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ORIGINAL ARTICLE

Corrected right ventricular end-diastolic volume and initial distribution volume of glucose correlate with cardiac output after cardiac surgery

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Abstract
Purpose Appropriate adjustment of cardiac preload is essential to maintain cardiac output (CO), especially in patients after cardiac surgery. This study was intended to determine whether index of right ventricular end-diastolic volume (RVEDVI), corrected RVEDVI using ejection fraction (cRVEDVI), index of initial distribution volume of glucose (IDVGI), or cardiac filling pressures are correlated with cardiac index (CI) following cardiac surgery in the presence or absence of arrhythmias.
Methods Eighty-six consecutive cardiac surgical patients were studied. Patients were divided into two groups: the non-arrhythmia (NA) group ($n = 72$) and the arrhythmia (A) group ($n = 14$). Three sets of measurements were performed: on admission to the ICU and daily on the first 2 postoperative days. The relationship between each cardiac preload variable and cardiac index (CI) was evaluated. A p value less than 0.05 indicated statistically significant differences.
Results Each studied variable was not different between the two groups immediately after admission to the ICU. cRVEDVI had a linear correlation with CI in both group (NA group: $r = 0.67$, $n = 216$, $p < 0.001$; A group: $r = 0.77$, $n = 42$, $p < 0.001$), but RVEDVI had a poor correlation with CI (NA group: $r = 0.27$, $n = 216$, $p < 0.001$; A group: $r = 0.19$, $n = 42$, $p = 0.036$). IDVGI had a linear correlation with CI (NA group: $r = 0.49$, $n = 216, p < 0.001$; A group: $r = 0.61, n = 42, p < 0.001$), Cardiac filling pressures had no correlation with CI.
Conclusion Our results demonstrated that cRVEDVI and IDVGI were correlated with CI in the presence or absence of arrhythmias. cRVEDVI and IDVGI have potential as indirect cardiac preload markers following cardiac surgery.

Keywords Cardiac surgery · Cardiac preload · Cardiac output

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Introduction

Appropriate adjustment of cardiac preload is essential to maintain cardiac output (CO), especially in patients following cardiac surgery, but the evaluation is not easily performed because either impairment of cardiac function [1–3] or internal bleeding may occur following cardiac surgery. Cardiac preload is traditionally assessed by its filling pressures, but edema or focal ischemia of myocardium after cardiac surgery may affect ventricular compliance, leading to poor correlation between these pressures and the end-diastolic volume, thus making these preload variables unreliable [4]. There is interest in the pulmonary artery catheter (PAC) that allows continuous measurements of CO and right ventricular end-diastolic volumes (RVEDV) on the basis of thermodilution technique [5], because RVEDV has been reported to reflect cardiac preload better than pulmonary artery wedge pressure (PAWP) and central venous pressure (CVP) [6]. However, RVEDV has also been shown to have a poor correlation with CO following cardiac surgery [7]. Considering that RVEDV is related to the patient's individual state of contractility by determining the difference between the estimated right

ventricular ejection fraction (RVEF), corrected RVEDV (cRVEDV) modified by RVEF has been proposed to promote the reliability of this method [8]. Thus, it remains unclear whether RVEDV or cRVEDV can reliably reflect cardiac preload following cardiac surgery.

The presence of arrhythmias also makes it difficult to use RVEDV to assess cardiac preload because RVEDV is calculated from stroke volume (SV) divided by RVEF and SV is not constant under arrhythmia conditions. However, it has not been studied adequately whether RVEDV or cRVEDV indicates cardiac preload in the presence of arrhythmias following cardiac surgery.

Initial distribution volume of glucose (IDVG) has been proposed as a marker of the central extracellular fluid (ECF) volume [9–12] using a small amount of glucose. The central extracellular fluid volume consists of the intravascular volume and the interstitial fluid volume of highly perfused organs such as brain, heart, lung, liver, and kidneys. Previous studies reported that IDVG rather than plasma volume has a better correlation with CO during early postoperative days of esophagectomy and that IDVG can predict the occurrence of subsequent hypovolemic hypotension early after major surgical procedures [13, 14]. Additionally, IDVG has been demonstrated to have a linear correlation with CO during hemodynamically unstable states early after esophagectomy, after percutaneous coronary intervention for acute myocardial infarction, and after major burns [11, 12, 15]. These results would allow us to speculate that IDVG has a potential as an alternative preload variable in critical ill patients, even though the concept of dilution volumetry is different from that of cardiac preload. Furthermore, considering the concept of IDVG measurement, IDVG would not be affected significantly, even in the presence of arrhythmia, unless its cardiovascular state changes obviously during measurement.

Additionally, decreased cardiac function after cardiac surgery may yield to changes in the relationship between cardiac preload and CO on the ascending part of the Frank–Starling curve and easily reach its descending part. Furthermore, a large variability of fluid volume status, from hypovolemia to hypervolemia, may occur in each individual patient following cardiac surgery. Assuming that each tested variable has a linear correlation with CO even in such heterogeneous conditions, it would be clinically relevant as a cardiac preload marker following cardiac surgery.

To examine these hypotheses, we measured cardiac preload variables including RVEDV, cRVEDV, IDVG, PAWP, and CVP as well as CO immediately after admission to the ICU and daily during the first 2 postoperative days following cardiac surgery in the presence or absence of arrhythmias. Additionally, we evaluated the effect of volume loading on each tested variable and CO when volume loading is clinically required during the first 24 h after admission to the ICU.

Materials and methods

The study was approved by our institutional Ethics Committee of the Hirosaki University Graduate School of Medicine, and each patient gave written informed consent. Eighty-six consecutive patients were enrolled into the study. Patients who underwent cardiac surgery including off-pump coronary artery bypass (OPCAB) and major thoracic aortic surgery were prospectively included, and a thermodilution pulmonary artery catheter was placed in each patient in the operating room. Patients with hyperglycemia (>250 mg/dl), neurological illness, apparent tricuspid regurgitation (diagnosed by transesophageal echocardiography during surgery), and mechanical cardiac support including intraaortic balloon pumping and/or percutaneous cardiac pulmonary support were excluded from the study.

A pulmonary artery catheter (Swan-GanzCCOmbo CCO/SvO_2, 744HF75; Baxter Healthcare, Irvine, CA, USA) was inserted into the right internal jugular vein and connected to a Vigilance Monitor system (Vigilance II Monitor, Model VG00765; Baxter Health Care), and arterial pressure, PAWP, CVP, continuous CO (CCO), RVEDV, and RVEF were recorded. A 3- to 5-min running average of CO determinations (CCOaverage mode) was used to record daily CO and RVEDV [16]. For the volume loading study, these were determined every 30 s (CCOstat mode).

On the basis of the presence or absence of arrhythmia, patients were divided into two groups: the non-arrhythmia (NA) group, patients who had normal sinus rhythm ($n = 72$), and the arrhythmia (A) group, patients who had atrial fibrillation, supraventricular premature contraction, ventricular premature contraction, or pacemaker with heart native electrical rhythm ($n = 14$). Three sets of measurements were performed: on admission to the ICU and daily at 10 AM on the first 2 postoperative days. IDVG was determined immediately after cardiovascular variables [CCOaverage, RVEDV, PAWP, CVP, RVEF, HR, and mean arterial pressure (MAP)] and other routine clinical variables were recorded. The corrected value of index of RVEDV (cRVEDVI) was also calculated using the following formula [8]:

$$\mathrm{cRVEDVI} = \mathrm{RVEDVI}/\exp(2.74 \times (0.4 - \mathrm{RVEF}(\%) \times 0.01))$$

To calculate IDVG, a bolus of 10 ml 50 % glucose (5 g) was injected through the proximal port of the pulmonary artery catheter. Heparinized blood samples were obtained from an arterial catheter immediately before and at 3 min

after the completion of glucose injection for measurement of approximated IDVG. The reported difference between the approximated IDVG and original IDVG using repeated samplings through 7 min after injection was -0.05 ± 0.54 (SD) l [17]. Plasma was separated immediately for glucose measurement, and plasma glucose levels were measured using the glucose oxidase method (glucose analyzer GA-1151; ARKRAY, Kyoto, Japan). Plasma glucose levels were measured in duplicate and averaged. The coefficient of variation was less than 2 % for repeated glucose measurements at a glucose concentration of 70–249 mg/dl. IDVG was calculated according to the following formula: IDVG (l) $= 24.4 \times \exp^{(-0.03 \times \triangle gl)} + 2.7$ [Δgl (mg/dl) is increase in glucose concentration] [18].

During the first 24 h postoperative after admission to the ICU, volume loading was performed in the NA group, when a diagnosis of hypovolemic hypotension was clinically made by attending ICU physicians not related to this study. Cardiovascular variables and IDVG were also measured immediately before volume loading and 10 min after completion of volume loading with 250 ml 5 % albumin over 20 min.

Statistical analysis

Calculated values are presented on the basis of reported basal body weight before surgery. The values are also indexed to body surface area when compared with cardiac index (CI). All data were presented as mean and standard deviation (SD) because all variables were normally distributed in ad hoc testing. Daily variables were assessed using a one-way analysis of variance for repeated measures. Post hoc testing was performed using Dunnett's test. Changes in variables before and after volume loading were assessed using the paired Student's *t* test, and comparisons between the NA and the A groups were assessed using the unpaired Student's *t* test. The Pearson product moment correlation using either actual values or changed values was performed. Actual values were defined as current values at each testing point. Changed values were defined as current values minus previous values. A *p* value less than 0.05 indicated statistically significant differences.

Results

Demographic data of 86 studied patients are shown in Table 1. All but 5 patients required a continuous infusion of vasoactive drugs such as noradrenaline and dobutamine during the study period without changes in an infusion rate during measurement.

Daily hemodynamic and volumetric variables are shown in Table 2. In the NA group, index of RVEDV (RVEDVI), cRVEDVI, and index of IDVG (IDVGI) were increased with CI on the second postoperative day when compared with the operative day ($p < 0.05$, respectively). However, PAWP, CVP, and body weight remained unchanged throughout the study period.

Table 1 Demographic data and type of operation

	Non-arrhythmia group	Arrhythmia group
Demographic data		
Sex (M/F)	49/23	9/5
Age (years)	67 ± 12	70 ± 8
Height (cm)	159.2 ± 9.8	158.2 ± 10.0
Preoperative body weight (kg)	60.2 ± 10.6	58.9 ± 9.6
Body surface area (m^2)	1.59 ± 0.19	1.57 ± 0.18
Types of operation		
OPCAB	13	1
On-pump CABG	12	3
Valve surgery	27	7
Major vascular surgery with CPB	20	3

Number of patients and mean ± SD

OPCAB off-pump coronary artery bypass, *CABG* coronary artery bypass grafting, *CPB* cardiopulmonary bypass

In the NA group, actual RVEDVI had a poor correlation with actual CI ($r = 0.27$, $n = 216$, $p < 0.001$) (Fig. 1a), but actual cRVEDVI had a linear correlation with actual CI ($r = 0.67$, $n = 216$, $p < 0.001$ for the latter, respectively) (Fig. 1c). IDVGI also had a linear correlation with actual CI ($r = 0.49$, $n = 216$, $p < 0.001$) (Fig. 1e). Neither actual PAWP nor actual CVP had a correlation with actual CI ($r = 0.10$ for the former and $r = -0.09$ for the latter, respectively). Changes in RVEDVI (ΔRVEDVI) had only a poor correlation with those in CI ($r = 0.22$, $n = 144$, $p = 0.007$) (Fig. 2a), but those in cRVEDVI (ΔcRVEDVI) had a linear correlation with CI ($r = 0.48$, $n = 144$, $p < 0.001$) (Fig. 2c). Changes in IDVGI (ΔIDVGI) also had a linear correlation with ΔCI ($r = 0.54$, $n = 144$, $p < 0.001$) (Fig. 2e).

In the A group, all studied variables remained unchanged throughout the study period. Between the NA and the A groups, all tested variables did not differ on each postoperative day. In the A group, actual cRVEDVI, but not RVEDVI, had a linear correlation with actual CI ($r = 0.77$, $n = 42$, $p < 0.001$ for the former and $r = 0.19$, $n = 42$, $p = 0.22$ for the latter, respectively) (Fig. 1b, d). Actual IDVGI had a linear correlation with actual CI ($r = 0.61$, $n = 42$, $p < 0.001$) (Fig. 1f). Actual CVP also had an inverse correlation with actual CI ($r = -0.41$, $n = 42$, $p = 0.007$), but actual PAWP did not. Only ΔcRVEDVI had a moderate correlation with ΔCI ($r = 0.58$, $n = 28$, $p = 0.001$) (Fig. 2d).

Table 2 Studied variables in the early postoperative days

	Non-arrhythmia group ($n = 72$)			Arrhythmia group ($n = 14$)		
	Day 0	Day 1	Day 2	Day 0	Day 1	Day 2
CI (l/min/m^2)	2.5 ± 0.5	2.5 ± 0.6	2.7 ± 0.5*,†	2.5 ± 0.6	2.4 ± 0.4	2.5 ± 0.5
RVEDVI (ml/m^2)	114 ± 23	111 ± 22	119 ± 22†	121 ± 25	121 ± 33	124 ± 30
cRVEDVI (ml/m^2)	86 ± 17	84 ± 17	91 ± 18†	91 ± 26	91 ± 14	92 ± 24
IDVGI (l/m^2)	4.0 ± 0.6	4.1 ± 0.4*	4.4 ± 0.5*,†	4.1 ± 0.6	4.2 ± 0.3	4.3 ± 0.4
PAWP (mmHg)	10 ± 4	9 ± 3	9 ± 3	8 ± 3	7 ± 4	11 ± 4
CVP (mmHg)	7 ± 3	7 ± 3	7 ± 3	8 ± 3	8 ± 3	9 ± 3
RVEF (%)	29 ± 6	29 ± 6	30 ± 6	29 ± 10	30 ± 11	29 ± 10
MAP (mmHg)	74 ± 13	69 ± 11*	73 ± 11	72 ± 12	71 ± 15	71 ± 14
HR (beats/min)	77 ± 14	79 ± 13	80 ± 13	78 ± 9	74 ± 7	78 ± 19
Body weight (kg)	61.3 ± 10.6	61.5 ± 10.6	61.4 ± 10.6	59.8 ± 8.9	60.0 ± 9.0	60.5 ± 8.9
IDVG/CO ratio	1.63 ± 0.32	1.73 ± 0.37	1.62 ± 0.29†	1.67 ± 0.33	1.75 ± 0.29	1.78 ± 0.28

Mean ± SD

CI cardiac index, *RVEDVI* indexed right ventricular end-diastolic volume, *cRVEDVI* corrected RVEDVI, *IDVGI* indexed initial distribution volume of glucose, *PAWP* pulmonary artery wedge pressure, *CVP* central venous pressure, *RVEF* right ventricular ejection fraction, *MAP* mean arterial pressure, *HR* heart rate

* $p < 0.05$ versus day 0

† $p < 0.05$ versus day 1

Volume loading was done in 14 patients. A small, but statistically significant, increase was observed in actual CI, cRVEDVI, IDVGI, CVP, and MAP after volume loading ($p < 0.01$ except for cRVEDVI; $p < 0.05$ for cRVEDVI) (Table 3). However, only actual cRVEDVI had a linear correlation with actual CI ($r = -0.48, n = 28, p = 0.009$).

Using all actual daily data, the IDVG/CO ratio was 1.66 ± 0.33 ($n = 216$) for the NA group and 1.73 ± 0.29 ($n = 42$) for the A group. The ratio was not different between the two groups ($p = 0.17$).

Discussion

The present results confirmed that cardiac filling pressures were unreliable in evaluating cardiac preload following cardiac surgery, because changes in cardiac compliance may have a significant impact on the pressure and cardiac preload relationship. In contrast, this study demonstrated that actual daily cRVEDVI and IDVGI had a positive linear correlation with actual CI regardless of the presence or absence of arrhythmias. These findings support the notion that these two variables can be used as a cardiac preload marker following cardiac surgery, because changes in cardiac compliance may have a negligible effect on the volume and cardiac preload relationship, even though volume loading in this study has only a limited effect as the result of a small increase in CI after volume loading.

Although two clinical studies have reported that RVEDVI was useful as a cardiac preload marker after cardiac surgery [6, 15], a poor correlation between RVEDVI and CI was found in both groups in this study, indicating that RVEDVI is not a reliable marker of cardiac preload following cardiac surgery. Inaccurate RVEDVI determinations have been reported when patients had a low RVEF because RVEDVI is calculated as the quotient of SV and RVEF [19, 20]. Diebel et al. [5] stated that RVEDV was reliable only when RVEF was 38 ± 9 %.The RVEF in this study was 29 ± 7 % ($n = 216$), which was similar to the previous study (31 ± 10 %; normal RVEF range, 40–60 %) [19]. A lower RVEF in this study would be responsible for the inaccuracy of RVEDVI measurement following cardiac surgery. To overcome the limitation of RVEDVI management, cRVEDVI modified by RVEF has been proposed [8]. In fact, cRVEDVI had a better correlation with CI regardless of the presence or absence of arrhythmias in this study. Malbrain et al. also revealed that changes in cRVEDVI had a good correlation with changes in CI even in which RVEFs (21–23 %) were lower than those in this study [8]. Therefore, cRVEDVI can be used as a reliable cardiac preload marker after cardiac surgery, even if patients have lower RVEF in the presence of arrhythmia. Although the RVEDV value is not shown on the monitor display when severe irregular rhythm developed, cRVEDVI in the presence of arrhythmias might be as reliable as cRVEDVI without arrhythmia so long as the RVEDV value is shown on the monitor display.

In our study, actual IDVGI had a linear correlation with actual CI in the presence or absence of arrhythmias following cardiac surgery because the initial volume of

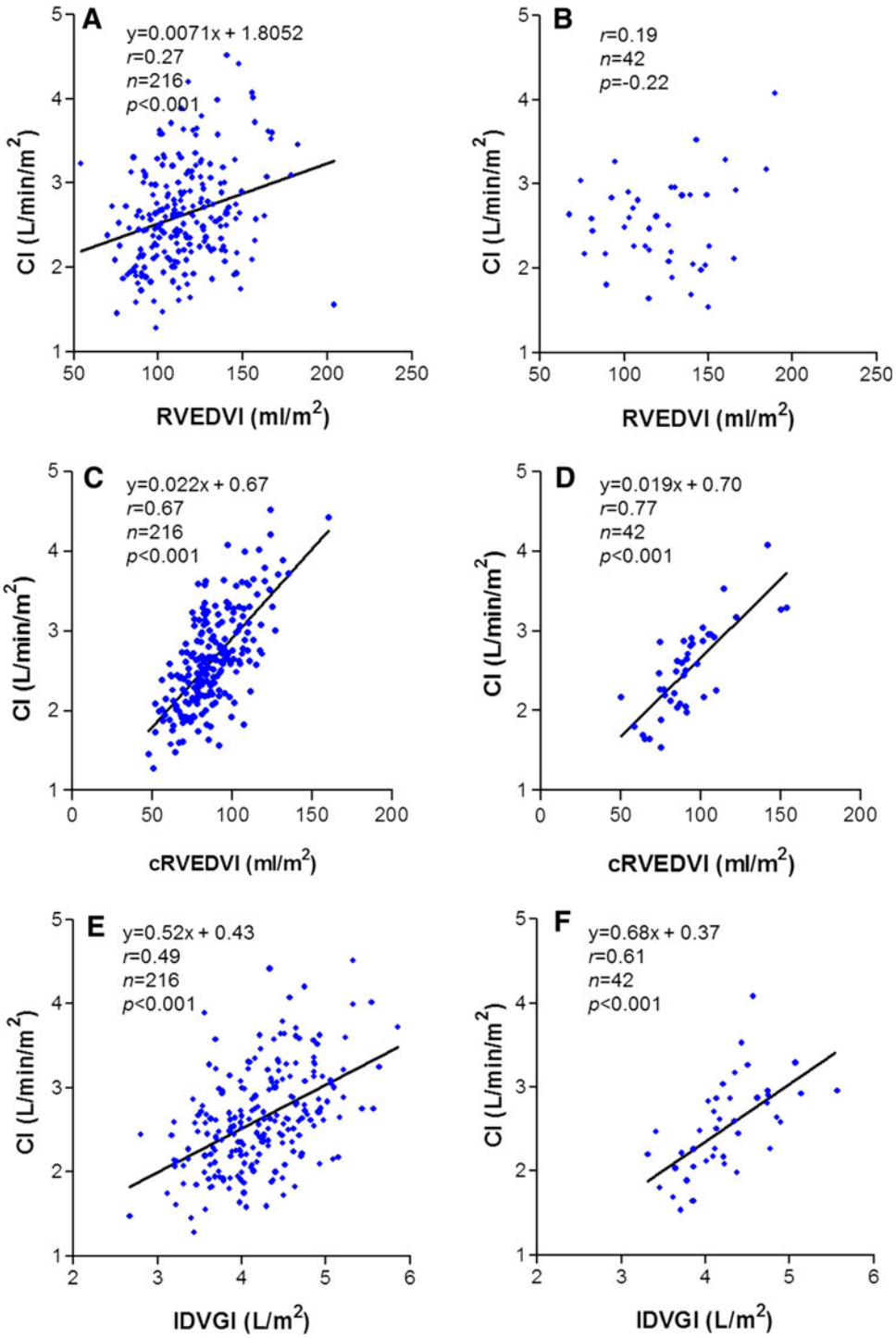

Fig. 1 Relationship with actual cardiac index in the presence or absence of arrhythmias. **a** *Top, left:* Indexed right ventricular end-diastolic volume (RVEDVI) versus cardiac index (CI) in the non-arrhythmia group ($r = 0.27$, $n = 216$, $p < 0.001$). **b** *Top, right:* RVEDVI versus CI in the arrhythmia group ($r = 0.19$, $n = 42$, $r = 0.22$). **c** *Middle, left:* cRVEDVI versus CI in the non-arrhythmia group ($r = 0.67$, $n = 216$, $p < 0.0001$). **d** *Middle, right:* cRVEDVI versus CI in the arrhythmia group ($r = 77$, $n = 42$, $p < 0.0001$). **e** *Bottom, left:* IDVGI versus CI in the non-arrhythmia group ($r = 0.49$, $n = 216$, $p < 0.001$). **f** *Bottom, right:* IDVGI versus CI in the arrhythmia group ($r = 0.61$, $n = 42$, $p < 0.001$). Actual values were defined as current values at each testing point. *RVEDVI* index of right ventricular end-diastolic volume, *CI* cardiac index, *cRVEDVI* corrected RVEDVI, *IDVGI* index of initial distribution volume of glucose

distribution of several drugs is determined by several factors including CO [21]. As CO depends on cardiac preload based on the Frank–Starling relationship, the better the filling of the heart, the better the resulting forward output. In fact, our previous experimental and clinical studies showed a relatively good correlation coefficient between IDVG and CO, ranging from 0.71 to 0.89 [9, 10, 22]. However, an excessive fluid volume loading (60 ml/kg) in dogs yielded a decrease in CO despite an increase in IDVG [23]. Additionally, IDVGI and CI did not consistently move together toward the same direction, as shown in Fig. 2f of this study and as described in nonsurgical critically ill patients [24]. These findings allow us to speculate that IDVGI only correlates with CI when cardiac preload is on the ascending part of the Frank–Starling curve, but not on its descending part, and that IDVGI itself is not

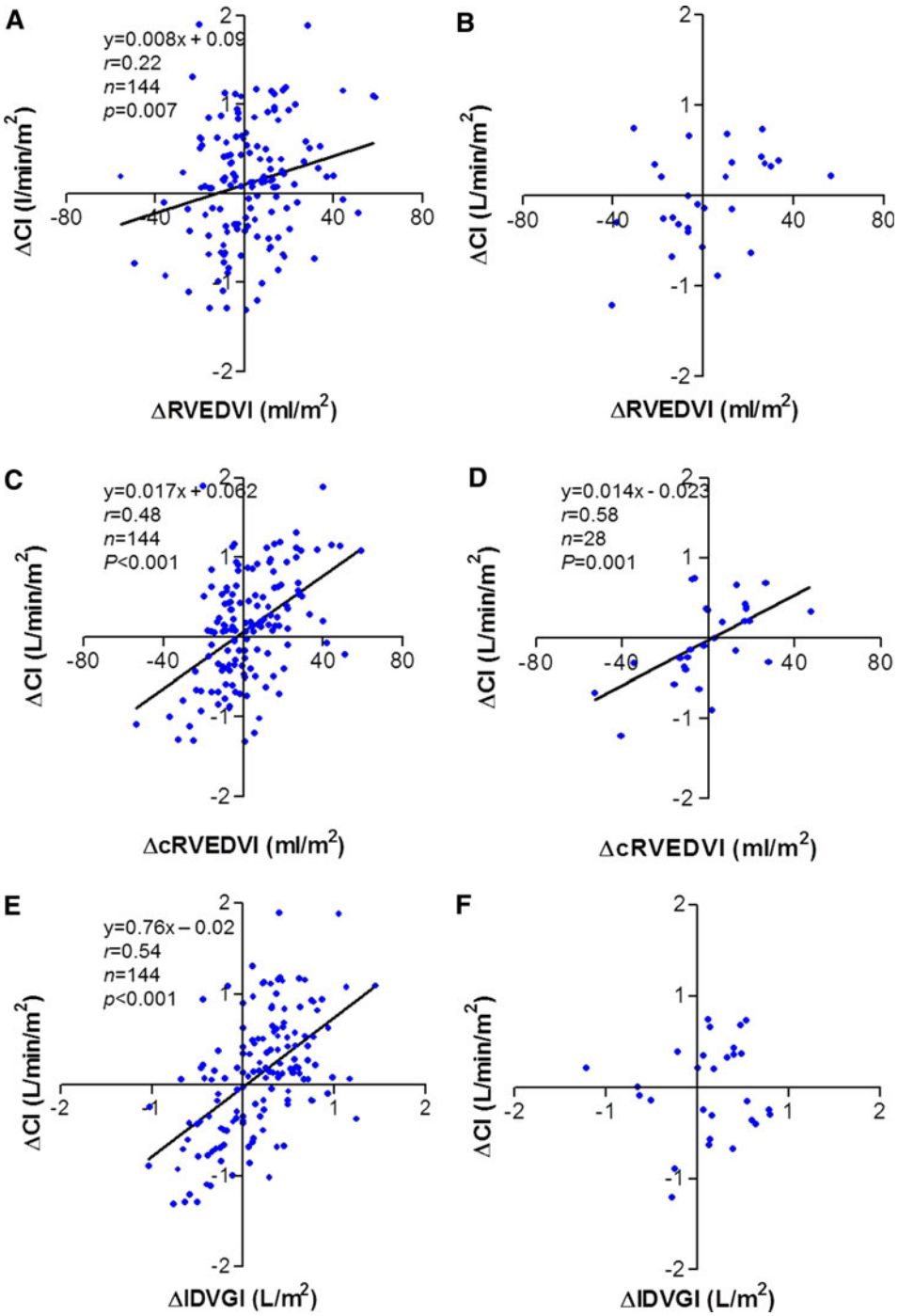

Fig. 2 Relationship with changes in cardiac index in the presence or absence of arrhythmias. **a** *Top, left:* RVEDVI versus CI in the non-arrhythmia group ($r = 0.22$, $n = 144$, $p = 0.007$). **b** *Top, right:* RVEDVI versus CI in the arrhythmia group ($r = 0.37$, $n = 28$, $p = 0.06$). **c** *Middle, left:* cRVEDVI versus CI in the non-arrhythmia group ($r = 0.48$, $n = 144$, $p < 0.0001$). **d** *Middle, right*: cRVEDVI versus CI in the arrhythmia group ($r = 0.58$, $n = 28$, $p = 0.0001$). **e** *Bottom, left:* IDVGI versus CI in the non-arrhythmia group ($r = 0.54$, $n = 144$, $p < 0.001$). **f** *Top, right:* IDVGI versus CI in the arrhythmia group ($r = 0.07$, $n = 28$, $p = 0.70$). Changed values were defined as current values minus previous values. *RVEDVI* index of right ventricular end-diastolic volume, *CI* cardiac index, *cRVEDVI* corrected RVEDVI, *IDVGI* index of initial distribution volume of glucose

consistently affected by CI, but rather reflects the central extracellular fluid volume status. Presumably, excessive increase in cardiac preload, decrease of myocardial contractility, and changes in cardiac afterload may also have a significant impact on the relationship between IDVGI and CI early after cardiac surgery. Furthermore, all but five patients required a continuous infusion of vasoactive drugs such as noradrenaline and dobutamine during the study period. These vasoactive drugs would change myocardial contractility and cardiac afterload and have a significant impact on the relationship between IDVGI and CI. Nevertheless, actual IDVGI had a linear correlation with actual CI in our study. Therefore, our results suggest that IDVGI is a reliable indirect cardiac preload marker, even following cardiac surgery. Furthermore, a regression line between actual IDVGI and actual CI in the A group was close to that in the NA group. This result therefore suggests that IDVGI is not affected even in the presence of arrhythmias.

Table 3 Changes of variables before and after volume loading

	Before	After
CI (l/min/m^2)	1.9 ± 0.3	2.2 ± 0.4*
RVEDVI (ml/m^2)	106 ± 12	108 ± 18
cRVEDVI (ml/m^2)	70 ± 13	75 ± 14**
IDVGI (l/m^2)	3.4 ± 0.4	3.6 ± 0.5*
PAWP (mmHg)	7 ± 4	8 ± 2
CVP (mmHg)	6 ± 3	7 ± 4*
SvO_2 (%)	60 ± 7	60 ± 6
MAP (mmHg)	62 ± 9	69 ± 11*
HR (beats/min)	78 ± 15	78 ± 15

Mean ± SD

CI cardiac index, *RVEDVI* indexed right ventricular end-diastolic volume, *cRVEDVI* corrected RVEDVI, *IDVGI* indexed initial distribution volume of glucose, *PAWP* pulmonary artery wedge pressure, *CVP* central venous pressure, *SvO_2* mixed venous oxygen saturation, *MAP* mean arterial pressure, *HR* heart rate

* $p < 0.01$ compared with before volume loading

** $p < 0.05$ compared with before volume loading

In the A group, no linear correlation was found between changes in each tested variable and ΔCI. However, the mean ΔCI in this group was only 0.02 ± 0.51 l/min/m^2. Biancofiore et al. [25] reported that a small change in CO (ΔCO) should be excluded to assess the accuracy of CO measurement. According to a report by Critchley et al. [26], a minimal ΔCO is required, 0.5–1.0 l/min, for this purpose. Applying this value to this study, about 68 % of data in the A group were included in the ΔCO exclusion criteria. Accordingly, in the A group, daily ΔCI was too small to assess the correlation between changes in cardiac preload variables and ΔCI. Further studies are needed to evaluate the relationship between these in the presence of arrhythmias.

Similarly, an increase in CI after volume loading in this study was only small, but significant (mean ΔCI = 0.3 l/min/m^2), because the amount of volume loading was relatively small (250 ml 5 % albumin solution) compared to the other fluid loading studies [25, 27]; data obtained for this study were collected during routine postoperative ICU management, rather than in a controlled research-oriented management situation, resulting in insufficient effect for evaluation of fluid loading. Additionally, the time interval between IDVG measurements before and after fluid loading was only 30 min in this study. Rose et al. [28] calculated IDVG using a one-compartment model with repeated sampling, and the bias of repeated IDVG measurements was only 0.08 ± 0.32 l at a 30-min interval in hemodynamically stable states, IDVG in this study was calculated from one-point incremental plasma concentration [18]. Therefore, one-point sampling as well as hemodynamically unstable states might affect the result that IDVGI has a poor correlation with CI, at least in part, when fluid loading was performed. Nevertheless, cRVEDVI, IDVGI, CVP, and MAP, but not RVEDV and PAWP, were increased after volume loading, even though no correlation was found between each tested variable and CI. Further studies are required to determine whether IDVGI can be correlated with CI in the fluid loading study.

To our knowledge, there have been two clinical reports describing the relationship between IDVG and fluid responsiveness after cardiac surgery. van Tulder et al. [29] reported that IDVG was insensitive to volume loading during the early postoperative period after cardiac surgery. However, they did not measure CO, even though they used a pulmonary artery catheter. Interestingly, their arterial pressure remained statistically unchanged despite an increase in CVP after volume loading. Harvey et al. [30] also reported that neither IDVG, systolic area variability, nor systolic blood pressure variability were predictive of preload responsiveness after cardiac surgery. Accordingly, evaluation of fluid responsiveness during hemodynamically unstable states early after cardiac surgery should be cautiously performed, because internal bleeding, temperature change, alternations in vasomotor tone, or fluid shift between compartments during the measurements may have a significant impact on the result [31].

Our previous study showed that patients with congestive heart failure (CHF) had a higher IDVG/CO ratio compared with patients without CHF: the ratio was 1.68 ± 0.47 for the former versus 1.16 ± 0.40 for the latter, respectively [24]. When applying this ratio in the present study, the result is comparable with the ratio observed in patients with CHF and suggests that following cardiac surgery the patients have either decreased cardiac function or relative fluid accumulation in the central extracellular compartment. Considering that actual IDVGI in NA group in this study was 4.2 ± 0.5 l/m^2 ($n = 216$) and reported IDVGI in 16 healthy volunteers was 4.0 ± 0.5 l/m^2 [32], the former was not apparently increased, and thus the high IDVG/CO ratio in this study may reflect decreased cardiac function rather than relative fluid accumulation in the central ECF compartment, even though some patients possibly had fluid accumulation. Considering our previous study, the normal IDVG range is approximately from 110 to 130 ml/kg. When decision making about fluid management is required, even in the presence of a high IDVG/CO ratio, a large IDVG (>130 ml/kg) indicates fluid removal to overcome excess fluid. On the other hand, a small IDVG (<110 ml/kg) indicates a low cardiac preload, and we should take volume loading into consideration.

In nearly one fourth (55/216) of our studied points, a low CO state (CI <2.2 l/min/m^2) was present. A low CO state might yield underestimation of IDVG, because the mixing of administered glucose would not be completed in

the central extracellular compartment within 3 min post infusion in a low CO state. However, Hashiba et al. [33] reported an unusual extremely larger IDVGI following volume loading in a patient with right ventricular myocardial infarction, even though a low CI (approximately 1.6 l/min/m^2) remained unchanged despite extensive volume loading. As judged by the fact that the velocity of glucose transfer across a capillary membrane is about 50 times greater than the linear capillary blood flow [34], a low CO state of itself would have a minimal effect on IDVG determination. Accordingly, we believe that IDVG values in this study are reliable even in a low CO state, even though further studies are required regarding the accuracy of IDVG determination in an extremely low CO state, such as less than 1.5 l/min/m^2.

Limitations

First, dynamic variables such as stroke volume variation and pulse pressure variation were not assessed in this study, because reliable measurement of dynamic variables consistently require a relatively large tidal volume (>8 ml/kg) without spontaneous breathing activity under heavy sedation, as well as regular sinus rhythm [35]. Measurement immediately after admission to the ICU may meet these essential underlying conditions for dynamic variables, but not thereafter. However, He et al. [36] recently showed an inverse correlation between IDVG and pulse pressure variation ($r = -0.65$) without volume loading in neurosurgical patients after induction of anesthesia. Further studies associated with volume loading are required to elucidate the relationship between them, even though the interpretation of the result should be cautiously carried out early after cardiac surgery [31]. Therefore, the relationship between IDVG and dynamic variables remains unclear.

Second, we did not simultaneously measure echocardiography. Left ventricular end-diastolic area derived from transesophageal echocardiography (TEE) was reported as a useful predictor of cardiac preload and fluid responsiveness in critically ill patients [37, 38]. However, after admission to the ICU, the use of TEE for cardiac preload assessment is not routinely performed because of its invasiveness, requiring heavy sedation. Thus, it is difficult to assess cardiac preload repeatedly using TEE following cardiac surgery, especially in the early postoperative days.

Conclusion

Our results demonstrate that cRVEDVI and IDVGI had a positive linear correlation with CI following cardiac surgery, regardless of the presence or absence of arrhythmias. These findings suggest that both cRVEDVI and IDVGI have potential as indirect cardiac preload markers following cardiac surgery.

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Conflict of interest The author(s) declare that they have no competing interests.

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