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ORIGINAL ARTICLE

Can a NICO monitor substitute for thermodilution to measure cardiac output in patients with coexisting tricuspid regurgitation?

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Abstract

Purpose The validity of measuring cardiac output (CO) using thermodilution via pulmonary artery catheterization in the presence of tricuspid regurgitation (TR) remains controversial.

Methods We compared the accuracy and precision of a non-invasive cardiac output (NICO) monitor and of thermodilution with those of transesophageal echocardiography (TEE) to measure CO in 50 patients who underwent elective valvoplasty to treat TR (26 mild and 24 moderate-to-severe) and in 25 normal controls (without TR). We used TEE as a reference method to measure CO and to intraoperatively grade TR.

Results The differences between NICO monitor and TEE measurements in patients without TR and in those with mild and with moderate-to-severe TR were -0.17 ± 0.88 ($n = 150$, $r^2 = 0.75$), -0.16 ± 0.82 ($n = 158$, $r^2 = 0.78$), and 0.17 ± 0.91 L/min ($n = 155$, $r^2 = 0.78$), respectively. The differences between bolus thermodilution cardiac output and TEE measurements in patients without TR and in those with mild and with moderate-to-severe TR were -0.08 ± 0.55 ($r^2 = 0.88$), 0.05 ± 0.61 ($r^2 = 0.86$), and 0.43 ± 1.37 L/min ($r^2 = 0.58$), respectively.

Conclusion These findings demonstrate that measuring CO using the thermodilution technique is less accurate in patients with moderate-to-severe TR and that the NICO monitor is more accurate for such patients. We postulate that the NICO monitor measures CO more accurately and reproducibly than thermodilution in patients with coexisting TR.

Keywords Cardiac output · Thermodilution · NICO monitor · Tricuspid regurgitation

Introduction

Thermodilution is a standard, accurate reference method of measuring cardiac output (CO) in the clinical setting. However, several reported pitfalls of CO measured by thermodilution include the effect of hypothermia, low flow, catheter dysfunction and position, intra and extra-cardiac shunt, injectate volume, and tricuspid valve insufficiency, which often interfere with evaluations of hemodynamics [1]. However, the reliability of thermodilution in the presence of tricuspid regurgitation (TR) is controversial. Because one report indicates that the incidence of TR ranges from 17 to 95% in the general population [2], whether thermodilution is reliable in the presence of TR (and, if not, which technique would be clinically accurate under these circumstances) are important questions. Early reviews without the support of experimental data indicated that TR invalidates thermodilution [3–6]. Subsequent studies reported underestimation [2, 7–9], overestimation [10, 11], and no difference [12–16]. The accuracy of thermodilution measured in patients with coexisting TR has been compared with several reference methods, for example an extracorporeal circuit, Fick methods, an

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electromagnetic flowmeter, or indocyanine green dye [2–17]. However, these methods are more specific and complicated than thermodilution and are thus less suitable for clinical applications.

A non-invasive cardiac output (NICO) monitor (Respironics-Novametrics, Wallingford, CT, USA) is a practical device based on the indirect Fick method and it calculates CO under controlled ventilation [18, 19]. The device is minimally invasive, easy to set up and its performance is operator-independent [20, 21]. The NICO monitor measures CO based on changes in respiratory CO_2 concentration caused by a brief period of rebreathing. The CO measurement is derived from combining signals from sensors that measure flow, airway pressure, and CO_2 concentration to calculate CO_2 elimination. Using these variables, the indirect Fick method is used to calculate CO. The NICO monitor could measure CO without the effect of the right heart system. Hence, we postulated that it could accurately measure CO in patients irrespective of TR. In this prospective study we compared the accuracy of CO measurements obtained using the NICO monitor and thermodilution with that of transesophageal echocardiography (TEE) in anesthetized, ventilated patients with TR.

Materials and methods

After obtaining institutional review board approval, we obtained written, informed consent from 50 patients who underwent elective valvoplasty to treat TR and 29 others who underwent elective coronary artery surgery (controls; without TR) at Kagoshima University Hospital between December 2006 and June 2009. We excluded patients with atrial fibrillation, and pulmonary or increased intracranial pressure, and those with other valve diseases located above the first degree of the aortic regurgitation jet depth to the anterolateral leaflet of the mitral valve and a regurgitant jet area <25% of the left ventricular outflow tract (LVOT) and above the first degree of aortic stenosis (aortic valve area <1.2 cm^2 and peak gradient <35 mmHg). A cardiovascular anesthesiologist induced anesthesia and then the presence of TR was evaluated by TEE.

Anesthesia was managed according to the study protocol. Morphine hydrochloride (0.2 mg/kg) was administered intramuscularly 30 min before the induction of anesthesia with midazolam (0.08 mg/kg) and fentanyl (5 μg/kg). Anesthesia was maintained with 40% O_2 and propofol 5 mg/kg/h and the total intraoperative dose of fentanyl was 20 μg/kg. Patients were paralyzed with vecuronium and mechanically ventilated using an Aestiva 7900 anesthesia machine (GE Healthcare, Buckinghamshire, UK). Tidal volume and respiratory rate were initially set at 10 mL/kg and 10 bpm, respectively, and adjusted to maintain $PaCO_2$ at between 35 and 45 mmHg. Intravenous crystalloid (1000–1500 mL) maintained preload during the sternotomy and before the cardiopulmonary bypass was established. The total volume of infused fluid ranged from 2500 to 3500 mL. The same surgeon performed all operations on all patients via a midline sternal incision.

The severity of TR was determined and CO was obtained after the induction of anesthesia before sternotomy in stabilized patients after preload optimization. The severity of TR was determined as the ratio of the regurgitant jet area to the right atrial area in mid-systole by an echocardiographer. Color Doppler TEE was completed on each patient using a multiplane transducer and a ProSound SSD-4000SV (Aloka, Mitaka, Tokyo, Japan). Nyquist limits were set between 40 and 50 cm/s, because changes in the color filter can alter regurgitant jet size. We semi-quantitatively graded mild or moderate-to-severe TR based on ratios of <20, and >20%, respectively [22, 23]. The values obtained from five consecutive cardiac cycles were averaged for each of the patients who were diagnosed with mild ($n = 26$) or moderate-to-severe ($n = 24$) TR. None of the patients had mild TR based on a ratio of <10%. We excluded four of the control patients who were diagnosed with mild TR. Thus, the control group finally comprised 25 patients without TR.

We simultaneously measured CO in 75 patients using TEE, NICO, and bolus thermodilution cardiac output (BCO). We compared the values with those of CO measured by TEE.

Cardiac output was determined by TEE using continuous Doppler measurements in the aortic valve. This is because of the flow characteristics of the aortic valve, in particular because the steerable multiplanar TEE probe allows uncomplicated investigation of the LVOT and the aortic valve opening area (AVA). Doppler investigation of the LVOT can best be achieved from the longitudinal transgastric view at an angle of 110°–130° or from the apical transgastric view at 0° rotation of the probe. The AVA is reliably planimetered using the triangular model from the transesophageal approach at a 25°–45° rotation of the probe. Three consecutive CW pulses were measured to determine the velocity–time integral (VTI) depending on the quality of the Doppler signal. Heart rate was determined from an electrocardiographic trace using the R–R interval between the first and last VTI. CO was calculated by multiplying the mean VTI by the mean AVA and heart rate [24–26]. To test intra-observer variability, measurements of CO by TEE were repeated twice by an echocardiographer. To test inter-observer variability, a videotape of the TEE findings was later reviewed by a second echocardiographer who was unaware of the results of the first evaluation. Variability was calculated as the mean percentage error, calculated as the difference between the two sets of measurements divided by mean of the observation.

An Opti Q catheter (Hospira, North Chicago, IL, USA) was inserted via the right internal jugular vein into all patients and CO was calculated using the Nihon Kohden algorithm (Nihon Kohden, Tokyo, Japan). Continuous cardiac output (CCO) and mixed venous oxygen saturation were continuously monitored with a Q2 Continuous Cardiac Output/Sos computer (Hospira).

The NICO monitor (Ver. 5.3) was placed between the endotracheal tube and the heat and moisture exchanger (Covidien, Dublin, Eire). An adequate rebreathing circuit volume was carefully maintained during monitoring. Data including average-mode and fast-mode CO were downloaded to a computer every 3 min. CO was measured as average-mode.

Bolus thermodilution cardiac output was continuously measured until induced cardiopulmonary bypass every 15 min after obtaining TEE and NICO measurements. Blood-gas data were input to the NICO monitor before each BCO measurement to enable precise estimation of shunt fraction and NICO values. Mean values at each time point were determined after four measurements within 3 min. Values of BCO were included in the analysis only if hemodynamic status was stable. Hemodynamic stability was arbitrarily defined as the absence of fluid challenge or change in pharmacological intervention for at least 5 min.

Relationships between CO determined by NICO and BCO were evaluated using linear regression analysis in the three TR groups. Mean differences between CO measured by NICO and BCO are expressed as mean ± 2 SD to estimate systematic bias and variances in differences. Bias and precision were compared using Bland–Altman plots [27, 28]. The interchangeability of either NICO or BCO against TEE was defined as a percentage error of less than ±20% in >75% of measured pairs [29]. The percentage error is defined as 100 × 2 SD of the difference/mean value of CO, and the relative error of each measurement pair (%) is defined as 100 × [(either NICO or BCO-TEE)/TEE] [30]. Data were analyzed using the statistical system SPSS 16.0.0. (SPSS, Chicago, IL, USA).

Results

The clinical characteristics of the patients, and the duration of surgery and anesthesia, did not significantly differ among groups (Table 1). The numbers of BCO measurements performed in patients without TR and with mild and moderate-to-severe TR were 150, 158, and 155, respectively.

Figure 1a shows the prediction equation for estimating TEE using NICO and BCO in patients without TR. Figure 1b shows the difference between NICO and TEE and between BCO and TEE measurements in patients without TR.

Figure 2a shows the prediction equation for estimating TEE using NICO and BCO in patients with mild TR. Figure 2b shows the difference between NICO and TEE and between BCO and TEE measurements in patients with mild TR.

Figure 3a shows the prediction equation for estimating TEE using NICO and BCO in patients with moderate-to-severe TR. Figure 3b shows the difference between NICO and TEE and between BCO and TEE measurements in patients with moderate-to-severe TR.

Table 2 summarizes differences between NICO and TEE and between BCO and TEE measurements in patients with different levels of TR severity.

Among patients without TR, with mild TR, and with moderate-to-severe TR, the errors for NICO were 35, 33, and 35%, respectively; those for BCO were and 23, 25, and 57%, respectively (Table 3). The relative errors of NICO were 3.5 ± 15.7, 4.3 ± 14.7, and 4.6 ± 15.7%, respectively, and those of BCO were −1.6 ± 10.5, −0.1 ± 10.8, and −6.2 ± 22.5%, respectively (Table 3). The relative error of NICO was within ±20% on 121 (81%), 130 (82%), and 117 (75%) occasions, respectively, and that of BCO on 140 (93%), 145 (92%), and 75 (49%) occasions, respectively (Table 3). The relative error of BCO of ±20% in

Table 1 Patient characteristics and intraoperative data

Variable	TR (−) ($n = 25$)	Mild TR ($n = 26$)	Moderate to severe TR ($n = 24$)	*P*
Age (years)	65 ± 10	64 ± 14	65 ± 9	NS
Height (cm)	159 ± 8.3	157 ± 7.4	159 ± 7.4	NS
Weight (kg)	63 ± 12	61 ± 14	62 ± 10	NS
Body surface area (m^2)	1.6 ± 0.2	1.6 ± 0.2	1.6 ± 0.2	NS
Male [*n* (%)]	20 (80)	17 (65)	19 (79)	NS
EF <40%, [*n* (%)]	2 (8)	1 (4)	1 (4)	NS
Surgical duration (min)	363 ± 46	401 ± 130	399 ± 81	NS
Anesthesia duration (min)	453 ± 40	471 ± 114	491 ± 84	NS

Values are presented as mean ± SD

TR tricuspid regurgitation, *EF* ejection fraction, *NS* not significant

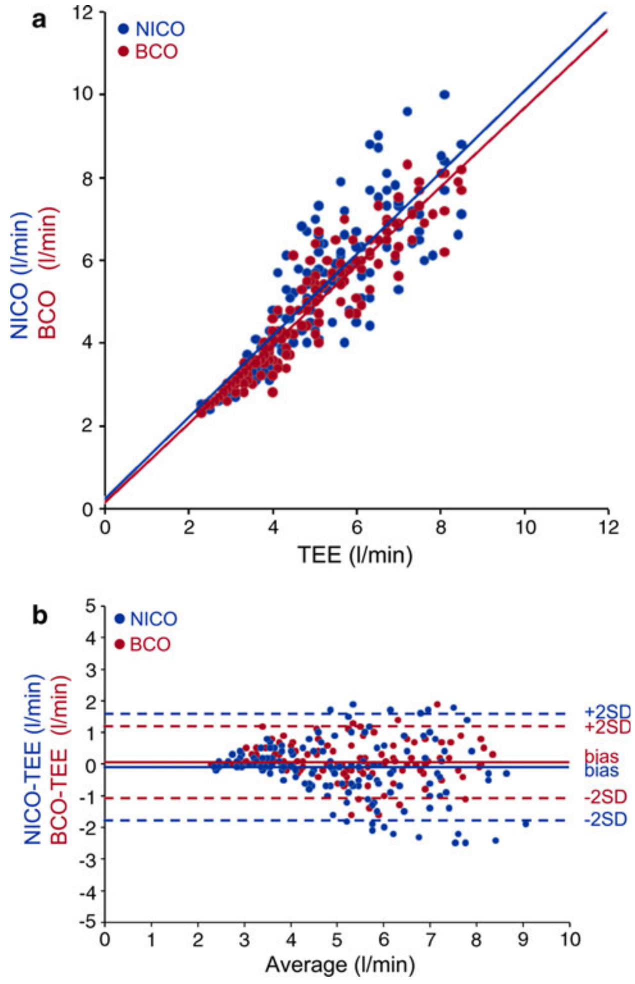

Fig. 1 NICO versus TEE and BCO versus TEE in patients without TR ($n = 150$). *Blue dots* are NICO, *red dots* are BCO. **a** Relationship between averaged value of NICO (*blue*, $r^2 = 0.75$, $P < 0.01$) and BCO (*red*, $r^2 = 0.88$, $P < 0.01$) with TEE. **b** Corresponding Bland–Altman plot representation: NICO bias ± precision (1 SD of bias) = −0.17 ± 0.88 L/min. BCO bias ± precision (1 SD of bias) = −0.08 ± 0.55 L/min. *Dashed line* indicates limits of agreement (±2 SD of bias). *NICO* Non-invasive cardiac output, *TEE* transesophageal echocardiography cardiac output, *BCO* bolus thermodilution cardiac output, *TR* tricuspid regurgitation

patients with moderate-to-severe TR fell far short of the 75% target.

Intra and Inter-observer variation in CO measurements by TEE was minimal. The mean percentage errors (SD) for intra and Inter-observer variability of CO were 1.5 (1.0)% and 1.4 (1.3)%, respectively.

Discussion

These results showed that measuring CO using the thermodilution technique is less accurate, particularly in patients with moderate-to-severe TR. The NICO monitor therefore measures CO more accurately in such patients. We postulated that NICO monitor is more accurate and reproducible than thermodilution in patients with coexisting TR.

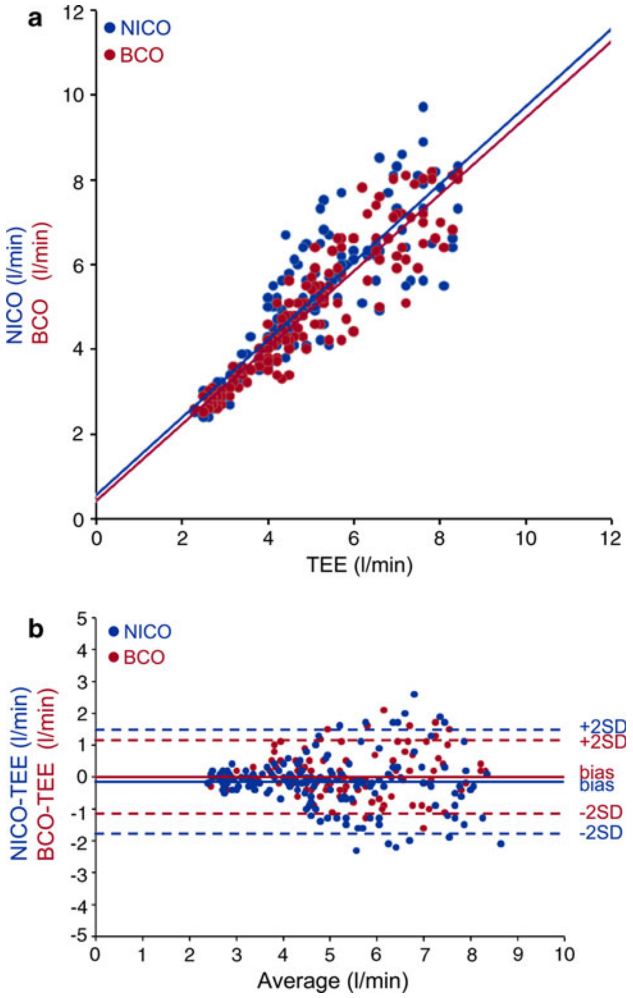

Fig. 2 NICO versus BCO and BCO versus TEE in patients with mild TR ($n = 158$). *Blue dots*, NICO; *red dots*, BCO. **a** Relationship between averaged value of NICO (*blue*, $r^2 = 0.78$, $P < 0.01$) and BCO (*red*, $r^2 = 0.86$, $P < 0.01$) with TEE. **b** Corresponding Bland–Altman plot representation: NICO bias ± precision (1 SD of bias) = −0.16 ± 0.82 L/min. BCO bias ± precision (1 SD of bias) = −0.05 ± 0.61 L/min. *Dashed line* indicates limits of agreement (±2 SD of bias)

We found that BCO had a smaller bias ± precision compared with NICO in patients without or with mild TR, whereas the NICO monitor had a smaller bias ± precision compared with BCO in patients with moderate-to-severe TR. Whether data from the NICO monitor and from BCO are interchangeable remains debatable, even though TR severity does not affect the accuracy or precision of the NICO monitor. The limits of agreement (2 SD of difference) should ideally fall within 28% of the average CO to claim interchangeability [29].

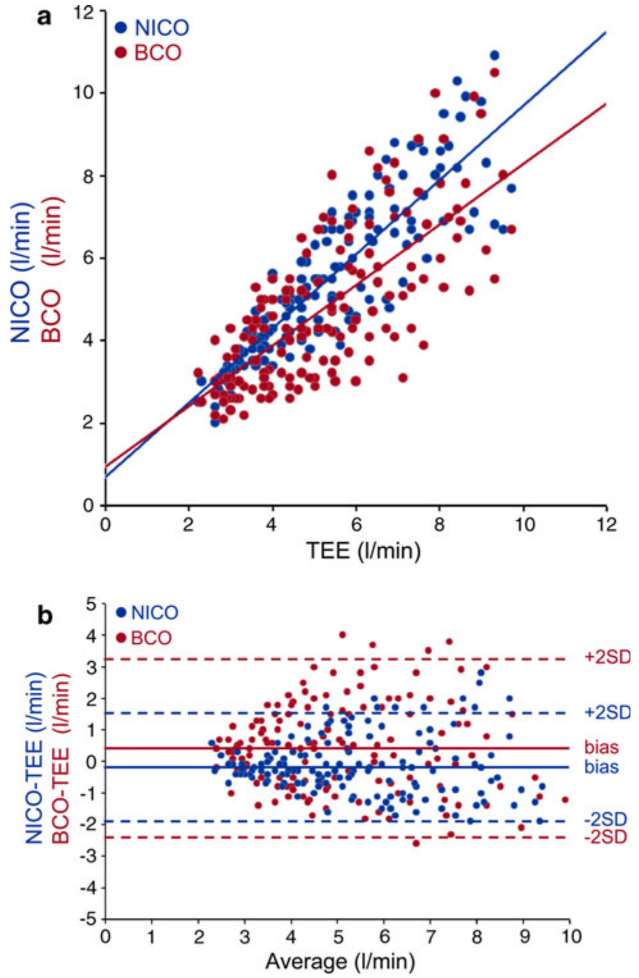

Fig. 3 NICO versus BCO and BCO versus TEE in patients without TR ($n = 155$). *Blue dots*, NICO; *red dots*, BCO. **a** Relationship between averaged value of NICO (*blue*, $r^2 = 0.78$, $P < 0.01$) and BCO (*red*, $r^2 = 0.53$, $P < 0.01$) with TEE. **b** Corresponding Bland–Altman plot representation: NICO bias ± precision (1 SD of bias) = 0.17 ± 0.91 L/min. BCO bias ± precision (1 SD of bias) = 0.43 ± 1.37 L/min. *Dashed line* indicates limits of agreement (±2 SD of bias)

Table 2 Differences between TEE and NICO values and between TEE and BCO values

	Mean ± SD (L/min)	Difference (L/min)	Pred. for TEE (L/min)	r^2
Without TR				
NICO	5.1 ± 1.8	−0.17 ± 0.88	0.98 NICO + 0.24	0.75
BCO	4.8 ± 1.6	0.08 ± 0.55	0.95 BCO + 0.15	0.88
Mild TR				
NICO	5.0 ± 1.7	−0.16 ± 0.82	0.92 NICO + 0.57	0.78
BCO	4.8 ± 1.6	0.05 ± 0.61	0.90 BCO + 0.42	0.86
Moderate-to-severe TR				
NICO	5.4 ± 1.9	0.17 ± 0.91	0.90 NICO + 0.69	0.78
BCO	4.8 ± 1.9	0.43 ± 1.37	0.73 BCO + 0.95	0.53

TR tricuspid regurgitation, *TEE* transesophageal echocardiography cardiac output, *NICO* non-invasive cardiac output, *BCO* bolus thermodilution cardiac output, r^2 correlation coefficient determined by regression analysis, Pred. for TEE, predictive equation used to estimate transesophageal echocardiography

Table 3 Severity of TR determined by NICO and BCO compared with TEE

	TR (−) ($n = 150$)	TR mild ($n = 158$)	TR moderate ($n = 155$)
Percentage error (%)			
NICO	35	33	35
BCO	23	25	57
Relative error (%)			
NICO	3.5 ± 15.7	4.3 ± 14.7	4.8 ± 15.4
BCO	−1.6 ± 10.5	−0.1 ± 10.8	−5.7 ± 24.9
Relative error less than ±20% (n)			
NICO	121	130	118
BCO	140	145	76
Relative error less than ±20% (%)			
NICO	81	82	76
BCO	93	92	49

NICO non-invasive cardiac output, *TEE* transesophageal echocardiography cardiac output, *BCO* bolus thermodilution cardiac output, *TR* tricuspid regurgitation

Alternatively, the results are interchangeable if the difference between the two methods is within ±20% on >75% of occasions [30]. Here, BCO fulfilled both criteria in patients without or mild TR, but not in those with moderate-to-severe TR. On the other hand, although NICO did not fulfill the former criterion, the latter was fulfilled in patients with or without TR. This finding showed that measuring CO using thermodilution is less accurate in parents with moderate-to-severe TR. We believe that the clinical usefulness of a hemodynamic monitor in patients with TR is not defined solely by accuracy but also by the added considerations of the balance between data quality and invasiveness, routine applicability, and operator-independence. From this perspective, data generated from NICO monitoring and thermodilution may not be interchangeable, but NICO monitoring can be used as a guide for hemodynamic management in patients with TR. We found here that CO measured using the NICO monitor and thermodilution correlated with CO measured by TEE in patients without and with mild TR. However moderate-to-severe TR did not affect the accuracy or precision of the NICO monitor, but did affect the accuracy or precision of thermodilution.

We found here that CO values measured by thermodilution significantly differed in the presence of moderate-to-severe TR. The algorithm cutoff is 30% of the peak height of the thermodilution curve when CO is determined [16]. The thermodilution curve could cut off more area in the presence than in the absence of moderate-to-severe TR, when 30% of the peak height algorithm was applied. We considered that this cutoff would affect thermodilution in the presence of simultaneous moderate-to-severe TR, because the thermodilution curve would cut off a larger area. Therefore, we considered that this algorithm could cause an error because the area of measurements decreases in the presence of moderate-to-severe TR.

Here, we used CO measured by TEE as a reference method. Bolus thermodilution has been widely accepted as a reference method in clinical practice [17]. However, the accuracy and precision of CO measurements obtained by thermodilution have been compared using the Fick principle, an electromagnetic flowmeter, indocyanine green dye, and TEE, as in our study [2–16, 26]. When CO is measured by TEE, the most reliable method of determining CO seems to continuous-wave Doppler measurements of valves [2, 24–26]. This method was originally described by Darmon et al. [24] and later confirmed by Poelaert et al. [25], and results correlate closely with those measured using thermodilution. Although CO can be accurately quantified by TEE, this procedure is often quite difficult to apply in clinical practice because a time-consuming optimal view is required. Therefore, we consider that the NICO monitor offers the clinical usefulness of a hemodynamic monitor in patients with coexisting TR.

This study has several limitations. All patients were anesthetized, paralyzed with vecuronium and mechanically ventilated, resulting in a constant tidal volume and stable carbon dioxide production. The patients were administered under control ventilation. Therefore, our results may not be directly extrapolated to populations of patients whose tidal volume and carbon dioxide production are unstable. Second, our patients had relatively normal lung mechanics, and their hemodynamics were stabilized at the time of entry into the study. Accuracy might be quite different among more seriously compromised patients. Last, this study only assessed the accuracy of the measurements, and not the usefulness of the NICO monitor. Further study is needed to evaluate the usefulness of NICO monitor in patients with coexisting TR.

In conclusion, we compared values obtained using a NICO monitor and by thermodilution with those obtained by TEE in patients with coexisting TR. We found that thermodilution is inaccurate for patients with moderate-to-severe TR, whereas the performance of the NICO monitor is accurate regardless of TR severity. The NICO monitor helps to prevent inaccurate measurements in patients with coexisting TR in the clinical setting.

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