Heart Surgery Forum 2023; 26(6): E770–E779 https://journal.hsforum.com/
doi: 10.59958/hsf.5921

Article

Association between Left Ventricular Longitudinal Strain (GLS) and Prognosis of the Patients Undergoing Heart Valve Surgery with Preserved Left Ventricular Ejection Fraction

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Submitted: 2 July 2023 Revised: 9 November 2023 Accepted: 29 November 2023 Published: 26 December 2023

Abstract

Purpose: Global longitudinal strain (GLS) seems accurate for detecting subclinical myocardial dysfunction. This study aimed to determine the association between GLS and postoperative intensity of inotropic support in the patients undergoing heart valve surgery with preserved left ventricular ejection fraction. **Methods**: 74 patients with preserved left ventricular ejection fraction who underwent valve surgery during the period between March 2021 and June 2022 were included in this prospective observational study. Transthoracic echocardiography including strain analysis with speckle tracking was performed before surgery. Patients were stratified according to the left ventricle (LV) GLS: LV-GLS ≥–16% (Impaired GLS group) and LV-GLS <–16% (Normal GLS group). The primary endpoint was postoperative vasoactive inotropic score. A high vasoactive inotropic score (VIS) was defined as a maximum VIS of ≥15 within 24 hours postoperatively. Postoperative adverse events, baseline clinical and echocardiographic data were also recorded. We invested the ability of preoperative GLS in predicting adverse postoperative outcomes, such as prolonged mechanical ventilation and the need for pharmacologic hemodynamic support after cardiac surgery. **Results**: Seventy-four patients were included and analyzed in this study, including thirty-three in impaired GLS group and forty-one in normal GLS group. In-hospital mortality was 1.27% (1/74). Patients in impaired GLS group were more likely to have prolonged mechanical ventilation (p = 0.041). Multivariable logistic regression analysis revealed that the apical four-chamber view of the left ventricle (A4C)-GLS was significantly associated with high VIS (OR 1.373, p = 0.007). A4C-GLS had a sensitivity of 62.5% and a specificity of 89.66% for predicting high VIS (area under the curve, 0.78). The relationships between GLS and other secondary outcome measures were not statistically significant. The optimal cutoff of A4C-GLS for postoperative high vasoactive inotropic score was –10.85%. **Conclusion**: Preoperative LV dysfunction is an independent risk factor for postoperative high VIS. A4C-GLS may be a reliable tool in predicting high VIS after cardiac surgery. Those patients with impaired contractility were at high risk for elevated inotropic support and prolonged mechanical ventilation after cardiac surgery. These findings suggest an important role for echocardiographic GLS in perioperative assessment of cardiac function in the patients undergoing cardiac surgery.

Keywords

two-dimensional speckle tracking imaging; left ventricular systolic function; cardiac surgery; vasoactive drug score

Introduction

Valvular heart disease is a frequent cardiovascular disease, with a prevalence of 5.3%–7.7% in Chinese population [1]. Heart valve surgery is an effective treatment for severe valvular disease [2]. Conversely, valvular surgery may cause myocardial damage and aberrant ventricular wall motion, leading to postoperative complications such as hemodynamic instability and arrhythmias that require inotropic drugs to maintain hemodynamic stability. Hence, perioperative left ventricle (LV) function evaluation is crucial to improve prognosis and reduce complication rate of patients after valve surgery. The left ventricular wall consists of three layers of myocardial fibers: endocardium, epicardium, and circular myocardium. The endocardium and epicardium of the left ventricle move along the longitudinal axis of the heart. Therefore, it is important to monitor the local contractility of the left ventricular longitudinal myocardium for the patients undergoing cardiac surgery. Bedside echocardiography is a commonly used method for monitoring postoperative cardiac function in a critical care unit. Compared to conventional echocardiography, two-dimensional speckle tracking imaging (2D-STI) can quantify the overall and regional myocardial function more accurately, which can be used for early diagnosis of subclinical cardiac dysfunction [3,4]. In addition, 2D-STI could also predict postoperative outcomes in the cardiac surgery patients [5,6]. However, those studies mainly focused on surgical timing and the identification of high-risk valve disease patients [7,8], rare studies focused on the application of left ventricular longitudinal strain measurement in the management of circulatory support after cardiac valve surgery. Recent studies indicated that high vasoactive inotropic score (VIS) within 24 hours after cardiac surgery could be used to predict worse outcomes in the patients receiving cardiac surgeries [9]. Therefore, this study aims to evaluate the relationship between left ventricular longitudinal strain and postoperative intensity of inotropic support in the patients with preserved left ventricular ejection fraction after heart valve surgery, for the purpose of guiding the perioperative hemodynamic management and improving the prognosis.

Materials and Methods

Patient Selection

Eighty-nine adult patients (age 18 and above) with valvular heart disease and preoperative left ventricular ejection fraction (LVEF) >50% were initially screened for potential enrollment between March 2021 and June 2022. The inclusion criteria involved adult patients scheduled for valve replacement or repair, including combined tricuspid annuloplasty, left atrial appendage ligation, or coronary artery bypass surgery. Patients were excluded from the study if they (1) with any congenital heart diseases such as atrial septal defect, or ventricular septal defect; (2) had thoracic trauma or rib fracture which may lead to failure of ultrasonic examination; (3) had poor echocardiographic image quality with transthoracic echocardiography (TTE); (4) aged more than 75 years old; (5) had any missing clinical variables; (6) had previously undergone valve or coronary artery bypass surgery. Finally, a total of seventy-four adult patients with heart valve surgery and a comprehensive and analyzable preoperative echocardiography were referred to this study.

After surgery, inotropic drugs (dopamine, dobutamine, epinephrine, milrinone, or levosimendan) were used to maintain cardiac index $\geq$2.0 L/min/m^2, and vasopressors (norepinephrine or vasopressin) were used to maintain the mean arterial pressure (MAP) $\geq$65 mmHg decided by the clinical physicians. Laboratory data including serum creatinine (CR), serum troponin I (TNI), serum troponin T (TNT), creatine phosphokinase-isoenzyme-MB (CK-MB), heart fatty acid binding protein (FABP) before operation (T0) and the day after operation (T1) of the patients were recorded and compared. Demographic and operative characteristics were also collected in this study. The Institutional Review Board for Clinical Research of Nanjing First Hospital approved the protocol. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Informed consent was obtained from all patients prior to their inclusion in the present study.

Echocardiography Data Collection

Comprehensive echocardiography was performed before surgery using Vivid Q systems (GE Healthcare, IL, USA), including conventional echocardiographic measures of systolic and diastolic function, standard 2-Dimensional apical four-, two-, and three-chamber views (4C, 2C, long-axis (LAX)). The longitudinal strain was computed using 2D-speckle-tracking analysis by automated function imaging (AFI). Global longitudinal strain (GLS) was only computed from patients with at least 15 of 18 segments tracked adequately. GLS >–16% was considered impaired GLS [10]. The global strain was calculated by averaging the values measured at the segmental level in the same frame, consistent with American Society of Echocardiography (ASE) guidelines. As shown in Fig. 1.

Outcome Assessments

The primary outcome was the highest score of vasoactive inotropic score (VIS) within 24 hours after operation. The doses of the inotropic and vasoactive drugs were recorded hourly in the first 24 hours after surgery. The VIS is a validated measure of hemodynamic status based on inotropic need after cardiac surgery and has been validated as a predictor of prolonged intubation, intensive care unit stay, and total hospitalization in prior studies. The VIS was calculated based on the following equation [11]: VIS = dopamine (μg·kg^{-1}·min^{-1}) + dobutamine (μg·kg^{-1}·min^{-1}) + 100 × adrenaline (μg·kg^{-1}·min^{-1}) + 50 × levosimendan (μg·kg^{-1}·min^{-1}) + 10 × milrinone (μg·kg^{-1}·min^{-1}) + 10,000 × vasopressin (units·kg^{-1}·min^{-1}) + 100 × noradrenaline (μg·kg^{-1}·min^{-1}). The patient was considered as high risk if the peak VIS was 15 or higher within 24 hours after surgery [9]. Secondary outcomes included malignant arrhythmia, cardiac arrest, respiratory failure, low cardiac output syndrome, delirium, and death in one week postoperatively.

Sample Size

The study aimed to estimate the correlation between perioperative echocardiographic LV-GLS and postoperative high vasoactive inotropic score (VIS $\geq$15). The sample size for the two groups was calculated by the formula $n = 2\bar{p}\bar{q}\left(Z_\alpha + Z_\beta\right)^2 / (p1 - p2)^2$. The sample size for the impaired GLS group and the normal GLS group was calculated by software PASS 15 (NCSS, Kaysville, UT, USA). Based on the results of the preliminary studies, the proportion of subjects with VIS $\geq$15 in the impaired GLS group was 40%, while in the normal GLS group, the proportion was 7%. With the two-sided α set at 0.05, the power of

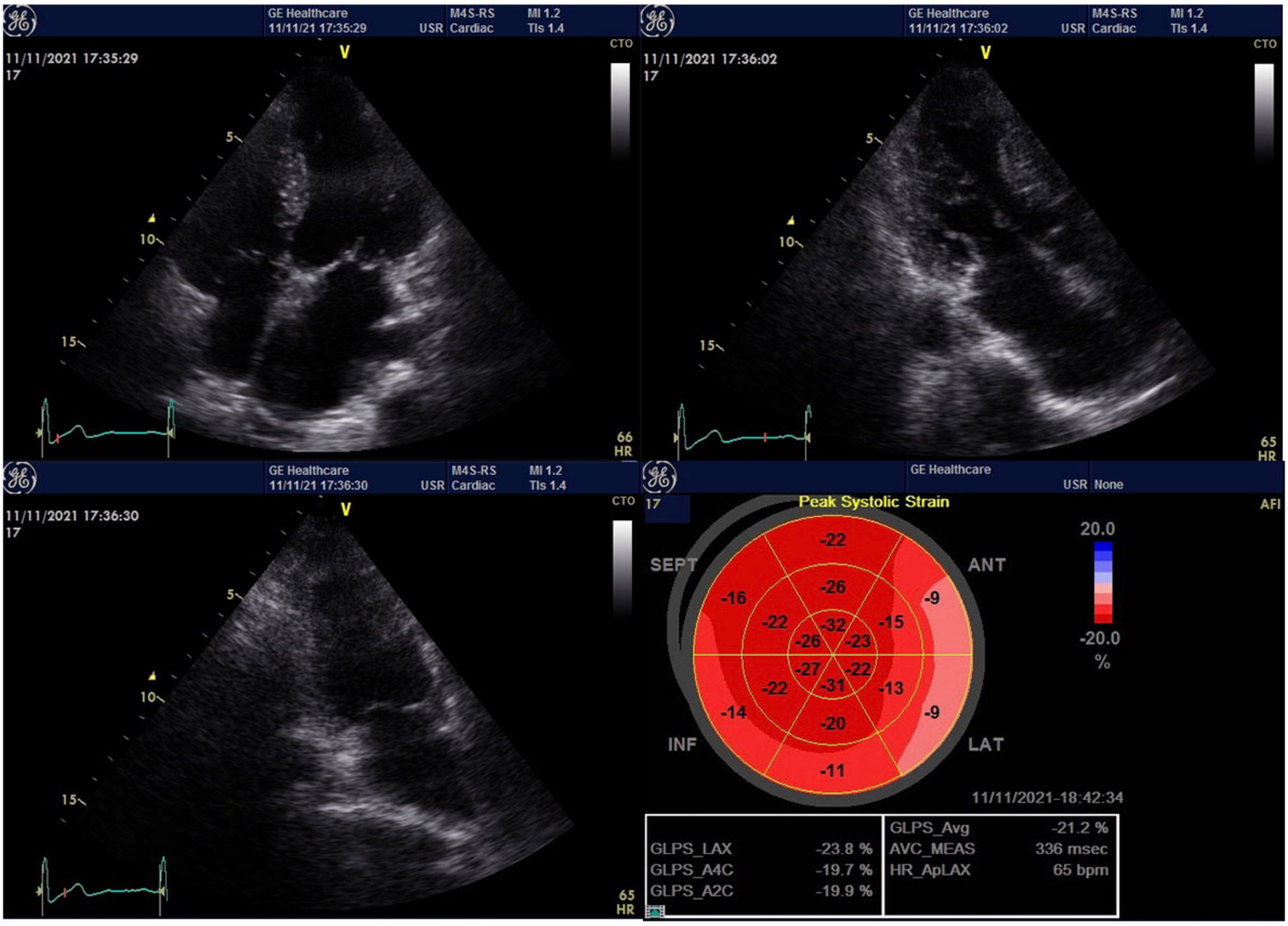

Fig. 1. Speckle-tracking strain of the left ventricle before valve operation. Numbers shown on the picture represent segmental and global systolic strain values of different Echocardiographic View.

1-β was 0.9, the sample size for each group was at least 33 cases. Taking into account a 20% loss to follow-up, the final requirement was for at least 42 cases in each group, giving a total sample size of 84 cases.

Statistical Analysis

The Shapiro-Wilk method was used to test the normality of variables. Continuous variables with a normal distribution were expressed as mean $\pm$ standard deviation (SD). Variables with a non-normal distribution were expressed as median (Q1, Q3). Independent *t*-test or Mann-Whitney U test were used to detect the differences between the two groups. Differences between categoric groups were assessed using the Chi-square test or Fisher exact test. The associations between variables and high VIS (VIS $\geq$15) were evaluated using multivariable logistic regression. Receiver operating characteristic (ROC) curves were operated and the area under the curve (AUC) was determined to assess the ability of the independent variables to predict the outcome. Two-sided $p < 0.05$ was considered statistically significant. SPSS 26.0 software (IBM Corp., Armonk, NY, USA) was used for statistical analysis.

Results

89 patients diagnosed with valvular heart disease and preoperative LVEF $>$50% who received surgical valve replacement or repair during the study period between March 2021 and June 2022 were enrolled in this study. A total of 15 patients were excluded from this study: 12 patients had inadequate echocardiographic images and 3 patients had no complete data available because they decided to withdraw from the study due to economic reasons. Therefore, 74 patients were included in the final analysis. Patients were divided into two groups according to preoperative GLS: impaired GLS group (LV-GLS $\geq$–16%, n = 33) and normal GLS group (LV-GLS $<$–16%, n = 41). One patient died within seven days of valve surgery because of malignant arrhythmia.

Comparison of Baseline Characteristics

Comparisons of the baseline characteristics of the patients in the two groups were displayed in Table 1. No significant differences were detected in terms of preoperative

Table 1. Baseline characteristics of the patients in the two groups.

	Normal GLS group (n = 41)	Impaired GLS group (n = 33)	*p* value
Male, n (%)	15 (36.6)	24 (72.7)	0.263
Age (y)	63.76 ± 10.27	63.41 ± 11.62	0.895
Weight (kg)	62.12 ± 10.56	63.78 ± 11.75	0.530
Height (cm)	163.18 ± 8.14	165.07 ± 8.63	0.340
BMI	23.28 ± 3.12	23.25 ± 2.98	0.965
APACHEII score	12.7 ± 2.77	12.72 ± 3.24	0.981
EURO score	6 (4, 6)	6 (5, 6)	0.969
Medical history, n (%)			
Hypertension n (%)	12 (29.3)	11 (33.3)	0.330
Diabetes mellitus n (%)	3 (7.32)	2 (6.06)	0.773
COPD n (%)	0 (0)	2 (6.06)	0.572
Pulmonary hypertension n (%)	15 (36.6)	17 (51.5)	0.730
Coronary heart disease n (%)	10 (24.4)	11 (33.3)	0.742
Acute myocardial infarction n (%)	1 (2.44)	1 (3.03)	0.876
Aortic cross-clamp time (min)	100.13 ± 36.71	90.61 ± 33.18	0.249
Duration of surgery (min)	264.55 ± 71.69	260.98 ± 61.82	0.819
Cardiopulmonary bypass time (min)	130.84 ± 42.27	121.01 ± 39.28	0.307
Surgical procedure, n (%)			
MVR, n (%)	8 (19.5)	11 (33.3)	0.800
AVR, n (%)	12 (29.3)	14 (42.4)	0.843
DVR, n (%)	11 (26.8)	12 (36.4)	0.707
MVP, n (%)	2 (4.88)	4 (12.1)	0.880
Combined CABG, n (%)	5 (12.2)	7 (21.2)	0.824
Vasoactive or inotropic drugs, n (%)			
Dobutamine, n (%)	20 (48.8)	21 (63.6)	0.419
Dopamine, n (%)	8 (19.5)	3 (9.09)	0.088
Adrenaline, n (%)	5 (12.2)	2 (6.06)	0.271
Noradrenaline, n (%)	12 (29.3)	14 (42.4)	0.843
Milrinone, n (%)	0 (0)	5 (15.2)	0.107
VIS (T0)	3.34 ± 4.73	3.13 ± 5.44	0.856
Peak VIS	4.82 ± 4.42	7.84 ± 7.3	0.044
VIS (T1)	2.56 ± 2.68	3.19 ± 3.02	0.352
Length of ICU stay (h)	20.6 (18.98, 23.59)	20.78 (17.89, 23.56)	0.625
MV time (h)	7.96 (5.50, 11.30)	9.58 (8.08, 12.24)	0.041
Length of hospital stay (d)	17 (15, 21)	15 (14, 18)	0.186
Acute renal injury, n (%)	5 (12.2)	7 (21.2)	0.296
Adverse event, n (%)	3 (7.32)	3 (9.09)	0.782
CR T0 (umol/L)	73.57 ± 19.66	75.21 ± 17.48	0.710
CR T1 (umol/L)	76.07 ± 22.56	76.03 ± 16.01	0.993
TNI T0 (ng/mL)	0.12 ± 0.06	0.11 ± 0.05	0.695
TNI T1 (ng/mL)	1.86 (1.03, 3.73)	1.50 (0.76, 4.25)	0.804
FABP T0 (pg/mL)	2.65 ± 0.54	2.79 ± 1.60	0.649
FABP T1 (pg/mL)	21.52 (13.11, 27.33)	18.19 (9.50, 26.78)	0.543
CK-MB T1 (U/L)	48.87 ± 37.06	40.79 ± 22.67	0.293
TNT T1 (ng/L)	580.15 ± 569.57	531.42 ± 491.48	0.724
Peak Lac (mmol/L)	3.60 ± 2.00	2.99 ± 1.88	0.178

GLS, Left ventricular longitudinal strain; APACHE II score, Acute Physiology and Chronic Health Evaluation II score; EURO score, European system for cardiac operative risk evaluation; COPD, Chronic obstructive pulmonary disease; VIS, Vasoactive inotropic score; MVR, Mitral valve replacement; AVR, Aortic valve replacement; DVR, Mitral valve and aortic valve replacement; MVP, Mitral valve plasty; CABG, coronary artery bypass surgery; CR, Serum creatinine; TNI, Troponin I; FABP, heart fatty acid binding protein; CK-MB, creatine phosphokinase-isoenzyme-MB; TNT, Troponin T; BMI, body mass index; MV, mechanical ventilation.

data including gender, age, body mass index (BMI), Acute Physiology and Chronic Health Evaluation II score (APACHE II score), European system for cardiac operative risk evaluation (EURO score), and medical history between the two groups. In terms of intraoperative variables, there were no significant differences in the duration of surgery, aortic cross-clamping time, and cardiopulmonary bypass time between the two groups. There were also no significant differences in surgical procedures and numbers of vasoactive or inotropic drugs. Dobutamine and norepinephrine were the most commonly used vasoactive drugs after valve surgery. Compared with the impaired GLS group, there were no statistically significant differences in preoperative creatinine, serum troponin I, and fatty acid binding protein ($p > 0.05$). In addition, no statistically significant differences were also detected in these biochemical indexes between the two groups on the first day after operation ($p > 0.05$).

Peak VIS in the impaired GLS group was significantly higher than those of the normal GLS group (7.84 ± 7.3 *vs.* 4.82 ± 4.42, $p = 0.044$), although VIS at the intensive care unit (ICU) admission (T0) and VIS at 24 hours after ICU admission (T1) were not statistically different between the two groups. No significant differences were shown in terms of ICU stay, hospital stay, in-hospital adverse events and incidence of acute renal injury between the two groups. However, mechanical ventilation time was significantly longer in the patients of the impaired GLS group (9.58 [8.08, 12.24] *vs.* 7.96 [5.50, 11.30], $p = 0.041$). There were three cases of postoperative adverse complications in the normal GLS group, including one patient complicated with III° atrioventricular block (AVB) that required permanent pacemaker treatment, one patient complicated with low cardiac output syndrome, and one patient complicated with respiratory failure required re-intubation. In the impaired GLS group, there were also three cases of adverse complications after surgery, including two patients developed low cardiac output syndrome and one patient suffered cardiac arrest. However, there were no significant differences in postoperative adverse events between the two groups ($p > 0.05$).

Comparison of Echocardiography Parameters

Table 2 represented the echocardiography parameters of the two groups. The preoperative velocity time integral (VTI) value in the patients of normal GLS group was 17.7 ± 4.32 cm, similar to those of impaired GLS group ($p = 0.641$). The preoperative LV-GLS value of the normal GLS group was –19% (–20.53%, –17.68%), while the preoperative LV-GLS value of the impaired GLS group was –13.1% (–14.63%, –10.73%). Compared with the normal GLS group, the impaired GLS group had a lower absolute value of LAX-GLS (–13.16 ± 3.81 *vs.* –20.18 ± 3.22, $p = 0.000$), apical four-chamber view of the left ventricle (A4C)-GLS (–12.60% [–15.2, –9.58] *vs.* –19.2% [–21.88, –17.68], $p = 0.000$) and A2C-GLS (–12.12 ± 3.40 *vs.* –18.14 ± 3.34, $p = 0.000$) at preoperation. Compared with the patients in impaired GLS group, there were no significant differences in values of left ventricular end diastolic diameter (LVDd), left ventricular end systolic diameter (LVDs), stroke volume (SV), left ventricular ejection fraciton (LVEF), and LAD in those of normal GLS group ($p > 0.05$). The LAX-GLS, A4C-GLS, A2C-GLS, and LV-GLS of the patients in normal GLS group all decreased markedly after surgery when compared with those before surgery ($p < 0.05$).

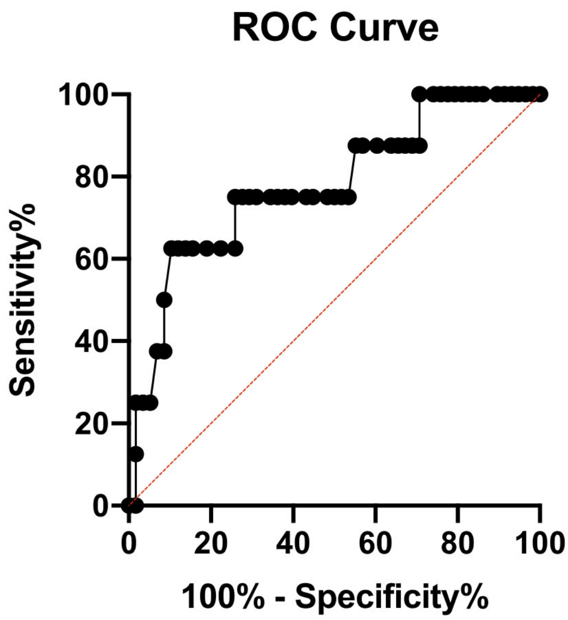

Fig. 2. Receiver operating characteristic curve analysis. Performance of the apical four-chamber view left ventricular longitudinal strain (A4C-GLS) in discriminating the risk of high vasoactive inotropic score (VIS).

Factors Correlating with VIS after Cardiac Valve Surgery

We further investigated the factors correlated with high VIS after cardiac valve surgery by Bivariate logistic regression analysis (Table 3 and Fig. 2). Univariate logistic regression analysis found that preoperative LV-GLS(T0), A2C-GLS(T0), A4C-GLS(T0), LAX-GLS(T0), CK-MB(T1), and FABP(T1) were correlated with postoperative high VIS value ($p < 0.05$). Further multivariate regression analysis including the above indexes showed that A4C-GLS (OR = 1.373, $p = 0.007$) was independently associated with high VIS after surgery. The ROC curve was plotted for the preoperative A4C-GLS with high independent VIS values, and the area under the curve (AUC) was calculated. The optimal threshold value of A4C-GLS be-

Table 2. Echocardiography parameters in the two groups.

	Normal GLS group (GLS <–16%, n = 41)	Impaired GLS group (GLS ≥–16%, n = 33)	*p* value
T0 (preoperation)			
VTI (cm)	17.70 ± 4.32	17.22 ± 4.14	0.641
LV-GLS (%)	–19.00 (–20.53, –17.68)	–13.10 (–14.63, –10.73)	0.000
LAX-GLS (%)	–20.18 ± 3.22	–13.16 ± 3.81	0.000
A4C-GLS (%)	–19.20 (–21.88, –17.68)	–12.60 (–15.2, –9.58)	0.000
A2C-GLS (%)	–18.14 ± 3.34	–12.12 ± 3.40	0.000
LVEF (%)	63.00 (59.50, 65.00)	62.00 (59.00, 64.00)	0.246
SV (mL)	103.00 (82.50, 114.50)	82.50 (68.75, 110.00)	0.096
LA (mm)	52.22 ± 12.76	51.83 ± 12.38	0.910
LVDs (mm)	37.68 ± 5.38	36.63 ± 6.49	0.531
LVDd (mm)	57.74 ± 7.34	54.39 ± 8.61	0.129
T1 (postoperation)			
VTI (cm)	16.71 ± 4.79	16.82 ± 4.42	0.936
LV-GLS (%)	–10.65 ± 3.57*	–11.50 ± 3.68	0.419
LAX-GLS (%)	–10.84 ± 3.99*	–11.92 ± 4.14	0.357
A4C-GLS (%)	–9.95 ± 3.97*	–10.56 ± 4.27	0.604
A2C-GLS (%)	–11.15 ± 4.83*	–11.93 ± 4.44	0.546

LV-GLS, left ventricular longitudinal strain; LAX-GLS, the apical three-chamber view left ventricular longitudinal strain; A4C-GLS, the apical four-chamber view left ventricular longitudinal strain; A2C-GLS, the apical two-chamber view left ventricular longitudinal strain; VTI, Velocity time integral; LVEF, left ventricular ejection fraction; SV, stroke volume; LA, left atrium diameter; LVDs, left ventricular end systolic diameter; LVDd, left ventricular end diastolic diameter. * $p < 0.05$ versus pre-op.

fore surgery was –10.85% (Sensitivity: 62.5%; Specificity: 89.66%), and the area under the ROC curve was 0.78.

Discussion

Left ventricular strain is regarded as an important parameter involved in the assesment of heart function, however, the study for the changes of strain during perioperative period in patients undergoing cardiac valve surgery is less, especially less reports about the clinical application of strain in the postoperative hemodynamic treatment. The main findings of the present study can be summarized as follows: (i) In the patients with valve disease undergoing valve surgery and preserved LVEF (≥50%), LV longitudinal strain could detect potential subclinical myocardial damage than LVEF; (ii) A4C-GLS is independently associated with postoperative elevated inotropic support in these patients; (iii) Patients with preserved LVEF (≥50%) but impaired LV-GLS (≥–16%) have prolonged mechanical ventilation compared with patients with normal LV-GLS (<–16%) after cardiac surgery.

The 2-Dimensional speckle tracking imaging (STI) is increasingly applied for clinical practice in patients before and after cardiac surgery in order to evaluated the impaired myocardial function and the influences of cardiac surgery. Ternacle *et al*. [12] showed that impaired GLS was associated with elevated plasma brain natriuretic peptide level, heart failure symptoms and early postoperative death in patients with preserved LVEF who referred for cardiac surgery. LV strain was sensitive to changes in intrinsic myocardial contractility than LVEF and thus served as an useful marker in the occurrence of low cardiac output syndrome during the perioperative period of cardiac surgery [13]. Zhang and colleagues [14] reported that LV-GLS was independently associated with prolonged hospitalization and the requirement for inotropic support in the patients undergoing aortic valve replacement surgery. These studies indicate that LV-GLS was an independent predictor for LV dysfunction in patients undergoing cardiac surgery.

Adverse cardiac remodeling is the major determinant of the prognosis of the patients with valvular heart disease, and indices such as chamber dilation or left ventricular ejection fraction are unable to reflect the changes of myocardial structure directly and accurately. Thus, management of valvular heart disease should shift from valve-centered to myocardium-centered [15]. The cardiac structure gradually changes which is manifested by the increase of the diameter of the atrium or ventricle and the adaptive thickening or thinner of the ventricular wall regardless of the type of valve

Table 3. **Univariate and multivariate logistic regression analysis of the risk factors for postoperative high VIS.**

	Univariate	*p* value	Multivariate	*p* value
	OR (95% CI)		OR (95% CI)	
LAX-GLS(T0)	1.19 (1.014, 1.397)	0.033		
A2C-GLS(T0)	1.313 (1.053, 1.638)	0.016		
A4C-GLS(T0)	1.245 (1.055, 1.468)	0.009	1.373 (1.092, 1.725)	0.007
LV-GLS(T0)	1.337 (1.083, 1.65)	0.007		
VTI(T0)	1.035 (0.873, 1.226)	0.693		
LVEF (%)	0.856 (0.72, 1.017)	0.077		
LA (mm)	0.996 (0.929, 1.068)	0.908		
LVDd (mm)	1.033 (0.93, 1.146)	0.546		
LVDs (mm)	0.99 (0.842, 1.164)	0.901		
SV (mL)	0.995 (0.963, 1.029)	0.768		
Apache II score	0.883 (0.678, 1.151)	0.359		
CPB time (min)	1.014 (0.997, 1.032)	0.117		
ACC time (min)	1.016 (0.996, 1.037)	0.121		
Duration of surgery (min)	1.007 (0.997, 1.018)	0.190		
CK-MB(T1)	1.023 (1.001, 1.045)	0.038		
FABP(T1)	1.082 (1.002, 1.169)	0.045		
Peak Lac	1.311 (0.934, 1.839)	0.118		
TNI(T1)	1.073 (0.877, 1.314)	0.494		
TNT(T1)	0.999 (0.997, 1.002)	0.533		
VTI(T1)	0.969 (0.808, 1.161)	0.730		
LV-GLS(T1)	1.036 (0.828, 1.295)	0.758		
LAX-GLS(T1)	1.002 (0.821, 1.224)	0.983		
A4C-GLS(T1)	1.123 (0.911, 1.386)	0.278		
A2C-GLS(T1)	0.974 (0.810, 1.169)	0.774		

CPB, Cardiopulmonary bypass; ACC, Aortic cross-clamp; Peak Lac, Peak Lactic acid.

disease. As a consequence, the chronic increase in left ventricular stress will lead to myocardial dysfunction, while the left ventricular ejection fraction still maintains normal [16]. Previous studies showed that LV longitudinal strain was more reflective for early myocardial dysfunction than LVEF [17]. The study by Mascle *et al*. [18] showed that the LV-GLS threshold of –18% may be related to the occurrence of left ventricular dysfunction after mitral valve surgery. The European Association of Cardiovascular Imaging (EACVI) and the American Society of Echocardiography (ASE) also recommended the use of LV-GLS measurement to assess heart function in clinical practice [19]. Our study showed that the median preoperative LV-GLS value was –19% (–20.53%, –17.68%) in the normal GLS group, and –13.1% (–14.63%, –10.73%) in the impaired GLS group ($p < 0.05$).

At present, the normal values of left ventricular strain used in different studies are different due to the type and severity of valve disease and operation types [20,21]. Stassen *et al*. [7] reported that LVEF $\geq$50% and |LV-GLS| $<$16% (HR, 2.467; 95% CI, 1.802–3.378; $p <$ 0 .001) was an independent predictor of all-cause mortality in patients with moderate aortic stenosis, while LVEF $\geq$50% and |LV-GLS| $>$16% was not associated with mortality. And in the other investigation, LV-GLS greater than –16% emerged as a significant and independent predictor of poor outcome in patients undergoing cardiac surgery [12]. Based on the forementioned analysis and according to the normal range of healthy adults, patients were divided into two groups according to whether LV-GLS was greater than –16%. In our study, the median preoperative LV-GLS value of all the patients with preserved left ventricular ejection fraction was –15.45%, which was lower than the LV-GLS strain value ranging from –15.9% to –22.1% (–19.7%, 95% CI, –20.4% to –18.9%) in healthy adults [10]. The result means that although EF remains normal, the patient's myocardium has been damaged.

The 28-day mortality of patients undergoing valve surgery in our center was 1.27% (1/74), which was similar to previous research result [22]. There were insignificant difference in the rates of complication occurrence and mortality between both the groups. However, compared with the normal GLS group, the time of mechanical ventilation of the impaired GLS group was prolonged. Many mechanisms involved in the ventilatory weaning process owing to cardiopulmonary interaction affect heart function, such as activation of the adrenergic system, increased oxygen consumption, and increased left ventricular preload as a result of decreased intrathoracic pressure [23]. Therefore, long-term mechanical ventilation is frequently associated with left ventricular dysfunction. One large-sample retrospective study of postoperative heart surgery populations has shown that left ventricular dysfunction was a powerful predictive factor for prolonged mechanical ventilation after heart surgery [24].

Our study investigated the relationship between preoperative LV-GLS and postoperative inotropic dose in the patients received heart valve surgery with preserved left ventricular ejection fraction. VIS is a score representing the amount of vasoactive and inotropic support which has been shown to predict mortality and morbidity in pediatric cardiac surgery. In a cohort of infants who had congenital heart surgery, a prior research study discovered an association between postoperative VIS over 20 and hospital mortality and prolonged mechanical ventilation [25]. Nevertheless, the cut-off VIS value of 5.5 at the end of the procedure was found to be linked to poor clinical outcomes in a group of adolescents undergoing cardiac surgery [26]. A single-center retrospective cohort study demonstrated that peak VIS in the first 24 hours after cardiac surgery was associated with adverse outcomes in adult heart surgery [27]. The study by Koponen *et al*. [9] revealed that a peak VIS range of 5 to 15 was correlated with ICU time (OR = 0.82) in the first 24 hours following cardiac surgery. Our finding that high VIS scores were not associated with postoperative adverse events was inconsistent with the above previous research, which could be affected by several reasons such as small sample size and the varying disease severity of surgical patients. Additionally, there might be confounding variables that were not taken into account, potentially impacting the relationship between hemodynamics and postoperative adverse events. Furthermore, the method and criteria used to assess VIS scores may need further scrutiny and validation through additional studies. The incidence of adverse events in the impaired GLS group reached 9.09%, which was higher than that of the normal GLS group, although the difference was not statistically significant. Further, our study confrmed the prognostic signifcance of preoperative A4C-GLS before surgery for elevated inotropic support after heart valve surgery in the cardiac patients with preserved LVEF ($\geq$50%), which might help to optimize hemodynamic management therapy in critically ill cardiac patients. Patients undergoing valve surgery may still require significant amounts of vasoactive medication therapy even if their left ventricular ejection fraction was normal before surgery.

In our study, apical four-chamber (A4C), apical two-chamber (A2C) and apical long-axis (LAX) strain curve throughout the cardiac cycle was derived and peak longitudinal strain value was calculated from the average of the 18 segments, but only the preoperative apical four-chamber (A4C) strain which reflect myocardial movement of the septum and lateral wall was independently related to high postoperative VIS value. The study by Salaun *et al*. [28] demonstrated that apical four-chamber longitudinal strain was independently associated with the mortality rate of the patients with aortic valve stenosis. An observational cohort study performed by Nam *et al.* [29] showed that the preoperative apical four-chamber longitudinal strain was also significantly related to all-cause mortality rate of 1773 patients who undergoing valve surgery. Apical two-chamber (A2C) and apical long-axis (LAX) strain did not independently predict high postoperative VIS value, possibly because of preserving subvalvular structure in mitral and aortic valve replacement surgery, which was beneficial for the functional recovery of the posterior and inferior walls of the left ventricle [30,31].

Perioperative hemodynamic optimization management for cardiac surgery and risk stratification in patients with severe valve disease is still challenging and therefore research has focused on identifying new and reliable prognostic parameters. The present study confirmed the prognostic value of LV-GLS in patients with preserved LVEF ($\geq$50%) undergoing valve surgery and showed that patients with normal LV-GLS have a significantly better outcome. However, there has been little research on VIS in adult heart surgery, particularly regarding the connection between VIS and left ventricular function. Thus our study numerically evaluated the correlation between the inotropic support during adult cardiac surgery with left ventricular myocardial strain. Early assessment of left ventricular strain variations might therefore indicate the possibility of postoperative hemodynamic instability in patients and the potential requirement for high inotropic medication therapy. A possible clinical benefit of LV strain is its capacity to detect hemodynamic instability and injured myocardium early in the postoperative period. The apical four-chamber view can be easily and effectively acquired in contemporary clinical practice. Therefore, it can be utilized as an option for LV longitudinal strain when the quality of the apical two-chamber (A2C) and apical long-axis (LAX) view is subpar. In the perioperative care of cardiac surgery, monitoring strain of a single apical four-chamber view allows us to rapidly identify changes in heart function and distinguish the shock's underlying cause. It is capable of formulating the subsequent therapeutic measures, particularly the modification of the kind and dosage of inotropic medications.

Additionally, we collected and analyzed a comprehensive set of variables between the two groups to assess any potential differences. While it is true that we did not observe significant differences in baseline characteristics and intra-operative variables between the groups, it is important to note that this does not necessarily indicate the absence of heterogeneity within the sample. The lack of significant differences could be attributed to several factors, including the sample size, the specific characteristics of the study population, or the precision of our measurements. Future research needs larger sample sizes or alternative study designs to further explore potential heterogeneity.

The main limitation of this study is inherent to the nature of a retrospective chart review. This type of study can only provide us with correlations and not causation. Considering the initial finding that LV-GLS encompasses the 6 segments of the whole LV and the calculation procedures for circumferential and radial strains are not contained in our machine software package, therefore, the study solely investigated the relationship between LV-GLS and the prognosis in patients referred for cardiac valve surgery. The study population was not homogenous and underwent a range of cardiac surgeries, including simple valvular surgery and combined surgery. No subgroup analysis was done for the study due to insufficient sample size. The sample size was small due to the occurrence of covid-19 during the study period led to decline in patient admissions. The generalizability of our findings may be limited to a certain extent due to the small sample size. It is important to conduct replication studies and further investigations in diverse populations to confirm the validity and applicability of our results. Future studies to guide the most efficient strategy for addressing hemodynamic management should be conducted in collaboration with LV-GLS.

Conclusion

Our study showed that preoperative A4C-GLS may be associated with postoperative peak VIS in the patients received heart valve surgery with preserved left ventricular ejection fraction. The preoperative A4C-GLS might be a predictive factor for the postoperative inotropic exposures. The echocardiographic myocardial strain analysis measures of LV contractility may have potential clinical utility in the patients receiving heart valve surgery to assist with myocardial protection and perioperative inotropic treatment strategy.

Availability of Data and Materials

All data generated or analyzed during this study are included in this published article.

Author Contributions

Conceptualization: YYX, XCS, CZ. Data curation: SYC, JLX, HX, LH, XS. Formal analysis: SYC. Investigation: JLX. Resources: XCS. Software: LH. Supervision: CZ. Validation: JLX. Writing – original draft: YYX, SYC, JLX. Writing – review & editing: XCS, CZ. 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

The institutional Ethics Committee of Nanjing First Hospital (KY20210118-01-KS-01) have approved for the conduction and data collection of this study. All patients were informed about the research and signed the consent form.

Acknowledgment

The authors gratefully acknowledge the contributions of the participating doctors: Yuting Li, Run Fu and Li Li.

Funding

This work was funded by the Nanjing Key Medical Science and Technology Development Foundation (ZKX 19021).

Conflict of Interest

The authors declare no conflict of interest.

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