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ORIGINAL ARTICLE

Hemodynamic Monitoring Using a Pulmonary Artery Catheter Versus the Vigileo/FloTrac System during Elective Cardiac Surgery Based on Real-world Data in Japan

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ABSTRACT

BACKGROUND

The controversy concerning the benefits of pulmonary artery catheter (PAC)-based hemodynamic monitoring in cardiac surgeries has not been adequately addressed. This study aims to compare the all-cause mortality between the PAC with venous oxygen saturation monitoring and the Vigileo/FloTrac (FloTrac) system with central venous oxygen saturation monitoring in cardiac surgeries.

METHODS

This nationwide retrospective study includes adult patients who underwent elective cardiac surgeries between April 2010 and October 2014, based on the Japanese health insurance claims database. The main outcome was 30-day all-cause mortality. Propensity scores (PS) were used to adjust for the confounding factors. Treatment effects were estimated using multivariable logistic regression analysis, including PS.

RESULTS

A total of 5,838 patients were included in this study. The crude 30-day mortality rates were 2.4% (8/334) and 1.7% (96/5,504) in the FloTrac and PAC groups, respectively. After PS matching, the ORs for 30-day all-cause mortality, in-hospital mortality after PAC placement (vs. FloTrac) were 0.36 (95% CI: 0.05–2.37; p = 0.28) and 0.59 (95% CI: 0.16–2.20; p = 0.43), respectively. The amount of dobutamine was larger in the PAC group (281 ± 31 mg vs 155 ± 19 mg; p < 0.001). There were no significant differences in the amounts of other inotropes, the volume of fluids, or blood transfusions.

CONCLUSIONS

The association between PAC (with venous oxygen saturation monitoring) and mortality in patients who underwent elective cardiac surgeries was unclear compared to FloTrac (with central venous oxygen saturation monitoring). Additional investigation is needed to evaluate the benefits of PAC-specific hemodynamic parameters in this population.

KEY WORDS

pulmonary artery catheter, arterial pressure wave analysis, Vigileo/FloTrac system, real-world data

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INTRODUCTION

A pulmonary artery catheter (PAC) has been utilized as a hemodynamic monitoring tool in critically ill patients for over five decades. However, the controversy concerning the benefits of PAC have not been adequately addressed. Several randomized controlled trials have yielded little evidence demonstrating the beneficial effects of PAC on survival in patients with acute respiratory distress syndrome, congestive heart failure, and high-risk surgical procedures [1–5]. In contrast, results from several observational studies have suggested that PAC improves outcomes in severely ill patients, such as intensive care patients with an Acute Physiology and Chronic Health Evaluation score greater than 31 and those with acute heart failure syndrome with hypotension [6, 7]. Notably, Ranka et al. used a nationwide database in the United States to explore the real-world impact of PAC and a decrease in mortality among patients with cardiogenic shock was observed [8].

Although the efficacy of PAC is unclear [9], PAC insertion in cardiac surgery patients is the standard procedure in many centers [10, 11]. Shaw et al. reported that PAC monitoring during adult cardiac surgeries was associated with a shorter hospital stay and lower cardiopulmonary morbidity than non-PAC in the United States during 2011–2015 [12].

The controversy over the effectiveness of PAC monitoring has led to a reduction in its use [13, 14]. Thus, less invasive hemodynamic monitoring devices have been increasingly utilized over the last 15 years. There are several devices that estimate cardiac output based on arterial pressure wave analysis, such as the Vigileo/FloTrac system (FloTrac; Edwards Lifesciences, Irvine, CA, USA) which measure arterial pressure-derived cardiac output (APCO) among others. The FloTrac system is the most commonly used alternative for less invasive hemodynamic monitoring [11]. The system displays the measurements derived from arterial wave analysis, including APCO and central venous oxygen saturation ($ScvO_2$) when connected to a central venous (CV) catheter with an oximetry sensor. However, the accuracy of APCO is limited in unstable patients, especially in those undergoing cardiac surgery [15–17].

Therefore, additional investigations into the benefits of PAC monitoring compared with FloTrac monitoring in patients undergoing cardiac surgery are warranted.

This study aimed to evaluate the impact of perioperative PAC monitoring (with SvO_2 monitoring) on all-cause mortality compared with FloTrac monitoring (and $ScvO_2$ monitoring) in cardiac surgery patients.

METHODS

This study was approved by the Kyoto University Graduate School and Faculty of Medicine Ethics Committee (Kyoto, Japan, E2324). The requirement for written informed consent was waived because of the retrospective design that used previously anonymized patient records.

STUDY DESIGN AND DATA SOURCE

This retrospective cohort study was performed using the administrative claims database accumulated by Medical Data Vision Co., Ltd. (MDV) (Tokyo, Japan). The MDV database contains health insurance claims from hospitals that participate in the Japanese Diagnostic Procedure Combination/Per-Diem Payment (DPC/PDPS) system—a case-mix-based inclusive fee schedule for inpatient care launched in 2002 [18]. As of December 2014, the MDV database had inpatient and outpatient claims data from 161 DPC/PDPS hospitals, which represented approximately 10.2% of all DPC/PDPS hospitals in Japan. The DPC/PDPS system covered approximately 55% of acute care beds nationwide in 2014. The database contained the following data for each patient: demographic information, diagnoses, comorbidities at admission, inpatient complications, surgical procedures (indicated by reimbursement codes specific to the Japanese health insurance system [K codes]), non-surgical procedures, drug administration, and medical device use.

DEFINITION OF EXPOSURE

Insurance claim codes for pulmonary artery "catheter" and the measurement of pulmonary artery pressure on the day of surgery were defined as PAC insertion. Insurance claim codes for the FloTrac disposable circuit on the day of surgery were defined as FloTrac use. Insurance claim codes for a PAC with oximetry or a CV oximetry catheter were defined as the use of mixed venous oxygen saturation (SvO_2) or $ScvO_2$ monitoring, respectively (**Supplementary Table 1**).

STUDY COHORT

The target population of this study included patients who underwent elective heart valve surgery and/or CABG. Patients aged ≥20 years who underwent cardiac surgeries with intraoperative transesophageal echocardiogram (reimbursement code: L008-00) between April 1, 2010, and October 31, 2014, were included. Patients were

excluded based on the following criteria: those who underwent thoracic aortic repair, abdominal aortic aneurysmectomy, isolated arrhythmia surgery, congenital heart surgery, ventricular septal perforation closure, left ventricular volume reduction, surgery for constrictive pericarditis, resection of cardiac tumor, exploratory thoracotomy, pulmonary embolectomy or insertion of artificial cardiac assist pump, those underwent emergency procedures, those who did not receive PAC or FloTrac monitoring, those who were not monitored for venous oxygen saturation (SvO_2 or $ScvO_2$) on the day of the surgery, those who received preoperative extracorporeal circulation, and those with pulmonary hypertension. The ICD10 codes and insurance claims codes used for the eligibility criteria are described in **Supplementary Table 1**.

PROPENSITY SCORE (PS) METHOD

Each participant's PS represented the probability of treatment (PAC) assignment based on the observed covariates [19]. PSs were estimated using a multivariable logistic regression model with potential confounding factors included as covariates. Potential confounders were identified based on clinical knowledge and previous reports, such as demographic data, preoperative factors, comorbidities, heart valve disease status, procedure factors, and institutional factors [20]. All missing body mass index (BMI) and Brinkman index values were imputed with 20 repeats using the multiple imputation method. Missing Canadian Cardiovascular Society (CCS) classifications in patients with a diagnosis of angina (defined by ICD10 codes) and missing New York Heart Association (NYHA) classifications in patients with a diagnosis of heart failure (defined by ICD10 codes) were also imputed with 20 repeats using the multiple imputation method. PSs were matched using a 1:1 protocol in each imputed dataset (so-called "within approach") [21] without replacement, with a caliper width of 0.1 logit of the standard deviation of estimated propensity scores, and exact matching on the procedure classification and the use of intraoperative cell salvage with SAS software (PSMATCH procedure in SAS v9.4; SAS Institute Inc., Cary, NC, USA). The use of intraoperative cell salvage was added as an exact matching variable after assessment of the initial PS model due to residual imbalance after matching. The participants' preoperative characteristics in continuous variables are described as mean and standard error of the mean (SEM) among 20 imputed datasets before and after PS matching. Those in categorical variables are described as mean and SEM of proportion among 20 imputed datasets before and after PS matching. The SEM of variables with no information missing are not indicated before PS matching). The basic statistics and test statistics (t-test for continuous variables and chi-square test for categorical variables) were combined using the MIANALYZE procedure in SAS software. The covariate balance was evaluated using the mean of the absolute values of the standardized mean difference (mean SMD) [22]. The cut-off value of the mean SMD representing imbalance was set at 0.1.

OUTCOMES

All participants in the study cohort were followed up until hospital discharge. The primary outcome was 30-day all-cause mortality (30-day mortality). The secondary outcomes were in-hospital all-cause mortality (in-hospital mortality), the incidence of postoperative sepsis, the amounts of inotropes, the volume of fluids, and blood transfusions from day 0 to day 2 (day 0 indicates the day of surgery), and the incidence of postoperative pulmonary embolism.

The crude all-cause mortality, incidence of postoperative sepsis, and pulmonary embolism were reported as counts and proportions. The all-cause mortality and incidence of postoperative sepsis after PS matching were reported as the mean ± SEM of the proportion.

The treatment effects on all-cause mortality and incidence of postoperative sepsis were estimated in the PS-matched cohort using a logistic regression model with the treatment exposure (PAC referenced by FloTrac) as an independent variable in each of the 20 imputed datasets. The results were reported as odds ratios (ORs) with 95% confidence intervals (CIs). The estimates and test statistics (chi-square test) were combined using the MIANALYZE procedure in the SAS software.

The amounts of inotropes, the volume of fluids, and blood transfusions from day 0 to day 2 (day 0 indicates the day of surgery) are described as the mean ± SEM. The basic statistics and test statistics (t-test) were combined using the MIANALYZE procedure in the SAS software.

SENSITIVITY ANALYSES

Several sensitivity analyses were performed: 1) PS covariate adjustment (estimated PSs were added to the covariate in the logistic regression model for the inference of treatment effects); 2) 1:2 PS matching; 3) excluding patients who underwent isolated valve surgery with aortic stenosis; 4) excluding low-volume centers, and 5) 1:1 PS matching with across approach (the mean PS across 20 imputations for each patient was used in a single outcome analysis) [21].

STATISTICAL ANALYSES

An academic biostatistician was in charge of statistical analyses. The study sample comprised of participants who met the eligibility criteria and without *a priori* power analysis. All reported probability values were two-sided. All data handling and statistical analyses were performed using SAS v9.4 (SAS Institute Inc., Cary, NC, USA). The definitions of the variables used are presented in **Supplementary Table 1**.

RESULTS

STUDY COHORT AND MATCHED COHORT

A flow diagram for the identification of the study cohort is shown in **Fig. 1**. Technical experts at MDV extracted the medical records of 10,972 patients who had undergone cardiovascular surgeries from the DPC/PDPS administrative claims database. We identified the study cohort of 5,838 patients after cleaning the data and applying the eligibility criteria. In the study cohort, 1,821 patients underwent isolated valve surgery, 559 underwent single-valve surgery and CABG, 1,093 underwent multiple valve surgeries and/or CABG, 769 underwent on-pump CABG, and 1,596 patients underwent off-pump CABG.

FloTrac and PAC monitoring on the day of surgery were used in 5.7% (334/5,838) and 94.3% (5,504/5,838) of patients in the study cohort, respectively. The proportions of the FloTrac measurements and PAC monitoring by procedure classification are listed in **Table 1**.

The baseline characteristics of the study cohort before and after PS matching are summarized in **Table 2**. The demographic characteristics and status of heart valve disease were similar between the treatment groups before and after PS matching. Regarding the preoperative factors, comorbidities, procedure factors, and institutional factors, there were several statistically significant differences between the FloTrac and PAC groups (before matching). For example, those in the PAC group had more severe CCS grades and were more likely to have a diagnosis of diabetes or arrhythmia than those in the FloTrac group. The proportion of high-volume centers

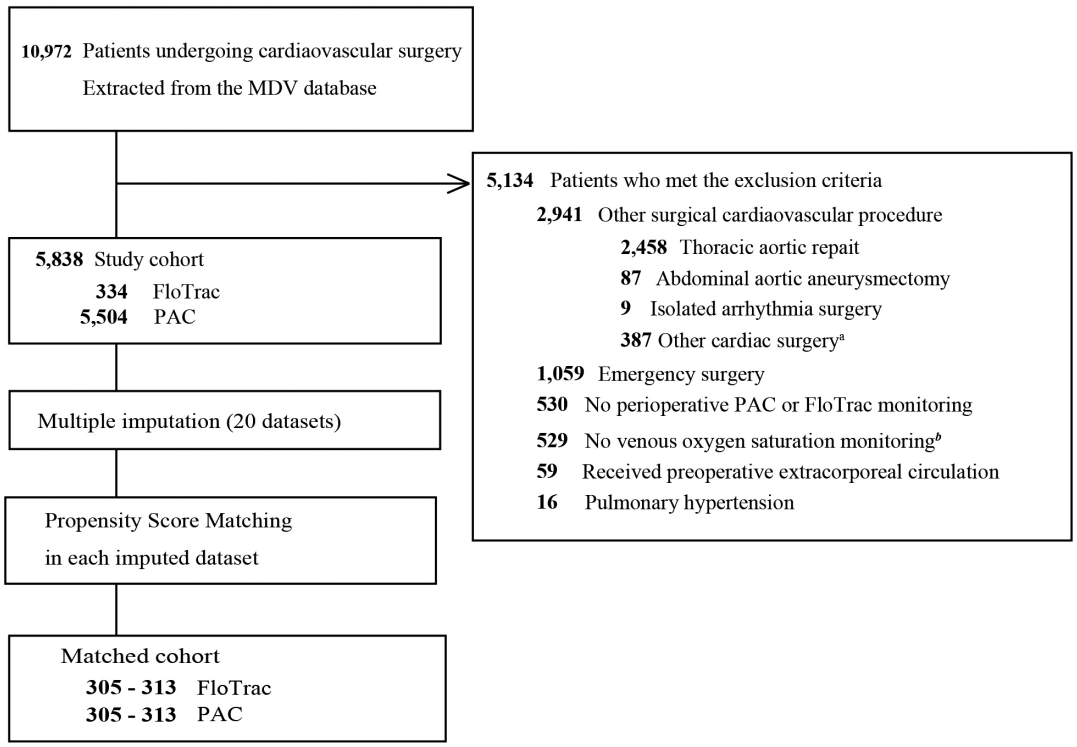

Fig. 1 Flow diagram depicting the selection of the study cohort.

a: congenital heart surgery, ventricular septal perforation closure, left ventricular volume reduction, surgery for constrictive pericarditis, resection of cardiac tumor, etc.
b: Mixed venous oxygen saturation (SvO_2) and central venous oxygen saturation ($ScvO_2$).
FloTrac; Vigileo/FloTrac system (Edwards Lifesciences, Irvine, CA, USA); MDV, Medical Data Vision Co., Ltd., PAC; pulmonary artery catheter

Table 1 Procedure classification and hemodynamic monitoring

Procedure classification	FloTrac	PAC
All	334 (5.7)	5,504 (94.3)
Isolated valve surgery	120 (6.6)	1,701 (93.4)
Single-valve surgery and CABG	32 (5.7)	527 (94.3)
Multiple valve surgeries and/or CABG	56 (5.1)	1,037 (94.9)
On-pump CABG	80 (10.4)	689 (89.6)
Off-pump CABG	46 (2.9)	1,550 (97.1)

Values are presented as count (proportion).
Abbreviations: PAC; pulmonary artery catheter with mixed venous oxygen saturation (SvO_2)-monitoring on the day of surgery, FloTrac; Vigileo/FloTrac system (Edwards Lifesciences, Irvine, CA, USA), CABG; coronary artery bypass grafting

(200 procedures per year) was higher in PAC group.

PS matching was conducted in each of the 20 imputed datasets (so-called "within approach") [21] based on PS, the procedure classification, and the use of intraoperative cell salvage and 305–313 pairs of patients were matched.

After PS matching, all characteristics were balanced between the FloTrac and PAC groups (mean SMD <0.1) (**Table 2**). The mean reduction in the mean SMD of all covariates was 82.2%. **Fig. 2** shows the histograms of the distribution of PS according to treatment type (FloTrac or PAC) before and after PS matching showing an adequate overlap.

OUTCOMES

The overall 30-day mortality rate was 2.5% (45/1,821) in isolated valvular surgery, 7.9% (44/559) in single-valve surgery and CABG, 6.5% (71/1,093) in multiple valve surgeries and/or CABG, 2.1% (16/769) in on-pump CABG, and 1.3% (20/1,596) in off-pump CABG. Before PS matching, the 30-day mortality rates were 2.4% (8/334) and 1.7% (96/5,504), in-hospital mortality rates were 3.3% (11/334) and 3.4% (185/5,504), the incidences of postoperative sepsis were 6.0% (20/334) and 6.8% (377/5,504), and the incidences of postoperative pulmonary embolism was 0.3% (1/334) and 0.4% (23/5,504) in the FloTrac and PAC groups, respectively. All patients with pulmonary embolism survived until their discharge.

After PS matching, the 30-day mortality rates were 2.6 ± 0.9% and 1.1 ± 0.8%, in-hospital mortality rates were 3.6 ± 1.1% and 2.3 ± 1.2%, and the incidences of postoperative sepsis were 6.0 ± 1.4% and 7.5 ± 1.8% in the FloTrac and PAC groups, respectively. The ORs for 30-day mortality, in-hospital mortality, and postoperative sepsis after PAC placement (vs. FloTrac) were 0.36 (95% CI: 0.05–2.37; p = 0.28), 0.59 (95% CI: 0.16–2.20; p = 0.43), and 1.26 (95% CI: 0.63–2.50; p = 0.51), respectively.

The amounts of inotropes, the volume of fluids and blood transfusions from day 0 to day 2 before and after matching are shown in **Table 3**. There were no significant differences in the amounts of noradrenaline and dopamine between the groups. The amount of dobutamine in the PAC group was greater than that in the FloTrac group (281 ± 31 mg vs 155 ± 19 mg; p < 0.001). Regarding the volume of fluids and blood transfusions, there were no significant differences between the FloTrac and PAC groups.

SENSITIVITY ANALYSES

As shown in **Table 4**, in all sensitivity analyses, there were no statistically significant differences in the mortality and incidences of postoperative sepsis. The amount of dobutamine in the PAC group was larger than that in the FloTrac group in all sensitivity analyses (**Supplementary Table 2**). In the analysis of PS matching with across approach, the treatment effect was not estimated because the covariates were not well-balanced (data not shown) after matching.

DISCUSSION

In this retrospective cohort study of 5,838 patients who underwent cardiac surgeries in Japan, the association between PAC exposure (with $ScvO_2$ monitoring) and all-cause mortality was not statistically significant when compared to that of Vigileo/FloTrac monitoring (with $ScvO_2$ monitoring). Although monitoring with and without PAC has been compared in previous studies, this is the first report on the real-world comparison of perioperative PAC and FloTrac monitoring in patients who underwent cardiac surgeries.

PAC monitoring provides hemodynamic information, such as central venous pressure, SvO_2, pulmonary artery pressure, pulmonary capillary wedge pressure, and continuous cardiac output. Although pulmonary artery pressure and pulmonary capillary wedge pressure are not available with the APCO system, central venous pressure and $ScvO_2$ can be measured using a central catheter, and the placement of a central catheter is considered standard care in many cardiac surgeries. $ScvO_2$ in patients with a central catheter was measured to be approximately the same as SvO_2 in patients without cardiac shunts. Patients who did not undergo SvO_2 (PAC group) or $ScvO_2$ (FloTrac group) were excluded. Therefore, the study

Table 2 The baseline characteristics of the study cohort before and after propensity score matching

	proportion of missing (%)	Combined the 20 imputed datasets (multiple imputation)					
		Before matching			After matching		
		FloTrac n = 334	PAC n = 5,504	mSMD	FloTrac n = 305–313	PAC n = 305–313	mSMD
Demographic factors							
Age (year)	0.0	71.3 ± 0.6[a]	70.4 ± 0.1[a]	0.08	71.3 ± 0.6	71.0 ± 0.8	0.05
Male sex	0.0	63.2	63.6	0.01	61.9 ± 2.8	60.2 ± 3.5	0.04
BMI (kg*m-2)	2.2	22.7 ± 0.2	23.1 ± 0.1	0.09	22.7 ± 0.2	22.7 ± 0.3	0.04
Preoperative factors							
Preoperative IV cardiovascular agent	0.0	5.1	5.7	0.03	4.8 ± 1.2	5.0 ± 1.8	0.04
NYHA classification -		51.1 ± 3.3	50.6 ± 0.9	0.03	49.9 ± 3.2	51.8 ± 4.0	0.05
NYHA classification 1		6.5 ± 1.6	8.0 ± 0.4	0.06	6.6 ± 1.6	6.5 ± 1.9	0.03
NYHA classification 2	57.9	24.7 ± 2.9	22.8 ± 0.8	0.05	25.0 ± 2.9	23.8 ± 3.4	0.04
NYHA classification 3		12.4 ± 2.2	12.4 ± 0.6	0.03	12.9 ± 2.3	12.4 ± 2.8	0.04
NYHA classification 4		5.3 ± 1.7	6.3 ± 0.5	0.05	5.6 ± 1.7	5.4 ± 1.9	0.03
CCS classification -		52.7 ± 2.9	45.1 ± 0.8	0.15	55.6 ± 3.0	53.9 ± 3.3	0.04
CCS classification 1		9.1 ± 1.7	13.1 ± 0.5	0.13	9.4 ± 1.8	10.0 ± 2.4	0.04
CCS classification 2	29.9	23.3 ± 2.5	20.9 ± 0.6	0.06	19.7 ± 2.4	19.6 ± 2.8	0.03
CCS classification 3		12.4 ± 2.0	17.3 ± 0.6	0.14	12.6 ± 2.1	13.1 ± 2.7	0.03
CCS classification 4		2.5 ± 1.0	3.6 ± 0.3	0.06	2.7 ± 1.0	3.5 ± 1.7	0.07
Lower ADL	3.1	16.6 ± 2.0	17.2 ± 0.3	0.02	16.4 ± 2.1	17.9 ± 2.9	0.05
Brinkman index	10.0	281.1 ± 24.2	360.6 ± 7.4	0.16	277.0 ± 25.7	283.8 ± 41.1	0.05
Comorbidities							
Myocardial infarction within 30 days preoperatively	0.0	3.9	3.7	0.01	3.7 ± 1.1	4.5 ± 1.6	0.06
Myocardial infarction >30 days preoperatively	0.0	16.5	17.5	0.03	14.0 ± 2.0	15.0 ± 3.0	0.05
Hypertension	0.0	83.2	79.8	0.09	82.3 ± 2.2	80.3 ± 3.0	0.06
Diabetes mellitus	0.0	23.4	42.4	0.41	25.2 ± 2.5	25.0 ± 3.2	0.03
Arrhythmia	0.0	4.8	11.4	0.25	5.2 ± 1.3	5.8 ± 1.8	0.03
Atrial fibrillation	0.0	36.2	38.0	0.04	38.0 ± 2.8	35.0 ± 3.6	0.07
Chronic renal failure	0.0	12.3	14.9	0.08	12.3 ± 1.9	11.2 ± 2.7	0.05

Propensity scores were estimated using the variables listed in this table except the procedure classification. The procedure classification was exactly matched between Vigileo/FloTrac and PAC groups. The basic statistics and test statistics (t-test in continuous variables and chi-square test in categorical variables) were combined by the MIANALYZE Procedure in SAS software. The values are indicated as mean ± SEM in age, BMI and Brinkman index. The values of all other variables are indicated as mean ± SEM of proportion. The SEM of categorical variables without missing are not indicated in before matching.

a; standard deviation

Abbreviations: PAC; pulmonary artery catheter with mixed venous oxygen saturation (SvO_2)-monitoring on the day of surgery, FloTrac; Vigileo/FloTrac system (Edwards Lifesciences, Irvine, CA, USA), CABG; coronary artery bypass grafting, mSMD; mean of standardized mean difference, BMI; body mass index, IV; intravenous, NYHA; New York Heart Association, CCS; Canadian Cardiovascular Society, ADL; activities of daily living, CABG; coronary artery bypass grafting, CPB; cardiopulmonary bypass, SEM; standard error of the mean

Table 2-2 The baseline characteristics of the study cohort before and after propensity score matching

	proportion of missing (%)	Combined the 20 imputed datasets (multiple imputation)					
		Before matching			After matching		
		FloTrac n = 334	PAC n = 5,504	mSMD	FloTrac n = 305–313	PAC n = 305–313	mSMD
Heart valve diseases							
Aortic stenosis	0.0	18.0	18.8	0.02	19.0 ± 2.3	18.0 ± 2.5	0.04
Aortic regurgitation	0.0	6.0	5.5	0.02	6.3 ± 1.4	7.6 ± 2.0	0.06
Mitral stenosis	0.0	0.9	1.3	0.04	1.0 ± 0.6	1.2 ± 0.8	0.04
Mitral regurgitation	0.0	13.8	12.2	0.05	14.9 ± 2.0	14.1 ± 2.7	0.05
Institute factor							
Procedure volume							
1–9/year	0.0	0	0.1	—	0	0	—
10–49/year	0.0	5.7	5.6	0.01	6.1 ± 1.4	5.5 ± 1.7	0.04
50–99/year	0.0	21.0	20.9	0.00	21.3 ± 2.4	20.2 ± 3.0	0.04
100–199/year	0.0	60.5	47.5	0.26	58.6 ± 2.8	62.3 ± 3.4	0.07
200–/year	0.0	12.9	26.0	0.34	13.9 ± 2.0	11.9 ± 2.4	0.06
Procedure factors							
Calendar year of surgery							
2010	0.0	1.8	5.0	0.18	1.9 ± 0.8	1.8 ± 1.0	0.03
2011	0.0	11.1	10.1	0.03	11.0 ± 1.8	10.4 ± 2.6	0.06
2012	0.0	17.7	13.9	0.10	17.2 ± 2.2	16.7 ± 2.6	0.04
2013	0.0	32.3	29.5	0.06	31.6 ± 2.7	32.4 ± 3.5	0.04
2014	0.0	37.1	41.5	0.09	38.3 ± 2.8	38.7 ± 3.4	0.03
Other factors							
Intraoperative cell salvage	0.0	46.7	89.9	1.05	50.4 ± 2.9	50.4 ± 2.9	0.00
Autologous blood transfusion	0.0	9.9	8.9	0.03	9.8 ± 1.7	8.9 ± 2.1	0.04
Procedure classification							
Isolated valve surgery	0.0	35.9	30.9	0.11	38.5 ± 2.8	38.5 ± 2.8	0.00
Single-valve surgery and CABG	0.0	9.6	9.6	0.00	9.4 ± 1.7	9.4 ± 1.7	0.00
Multiple valve surgeries and/or CABG	0.0	16.8	18.8	0.05	18.1 ± 2.2	18.1 ± 2.2	0.00
On-pump CABG	0.0	24.0	12.5	0.30	19.2 ± 2.3	19.2 ± 2.3	0.00
Off-pump CABG	0.0	13.8	28.2	0.36	14.8 ± 2.0	14.8 ± 2.0	0.00

Propensity scores were estimated using the variables listed in this table except the procedure classification. The procedure classification was exactly matched between Vigileo/FloTrac and PAC groups. The basic statistics and test statistics (t-test in continuous variables and chi-square test in categorical variables) were combined by the MIANALYZE Procedure in SAS software. The values are indicated as mean ± SEM in age, BMI and Brinkman index. The values of all other variables are indicated as mean ± SEM of proportion. The SEM of categorical variables without missing are not indicated in before matching.

a; standard deviation

Abbreviations: PAC; pulmonary artery catheter with mixed venous oxygen saturation (SvO_2)-monitoring on the day of surgery, FloTrac; Vigileo/FloTrac system (Edwards Lifesciences, Irvine, CA, USA), CABG; coronary artery bypass grafting, mSMD; mean of standardized mean difference, BMI; body mass index, IV; intravenous, NYHA; New York Heart Association, CCS; Canadian Cardiovascular Society, ADL; activities of daily living, CABG; coronary artery bypass grafting, CPB; cardiopulmonary bypass, SEM; standard error of the mean

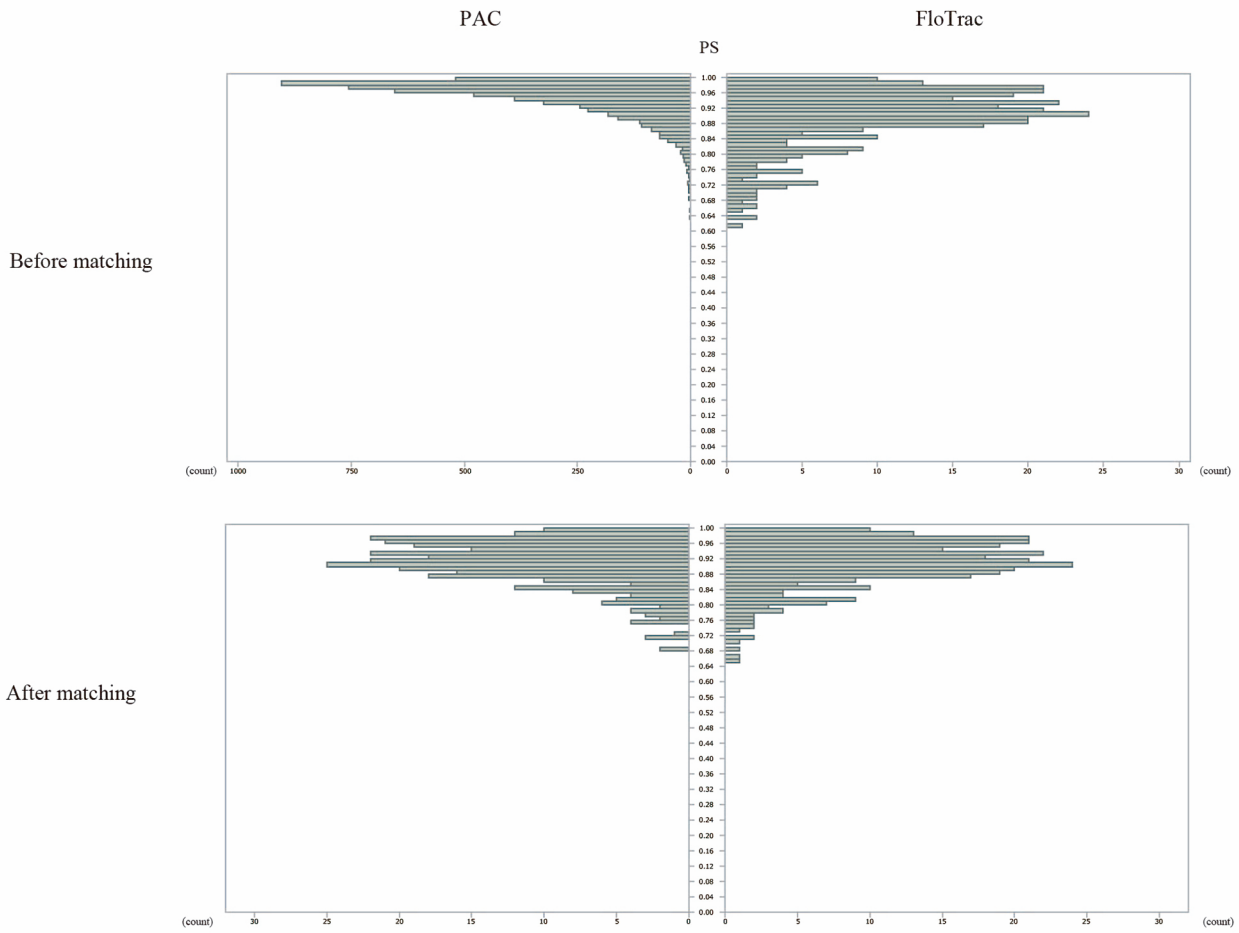

Fig. 2 Propensity score distribution of the study cohort according to the treatment type (FloTrac or PAC) before and after propensity score matching.

PAC: pulmonary artery catheter with mixed venous oxygen saturation (SvO_2)-monitoring on the day of surgery, FloTrac; Vigileo/FloTrac system (Edwards Lifesciences, Irvine, CA, USA) with central venous oxygen saturation ($ScvO_2$)-monitoring on the day of surgery; PS, propensity score

Table 3 The administration of inotropes, fluids, and blood transfusions from day 0 to day 2 before and after propensity score matching

	Combined the 20 imputed datasets (multiple imputation)				
	Before matching		After matching		
	FloTrac n = 334	PAC n = 5,504	FloTrac n = 305–313	PAC n = 305–313	p value
Nad, mg	2.9 ± 0.3	4.9 ± 0.1	2.9 ± 0.3	3.8 ± 0.6	0.23
Dopamine; mg	460 ± 23	404 ± 7	466 ± 25	458 ± 40	0.86
Dobutamine; mg	154 ± 18	234 ± 5	155 ± 19	281 ± 31	<0.001
Fluids; mL	22990 ± 603	26290 ± 136	23420 ± 641	25172 ± 655	0.06
Allogenic red cell transfusion; mL	944 ± 62	1042 ± 16	960 ± 66	964 ± 75	0.97
Fresh frozen plasma transfusion; mL	603 ± 42	598 ± 11	615 ± 44	496 ± 57	0.10

The results were described as mean ± SEM. The basic statistics and test statistics (t-test) were combined by the MIANALYZE Procedure in SAS software.
Abbreviations: PAC; pulmonary artery catheter with mixed venous oxygen saturation (SvO_2)-monitoring on the day of surgery, FloTrac; Vigileo/FloTrac system (Edwards Lifesciences, Irvine, CA, USA), Nad; noradrenaline, SEM; standard error of the mean

Table 4 The results of sensitivity analyses

Analysis	Number of patients	Reduction of mSMD (%)	30-day mortality			In-hospital mortality			Postoperative sepsis		
			OR	(95%CI)	p value	OR	(95%CI)	p value	OR	(95%CI)	p value
Main analysis	5,838	82.2	0.36	(0.05–2.37)	0.28	0.59	(0.16–2.20)	0.43	1.26	(0.63–2.50)	0.51
Sensitivity analysis 1	5,838	—	0.37	(0.082–1.71)	0.20	0.80	(0.22–2.86)	0.73	1.13	(0.44–2.94)	0.80
Sensitivity analysis 2	5,838	80.5	0.38	(0.11–1.39)	0.14	0.62	(0.22–1.73)	0.36	1.17	(0.64–2.15)	0.60
Sensitivity analysis 3	5,063	83.0	0.57	(0.09–3.47)	0.54	0.65	(0.15–2.71)	0.56	1.01	(0.50–2.42)	0.81
Sensitivity analysis 4	5,510	72.5	0.43	(0.06–3.06)	0.40	0.84	(0.29–2.40)	0.74	1.01	(0.53–1.92)	0.98
Sensitivity analysis 5	5,838	—[a]	The outcome analysis was not conducted.								

Main analysis; entire study cohort (1:1 within matching)
Sensitivity analysis1; entire study cohort (PS covariate adjustment)
Sensitivity analysis2; entire study cohort (1:2 within matching)
Sensitivity analysis3; excluding isolated valve surgery with AS (1:1 within matching)
Sensitivity analysis4; excluding low-volume center (1:1 within matching)
Sensitivity analysis5; entire study cohort (1:1 across matching)
The treatment effects of PAC (vs. FloTrac) on outcomes were estimated using a logistic regression model with the treatment exposure (PAC referenced by FloTrac).The OR estimates and test statistics were combined by the MIANALYZE Procedure in SAS software.
[a]; The outcome analysis was not conducted due to the residual imbalance after PS matching.
Abbreviations: mSMD; mean of standardized mean difference, PAC; pulmonary artery catheter with mixed venous oxygen saturation (SvO_2)-monitoring on the day of surgery, FloTrac; Vigileo/FloTrac system (Edwards Lifesciences, Irvine, CA, USA), OR; odds ratio, CI; confidence interval.

design allows the assessment of whether the measurement of PAC-specific hemodynamic parameters, which cannot be obtained using the FloTrac system, affected postoperative mortality.

Currently, no randomized controlled trial has reported the advantages or disadvantages of PAC measurement in mortality after cardiac surgery. In an international observational study between 1996 and 2000, Schwann et al. reported that PAC use during on-pump CABG was associated with a higher risk of mortality compared with the non-PAC group [9]. However, it is difficult to compare these results to ours due to the large time interval and the differences in study settings. First, the FloTrac system was not available during the study period. Second, there were variations in the study population. Their study included on-pump CABG only, while our study included valve surgery, CABG with/without CPB, and concomitant surgery. Our study cohort did not include sufficient cases of on-pump CABG for subgroup analysis. This was partly driven by the fact that the number of off-pump CABG was quite high in Japan. Additionally, the number of matched pairs was very small because the proportion of PAC insertion was very high (89.6% in on-pump CABG) in this study cohort.

In 2018, Shaw et al. reported in their retrospective cohort study based on an electronic hospital record database in the United States that PAC use during adult cardiac surgery was not statistically associated with an increased risk of in-hospital 30-day mortality compared with non-PAC use [12]. They included patients who underwent CABG, valve surgery, complex valvular procedures, and aortic procedures. Their report and this study have similar study settings. First, their matched cohort was similar to this study because only one matched pair of aortic procedures was included in the analyses. Second, both studies were based on a retrospective observational study design that represented "real-world performance." The results were comparable to ours which showed no increase in 30-day in-hospital mortality.

The number of matched pairs was small because the proportion of patients monitored by the FloTrac system was lower than expected. Therefore, PS covariate adjustment analyses (sensitivity analysis 1) or 1:2 PS matching (sensitivity analysis 2) were conducted. However, neither had a clear impact on the results.

Sensitivity analyses 3 were conducted excluding patients who underwent isolated valve surgery with a diagnosis of aortic stenosis without a diagnosis of mitral

valve disease. This is because there could be an association between the FloTrac measurement and isolated aortic valve surgery for aortic stenosis, a known cause of high perioperative mortality. However, exclusion of these patients did not affect the results. In addition, sensitivity analysis 4, which excluded low-volume centers, did not affect the results.

The amounts of inotropes, fluids, and blood transfusions were analyzed to gain insight into the potential mechanisms by which PAC use affects outcomes. In the current study, the amount of dobutamine in the PAC group was significantly larger than that in the FloTrac group. The amount of noradrenaline tended to be larger in the PAC group, although the difference was not statistically significant. There may be several explanations for these results. First, the PAC-specific measurements led the doctor to choose different inotropes. For example, systemic hypotension and left ventricular dysfunction with elevated pulmonary artery pressure may lead to the choice of dobutamine with noradrenaline. Second is an association between doctors' preference of inotropes and in choice of PAC monitoring. In Schwan's international observational study that reported a higher risk of mortality in patients who underwent on-pump CABG, a larger positive IV fluid balance and a higher proportion of inotrope administration were observed [9]. They pointed out that intensive hemodynamic manipulations and interventions as a result of the presence of a PAC might be responsible for the deleterious effect on mortality. In this study, there were no significant differences in the fluid administration or blood transfusions. Therefore, the results suggest that PAC use does not have a deleterious impact on mortality due to the larger amounts of inotropes.

This study had several strengths. It incorporated nationwide administrative data, and the findings may be applied to cardiac surgeries performed in a variety of settings. The retrospective observational analysis of the nationwide data from the DPC/PDPS claims database made it possible to investigate the "real-world performance" of the monitoring systems while incorporating factors such as surgical procedure heterogeneity, varying anesthesia techniques, and different levels of perioperative care.

However, this study has several limitations. First, we lacked echocardiogram and laboratory test results (e.g., left ventricular ejection fraction and serum creatinine level) because the data source was based on health insurance claims data and not health records. Therefore, some confounding variables were not included in the analysis. However, 24 confounders, including important factors identified in previous studies, were adjusted for in the analysis [20]. Second, out-of-hospital mortality within 30 days was not captured because the data source was a facility-level database. There may be some cases of mortality that could not be specified. Third, this study was based on a commercial data vendor in the Japanese healthcare system. Hospitals with a contract with the vendor may be cost conscious. However, it was unclear in which direction (i.e., PAC or FloTrac), their cost-consciousness would direct their behavior. Therefore, cost consciousness is assumed to have a small impact on the choice of monitoring. Fourth, there were some sources of bias specific to research using administrative data (e.g., coding errors occurring at the hospitals, inexactness of the diagnosis, and date of onset). Fifth, generalization to international patient populations may be limited. Lastly, the results were underpowered due to the small sample size, despite using a large database. This is due to the high proportion of PAC placement (94.3% of the overall study cohort), and the study period was relatively old and short. Given the proportion of deaths after cardiac surgery and a high frequency of PAC placement, a much larger cohort may be needed to achieve sufficient power for statistical analysis.

CONCLUSIONS

The association between PAC (with SvO_2 monitoring) and all-cause mortality was not statistically significant when compared to FloTrac with $ScvO_2$ monitoring. Additional investigation is needed to evaluate the benefits of PAC-specific hemodynamic parameters (pulmonary artery pressure and pulmonary capillary wedge pressure) in this population.

CONFLICT OF INTERESTS

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