RESEARCH

The relationship between tricuspid annular plane systolic excursion on transesophageal echocardiography and the incidence of postoperative acute kidney injury in patients undergoing coronary artery bypass grafting surgery: a multicenter prospective cohort study

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Abstract

Background To date, the relationship between the Transesophageal Echocardiography (TEE) monitoring indicator tricuspid annular plane systolic excursion (TAPSE) and the incidence of postoperative acute kidney injury (AKI) in Coronary Artery Bypass Grafting(CABG) patients remains unknown. The main objective of this study was to explore the relationship between the TAPSE and the incidence of AKI in CABG patients.

Methods This was a multicenter prospective cohort study was conducted between September 2021 and July 2022. Among 266 patients aged at least 18 years who underwent elective CABG, 140 were included.

Results We measured TAPSE via M-mode TEE via the mid-esophageal (ME) right ventricle(RV) inflow-outflow view (60°). All echocardiographic measurements were performed three separate times at each time point: T0 (before the start of CABG), T2 (approximately 5∼10 min after neutralization of protamine) and T3 (before leaving the operating room), and then averaged. Serum creatinine was measured 1 day before and within 7 days after CABG. There was no statistically significant association between the TEE-monitoring indicator TAPSE and the incidence of postoperative AKI in patients who underwent CABG.

Conclusions The TAPSE was not significantly correlated with postoperative AKI incidence and could not predict the early occurrence of postoperative AKI in CABG patients. TEE needs more evaluation for clinical efficacy of predicting the early occurrence of postoperative AKI in isolated CABG.

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Liu *et al. BMC Anesthesiology*   (2024) 24:328

Page 2 of 9

Introduction

Acute kidney injury (AKI) is the most common major postoperative complication of CABG and is independently related to hospitalization and long-term mortality [1]. Therefore, early recognition of AKI is important for effectively improving the prognosis of CABG patients. In CABG patients, AKI is associated with renal hypoperfusion in addition to these surgery-related factors [2]. The condition of these patients is often complicated by myocardial infarction, severe multivessel coronary artery disease, or right heart insufficiency, which can cause venous congestion. Venous congestion and fluid overload may reduce renal blood flow and promote the occurrence of AKI [3]. Indicators of venous congestion, such as fluid balance and central venous pressure, have been shown to be correlated with AKI [4, 5]. At present, studies on the relationships between transesophageal echocardiography and postoperative clinical outcome and prognosis are rare, and the conclusions are unclear [6–10]. Although the TAPSE is an ideal indicator for assessing of right ventricular systolic insufficiency [11], its value in predicting the incidence of postoperative AKI in CABG patients remains unknown. Therefore, we designed a multicenter prospective cohort study [12] to explore the effectiveness and guiding role of the TAPSE in reducing the incidence of postoperative AKI and improving the clinical prognosis of CABG patients. The hypothesis of this study is that the TAPSE can predict AKI in CABG surgery patients. The main objective of this study was to investigate the relationship between the TAPSE and postoperative AKI in CABG patients.

Materials and methods

Study design

This was a multicenter prospective observational cohort study that was conducted according to the guidelines of the Declaration of Helsinki and was approved by the Ethics Committee of The First Affiliated Hospital of Shandong First Medical University, Jinan, and Zibo Central Hospital, Zibo, China. We have published our study protocol in the journal BMJ Open [12]. A total of 266 patients who underwent elective CABG at Qianfoshan Hospital in Shandong Province and Zibo Central Hospital in Shandong Province, China between September 6, 2021 and September 30, 2022, were enrolled. The inclusion criteria were as follows: patients ≥ 18 years who were scheduled to undergo CABG surgery and whose consent forms were signed by the patients themselves or their authorized family members. We interviewed the patients, and they signed the informed consent form 1 day before the procedure. Informed consent was obtained to publish the information/images in an online open access publication. The specific exclusion criteria are described in our protocol [12] that was published in BMJ Open. The clinical data of 140 patients were ultimately analyzed (Fig. 1).

Data collection

After the inclusion of patients, preoperative data on the following variables were collected: anthropomorphic data, risk factors for AKI, EuroSCORE II, preoperative left ventricular ejection fraction (LVEF), pulmonary arterial systolic pressure (PASP), tricuspid regurgitation pressure gradient (TRPG), preoperative Scr levels, preoperative estimation of the glomerular filtration rate (eGFR) and preoperative coexisting disease. Additionally, the following intraoperative data were collected: the type of CABG surgery, graft number, red blood cell (RBC) transfusion, bleeding volume, urine volume, total liquid input, total liquid excretion, operation time, cardiopulmonary bypass (CPB) time, aortic cross-clamp time, Systolic Blood Pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and serum lactate level. The postoperative data obtained in the intensive care unit (ICU) included the incidence of AKI, the incidence of major postoperative cardiovascular and cerebrovascular adverse events (MACCEs) within 30 days after surgery, the incidence of postoperative pulmonary complications (POPC), the duration of tracheal intubation in the ICU (EIT-ICU), the ICU length of stay (D-ICU), the length of stay (LOS), and the cost of hospitalization (HE) (Table 1).

The venous blood of patients was collected, and the Scr level was measured 1 day before and within 7 days after CABG. AKI was also diagnosed according to the Kidney Disease: Improving Global Outcomes (KDIGO) diagnostic guidelines [18, 19]. Patients were divided into the following two groups according to the occurrence of postoperative AKI: the acute kidney injury group (AKI group) and the nonacute kidney injury group (non-AKI group).

Anesthesia management

According to the American Society of Anesthesiologists (ASA) guidelines, continuous monitoring of parameters, including noninvasive blood pressure, heart rate, ECG, SpO_2, bispectral index (BIS) and invasive blood pressure, is recommended following admission to the operating room. Midazolam (0.01–0.05 mg/kg), etomidate (0.2 mg/kg), sufentanil (1–3 μg/kg), and cisatracurium besylate (0.2–0.3 mg/kg) or rocuronium (0.6–0.8 mg/kg) were administered intravenously for general anesthesia
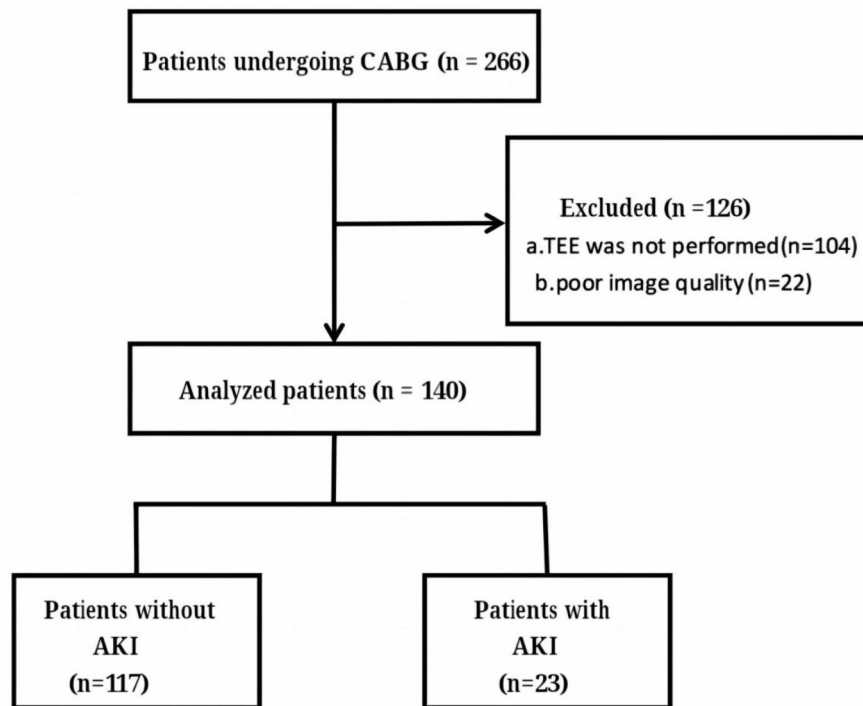
Liu *et al. BMC Anesthesiology*   (2024) 24:328

Page 3 of 9

Fig. 1 Flow chart of study selection

induction. Combined intravenous and inhalational anesthesia was used to maintain general anesthesia. We adopted a low tidal volume ventilation strategy with the tidal volume set at 6 ml/kg and the PEEP set at 0 mmHg. After induction of general anesthesia, the right internal jugular vein was prepared for central venous pressure (CVP) monitoring and infusion. In the supine position, the central vein pressure sensor was zeroed at the level of the right atrium. We placed the TEE probe before the start of the CABG procedure.

Transesophageal echocardiography measurements
An anesthesiologist who is highly trained and experienced in the use of esophageal ultrasound performed a full TEE examination with a multiplanar TEE probe (Philips X7-2t) (Philips EPIQ 5, Washington, USA). Ultrasound measurements included measurements of inferior vena cava and right ventricular function. The detailed measurement methods and processes can be found in our research protocol (Fig. 2) [12]. All echocardiographic measurements were performed three separate times at each time point: T0 (before the start of coronary artery bypass graft), T2 (approximately $5 \sim 10$ min after neutralization of protamine) and T3 (before leaving the operating room after sternal closure), and the average values were calculated [12].

Outcome measures
The primary outcome was the incidence of postoperative AKI, which was diagnosed according to the KDIGO guidelines [13, 14].

The secondary outcomes included the incidence of MACCEs, the incidence of POPC, the duration of tracheal intubation in the ICU, the length of ICU stay, the LOS and the hospitalization expenses (Table 1) [12].

Statistical methods
Sample size
According to previous studies [2, 15], the incidence of AKI after CABG is approximately 5-57.7%. The sample size of this study was estimated on the basis of the Event Per Variable principle (EPV) in multivariate logistic regression analysis [16], and a total of 135 patients were needed. The minimum sample size is 150, which is based on a 10% loss rate. A total of 266 patients who met the test requirements were included in this study.

Statistical analysis
The statistical analysis was performed according to the prespecified protocol [12], with any deviations justified and conducted by R4.0.2 and Free V1.7 statistical software. All the data subjected to statistical analyses in this study were considered statistically significant if the two-tailed P value was < 0.05.

Liu *et al. BMC Anesthesiology*   (2024) 24:328

Page 4 of 9

Table 1 Patients' characteristics and perioperative data

Patients'characteristics and perioperative data	No AKI(*n* = 117)	AKI(*n* = 23)	*P*-value
Anthropomorphic and preoperative data			
male, *n* (%)	83 (70.9)	16 (69.6)	0.895
Age(year)	62.7 ± 8.4	66.7 ± 7.2	0.032
BMI (kg.m-2)	25.6 ± 3.4	25.2 ± 3.4	0.553
Smoke, *n* (%)	51 (43.6)	10 (43.5)	0.992
Alcohol, *n* (%)	44 (37.6)	7 (30.4)	0.513
EuroSCORE II	6.0 (5.0, 9.0)	7.0 (6.0, 9.0)	0.448
LVEF(%)	60.0 (53.0, 64.0)	57.0 (47.0, 65.0)	0.733
MAP(mmHg)	98.6 ± 15.1	101.3 ± 12.0	0.414
Preoperative serum creatinine (mmol/L)	73.0 (65.0, 83.0)	77.0 (62.5, 85.0)	0.942
Comorbidities			
Hypertension, *n* (%)	75 (64.1)	19 (82.6)	0.084
Diabetes mellitus, *n* (%)	48 (41)	10 (43.5)	0.827
Heart failure, *n* (%)	6 (5.1)	1 (4.3)	1.000
Cerebral infarction, *n* (%)	26 (22.2)	4 (17.4)	0.783
Myocardial infarction, *n* (%)	44 (37.6)	8 (34.8)	0.798
Intraoperative data			
Type of CABG			0.064
off-pump, *n* (%)	55 (47)	6 (26.1)	
on-pump, *n* (%)	62 (53)	17 (73.9)	
grafts.number(*n*)	3.3 ± 1.0	3.4 ± 0.8	0.682
RBC transfusion(ml)	400.0 (0.0, 600.0)	400.0 (400.0, 700.0)	0.398
Bleeding volume(ml)	520.5 ± 153.4	604.3 ± 302.2	0.049
Urine volume(ml)	1780.8 ± 967.5	1795.7 ± 722.2	0.944
Operation time(h)	5.2 ± 0.9	5.8 ± 1.6	0.008
CPB time(min)	110.0 (0.0, 156.0)	146.0 (43.5, 207.5)	0.069
Cross-clamp time (min)	60.0 (0.0, 104.0)	76.0 (24.5, 123.5)	0.085
TAPSE0(mm)	18.5 ± 3.7	19.9 ± 3.8	0.119
TAPSE2(mm)	16.6 ± 3.0	17.2 ± 3.2	0.236
TAPSE3(mm)	16.1 ± 3.1	15.7 ± 3.0	0.541
Postoperative data			
EIT-ICU(h)	19.0 (18.0, 20.0)	20.5 (18.2, 39.5)	0.062
D-ICU(h)	44.5 (43.0, 68.0)	61.5 (43.5, 97.8)	0.363
LOS(d)	20.0 (17.0, 24.0)	20.0 (15.5, 25.5)	0.780
HE(10k)	10.8 (9.0, 13.8)	11.5 (9.0, 14.0)	0.265

Data are presented as mean±(SD), as medians and interquartile range [IQR: 25th to 75th percentiles] or frequency (proportion). The *P*-value refers to comparison between groups(No AKI versus AKI). All tests of significance were 2-tailed, and results of comparisons were considered statistically significant when the *P*-value was ≤0.05. Abbreviations: BMI: body mass index; EuroSCORE: European system for cardiac operative risk evaluation; LVEF: left ventricular ejection fraction; CABG: coronary artery bypass graft; RBC: red blood cells; CPB: cardiopulmonary bypass; MAP: mean arterial pressure; TAPSE: tricuspid annular plane systolic excursion; EIT: endotracheal intubation time; ICU: Intensive Care Unit; LOS: length of stay; HE: hospitalisation expenses

Table 2 Association between TAPSE and AKI in this study

	Nonadjusted	*P* value	Adjust I	*P* value	Adjust II	*P* value
TAPSE0	1.10 (0.98 ~ 1.23)	0.121	1.12 (0.98 ~ 1.29)	0.088	1.12 (0.98 ~ 1.29)	0.097
TAPSE2	1.06 (0.91 ~ 1.24)	0.447	1.10 (0.92 ~ 1.31)	0.294	1.12 (0.92 ~ 1.34)	0.254
TAPSE3	0.95 (0.81 ~ 1.11)	0.538	0.96 (0.82 ~ 1.14)	0.666	0.97 (0.81 ~ 1.15)	0.709

Notes: data presented are ORs and 95% CIs. Adjust I model adjusts for age, gender, operation time, grafts number, cardiopulmonary bypass condition; adjust II model adjusts for adjust I+body mass index, cardiopulmonary bypasstime, red blood cell, High blood pressure, Alcohol, Aortic cross-clamp time. Abbreviations: TAPSE, tricuspid annular plane systolic excursion

Baseline data were obtained throughout the cohort and stratified according to whether patients developed AKI. Depending on whether the data adhere to a normal distribution per the Shapiro−Wilk test, continuous variables are expressed as the means and standard deviations (SDs) or medians and IQRs. Categorical variables are presented as counts (percentages) and were analyzed by means of Fisher's exact test or the χ2 analysis.

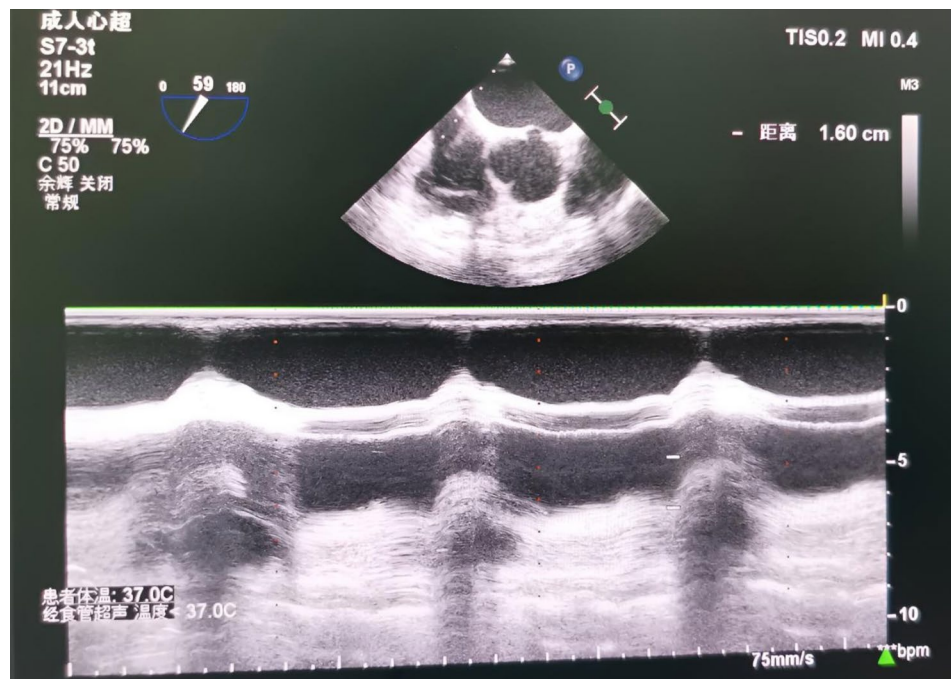Multivariate logistic regression analysis and smoothing function analysis (Fig. 3) were used to analyze the

Liu *et al. BMC Anesthesiology*   (2024) 24:328

Page 5 of 9

Fig. 2 Example of echographic time-motion recording of tricuspid annular plane systolic excursion (TAPSE)

association between the TAPSE and the incidence of postoperative AKI in patients who underwent CABG. Adjustments were made for the following variables, which were important to the prognosis: age, sex, operation time, graft number, cardiopulmonary bypass condition, body mass index, cardiopulmonary bypass time, red blood cell count, high blood pressure, alcohol use, and aortic cross-clamp time. The associations between the TAPSE and the secondary outcomes were also analyzed via multivariate logistic regression analysis. In addition, we stratified patients with or without AKI after CABG descriptively according to sex, number of grafts, and cardiopulmonary bypass. A receiver operating characteristic (ROC) curve was generated for TAPSE at T0 (before the start of CABG). The area under the ROC curve (AUC) and 95% confidence interval (CI) of TAPSE0 were calculated to analyze its predictive ability.

Results

In the present study, 266 patients were included, and 126 were excluded for the following reasons: (a) patients for whom TEE examination could not be performed because the TEE probe was difficult to place or unavailable and (b) patients with too much gas in the stomach or an unclear ultrasonic image. Ultimately, 140 patients were analyzed (Fig. 1).

AKIs were diagnosed in 16.4% (23/140) of the patients. There were 23 patients with AKI (16.4%) and 117 patients without AKI (83.6%). The baseline characteristics of the two groups are shown in Table 1. There were

no significant differences in sex, BMI, smoking status, alcohol consumption, EuroSCORE II, LVEF, comorbidities, type of CABG, graft number, RBC transfusion, urine volume, total liquid input, total liquid excretion, CPB time, aortic clamping time, POPC, EIT-ICU, D-ICU, LOS, or HE between the two groups; however, there were significant differences in age (62.7±8.4 versus 66.7±7.2, $P=0.032$), bleeding volume (520.5±153.4 versus 604.3±302.2, $P=0.049$), operation time (5.2±0.9 versus 5.8±1.6, $P=0.008$) between the two groups. The incidence of MACCEs in the AKI group was higher than that in the non-AKI group(39.1% versus 10.3%, $P=0.002$).

The smoothing function analysis(Fig. 3) and multivariate regression analysis (Table 2) revealed that the TEE monitoring index TAPSE at all three time points was not significantly associated with the incidence of postoperative AKI in patients who underwent CABG. Moreover, there was no statistically significant association between the TAPSE measured by TEE at any of the three time points and the secondary outcome of CABG (Table 3).

Discussion

In this prospective cohort study, we found that there was no statistically significant relationship between the TAPSE measured by TEE and the incidence of postoperative AKI. Cardiac surgery associated-acute kidney injury (CSA-AKI) is a major postoperative complication of CABG and is independently correlated with high morbidity and mortality rates. The incidence of CSA-AKI in this study was 16.4%, which was comparable to the results of
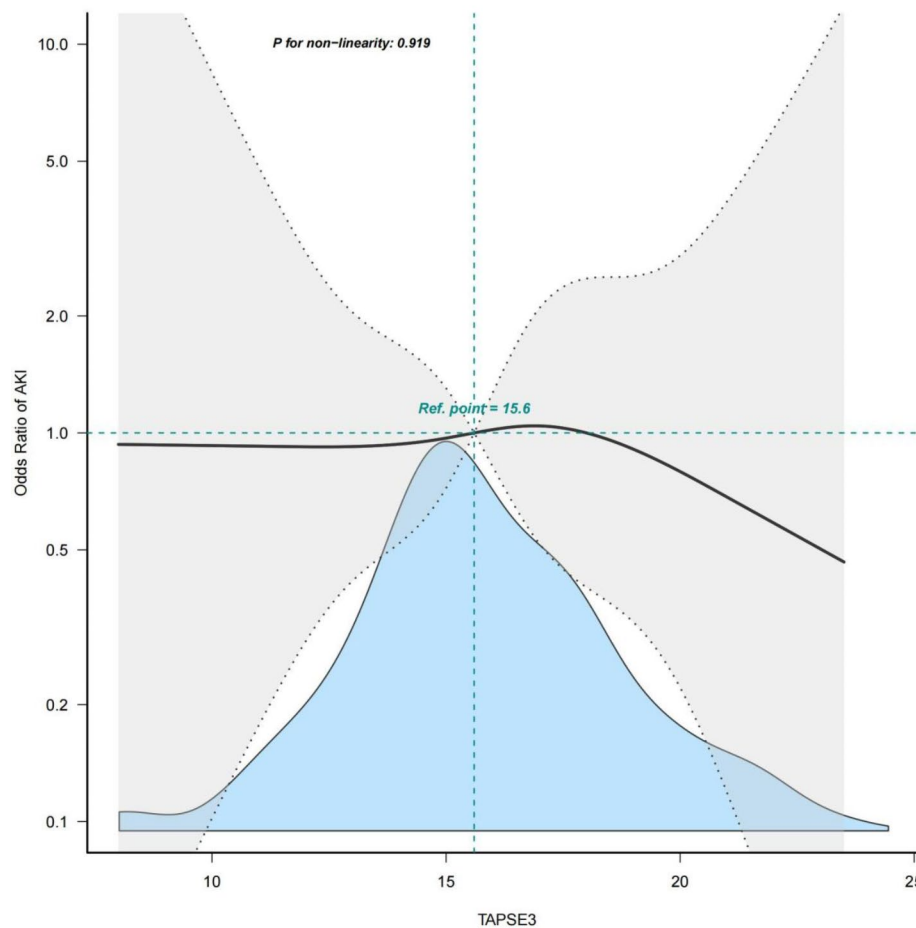
Liu *et al. BMC Anesthesiology*   (2024) 24:328

Page 6 of 9

Fig. 3 Smoothing function curve between TAPSE3 and AKI in this study

Table 3 Association betweenTAPSE and MACCE in this study

	Nonadjusted	*P* value	Adjust I	*P* value	Adjust II	*P* value
TAPSE0	0.98 (0.86~1.11)	0.729	1.08 (0.93~1.25)	0.332	1.11 (0.95~1.30)	0.185
TAPSE2	0.88 (0.75~1.03)	0.111	1.00 (0.82~1.22)	0.985	0.99 (0.79~1.25)	0.952
TAPSE3	0.95 (0.80~1.12)	0.521	1.07 (0.87~1.31)	0.532	1.06 (0.84~1.32)	0.639

Notes: data presented are ORs and 95% CIs. Adjust I model adjusts for age, gender, operation time, grafts number, cardiopulmonary bypass condition; adjust II model adjusts for adjust I+body mass index, cardiopulmonary bypasstime, red blood cell, High blood pressure, Alcohol, Aortic cross-clamp time. Abbreviations: TAPSE, tricuspid annular plane systolic excursion

several previous studies [15]. Traditional diagnostic indicators of AKI, such as serum creatinine (Scr) levels and urine volume, are time-delayed and influenced by many factors [2, 17, 20]. New biomarkers related to AKI, such as neutrophil gelatinase-associated lipoprotein (NGAL) and cystatin-C, are more sensitive for early detection but are not routinely used [2, 21]. Therefore, identifying a new indicator for the early prediction of postoperative AKI is highly important. However, no study has indicated that the TEE-monitoring indicator TAPSE can predict the occurrence of postoperative AKI in CABG patients.

According to the guidelines and previous literatures [11, 22], TAPSE is an ultrasound indicator that has a good

correlation with right ventricular systolic function and a good reflection of right ventricular function. In clinical practice, TAPSE is one of the most frequent measures to assess RV function given its simplicity and reproducibility. Although the TAPSE is strongly correlated with global right ventricular function and has been routinely used to assess RV function [22–24], its value in predicting AKI after CABG surgery remains unclear. However, the relationship between intraoperative TAPSE and postcoronary bypass AKI remains to be verified in these patients. Wiersema and colleagues reported a statistically independent association between a lower TAPSE and the development of AKI in critically ill patients [3].

Shuangshuang Zhu et al. found that the TAPSE appears to be a reliable predictor of AKI after heart transplantation [25]. Guinot et al. showed that patients with RV dysfunction prior to surgery had a higher incidence of AKI after cardiac surgery [26].

However, a retrospective cohort study revealed that TEE was not associated with a reduced incidence of newly hospitalized AKI in adult patients undergoing isolated CABG surgery in the United States [8]. The results of our study revealed no statistically significant relationship between the TAPSE monitored by TEE and the incidence of postoperative AKI, which was similar to the findings of previous studies. We may consider this for several reasons as follows. First, the TAPSE in our study was derived from TEE measurements rather than from traditional transthoracic echocardiography (TTE), and this is different from the methods used in the above studies [3, 25, 26]. In previous studies, the TAPSE and other indicators reflecting right heart function were generally measured via TTE [3, 22–26]. Unlike the apical 4-chamber view in TTE, the ultrasound was not aligned with the lateral tricuspid annulus in TEE's 4-chamber view. Mauermann E et al. reported that the TAPSE measured by the 4-chamber TEE view of the midesophagus was significantly lower than that measured by the reference standard TTE view [27]. Munaf and colleagues showed that high interobserver and intraobserver variability in both adult and pediatric patients warrant further studies to evaluate the feasibility of using transgastric RV inflow TAPSE in cardiac surgery [28]. Second, our study revealed a common problem with TEE: there are currently no guidelines comparing the gold standard for TEE measurements of right ventricular function in patients under anesthesia and ventilation [27]. Angle dependence is an important factor that severely hinders the measurement of the right ventricle. Third, longitudinal RV function may not reflect global performance. A study showed that right ventricular longitudinal strain reflects longitudinal myocardial tissue volume and accounts for 80% of the RV stroke volume [29]. Prior studies have shown that commonly used indices of RV function, such as the TAPSE, can be altered by pericardiotomy itself. Our results also revealed that the TAPSE was significantly reduced with sternotomy and pericardiotomy, which may also indicate deteriorated longitudinal RV function. A decrease in longitudinal shortening has been shown to result in gains in transverse shortening, which further limits traditional longitudinal measurements of RV performance, such as TAPSE [30]. Fourth, there are many influencing mechanisms and factors that cause AKI in CABG surgery [2, 8, 10], which also influences the ability of the TAPSE to predict the occurrence of postoperative AKI.

To our knowledge, this is a rare prospective multicenter cohort study examining the association between the TAPSE, an intraoperative TEE-monitoring indicator, and prognosis in patients with CABG. Furthermore, we registered the clinical study at ClinicalTrial.com and published the study protocol [12] in advance. Our study was designed in accordance with the strengthening the reporting of observational studies in epidemiology (STROBE) statement [31], and statistical analyses of the data and subject information were conducted in strict accordance with the research protocol, thereby increasing the transparency and internal validity of the research.

Our study has several limitations. First, the inherent limitation of this study was its observational design, which is well known to result in incomplete data collection and have an increased risk of missing data and follow-up information, which may introduce confounding bias and compromise the accuracy of the data. However, our study was implemented in strict accordance with the published research protocol [12], and multifactor logistic regression analysis was used to control for potential confounding factors. Second, the multifactorial nature of AKI makes the study susceptible to residual confounding factors, such as postoperative transient hypotension, pressor drug requirements and other influencing factors, which may lead to renal hypoperfusion, resulting in oliguria and acute kidney injury [33]. Third, according to the KDIGO guidelines, creatinine levels and urine volume are included in the diagnosis of AKI [13, 14]. However, we calculated the incidence of postoperative AKI on the basis of only blood creatinine levels, which may have led to the underestimation of AKI incidence in this study. Fourth, TAPSE is derived from the ME-RV inflow/outflow view, which is not one of the most commonly used methods and may affect results and repeatability. Although TAPSE measurements and analyses derived from TTE can more accurately assess right ventricular systolic function, it is less commonly used in open heart surgery and is more difficult to obtain. It has been reported that TEE values from the transgastric view RV-inflow view demonstrated high performance throughout surgery and a good agreement with TTE TAPSE measurements [33], which is similar and consistent with our research. The ME-RV inflow/outflow view(60°) avoids the simple evaluation of the longitudinal deep muscle systolic function of the right ventricular free wall, but more considers that the left and right ventricular muscle fibers combine the systolic function of the left and right ventricles through the fusion of the superficial muscle of the ring, taking into account the combined contraction function of the deep longitudinal muscle and the superficial muscle of the ring, which seems to better reflect the true right ventricular function [34].

Liu *et al. BMC Anesthesiology* (2024) 24:328

Page 8 of 9

In summary, the TAPSE, a TEE-based monitoring indicator, was not significantly correlated with postoperative AKI incidence and could not predict the early occurrence of postoperative AKI in CABG patients. These findings highlight the need for further and more significant additional studies to validate the clinical efficacy of TEE in isolated CABG surgery.

Data availability
The obtained data and other information from the included participants will be held in strict confidence by the investigators, research staff, and sponsoring institute. No information or data concerning the study will be released by any unauthorsized third party, without a prior written approval of the sponsoring institution. Authorized representatives from the sponsoring institution may inspect all the documents and records required to be maintained by the investigator (Binghua Liu: liubinghua042525@126.com).

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of The First Affiliated Hospital of Shandong First Medical University, Jinan, and Zibo Central Hospital, Zibo, China. Informed consent was obtained from all the subjects involved in the study. Written informed consent has been obtained from the patient(s) to publish this paper.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Presentation
Our article has not been presented at any conference.

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Liu *et al. BMC Anesthesiology*   (2024) 24:328

Page 9 of 9

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