Heart Surgery Forum 2023; 26(3): E264–E270
doi: 10.1532/hsf.5623

Article

A Potential Marker for Prognosis in Giant Left Ventricular Patients Undergoing Valve Surgery

Linglin Fan[1,†], Yuan Wu[1,*], Fei Liu[1,†], Xijie Wu[1,*]

[1]Department of Cardiac Surgery, Xiamen Cardiovascular Hospital of Xiamen University, School of Medicine, Xiamen University, 361000 Xiamen, Fujian, China

*Correspondence: wuyuan0559@163.com (Yuan Wu); wuxijie0701@xmu.edu.cn (Xijie Wu)

[†]These authors contributed equally.

Submitted: 19 March 2023 Revised: 12 April 2023 Accepted: 19 April 2023 Published: 19 June 2023

Abstract

Background: Although many clinicians have made efforts to improve the prognosis for giant left ventricular with valve disease patients, potential markers to judge the prognosis of giant left ventricular patients undergoing valve surgery are still unknown. The purpose of this study was to explore the possible impact factors for giant left ventricle prognosis. **Methods**: From September 2019 to September 2022, 75 patients with preoperative valvular disease with a giant left ventricle (left ventricular end diastolic diameter (LVEDD) >65 mm) underwent cardiac valve surgery. The changes in cardiac function one year after surgery were used to describe prognosis and analyze the potential independent factors affecting surgical prognosis. The left ventricular ejection fraction (LVEF) was considered to be recovered if it was ≥50% on follow-up echocardiography at least 6 months after the diagnosis. **Results**: The cardiac function of patients with a giant left ventricular and valve disease improved. Compared with preoperation, the left ventricular end diastolic diameter (LVEDD), left ventricular end-systolic dimension (LVESD), pulmonary artery systolic pressure (PASP), NT-proBNP, and cardio thoracic ratio (CTR) were significantly decreased ($p < 0.05$), and the ratio of severe heart failure was decreased from 60% to 37.33%. In the univariate analyses, the preoperative NT-proBNP levels and PASP were significantly associated with the cardiac function recovery (odds ratio [OR] = 1.001, 95% CI 1.000–1.002, $p = 0.027$; OR = 1.092, 95% CI 1.015–1.175, $p = 0.018$). However, during the diagnostic test, PASP did not account for cardiac function recovery (AUROC = 0.505, 95% CI = 0.387–0.713, $p = 0.531$). Based on the cutoff value in the experiment, we found that a NT-proBNP >753 pg/mL (AUROC = 0.851, 95% CI = 0.757–0.946, $p < 0.0001$) was a potential prognostic marker for patients with a giant left ventricular valve disease. **Conclusions**: We have demonstrated that an elevated preoperative NT-proBNP level is an independent predictor of cardiac function recovery in a cohort of giant left ventricular patients undergoing valve surgery, and this is the first study about this specific cohort of patients.

Keywords

giant left ventricle; valve disease; surgery; prognosis

Introduction

Patients with a giant left ventricular and heart valve disease have a left ventricular end-diastolic diameter (LVEDD) ≥65 mm [1]. Incomplete statistics have demonstrated a 5-year mortality rate of 20% [2], and surgery is the recommended approach for the management of giant left ventricular valve disease patients [3,4]. However, the efficacy of surgery is still a difficult problem that influences the best surgical opportunity [5]. The purpose of this study was to explore the clinical outcomes after surgery and identify the likely impact factors for giant left ventricle prognosis.

Materials and Methods

Patient Selection

The clinical data of 75 patients with giant left ventricles confirmed by Doppler ultrasound before surgery in the Department of Cardiac Surgery at Xiamen Hospital of Xiamen University from September 2019 to September 2022 were retrospectively collected. This study was approved by the Ethics Review Committee of the Xiamen Cardiovascular Hospital of Xiamen University, and all patients or their authorized representatives gave their informed consent in writing before the operation. Patients with heart valve disease and an LVEDD >65 mm were included. However, patients with dilated cardiomyopathy, hypertensive cardiomyopathy, idiopathic cardiomyopathy, ischemic cardiomyopathy, a history of ventricular aneurysm or congenital heart disease were excluded.

Surgical Procedures and Perioperative Management

The preoperative evaluation included a detailed clinical history, physical examination, laboratory examination,

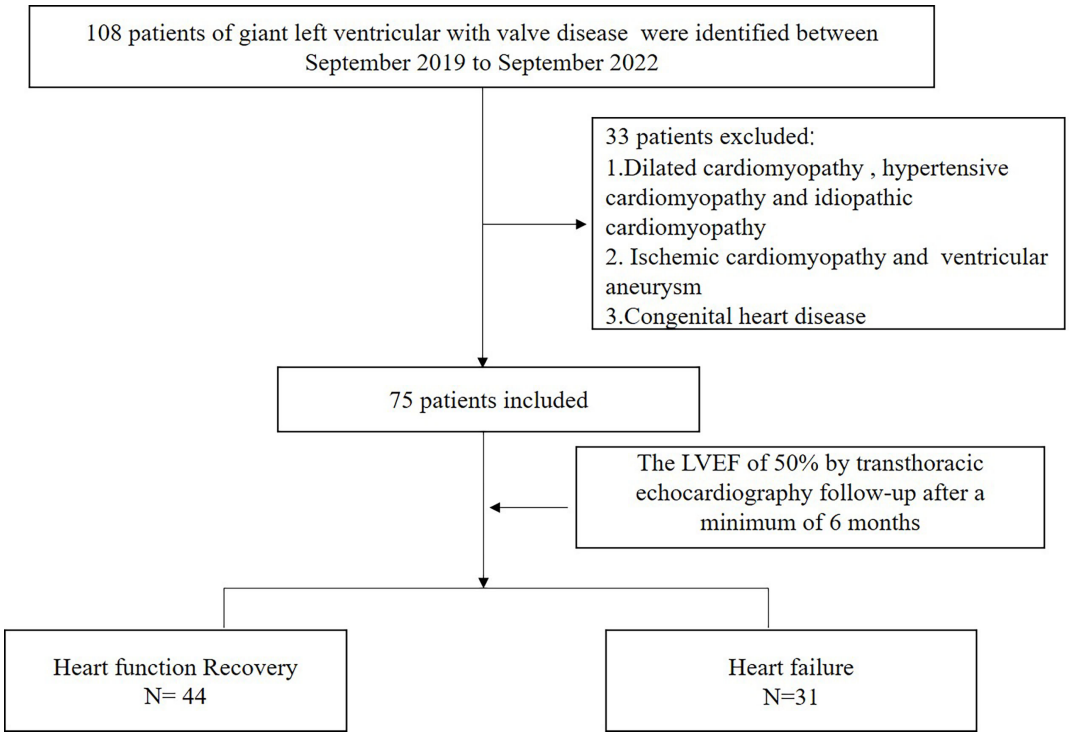

Fig. 1. Patient enrollment process.

and imaging examination including ultrasound. All patients underwent sawing of the sternum to open the heart under general anesthesia, and valve replacement under deep hypothermic cardiopulmonary bypass according to the involved valves. If necessary, additional examinations such as cardiac computed tomography (CT), magnetic resonance imaging (MRI), and myocardial nuclides were performed before surgery. All patients were treated with similar postoperative treatment. Postoperative laboratory examinations were performed every other day. All patients underwent echocardiography one week after surgery. All patients underwent follow-up examinations including echocardiography one year after surgery. An LVEF $\geq$50% on transthoracic echocardiography at the 6-month follow-up was defined as LV function recovery.

Statistical Analysis

Continuous variables with normal distribution are expressed as mean $\pm$ standard deviation (SD), and nonnormal continuous variables are expressed as the median (interquartile range). The independent sample *t* test was used to compare the continuous normal distribution variables. The Mann–Whitney *U* test was used to compare the continuous normally distributed variables. The Pearson chi-square test or Fisher's exact probability method was used to compare the categorical data. The cutoff was to analyze the possible markers for prognosis. Baseline variables with a $p < 0.05$ in the univariate analysis were included in the regression analysis. All statistical analyses were performed by using the IBM SPSS software package (version 26.0; SPSS, Chicago, IL, USA). A value of $p < 0.05$ was considered statistically significant.

Results

Basic Characteristics of the Patients

Adherence to the inclusion and exclusion criteria resulted in the attainment of 75 study participants (Fig. 1). The patients' characteristics are presented in Table 1, and the types of surgery procedures are presented in Fig. 2. The mean age was 54.9 years. The mean body mass index (BMI) was 22.6 kg/m^2. The mean cardio thoradic ratio (CRI) was 0.59. The population was a standard population of heart surgery patients. Of the included patients, 78.7% had a new york heart association (NYHA) score above 3.7% had hypertension, and 36% were smokers. A total of 5.3% had consumed alcohol, and 54.7% had taken vasoactive drugs. The median preoperative N-terminal pro-B-type natriuretic peptide (NT-proBNP) was 1952 ng/L [interquartile range (IQR) 852–4014]. The mean length of hospital stay was 25 days. The mean length of stay in the ICU was 25 days. The mean length of extracorporal circulation was 158 minutes. The mean length of aortic occlusion was 109 minutes. All cases were caused by diseased rheumatic valvular disease, including 42 cases of aortic valve disease (AVD), 16 cases of mitral valve disease (MVD), and the remaining 17 cases were double valve disease (DVD) (Fig. 2).

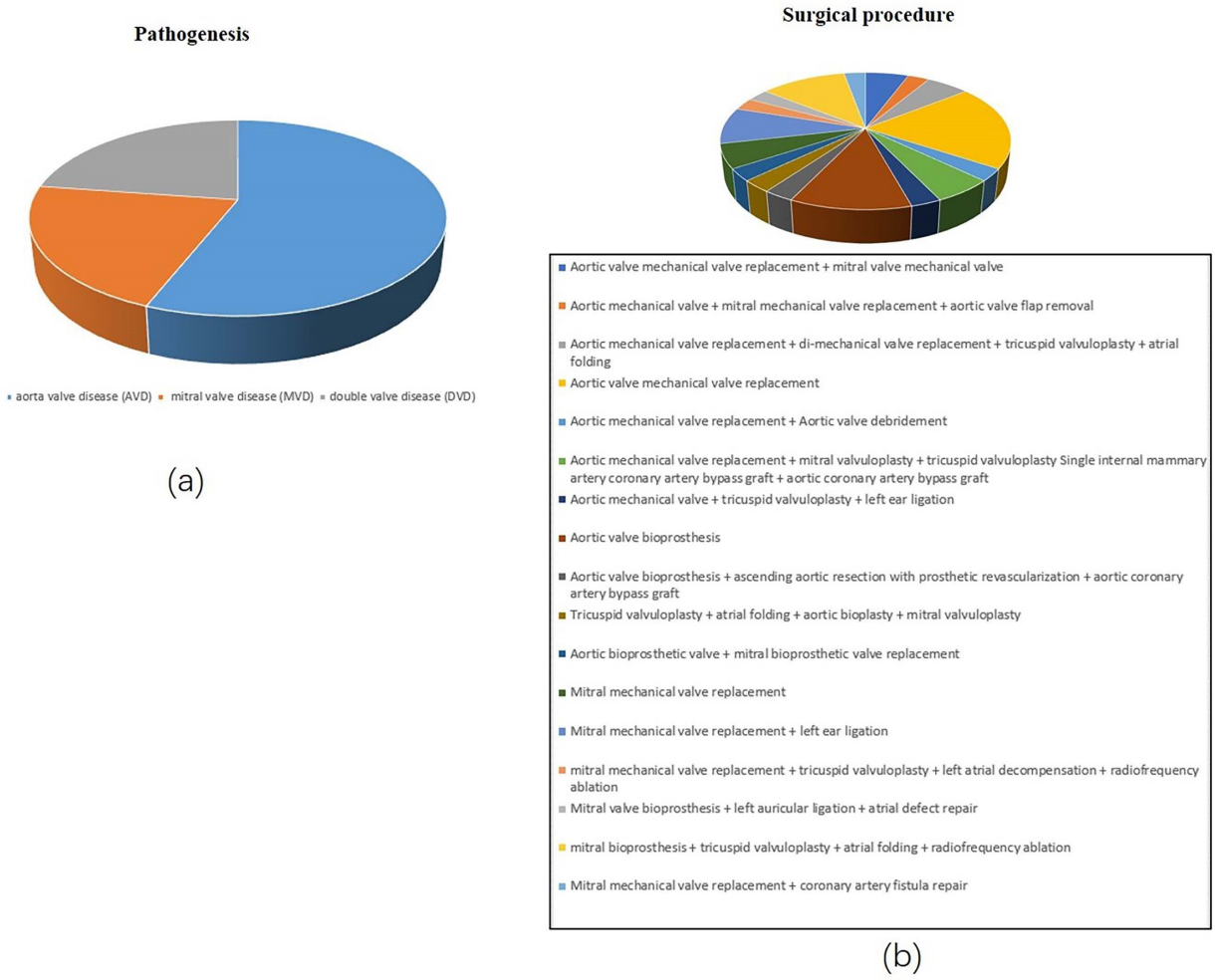

Fig. 2. Pathpgenesis and surgical procedures. (a) The pathogenesis for giant left ventricular with valve disease. (b) The surgical procedure for giant left ventricular with valve disease.

Univariate Analysis

Through a univariate analysis to explore the relationship between preoperative factors and prognosis variables, we found that 36 patients had significantly improved cardiac function postoperatively (A LVEF ≥50% on transthoracic echocardiography at the 6-month follow-up was defined as LV function recovery), and univariate and multivariate logistic analyses found that preoperative NT-proBNP and PASP were independent risk factors for postoperative improvement of cardiac function (Tables 1,2).

Performance of NT-pro BNP

Compared with the perioperative group, the NYHA class IV decreased from 60% to 37.3%, and the differences between the preoperative group and the postoperative group were significant (Kruskal-Wallis test: $\chi^2 = -2.844$, p value = 0.004) (Table 3).

ROC Analysis

The ROC analysis showed that preoperative BNP adequately discriminated the prognosis of giant left ventricular valve disease patients with an AUROC of 0.851 (95% CI 0.757–0.946; p value < 0.0001). PASP did not show better discrimination with an AUROC of 0.505 (95% CI 0.387–0.713; p value = 0.531) (Fig. 3). The best cut-off of NT-proBNP of 753 pg/mL may serve as a likely marker to predict postoperative cardiac function recovery (**Supplementary material**).

Discussion

Although heart valve replacement is an established intervention for patients with giant left ventricles with valve disease, it has not been adequately studied to accurately predict the prognosis of giant left ventricles with valve disease patients, because of always delaying the best opportunity

Table 1. Univariate analysis of risk factors for cardiac function recover.

Variable	Total (N = 75)	Heart function recovery (N = 44)	Heart failure (N = 31)	*p*
Age (years)	54.85 ± 11.04	54.32 ± 10.58	55 ± 12.12	0.800
BMI (Kg/m^2)	22.62 ± 3.11	22.51 ± 3.06	22.5 ± 3.11	0.987
Gender (male)	70 (93.3%)	40 (90.9%)	30 (96.7%)	0.248
Smoking	36 (48%)	23 (52.3%)	13 (41.9%)	0.238
Drinking	4 (5.3%)	1 (2.3%)	3 (9.6%)	0.131
Hypertension	7 (9.3%)	5 (11.4%)	2 (6.45%)	0.759
CRI	0.585 ± 0.07	0.59 ± 0.07	0.575 ± 0.07	0.365
hs-CTNT (ng/L)	23.93 (15.33~41.1)	27.15 (18.3~46.88)	14.9 (11.5~22.72)	0.124
Cr (umol/L)	79 (69.45~95.1)	78.8 (69~99.3)	79.1 (69.9~88.8)	0.277
BUN (mmol/L)	7.72 ± 4.37	8.16 ± 5.02	7.07 ± 3.12	0.302
Vasoctive drugs	41 (54.7%)	29 (65.9%)	12 (38.7%)	0.051
LOS (days)	24.87 ± 14.51	31.16 ± 16.7	23.17 ± 9.6	0.023
ICU (days)	15.03 ± 10.51	17 ± 12.5	11.9 ± 5.12	0.043
CPAP (days)	10 (5~18)	14 (4~18.7)	7 (5~17)	0.343
ECC (minutes)	158 ± 52	147.53 ± 48.09	174.72 ± 55.37	0.030
AO (minutes)	108.6 ± 42.9	100.56 ± 38.99	123.04 ± 46.95	0.035
BL (mL)	625.9 ± 253.6	607.91 ± 246.4	648.97 ± 276.64	0.511
LVEDD (mm)	71.44 ± 6.47	72.73 ± 7.03	69.48 ± 5.04	0.035
LVESD (mm)	50.48 ± 8.5	52.07 ± 9.24	48.07 ± 6.67	0.048
EF value (%)	53.66 ± 12.93	52.59 ± 13.5	55.28 ± 12.07	0.389
LVFS value (%)	32.29 ± 9.97	30.15 ± 7.86	35.35 ± 12.92	0.054
PASP (mmHg)	52.27 ± 19	55.58 ± 17.72	47.09 ± 20.15	0.094

BMI, body mass index; CRI, cardio thoradic ratio; hs-CTNT, high-sensitivity cardiac troponinl; Cr, creatinine; BUN, blood urea nitrogen; LOS, length of stay; ICU, intensive care unit; CPAP, continueous positive airway pressure; ECC, extracorporal circulation; AO, aortic occlusion; BL, blood loss; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end-systolic dimension; EF, jection fraction; LVFS, left ventricular fraction shortening; PASP, pulmonary artery systolic pressure.

for surgery [6]. The current clinical feature of giant left ventricular heart valve replacement is that the operative death rate is high, and the long-term outcome is generally poor [5,7].

LV function recovery was defined as an LVEF >50% via transthoracic echocardiography at 6-month follow-up [8]. This study points out that preoperative NT-proBNP level is associated with postoperative cardiac function recovery and this is the first study that considers a cohort made up of only giant left ventricular patients who underwent valve surgery. In the first study of the specific patient population, we found that an elevated preoperative NT-proBNP levels is an independent predictor of postoperative cardiac function recovery. This study has shown that preoperative NT-proBNP is a sensitive and specific predictor of prognosis for giant left ventricular patients.

According to the ROC curve analysis of the validation cohort, a NT-proBNP value of 753 pg/mL was identified as the optimal cutoff point for the prediction of cardiac function recovery. A value higher than this cutoff point may indicate the optimal outcome of intervention and necessitate to surgery as soon as possible. By using a cutoff preoperative NT-proBNP value of 753 pg/mL as the cutoff value, we have identified a population of patients with an almost sixfold increase in cardiac function in the postoperative period.

According to the 2005 American Society of Echocardiography standards, there are four categories of left ventricular size: normal, mildly enlarged, substantially enlarged, and severely enlarged [9]. Han *et al.* [3] studied the factors associated with the outcome of giant LV valve replacement surgery, and all 55 patients with chronic rheumatic heart disease with LVEDD ≥70 mm underwent mechanical valve replacement. The perioperative mortality rate increased significantly to 8.8% [3], indicating that a giant left ventricle is an important factor in perioperative mortality [6,7]. In previous studies, the researchers preferred to assess left ventricular changes by ultrasound, but there are no standardized parameters of left ventricular function [10]. Although many novel radiographic examinations, such as cardiac magnetic resonance imaging (CMRI), have been used to assess morphologic changes in the left ventricular, these methods have been proven to be ineffective [11,12]. Although some similar studies have focused on myocardial fibrosis markers, these markers are not widely used in clinical practice [13,14].

Table 2. Multivariate Logistic regression analysis of independent risk factors for cardiac function recover.

Variables	B	SE	Wald χ^2	p	OR	95% CI
NT-proBNP (pg/mL)	0.002	0.001	4.045	0.044	1.002	1.000–1.004
PASP (mmHg)	0.084	0.043	3.765	0.050	1.088	0.999–1.183
LOS (days)	–0.074	0.092	0.642	0.423	0.929	0.775–1.113
ICU (days)	0.175	0.174	1.014	0.314	1.191	0.847–1.674
ECC (minutes)	–0.070	0.047	2.221	0.136	0.933	0.851–1.022
AO (minutes)	0.032	0.048	0.466	0.495	1.033	0.941–1.134
LVEDD (mm)	–0.497	0.353	1.984	0.159	0.608	0.305–1.215
LVESD (mm)	0.530	0.357	2.199	0.138	1.699	0.843–3.424

AO, aortic occlusion; ECC, extracorporal circulation; LOS, length of stay; ICU, intensive care unit; LVEDD, left ventricular end diastolic diameter; LVESD, left ventricular end-systolic dimension; NT-proBNP, N-terminal brain natriuretic peptide; PASP, pulmonary artery systolic pressure; B, regression coefficient; SE, standard error.

Table 3. Comparison between Preoperative group and Postoperative group by NYHA classificaction.

Comparison of preoperative and postoperative cardiac function classification [N = 75, N (%)]				
Variable	Preoperative group	Postoperative group	χ^2	p
NYHA II	6 (8.00)	13 (17.33)		
NYHA III	14 (18.67)	24 (32.00)	–2.844	0.004
NYHA IV	45 (60.00)	28 (37.33)		

Differences between before and after surgery are significant (Kruskal-Wallis test; $\chi^2 = -2.844$, $p = 0.004$). NYHA, New York heart association.

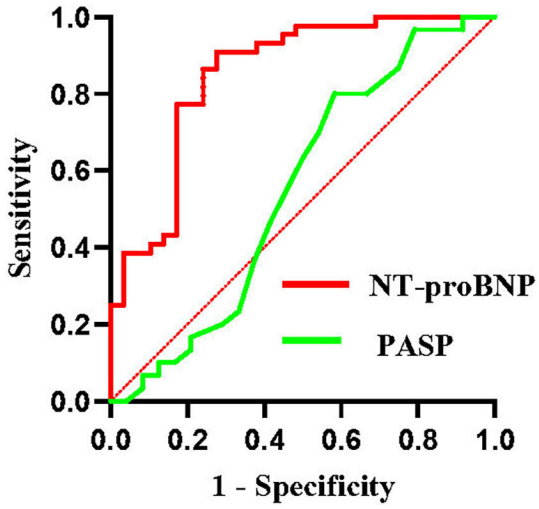

Fig. 3. ROC Analysis for Heart function recovery. NT-proBNP and PASP accurately discriminated heart function recovery (with AUROC: 0.851 (95% CI 0.757–0.946), p value < 0.0001 and 0.505, 95% CI (0.387–0.513), $p = 0.531$). NT-proBNP, N-terminal pro-B-type natriuretic peptide; PASP, pulmonary artery systolic pressure.

In several studies, preoperative NT-proBNP values have been shown to be useful in predicting cardiac events [15–17]. The prognosis of aortocoronary grafting can now be predicted by the preoperative NT-proBNP value [16]. During lung cancer, Nojiri *et al.* [18] discovered that the preoperative NT-proBNP value was a predictor of atrial fibrillation. This result has been confirmed in population of vascular surgical patients [19,20]. In our analysis, there were statistically significantly difference in the PASP and the NT-proBNP value between the patients with and without cardiac function recovery.

Until now, no other authors have predicted the prognosis in a cohort solely composed of patients with a giant left ventricle who underwent valve surgery to; for this reason, this study is an innovation for the prognosis of giant left ventricular patients in valve surgery. This has been confirmed in the ROC analysis, where a preoperative NT-proBNP level of 753 pg/mL was the only independent variable that was correlated with postoperative cardiac function.

There were several limitations in our study. First, the number of patients collected for the survey was relatively small. Second, the test time of preoperative NT-proBNP was not completely synchronized. Second, because this was a retrospective study, potential misclassification bias could not be completely excluded. Furthermore, there may exist some heart failure patients who still have normal values of NT-proBNP before surgery.

Conclusions

In conclusion, our data demonstrated that a preoperative assessment of NT-proBNP plasma levels seems to be of a great utility for long-term prognosis in giant left ventricular patients undergoing valve surgery.

Abbreviations

AO, aortic occlusion; BL, blood loss; BMI, body mass index; BUN, blood urea nitrogen; CRI, cardio thoradic ratio; Cr, creatinine; CPAP, continueous positive airway pressure; EF, ejection fraction; ECC, extracorporal circulation; LOS, length of stay; ICU, intensive care unit; LV, left ventricular; LVDD, left ventricular end diastolic diameter; LVESD, left ventricular end-systolic dimension; LVFS, left ventricular fraction shortening; PASP, pulmonary artery systolic pressure.

Availability of Data and Materials

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Author Contributions

YW and XW designed the research study. LF and FL performed the research. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Review Committee of the Xiamen Cardiovascular Hospital of Xiamen University ((2020) Medical Lunke No. (2)), and all patients or their authorized representatives gave their informed consent in writing before the operation.

Acknowledgment

Not applicable.

Funding

This project was supported by Natural Science Foundation of Fujian (grant number: 2020D022).

Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.1532/hsf.5623.

References

[1] Nishimura RA, Otto CM, Bonow RO, Carabello BA, Erwin JP 3rd, Guyton RA, *et al*. 2014 AHA/ACC Guideline for the Management of Patients With Valvular Heart Disease: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines [published correction appears in Circulation. 2014; 129: e650]. Circulation. 2014; 129: 2440–2492.

[2] Zhang H, Xu HS, Wen B, Zhao WZ, Liu C. Minimally invasive beating heart technique for mitral valve surgery in patients with previous sternotomy and giant left ventricle. Journal of Cardiothoracic Surgery. 2020; 15: 122.

[3] Han D, Zhang Y, Xue DM, Wang WL, Yan WJ. Valve replacement for valvular heart disease with giant left ventricle. European Review for Medical and Pharmacological Sciences. 2015; 19: 3001–3005.

[4] Sanz J, Sánchez-Quintana D, Bossone E, Bogaard HJ, Naeije R. Anatomy, Function, and Dysfunction of the Right Ventricle: JACC State-of-the-Art Review. Journal of the American College of Cardiology. 2019; 73: 1463–1482.

[5] Ross J, Jr. Left ventricular function and the timing of surgical treatment in valvular heart disease. Annals of Internal Medicine. 1981; 94: 498–504.

[6] Lomivorotov VV, Efremov SM, Kirov MY, Fominskiy EV, Karaskov AM. Low-Cardiac-Output Syndrome After Cardiac Surgery. Journal of Cardiothoracic and Vascular Anesthesia. 2017; 31: 291–308.

[7] Buckberg G, Athanasuleas C, Conte J. Surgical ventricular restoration for the treatment of heart failure. Nature Reviews. Cardiology. 2012; 9: 703–716.

[8] Liang YD, Xu YW, Li WH, Wan K, Sun JY, Lin JY, *et al*. Left ventricular function recovery in peripartum cardiomyopathy: a cardiovascular magnetic resonance study by myocardial T1 and T2 mapping. Journal of Cardiovascular Magnetic Resonance. 2020; 22: 2.

[9] Lang RM, Bierig M, Devereux RB, Flachskampf FA, Foster E, Pellikka PA, *et al*. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. Journal of the American Society of Echocardiography. 2005; 18: 1440–1463.

[10] Allen HD, Lange LW, Sahn DJ, Goldberg SJ. Ultrasound cardiac diagnosis. Pediatric Clinics of North America. 1978; 25: 677–706.

[11] Caenen A, Pernot M, Nightingale KR, Voigt JU, Vos HJ, Segers P, *et al*. Assessing cardiac stiffness using ultrasound shear wave elastography. Physics in Medicine and Biology. 2022; 67.

[12] Pedrizzetti G, Claus P, Kilner PJ, Nagel E. Principles of car-

diovascular magnetic resonance feature tracking and echocardiographic speckle tracking for informed clinical use. Journal of Cardiovascular Magnetic Resonance. 2016; 18: 51.

[13] de Boer RA, Daniels LB, Maisel AS, Januzzi JL, Jr. State of the Art: Newer biomarkers in heart failure. European Journal of Heart Failure. 2015; 17: 559–569.

[14] López B, González A, Ravassa S, Beaumont J, Moreno MU, San José G, *et al*. Circulating Biomarkers of Myocardial Fibrosis: The Need for a Reappraisal. Journal of the American College of Cardiology. 2015; 65: 2449–2456.

[15] Ma J, Xin Q, Wang X, Gao M, Wang Y, Liu J. Prediction of perioperative cardiac events through preoperative NT-pro-BNP and cTnI after emergent non-cardiac surgery in elderly patients. PLoS ONE. 2015; 10: e0121306.

[16] Fox AA, Shernan SK, Collard CD, Liu KY, Aranki SF, DeSantis SM, *et al*. Preoperative B-type natriuretic peptide is as independent predictor of ventricular dysfunction and mortality after primary coronary artery bypass grafting. The Journal of Thoracic and Cardiovascular Surgery. 2008; 136: 452–461.

[17] Fox AA, Body SC. Assessment of preoperative B-type natriuretic peptide in adult surgeries: is it useful? Anesthesia and Analgesia. 2011; 112: 1005–1007.

[18] Nojiri T, Maeda H, Takeuchi Y, Funakoshi Y, Kimura T, Maekura R, *et al*. Predictive value of B-type natriuretic peptide for postoperative atrial fibrillation following pulmonary resection for lung cancer. European Journal of Cardio-Thoracic Surgery. 2010; 37: 787–791.

[19] Goei D, Flu WJ, Hoeks SE, Galal W, Dunkelgrun M, Boersma E, *et al*. The interrelationship between preoperative anemia and N-terminal pro-B-type natriuretic peptide: the effect on predicting postoperative cardiac outcome in vascular surgery patients. Anesthesia and Analgesia. 2009; 109: 1403–1408.

[20] Rodseth RN, Padayachee L, Biccard BM. A meta-analysis of the utility of pre-operative brain natriuretic peptide in predicting early and intermediate-term mortality and major adverse cardiac events in vascular surgical patients. Anaesthesia. 2008; 63: 1226–1233.