Measurements of Right Ventricular Volumes during Fluid Challenge*

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The effects of fluid loading on RV function were studied in 41 acutely ill patients monitored with a modified pulmonary artery catheter equipped for measuring RVf. Hemodynamic evaluation was performed before and after infusion of 300 ml of 4.5 percent albumin solution in 30 min. Changes in SI did not correlate with Pra or Ppa but did with RVEDV1. For the entire group, RVef was unchanged (27 ± 9 vs 27 ± 9 percent). In the eight patients with an initial RVEDVi > 140 ml/m², the fluid challenge increased Pra and Ppa and reduced LSVSWI without any other significant effect. There was no significant correlation between RVEDVi and Pra and only a weak correlation between RVESVi and Ppa. However, there was a highly linear correlation between both RVEDVi and RVESVi and changes in RVEDVi and in RVESVi, suggesting that the absence of severe pulmonary hypertension RV output is primarily dependent on RV preload.

(Method) RVef = right ventricular ejection fraction; Pra = right atrial pressure; Ppa = pulmonary artery pressure; RVEDVi = right ventricular end-diastolic volume index; RVESVi = right ventricular end-systolic volume index; Ppa = pulmonary artery pressure; Pa = mean arterial pressure; SI = stroke index; LSVSWI = left ventricular stroke work index; RVSWI = right ventricular stroke work index; ANOVA = analysis of variance; LVef = left ventricular ejection fraction

Maintenance of adequate venous return is central in the management of the hemodynamically unstable patient. In this regard, intravascular fluid challenges often are employed to define preload dependency of cardiovascular function. A central mechanism in the hemodynamic response to fluid challenge consists of the relationship between cardiac preload and cardiac work output as it was initially described by Starling and Sarnoff and Berglund. Preload represents the degree of stretch of the myocardial fibers at the onset of contraction or in the intact heart, the ventricular volume at end-diastole. As ventricular volumes are difficult to obtain at the bedside, cardiac filling pressures usually are measured clinically to assess the patient's volume status and response to fluid therapy. However, cardiac filling pressures might not accurately reflect cardiac preload, as the end-diastolic pressure-volume relationship of either ventricle can be influenced by both intrinsic and extrinsic factors.

Recently, bedside measurements of RVf by the thermodilution technique have become available. Several groups of investigators demonstrated similar degrees of accuracies between gated radionuclide, first-pass radionuclide and thermodilution techniques in estimating RVf in man. The thermodilution RVf method has been used to characterize various disease states as well as the response to various therapeutic interventions. In the present study, we tested the hypothesis that measurements of RV volumes are more accurate than measurements of cardiac filling pressures to define the hemodynamic response of the acutely ill patient to fluid therapy. This study also helped to characterize the RV response to fluid challenge.

Patients and Methods

The study included 41 adult patients (58 ± 14 years) hospitalized in our Department of Intensive Care and monitored with a pulmonary artery catheter for acute respiratory failure, cardiovascular failure or fluid imbalance. Eighteen patients had evidence of bacterial infection. Thirty-one patients (76 percent) were mechanically ventilated on assisted-controlled mode, using tidal volumes of 10 to 15 ml/kg; PEEP did not exceed 10 cm H₂O. Twenty-one patients (51 percent) were treated with dopamine, dobutamine or both. Nineteen patients (46 percent) survived hospitalization.

Each patient had been monitored with a modified pulmonary artery catheter equipped with a fast response thermistor (39A-431 H-7.5 F) allowing measurement of RVf by the thermodilution technique. Normal RVf is 40 percent. The use of this modified pulmonary artery catheter had been approved by the hospital's human studies committee.

In each patient, a fluid challenge was motivated by the occurrence of one of several signs including the following: a decreased arterial pressure (systolic blood pressure below 90 mm Hg), a low CI (below 2.5 L/min m²), an increased HR (more than 120 beats per min) or a decreased urine output (less than 25 ml/h). Hence, this fluid challenge was part of their standard therapy.

Hemodynamic evaluation was performed before and after a central intravenous infusion of 300 ml of a 4.5 percent albumin solution (Stable Solution of Plasma Proteins, Red Cross of Belgium) administered in 30 min using a volumetric pump. This evaluation included measurements of mean Pa, mean Ppa, Ppa and Pra obtained at end-expiration from a paper trace (recorder HP 7404 A, Hewlett Packard). Cardiac output and RVf were measured by the thermodilution technique using three to five 10-ml injections of

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Table 1—Hemodynamic Effects of Fluid Challenge

<table>
<thead>
<tr>
<th></th>
<th>Total population (n = 41)</th>
<th>Responders (n = 26)†</th>
<th>Nonresponders (n = 15)</th>
<th>RVEDVI &lt;140 ml/m² (n = 33)</th>
<th>RVEDVI &gt;140 ml/m² (n = 8)</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Before Fluid Challenge</td>
<td>After Fluid Challenge</td>
<td>Before Fluid Challenge</td>
<td>After Fluid Challenge</td>
<td>Before Fluid Challenge</td>
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<tr>
<td>Pa, mmHg</td>
<td>69.4 ± 18.0</td>
<td>73.5 ± 17.2</td>
<td>69 ± 19</td>
<td>76 ± 18</td>
<td>71 ± 16</td>
</tr>
<tr>
<td>Ppa, mmHg</td>
<td>21.9 ± 6.1</td>
<td>23.6 ± 6.8†</td>
<td>22.7 ± 5.9</td>
<td>25.2 ± 7.3‡</td>
<td>20.2 ± 6.0</td>
</tr>
<tr>
<td>Ppao, mmHg</td>
<td>9.7 ± 3.6</td>
<td>12.8 ± 3.9‡</td>
<td>9.7 ± 3.8</td>
<td>13.5 ± 4.3‡</td>
<td>9.6 ± 3.2</td>
</tr>
<tr>
<td>Pra, mmHg</td>
<td>8.4 ± 4.2</td>
<td>10.6 ± 4.1‡</td>
<td>8.5 ± 4.4</td>
<td>10.9 ± 4.2‡</td>
<td>8.4 ± 3.5</td>
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<tr>
<td>CI, L/min/m²</td>
<td>3.1 ± 1.2</td>
<td>3.3 ± 1.3‡</td>
<td>3.0 ± 1.1</td>
<td>3.5 ± 1.2‡</td>
<td>3.2 ± 1.4</td>
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<tr>
<td>HR, beats/min/m²</td>
<td>113 ± 20</td>
<td>110 ± 19</td>
<td>112 ± 16</td>
<td>110 ± 15</td>
<td>115 ± 28</td>
</tr>
<tr>
<td>SI, ml/m²</td>
<td>27.7 ± 11.0</td>
<td>30.6 ± 11.6†</td>
<td>27.6 ± 11.2</td>
<td>32.2 ± 12.0‡</td>
<td>27.9 ± 10.5</td>
</tr>
<tr>
<td>RVef, %</td>
<td>27 ± 9</td>
<td>27 ± 9</td>
<td>27 ± 8</td>
<td>26 ± 8</td>
<td>27 ± 12</td>
</tr>
<tr>
<td>RVEDVI, ml/m²</td>
<td>108 ± 35</td>
<td>117 ± 35‡</td>
<td>104 ± 27</td>
<td>115 ± 30‡</td>
<td>117 ± 46</td>
</tr>
<tr>
<td>LVSWI, g/m²/m²</td>
<td>40.2 ± 18.6</td>
<td>45.3 ± 19.9†</td>
<td>39.6 ± 21.2</td>
<td>49.2 ± 24.4†</td>
<td>41.3 ± 16.6</td>
</tr>
<tr>
<td>RSVWI, g/m²/m²</td>
<td>9.2 ± 5.7</td>
<td>9.9 ± 5.1†</td>
<td>9.8 ± 6.9</td>
<td>11.4 ± 7.1†</td>
<td>8.2 ± 4.5</td>
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*All values are mean ± SD.
†p<0.05.
‡p<0.01 vs after fluid challenge.

Cold (<8°C) 5 percent dextrose in water via a closed system (COSet, Edwards Laboratories) and a prototype computer (REF 1, Edwards Laboratories). The injection of the cold water was started at end-inspiration to minimize the variability of cardiac output and RVef measurement. The RVef was calculated from the exponential decay of the thermodilution curve. The RVef computer used an algorithm to correct a damping effect related to catheter mounting. Stroke index was obtained by dividing CI by HR and RVEDVI by dividing SI by RVef. Left ventricular stroke work index and RVSWI were calculated by the following formulas:

\[
\text{LVSWI (in g mm Hg/m²)} = 0.0136 \text{ SI (Pa – Ppao)} \\
\text{RVSWI (in g mm H/m²)} = 0.0136 \text{ SI (Ppa – Pra)}
\]

Results were analyzed by ANOVA. A p value less than 0.05 was considered statistically significant. Results are presented as mean ± SD.

Results

For the entire population of 41 patients, the colloid infusion resulted in significant increases in Pra, Ppao, Ppa, CI and SI. Arterial pressure and HR did not change significantly. Accordingly, LVSWI and RSVWI increased significantly. The RVef, which was relatively low, remained constant so that mean SI increased proportionally to the increase in RVEDVI (Table 1). Changes in SI did not correlate with either Pra or Ppao (r = 0.21 and r = 0.12, respectively). However, there was a weak but significant correlation between the increase in RVEDVI and SI (ΔSI = 0.10 ΔRVEDVI + 2; r = 0.44, p<0.01).

The patient population was divided into two groups depending on their cardiac response to fluid challenge. In a first group of patients, CI increased (responders, n = 26). In the second group, CI either was unchanged or decreased (nonresponders, n = 15 [Table 1]). Initially, no clinical or hemodynamic parameter could distinguish the responders from the nonresponders. The responders demonstrated a significant increase in Pa, Ppa, LVSWI and RVSWI. Since RVef was unchanged in both groups, RVEDVI increased significantly only in the responders.

Patients also were divided into two groups according to their initial RVEDVI. In the eight patients with an initial RVEDVI >140 ml/m², the fluid challenge only increased Ppao and Pra, while decreasing LVSWI. These patients initially had slightly higher Ppa, SI and RSVWI, but these differences were not significant. Despite the marked difference in RVEDVI between the two groups, there were no differences in Ppao or Pra suggesting significant differences in ventricular compliance between the two groups of patients.

There was no significant correlation between Pra and RVEDVI. The mean difference in RVEDVI was 33.0 ± 14.2 ml/m² (p<0.05) (Table 1, Figure 1).

![Figure 1](http://journal.publications.chestnet.org/pdfaccess.ashx?url=/data/journals/chest/21622/ on 04/18/2017)
and RVEDVI (Fig 1) indicating various degrees of RV compliance in these patients. No patient had a mean Ppa greater than 35 mm Hg. The correlation was weak between systolic Ppa and RVESVI (Fig 2) or between mean Ppa and RVESVI (r = 0.28, p < 0.02). However, there was a strong relationship between RVESVI and RVEDVI or between changes in RVESVI and changes in RVEDVI in the 41 patients (Fig 3).

**DISCUSSION**

The determinants of the cardiovascular response to fluid challenge are complex and vary in importance in different disease states. We studied a heterogeneous population of acutely ill patients susceptible to benefit from fluid therapy. Thus, it is not surprising that the hemodynamic response to fluid challenge was variable within this population. None of the currently monitored parameters could predict the response to fluid challenge. However, we found a significant and important positive correlation between response to fluid challenge and baseline RVEDVI, suggesting that in acutely ill patients fluid resuscitation is more effective at increasing cardiac output if RVEDI is less than 140 ml/m². Interestingly, in patients with elevated RVEDVI, fluid challenge often decreased CI suggesting that ventricular overdistension could even compromise oxygen transport. As in previous studies, we saw no significant relationship between RVESVI and Rpa.

Thus, measurements of thermodilution RV volumes can be superior to measurements of cardiac filling pressures to assess the fluid requirements in the acutely ill. These measurements can be particularly helpful to recognize the patients with maximally dilated RV who are therefore not likely to benefit from fluid therapy.

The effects of fluid challenge on LVEf and RVEf are not well defined. More than 30 years ago, Sarnoff and Berglund suggested a linear relationship between fluid challenge...
stroke work and end-diastolic volume. More recently, Glower et al. induced changes in ventricular preload in chronically instrumented dogs and observed a highly linear relationship between LV stroke volume or LV stroke work and LV end-diastolic volume. On the other hand, if the relationship between stroke volume and end-diastolic volume is curvilinear, changes in LVEf should be dependent on the initial end-diastolic volume. Indeed, in dogs on right ventricular bypass, Palacios et al. observed that LVEf increased when LV end-diastolic volume was initially low, but this increase vanished at higher end-diastolic volumes.

In normal individuals, LVEf usually increases moderately following fluid challenge.24,25 After myocardial revascularization, LVEf has been found to increase,24 to remain stable26 or to decrease26 during fluid challenge in some patients. In critically ill patients with or without sepsis, three different studies have shown that LVEf was very constant during fluid challenge.27-29

The effects of fluid challenge on RV volumes have been less studied, in part because measurements of RV volumes have been more difficult. In a heterogeneous group of 28 acutely ill patients similar to ours, Calvin et al.27 observed a minor decrease in radionuclide RVEf from 30 to 28 percent during a similar fluid challenge. Responders and nonresponders had a similar hemodynamic profile. Studying the effects of volume loading in 25 patients after coronary artery bypass graft, Boldt et al.29 recently observed that the thermodilution RVEf increased in 17 patients but decreased in eight patients. Patients in this latter subgroup only had evidence of right coronary artery stenosis. In patients with septic shock, Schneider et al.28 observed a small but significant decrease in radionuclide RVEf from 45 to 41 percent during fluid challenge. The nonresponders could have a more altered RV coronary perfusion, since they had a lower Pa and a higher Ppa than the responders.

The behavior of the RV in response to fluid challenge in our study was both variable and constant between patients. It was variable in both the degree to which RV EDVI and SI changed, and it was constant in the relationship to initial RVEf despite hemodynamic changes for each patient.

The striking constancy of RVEf as RV EDVI is varied resulted in a highly linear relationship between either RV EDVI or RVESVI for all patients. Although absolute values of RV EDVI and RVESVI are mathematically coupled when they are derived from measurements of SI and RVEf, their changes are not, and similar LV volume analyses do not demonstrate this linear relationship. On the other hand, changes in RVESVI occurred independently of changes in Ppa. These observations are limited by the fact that transmural Ppa were not measured, and Ppa was measured in various ventilatory conditions. Also, Ppa was usually not elevated. The data, however, suggest that in the absence of severe pulmonary hypertension the RV is more dependent on RV EDVI than Ppa for the final RV ESVI. From this study, it appears that preload-dependent changes in SI during fluid challenge result in an obligatory directionally similar change in RV ESVI. The implications that such changes may have on RV wall stress, myocardial blood flow and systolic function remain to be defined.

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