The Splanchnic Blood Volume in Congestive Heart Failure

By Elliot Rapaport, Myron H. Weisbart, and Milton Levine

With the technical assistance of Pasquale Cifarelli and Armen Renjilian

Little data have been accumulated regarding the contribution of regional volumes to the increased total blood volume observed in congestive heart failure. This report deals with the measurement of splanchnic blood volume in 12 patients in congestive heart failure compared with results obtained in 10 control subjects similarly studied.

The total blood volume in congestive heart failure has been the subject of extensive investigation. Although there are isolated reports failing to demonstrate a consistently increased volume,1,2 the overwhelming body of evidence obtained with both plasma3-5 and red-cell tags6-8 leaves little doubt that total blood volume is increased in the majority of patients having overt evidence of congestive heart failure.

Lack of suitable methodology has limited the knowledge of the contribution of various regional volumes to total blood volume. An exception is the attention that has been focused on the cardiopulmonary blood volume measured by the Stewart-Hamilton indicator-dilution technique. An expanded cardiopulmonary blood volume in association with heart failure has been found by Kopelman and Lee,9 by Borden, Ebert, Wilson and Wells,10 and by Doyle, Wilson, Lepine and Warren.11 Bradley, Marks, Reynell and Meltzer12 have recently introduced a method of measurement of splanchnic blood volume. The purpose of the study here described was to assess the possibility that an expanded splanchnic blood volume contributes to the increased total blood volume in patients manifesting congestive heart failure.

Methods and Procedures

Splanchnic plasma volume (T 1824 space) was measured in 12 patients with moderate-to-severe congestive heart failure, and splanchnic blood volume was approximated by use of the hematocrit level of blood from a large vessel. Similar studies were made of 10 normal control subjects of comparable age. The normal cases either had been hospitalized for study of nonorganic complaints or were convalescing from minor illnesses; none had evidence of significant cardiovascular disease. All of the patients and controls were males. Studies were carried out in the fasting, unsedated state and with the subject recumbent. A priming dose of 100 mg. bromsulphalein was injected intravenously, following which a solution of bromsulphalein in 5 per cent dextrose in water was infused at a constant rate with a Bowman pump. An average of 3.9 mg. of bromsulphalein per minute was administered. Right heart catheterization was performed in the usual manner, after which the catheter was placed in a branch of the right hepatic vein. Pressures were recorded in the wedged and free positions. Three to 4 brachial arterial and hepatic vein samples were then simultaneously withdrawn at 8- to 10-minute intervals for determination of hepatic blood flow. Samples were also taken midway through the last period for oxygen analysis. One minute after withdrawal of the last samples, a measured amount of T 1821 was injected intravenously. Coincident with injection, sampling was begun from the brachial artery and hepatic vein by means of a constant suction pump.13 Multiple samples were collected continuously at 45-second intervals for a period of 225 to 280 seconds. Samples for determination of total blood volume were obtained at 10 and 20 minutes after injection or occasionally at 20 and 30 minutes. Samples taken for bromsulphalein analyses were centrifuged and a 1:30 dilution of plasma was analyzed in duplicate in a Coleman colorimeter at a wavelength of 580 mμ, following addition of 1 to 2 drops of 10 per cent sodium hydroxide. The samples collected for T 1824 dye analyses were centrifuged, and the undiluted plasma was analyzed in a Beckman D. U. spectrophotometer at a wavelength of 620 mμ. Hematocrit levels were corrected for trapped plasma as suggested by Gregersen.14 Oxygen analyses were performed by the method of Van Slyke and Neill.15 Cardiac output was determined by the direct Fick

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method. Estimated hepatic blood flow was calculated by the method of Bradley and associates.\textsuperscript{25} Values obtained only during periods when the plasma bromsulphalein concentration was changing at a rate of less than 0.0003 mg. per minute were utilized. Splanchnic blood volume was calculated according to the method introduced by Bradley\textsuperscript{23} as modified for errors in delay time or collection as suggested by Rabinowitz and Rapaport. Equilibration was assumed to have occurred when hepatic and arterial concentrations of T 1524 approached to within 5 per cent of equality and did not significantly diverge thereafter. The ratio of hepatic vein-arterial concentration difference in the equilibration samples to the final equilibration concentration averaged 2.1 per cent.

**RESULTS**

The results of this study are summarized in tables 1 and 2. The coefficient of variability is significantly less when the splanchnic and total blood volumes are calculated at the time of study in terms of body weight rather than body surface area. Therefore the volumes in table 2 are expressed in ml. per Kg. The flow data in tables 1 and 2 are corrected for body surface area, as is customary.

Although therapeutic measures had been started in most of the cases of congestive fail-

![Image](http://circ.ahajournals.org/)

**Table 1.—Hemodynamic Data in Twelve Patients with Congestive Heart Failure**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Age (yrs.)</th>
<th>Weight (Kg.)</th>
<th>Surface Area (M²)</th>
<th>Total O₂ consumption (ml/min./M²)</th>
<th>Arterial-venous O₂ difference (ml./l.)</th>
<th>Direct Fick cardiac index (l./min./M²)</th>
<th>R.A. (mm. Hg.)</th>
<th>P.A. (mm. Hg.)</th>
<th>Wedged hepatic vein (mm. Hg.)</th>
</tr>
</thead>
<tbody>
<tr>
<td>G.C.</td>
<td>H.C.V.D.</td>
<td>62</td>
<td>55.7</td>
<td>1.55</td>
<td>154</td>
<td>63</td>
<td>2.5</td>
<td>209/104</td>
<td>53/23</td>
<td>5</td>
</tr>
<tr>
<td>H.F.</td>
<td>Cor P.</td>
<td>62</td>
<td>63.4</td>
<td>1.76</td>
<td>112</td>
<td>40</td>
<td>2.8</td>
<td>135/73</td>
<td>41/22</td>
<td>6</td>
</tr>
<tr>
<td>A.H.</td>
<td>R.H.D.</td>
<td>61</td>
<td>55.9</td>
<td>1.61</td>
<td>139</td>
<td>43</td>
<td>3.2</td>
<td>157/73</td>
<td>50/21</td>
<td>9</td>
</tr>
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<td>47</td>
<td>78.0</td>
<td>1.94</td>
<td>149</td>
<td>51</td>
<td>2.9</td>
<td>119/82</td>
<td>28/20</td>
<td>6</td>
</tr>
<tr>
<td>J.M.</td>
<td>Cor P.</td>
<td>66</td>
<td>63.6</td>
<td>1.75</td>
<td>125</td>
<td>53</td>
<td>2.4</td>
<td>128/77</td>
<td>52/28</td>
<td>7</td>
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<tr>
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<td>R.H.D.</td>
<td>41</td>
<td>79.1</td>
<td>2.00</td>
<td>131</td>
<td>92</td>
<td>1.4</td>
<td>122/83</td>
<td>112/53</td>
<td>18</td>
</tr>
<tr>
<td>W.P.</td>
<td>R.H.D.</td>
<td>60</td>
<td>72.3</td>
<td>1.92</td>
<td>155</td>
<td>84</td>
<td>1.8</td>
<td>152/95</td>
<td>83/41</td>
<td>15</td>
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<td>J.P.</td>
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<td>89.5</td>
<td>2.05</td>
<td>131</td>
<td>69</td>
<td>1.9</td>
<td>119/70</td>
<td>73/40</td>
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<tr>
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<td>Cor P.</td>
<td>60</td>
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<td>1.88</td>
<td>82</td>
<td>56</td>
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<td>136/78</td>
<td>67/27</td>
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<td>1.89</td>
<td>134</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
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</tr>
<tr>
<td>W.K.</td>
<td>R.H.D.</td>
<td>47</td>
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<td>1.72</td>
<td>125</td>
<td>106</td>
<td>1.2</td>
<td>109/68</td>
<td>68/43</td>
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<td>C.B.</td>
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<td>75</td>
<td>2.7</td>
<td>126/76</td>
<td>66/40</td>
<td>20</td>
</tr>
</tbody>
</table>

B.A., brachial artery; P.A., pulmonary artery; R.A., right atrium; H.C.V.D., hypertensive cardiovascular disease; Cor P., cor pulmonale; R.H.D., rheumatic heart disease; A.S.H.D., arteriosclerotic heart disease.
congestive heart failure patients as a group. The average flow in the heart failure cases was 674 ml. per minute per M² (S.D. 257). The differences between the means of the 2 groups is 1.5 times the standard error of the differences of the means.

Splanchnic oxygen consumption was similar in the 2 groups, averaging 41.7 ml. per M² (S.D. 11) in the normal subjects and 42.6 (S.D. 4.3) in the failure group. Mean arterial-hepatic venous oxygen difference was 71 ml. per L. (S.D. 32) in the congestive heart failure group as contrasted to a mean of 51 ml. per L. (S.D. 10) in the normal group.

Total blood volume was markedly elevated in the congestive heart failure group and averaged 79.8 ml. per Kg. (S.D. 12.5) compared to a mean of 62.1 ml. per Kg. (S.D. 7) in the normal group. Splanchnic blood volume (average 20.8 ml. per Kg., S.D. 5.6) was similarly increased among the patients with congestive heart failure compared to the normal subjects (12.7 ml. per Kg., S.D. 2.2). The differences of both parameters are statistically highly significant.

Comments

Blood Flow

Cardiac output was reduced in this group of patients with congestive heart failure. This finding is in agreement with a number of previous studies.17-20

It was of interest that the reduction in estimated hepatic blood flow in 5 of the 12 cases in which it occurred was roughly proportional to the reduction in cardiac output. Thus the ratio of estimated hepatic blood flow to cardiac output either remained normal or was increased in the group with congestive heart failure over the normal controls. Myers and Hickam17 found an estimated hepatic blood flow significantly reduced in patients with congestive heart failure. They noted that the fall in hepatic blood flow was proportional to the fall in cardiac output. The importance of these observations is that they suggest no mechanism for selective reduction in splanchnic blood flow in patients with congestive failure. They serve to emphasize that maintenance of hepatic blood flow is important to the body economy and that the reduction that may occur in congestive heart failure is not out of proportion to the general reduction in cardiac output. In this respect the action of the splanchnic bed differs strikingly from that of the kidney, where a reduction in blood flow occurs much out of proportion to the reduction in cardiac output in patients with congestive heart failure.20

There was close agreement between splanchnic oxygen uptake in the normal control group and that in the patients with congestive heart failure. Since hepatic blood flow tended to be reduced, it follows that the extraction of oxygen by the splanchnic bed was greater in the congestive heart failure group than in the controls.

The extraction ratios of bromsulphalein averaged 36 per cent (range 15 to 60 per cent) in the failure patients compared to 40 per cent (range 18 to 74 per cent) in the controls. In no case did extraction fall below 15 per cent, and therefore the validity of the flow data was not considered jeopardized. Extraction ratios of bromsulphalein vary inversely with the arterial concentration. Thus the absence of an apparent difference between the 2 groups of subjects is misleading. When the data are expressed as milliliters of arterial plasma completely cleared of bromsulphalein per minute per M² (table 2), a definite impairment in the ability of the congestive heart failure group to remove bromsulphalein is seen. Bromsulphalein clearance averaged 205 ml. of plasma per minute per M² (S.D. = 89) in the normal group as compared to 116 ml. per minute per M² (S.D. = 55) in the group with congestive heart failure (p = .01).

Blood Volume

The basic tenets of the Bradley method for determination of splanchnic blood volume are described in detail elsewhere.12 Among these is the assumption that all the plasma tag within the splanchnic bed remains in the intravascular space during the 4 minutes or so necessary for equilibration. This assumption
TABLE 2.—Hemodynamic Data of Hepatic and Splanchnic Circulation in 12 Patients with Congestive Heart Failure

<table>
<thead>
<tr>
<th>Patient</th>
<th>Estimated hepatic blood flow (ml./min./M.²)</th>
<th>Ratio hepatic blood flow/cardiac output (%)</th>
<th>Arterial-venous oxygen difference (ml./l.)</th>
<th>Splanchnic G uptake (ml/min./M.²)</th>
<th>Splanchnic blood vol. (ml./kg.)</th>
<th>Total blood vol. (ml./kg.)</th>
<th>Ratio splanchnic blood vol./total blood vol. (%)</th>
<th>Derived mean transit time (sec.)</th>
<th>Plasma HSP (mg./ml.)</th>
<th>Hematocrit</th>
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<td>36.0</td>
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<tr>
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<td>47.3</td>
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Congestive failures

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<th>71</th>
<th>42.6</th>
<th>29.8</th>
<th>79.8</th>
<th>26.5</th>
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<td>12.5</td>
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Normal

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<th>51</th>
<th>41.7</th>
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<th>295</th>
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<tbody>
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<td>11.0</td>
<td>2.2</td>
<td>7.0</td>
<td>5.1</td>
<td>7.5</td>
<td>89</td>
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</table>

Significance of differences:

\[ p > .1 \quad \text{and} \quad p > .05 \quad \text{and} \quad p > .01 \quad \text{and} \quad p < .01 \quad \text{and} \quad p < .05 \quad \text{and} \quad p < .001 \]

in means.

may be a tenuous one in respect to patients with congestive heart failure, where some extravascular loss and removal by lymphatic drainage could occur during this interval. However, Milnor and Crary were unable to demonstrate evidence of rapid loss of T 1824 from the plasma of patients with congestive heart failure; unfortunately their methods were not designed to study the disappearance rate during the first 2 to 4 minutes after injection. Samet and co-workers concluded that an abnormal rate of plasma T 1824 loss is unlikely in patients with congestive heart failure, since the concentration obtained by extrapolating to zero time was independent of the amount of dye injected or of the time interval over which the injection was made. Calculations in our cases based on subsequent disappearance slopes of dye concentrations, and the assumption that approximately 25 per cent of the total loss took place in the splanchnic bed, together with the observation that hepatic venous concentration of T 1824 is not demonstrably lower than the arterial following equilibration, suggest that splanchnic extravascular loss during the first 4 minutes is not sufficient to affect materially the calculated volumes. The defense of plasma tags for measurement of total blood volume by Schreiber and co-workers in patients with
SPLANCHNIC BLOOD VOLUME IN CONGESTIVE HEART FAILURE

Congestive heart failure is particularly applicable, because the total duration of measurement from injection to regional equilibration is brief.

The use of any plasma tag and the large vessel hematocrit for calculation of splanchnic blood volume will result in values somewhat greater than those that actually exist, because the ratio of splanchnic to large vessel hematocrit is less than unity. Comparisons by Lilienfield and associates,23 of mean circulation times across the splanchnic bed following simultaneous injection of plasma and red cell tags suggest that this ratio is in the vicinity of 0.84 in patients with heart failure. A splanchnic-to-large vessel hematocrit ratio of 0.91 has been observed in normal subjects.24 Thus, depending on the large vessel hematocrit in any given case, the use of only a plasma tag will result in overestimation of splanchnic blood volume of approximately 8 per cent in the failure cases and around 4 per cent in the normal persons. The differences in splanchnic blood volume observed in this study are considerably greater than this, and differences between large vessel and splanchnic bed hematocrit are thought to play no significant role in the results obtained.

The possibility exists that the blood samples for T-1824 concentration obtained with the catheter from one of the hepatic veins are not representative of the T-1824 concentration of blood simultaneously emerging from other areas of the liver. The same theoretic objection applies to the measurement of hepatic blood flow by the bromsulphalein technic. The random use of different branches of the right hepatic vein in both patients and control subjects might produce some variation in results in any individual case; however, it seems unlikely that sampling variation in itself could be responsible for the significant mean increase in splanchnic blood volume observed in the congestive heart failure patients compared to the control group.

This increase in splanchnic blood volume in the congestive heart failure cases is even more strikingly reflected in terms of the average of the mean transit times across the splanchnic bed. Mean transit time calculated by dividing the splanchnic volume by the respective splanchnic flow averaged 85.6 seconds for the failure population as contrasted to 36.9 seconds for the normal group.

The average increase in splanchnic blood volume exceeded that observed in total blood volume. The mean ratio of splanchnic blood volume to total blood volume averaged 20.8 per cent in the normal controls, a value similar to that found by others.25 This ratio was increased to 26.5 per cent in the patients with congestive heart failure. Thus, the splanchnic bed as well as the heart and lungs contributes to the increased total blood volume seen in congestive heart failure. The data imply that the splanchnic bed is relatively more distensible than other comparable venous beds, accepting a proportionally greater volume of blood in response to the same common elevated central venous pressure. This is not meant to infer that augmented venomotor tone, generally regarded as largely responsible for the increased venous pressure in congestive heart failure,26 does not involve the splanchnic bed. However, the demonstration that there is more than a 50 per cent mean increase in the amount of blood normally present in the splanchnic bed in congestive failure, or a volume out of proportion to the increase in total blood volume, makes it reasonable to assume that the increased volume within the splanchnic bed plays an important role in maintaining the venous hypertension of this bed, irrespective of whether or not increased venomotor tone is present.

Anatomic studies suggest that the bulk of the splanchnic blood volume is contained within the hepatic and portal venous systems.27 If one views the splanchnic reservoir as a passive elastic container, one expects the volume contained within to vary, within wide limits, as a function of the distending venous pressure.28 Table 1 lists the values observed for right atrial mean and wedged hepatic vein pressures in these cases. The pressure gradient between the wedged and free hepatic vein positions did not exceed 2 mm. Hg in
any subject. Four of the patients (G.C., H.F., G.K. and E.S.) had atrial and portal venous pressures (as estimated by the hepatic vein wedge technic) within the normal range. Although still edematous at the time of study, these patients had responded to therapy with considerable diuresis and a reduction of venous pressure into the normal range. In these patients with normal intrahepatic sinusoidal and portal vein pressures, no significant increase in the volume of blood within the splanchnic bed was observed. The significant correlation of relatively moderate degree noted between wedged hepatic venous pressure and the splanchnic blood volume \( (r = +.64, p < .05) \) suggests that the amount of blood contained within the splanchnic bed in congestive heart failure is intimately associated with the level of the distending venous pressure.

**SUMMARY**

The splanchnic blood volume was measured in 12 patients with congestive heart failure, and the results were compared with 10 normal persons.

Although splanchnic blood flow may be reduced in congestive failure, splanchnic blood volume is consistently increased. The splanchnic bed acts as a major reservoir for the increased total blood volume observed in these patients.

It is suggested that the enlarged splanchnic reservoir observed in congestive failure is an important factor in maintaining the venous hypertension of this bed.

**SUMMARIO IN INTERLINGUA**

Le volumine de sanguine splanchnic esseva mesurate in 12 patientes con congestive disfallimento cardiae. Le resultatos esseva comparate con illos obtenite in 10 casos normal.

Ben que le fluxo del sanguine splanchnic es rednicate congestive disfallimento cardiae, su volumine es uniformemente augmentate. Le vasculatura splanchnic age como un major reservoir pro le augmentate volumine total de sanguine que es observate in iste patientes.

Es suggerite que le allargate reservoir splanchnic observate in disfallimento congestive es un factor importante in mantenere le hypertension de iste vasculatura.

**REFERENCES**


11. Doyle, J. T., Wilson, J. S., Lepine, C., and Warren, J. V.: An evaluation of the meas-

A physician may possess the science of Harvey and the art of Sydenham, and yet there may be lacking in him those finer qualities of heart and head which count for so much in life.—British Medicine in Greater Britain. Montreal Med. Journal, 1897.
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