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ORIGINAL ARTICLE

Tissue Doppler imaging is useful for predicting the need for inotropic support after cardiac surgery

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Abstract

Purpose Low preoperative left ventricular ejection fraction (EF) is a predictor of the need for inotropic support after cardiac surgery. However, EF can be misinterpreted and difficult to measure in some cases. The purpose of this study was to compare the value of preoperative EF and intraoperative tissue Doppler imaging variables in predicting the need for postoperative inotropic support.

Methods Forty-eight consecutive adult patients undergoing cardiac surgery were enrolled in this study. Systolic mitral annular velocity (S_m), early diastolic mitral annular velocity (E_m), the ratio of E_m to late diastolic mitral annular velocity (E_m/A_m), and the ratio of early diastolic transmitral velocity to E_m (E/E_m) were measured using transesophageal echocardiography before median sternotomy. The primary outcome was the need for inotropic support for 12 or more hours after surgery. Preoperative, intraoperative, and echocardiographic characteristics were analyzed to determine the independent predictors of the need for postoperative inotropic support.

Results Postoperative inotropic support was required for $\geq$12 h in 26.7% of patients. Multivariate logistic regression identified only cardiopulmonary bypass (CPB) time as an independent predictor of inotropic support (odds ratio, 1.015; 95% CI, 1.004–1.025; $P = 0.004$). Additional analysis was performed in the 25 patients with a CPB time of $\geq$200 min. In this analysis, only S_m was significantly associated with the need for inotropic support for $\geq$12 h.

Conclusions This study suggests that those patients who have decreased S_m and extended CPB times are more likely to require inotropic support after surgery, independent of a preserved left ventricular EF.

Keywords Tissue Doppler imaging (TDI) · Mitral annular velocity · Inotropic support · Cardiac surgery

Introduction

For cardiac anesthesiologists, the ideal intraoperative assessment of cardiac function with transesophageal echocardiography (TEE) should be easily applicable to the perioperative clinical setting, sensitive to changes in inotropy, and independent of heart size, mass, and loading conditions [1]. Echocardiographic quantitative assessment of left ventricular systolic function has centered on ejection fraction (EF). However, the assessment of EF and other volumetric measurements can be difficult in patients with abnormally shaped ventricles, regional wall motion abnormalities, ventricular hypertrophy, or poor endocardial border identification [2, 3]. Moreover, these assessments depend on loading conditions and are prone to technical errors caused by foreshortened views [3].

Positive inotropic drug support is frequently needed after cardiac surgery. Previous studies have demonstrated that the need for inotropic support after cardiac surgery is predictive of ventricular dysfunction and adverse short-term outcomes [4–6]. Reduced left ventricular EF has been identified as a predictor of the need for postsurgical inotropic support in patients undergoing coronary artery

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bypass grafting (CABG) or valve surgery [7, 8]. However, misestimation of EF can occur in the case of aortic stenosis, mitral regurgitation, or left ventricular hypertrophy [1]. Furthermore, almost half of patients with heart failure have a normal left ventricular EF but abnormal systolic function in the long axis [9].

Tissue Doppler imaging (TDI) is a relatively novel echocardiographic method to measure myocardial velocities. TDI has been used to assess systolic and diastolic left ventricular function in a variety of clinical conditions [10]. Mitral annulus velocities that reflect left ventricular function in the long axis can be easily measured by TDI [11]. Recent studies have shown that TDI variables are useful for determining the long-term prognosis of patients with various major cardiac diseases as well as the general population [12, 13]. Most echocardiographic equipment can be used for TDI to assess global left ventricular function. Thus, TDI may be the ideal method for intraoperative assessment of cardiac function during the anesthetic management of patients undergoing cardiac surgery. However, it is unknown whether TDI variables can predict short-term outcomes after cardiac surgery. The purpose of this study was to test the hypothesis that, compared with preoperative EF, intraoperative TDI variables are better able to predict the need for postoperative inotropic support.

Methods

Study population and data collection

The study was approved by the Institutional Ethical Committee of Niigata University Medical and Dental Hospital, Niigata, Japan. All participants gave written informed consent. Forty-eight consecutive adult patients undergoing cardiac surgery from October 2007 to September 2009 were included in this study. Patients with paced or non-sinus rhythm were excluded. Data collected included age, sex, and complications including hypertension, diabetes, hyperlipidemia, renal failure, peripheral vascular disease, and preoperative left ventricular EF. EF was measured with transthoracic echocardiography, and the most recent preoperative value was recorded. Surgical data included the type of surgery, cardiopulmonary bypass (CPB) time, and aortic cross-clamping time.

Anesthetic management and CPB

Anesthesia was induced with a combination of either midazolam or propofol with fentanyl and remifentanil. Muscle paralysis was achieved with vecuronium or rocuronium. Anesthesia was maintained with a combination of either sevoflurane or propofol with fentanyl and remifentanil. The bispectral index (Aspect Medical Systems, Norwood, MA, USA) was monitored, with a target level of 40–50 during surgery. Patients were monitored by 5-lead electrocardiogram, pulse oximetry, capnography, radial artery catheter, thermometer codes in the nasopharynx and urinary bladder, pulmonary artery catheter, and TEE.

CPB was performed at moderate hypothermia (32°–33.5°C) with α-stat pH management, a mean perfusion pressure of 60–80 mmHg, pump flow rates of 2.4–2.6 l/min/m, a hematocrit of 23–26%, and a membrane oxygenator. Myocardial protection was performed with intermittent antegrade and occasional retrograde cold blood cardioplegia at roughly 20-min intervals during aortic cross-clamping.

TEE examinations

After induction of general anesthesia and endotracheal intubation, a 5-MHz multiplane TEE probe (UST-5293S-5 or UST-52115S; Aloka, Tokyo, Japan) was inserted and connected to an ultrasound system (ProSound ALPHA 10; Aloka). TEE examinations were performed during a period of hemodynamic stability before median sternotomy. TDI variables were measured using pulsed-wave TDI with the preset TDI control on the ultrasound system. The sample volume was placed at the lateral mitral annulus in the midesophageal four-chamber view (Fig. 1). The sample volume was set at 3 mm in axial length, and the sweep speed was set at 66.7 mm/s. The recordings were stored on an S-VHS videotape for offline analysis. Systolic mitral annular velocity (S_m), early diastolic mitral annular velocity (E_m), and the ratio of E_m to late diastolic mitral annular velocity (E_m/A_m) were measured. Transmitral Doppler flow was obtained at the tip of the mitral leaflets in the midesophageal four-chamber view. The ratio of early diastolic transmitral velocity to E_m (E/E_m) was calculated. All measurements were obtained for three consecutive cardiac cycles at end-expiration, and the average was determined. Intraoperative EF using TEE was measured in 36 consecutive patients from February 2008 to September 2009 in the transgastric left ventricular midpapillary short-axis view just after recording the TDI waveform. All TEE examinations were performed by a single investigator (H.I.) certified by the Japanese Board of Perioperative Transesophageal Echocardiography.

Study outcomes

The primary outcome in this study was inotropic support for $\geq$12 h after cardiac surgery. Patients were defined as having received inotropic support if they received intravenous infusions of dopamine, dobutamine, epinephrine,

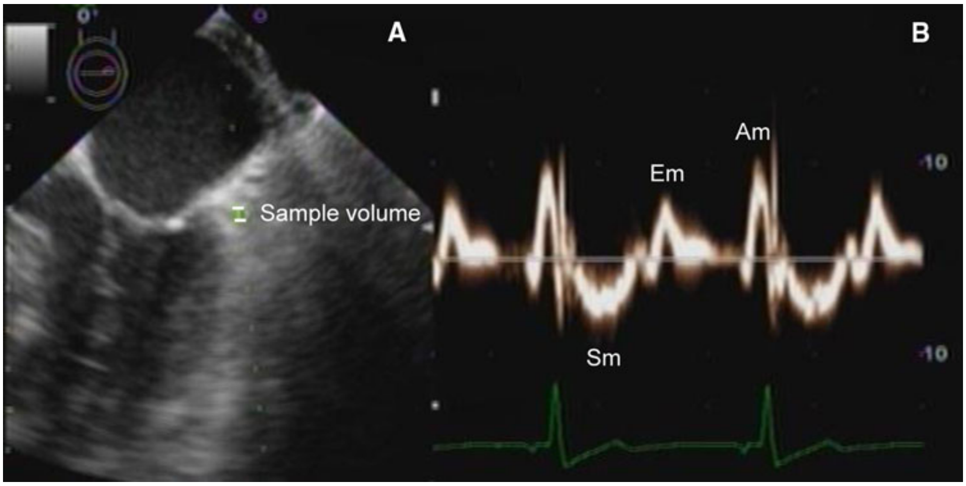

Fig. 1 Tissue Doppler imaging of the lateral mitral annulus of a patient with aortic valve stenosis. **a** Position of the pulsed-wave Doppler sample volume is demonstrated in the two-dimensional transesophageal echocardiographic image of the midesophageal four-chamber view. **b** A spectrum of myocardial velocities. S_m systolic mitral annular velocity, E_m early diastolic mitral annular velocity, A_m late diastolic mitral velocity

olprinone, or milrinone. Based on previous reports, a dopamine infusion of $\geq$4 μg/kg/min was considered as inotropic support [4, 5, 7, 8]. At our institution, in contrast to previous reports, inotropic drugs are frequently administered during and after weaning from CPB [6–8, 14]. Inotropic drugs are usually tapered and then discontinued by the next morning if a systolic blood pressure of $\geq$90 mmHg and cardiac index of $\geq$2.2 l/min/m^2 are maintained in the intensive care unit (ICU). Therefore, inotropic support for $\geq$12 h was considered to be an adverse outcome in this study. The cardiac surgeon, who was blinded to the TDI measurements, conducted postoperative hemodynamic management of patients.

Statistical analysis

Continuous variables were expressed as mean ± SD and compared using the Mann–Whitney *U* test. Categorical variables were expressed as number of patients (percentages) and compared using the chi-square test or Fisher's exact test. Multivariate logistic regression analysis was used to identify independent predictors of the need for inotropic support after cardiac surgery. Variables that had a univariate probability value <0.05 were selected for inclusion in a logistic regression model by stepwise selection. A P value <0.05 was considered statistically significant. Statistical analysis was performed using Stat-Flex software, Version 6 (Artech, Osaka, Japan).

Results

No patients who underwent urgent operations were included in this study. Two patients were excluded from the study because of intermittent atrial arrhythmias or hemodynamic instability during TEE examinations. One other patient was excluded because of sudden cardiac arrest on the operative day. Of the remaining 45 patients, 14 underwent CABG (on-pump, 6; off-pump, 8), 18 underwent valve surgery (aortic alone, 10; mitral alone, 3; aortic and mitral, 1; aortic, mitral, and tricuspid, 4), 6 underwent combined aortic valve surgery and CABG, and 7 underwent other procedures (Bentall procedure, 4; resection of left atrial myxoma, 2; atrial septal defect closure, 1). One patient who received inotropic support for $\geq$12 h had suboptimal views to obtain A_m. One patient who received inotropic support for <12 h had suboptimal views to obtain E. All TEE-derived variables were available for analysis in the remaining 43 patients.

A good correlation was found between preoperative EF and intraoperative EF ($r = 0.78$; $P < 0.001$).

Inotropic support for $\geq$12 h after cardiac surgery was required in 12 patients (26.7%). Preoperative, intraoperative, and echocardiographic characteristics of patients who did or did not require postoperative inotropic support for $\geq$12 h are listed in Table 1. Univariate analysis revealed that inotropic support was significantly associated with CPB time, aortic cross-clamping time, and S_m. Preoperative EF was not statistically different between the two groups. Patients with inotropic support for $\geq$12 h required longer ventilatory support (8.8 ± 39.1 vs. 13.7 ± 21.8 h; $P = 0.006$) and a longer postoperative ICU stay (1.5 ± 2.1 vs. 2.3 ± 1.6 days; $P < 0.001$).

Multivariate logistic regression identified only CPB time as an independent predictor of the need for $\geq$12 h of inotropic support after cardiac surgery (odds ratio, 1.015; 95% CI, 1.004–1.025; $P = 0.004$). The distribution of CPB time in both groups is presented in Fig. 2. All 12 patients who required $\geq$12 h of inotropic support had CPB times of $\geq$200 min, whereas only 13 patients (39.4%) who required <12 h of inotropic support had CPB times of $\geq$200 min. Additional analysis was performed in these 25 patients with CPB times of $\geq$200 min to adjust for CPB time. CPB time was 263 ± 70 min in the <12-h group and

Table 1 Patient characteristics

	Inotropic support		P
	<12 h	$\geq$12 h	
Number of patients	33 (73.3)	12 (26.7)	
Preoperative data			
Age (years)	66.7 ± 13.6	62.0 ± 14.6	0.22
Sex			
Male	19 (57.6)	10 (83.3)	0.11
Female	14 (42.4)	2 (16.7)	
Hypertension	20 (60.6)	4 (33.3)	0.10
Diabetes	8 (24.2)	2 (16.7)	0.59
Hyperlipidemia	8 (24.2)	2 (16.7)	0.59
Renal failure	3 (9.1)	4 (33.3)	0.07
Peripheral vascular disease	4 (12.1)	1 (8.3)	1.00
Ejection fraction (%)	63.5 ± 13.5	57.7 ± 17.5	0.22
Type of surgery			
Off-pump CABG	8 (24.2)	0	0.09
CABG	4 (12.1)	2 (16.7)	1.00
Valve surgery	13 (39.4)	5 (41.6)	0.89
Valve and CABG	3 (9.1)	3 (25.0)	0.32
Others	5 (15.2)	2 (16.7)	1.00
Cardiopulmonary bypass time (min)	150 ± 114	283 ± 46	<0.001
Aortic cross-clamping time (min)	88 ± 81	159 ± 82	0.008
Intraoperative TDI data			
S_{m} (cm/s)	7.4 ± 2.5	5.2 ± 1.7	0.002
E_{m} (cm/s)	6.6 ± 2.8	6.1 ± 3.9	0.24
$E_{\mathrm{m}}/A_{\mathrm{m}}$ <1	17 (51.5)	6 (54.5)[a]	0.86
E/E_{m} >15	10 (31.3)[b]	6 (50.0)	0.17

Data are expressed as mean ± SD or number of patients (%)

CABG coronary artery bypass grafting, *TDI* tissue Doppler imaging, S_{m} systolic mitral annular velocity, E_{m} early diastolic mitral annular velocity, A_{m} late diastolic mitral annular velocity, E early diastolic transmitral velocity

[a] One patient with views that were suboptimal for obtaining A_{m} was excluded from the analysis ($n = 11$)

[b] One patient with views that were suboptimal for obtaining E was excluded from the analysis ($n = 32$)

283 ± 46 min in the $\geq$12-h group ($P = 0.20$). In this analysis, only S_{m} was associated with the need for $\geq$12 h of inotropic support after surgery (6.5 ± 1.7 vs. 5.2 ± 1.7 cm/s; $P = 0.027$). The association between inotropic support and $S_{\mathrm{m}} \leq 5$ cm/s is presented in Table 2 ($P = 0.009$). Other variables, including preoperative EF (58.2 ± 14.3% vs. 57.8 ± 17.5%; $P = 0.91$) and surgery type, were not statistically different between the two groups (Table 2). Scatter plots of S_{m} and EF in patients who had CPB times of $\geq$200 min are presented in Fig. 3.

Ten records were randomly selected and used to assess intraobserver and interobserver (H.I. and M.T.) variability in the measurement of TDI variables. Variability was calculated as the difference between the measurements divided by the mean values. Intraobserver and interobserver variability for S_{m} were 3.2 ± 2.9% and 6.5 ± 4.8%, respectively.

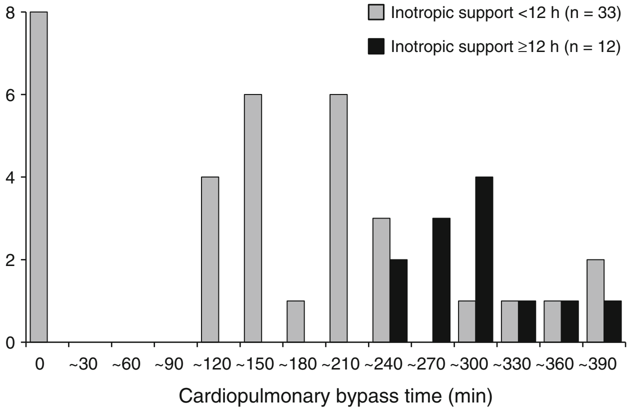

Fig. 2 Distribution of cardiopulmonary bypass time in patients who required <12 or $\geq$12 h of postoperative inotropic support. Data are expressed as number of patients at 30-min intervals

Discussion

To our knowledge, this is the first report focusing on the association between intraoperative TDI variables and the need for inotropic support after cardiac surgery. In this study, 27% of patients required inotropic support for $\geq$12 h. These patients required longer ventilatory support and a longer postoperative ICU stay. On this basis, the primary outcome we set in our study, namely, the need for inotropic support for $\geq$12 h, is efficient for identification of patients who require highly intensive care. CPB time was the strongest predictor of the need for inotropic support. None of the TDI variables was an independent predictor. The most important finding of this study is that decreased intraoperative S_{m}, but not preoperative EF, was significantly associated with the need for postoperative inotropic support, even after adjustment for CPB time.

Our findings are inconsistent with previous studies that described reduced left ventricular EF as a predictor of low cardiac output syndrome and the need for inotropic support after cardiac surgery [4, 5, 7, 8]. However, several studies have suggested that volumetric assessments of cardiac function are not associated with inotropic support [14, 15]. Zaroff et al. [16] found that although low preoperative EF is a known predictor of poor immediate postoperative outcome after cardiac surgery, not all patients with low preoperative EF required postoperative inotropic support.

TDI variables were easily obtained in this study with the exception of two patients for whom A_{m} and E values could

Table 2 Association between S_{m} of ≤ 5 cm/s, type of surgery, and inotropic support in patients with a cardiopulmonary bypass time of ≥ 200 min

	Inotropic support		Row total
	<12 h	≥12 h	
Number of patients	13	12	
$S_{\mathrm{m}} \leq 5$ cm/s	3 (23.1)	9 (75.0)	12
$S_{\mathrm{m}} > 5$ cm/s	10 (76.9)	3 (25.0)	13
Type of surgery			
CABG	3 (23.1)	2 (16.7)	5
Valve surgery	5 (38.4)	5 (41.6)	10
Valve and CABG	3 (23.1)	3 (25.0)	6
Others	2 (15.4)	2 (16.7)	4

Data are expressed as number of patients (%)

CABG coronary artery bypass grafting, S_{m} systolic mitral annular velocity

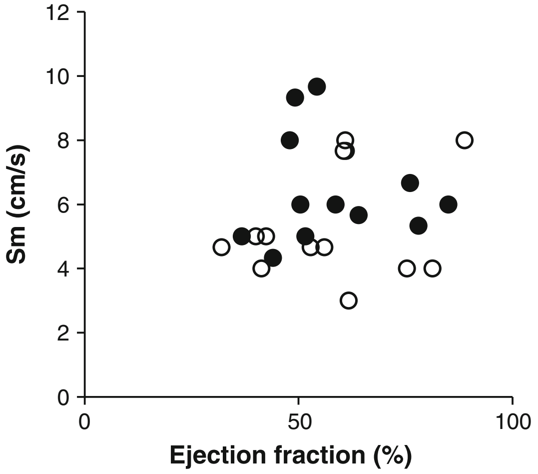

Fig. 3 Scatter plots of systolic mitral annular velocity and ejection fraction in patients with a cardiopulmonary bypass time of ≥ 200 min. *White circles* patients who required ≥ 12 h of inotropic support, *black circles* patients who required <12 h of inotropic support. S_{m} systolic mitral annular velocity

not be determined. S_{m} was significantly associated with inotropic support following univariate analysis. S_{m} is a sensitive marker of mildly impaired left ventricular systolic function with a normal EF or apparently preserved left ventricular systolic function [9]. Although EF can assess only systolic function, TDI can simultaneously assess both systolic and diastolic functions. Contrary to expectations, E_{m}, $E_{\mathrm{m}}/A_{\mathrm{m}}$, and E/E_{m}, which represent diastolic function, were not associated with the need for inotropic support. Bernard et al. [14] described preoperative left ventricular diastolic dysfunction as an independent predictor of inotropic support after CPB. In their study, diastolic function was assessed with conventional Doppler measurements in 66 patients undergoing cardiac surgery, including 56 (85%) patients undergoing isolated CABG. Here, we assessed diastolic function with TDI rather than conventional Doppler measurements. With conventional Doppler measurements, both transmitral and pulmonary venous Doppler flow variables must be measured to assess diastolic function [17]. In addition, these variables are often difficult to determine because of changes in preload or left atrial pressures [10, 18, 19]. By contrast, E_{m} is a relatively preload-independent assessment of diastolic function [18, 19]. Several studies have demonstrated that E_{m} is a powerful predictor of cardiac mortality [20, 21]. Parameters of diastolic function, including E_{m}, $E_{\mathrm{m}}/A_{\mathrm{m}}$, and E/E_{m}, were not graded according to severity in our study, which differs from previous reports [14, 22]. We measured only peak velocity of the TDI spectrum because it is simple and is easily and rapidly performed intraoperatively. We consider that complex measurements of diastolic function are unsuitable for intraoperative online monitoring. Diastolic TDI variables might not have been an effective predictive index in our study because of these different processes. Nevertheless, we believe that TDI diastolic variables, which can be measured easily and rapidly, may have potential practical value in perioperative management of patients undergoing cardiac surgery.

Intraoperative TDI variables were measured only before CPB in our study. Those values after CPB are probably affected by several factors related to CPB or vasoactive medications [23, 24]. In our preliminary study, we experienced frequent difficulty in the clear identification of S_{m} and E_{m}. The reasons for this difficulty were not identified, but they might have been related to myocardial stunning or reduced compliance of the left ventricle. We consider, therefore, that intraoperative TDI variables after CPB are not suitable for application to prediction of the inotropic support requirement.

CPB time was, not surprisingly, the strongest predictor of the need for postoperative inotropic support in this study. Our findings are consistent with those of several studies that used multivariate logistic regression analysis to show that CPB time is an independent predictor of the need for inotropic support [14, 15]. Compared with these previous studies, however, the patients in this study had longer CPB times. In fact, all patients who required inotropic support for ≥ 12 h had CPB times of ≥ 200 min (Fig. 2). In addition, no patients undergoing off-pump CABG required inotropic support for ≥ 12 h. These findings suggest that our results might be highly affected by CPB time.

To exclude the effect of CPB time on the need for inotropic support, an additional analysis was performed in patients with CPB times of ≥ 200 min. Only S_{m} was significantly associated with inotropic support in this additional analysis. Wang et al. [20] showed that the hazard ratio of cardiac death is significantly increased in subjects with $S_m \leq 5$ cm/s compared with those with $S_m > 5$ cm/s. Based on this report, we determined the number of patients with CPB times ≥200 min who had S_m values of ≤5 and >5 cm/s. Most patients with S_m of ≤5 cm/s (75%) needed inotropic support for ≥12 h (Table 2). Taken together, our results suggest that patients with decreased S_m who must undergo prolonged CPB will be more likely to require inotropic support after cardiac surgery (Fig. 3).

These observations have clinical implications for the perioperative management of patients undergoing cardiac surgery. Low cardiac output syndrome will occur even in the presence of preserved left ventricular EF. Intraoperative assessment of cardiac function with TDI can be useful to identify patients who might suffer from longer inotropic support. A surgical strategy in which CPB time can be shortened may preferentially be considered in patients with decreased S_m.

Although the use of positive inotropic drugs is an important approach in treating postoperative low cardiac output syndrome, little is known about the relationship between TDI variables and inotropic support after cardiac surgery. Our study indicates that the TDI variable S_m was significantly and negatively associated with the need for prolonged postoperative inotropic support. However, this study has some limitations. First, the sample size is insufficient to confirm whether S_m could be considered as a risk factor for inotropic support after cardiac surgery. Based on the regression coefficient of our results, a study that includes 106 patients in each group (<12 and ≥12 h of inotropic support) would be necessary to evaluate the interaction between S_m and inotropic support using multivariate logistic regression analysis with a statistical power of 0.80 and a statistical significance of 0.05. Second, EF was measured with transthoracic echocardiography, whereas TDI variables were measured with TEE under general anesthesia. Because intraoperative EF under general anesthesia tends to be affected by loading conditions that are induced by anesthetic agents, we adopted preoperative EF in this study. No patients who underwent urgent operations were included in this study. All preoperative EF data were measured under steady conditions. In fact, we found a good correlation between preoperative EF and intraoperative EF. Therefore, we consider that our results will not change if we adopt intraoperative EF. Third, the anesthetic agents used in each patient were left to the discretion of the attending anesthesiologists in the present study. Anesthesia was maintained with sevoflurane in the majority of the patients (84%), whereas anesthesia was maintained with propofol in the remaining patients. Filipovic et al. [25] reported no differences in E_m, A_m, or S_m between the sevoflurane and propofol groups with intermittent positive pressure ventilation. On this basis, we consider that the choice of the anesthetic agents in our study did not affect the TDI variables.

In conclusion, the intraoperative TDI variable S_m, but not preoperative EF, is closely related to the need for inotropic support after surgery, even when CPB time is ≥200 min. The need for inotropic support after cardiac surgery was increased in patients with decreased S_m and who must undergo prolonged CPB. This study suggests that TDI variables can identify patients who require inotropic support, even in the presence of preserved left ventricular EF.

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