mmHg	134.0 ± 108.9
Diastolic blood pressure, mmHg	67.8 (61.0-76.0)
Heart rate, beat/min	66.0 ± 15.2
STS score	5.91 (4.39-8.47)
Logistic EuroScore	11.44 (8.52-18.06)
Comorbidities, n (%)	
Coronary disease	26 (25.5 %)
Hypertension	74 (72.5 %)
Diabetes mellitus	27 (26.5 %)
Dyslipidemia	44 (43.1 %)
Chronic kidney disease	47 (46.1 %)
Dialysis	0 (0 %)
Pulmonary dysfunction	29 (28.4 %)
Atrial fibrillation	20 (19.6 %)
Previous open chest surgery	4 (3.9 %)
Cranial infarction	12 (11.8 %)
Blood examination	
Serum BNP concentration, pg/mL	201 (93-365)
Creatinine, mg/dL	0.87 (0.69-1.12) mg/dL
Hemoglobin, g/dl	11.3 (10.2-12.3) g/dL
Echocardiography	
LV end-diastolic volume, mL	60.9 ± 22.9
LV end-systolic volume, mL	21.0 ± 10.6
LV ejection fraction	65.7 ± 7.8
LV mass index, g/m^2	112.5 (90.5-135.5)
LA volume index, mL/m^2	55.1 (42.9-71.9)
E wave velocity, cm/s	76.0 ± 32.2
E/e’	19.6 ± 9.9

Aortic valve area, cm^2	0.63 ± 0.18
Indexed aortic valve area, cm^2/m^2	0.44 ± 0.13
Mean transaortic pressure gradient, mmHg	51.8 (43.0-61.1)
Global longitudinal strain, %	12.8 ± 3.4

Values are mean ± SD for normally distributed data and median and interquartile range for non-normally distributed data, or n (%).

STS, The Society of Thoracic Surgeons; BNP, B-type natriuretic peptide; LV, left ventricular; LA, left atrial; E, peak early diastolic mitral flow velocity; e', spectral pulsed-wave Doppler-derived early diastolic velocity from the septal mitral annulus;

Table 2

Baseline clinical and echocardiographic characteristics of the patients with acute improvement and non-acute improvement in GLS after TAVI

Variables	Patients with acute improvement in GLS after TAVI (N=92)	Patients with non-acute improvement in GLS after TAVI (N=59)	P value
Clinical Data			
Age, year	85.1 ± 0.9	85.3 ± 1	0.778
Gender (men), n (%)	24 (26.4)	19 (31.7)	0.482
Body surface area, m^2	1.46 ± 0.04	1.48 ± 0.04	0.422
Systolic blood pressure, mmHg	133.3 ± 3.7	133.4 ± 5.5	0.975
Diastolic blood pressure, mmHg	68.3 ± 2.2	65.4 ± 3.3	0.137
Heart rate, beat/min	68.2 ± 4.2	65.5 ± 2.8	0.341
STS score	5.7 (4.0 - 7.4)	5.9 (4.5 - 7.8)	0.288
Logistic EuroScore	11.2 (8.2 - 15.3)	11.4 (8.6 - 16.1)	0.758
Comorbidities, n (%)			
Coronary disease	27 (29.7)	9 (15.3)	0.039
Hypertension	63 (69.2)	46 (76.7)	0.320
Diabetes mellitus	25 (27.5)	14 (23.3)	0.571
Dyslipidemia	47 (51.6)	22 (36.7)	0.072
Chronic kidney disease	50 (54.9)	36 (61.0)	0.541
Dialysis	0 (0)	0 (0)	1.0
Pulmonary dysfunction	20 (21.7)	15 (25.4)	0.668
Atrial fibrillation	18 (19.8)	16 (26.7)	0.323
Previous open chest surgery	6 (6.6)	2 (3.3)	0.383

Cranial infarction	10 (10.9)	7 (11.7)	0.898
Blood examination			
Serum BNP concentration, pg/mL	171.9 (95.8 - 319.1)	253.4 (119.0 - 393.4)	0.144
Creatinine, mg/dL	0.79 (0.60 - 1.07)	0.84 (0.68 - 1.12)	0.133
Hemoglobin, g/dl	10.5 (9.7 - 11)	10.3 (9.55 - 11.1)	0.602
Echocardiography			
LV end-diastolic volume, mL	63.6 ± 4.4	67.2 ± 6.5	0.339
LV end-systolic volume, mL	22.5 ± 2.2	23.3 ± 2.8	0.654
LV ejection fraction	65.6 ± 1.6	65.6 ± 2	0.999
LV mass index, g/m^2	111.9 (90.5 - 142.4)	110.7 (86.9 - 141.5)	0.747
LA volume index, mL/m^2	52.8 (41.9 - 64.8)	56.6 (45.2 - 67.9)	0.294
E wave velocity, cm/s	85.5 ± 7.4	83.9 ± 7.6	0.767
E/e’	19.6 (15.2 - 25.2)	17.3 (13.2 - 23.7)	0.385
Aortic valve area, cm^2	0.63 (0.53 - 0.77)	0.67 (0.57 - 0.77)	0.242
Indexed aortic valve area, cm^2/m^2	0.44 (0.35 - 0.49)	0.45 (0.38 - 0.53)	0.331
Mean transaortic pressure gradient, mmHg	51.5 ± 2.8	52.1 ± 3.5	0.809
Global longitudinal strain, %	12.1 ± 0.7	13.8 ± 0.9	0.002

Values are mean ± SD for normally distributed data and median and interquartile range for non-normally distributed data, or n (%).

STS, The Society of Thoracic Surgeons; BNP, B-type natriuretic peptide; LV, left ventricular; LA, left atrial; E, peak early diastolic mitral flow velocity; e’, spectral pulsed-wave Doppler-derived early diastolic velocity from the septal mitral annulus;

Table 3

Univariate and multivariate Cox proportional hazards analyses

Covariate	Univariate analysis			Multivariate analysis		
	HR	95% CI	p value	HR	95% CI	p value
Age	0.987	0.859 - 1.134	0.853			
Gender (Male)	0.675	0.146 - 3.131	0.616			
Body surface area	0.120	0.003 - 5.031	0.266			
Hemoglobin	0.788	0.498 - 1.248	0.311			
Creatinine	0.866	0.216 - 3.476	0.839			
Brain natriuretic peptide	1.000	0.999 - 1.002	0.568			
LA volume index	1.000	0.974 - 1.026	0.968			
LV mass index	0.997	0.978 - 1.015	0.709			
E wave velocity	0.999	0.980 - 1.017	0.881			
Mean transaortic pressure gradient	0.951	0.905 - 0.999	0.045	0.931	0.872-0.993	0.03
LV ejection fraction (before TAVI)	0.984	0.910 - 1.065	0.692			
GLS (before TAVI)	0.961	0.809 - 1.141	0.647			
Non-acute improvement of GLS after TAVI	0.234	0.062 - 0.882	0.032	0.123	0.024-0.592	0.009

LA, left atrial; LV, left ventricular; E, peak early diastolic mitral flow velocity; TAVI, transcatheter aortic valve implantation; GLS, global longitudinal strain