Volume expansion is frequently used in critically-ill patients to improve hemodynamics. However, the Frank–Starling curve (stroke volume (SV) expressed as a function of preload), is steep in its early phase and then levels out to a plateau. When the plateau is reached, vigorous fluid resuscitation risks generating a volume overload without improving the hemodynamics. Therefore, assessing the cardiac preload accurately and predicting the response to fluid challenge (fluid responsiveness) is important when attempting to avoid unnecessary volume expansion. Using the Frank–Starling principle, ventricular preload is defined as the myocardial muscle-fiber length that is present at the end of diastole. Ideally, the appropriate clinical correlate would be left ventricular end-diastolic volume (LVEDV), but this parameter is not easily measured. Therefore, preloads have often been assessed by measuring pressure, such as the pulmonary capillary wedge pressure (PCWP) or the central venous pressure (CVP). However, changes in functional cardiac compliance can lead to poor correlations between pressure and the left ventricular preload. Because of this unpredictable relationship between pressure and volume, it is sometimes difficult to predict fluid responsiveness from the pressure parameters of preload. It is particularly important to monitor pressure and volume in patients after cardiac surgery, because marked changes in cardiac compliance are expected due to edema or focal ischemia caused by the operation.

Recently, a modified Swan–Ganz catheter, which has a rapid-response thermistor, became available. This permits almost continuous assessment of cardiac output (CO), right ventricular ejection fraction (RVEF) and right ventricular end-diastolic volume (RVEDV). Because RVEDV represents a true volumetric assessment of ventricular filling, as opposed to pressure, it has been suggested that RVEDV may provide a more useful bedside assessment of ventricular filling. The purpose of the present study was to evaluate the accuracy of RVEDV measurements and commonly used pressure parameters in predicting the response of SV to volume expansion in postoperative cardiac surgery patients.

**Methods**

After the ethical approval was received from the Departments of Cardiovascular Surgery and Anesthesiology and Intensive Care Medicine, we conducted a retrospective study of the hemodynamic changes following fluid challenge after cardiac surgery. In 16 patients who had...
undergone cardiac surgery (coronary artery bypass graft (CABG) (n=7), mitral valve surgery (n=2), aortic valve surgery (n=4), surgery of ascending aorta (n=2), and closure of atrial septal defect (n=1)), CO, RVEDV and RVEF were monitored continuously in the intensive care unit after the operations during routine postoperative monitoring. A right-heart ejection fraction pulmonary artery catheter (CCOMboV 774HF; Edwards Lifesciences, Irvine, CA, USA), which was connected to a Vigilance Monitor system (Edwards Lifesciences), was used for the continuous measurement of these parameters. Parameters were updated every 30 s and were recorded automatically. Written informed consent was given by the patients for insertion of a pulmonary artery catheter and monitoring.

Based on the pulse warm thermodilution technique, CO was continuously calculated from the area under the thermodilution curve. The calculation of RVEF was based on the exponential decay time constant (D) of the thermodilution washout decay curve and heart rate (HR): RVEF=1− exp(−60/(D×HR)). RVEDV, which is based on CO, HR and RVEF, was calculated as: RVEDV=(CO/HR)/RVEF.

Simultaneously, all patients received an arterial catheter to allow continuous monitoring of arterial blood pressure. Pulmonary artery pressure, PCWP and CVP were also measured using the pulmonary artery catheter.

Because the present study was a retrospective observational study, the same as the clinical practice of usual postoperative care, the decision to conduct a fluid challenge was made by the intensive-care specialists in response to one or more clinical conditions that suggested the possibility of inadequate preload. These were no fluid challenges specifically carried out for this study. The volume of the fluid challenge was also decided by the intensive-care specialists based on the clinical conditions and was not affected by the present study. Therefore, informed consent was not sought specifically for these fluid challenges in routine clinical practice. Approval of this retrospective observational study was given by the Ethical Committee of the Departments of Cardiovascular Surgery and Anesthesiology and Intensive Care Medicine of the Gifu Prefectural Tajimi Hospital and the committee waived the requirement for consent for fluid therapy in the present study.

In the present study, among fluid challenges carried out in various ways, we only analyzed fluid challenges using either 480 or 500 ml colloid solutions (5% albumin, fresh frozen plasma or 6% hydroxyethyl starch), which were administered in 30–60 min. The fluid challenge using crystalloids, or other blood products, was not analyzed. In addition, the fluid administration of other volumes was not included in the analysis. If the doses of inotropic agents or other vasoactive agents were changed during the fluid administration, the fluid challenge was also excluded from the analysis. The cases in which there was active bleeding (50 ml during the fluid administration) were not included.

Finally, all 17 fluid challenges (8 CABG cases and 9 non-CABG cases) that satisfied these criteria were analyzed. There was no case that had a residual intra-cardiac shunt or significant tricuspid regurgitation. All cases had 20% or more RVEF. Tachycardia at a rate in excess of 150 beats/min was not observed when patients had these fluid challenges and all patients were in sinus rhythm. Patients were intubated and mechanically ventilated with 5–10 mmHg of positive end-expiratory pressure.

Hemodynamic parameters were measured before the start of fluid challenge and 12 min after its completion. The percentage change in SV after fluid challenge was used as the principal indicator of volume responsiveness. Responders were defined as those individuals who had a 10% or greater increase in SV (and SV index (SVI)). Dynamic variables, such as pulse and pressure variation, were not measured to assess fluid responsiveness in the present study.

Statistical Analysis

For statistical analysis, all volume variables were indexed to the body surface area. Student’s t-test was used to compare variables. We conducted linear regression analyses between the changes in variables that reflected preload and the changes in SVI. Statistical analysis was carried out using the JMP 6 software (SAS Inc, Cary, NC, USA). A value of p<0.05 was considered to be statistically significant. Data are presented as the mean ± standard deviation.

Results

The changes in hemodynamic parameters following fluid challenge are described in Table 1. Cardiac index increased from 3.08 to 3.46 L·min⁻¹·m⁻² (p<0.01) and SVI increased from 33.6 to 38.5 ml/m² (p=0.011). PCWP increased from 14.3 to 15.5 mmHg (p=0.046); however, changes in the RVEDV index (RVEDVI) (from 108.2 to 115.3 ml/m²) were not significant. The volume-induced increase in SVI was 10% or greater in 9 fluid challenges (53%; defined as responders).

Linear regression analysis between the percentage of change in SVI and baseline RVEDVI revealed a statistically significant but weak correlation (r²=0.249, p=0.041) (Fig 1). However, linear regression analysis between the percentage change in SVI and the pressure variables reflecting preload (CVP and PCWP) did not reveal any significant relationships (r²=0.12, p>0.05 for CVP; and r²=0.057, p>0.05 for PCWP (Fig 2)). Although the baseline RVEDVI was higher in non-responders than in responders (112.4±6.1 vs 104.4±5.8 ml/m², p=0.05), there was marked overlap of baseline RVEDVI values between responders and non-responders, as shown in Fig 1. Therefore, there was no specific RVEDVI threshold that could reliably discriminate responders and non-responders before fluid was administered.

### Table 1 Change in Hemodynamic Parameters Before and After Fluid Challenge

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Baseline</th>
<th>Post-fluid challenge</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>94.8±18.4</td>
<td>93.4±20.2</td>
<td>NS</td>
</tr>
<tr>
<td>MAP (mmHg)</td>
<td>64.1±7.9</td>
<td>75.4±11.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CVP (mmHg)</td>
<td>10.6±4.7</td>
<td>12.3±5.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PCWP (mmHg)</td>
<td>14.3±2.5</td>
<td>15.5±4.3</td>
<td>0.046</td>
</tr>
<tr>
<td>MPAP (mmHg)</td>
<td>18.7±4.1</td>
<td>21.2±4.0</td>
<td>0.005</td>
</tr>
<tr>
<td>CI (L·min⁻¹·m⁻²)</td>
<td>3.08±0.88</td>
<td>3.46±0.97</td>
<td>0.009</td>
</tr>
<tr>
<td>RVEDVI (ml/m²)</td>
<td>108.2±17.3</td>
<td>115.3±21.9</td>
<td>NS</td>
</tr>
<tr>
<td>RVEF (%)</td>
<td>31.1±8.7</td>
<td>34.4±13.5</td>
<td>0.05</td>
</tr>
<tr>
<td>SVI (ml/m²)</td>
<td>33.6±9.9</td>
<td>38.5±12.9</td>
<td>0.011</td>
</tr>
<tr>
<td>SvO₂ (%)</td>
<td>60.0±11.0</td>
<td>63.5±9.5</td>
<td>0.0043</td>
</tr>
</tbody>
</table>

Comparison was carried out using a paired t-test. Data are mean±SD. p<0.05 was considered to be statistically significant. HR, heart rate; NS, not stated; MAP, mean arterial pressure; CVP, central venous pressure; PCWP, pulmonary capillary wedge pressure; MPAP, mean pulmonary arterial pressure; CI, cardiac index; RVEDVI, right ventricular end-diastolic volume index; RVEF, right ventricular ejection fraction; SVI, stroke volume index; SvO₂, mixed venous oxygen saturation.
Using previously suggested criteria\textsuperscript{4,5} the response to fluid when RVEDVI was very high (>138 ml/m\textsuperscript{2}) or very low (<90 ml/m\textsuperscript{2}) was also analyzed. One of 2 cases in which RVEDVI was greater than 138 ml/m\textsuperscript{2} had a positive response to fluid challenge, and one of 3 cases in which RVEDVI was less than 90 ml/m\textsuperscript{2} did not have a positive response. Thus, even at these extremes, baseline RVEDVI failed to discriminate between responders and non-responders.

There was no significant difference in aortic cross-clamp time between responders and non-responders (98.7±42.9 vs 78.3±59.9 min, p>0.05). Linear regression analysis between the percentage of change in SVI and aortic cross-clamp time did not reveal any relationships ($r^2=0.04$, p>0.05).

There was no significant difference in the incidence of responders between CABG cases and non-CABG cases (0.50 vs 0.56, p>0.05). These results suggested that the influence of the types of operations on fluid responsiveness was relatively weak.

**Discussion**

A reliable bedside predictor of fluid responsiveness would be desirable in cardiac postoperative care because it would encourage aggressive fluid resuscitation when preload is inadequate and would avoid excessive volume expansion when preload is adequate.

Although cardiac filling pressures, such as CVP and PCWP, have commonly been used to guide the postoperative management of cardiac surgery, our study shows that PCWP did not provide a reliable guide to cardiac preload and fluid responsiveness as there was no correlation between PCWP and the increase in SVI. By contrast, some previous studies (which did not include cardiac surgery patients) concluded that the pressure parameters were still reliable indicators of preload and fluid responsiveness\textsuperscript{6}. The possible reason for this discrepancy is that our study specifically assessed postoperative patients who had undergone cardiac surgery. The factors that are often observed after cardiac surgery, such as edema or focal ischemia of the myocardium, easily affect ventricular compliance. Changes in cardiac compliance can lead to poor correlations between pressure and LVEDV, which make the pressure parameters of preload unreliable.

In the present study, there was a weak but significant correlation observed between baseline RVEDVI and the change in SVI following fluid challenge. Therefore, RVEDVI, as the volumetric measurement, was to some extent superior to the pressure measurements. However, although statistically significant, because the relationship between them was weak, and there was marked overlap of the RVEDVI values in responders and non-responders, RVEDVI could not be used to discriminate between responders and non-responders before fluid was administered. In particular, it should be noted that even in one case with a very high RVEDVI, there was a positive response to fluid challenge, whereas in one case with a very low RVEDVI, there was a negative response.

There were several possible reasons for RVEDVI not being an absolutely reliable marker of fluid responsiveness. First, the left ventricular response to fluid loading may be predicted by the right ventricular volume only in a limited manner. Second, the terms “cardiac preload” and “fluid responsiveness” are not always exchangeable. Because a decrease in ventricular contractility decreases the slope of the relationship between end-diastolic volume and SV and moves the Frank–Starling curve to the right. Therefore, patients with a dilated left ventricle could still respond to fluid challenge despite increased preload\textsuperscript{1,7}. It should be noted that not only baseline preload, but cardiac contractility (pressure-volume loops of each patient) affect fluid responsiveness significantly.

In conclusion, we showed that RVEDVI, which is a volumetric measurement of cardiac preload, reflected fluid responsiveness after cardiac surgery only to a limited degree. Pressure measurements, such as CVP or PCWP, did not reflect fluid responsiveness after cardiac surgery—probably as a result of changes in functional cardiac compliance due to the operation.

However, patients should not be resuscitated to an absolute RVEDVI alone; resuscitation should instead be based on their individual response to fluid administration. Because neither pressure-based nor volumetric measurements were sufficiently reliable to obviate the need for empirical fluid challenge, empirical fluid challenge should still be required in critically-ill postoperative cardiac surgery patients whose clinical picture suggests inadequate preload.
Acknowledgments

The authors thank Drs Jyunji Yamazaki, Tomio Yamada, Masaaki Inagaki, Takehiko Takayanagi, Mitsunori Miyazu and the ICU nurses at Gifu Prefectural Tajimi Hospital for their assistance.

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