The Influence of Atrial Pressure on Cardiac Performance Following Myocardial Infarction Complicated by Shock

By R. D. Bradley, B.Sc., M.B., B. S. Jenkins, M.B., M.R.C.P.,
and M. A. Branthwaite, M.R.C.P., F.F.A.R.C.S.

SUMMARY
Performance curves for both sides of the heart were derived in six patients with acute myocardial infarction complicated by cardiogenic shock. Stroke index and right and left ventricular stroke work index were related to mean atrial pressures which were lowered by venesection. Values for cardiac index, stroke index, and stroke work index were all low, and little change occurred with alterations in atrial pressures. The relationship of right and left atrial pressures to the genesis of pulmonary edema is discussed, and the effects of isoproterenol (isoprenaline) are described.

Additional Indexing Words:
Bilateral function curves Pulmonary edema Transseptal puncture
Isoproterenol

ACUTE myocardial infarction accompanied by signs of clinical shock carries a high mortality.\(^1,2\) Accurate hemodynamic information may be difficult to obtain in such patients,\(^3\) but it is widely accepted that cardiac output and stroke volume are reduced.\(^4,6\)

One determinant of stroke volume is ventricular filling pressure,\(^7,8\) and this may be reduced if there is a fall in blood volume. Several studies have reported a decrease in blood volume in cardiogenic shock,\(^9,10\) and infusion of fluid has been advocated to restore ventricular filling pressure, or even to elevate it to greater than normal levels, in an attempt to increase stroke volume.\(^9,11-13\) The normal heart responds to an increase in filling pressure by raising stroke volume and stroke work, but this ability is impaired in heart failure\(^14\) so that the benefit of volume expansion following myocardial infarction remains uncertain. An increased blood volume may be hazardous because myocardial infarction selectively depresses the function of the left ventricle in most instances. A small increment in right ventricular filling pressure is then accompanied by a much larger increase in left ventricular filling pressure, and mean left atrial pressure may rise therefore to the level at which pulmonary edema occurs.\(^15\)

The present study was undertaken to evaluate the effect of alterations of filling pressure in patients suffering from acute myocardial infarction complicated by cardiogenic shock and pulmonary edema.

Methods
Six patients were studied 36 hours to 10 days following acute myocardial infarction confirmed by ECG and enzyme studies. All showed the clinical features of cardiogenic shock which were defined\(^16\) as pallor, hypotension, restlessness, disturbance of consciousness, peripheral vasoconstriction, and anuria with or without a raised central venous pressure. All but patient 5 had clinical and radiologic evidence of pulmonary edema at the time of the study, which was only undertaken when it was judged that survival was...
improbable with conventional treatment. The disturbance of consciousness in these critically sick patients was such that informed consent could be obtained in only one instance (case 6). Clinical details and initial hemodynamic data are given in tables 1 and 2.

The patients lay either supine (case 5) or with the head of the bed elevated 45°. Four were breathing oxygen-enriched air throughout the study; cases 1 and 4 were studied during intermittent positive pressure ventilation.

Pressure measurements were all referred to zero at the sternal angle and were made using Statham P23Db transducers and recorded on an Elema-Schönander Mingograf recorder. The frequency response of this system with the finest catheters used in the study is linear to 10 Hz, falling to 50% at 20 Hz, with no resonant frequency. Mean pressures were obtained electronically.

Cardiac output was measured by the thermal dilution technic, and standard formulae were used to calculate stroke volume, cardiac index, left and right ventricular stroke work, and systemic and pulmonary vascular resistance. The ECG was recorded continuously and no disturbance of rhythm could be attributed to the procedure.

Systemic arterial pressure was recorded through a short cannula in the femoral artery. Right atrial pressure was measured through a 20-cm catheter inserted into the right internal jugular vein and advanced to the junction of the superior vena cava and right atrium. This catheter was also used for the injection of the thermal indicator (5% dextrose at room temperature).

A nylon catheter (ID, 0.5 mm) carrying a thermistor at its tip was floated into the pulmonary artery and was used to record both pulmonary arterial pressure and the thermal dilution signal.

Left atrial pressure was derived from end-diastolic pulmonary arterial pressure in cases 1, 2, and 3. In cases 4, 5, and 6, left atrial pressure was recorded directly by use of a modified transseptal technic. This approach was chosen in preference to retrograde left ventricular catheter-

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr), sex</th>
<th>Time since onset</th>
<th>Outcome</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>56 M</td>
<td>4 days</td>
<td>Survived</td>
<td>Inferior infarct 2 yr previously; mild angina since; new massive anterolateral infarct</td>
</tr>
<tr>
<td>2</td>
<td>62 F</td>
<td>5 days</td>
<td>Died</td>
<td>Diabetic with extensive arterial disease; inferior infarct, complicated by diabetic ketosis; no PM</td>
</tr>
<tr>
<td>3</td>
<td>66 M</td>
<td>2 days</td>
<td>Died</td>
<td>PM confirmed massive LV infarct (lateral wall and septum); multiple acute duodenal ulcers; one perforated with acute generalized peritonitis</td>
</tr>
<tr>
<td>4</td>
<td>55 M</td>
<td>36 hr</td>
<td>Died</td>
<td>Inferior infarct 2 yr previously; angina since; PM showed 75% infarction of LV; multiple acute gastric ulcers; one perforated</td>
</tr>
<tr>
<td>5</td>
<td>58 M</td>
<td>10 days</td>
<td>Died</td>
<td>Anterolateral infarct 10 days previously with pulmonary edema, shock, and arrhythmias. Subsequent recovery followed by further collapse on 10th day, with cardiac arrest just prior to study. Calculated PVR (7 units) suggested pulmonary embolism rather than further infarction. PM showed pulmonary embolism and extensive infarction of both ventricles. Terminal hematemesis from acute gastro-duodenal erosions</td>
</tr>
<tr>
<td>6</td>
<td>53 M</td>
<td>4 days</td>
<td>Survived</td>
<td>Anterolateral infarct; condition improved following venesection; isoprenaline therefore withheld</td>
</tr>
</tbody>
</table>

Abbreviations: PM = postmortem examination; PVR = pulmonary vascular resistance.
Hemodynamic Data Prior to Manipulation of Filling Pressure

<table>
<thead>
<tr>
<th>Case</th>
<th>SA (m²)</th>
<th>CI (L/min/m²)</th>
<th>Rate &amp; rhythm</th>
<th>SAP (mm Hg)</th>
<th>PAP (mm Hg)</th>
<th>MLAP (mm Hg)</th>
<th>MRAP (mm Hg)</th>
<th>SVR (units)</th>
<th>PVR (units)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.6</td>
<td>2.1</td>
<td>120 SR</td>
<td>100/70</td>
<td>40/30</td>
<td>30</td>
<td>6.5</td>
<td>19.8</td>
<td>0.9</td>
</tr>
<tr>
<td>2</td>
<td>1.7</td>
<td>1.2</td>
<td>90 SR</td>
<td>80/40</td>
<td>35/24</td>
<td>24</td>
<td>10.0</td>
<td>19.8</td>
<td>1.8</td>
</tr>
<tr>
<td>3</td>
<td>1.53</td>
<td>2.3</td>
<td>140 SR</td>
<td>90/40</td>
<td>30/15</td>
<td>15</td>
<td>2.0</td>
<td>14.3</td>
<td>1.2</td>
</tr>
<tr>
<td>4</td>
<td>1.65</td>
<td>1.0</td>
<td>60 SR</td>
<td>80/50</td>
<td>26/12</td>
<td>12.5</td>
<td>2.0</td>
<td>22.0</td>
<td>3.0</td>
</tr>
<tr>
<td>5*</td>
<td>1.8</td>
<td>1.15</td>
<td>100 SR</td>
<td>85/55</td>
<td>53/34</td>
<td>24</td>
<td>6.0</td>
<td>27.0</td>
<td>8.3</td>
</tr>
<tr>
<td>6</td>
<td>1.7</td>
<td>2.4</td>
<td>100 SR</td>
<td>85/70</td>
<td>43/26</td>
<td>25.5</td>
<td>4.0</td>
<td>17.1</td>
<td>1.2</td>
</tr>
</tbody>
</table>

*Patient was already receiving isoproterenol.

Abbreviations: SA = surface area; CI = cardiac index; SAP = systemic arterial pressure; PAP = pulmonary arterial pressure; MLAP = mean left atrial pressure; MRAP = mean right atrial pressure; SVR = systemic vascular resistance; PVR = pulmonary vascular resistance.

zation to avoid arrhythmias provoked by the passage of a catheter through the left ventricular outflow tract. Use of pulmonary wedge pressure to obtain repeated, simultaneous measurements of both left atrial and pulmonary arterial pressure is inconvenient, and the small right heart catheters used in this study do not wedge. It was felt that use of a larger right heart catheter would increase the risk of arrhythmias and that the modified transseptal technic described below would carry least hazard. The method enables transseptal puncture to be performed at the bedside in orthopaedic subjects. The apparatus is illustrated in figure 1.

A Teflon catheter (ID, 1.15 mm; OD, 1.75 mm; length, 33 cm) with a Luer hub on the proximal end, is inserted into the right internal jugular vein by the Seldinger technic. The tip of this catheter is pulled down so that it will just permit the passage of a 19-gauge wire. A constant flushing device is connected to the hub of the catheter, and this has a shaft seal at its proximal end through which the transseptal needle assembly is introduced.

The transseptal needle is made from two concentric lengths of steel tubing, the outer 19 gauge, and the inner 26 gauge. The outer shaft, 40 cm long, is blunt and its distal 5 cm is bent into a shallow curve. When the inner needle (41 cm long) is protruded, its tip continues the curve of the outer shaft. The bevel of the inner needle is on the concavity of this curve. At the proximal end, the needles are mounted separately in two solid Teflon blocks, drilled to continue the lumen of each. These two blocks are joined by stainless steel guide rods, and by moving the Teflon block supporting the inner needle along these rods, the sharp tip of the inner needle may be protruded or withdrawn within the outer shaft.

The Teflon block supporting the outer shaft carries an insulated socket which permits intracardiac ECG recording. This socket also indicates the direction in which the curved tip of the needle is pointing.

The needle assembly, with the inner needle sheathed, is introduced through the shaft seal of the flushing device until its tip protrudes 1 cm beyond the end of the Teflon catheter in the right atrium (this distance is determined by previous measurement). The mid-atrial point is located by means of a portable image intensifier, or by using the shaft of the needle as an ECG probe. At this level, the needle is rotated so that the curve points posteromedially, and with the outer shaft held firmly against the septum, the inner needle is protruded and passes through the septal wall. Entry into the left atrium is confirmed by a change of pressure and by the aspiration of oxygenated blood. The whole catheter system is then advanced about 1 cm, and this movement carries the outer shaft through the septum. The

---

**Figure 1**

Catheter and needle used for transseptal puncture.
inner needle is withdrawn into the shaft and the Teflon catheter is advanced with the shaft into the left atrium. The needle assembly is then withdrawn through the shaft seal and is replaced by a fine Teflon catheter (ID, 0.4 mm) which can be advanced into the left ventricle. In this study, the fine Teflon catheter was withdrawn to the left atrium to minimize the risk of ventricular arrhythmias.

Serial measurements of pressure and flow were obtained when atrial pressure was decreased by controlled, rapid venesection. On each occasion, both dynamic and mean pressures were recorded; cardiac output and pulse rate were measured simultaneously immediately afterward. Each value for cardiac output was the mean of at least three determinations which were made in rapid succession.

In subject 1, with gross pulmonary edema (see fig. 4A), the initial value for mean left atrial pressure was 30 mm Hg and for mean right atrial pressure, 7 mm Hg, falling to 21 and 3 mm Hg, respectively, with the institution of intermittent positive pressure ventilation. In cases 3 and 4, the initial value for mean left atrial pressure was 15 mm Hg or less, and this was raised by the transfusion of dextran or dextrose. During transfusion, mean left atrial pressure was never elevated above 24 mm Hg, and repeated measurements of oxygen tension, respiratory rate, or inflation pressure in subjects maintained on intermittent positive pressure ventilation did not suggest any accumulation or worsening of pulmonary edema.

Hemodynamic observations were made when the mean left atrial pressure was elevated, either spontaneously or following transfusion, and were repeated serially 5 min after the withdrawal of 100 to 200 ml of blood, up to a maximum of 600 ml. In case 6, mean left atrial pressure had only fallen 5 mm Hg as a result of venesection. Bilateral thigh cuffs were therefore applied and measurements were repeated with one and then both cuffs inflated.
In view of the poor cardiac performance of these subjects, in infusion of isoproterenol (isoprenaline, 1 to 2 μg/min), was established in all but case 6. The blood (which had been collected in sterile acid-citrate-dextrose solution) was reinfused, keeping the mean left atrial pressure below 24 mm Hg. The entire procedure, recording pressure and flow during controlled venesection, was then repeated while isoprenaline was infused. One patient (case 5) was unable to maintain a circulation without the support of this drug and was only studied therefore during infusion of isoprenaline. In case 3, the effect of an infusion of adrenaline (10 μg/min) was also recorded in the same manner.

Results

The results are presented graphically in figure 2 and show the relation between mean atrial pressure and stroke work index, stroke index, and cardiac index for each side of the heart. The changes in heart rate, pulmonary and systemic arterial pressure, stroke work index, stroke index, and cardiac index, which were produced by altering atrial pressure, are shown for each individual patient in figure 3A to F, and the effects of isoprenaline or adrenaline are also shown when applicable.

Discussion

Cardiac performance is frequently related to ventricular end-diastolic pressure.8, 14 In the normal heart, there is little difference between mean atrial and ventricular end-diastolic pressure, but in the presence of left ventricular failure, these pressures may differ considerably.20 The relationship between mean atrial pressure and stroke index or stroke work index then reflects the combined performance of the atrium and ventricle,21 and in the cases reported here, all indices of performance are related to mean atrial pressure for each side of the heart. Knowledge of overall performance, rather than that of the ventricle alone, may be of greater value in the management of patients with severe circulatory failure. An additional advantage gained from the recording of mean left atrial pressure is that it provides an indication of pulmonary venous pressure which is one of the principal determinants of the development of pulmonary edema.22

The value of end-diastolic pulmonary arterial pressure as an indirect estimate of mean left atrial pressure has been investigated in a previous study when it was shown that there is close correlation between these two values when the pulmonary vascular resistance is normal (r = 0.95). In the present series end-diastolic pulmonary arterial pressure was used instead of mean left atrial pressure in the first three cases. One patient (case 1) had sustained a myocardial infarct 2 years previously and had suffered from mild angina since. Apart from this instance, none of these three patients had any previous history of cardiorespiratory disease or any evidence of pulmonary embolism. Arterial oxygen tension exceeded 55 mm Hg while the subjects were breathing oxygen-enriched air; arterial carbon dioxide tension lay between 33 and 49 mm Hg and pH between 7.27 and 7.42.

Measurements of cardiac output using the Fick or indicator-dilution technics may prove unreliable when stable conditions cannot be achieved, or if the circulation time is prolonged as it is when the cardiac output is low or the central blood volume is enlarged.8, 23 Errors in the indicator-dilution technic are largely due to recirculation, and this may be minimized by approximating the sites of injection and sampling4, 23 or avoided by eliminating recirculation. In the thermal dilution technic, the indicator is injected into the right atrium, and temperature change is recorded in the pulmonary artery; with this technic, recirculation has not been detected in man. The absence of recirculation enables the area under the curve to be derived by use of a simple integrating device, and with the addition of a computing element, a numerical value for cardiac output can be displayed within a few seconds of the complete inscription of the curve.24 Multiple measurements can be made in rapid succession and produce no measurable change in body temperature. The effect of variations in stroke volume caused by atrial fibrillation or ectopic beats can be minimized by recording six or more thermal dilution curves as quickly as possible and calculating the mean value.
Figure 3
ATRIAL PRESSURE AND CARDIAC PERFORMANCE

The relationship between stroke work or stroke volume and filling pressure obtained in this investigation is not a "ventricular function curve" such as might be demonstrated in an isolated heart preparation under conditions of constant heart rate, afterload, and sympathetic stimulation. It is rather a description of the activity of each side of the heart in response to changes in filling pressure when the heart is integrated in a reactive circulation. When the circulation is intact, variations in intravascular volume provoke a variety of reflex changes which tend to minimize changes in stroke volume or stroke work. However, it has been shown that a decrease in ventricular end-diastolic pressure achieved by balloon inflation in the inferior vena cava is followed by a decrease in cardiac index, stroke volume, and stroke work. In patients with impaired left ventricular function, the response is similar, but the curves relating stroke volume or stroke work to ventricular end-diastolic pressure are lower and flatter than those obtained in normal subjects.

It is preferable to express myocardial performance in terms of the relationship between stroke work and filling pressure rather than stroke volume and filling pressure. In the cases reported here, all values for stroke work index are low, and there is little variation, particularly in left ventricular stroke work index, with changes in atrial pressure. It is perhaps worthy of note that the two surviving subjects (nos. 1 and 6) had the highest initial values for left ventricular stroke work index (more than 10 g-m/m²). The values for both stroke index and cardiac index are also low, and the changes produced by alterations in atrial pressure are very small. Again the two surviving subjects differ from the rest in that they show some decrease in cardiac index with a fall in atrial pressure; in case 6, stroke index as well as cardiac index fell when atrial pressure was reduced.

The relationship between the performance of the two sides of the heart is illustrated in figures 2 and 3, and the slope of the line relating stroke index to mean atrial pressure is less for the left than the right heart in cases 1, 4, 5, and 6 so that small changes in right atrial pressure are accompanied by large changes in the corresponding left atrial pressure. A small increase in right atrial pressure can therefore raise left atrial pressure to the level at which pulmonary edema develops, and similarly, a small decrease in right atrial pressure (produced by drugs, diuresis, or the hypovolemia of prolonged vasoconstriction) may be sufficient to decrease left atrial pressure below the threshold value for the formation of pulmonary edema. Once pulmonary edema has developed, it may take some time to clear, and this could explain the demonstration of a low left atrial pressure with pulmonary edema in patients following myocardial infarction. Alternatively, capillary permeability could be abnormal or the concentration of plasma proteins reduced. The plasma protein concentration for all subjects reported here was within normal limits.

The clinical implication of these findings is that in patients with poor myocardial performance, increases in atrial pressure do little to improve cardiac output. Unless therapy is guided by measurements of left atrial pressure, pulmonary edema can be

Figure 3

(A to F). The influence of changes in atrial pressure on systemic and pulmonary arterial pressure, heart rate, stroke work index, stroke index and cardiac index for individual cases; the effect of isoprenaline or adrenaline. Symbols and abbreviations: = without isoprenaline; × = with isoprenaline; = with adrenaline; R = right heart; L = left heart PAP = mean pulmonary arterial pressure (mm Hg); FAP = mean femoral arterial pressure (mm Hg), in case 2 pressure was measured in the radial artery; HR = heart rate (beats/min); SWI = stroke work index (g-m/m²); SI = stroke index (ml/m²); CI = cardiac index (L/min/m²).

Circulation, Volume XLII, November 1970
Figure 4

Case 1. X-rays (A) before and (B) 12 hours after the study.

Figure 5

Case 6. X-rays (A) before and (B) 12 hours after the study.

precipitated with only small changes in right atrial pressure. In patients with less severely disordered function, changes in atrial pressure may be of greater value in improving output. By applying these conclusions to the cases reported here, it was possible to select for each patient a right atrial pressure which would yield the maximum stroke output.
ATRIAL PRESSURE AND CARDIAC PERFORMANCE

Commensurate with a left atrial pressure which allowed the reabsorption of pulmonary edema. The chest x-rays of cases 1 and 6 before and 12 hours after treatment are reproduced in figures 4 and 5.

In case 2, stroke work index, stroke index, and cardiac index rose when mean atrial pressure was reduced, suggesting an apparent negative slope to the function curve. Similar findings were recorded in dogs by Case and associates who demonstrated a selective descending limb of the left ventricular function curve when left ventricular stroke work was related to mean left atrial pressure during the restriction of left coronary flow. The instability of a descending limb to the function curve has been discussed by Katz and Ross and Braunwald who were unable to demonstrate a descending limb to the ventricular function curve in patients with left ventricular failure who were subjected to changes in left ventricular end-diastolic pressure produced by balloon inflation in the cava. The same authors, however, have demonstrated a descending limb in some patients with impaired left ventricular function when left ventricular end-diastolic pressure rose following the elevation of aortic pressure with an infusion of angiotensin and the changes seen in our case 2 may reflect the effect of an alteration in afterload.

There is a logical difficulty to accepting the possibility of a decrease in stroke volume with an increase in filling pressure for both ventricles. Such a configuration implies inverse changes in stroke output from the two sides of the heart and either an ever-increasing or decreasing central blood volume. The negative slopes recorded here may not be significant. Alternatively, they could exist within the framework of a stable circulation if each of the points contributing to the negative slope lay upon a separate curve of ventricular function, each with a positive slope, the ventricle improving its state of contractility between each set of observations. Finally, cardiac performance was related here to mean atrial pressure, so that the effect on ventricular performance alone may be obscured by changes in atrial behavior or the competence of the atrioventricular valves.

The effects of isoprenaline are shown in figure 3A to F, and improved performance of varying magnitude was demonstrated in cases 1, 2, and 4 and presumed in case 5 in which circulation could not be maintained without the support of this drug. In addition to the increase in cardiac index, stroke index, and stroke work index at any atrial pressure, the slope of the performance curves is increased; this implies restoration or improvement in the ability of the heart to respond favorably to a rise in atrial pressure.

In case 3 no change in cardiac performance could be demonstrated following the infusion of isoprenaline and the change produced in case 4 was very small. Marginal improvement in performance followed the infusion of adrenaline in case 3.

Occasional ventricular extrasystoles were present in several subjects; the infusion of isoprenaline produced no apparent increase in the frequency of these ectopic beats, and their incidence did not warrant therapy in any subject.

Acidosis or hypoxia impair the ability of the heart to respond to catecholamines and Lockett has demonstrated a detrimental effect when isoprenaline is used to perfuse the isolated, failing heart. Isoprenaline increases myocardial oxygen consumption and a limited coronary flow may be unable to meet this demand, particularly if coronary perfusion pressure is decreased by the effect of the drug on systemic vascular resistance. Angina during the infusion of isoprenaline has been reported and it is possible that the massive infarction commonly reported in patients following a prolonged period of cardiogenic shock treated with inotropic agents is a reflection of this therapy. Postmortem information was available in three of the four fatal cases in this group and showed evidence of massive myocardial infarction. These three patients also suffered some complication of peptic ulceration as a terminal event. The relation of this to the severity of the disease or
the nature and duration of therapy remains uncertain.

References
1. OLIVER MF, JULIAN DG, DONALD KW: Problems in evaluating coronary care units: Their responsibilities and their relation to the community. Amer J Cardiol 20: 465, 1967

Circulation, Volume XLII, November 1970
32. Ross J Jr, Braunwald E: The study of left ventricular function in man by increasing resistance to ventricular ejection with angiotensin. Circulation 29: 739, 1964
The Influence of Atrial Pressure on Cardiac Performance Following Myocardial Infarction Complicated by Shock

R. D. BRADLEY, B. S. JENKINS and M. A. BRANTHWAITE

_Circulation_. 1970;42:827-837
doi: 10.1161/01.CIR.42.5.827

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1970 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/42/5/827

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/