Potential adverse effects of volume loading on perfusion of vital organs during closed-chest resuscitation

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ABSTRACT To determine whether expansion of blood volume improves vital organ perfusion pressures and blood flow during closed-chest cardiopulmonary resuscitation in dogs, we recorded intracranial and high-fidelity ascending aortic and right atrial pressures and measured total and regional blood flow with radioactive microspheres during cardiopulmonary resuscitation before and after rapid infusion of 1 liter of saline or dextran in 12 animals. Volume loading increased total forward blood flow from 327.1 ± 50.9 to 692.7 ± 105.9 ml/min (p < .01). However, blood flow to the cerebral hemispheres, cerebellum, brainstem, and ventricular myocardium all decreased significantly. For example, blood flow to the left cerebral hemisphere fell from 16.5 ± 2.4 to 5.5 ± 1.7 ml/min/100 g (p < .001), while left ventricular myocardial blood flow fell from 12.0 ± 3.1 to 4.1 ± 0.8 ml/min/100 g (p < .05). These changes in critical regional flow were accompanied by disproportionate increases in right atrial and intracranial pressures (relative to aortic pressure), which reduced the average pressure differences generated across the coronary and cerebral circulations from 11.0 ± 2.5 to 3.7 ± 1.3 mm Hg (p < .01) and from 16.1 ± 2.3 to 10.5 ± 1.5 mm Hg (p < .01), respectively. The overall rise in forward flow was associated with a marked increase in extracranial, brachiocephalic blood flow. These findings suggest that large increments in blood volume can reduce vital organ perfusion during cardiopulmonary resuscitation despite an increase in total forward blood flow.


SEVERAL years ago, Harris et al.¹ demonstrated that administration of intravenous fluid increases carotid blood flow and, in some cases, the arterial pressure generated by external chest compression. However, we suspected that these apparently beneficial effects might not be accompanied by improved vital organ perfusion for several reasons. First, coronary blood flow during cardiopulmonary resuscitation (CPR) is a function of the pressure difference generated across the coronary circulation² and occurs primarily during the relaxation or release phase of each cycle of chest compression.² ³ It seemed reasonable to expect that volume loading, by filling venous capacitance vessels, would raise right atrial as well as aortic pressure during this phase and that this effect would limit any improvement in the driving force for coronary blood flow. Second, intracranial pressure rises more during chest compression when resting intracranial pressure is elevated.⁴ By increasing cerebral blood volume, volume loading would be expected to increase resting intracranial pressure, and therefore intracranial pressure during CPR. It seemed likely that this effect would limit any improvement in the driving force for cerebral blood flow. Increased carotid¹ and total forward blood flow after volume loading could be due entirely to enhanced flow through extrathoracic, extracranial vascular beds.

The purpose of this study was to determine the effects of expansion of blood volume on vital organ perfusion pressures and blood flow during CPR. This was accomplished by recording ascending aortic, right atrial, and intracranial pressures and measuring total and regional blood flow with radioactive microspheres during CPR performed before and after rapid intravenous infusion of a large volume of saline or dextran.

Methods

Studies were performed in 12 closed-chest, mongrel dogs weighing 21.4 to 48.2 kg. A preliminary left lateral thoracotomy was performed to allow placement of a polyethylene catheter in the left atrium. In addition, a bipolar electrode was sewn to the surface of the left ventricular free wall. The left atrial
catheter and the electrical leads from the epicardial electrode were exteriorized through small incisions in the neck. The chest then was closed in layers, and the animals were allowed to recover for several days.

On the day of study, dogs were anesthetized (pentobarbital 30 mg/kg iv), intubated, and mechanically ventilated with 100% oxygen. Peak inspiratory airway pressure was adjusted to maintain arterial pH and POCO2 in the normal range when the lungs were inflated for 1 sec 12 times per minute. Sodium bicarbonate solution and additional pentobarbital were given before collection of data, when necessary. High-fidelity, micromanometer-tipped catheters (Millar), each with a separate lumen for recording fluid-filled pressures, were inserted via a femoral artery and vein and positioned in the ascending aorta and right atrium, respectively. Catheter position was confirmed fluoroscopically and by appropriate pressure recordings in all cases. The lumen of each Millar catheter was connected to a Gould P23Db pressure transducer with zero reference set at the midchest level. The solid-state pressure transducers were calibrated before insertion, and high-fidelity and fluid-filled pressures were matched before each set of pressure recordings to correct for baseline drift. In addition, a large-bore plastic catheter was positioned in the inferior vena cava to allow rapid fluid administration, and the male connector of a fluid-filled extension tube (Travenol) was inserted into a twistdrill hole in the skull to allow measurement of intracranial pressure. The proximal end of the intracranial tube was connected to a third Gould transducer, also set at the midchest level. Carotid blood flow was measured in all animals by either a Carolina Medical Electronics Model 501 or 501D square-wave electromagnetic flowmeter and a circumferential probe, or a Biotronex BL-610-2A pulsed-logic electromagnetic flowmeter with a cannulating probe placed in the left common carotid artery several centimeters above the thoracic outlet. Flow probe calibrations were performed in vitro. Reference for zero flow was determined by recording flow signals after intravascular pressures had equilibrated following induction of ventricular fibrillation. Pressures and flow signals were recorded on a Beckman Model R611 or R612 eight-channel recorder. The instantaneous difference between ascending aortic and right atrial pressures was recorded on a separate channel by means of an electronic subtraction circuit. A single intravenous dose of heparin (5000 U) was given before collection of data to retard clot formation.

Estimates of regional blood flow distribution were made with radioactive microspheres (approximately 15 μm in diameter), labeled with 113mCe, 55Co, 51Cr, 153Gd, 99mTc, 109Ru, 125I, or 111In. The microspheres were suspended in a 10% dextran solution with 0.02% polysorbate 80 (Tweem 80) and agitated for several minutes before injection to minimize aggregation. At least 2 million microspheres, followed by a 5 ml saline flush, were injected through the left atrial catheter for each measurement. The radioisotopes used and the order of injection were varied between studies.

The first microsphere injection was made under control (prearrest) conditions. Slightly before microsphere injection, blood samples were withdrawn at a constant rate through a catheter positioned in the ascending aorta. Sequential 20 sec collections were obtained in preweighed vials for a total of from 2 min and 40 sec to 3 min and 40 sec, after which pressures and carotid flow signals were recorded with respiration temporarily suspended at end-expiration. In six dogs, an additional set of samples was collected simultaneously from a second catheter positioned in the descending (abdominal) aorta.

Ventricular fibrillation then was induced by applying a low-voltage alternating current to the epicardial electrode. After recording pressures and flow signals under conditions of zero flow, anteroposterior chest compression was initiated with a modified, pneumatic chest-compression device (Michigan Instruments Life Aid Model X1004 Cardiopulmonary Resuscitator). The chest was compressed 60 times per minute with a force of 140 pounds and a compression duration equal to 50% of each cycle. The relaxation phase of the cycle was prolonged by 0.5 sec every fifth compression to allow synchronized lung inflation to the same peak inspiratory pressure used during control (prearrest) studies. Measurements of pressure and carotid blood flow were then repeated, after which two additional microsphere injections, separated by an interval of 20 sec, were performed with different radioisotopes. Slightly before the first of these injections, ascending and descending (n = 6) aortic blood samples were withdrawn at a constant rate for a total of 8 min, after which analysis of arterial blood gas and measurements of pressure and carotid flow were repeated. CPR was interrupted briefly before and after each set of recordings to correct signals for baseline drift.

One liter of either 0.9% saline or 10% dextran solution then was administered as rapidly as possible by consecutive 50 ml injections through the inferior vena caval catheter. In addition, an ampule of sodium bicarbonate solution (44.6 meq in 50 ml of water) was injected through the right atrial catheter. Pressure and flow recordings were repeated, and signals were checked for baseline drift. Two final microsphere injections, again separated by an interval of 20 sec, were then performed, and aortic blood samples were collected for a total of 8 min as described above. When collection was complete, pressure and carotid flow recordings again were repeated, and a final arterial blood sample was obtained for gas analysis.

At the conclusion of the study, aortic blood samples were reweighed, and the volume of each collection sample was calculated assuming a specific gravity for blood of 1.064. The heart, brain, brainstem, kidneys, and large samples of the temporalis muscles were removed, and the right and left ventricles, right and left cerebral hemispheres, cerebellum, temporalis muscles, and right and left kidneys were homogenized separately. Three samples of each homogenate and the entire pons and medulla were placed in vials, weighed, and counted for radioactivity along with each set of blood samples and a reference standard for each microsphere in a three-channel, well-type gamma scintillation counter (Packard Model 5230 Auto-Gamma Scintillation Spectrometer). Samples were counted for 4 min or a maximum of 2 million counts, with energy windows calibrated and adjusted for the peak emissions of the isotopes used in each animal. Specific blood and tissue activities then were corrected for radioactive "cross-talk" between isotopes.

Total forward blood flow was calculated for each microsphere injection by the following formula:

$$Q_F = \frac{C_I \times Q_B}{C_B}$$

where $Q_F$ = total forward blood flow (ml/min), $C_I$ = radioactivity of the net injectate (counts/min), $C_B$ = the sum of radioactivity in individual (20 sec) blood collections (counts/min), and $Q_B$ = the total volume of blood collected divided by the collection time (ml/min). Analysis of sequential aortic samples invariably demonstrated a residual blood radioactivity in the final sample of less than 2% of the peak level. Tissue blood flow was then calculated from each set of microsphere data according to the following relationship:

$$Q_T = \frac{C_T \times Q_I}{C_I}$$

where $Q_T$ = tissue blood flow (ml/min/100 g), $C_T$ = tissue activity (counts/min/100 g), $C_I$ = activity of the net injectate (counts/min), and $Q_I$ = total forward blood flow (ml/min).
Pressures and carotid flow signals during CPR were averaged over five compression cycles. Carotid flow recordings in two dogs were technically inadequate and were excluded from analysis. Since recordings were made before and after each 8 min period of microsphere collection during CPR, the effects of volume loading on pressures and carotid blood flow during CPR were analyzed in two ways. First, all four sets of measurements were compared. This included a comparison of measurements immediately before and after volume loading (i.e., from the end of control CPR and the beginning of volume-loaded CPR, respectively), when the opportunity for spontaneous hemodynamic changes between measurements was minimal. Second, measurements from the beginning and end of each microsphere collection period were averaged to provide representative values for control and volume-loaded CPR conditions. Total and regional blood flow during CPR before and after volume loading were analyzed by averaging the two microsphere measurements made under each set of study conditions and by comparing paired measurements under the same conditions to assess reproducibility. Data are expressed as mean values ± SEM. Statistical significance was tested either by the two-tailed Student’s t test for paired samples or by analysis of variance with multiple comparison testing (Student-Newman-Keuls) when more than two data groups were compared.

Results

Pressures during prearrest and both CPR conditions are summarized in Table 1. The mean ascending aortic–right atrial pressure difference produced by CPR decreased from 9.8 ± 2.7 mm Hg immediately before to 4.0 ± 1.4 mm Hg immediately after volume loading (p < .01). This resulted primarily from a disproportionate increase in right atrial pressure (relative to aortic pressure) during the relaxation phase of each cycle chest compression (Figure 1). The mean aortic-intracranial pressure difference during CPR averaged 14.7 ± 2.5 mm Hg immediately before and 11.8 ± 2.0 mm Hg immediately after volume loading (a decrease of borderline statistical significance). This trend toward a lower cerebral perfusion pressure resulted primarily from a disproportionate increase in intracranial pressure (relative to aortic pressure) during the compression phase of each cycle (Figure 2). The mean aortic–external jugular pressure difference generated during CPR decreased immediately after volume loading in four of five dogs in which external pressures were measured, although mean values did not differ significantly (Table 1). Mean aortic–right atrial, aortic–intracranial, and aortic–external jugular pressure differences based on averages of values from the beginning and end of each period of microsphere collection were all significantly lower after volume loading (Table 2). Peak aortic pressure, which increased immediately after volume loading (Table 1), did not differ significantly between the two CPR conditions when averages of values from the beginning and end of each period of microsphere collection were compared. This reflected the fact that all recorded pressures tended to increase during the time required for microsphere collections both before and after volume loading (Table 1). Mean circulatory and resting intracranial pressures increased after volume loading by both methods of analysis (all p < .01).

The effects of volume loading on microsphere estimates of total and regional blood flow during CPR are

### Table 1

<table>
<thead>
<tr>
<th>Pressure (mm Hg) and carotid blood flow (ml/min)</th>
<th>Mean aortic–right atrial pressure difference</th>
<th>Mean aortic–intracranial pressure difference</th>
<th>Mean aortic–external jugular pressure difference</th>
<th>Mean resting circulatory pressure</th>
<th>Mean cerebral pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peak aortic pressure</strong></td>
<td><strong>Peak right atrial pressure</strong></td>
<td><strong>Peak intracranial pressure</strong></td>
<td><strong>Carotid blood flow</strong></td>
<td><strong>Mean aortic–right atrial pressure difference</strong></td>
<td><strong>Mean aortic–intracranial pressure difference</strong></td>
</tr>
<tr>
<td>(n = 12)</td>
<td>(n = 12)</td>
<td>(n = 12)</td>
<td>(n = 10)</td>
<td>(n = 12)</td>
<td>(n = 12)</td>
</tr>
<tr>
<td>Prearrest</td>
<td>148.6±6.5</td>
<td>0.8±0.7</td>
<td>9.4±2.4</td>
<td>189.2±29.8</td>
<td>141.1±5.7</td>
</tr>
<tr>
<td>Control CPR</td>
<td>47.9±4.7</td>
<td>42.7±4.5</td>
<td>19.5±1.9</td>
<td>26.7±6.0</td>
<td>12.3±2.5</td>
</tr>
<tr>
<td>Control CPR</td>
<td>40.1±5.6</td>
<td>38.8±5.3</td>
<td>12.1±2.7</td>
<td>14.9±3.8</td>
<td>9.8±2.7</td>
</tr>
<tr>
<td>Volume CPR</td>
<td>54.3±5.7</td>
<td>57.8±5.3</td>
<td>30.2±3.7</td>
<td>43.9±6.1</td>
<td>4.0±1.4</td>
</tr>
<tr>
<td>Volume CPR</td>
<td>37.9±3.4</td>
<td>41.5±3.5</td>
<td>17.7±1.8</td>
<td>36.3±4.4</td>
<td>3.3±1.4</td>
</tr>
</tbody>
</table>

Resting intracranial pressure = intracranial pressure during ventricular fibrillation without CPR; mean circulatory pressure = equilibrated aortic and right atrial pressures during ventricular fibrillation without CPR; control CPR and control CPR = measurements before and after microsphere collection during control CPR; volume CPR, and volume CPR = measurements before and after microsphere collection during volume-loaded CPR. Prearrest values are shown for comparison but were not included in statistical analyses.

*Phasic intracranial pressures were not recorded before microsphere collection during control CPR in one dog.

<table>
<thead>
<tr>
<th>p &lt; .05 vs control CPR</th>
<th>p &lt; .05 vs control CPR</th>
<th>p &lt; .01 vs control CPR</th>
<th>p &lt; .01 vs control CPR</th>
<th>p &lt; .01 vs volume CPR</th>
</tr>
</thead>
</table>
| The observed and the critical differences between means for p < .05 vs Control CPR were 2.9 and 3.7 mmHg, respectively.

Vol. 69, No. 1, January 1984
summarized in table 3. Volume loading increased total forward blood flow from 327.1 ± 50.9 to 692.7 ± 105.9 ml/min (p < .01) (based on an average of the two measurements made under each set of CPR conditions). However, blood flow to the cerebral hemispheres, cerebellum, brainstem, kidneys, and ventricular myocardium all decreased significantly. For example, blood flow to the left cerebral hemisphere decreased from 16.5 ± 2.4 to 5.5 ± 1.7 ml/min/100 g (p < .001), and average left ventricular myocardial blood flow decreased from 12.0 ± 3.1 to 4.1 ± 0.8 ml/min/100 g (p < .05). However, extracranial, brachiocephalic blood flow increased substantially after volume loading, as indicated by a rise in flow to the temporalis muscles from 1.2 ± 0.2 to 6.0 ± 1.2 ml/min/100 g (p < .01). This was accompanied by a significant increase in common carotid blood flow whether measurements immediately before and after volume loading (table 1) or an average of values from the beginning and end of each period of microsphere collection were compared (table 2) (both p < .01). There were no apparent differences between the effects

FIGURE 1. Aortic and right atrial pressure recordings during CPR immediately before and after volume loading. Small solid arrows indicate the onset of consecutive chest compressions; large solid arrows indicate the onset of synchronized lung inflation. Volume loading increased the aortic pressure generated during CPR but decreased the mean pressure difference across the coronary circulation. This was due to a greater increase in right atrial pressure, particularly during the relaxation phase of each cycle of chest compression (large open arrow). Control CPR and Volume CPR = CPR immediately before and after volume loading, respectively.

FIGURE 2. Carotid blood flow and aortic and intracranial pressure recordings during CPR before and after volume loading. Volume loading increased intracranial pressure more than aortic pressure, particularly during the compression phase of each CPR cycle. Increased carotid flow was due to a marked increase in extracranial, brachiocephalic blood flow. Arrows and labels are defined in the legend for figure 1.
TABLE 2
Average pressures (mm Hg) and carotid blood flow (ml/min) during CPR

<table>
<thead>
<tr>
<th></th>
<th>Peak aortic right pressure</th>
<th>Peak intra-cranial pressure</th>
<th>Carotid blood flow</th>
<th>Mean aortic-right atrial pressure difference</th>
<th>Mean aortic-intra-cranial pressure difference</th>
<th>Mean aortic-external jugular pressure difference</th>
<th>Resting intra-cranial pressure</th>
<th>Mean circulatory pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control CPR</td>
<td>44.0 ± 4.8</td>
<td>40.7 ± 4.4</td>
<td>15.8 ± 2.1</td>
<td>11.0 ± 2.5</td>
<td>16.1 ± 2.3</td>
<td>28.3 ± 6.1</td>
<td>5.7 ± 0.5</td>
<td>5.7 ± 0.8</td>
</tr>
<tr>
<td>Volume CPR</td>
<td>46.1 ± 4.3</td>
<td>49.7 ± 4.1</td>
<td>24.0 ± 2.6</td>
<td>3.7 ± 1.3</td>
<td>10.5 ± 1.5</td>
<td>16.7 ± 4.9</td>
<td>11.4 ± 1.4</td>
<td>10.5 ± 1.6</td>
</tr>
</tbody>
</table>

Pressures and flows were calculated by averaging measurements made before and after microsphere collection under each CPR condition. Definitions are the same as in table 1. Control CPR and volume CPR represent CPR before and after volume loading.

*p < .05 vs control CPR.

*p < .01 vs control CPR.

*p < .001 vs control CPR.

of saline and dextran on either coronary or cerebral perfusion pressures or blood flow during CPR.

Duplicate estimates of total and regional blood flow under the same CPR conditions did not differ significantly. Figures 3 to 5 demonstrate the reproducibility of these measurements with regard to total forward blood flow and regional flow to the cerebral hemispheres and ventricular myocardium.

Total flow calculations based on paired ascending and descending aortic reference samples did not differ significantly for any of the four measurements made during CPR. Likewise, blood flow to paired organs was comparable under all conditions. Specifically, mean tissue flows did not differ significantly between the right and left kidneys, the right and left cerebral hemispheres, or the right and left cardiac ventricles, either before or after volume loading (table 3).

Blood gas analyses are summarized in table 4.

Discussion

The results of this study suggest that expansion of blood volume during CPR can decrease coronary and cerebral perfusion and increase both carotid and total forward blood flow. Before considering possible explanations for these paradoxic effects, it is important to establish that the microsphere techniques used in this study were valid under the present experimental conditions. This method of estimating total and regional blood flow requires uniform mixing of microspheres with blood.5,6 Theoretically, the low flow conditions of CPR might permit nonuniform streaming of microspheres due to inadequate proximal mixing or sedimentation. However, we found no evidence of unequal blood flow to paired organs either before or after volume loading (table 3) and obtained comparable estimates of total forward flow with reference samples from two different arterial sites. Furthermore, total and regional blood flow measurements during CPR were highly reproducible both before and after volume loading (figures 3 to 5), and changes in both coronary and cerebral blood flow after volume loading followed similar directional changes in perfusion pressures. These observations are consistent with the results of other recent studies that have validated these methods under similar experimental conditions7 and are strong evidence against a systematic error in our results due to nonuniform streaming of microspheres.
TABLE 3

<table>
<thead>
<tr>
<th>Total and regional blood flow</th>
<th>Tissue blood flow (ml/min/100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total forward blood flow (ml/min)</td>
</tr>
<tr>
<td>Prearrest</td>
<td>2906.3 ± 422.4</td>
</tr>
<tr>
<td>Control CPR</td>
<td>327.1 ± 50.9</td>
</tr>
<tr>
<td>Volume CPR</td>
<td>692.7 ± 105.9</td>
</tr>
</tbody>
</table>

Prearrest values are shown for comparison but were not included in statistical analyses. CPR data represent an average of the two microsphere measurements made under each condition. Abbreviations are explained in the legends for tables 1 and 2.

The decrease in blood flow to the right kidney after volume loading was of borderline statistical significance (p < .07).

* p < .05 vs control CPR.

** p < .01 vs control CPR.

*** p < .001 vs control CPR.

** p = NS vs right cerebrum.

** p = NS vs right ventricle.

** p = NS vs right kidney.

Since control CPR was performed first in each of our experiments, it is also important to establish that the changes in regional perfusion pressures and blood flow distribution observed after volume loading were not caused by spontaneous hemodynamic deterioration. We found that all recorded pressures tended to decrease during the course of microsphere collections both before and after volume loading (table 1). However, two observations indicate that the changes in pressures and blood flow observed after volume loading in our studies were primarily caused by expansion of blood volume. First, decrements in both coronary and cerebral perfusion pressures were apparent immediately after volume loading (table 1), when the opportunity for spontaneous changes between measurements was minimal. Second, coronary and cerebral perfusion decreased after volume loading despite an increase in both carotid and total forward blood flow. Therefore the hemodynamic changes that followed volume loading were not the result of a progressive failure of CPR to maintain an artificial circulation. Although we had reasoned that the effects of volume loading on right atrial and intracranial pressures might prevent an increase in coronary and cerebral blood flow after volume loading, we did not expect driving pressures and blood flow to these organs to decrease. To explain these findings, it is necessary to consider more carefully how coronary and cerebral perfusion pressures are generated during CPR and to speculate on the mechanism by which volume loading increases total forward blood flow.

Since circulatory pressures equilibrate during ventricular fibrillation, the genesis of a pressure difference across the coronary circulation during CPR re-
TABLE 3
(Continued)

<table>
<thead>
<tr>
<th>Tissue blood flow (ml/min/100 g)</th>
<th>Left ventricle</th>
<th>Temporalis muscles</th>
<th>Right kidney</th>
<th>Left kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>78.4 ± 5.7</td>
<td>15.4 ± 3.8</td>
<td>293.3 ± 26.0</td>
<td>298.4 ± 29.6</td>
<td></td>
</tr>
<tr>
<td>12.0 ± 3.1(\text{a})</td>
<td>1.2 ± 0.2</td>
<td>31.5 ± 7.9</td>
<td>28.5 ± 7.7(\text{c})</td>
<td></td>
</tr>
<tr>
<td>4.1 ± 0.8(\text{a})</td>
<td>6.0 ± 1.2(\text{c})</td>
<td>17.0 ± 4.0(\text{a})</td>
<td>14.8 ± 3.3(\text{a},\text{g})</td>
<td></td>
</tr>
</tbody>
</table>

requires a net transfer of blood from the venous to the arterial circulation. The magnitude of the pressure difference created during each cycle of chest compression depends on the net amount of blood transferred from veins to arteries and on the pressure-volume relationships of the arterial and venous vascular beds. For example, if only a small volume of blood were shifted from the venous to the arterial system, and both vascular beds were highly compliant, CPR would cause a slight increase in transmural arterial pressure, a slight decrease in transmural venous pressure, and only a small arteriovenous pressure difference. Transfer of a larger volume of blood, or of the same volume between less compliant vessels, would cause greater changes in transmural arterial and venous pressures and a larger mean pressure difference. Since blood vessels, like other biologic tissues, possess nonlinear pressure-volume characteristics, their operative level of compliance decreases as a function of volume. As a result, the same net transfer of blood from veins to arteries during CPR would be expected to create a greater mean central arteriovenous pressure difference (averaged throughout the two systems) after volume loading (figure 6). A lower mean pressure difference (as suggested by the fall in both aortic–right atrial and aortic–external jugular pressure differences in our study) can result only from a smaller net change in blood volume distribution. This is true regardless of the specific relationships between arterial and venous volumes and compliances or the mechanism of blood flow during CPR (assuming that intrathoracic and other extravascular pressures are applied in the same proportion to arteries and veins before and after volume loading).

How, then, can volume loading increase total forward blood flow yet reduce the net amount of blood shifted from the venous to the arterial circulation during CPR? Although this study was not designed to answer this question, the observation that temporalis muscle blood flow increased several times despite a fall in the aortic–external jugular pressure difference suggests that volume loading increases forward blood flow during CPR primarily by decreasing systemic vascular resistance. We believe that this effect (presumably due to vascular distention and decreased blood viscosity) creates a circumstance in which the flow of blood can increase with less net translocation of blood volume. Conceptually, if fluid is pumped through a closed system consisting of two rigid tubes separated by a source of resistance, pressure will rise abruptly in the tube that receives fluid from the pump, and flow will occur without significantly changing the volume of fluid in either tube (figure 7). However, if the tube into which fluid is pumped is distensible, its volume will increase until the pressure difference across the resistance rises sufficiently to allow forward flow. The volume of fluid redistributed at equilibrium will depend on both the resistance to flow and the compliance of the tubes. Specifically, the lower the resistance and the stiffer the tubes, the less the net change in volume. Assuming that these considerations apply in principle to pulsatile flow during CPR, it is apparent that a substantial decrease in systemic vascular resistance theoretically could increase forward flow.

![FIGURE 5](image-url)

FIGURE 5. Duplicate measurements of myocardial blood flow during CPR before and after volume loading. Paired measurements made under the same conditions were reproducible and demonstrated comparable directional changes for both ventricles. Data groups are defined in the legend for figure 3.
while reducing both blood volume redistribution and central arteriovenous pressure differences. We cannot be certain to what extent a spontaneous decrease in vasomotor tone may have contributed to lower resistance and its consequences after volume loading in our studies. However, the immediate (and opposite) effects of expansion of blood volume on brachiocephalic perfusion pressures and carotid blood flow (table 1) suggest that volume loading itself can have a major effect on systemic vascular resistance during CPR.

Although standard CPR generates substantial brachiocephalic arteriovenous pressure differences, the driving force for cerebral blood flow during CPR is limited by the increase in intracranial pressure caused by chest compression. Large increments in blood volume presumably potentiate this adverse effect by expanding intracranial contents to the limits of the cranial vault. Since the skull is effectively rigid, any additional increase in intracranial volume causes a significant increase in pressure. As a result, volume loading not only increases resting intracranial pressure but also greatly exaggerates the further rise in pressure caused by additional, small increments in intracranial volume during chest compression. We cannot be certain whether these effects in our study were due primarily to an increase in cerebral blood volume or to cerebral edema. However, the aortic-intracranial pressure difference generated during CPR fell immediately after volume loading (table 1), and saline and dextran had similar effects, suggesting that increased blood volume was an important factor.

The distribution of blood flow during CPR ultimately depends on regional differences in both perfusion pressures and vascular resistance. Although not well documented in this setting, autoregulatory mechanisms presumably cause coronary and cerebral resistance vessels to dilate maximally in response to the low perfusion pressures present during CPR. By reducing driving pressures when flow is primarily pressure dependent, volume loading decreases both coro-
nary and cerebral blood flow. In addition, cerebral vascular resistance may actually increase as a result of local edema (a possibility suggested by the finding that cerebral blood flow fell proportionately more after volume loading than did the aortic-intracranial pressure differences generated by CPR) (tables 1 to 3). In contrast, vascular resistance in peripheral organs such as skeletal muscle is ordinarily high in low output states because of low resting oxygen requirements and sympathetic nervous system-mediated vasoconstriction. By decreasing resistance in these vascular beds, volume loading allows local blood flow to increase even though perfusion pressures fall. This is exemplified by the more than fourfold increase in blood flow to the temporalis muscles observed after volume loading despite lower mean aortic-external jugular pressure differences. The observation that renal blood flow decreased after volume loading is more difficult to explain, since it is likely that renal vascular resistance was high during control CPR studies. It is possible that CPR provoked more intense vasoconstriction in the kidneys than in skeletal muscle and that this effect prevented a fall in renal vascular resistance after volume loading.

The basic observation that expansion of blood volume can increase both total and carotid blood flow while decreasing flow to the heart and brain emphasizes the quantitative importance of blood flow to nonvital organs during CPR and has important implications for both the clinical application and study of resuscitation techniques. We recently reported that standard CPR is several times more effective in producing carotid blood flow than coronary blood flow. Although we still believe that generalized changes in intrathoracic vascular pressures intrinsically limit the driving force for coronary flow during CPR, our previous comparisons of carotid and coronary blood flow were based on observations made in animals given saline before induction of ventricular fibrillation. In retrospect, it is likely that this exaggerated the observed differences in relative blood flow by increasing carotid flow and decreasing coronary flow. Although external chest compression produces higher arteriovenous pressure differences across extrathoracic, bra-chiocephalic vascular beds than across the coronary circulation, extracranial carotid blood flow in the absence of hypervolemia is limited by high vascular resistance.

In conclusion, we found that coronary and cerebral blood flow during CPR decreased after volume loading, even though carotid and total forward blood flow increased. The amount of fluid administered in each of our experiments was large relative to the size of the animals studied, and it is not known whether smaller changes in blood volume would have similar effects. Furthermore, the hemodynamic changes observed after volume loading in our studies may have been influenced to some extent by a spontaneous fall in systemic vascular resistance. It is possible that volume expansion would have different effects on regional blood flow distribution during CPR if accomplished immediately after the onset of ventricular fibrillation, or if vascular resistance were maintained pharmacologically. However, our findings point out a potentially important dissociation between the effects of volume loading on total forward blood flow and coronary and cerebral perfusion and suggest that blood volume expansion is unlikely to be beneficial as an isolated intervention during CPR.

We thank Stephen Bell, Holly Collier, Donna Orchison, Jane Smoak, and Victoria Travis for their expert technical assistance, and Barbara Breckenridge, Carole Becker, and Jeanne Boschi for typing the manuscript.

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Circulation. 1984;69:181-189
doi: 10.1161/01.CIR.69.1.181

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