Circulation Reports
Circ Rep 2025; 7: 365–371
doi:10.1253/circrep.CR-24-0139

ORIGINAL ARTICLE
Valvular Heart Disease

Early Changes in Left Ventricular Myocardial Mechanics After Transcatheter Aortic Valve Replacement for Severe Aortic Stenosis

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Background: Transcatheter aortic valve replacement (TAVR) improves left ventricular (LV) deformation by aortic stenosis (AS). However, the early effects of TAVR on LV mechanics as assessed by echocardiography have not been fully elucidated.

Methods and Results: Between 2021 and 2024, we included 81 patients who underwent transfemoral TAVR for severe AS. We used the natural logarithm of B-type natriuretic peptide (lnBNP) 1 week after TAVR as an indicator of the early effects on LV mechanics. To determine the association with echocardiographic parameters (LV ejection fraction [LVEF], global longitudinal strain [GLS], E/e′, and Tei index) and postprocedural lnBNP, we used regression models while adjusting for covariates. There were no significant differences in LVEF, GLS or E/e′ between before and after TAVR, but the postprocedural Tei index was significantly higher than the preprocedural Tei index (0.40 vs. 0.26, P<0.01). In a univariate linear regression, the preprocedural LVEF (β=–0.28, P=0.01), GLS (β=–0.24, P=0.04), E/e′ (β=0.36, P<0.01), and Tei index (β=0.27, P=0.02) correlated with postprocedural lnBNP. Regarding the postprocedural parameters, GLS (β=–0.27, P=0.02) and E/e′ (β=0.36, P<0.01) also correlated with postprocedural lnBNP, but the LVEF and Tei index did not. After adjustment for covariates, these correlations remained significant.

Conclusions: Preprocedural echocardiographic parameters reflecting LV function correlated with BNP after TAVR, but the utility of postprocedural parameters may depend on preprocedural LV function or perioperative factors.

Key Words: Aortic stenosis; Echocardiography; Tei index; Transcatheter aortic valve replacement

Transcatheter aortic valve replacement (TAVR) is a less invasive alternative to surgical aortic valve replacement (SAVR).[1] Because recent studies have shown that TAVR is effective for patients in all surgical risk categories, TAVR has become the dominant therapy for patients with severe aortic stenosis (AS).[2–4] Severe AS is characterized by changes in left ventricular (LV) geometry and function, resulting from prolonged pressure overload.[5,6] Geometric changes in the LV include increased wall thickness, while functional changes initially present as diastolic dysfunction and progress to systolic dysfunction, resulting in adverse cardiac events.[7] TAVR improves clinical outcomes, LV function, and LV myocardial deformation by reducing the afterload caused by AS. However, the early effects of TAVR on LV mechanics, as assessed by echocardiography, and their prognostic value have not been fully elucidated.

LV ejection fraction (LVEF) is well established as a prognostic value after TAVR.[8,9] However, LVEF often remains preserved even after the progression of AS and is inaccurate for detecting subtle changes in cardiac function.[10] Previous studies have reported that echocardiographic parameters related to LV function (i.e., global longitudinal strain [GLS],[11] E/e′[12] and Tei index[13]) have prognostic value in patients with severe AS who have undergone TAVR. Although GLS can be used to assess subtle LV systolic dysfunction earlier than LVEF, the measurement of GLS requires high-quality images,[14] and there

Received November 4, 2024; revised manuscript received January 12, 2025; accepted January 29, 2025; J-STAGE Advance Publication released online March 27, 2025 Time for primary review: 22 days

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S.M. is a member of *Circulation Reports*' Editorial Team.

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ISSN-2434-0790

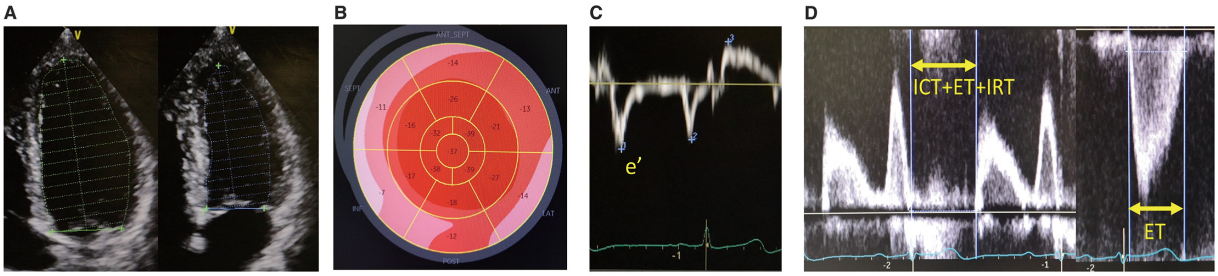

Figure 1. Echocardiographic parameters related to left ventricular function. (**A**) LVEF, (**B**) GLS, (**C**) E/e′, and (**D**) Tei index. ET, ejection time; GLS, global longitudinal strain; ICT, isovolumic contraction time; IRT, isovolumic relaxation time; LVEF, left ventricular ejection fraction.

Table 1. Baseline Clinical Characteristics of the Study Patients

	Entire cohort (n=81)
Age, years	84.9±5.1
Male, n (%)	37 (45.7%)
BMI	22.6±3.5
NYHA ≥III, n (%)	28 (34.6%)
STS score	5.3 [3.6, 7.4]
EURO SCORE II	3.8 [2.1, 5.2]
Permanent pacemaker, n (%)	5 (6.2%)
Atrial fibrillation, n (%)	12 (14.8%)
Coronary artery disease, n (%)	15 (18.5%)
Hypertension, n (%)	65 (80.2%)
Dyslipidemia, n (%)	53 (65.4%)
Diabetes mellitus, n (%)	23 (28.4%)
Procedure time, min	91.0 [76.8, 116.0]
Valve type	
Edwards SAPIEN series	51 (63.0%)
SAPIEN 3	39 (48.1%)
SAPIEN 3 Ultra RESILIA	12 (14.8%)
Medtronic Evolut family	30 (37.0%)
Evolut PRO+	13 (16.0%)
Evolut FX	17 (21.0%)

Data are presented as the mean±standard deviation or median (interquartile range) for continuous variables or the number (percent) of patients for categorical variables. BMI, body mass index; NYHA, New York Heart Association functional classification; STS, Society of Thoracic Surgeons.

are differences between the equipment of vendors.[15] Although E/e′ is recommended for estimating diastolic LV function by current Doppler echocardiography guidelines, it should be interpreted in the context of other echocardiographic parameters (left atrial volume index and E/A).[16] The Tei index is a simple assessment of both systolic and diastolic LV function,[17] but it significantly changes after SAVR regardless of LV function, as the impedance to LV ejection affects the ejection time (ET).[18] Despite the utility of the Tei index being limited in SAVR, Asami et al. recently reported that the Tei index was associated with impaired clinical outcomes after TAVR.[13]

B-type natriuretic peptide (BNP) reflects volume loading and stretch and stress on the LV, and is widely used in the prediction and diagnosis of heart failure.[19] The utility of BNP in stratifying long-term death and cardiovascular risk is well established in patients with heart failure, and some studies have identified BNP as a predictor of postoperative survival in patients with severe AS undergoing TAVR.[20,21] In addition, BNP levels following TAVR have been reported to be associated with short- and mid-term mortality and serve as an indicator of subtle effects on the LV. Mizutani et al. reported that elevation of BNP at discharge is associated with 2-year all-cause death and hospitalization for heart failure after TAVR.[22] In their report, the median time from TAVR to BNP measurement was 8 days, and hospitalization length was 10 days. In this study, we sought to identify the echocardiographic parameters associated with BNP 1 week after TAVR for detecting subtle changes in LV function after TAVR.

Methods

Study Population

This was an observational cohort study of consecutive symptomatic severe AS patients undergoing transfemoral TAVR between August 2021 and February 2024. Exclusion criteria included unavailable echocardiographic and laboratory data within 1 week before and after TAVR, previous AVR, and dialysis. Further, we excluded cases differing cardiac rhythm between before and after TAVR. TAVR was performed under general anesthesia using the following valves: SAPIEN 3 and SAPIEN 3 Ultra RESILIA (Edwards Lifesciences, Irvine, CA, USA), and Evolut Pro+ and Evolut FX (Medtronic, Dublin, Ireland). This study was performed according to the Declaration of Helsinki regarding investigations in humans and approved by the Ethics Committee of Fukuoka University Hospital (EC/IRB: U23-04-012). Informed consent was given in the form of opt-out on the website.

Echocardiography

Analysis was conducted by transthoracic echocardiography (TTE) using a commercially available ultrasound system and software (Vivid-S70N and EchoPAC version 206, General Electric Vingmed Ultrasound AS, Strandpromenaden, Horten, Norway). TTE was performed within 1 week before and after TAVR. Echocardiography parameters were evaluated according to the American Society of

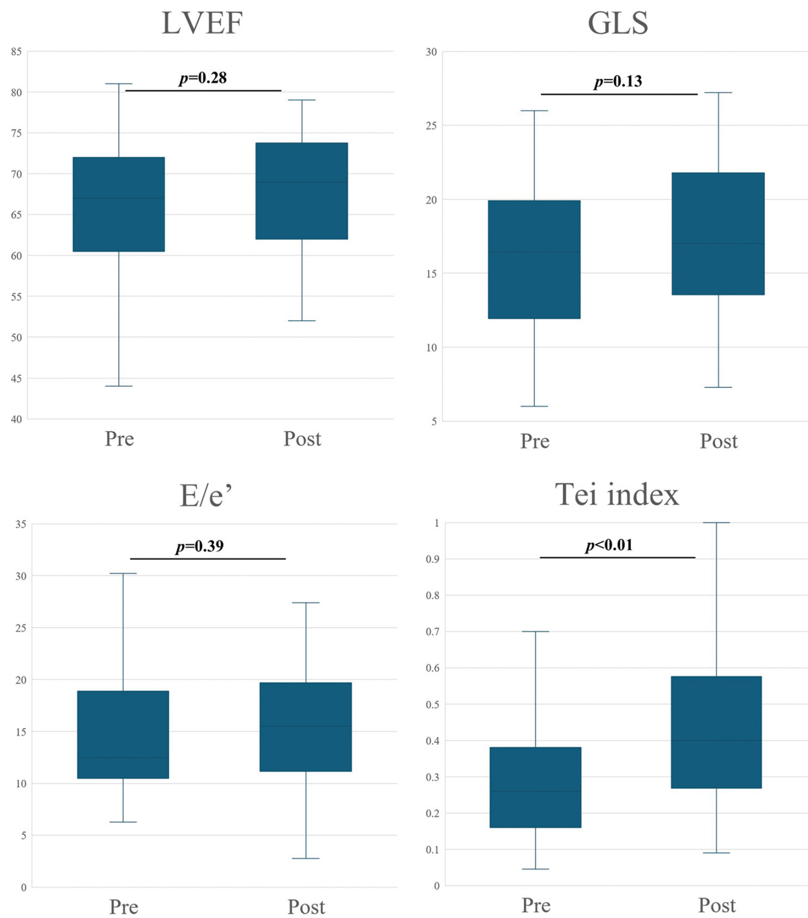

Figure 2. Comparison of pre- and postprocedural echocardiographic parameters related to left ventricular function. GLS, global longitudinal strain; LVEF, left ventricular ejection fraction.

Echocardiography guidelines.[23] The echocardiographic measurement was performed by a single cardiologist who was blinded to the patient's clinical status. We averaged the echocardiographic parameters from 3 consecutive heartbeats. LVEF was measured with Simpson's rule. GLS was measured using 2-dimensional speckle-tracking strain from conventional apical 2- and 4-chamber and apical long-axis views.[24] Average E/e′ was calculated using early transmitral velocities (E wave) by the mitral inflow velocity pattern on spectral pulsed-wave Doppler imaging and the peak early diastolic velocity (e'), measured using the tissue Doppler imaging at the lateral and septal mitral annular on the apical 4-chamber view.[16] ET and mitral valve closure to opening time (MCO) were measured by the LV outflow velocity pattern and the mitral inflow velocity pattern on spectral pulsed-wave Doppler imaging, respectively. The sum of isovolumetric contraction time (ICT) and isovolumetric relaxation time (IRT) was obtained by subtracting ET from MCO. The Tei index was calculated as (ICT + IRT) / ET[17] (**Figure 1**). The peak aortic velocity was measured using continuous-wave Doppler. The aortic gradient was estimated by using the modified Bernoulli formula. The aortic valve area (AVA) was calculated by the continuity equation.

Statistical Analysis

Continuous data are reported as mean ± standard deviation or median (interquartile range) depending on the distribution. The Shapiro-Wilk test was used to assess whether or not data were normally distributed. Categorical data are presented as percentages. Groups were compared using Student's t-test or the Wilcoxon test for continuous values, and the chi-squared test for categorical data, as appropriate. We used the BNP measurement 1 week after TAVR as an indicator of the early effects on LV mechanics. Additionally, BNP levels were transformed to natural logarithms (lnBNP) in the analysis because they were not normally distributed.[25] To determine the association of pre- and postprocedural echocardiographic parameters with postprocedural lnBNP, we conducted a linear regression analysis. The models were adjusted for conventional BNP-affecting factors (e.g., age, body mass index [BMI], and sex). Subsequently, similar supplementary analyses were performed on cases excluded for atrial fibrillation (AF). A two-tailed $P<0.05$ was considered statistically significant. All statistical analyses were performed with R4.1.2 (CRAN) and JMP 16 (SAS Institute Inc., Cary, NC, USA).

Results

Patients' Characteristics

Between August 2021 and February 2024, 89 patients underwent TAVR. Of them, 6 with different cardiac

Table 2. Comparison of Pre- and Postprocedural Laboratory Data and Echocardiographic Parameters

	Preprocedural	Postprocedural	P value
Laboratory data			
Creatinine, mg/dL	0.80 [0.67, 1.04]	0.72 [0.54, 0.92]	<0.01
BNP, pg/mL	187.7 [80.8, 403.0]	127.8 [67.0, 270.8]	0.06
lnBNP, pg/mL	5.21±1.14	4.90±0.94	0.06
Echocardiographic parameters			
LVEF, %	67.0 [61.0, 72.0]	69.0 [62.0, 73.0]	0.28
GLS, %	16.3±4.7	17.5±4.9	0.13
E/e′	12.4 [10.6, 18.7]	15.5 [11.3, 19.7]	0.39
Tei index	0.26 [0.16, 0.37]	0.40 [0.27, 0.57]	<0.01
ET, ms	339.3±41.2	310.1±34.0	<0.01
ICT+IRT, ms	88.0 [59.0, 115.0]	126.0 [88.0, 165.0]	<0.01
MR ≥moderate, n (%)	14 (17.3%)	11 (13.6%)	0.51
AR ≥moderate, n (%)	5 (6.2%)	2 (2.5%)	0.25
Peak aortic velocity, m/s	4.3 [4.1, 5.1]	2.0 [1.7, 2.3]	<0.01
Mean aortic PG, mmHg	43.0 [39.0, 53.0]	8.0 [6.0, 11.0]	<0.01
AVA (EOA), mm²	0.59 [0.50, 0.82]	1.63 [1.31, 1.91]	<0.01

Data are presented as mean±standard deviation or median (interquartile range) for continuous variables or the number (per cent) of patients for categorical variables. AR, aortic regurgitation; AVA, aortic valve area; BNP, B-type natriuretic peptide; EOA, effective orifice area; ET, ejection time; GLS, global longitudinal strain; ICT, isovolumic contraction time; IRT, isovolumic relaxation time; lnBNP, natural logarithm of B-type natriuretic peptide; LVEF, left ventricular ejection fraction; MR, mitral regurgitation; PG, pressure gradient.

Table 3. Univariate Linear Regression Between Postprocedural lnBNP and Echocardiographic Parameters Related to Left Ventricular Function

	β (Standardized coefficients)	P value
Preprocedural		
Pre LVEF	−0.28	0.01
Pre GLS	−0.24	0.04
Pre E/e′	0.36	<0.01
Pre Tei index	0.27	0.02
Pre ET	−0.02	0.85
Pre ICT+IRT	0.31	<0.01
Postprocedural		
Post LVEF	−0.21	0.06
Post GLS	−0.27	0.02
Post E/e′	0.36	<0.01
Post Tei index	0.20	0.07
Post ET	−0.14	0.22
Post ICT+IRT	0.16	0.14

Abbreviations as in Table 2.

rhythms before and after TAVR were excluded (4 patients required permanent pacemaker implantation, 1 patient developed new-onset AF, and 1 patient recovered from AF to sinus rhythm within 1 week), and 2 patients were excluded due to the absence of postprocedural echocardiographic data 1 week after TAVR (no deaths within the first week). Therefore, a total of 81 patients were included in the study. **Table 1** summarizes the baseline clinical characteristics of the study patients. Their mean age was 85 years, 37 (45.7%) were male, 28 (34.6%) were New York Heart Association functional classification (NYHA) III or IV, the median Society of Thoracic Surgeons (STS) score was 5.3, 5 (6.2%) were already implanted with permanent pacemakers before TAVR, and 12 (14.8%) had shown AF. Balloon-expandable valves were implanted in 51 patients (63.0%), and self-expanding valves were implanted in 30 (37.0%).

Pre- and Postprocedural Laboratory Data and Echocardiographic Parameters

Postprocedural creatinine levels were significantly lower than preprocedural (0.72 vs. 0.80 mg/dL, P<0.01), and postprocedural BNP tended to be lower than preprocedural BNP (127.8 vs. 187.7 pg/mL, P=0.06). There were 19 patients (23.5%) with moderate to severe mitral regurgitation (MR) or aortic regurgitation (AR) before TAVR, and 13 (16.0%) after TAVR. There were no significant differences in LVEF, GLS, or E/e′ before and after TAVR, but the postprocedural Tei index was significantly higher than the preprocedural value (0.40 vs. 0.26, P<0.01) (**Figure 2**). It is noteworthy that the postprocedural ET was lower than the preprocedural ET (310.1 vs. 339.3 ms, P<0.01), and the postprocedural ICT+IRT was higher than the preprocedural ICT+IRT (126.0 vs. 88.0 ms, P<0.01) (**Table 2**). As for LVEF, 74 patients had preserved EF (pEF, LVEF ≥50%), 5 had mid-range EF (mrEF, 50>LVEF ≥40%), and 2 had reduced EF (rEF, LVEF <40%) before TAVR. After TAVR, 79 patients had pEF, 1 had mrEF and 1 had rEF. Of the 7 patients with mrEF or rEF, 6 improved to pEF following TAVR. Regarding conduction disturbances, 5 patients (6%) had left bundle branch block (LBBB) before TAVR, and 20 (24.7%) had LBBB after TAVR.

Association With Echocardiographic Parameters and Outcome

In a univariate linear regression, the preprocedural parameters, including LVEF (β=−0.28, P=0.01), GLS (β=−0.24, P=0.04), E/e′ (β=0.36, P<0.01), and the Tei index (β=0.27, P=0.02), correlated with postprocedural lnBNP. Of the postprocedural parameters, GLS (β=−0.27, P=0.02) and

Table 4. Multiple Linear Regression for Postprocedural lnBNP Including Preprocedural Echocardiographic Parameters								
	β (standardized coefficients)	P value	β (standardized coefficients)	P value	β (standardized coefficients)	P value	β (standardized coefficients)	P value
Age	0.29	<0.01	0.28	0.01	0.24	0.02	0.28	<0.01
BMI	–0.21	0.06	–0.25	0.02	–0.20	0.07	–0.23	0.03
Female	–0.01	0.94	–0.03	0.76	–0.05	0.63	0.01	0.96
Pre LVEF	–0.24	0.03						
Pre GLS			–0.23	0.03				
Pre E/e′					0.27	0.01		
Pre Tei index							0.23	0.03

Adjusted for age, BMI, sex and each echocardiographic parameter. Abbreviations as in Tables 1,2.

Table 5. Multiple Linear Regression for Postprocedural lnBNP Including Postprocedural Echocardiographic Parameters								
	β (standardized coefficients)	P value	β (standardized coefficients)	P value	β (standardized coefficients)	P value	β (standardized coefficients)	P value
Age	0.26	0.02	0.26	0.02	0.23	0.03	0.26	0.02
BMI	–0.25	0.02	–0.25	0.02	–0.21	0.05	–0.25	0.02
Female	–0.03	0.76	–0.03	0.75	–0.09	0.37	–0.03	0.76
Post LVEF	–0.13	0.20						
Post GLS			–0.24	0.03				
Post E/e′					0.28	<0.01		
Post Tei index							0.11	0.30

Adjusted for age, BMI, sex and each echocardiographic parameter. Abbreviations as in Tables 1,2.

E/e′ (β=0.36, P<0.01) showed a correlation with postprocedural lnBNP, but LVEF and the Tei index did not (**Table 3**). After adjustment for covariates, all the preprocedural parameters (LVEF, GLS, E/e′, and Tei index), and the postprocedural parameters, GLS and E/e′, remained significantly correlated with postprocedural lnBNP (**Tables 4**,**5**).

Supplementary Tables 1 and **2A/2B** shows the results of a univariate linear regression and a multiple linear regression for postprocedural lnBNP in the cases excluded for AF. Regardless of the presence of AF, both the univariate and multiple linear regression analyses showed results similar to those observed for the entire cohort.

Discussion

The main findings from our study investigating the echocardiographic parameters of LV function in patients with severe AS undergoing TAVR are: (1) the Tei index increased after TAVR, whereas LVEF, GLS, and E/e′ remained unchaged, and (2) GLS and E/e′ were associated with lnBNP in both the preprocedural and postprocedural phases, whereas the associations of the Tei index and LVEF with lnBNP were limited to the preprocedural phase. Previous studies have reported that LVEF, GLS, E/e′, and the Tei index have prognostic value in patients with severe AS who have undergone TAVR,[8,9,11–13] but in our study, the postprocedural LVEF and the Tei index showed different results.

In previous studies, the Tei index has been demonstrated to have a prognostic value in various heart diseases, including myocardial infarction,[26] heart failure,[27] and cardiac amyloidosis.[28] Furthermore, it has been suggested that the Tei index is a potentially useful predictor of increased risk of peri-operative death or congestive heart failure in patients with MR undergoing mitral valve surgery.[29] However, the usefulness of the Tei index for assessing LV function in patients with valvular heart disease is controversial. In a study of patients who underwent SAVR, the preprocedural Tei index may have been underestimated, because the preprocedural ET was prolonged by resistance of LV ejection regardless of LV function.[18] Recently, Asami et al. reported that the preprocedural Tei index was associated with impaired clinical outcomes during short- and longer-term follow-up after TAVR.[13] In our study as well, the preprocedural ET was prolonged, and the preprocedural Tei index was associated with postprocedural lnBNP. However, preprocedural ET was not associated with postprocedural lnBNP, whereas preprocedural ICT+IRT correlated with postprocedural lnBNP. Because ICT+IRT reflects both systolic and diastolic LV functions, the Tei index is considered useful for evaluating LV function.

Asami et al. also reported that the postprocedural Tei index was associated with impaired clinical outcomes after TAVR; however, in our study, it was not associated with outcome. Although it has been shown that ICT+IRT remain unchanged after SAVR,[16] it was prolonged in our study. Early after TAVR, LBBB is more likely to occur due to the expansion of the prosthetic valve, and the occurrence of LBBB is associated with prolonged ICT+IRT.[30] Furthermore, AR prolongs ET.[18] In our study, when cases of postprocedural LBBB (23%) or moderate to severe AR (2%) were excluded, the postprocedural Tei index was associated with postprocedural lnBNP (β=0.26, P<0.05). The utility of the postprocedural Tei index early after TAVR to assess LV function may be influenced by intraventricular conduction disturbances or AR.

In our study, the preprocedural LVEF was associated with postprocedural lnBNP, whereas the postprocedural LVEF was not. Although 91% of patients had pEF before TAVR, this increased to 97% after TAVR. With preserved LV systolic function, LVEF is limited as an indicator of LV function. As aortic valve stenosis progresses, diastolic dysfunction proceeds to irreversible systolic dysfunction.[7] Our study population may have been in the phase in which systolic impairment has begun in addition to diastolic dysfunction. The optimal echocardiographic parameters reflecting LV function may differ depending on the phase of AS.

Study Limitations

This study has several limitations that warrant discussion. First, our study was a retrospective analysis performed at a single tertiary referral center with a limited number of study patients, and there was a potential selection bias. Previous studies have shown that echocardiographic parameters improve 30 days after TAVR.[31] However, in our study, no significant changes were observed in LVEF, GLS, or E/e′. This may be attributed to either the earlier timing of echocardiographic assessments compared with previous studies or potential selection bias. Next, this study included patients with AF, permanent pacemaker implantation, BBB, other valvular diseases, and coronary artery disease, which may have affected the echocardiographic parameters. Considering the measurement of the Tei index, we excluded cases of patients with different cardiac rhythms between pre- and postprocedural echocardiography. However, even after we excluded patients with AF, the usefulness of the echocardiographic parameters of LV function remained. Finally, although we used postprocedural lnBNP as an indicator reflecting subtle effects on LV after TAVR, BNP is influenced by several factors (e.g., medication and hemodynamics). The results of this study need to be further validated in a larger prospective study.

Conclusions

Preprocedural echocardiographic parameters reflecting LV function correlated with BNP after TAVR, but the utility of postprocedural parameters may depend on preprocedural LV function or perioperative factors.

Acknowledgment

During the preparation of this manuscript, the authors used ChatGPT in order to translate.

Disclosures

None of the authors have conflicts of interest to disclose. S.M. is a member of the Editorial Boards of *Circulation Journal*/ *Circulation Reports*.

IRB Information

This study was approved by the Ethics Committee of Fukuoka University Hospital (EC/IRB: U23-04-012).

Data Availability

The de-identified participant data will not be shared.

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Supplementary Files

Please find supplementary file(s);
https://doi.org/10.1253/circrep.CR-24-0139