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Prognostic value of preoperative left ventricular global longitudinal strain for predicting postoperative myocardial injury and mortality in patients undergoing major non-cardiac surgery (SOLOMON study)

Minkwan Kim [a,1], Inki Moon [b,1], SungA Bae [a], HyeSun Seo [b,**], In Hyun Jung [a,*]

[a] Division of Cardiology, Department of Internal Medicine, Yonsei University College of Medicine and Cardiovascular Center, Yongin Severance Hospital, Yongin, Republic of Korea
[b] Division of Cardiology, Department of Internal Medicine, Soonchunhyang University Bucheon Hospital, Bucheon, Republic of Korea

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ABSTRACT

Background: The usefulness of preoperative measurement of left ventricular global longitudinal strain (LVGLS) for predicting prognosis in patients undergoing non-cardiac surgery has not been evaluated. We analyzed the prognostic value of LVGLS in predicting postoperative 30-day cardiovascular events and myocardial injury after non-cardiac surgery (MINS).

Methods: This prospective cohort study was conducted in two referral hospitals and included 871 patients who underwent non-cardiac surgery <1 month after preoperative echocardiography. Those with ejection fraction <40%, valvular heart disease, and regional wall motion abnormality were excluded. The co-primary endpoints were the (1) composite incidence of all-cause death, acute coronary syndrome (ACS), and MINS and (2) composite incidence of all-cause death and ACS.

Results: Among the 871 participants enrolled (mean age: 72.9 years; female: 60.8%), there were 43 cases of the primary endpoint (4.9%): 10 deaths, 3 ACS, and 37 MINS. Participants with impaired LVGLS (≤16.6%) had a higher incidence of the co-primary endpoints (log-rank $P < 0.001$ and 0.015) than those without. The result was similar after adjustment with clinical variables and preoperative troponin T levels (hazard ratio = 1.30, 95% confidence interval [CI] = 1.03–1.65; $P = 0.027$). In sequential Cox analysis and net reclassification index, LVGLS had an incremental value for predicting the co-primary endpoints after non-cardiac surgery. Among the 538 (61.8%) participants who underwent serial troponin assay, LVGLS predicted MINS independently from the traditional risk factors (odds ratio = 3.54, 95% CI = 1.70–7.36; $P = 0.001$).

Conclusions: Preoperative LVGLS has an independent and incremental prognostic value in predicting early postoperative cardiovascular events and MINS.

Clinical Trial Registration: URL: https://trialsearch.who.int/. Unique identifiers: KCT0005147.

1. Introduction

Annually, 4% of the world's population undergoes surgery, and 30% of the population undergoes major non-cardiac surgery with at least one cardiovascular risk factor [1,2]. The 30-day mortality rate after major non-cardiac surgeries is reported to be 0.5–2.8% [3–6], and the most common cause of death is a major cardiovascular event, mainly postoperative myocardial infarction [7]. In addition, regardless of the cause of death, the 30-day mortality rate reaches 8% when new-onset heart failure occurs after non-cardiac surgery [8]. Therefore, predicting the

Abbreviation: ACS, acute coronary syndrome; CI, confidence interval; COVID-19, coronavirus disease 2019; EF, ejection fraction; HR, hazard ratio; IQR, interquartile range; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain; MINS, myocardial injury after non-cardiac surgery; RCRI, revised cardiac risk index.

* Corresponding author at: Division of Cardiology, Cardiovascular Center, Yongin Severance Hospital, 363 Dongbaekjukjeon-daero, Giheung-gu, Yongin-si, Gyeonggi-do 16995, Republic of Korea.
** Corresponding author.
E-mail addresses: haesun@schmc.ac.kr (H. Seo), saveheart@yuhs.ac (I.H. Jung).
[1] These two authors contributed equally to this work.

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occurrence of major cardiovascular events or heart failure before surgery may help improve postoperative mortality. Recent studies that focused on assessing myocardial injury after non-cardiac surgery (MINS) used serial high-sensitivity troponin assay as a perioperative prognostic marker. Assessing MINS can lead to an earlier diagnosis of perioperative myocardial infarction and improved 30-day, 6-month, and 1-year outcomes [4,9]. Studies have shown that preoperative troponin elevation alone is an independent predictor of 30-day and long-term mortality [9,10]. However, high-sensitivity troponin has low specificity because it is elevated in various conditions other than myocardial ischemia, and it does not provide any information about the structure and function of the heart.

Preoperative echocardiography has been utilized in symptomatic patients with reduced ejection fraction (EF) or severe valvular heart disease. However, routine echocardiography in asymptomatic patients is not recommended [2]. Moreover, routine preoperative cardiac function evaluation with EF only has modest predictive power over clinical risk factors [11,12]. Recently, it was found that left ventricular global longitudinal strain (LVGLS), which measures myocardial longitudinal fiber shortening, can evaluate cardiac pumping function more precisely than and predict prognosis independently of other traditional risk factors, including clinical variables and EF, in patients with valvular heart disease, heart failure, and cardiomyopathy [13–16]. However, the usefulness of preoperative measurement of LVGLS for predicting prognosis in patients undergoing non-cardiac surgery has not been evaluated. Therefore, in this study, we aimed to evaluate the clinical utility of preoperative LVGLS, measured using transthoracic echocardiography, for predicting the cardiovascular outcomes and prognosis of patients who underwent non-cardiac surgery.

2. Methods

2.1. Study participants

This was a prospective, multicenter observational cohort study conducted in two referral hospitals (URL: https://trialsearch.who.int. Unique identifiers: KCT0005147). Eligible participants were patients aged ≥65 years who were scheduled for major non-cardiac surgery under general anesthesia and underwent preoperative transthoracic echocardiography or patients aged ≥45 years who had at least one cardiovascular risk factor (including previous coronary artery disease, peripheral artery disease, stroke or transient ischemic accident, diabetes mellitus, chronic kidney disease, congestive heart failure, and uncontrolled hypertension) or abnormal electrocardiogram parameters, such as Q wave, T inversion, and ST depression. Patients who underwent surgery less than one month after echocardiography were enrolled. We excluded patients who had minor surgeries, such as ophthalmology, ears/nose/throat, hand, herniated disc, arthroscopic knee, parathyroid, thyroid, breast, or hemorrhoid surgery; oophorectomy or salpingectomy only (without hysterectomy); transurethral resection; or underwent any operation performed under local anesthesia. Patients who had EF <40%, regional wall motion abnormality, moderate to severe valvular heart disease, left bundle branch block, atrial fibrillation, or poor image quality that would interfere with LVGLS analysis were also excluded. All participants provided informed consent before the surgery. Among the 889 participants, 17 were subsequently excluded because of delayed ($n = 5$) or canceled ($n = 8$) operations or transfer to other hospitals ($n = 4$). Finally, from 2020 June to 2022 March, 871 participants were enrolled. This study was approved by the institutional review boards of both participating hospitals (IRB number: 9–2020-0042 and schbc202006022). All participants provided written informed consent.

2.2. Data collection

The participants' demographic information, past medical history, social history, medication history, and preoperative laboratory findings were collected if the attending physician or surgeon performed the evaluation. High-sensitivity troponin T was measured with the Cobas e810 analyzer (Roche Diagnostics, Rotkreuz, Switzerland) using the electrochemiluminescence immunoassay method, and high-sensitivity troponin I was measured using DxI 600 (Beckman Coulter, Brea, CA), with the 99th percentile of the upper reference limits at 14 pg/mL and 8 ng/L, respectively [17]. Conventional two-dimensional echocardiography parameters were measured at rest using Vivid E9/E95 (GE healthcare, Horton, Norway) based on the guidelines established by the American Society of Echocardiography [18]. Left ventricular EF (LVEF) was calculated using the biplane Simpson's disc summation method. LVGLS was measured using a commercially available software (EchoPAC version 204, GE Healthcare) through speckle-tracking and semi-automatic analysis method, in accordance with the guidelines specified by Voigt et al. [19] In brief, simultaneous echocardiogram tracing of three apical standard views was performed. The observer manually edited the region of interest along the endocardial and epicardial borders, which were automatically assessed at first. LVGLS was calculated from an average of three apical standard views of global longitudinal strain values. All participants enrolled in the study had good-quality examinations, with less than two missing segments. LVGLS is presented as absolute values throughout the manuscript. For simple comparison, "lower" or "impaired" LVGLS values indicate smaller absolute LVGLS values.

2.3. Study endpoint

The co-primary endpoints were (1) the composite incidence of all-cause death, acute coronary syndrome (ACS), including non-fatal myocardial infarction that needed urgent revascularization, and MINS; and (2) the composite incidence of all-cause death and ACS in the early postoperative period of 30 days. MINS was defined as an absolute increase in high-sensitivity troponin levels of at least 14 pg/mL between two measurements [4]. The index date was determined when the non-cardiac surgery was performed. The study was performed during the coronavirus disease 2019 (COVID-19) pandemic, and some participants were not able to visit the clinic easily. We contacted the participants via telephone calls when they did not visit the clinic between 4 and 5 weeks from the date of operation.

2.4. Statistical methods

The participants were divided into two groups according to LVGLS and the primary endpoint. Due to the low incidence of the primary endpoint, we expressed continuous variables as median (interquartile range [IQR]) and compared them using Mann–Whitney *U* test. Categorical variables were expressed as numbers (percentages) and compared using chi-squared test or Fisher's exact test, as appropriate. Receiver operating characteristics curve analysis was conducted based on the Youden index to determine the optimal cutoff value of LVGLS for the primary endpoint [20]. Survival analysis was performed using Kaplan–Meier curve, and the difference was compared using log-rank test. Missing data imputation was performed with the missForest algorithm [21]. Univariable Cox regression analysis was performed, and variables that had *P*-value <0.10 were used for multivariable Cox regression analysis to predict the primary endpoint of composite incidence of all-cause death and ACS. To assess the incremental value of LVGLS, we performed sequential Cox regression analysis, C-statistics, and category-free net reclassification index-constructed multivariable models: model 1 (age and sex), model 2 (model 1, diabetes mellitus, and body mass index), model 3 (model 2 and preoperative troponin T), and model 4 (model 3 and LVGLS). Logistic regression analysis was performed to evaluate the diagnostic performance of LVGLS for estimating MINS in participants who had more than two serial measurements of perioperative troponin. All statistical analyses were performed using R version 3.6.0 (R Development Core Team, Vienna, Austria), and two-

sided *P*-value <0.05 was considered statistically significant.

3. Results

3.1. Baseline characteristics and echocardiographic parameters of the study participants

Among the 871 patients (mean age, 72.9 ± 9.3 years), 60.8% (n = 530) were females, and 22% had diabetes. The most common type of surgery was orthopedic (42.4%), followed by gastrointestinal and pancreatico-biliary surgery (38%) (**Supplementary Table I**). Preoperative transthoracic echocardiography parameters are summarized in **Supplementary Table II**. There were no significant differences in the systolic and diastolic parameters, including LVEF. The median value of LVGLS was 17.5 (IQR = 16.0–19.1), and participants who met the primary endpoint tended to have impaired LVGLS values compared to those who did not (16.2 [14.1–17.6] vs. 17.5 [16.1–19.1], P = 0.032) (**Supplementary Table II).** The optimal cutoff value of LVGLS with the highest Youden index calculated from the receiver operating characteristic curve was 16.6%. Participants with impaired LVGLS were older and had higher blood pressure, white blood cell count, and random blood glucose. They also had higher prevalence of history of hypertension and stroke and use of loop diuretics, but they had a lower glomerular filtration rate (Table 1).

3.2. Outcomes and prognostic impact of LVGLS

There were 43 cases of the primary endpoint (4.9%): 10 cases of death, three cases of ACS (including one case of ST-elevation myocardial infarction), and 37 cases of MINS. One participant experienced both ACS and death, and the first event, i.e., ACS, was included in the primary endpoint analysis. Congestive heart failure did not occur in any patient. Participants that met the primary endpoint were more likely to have diabetes, lower body mass index, and higher white blood cell count and high-sensitive troponins (**Supplementary Table III**). There were no differences between the two groups regarding age, sex, level of hemoglobin, and glomerular filtration rate. There was also no difference in the revised cardiac risk index (RCRI) between the groups.

There was no difference in the cumulative incidence of LVEF between the groups in the Kaplan–Meier survival analysis (**Supplementary Fig. I**), but participants with lower LVGLS values (≤16.6%) had a higher incidence of the co-primary endpoints (relative risk = 1.94 and 2.00; log-rank P < *0.001* and 0.015) than those who had no LVGLS impairment (Table 2, Fig. 1A and B). Cumulative incidence curves of composite event of all-cause death and ACS for LVGLS started to diverge during the first week and continued to diverge throughout the early postoperative period (Fig. 1B).

To predict the primary endpoint, multivariable Cox regression analysis was performed with the variables that met the standard described in section 2.4 in the univariable Cox analysis (Table 3). LVGLS, as a continuous variable, was an independent prognostic marker that predicted the primary endpoint (adjusted hazard ratio [HR] = 1.30, 95% confidence interval [CI] = 1.03–1.65, P = 0.027).

We conducted sequential Cox analysis and category-free net reclassification index analysis to identify the incremental value of LVGLS over traditional risk factors for predicting the primary endpoint. Compared to demographic variables (model 1), clinical risk factors (model 2), and preoperative troponin (model 3), LVGLS (model 4) improved the global chi-squared values significantly (P = 0.039 from model 3) (Fig. 2). The C-statistics for model 4, which included model 3 and LVGLS, was 0.846 (95% CI = 0.723–0.968), but it was not significantly different from that of model 3 (P for difference = 0.391). However, the category-free net reclassification index demonstrated the incremental value of LVGLS for predicting the primary endpoint (0.665, 95% CI = 0.128–1.188, P for difference = 0.015) (Table 4).

Table 1
Baseline clinical characteristics of the study population according to the primary endpoint.

Characteristic	LVGLS < 16.6% (n = 292)	LVGLS ≥ 16.6% (n = 576)	*P*-value
Age at enrollment, years	74.3 ± 9.2	72.1 ± 9.3	0.001
Female sex, n (%)	176 (59.7)	354 (61.5)	0.659
Systolic blood pressure, mmHg	136.9 ± 19.3	133.5 ± 16.8	0.010
Diastolic blood pressure, mmHg	77.4 ± 11.5	76.7 ± 30.0	0.642
Body mass index, kg/m^2	24.5 ± 3.6	24.6 ± 3.9	0.871
Cardiovascular risk factors			
Hypertension	243 (82.4)	403 (70.3)	<0.001
Diabetes mellitus	131 (44.4)	218 (37.8)	0.072
Coronary artery disease	19 (6.4)	30 (5.2)	0.566
Heart failure	5 (1.7)	7 (1.2)	0.796
Previous stroke	39 (13.2)	37 (6.5)	0.001
Dyslipidemia	111 (37.6)	217 (37.9)	>0.999
Current smoking	21 (7.1)	52 (9.1)	0.393
Major laboratory findings			
White blood cell, ×10^6 /μL	8.1 ± 3.4	7.4 ± 2.8	0.001
Hemoglobin, g/dL	12.5 ± 1.9	12.4 ± 1.9	0.616
Platelets, ×10^6 /μL	240.3 ± 84.6	237.5 ± 80.8	0.637
GFR, mL/min/1.73m^2	75.0 ± 25.7	81.8 ± 22.0	<0.001
Random blood glucose, mg/dL	139.4 ± 64.2	125.6 ± 42.8	0.001
Hemoglobin A1c, % (valid = 505)	6.8 ± 1.5	6.7 ± 1.4	0.501
CRP, mg/L (valid = 460)	23.0 ± 45.2	17.7 ± 39.3	0.103
Troponin I, pg/mL (valid = 152)	7.3 ± 7.6	7.0 ± 11.6	0.838
Troponin T, pg/mL(valid = 489)	38.9 ± 193.5	13.5 ± 10.9	0.080
Preoperative medications	86 (29.2)	146 (25.6)	0.295
Antiplatelet			
RAS blocker	155 (52.5)	268 (46.9)	0.136
Beta-blocker	43 (14.6)	80 (14.0)	0.902
Loop diuretic	15 (5.1)	11 (1.9)	0.018
Aldosterone receptor blocker	4 (1.4)	7 (1.2)	>0.999
Statin	136 (46.1)	249 (43.6)	0.530
Insulin	19 (6.4)	23 (4.0)	0.153
Revised cardiac risk index			0.315
0	118 (40.0)	242 (42.0)	
1	140 (47.5)	280 (48.6)	
2	33 (11.2)	51 (8.9)	
3	4 (1.4)	2 (0.3)	
4	0 (0.0)	1 (0.2)	

Categorical variables are presented as number (percentage). Continuous variables are presented as mean ± standard deviation.
LVGLS, left ventricular global longitudinal strain; GFR, estimated glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration equation; CRP, C-reactive protein; RAS, renin-angiotensin system.

Table 2
Clinical outcomes according to LVGLS value.

	LVGLS < 16.6% (N = 295)	LVGLS ≥ 16.6% (N = 576)	Relative risk (95% CI)	Log-rank *P-value*
Co-primary outcome 1				
Composite of all-cause death, ACS, and MINS	27 (9.2)	16 (2.8)	1.94 (1.51–2.49)	<0.001
Co-primary outcome 2				
Composite of all-cause death and ACS	8 (2.7)	4 (0.7)	2.00 (1.32–3.00)	0.020

LVGLS, left ventricular global longitudinal strain; CI, confidence interval; ACS, acute coronary syndrome; MINS, myocardial injury after non-cardiac surgery.

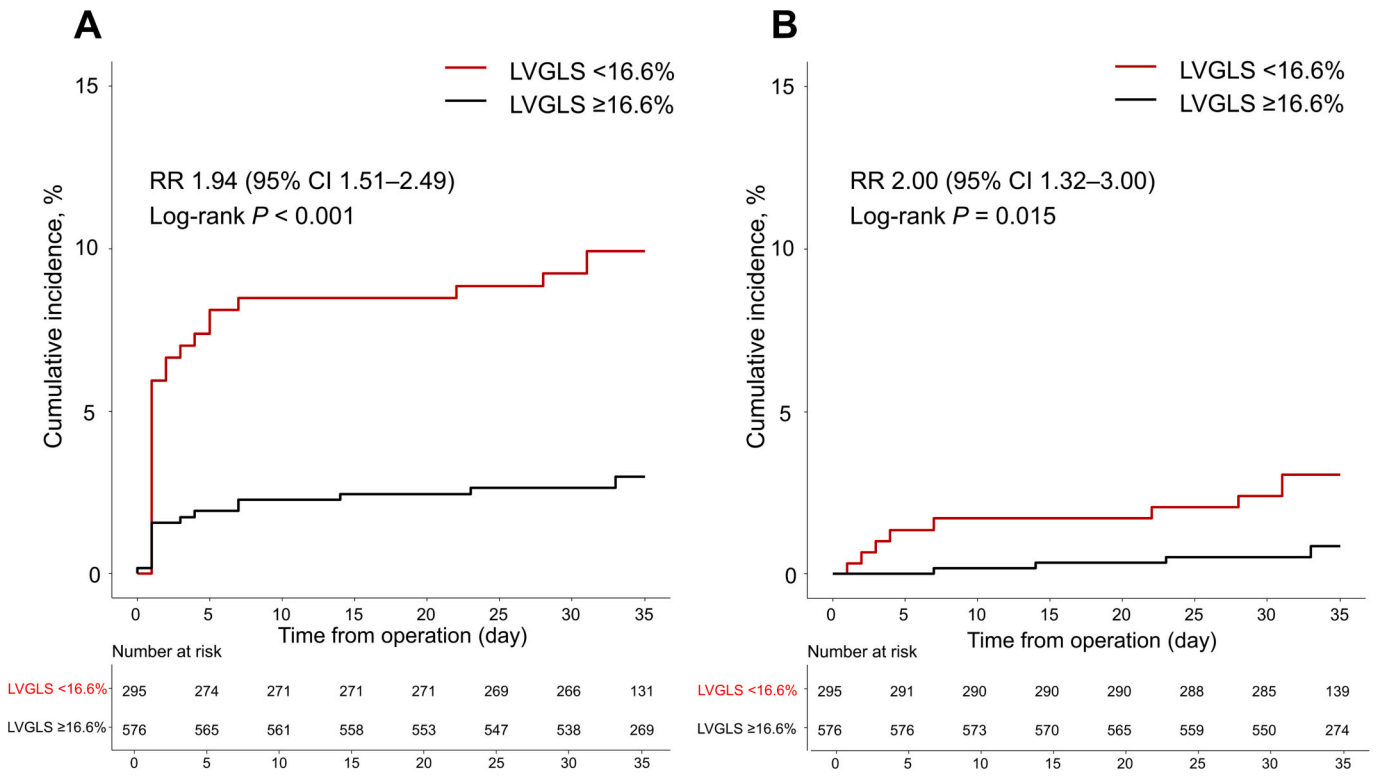

Fig. 1. Kaplan–Meier curve of the cumulative incidence of the primary endpoint.
Kaplan–Meier curve of the cumulative incidence of the co-primary endpoints, namely the composite incidence of all-cause death, ACS (including non-fatal myocardial infarction that needed urgent revascularization), and MINS **(A)**; and the composite incidence of all-cause death and ACS **(B)** according to LVGLS of 16.6%.
LVGLS, left ventricular global longitudinal strain; ACS, acute coronary syndrome; MINS, myocardial injury after non-cardiac surgery.

Table 3
Univariable and multivariable Cox regression analyses of prediction of the primary endpoint in patients who underwent non-cardiac surgery.

	Univariable HR (95% CI)	Multivariable HR (95% CI)	*P*-value*
Age	1.06 (0.99–1.14)	1.00 (0.94–1.07)	0.991
Body mass index	0.84 (0.72–0.98)	0.81 (0.66–1.00)	0.055
Diabetes mellitus	4.44 (1.20–16.41)	4.61 (1.06–20.12)	0.042
Furosemide	6.55 (1.43–29.88)	2.23 (0.42–11.90)	0.348
White blood cell ($\times 10^6$ all)	1.11 (0.99–1.24)	1.11 (0.98–1.25)	0.106
Uric acid (mg/dL)	0.68 (0.44–1.05)	0.68 (0.46–1.02)	0.062
Troponin T (≥14 pg/mL)	6.54 (1.96–21.81)	4.05 (0.98–16.67)	0.053
Deceleration time (ms)	0.99 (0.97–1.00)	0.99 (0.98–1.01)	0.389
LVGLS (%)	1.27 (1.05–1.54)	1.30 (1.03–1.65)	0.027

HR, hazard ratio; CI, confidence interval; LVGLS, left ventricular global longitudinal strain.
* *P*-value for multivariable Cox regression analysis.

3.3. Diagnostic performance of LVGLS for estimating MINS

Among the 871 participants in this study, 538 participants had both pre- and postoperative measurements or more than two serial measurements of postoperative troponin. Among them, 36 participants had MINS (6.7%). Participants with MINS were older and had lower body mass index; higher levels of white blood cells, C-reactive protein, and preoperative troponins; and lower glomerular filtration rate (**Supplementary Table IV**). LVEF was not significantly different between the participants with and without MINS. However, participants with MINS had significantly greater impairment in LVGLS than those without (median [IQR] = 15.9 [14.6–18.1] vs. 17.4 [16.0–18.9], $P = 0.003$) (Fig. 3). In the multivariable logistic regression analysis, LVGLS displayed a powerful diagnostic performance in estimating MINS compared to traditional risk factors, including troponin (odds ratio = 3.54, 95% CI = 1.70–7.36, $P = 0.001$) (Fig. 4 **and Supplementary Table IV**).

4. Discussion

The present prospective cohort study of participants who underwent echocardiography before major non-cardiac surgery demonstrated that LVGLS is independently associated with the primary endpoint after adjustment for traditional risk factors, including preoperative troponin level. LVGLS also had an incremental prognostic value for predicting a composite of early preoperative cardiovascular events. To the best of our knowledge, this is the first prospective observational study that demonstrated the clinical utility of echocardiography-measured preoperative LVGLS in patients with cardiovascular risk factors. Additionally, our study was performed in a population without systolic dysfunction or significant valvular heart disease, which has been previously known to demonstrate poor echocardiographic parameters. Thus, we suggest that assessing LVGLS, in addition to traditional risk assessment using high-sensitivity troponin level and clinical variables, may be of benefit to patients undergoing non-cardiac surgery.

The guidelines for non-cardiac surgery recommend that if the patient's physical activity is >4 metabolic equivalents of task and no acute cardiac condition is present, surgery could be performed without additional examination [1,2]. Stress tests are needed for specific populations who have impaired physical activity and cardiovascular risk factors. Most elderly patients have impaired or indeterminate physical activity, and exercise stress test is often challenging in this population due to their comorbidities, such as orthopedic problems. In addition, because the pharmacological stress test is expensive and time-consuming, it is difficult to conduct it for all candidates who have intermediate risk and are scheduled for non-cardiac surgery. Recent studies have reported an

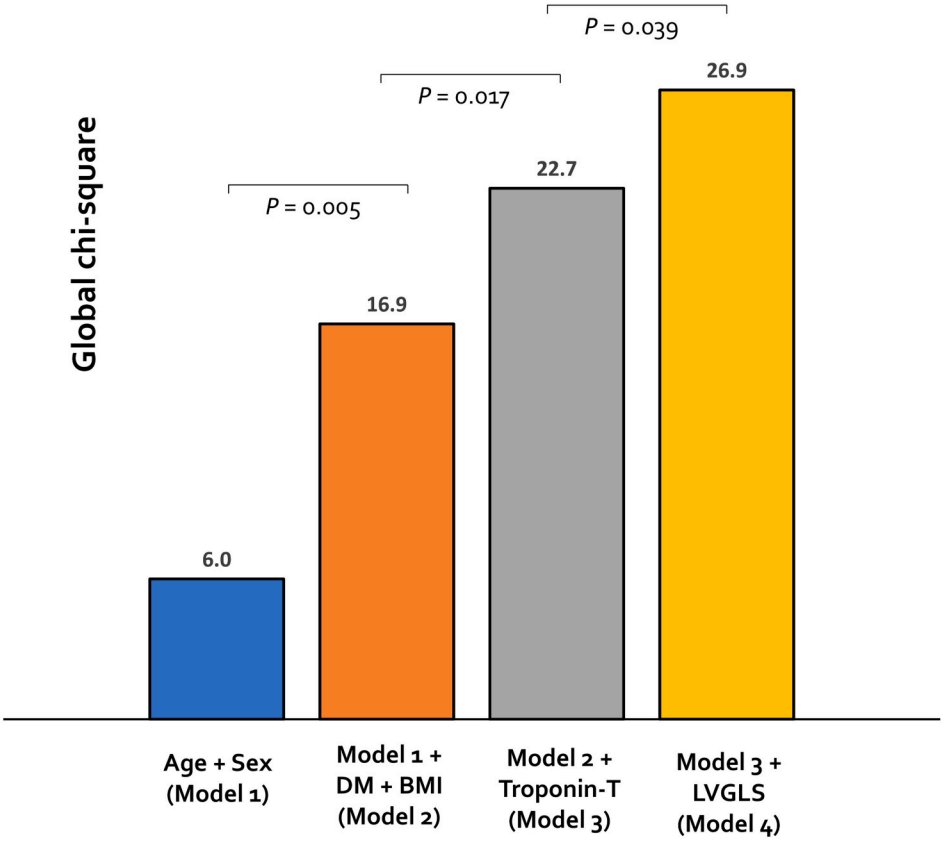

Fig. 2. Incremental value of left ventricular global longitudinal strain over clinical variables and high-sensitivity cardiac troponin T for predicting the primary endpoint, based on global chi-squared changes in sequential Cox analysis.
Model 1: age and sex; model 2: model 1 and clinical risk factors that had statistical significance in univariable Cox regression analysis, including DM and BMI; model 3: Model 2 and high-sensitivity troponin T; model 4: model 3 and LVGLS, an echocardiographic systolic function parameter.
DM, diabetes mellitus; BMI, body mass index; LVGLS, left ventricular global longitudinal strain.

Table 4
Incremental value of left ventricular global longitudinal strain compared to traditional risk factors for predicting the primary endpoint in patients who underwent non-cardiac surgery.

	C-statistic		Net reclassification index	
	95% CI	*P*-value for difference	95% CI	*P*-value for difference
Model 1 (age, sex)	0.658 (0.468–0.848)			
Model 2 (Model 1 + DM + BMI)	0.785 (0.626–0.943)	0.029	0.857 (0.363–1.350)	<0.001
Model 3 (Model 2 + Troponin T*)	0.825 (0.692–0.957)	0.220	0.880 (0.344–1.417)	0.001
Model 4 (Model 3 + LVGLS†)	0.846 (0.723–0.968)	0.391	0.665 (0.128–1.188)	0.015

* Categorical variable with the threshold of 14 pg/mL. † LVGLS value showing both per 1% decrease and < 16.6%.
LVGLS, left ventricular global longitudinal strain; CI, confidence interval; DM, diabetes mellitus; BMI, body mass index.

association between preoperative echocardiography and prognosis in specific populations, such as those with reduced EF or significant valvular heart disease [11,22,23]. However, the interpretation of study results based on routine preoperative echocardiography is limited because of the relatively small sample size or low incidence of 30-day cardiovascular events [12,24]. In previous studies, the incremental value of echocardiography was insignificant compared to the combination of traditional clinical variables and risk stratification models such as RCRI [12,25]. RCRI, a representative risk assessment tool for non-cardiac surgery patients, achieved good risk stratification in some cohorts [26]. However, recent studies have shown that RCRI had poor performance (C-statistics of 0.666 in vascular surgery and 0.566 in non-vascular surgery) and did not predict MINS as well as our study results did [1,2,27]. The prognostic value of LVGLS, a systolic function parameter, was previously identified in various disease conditions, such as valvular heart disease, heart failure, and cardiomyopathy [13–16]. The present study, for the first time, demonstrated the association between LVGLS and early postoperative cardiovascular events and the incremental prognostic value of LVGLS when combined with clinical variables and preoperative troponin levels. This suggests that preoperative echocardiography may provide additional information to surgical teams and anesthesiologists in the management of patients undergoing non-cardiac surgery.

Many studies conducted in large populations have utilized cardiac troponin to identify the postoperative risk in non-cardiac surgery patients. Elevated troponin levels before surgery is an independent postoperative predictor of 30-day and long-term mortality [9,10]. MINS is defined as myocardial damage due to ischemia that occurs during the intraoperative and early postoperative period, and non-ischemic myocardial damage resulting from conditions such as sepsis or pulmonary embolism is not considered as MINS [28]. Although the diagnosis of MINS is difficult because it often occurs without typical symptoms or electrocardiogram features of myocardial ischemia, previous studies have reported that patients with MINS have poor 30-day, 6-month, and 1-year prognosis [4,5,9]. Based on this, recent guidelines have recommended postoperative high-sensitivity troponin tests after 24 and 48 h for patients who underwent major non-cardiac surgery [29,30]. However, high-sensitivity troponin may be elevated in other situations, such as sepsis and renal insufficiency [9,31]. Acute and chronic heart failure also cause cardiac troponin elevation due to myocardial stretching following increased left ventricular filling pressure [31]. Our study found that LVGLS is an independent prognostic marker from cardiac troponin and has incremental value for estimating early postoperative

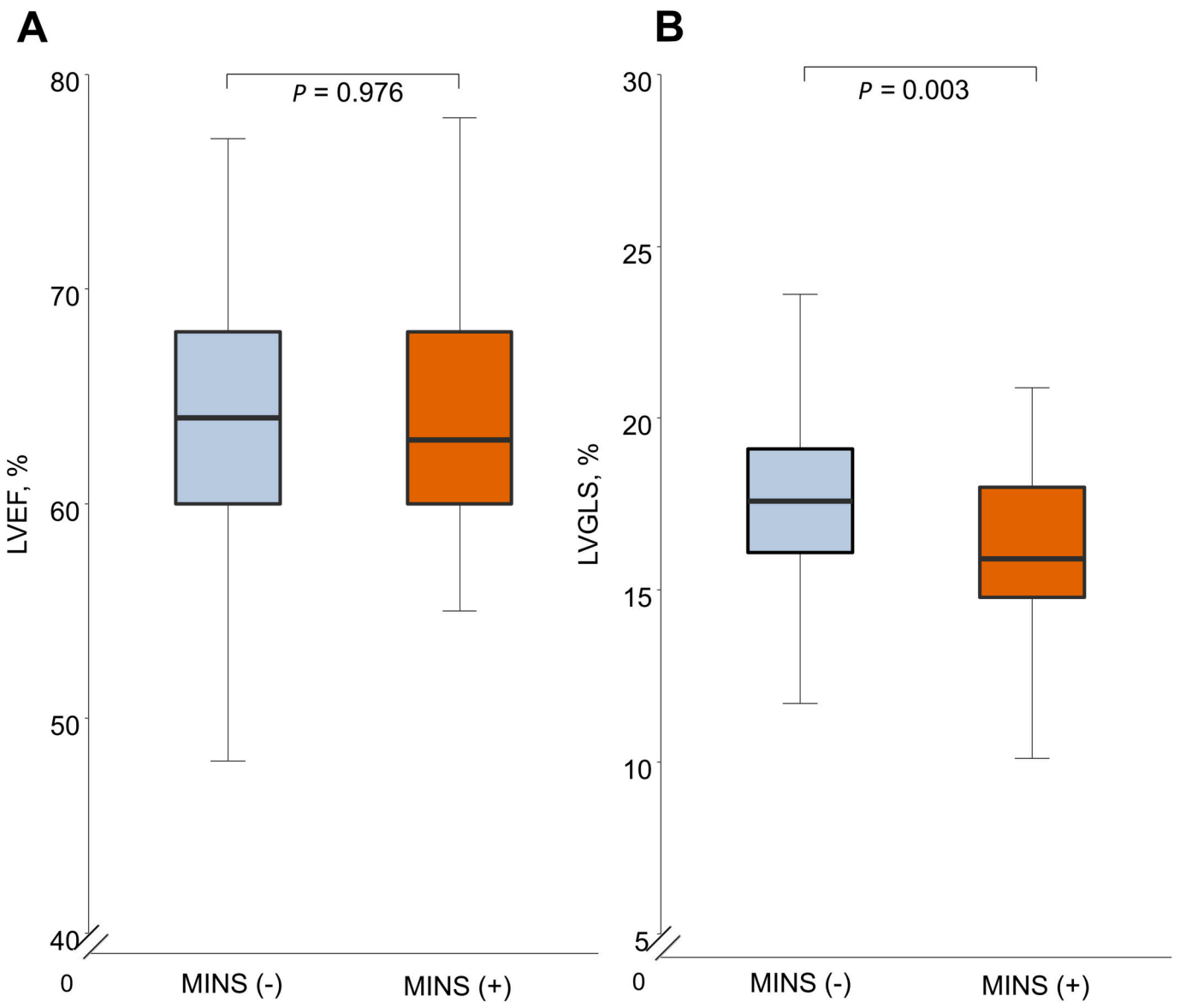

Fig. 3. Box plot of (A) LVEF and (B) LVGLS according to the presence of MINS in participants who underwent more than two serial measurements of high-sensitive troponin. There was no missing value of high-sensitivity cardiac troponin in this analysis.
MINS, myocardial injury after non-cardiac surgery; LVEF, left ventricular ejection fraction; LVGLS, left ventricular global longitudinal strain.

events when used in combination with high-sensitivity troponin. Furthermore, preoperative LVGLS predicts MINS independently from several traditional risk factors. Therefore, combining LVGLS with traditional risk assessment, including cardiac troponin, may be useful for predicting cardiovascular events and MINS before a major non-cardiac surgery.

4.1. Study limitations

The present study has some limitations. First, due to its design as an observational trial to investigate the prognostic value of preoperative echocardiographic parameters, including LVGLS, selection bias may exist. The incidence of the primary endpoint was similar to or slightly lower than that obtained in previous studies; thus, our study may have enrolled participants with lower risk of early postoperative cardiovascular events than participants in previous studies [2,5,32]. Second, due to the study design, not all participants were available to undergo pre- and postoperative high-sensitivity troponin assays. However, we tried to demonstrate the independent and incremental value of LVGLS over troponin assay by using several statistical methods, including imputation and subpopulation of participants with serial troponin results. A further well-designed study, such as a randomized control study, will be needed to identify the incremental or synergistic value of troponin and echocardiographic parameters, including LVGLS. Furthermore, because this study was conducted during the COVID-19 pandemic when many elective surgeries were canceled or delayed, our sample size was slightly smaller than initially planned. However, our multivariable regression analysis showed that LVGLS has a prognostic value in predicting the primary outcome and estimating MINS. Lastly, our study did not evaluate long-term outcome beyond 1 year. It is also uncertain whether preoperative intervention based on LVGLS will improve the prognosis of patients who undergo non-cardiac surgery. However, this preliminary study has demonstrated the clinical utility of LVGLS in evaluating the preoperative risk for cardiovascular events after non-cardiac surgery. Further studies that explore long-term prognosis or randomized controlled studies based on LVGLS may clarify the prognostic value of LVGLS.

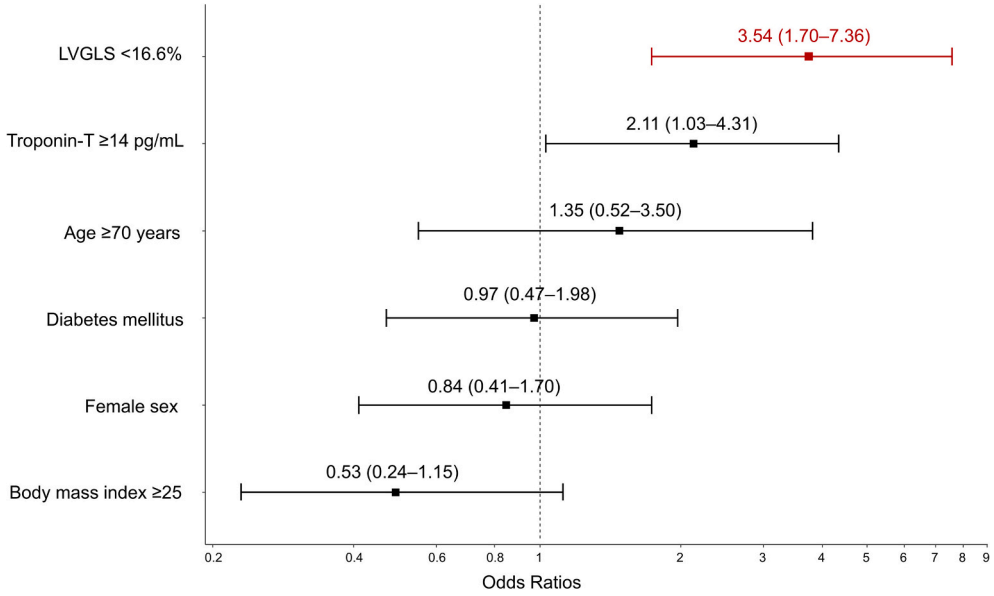

Fig. 4. Forest plot for estimating MINS analyzed by multivariable logistic regression analysis in participants who underwent more than two serial measurements of high-sensitivity troponin. There was no missing value of high-sensitivity cardiac troponin in this analysis.
MINS, myocardial injury after non-cardiac surgery; OR, odds ratio; CI, confidence interval.

4.2. Conclusion

Preoperative LVGLS has an independent and incremental value in predicting early postoperative cardiovascular events and MINS. LVGLS may provide additional preoperative risk information to known prognostic factors. The possibility of improving postoperative prognosis by preoperative intervention based on LVGLS warrants further investigations.

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Declaration of Competing Interest

All authors have no relevant disclosures.

Data availability

The data presented in this article are included in the manuscript or supplementary materials. Further information will be shared on reasonable request to the corresponding author.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcard.2023.02.046.

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