CARDIOGENIC SHOCK AND ITS CURRENT TREATMENT

PARKLAND MEMORIAL HOSPITAL

MEDICAL GRAND ROUNDS

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James T. Willerson, M. D.

Each year more than 600,000 people in this country die from coronary artery disease. Power failure of the heart and its most extreme manifestation, cardiogenic shock, remain the single most common cause of hospital mortality in acute myocardial infarction. The definition of cardiogenic shock as provided by the myocardial infarction research units of the National Heart and Lung Institute is listed in Table 1.

Table 1

Definition of Cardiogenic Shock

1. A peak systolic arterial pressure of less than 90 mm Hg or 30 mm Hg below the previous basal level
2. Evidence of reduced blood flow as shown by:
   a. Urine output of less than 20 ml/hr
   b. Impaired mental function
   c. Peripheral vasoconstriction associated with a cold, clammy skin

Specifically excluded from the definition of cardiogenic shock are the phenomena listed in Table 2 below.

Table 2

Shock Other Than Cardiogenic Shock

1. Hypotension related to pain
2. Hypotension related to vasovagal reaction
3. Hypotension related to cardiac rhythm disturbances such as a ventricular or AV junctional rhythm and loss of atrial contribution to cardiac output
4. Drug reactions especially those related to cardiac medications such as parenteral quinidine or procaine amide
5. Hypotension related to hypovolemia

Summary

Cardiogenic shock means the occurrence of a shock syndrome resulting from primary cardiac dysfunction.

Problems related to the definition of cardiogenic shock are listed in Table 3.

Table 3

Problems Related to Identification of Cardiogenic Shock

1. There are clear differences in arterial pressure measured by the standard blood pressure cuff and those measured with a direct arterial needle. The latter may be 10-20 mm Hg higher than those measured with a cuff so classification does depend on how measurements are made.
2. Urine volume or cerebral function may be preserved in individuals who otherwise appear to be clearly in cardiogenic shock.
3. There is as yet no precise hemodynamic characterization of these patients though generally (*but not always*) they do have a depressed cardiac output and cardiac index, increased left ventricular end-diastolic pressure, or mean pulmonary capillary wedge pressure, and decreased left ventricular stroke work.

CLINICAL GROUPS OF PATIENTS WITH CARDIOGENIC SHOCK

1. Group I. Patients admitted with severe circulatory collapse and hypotension. These patients generally have a large area of acutely developing left ventricular ischemia that is the result of occlusion of the proximal portion of a major coronary artery. These patients usually die within minutes or hours following their admission. The occasional young patient with his first myocardial infarction that presents in cardiogenic shock is usually in this group of patients.

2. Group II. Patients develop cardiogenic shock while in the hospital as a relatively late or late complication of their myocardial infarction. This most commonly is the result of an extension of the area of myocardial infarction and this group is usually composed of patients with several previous myocardial infarctions.

NECESSARY HEMODYNAMIC MEASUREMENTS

Table 4 describes the recommended measurements that should be made in patients in cardiogenic shock. The frequency with which these measurements are made depends on the given clinical situation. Figure 1 demonstrates the recently developed Swan-Ganz catheter for measuring pulmonary artery and pulmonary capillary wedge pressures. This catheter has a balloon cuff near the tip. The catheter is inserted into a peripheral vein and from there passed into the right atrium. At that location 0.4 cc of air is

placed into the balloon and the catheter is then "floated" ("flow directed") out into the pulmonary artery where pulmonary artery pressures can be measured. Inflation of the balloon with 0.8 cc of air occludes the pulmonary artery and pulmonary venous pressure as transmitted through the pulmonary capillaries can be measured from the tip of the catheter distal to the balloon. The mean pulmonary capillary wedge pressure is the same as the left ventricular end-diastolic pressure in the absence of mitral valve disease (Fig. 2). This catheter can be positioned in the pulmonary artery without the aid of fluoroscopy but despite advertisement to the contrary it is much easier to do under fluoroscopy. This catheter seems to produce fewer ventricular ectopic beats in its passage through the right ventricle than do the larger and previously more commonly used catheters to measure pulmonary artery pressures. Complications related to passage and relatively long-term placement of the Swan-Ganz catheter have been few in number but include sepsis, breakage, and pulmonary embolization of the balloon material, and rarely ventricular tachycardia and/or ventricular fibrillation related to the presence of the catheter in the right ventricle.

Table 4

Hemodynamic Monitoring of Patients in Cardiogenic Shock

Continuous

1. Electrocardiogram
2. Systemic arterial pressure (indwelling radial, brachial, or femoral arterial catheter)
3. Pulmonary arterial pressure (Swan-Ganz catheter)
4. Urine flow (indwelling Foley catheter)

Intermittent

1. Pulmonary capillary wedge pressure (Swan-Ganz catheter)
2. Central venous pressure (optional measurement)
3. Arterial pO_2, pCO_2, and pH
4. Cardiac output
5. Chest film
6. Temperature
7. Hematological parameters
8. Renal function tests
9. Serial complete electrocardiograms
10. Cardiac enzymes

Figure 1

Swan-Ganz Catheter for Measuring Pulmonary Artery and Pulmonary Capillary Wedge Pressures

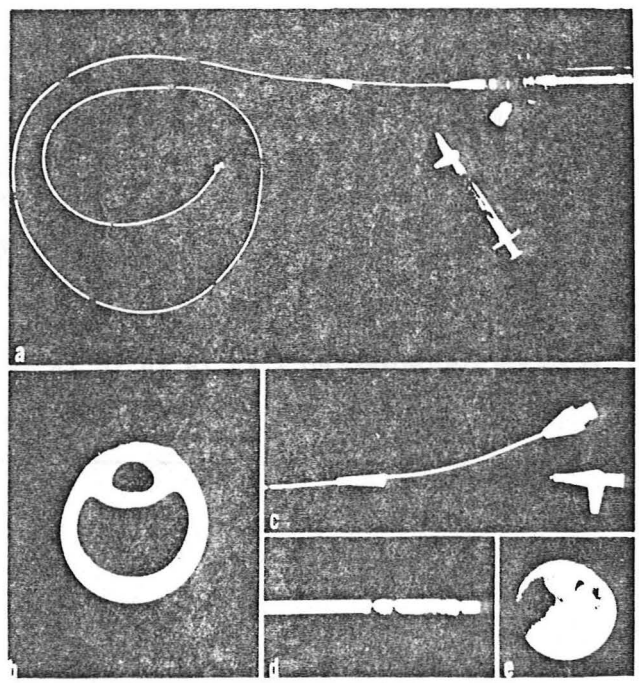
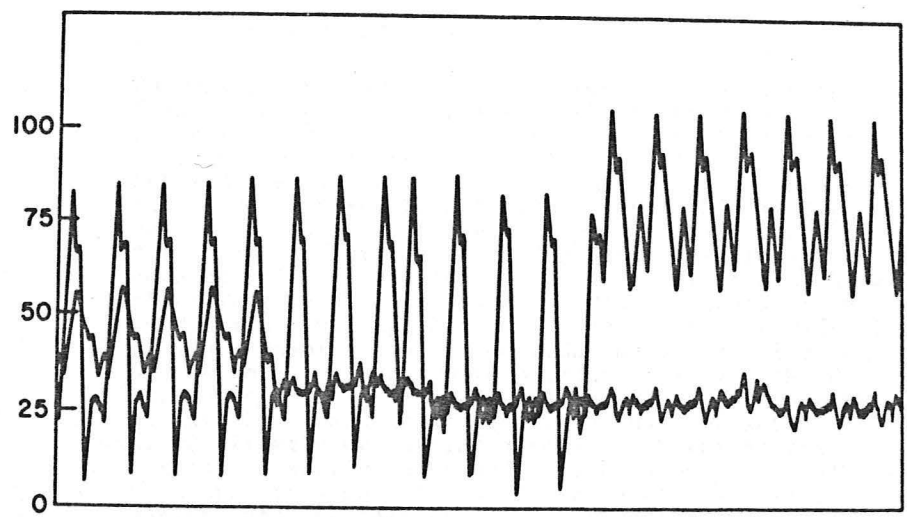


Figure 2

Relationship Between Left Ventricular End-Diastolic Pressure and Pulmonary Capillary Wedge Pressure (Swan-Ganz Catheter)



Legend: Shown above are simultaneous pulmonary artery and left ventricular pressures (left), pulmonary capillary wedge and left ventricular pressures (center), and pullback from left ventricle to aorta (right).

MEASUREMENTS OF LEFT VENTRICULAR FILLING PRESSURE (LVEDP)

This hemodynamic measurement is of crucial importance in patients in cardiogenic shock in order to assure that volume expansion is not a therapeutic consideration and in order to assess the efficacy of therapeutic measures employed. Table 5 summarizes the different methods used to measure LVEDP.

Table 5

Methods Used to Measure LVEDP

1. Pulmonary capillary wedge pressure (Swan-Ganz catheter). This is the most common way in which LVEDP is measured currently and the one that we employ in the coronary care unit at Parkland Memorial Hospital.
2. Scheinman *et al.* have used pulmonary artery end-diastolic pressure and have suggested that this is the equivalent of mean left atrial pressure and LVEDP in the absence of mitral valve disease. This is a much debated point currently though as recent studies have shown that in patients with LVEDP's in excess of 20 mm Hg with acute myocardial infarction the PA diastolic pressure underestimates the LVEDP by a mean of 11 mm Hg. Also in patients with pulmonary disease the PA diastolic pressure is not an accurate gauge of LVEDP.
3. Gunnar, Loeb, and their associates have measured LVEDP directly by passing a small catheter retrograde across the aortic valve under fluoroscopic guidance.
4. Cohn and his associates have used a coiled catheter passed into the left ventricle without visual guidance to measure LVEDP.

Summary

There are then several ways in which one may measure LVEDP in the setting of acute myocardial infarction. All of these are safest and most easily performed if one has fluoroscopic guidance of the catheter. Those that involve the direct measurement of LVEDP by passing a catheter across the aortic valve require an arteriotomy and have the potential of producing serious ventricular irritability and possible thrombus formation if the catheter remains in the left ventricle for any extended period of time.

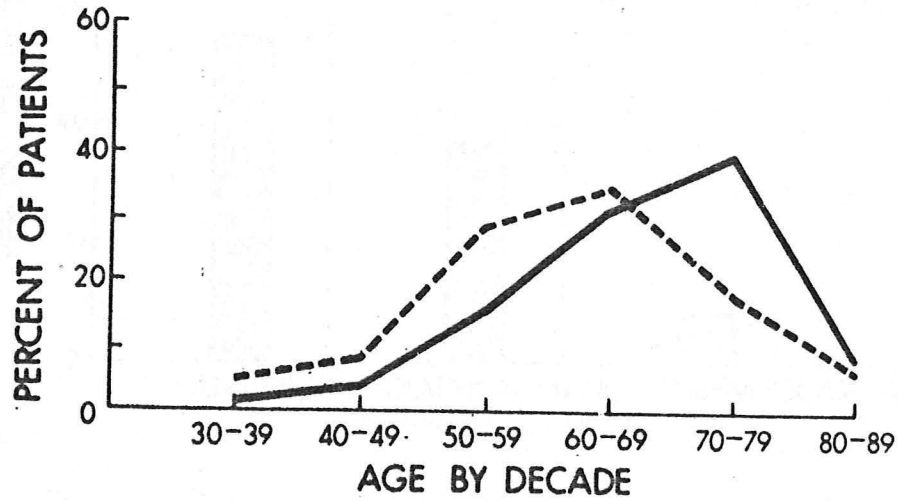
CHARACTERISTICS OF PATIENTS IN CARDIOGENIC SHOCK

Killip and his associates in a study done in the New York Hospital coronary care unit at the New York Hospital-Cornell Medical

Center between January 1, 1965 and February 1, 1969 found that cardiogenic shock developed in 73 of 547 patients (15%) with an established diagnosis of acute myocardial infarction.

The patients in the above series with cardiogenic shock tended to be older than those who did not develop cardiogenic shock as shown in Figure 3. The mean age of patients without shock was 63 years and with shock was 68 years. Although women are less likely to present with acute infarction than men, shock was more likely to develop in women with infarction. Only 25% of the total group of patients were women but 37% of those with shock were women ($p < 0.01$).

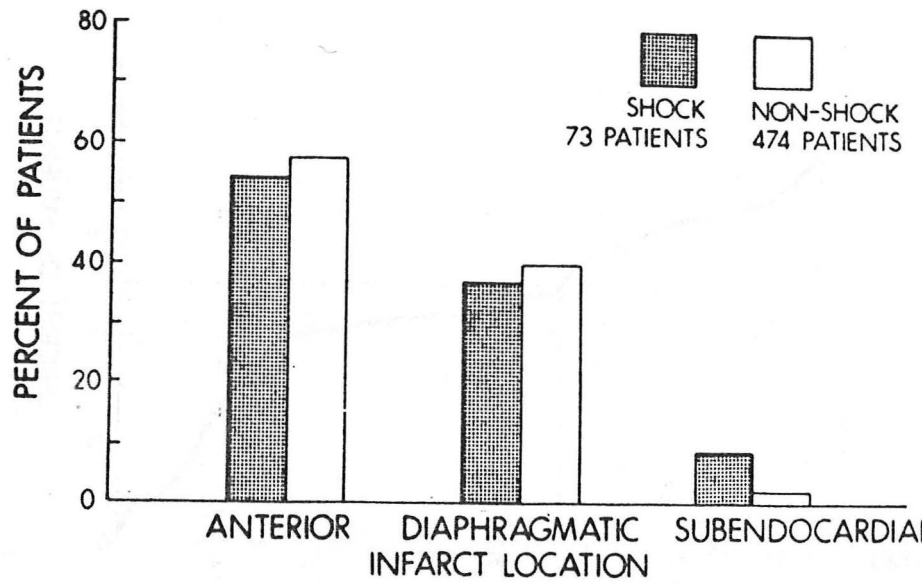
Figure 3



Legend: Age distribution of 72 patients with cardiogenic shock (solid line) and 474 patients without shock (broken line) is shown above. The mean age of patients with shock is greater than that of patients without shock.

The location of the myocardial infarction in patients with cardiogenic shock as compared to those without in the study of Killip *et al*. is shown in Figure 4.

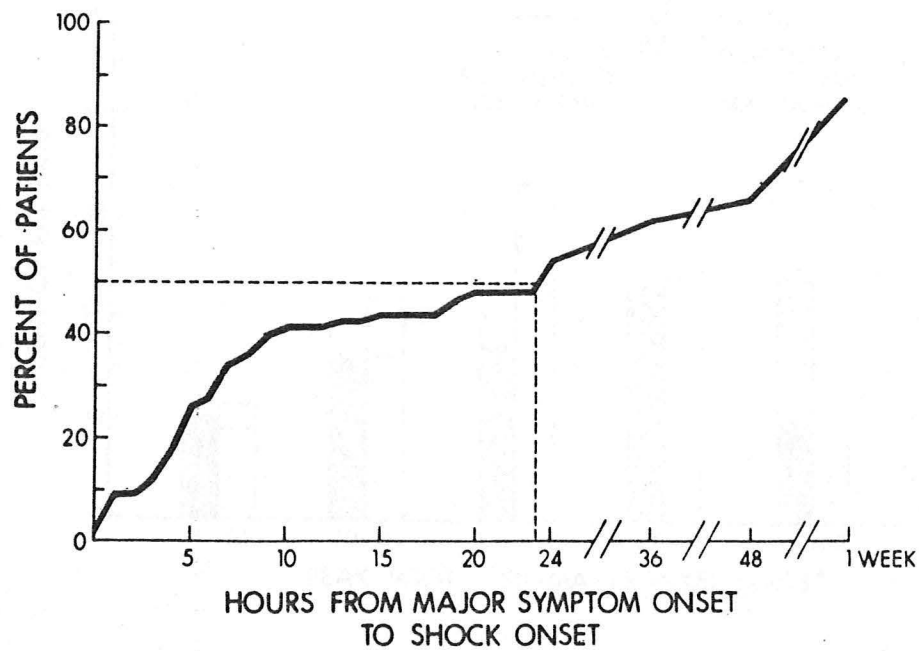
Figure 4



Legend: Electrocardiographic location of myocardial infarction in patients with cardiogenic shock and those without cardiogenic shock. The location of the myocardial infarction is similar in the two groups.

The interval from the onset of cardiogenic shock was somewhat variable but only 7% of the patients in whom cardiogenic shock ultimately developed were in shock within the first hour after their myocardial infarction (Fig. 5). Approximately one-third of all patients developing cardiogenic shock did so within 6 hours of clinical onset of myocardial infarction; half of the patients experienced it within 24 hours; and about two-thirds of the patients developed it within 36 hours. However, in 13% shock did not develop until one week or more after the acute myocardial infarction.

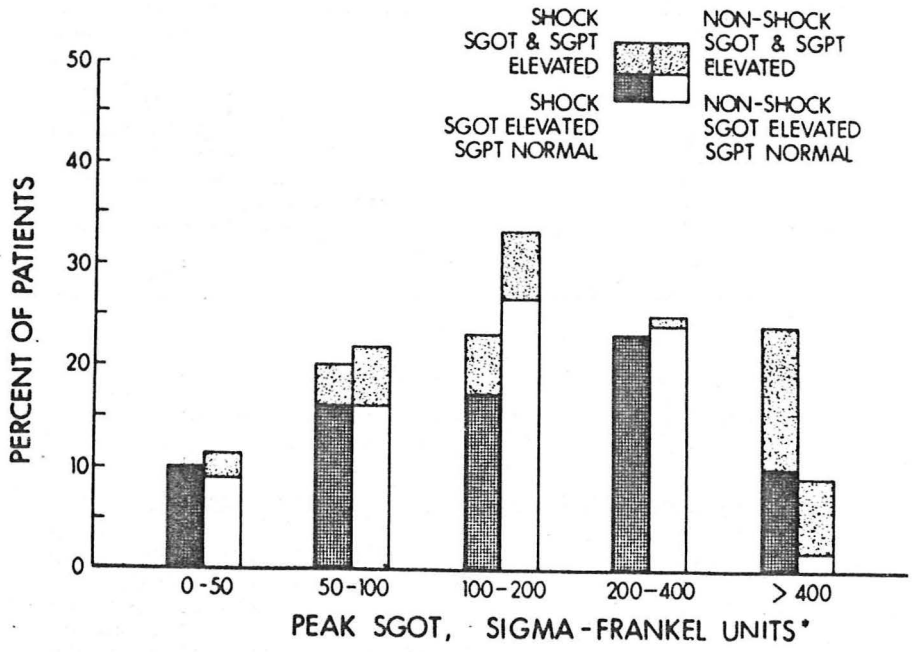
Figure 5



Legend: Delay from onset of major clinical symptoms to onset of shock.

Figure 6 demonstrates that increased serum SGOT activity was common in patients with cardiogenic shock. A peak SGOT value over 400 Sigma-Frankel units occurred almost entirely in patients with shock. Similar recent claims have been made by Sobel and his associates using serum creatine phosphokinase (CPK) to measure "infarct size" with the finding that larger infarcts have higher serum CPK levels.

Figure 6



Legend: Peak SGOT and SGPT values in patients with and without cardiogenic shock.

Further clinical characteristics of the group of patients in cardiogenic shock in the study by Killip *et al.* are shown in

Tables 6, 7, and 8. The incidence of previous myocardial infarction, angina pectoris, and hypertension was similar in patients with and without shock. Additional factors including prior digitalis therapy, heart failure, and smoking were not clearly different between the two groups.

Table 6

Historical Data in Patients With Cardiogenic Shock (Killip et al. *Series)*

Historical Data	Per Cent of Patients With Positive History
Angina pectoris	52
Previous acute myocardial infarction	38
Prior digitalis therapy	34
Hypertension	29
Heart failure	25
Cigarette smoking	25
Prior anticoagulant therapy	18
Diabetes mellitus	15
Chronic obstructive pulmonary disease	7

Table 7

Potential Precipitating Factors Within 12 Hours of Onset of Shock (Killip et al. *Series)*

Precipitating Factors	Number of Patients*
None	24
Unexplained fever > 38° C	14
Circulatory arrest	13
Pulmonary edema	10
Pneumonia	7
Hypotension without peripheral manifestations of shock	4
Ventricular tachycardia	3
Ventricular septal defect	2
Coronary arteriography	2
Surgery	1
Preexisting congenital heart disease	1
Grand mal seizure	1

* Some patients had more than one potential precipitating factor.

Table 8

Cardiac Rhythm at Time of Onset of Shock in 68 Patients (Killip et al. *Series)*

Cardiac Rhythm	Per Cent of Patients
Sinus rhythm	35
Sinus tachycardia	28
Sinus bradycardia	4
Atrial fibrillation	6
Nodal rhythm (AV junctional)	4
Ventricular tachycardia	6
Second or third degree heart block	10
Other or changing rhythms	6

HEMODYNAMICS OF PATIENTS IN CARDIOGENIC SHOCK FOLLOWING ACUTE MYOCARDIAL INFARCTION

1. Angiographic Findings

Leinbach and his associates have shown that all of the 11 patients with cardiogenic shock following acute myocardial infarction in their series who underwent coronary arteriography had significant obstruction of their left anterior descending coronary artery (with invariable angiographic evidence of cardiac apex dysfunction). In all but one patient another major coronary artery (eigher right coronary or circumflex coronary artery but usually the right coronary artery) was severely stenotic. These coronary arteriographic findings are demonstrated in Table 9.

Table 9

Coronary Arteries With Significant Obstruction or Occlusion in Patients With Cardiogenic Shock (Leinbach et al. *Series)*

Number	Patient	Vessels 75% or More Obstructed		Major Open Vessel
1	AW	RCA	LAD	C-CM
2	EP	RCA	LAD C	None
3	CM	RCA	LAD	CM
4	AK	RCA	LAD	C-CM
5	HM	RCA	LAD C	CM
6	AS	RCA	LAD C	None
7	JW	RCA	LAD	C
8	JD	RCA	LAD C	None
9	GP		LAD	RCA-C
10	HW	RCA Main L	LAD	None
11	AF		LAD C	RCA

Abbreviations: RCA = right coronary artery; LAD = left anterior descending; C = circumflex; CM = circumflex marginal.

Leinbach and his associates further defined the angiographic appearances of the left ventricles of the 11 patients they studied in cardiogenic shock by dividing the left ventricle into 6 separate segments. These segments were 1) anterolateral, 2) apex, 3) anteroseptal, 4) inferior, 5) posterolateral, and 6) posteromedial. The left anterior descending coronary artery and its branches perfuse the anterolateral, apical, and anteroseptal segments. The posterior descending branch of the right coronary artery usually supplies the inferior segment. Posteromedial segments may be supplied by posterior left ventricular branches of the right coronary artery or distal branches of the circumflex. Generally the posterolateral segment is perfused by the circumflex marginal vessel. There is some variation in these patterns as the exact location of the watershed area between "feeding vessels" may vary some and in 10% of cases the posterior descending artery is a branch of the left coronary artery. The contraction and perfusion of each of the above segments in these 11 patients are shown in Table 10.

Table 10

Contraction and Perfusion of 6 Myocardial Segments in Patients in Cardiogenic Shock (Leinbach et al.*)*

Number	Patient	AL	Apex	AS	I	PM	PL
1	AW	3/4	5/4	2/4	2/3	2/?	1/1
2	EP	4/5	5/5	/5	3/4	3/3	/3
3	CM	4/3	4/3	/3	2/3	2/2	/1
4	AK	3/4	5/4	3/4	4/5	3/1	1/1
5	HM	3/3	4/4	3/4	3/?	1/3	1/2
6	AS	3/3	5/4	/3	3/3	2/3	/3
7	JW	4/4	5/4	3/4	3/4	1/1	1/4
8	JD	4/5	4/5	/5	4/4	3/3	/3
9	GP	4/5	5/5	/5	2/1	1/1	/4
10	HW	4/5	4/5	/5	4/4	3/3	/3
11	AF	4/5	4/5	/5	3/1	3/4	/3

* The numerator represents contraction as assessed angiographically. Scale: 1 = normal; 2 = mildly reduced; 3 = moderately reduced; 4 = absent; 5 = paradoxical. The denominator represents perfusion from the corresponding coronary artery. Scale: 1 = normal; 2 = moderate obstruction (50-75%); 3 = severe obstruction (> 75%); 4 = occlusion with filling by collateral; 5 = occlusion without collateral. A question mark indicates insufficient clarity of coronary opacification.

Leinbach and his associates feel that a poor prognosis is present for patients who have more than three segments with avascularity and akinesis. Avascularity and akinesis at angiography correlated well with completely occluded vessels and necrosis at the time of postmortem examination.

Scheidt, Killip, and their associates also found a higher incidence of three-vessel coronary artery disease in patients with cardiogenic shock as compared to those without (Table 11) in patients that subsequently had postmortem examinations.

Table 11

Extent of Coronary Atherosclerosis in 68 Autopsied Cases of Acute Myocardial Infarction

	Per Cent of Patients With Shock (n = 43)	Per Cent of Patients Without Cardiogenic Shock (n = 25)
Obstruction > 70% of Lumen		
1 artery	26	44
2 arteries	16	32
3 arteries	53	24
Arterial Occlusions		
None	37	40
1 artery	56	56
2 arteries	7	4
Vessels Occluded		
Right coronary	14	7
Left anterior descending	10	5
Left circumflex	6	4

Roberts has also documented the fact that the coronary arteries are diffusely involved by atherosclerotic plaques in patients with fatal acute myocardial infarctions. An example of the postmortem coronary arteriograms from such a patient are shown in Figure 7. Roberts' studies of the coronary arteries of patients in the above category have also shown the following: 1) thrombi in extramural coronary arteries are infrequent in patients dying suddenly and in those with subendocardial necrosis; 2) thrombi when found in extramural coronary arteries in transmural infarction generally indicate the presence of "pump failure" for some time before death; 3) thrombi in coronary arteries usually are located at, and just proximal to, sites already severely narrowed by old atherosclerotic plaques; and 4) that coronary atherosclerosis does not involve intramural coronary arteries.

Figure 7

Coronary Arteries From a 54-Year-Old Woman That Died Suddenly Following Acute Myocardial Infarction

Legend: a) Right coronary artery 3 cm from aortic ostium; b) left main coronary artery; c) left circumflex artery in the first circumflex marginal; d) left anterior descending coronary artery 3 cm from the bifurcation of the left main artery. The luminal narrowing in each case was due entirely to old plaques.

The hemodynamics of a group of patients with acute myocardial infarction studied by Swan and his associates are shown in Table 12 below. These values are similar to those reported by Hamosh and Cohn and their associates.

Table 12

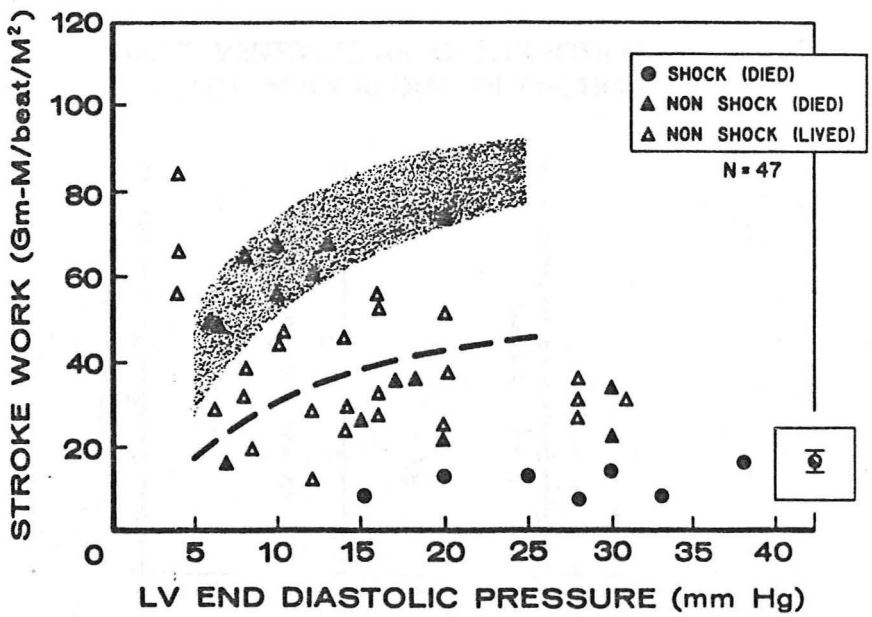
Hemodynamic Characterization of Patients With Acute Myocardial Infarction (Swan et al.*) (123 Patients Studied at Admission)*

Parameter	Shock	No Pts	Nonshock	No Pts
Heart rate	94 ± 17	30	89 ± 21	93
Mean arterial pressure	71 ± 20	27	100 ± 21	86
Cardiac output	2.5 ± 0.8	22	4.6 ± 1.2	53
LV filling pressure	27 ± 8	18	15 ± 8	68
LV dp/dt	710 ± 216	8	1941 ± 1067	9
Stroke volume	27 ± 10	22	55 ± 20	53
Stroke work	26 ± 10	22	81 ± 36	52
Total systemic vascular resistance	2530 ± 1190	22	1880 ± 580	52

Figure 8 demonstrates that patients with cardiogenic shock that subsequently died had very depressed ventricular function curves in the patients with acute myocardial infarction studied by Swan.

Figure 8

Ventricular Function Curves in Patients With Acute Myocardial Infarction



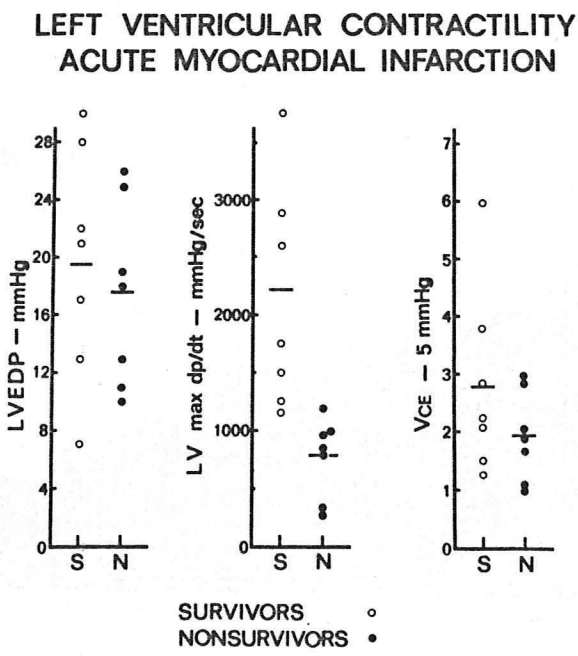
Legend: LV function in acute myocardial infarction in 47 patients. Stroke work index is plotted against LVEDP. Note the most severe depression occurred in patients with cardiogenic shock that died. The stippled area represents the normal range of left ventricular function. The level of left ventricular function predicted for a myocardial infarction that involved 40% of the LV is shown by the dashed line.

Figure 9 demonstrates some additional measurements of left ventricular contractility made by Parmley and his associates from patients with acute myocardial infarction. The only statistically

significant differences are between LV dp/dt from patients that survived and those that did not survive.

Figure 9

Left Ventricular Contractility in Acute Myocardial Infarction (Parmley et al.*)*

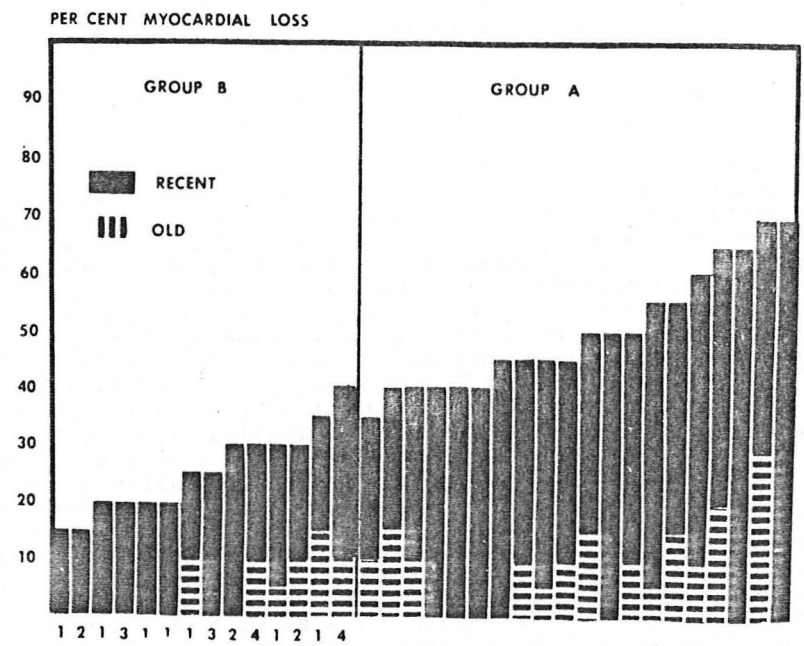


Legend: Measurements of left ventricular end-diastolic pressure (LVEDP), LV max dp/dt, and V_{CE} at 5 mm Hg.

Page, Caufield, and their associates have correlated postmortem findings as regards the extent of myocardial necrosis with premortem hemodynamic findings. Their findings are shown in Figure

10. From their data one may conclude that patients with cardiogenic shock have necrosis that involves 40% or more of their left ventricle.

Figure 10



Legend: Percentage loss of left ventricle in patients with (group A) and without (group B) cardiogenic shock.

SKELETAL MUSCLE METABOLIC STUDIES IN PATIENTS WITH CARDIOGENIC SHOCK

Recently studies have been done in the coronary care unit at Parkland Memorial Hospital in 12 patients in cardiogenic shock

using a needle biopsy technique to obtain lateral thigh skeletal muscle samples. Muscle lactates in 3 survivors averaged 4.7 (3.0-6.1) mmoles/kg compared to 16.2 (9.1-34.1) mmoles/kg in 9 who died. Blood lactates for the whole group ranged from 3.1 to 24.3 mmoles/liter with overlap between survivors and nonsurvivors. In 5 of these patients there was a marked concentration gradient between muscle and blood lactate values. ATP, CP, and glycogen determinations in the muscle biopsies of these patients also demonstrated evidence of anaerobic glycolysis. Arterial lactates and pH values did not necessarily predict skeletal muscle lactate values.

PHYSIOLOGY OF ACUTE MYOCARDIAL INFARCTION WITH EXTENSIVE PUMP DAMAGE

The important factors determining the ultimate fate of a patient with an acute myocardial infarction are 1) the magnitude and location of the myocardial infarction, 2) the functional state of the noninfarcted myocardium, 3) the absolute effectiveness of compensatory mechanisms, and 4) the presence of additional factors which increase mechanical load. It is obvious that total occlusion of a major coronary artery that is responsible for supplying blood to a large portion of myocardium may create such an extensive area of heart muscle dysfunction that survival for more than minutes to hours is impossible. "Late shock" deaths occurring several days following an acute myocardial infarction are generally associated with extensive three-vessel coronary artery disease and usually a history of previous myocardial infarction. These patients usually have hearts that at postmortem examination exhibit extensive myocardial destruction which is almost always greater than 40% of the left ventricular mass. In these latter patients the shock syndrome may be precipitated by secondary factors like abnormalities in heart rate or rhythm, hypovolemia, hypoxemia, or the use of agents or techniques that increase myocardial oxygen demands in a situation in which oxygen availability is limited. The result of increasing oxygen demand in such a situation may be to extend the area of preexisting myocardial damage.

It might be useful to look even more closely at the myocardium inflicted with an acute infarction. Heart muscle in this situation can be separated into two portions: 1) a totally noncontractile area or in some cases noncontractile areas of variable size ultimately developing reduced compliance and 2) a remaining noninfarcted area with either normal or near normal contractility. The normal area should be capable of responding to increases in fiber stretch and demands for an increase in contractile state. This normal myocardium has normal compliance. One would expect that immediately following myocardial infarction the endogenous catecholamine production resulting from pain and reduced perfusion would increase the contractility of the noninfarcted portion of myocar-

dium. Subsequent changes in myocardial contractility would be largely a function of infarct size. In the setting of extremely large myocardial infarcts then even maximal stimulation of a small portion of noninfarcted myocardium (through both endogenous and exogenous catecholamines) will be insufficient to sustain life. In those patients that survive smaller myocardial infarctions the changes in the contractile state of noninfarcted myocardium return to normal.

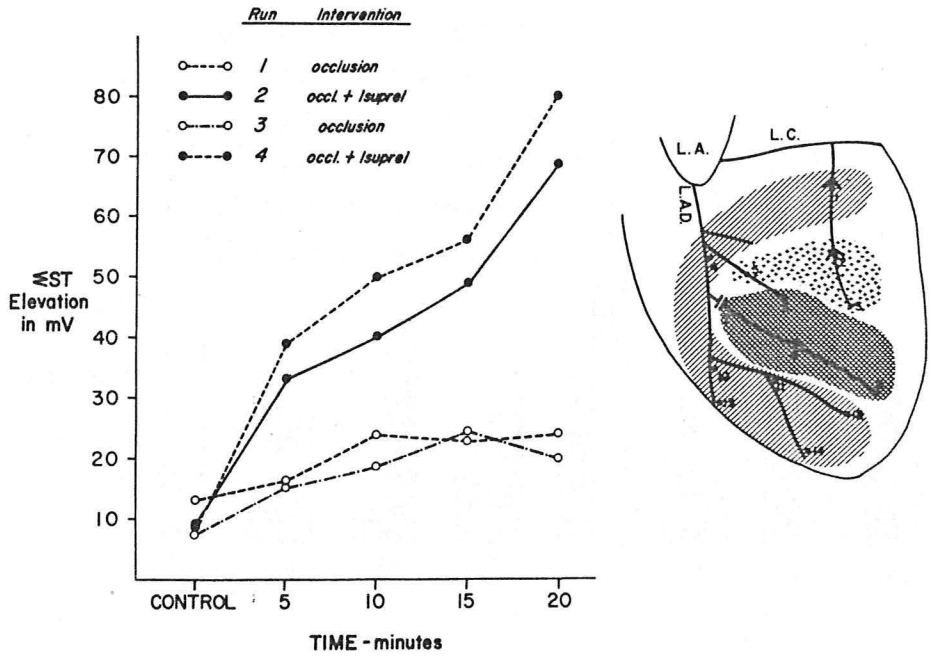
The addition of a mechanical load, *i.e.*, either acute mitral regurgitation, ventricular septal defect, or the development of a significant area of ventricular aneurysm, creates additional hemodynamic problems in the setting of acute myocardial infarction. Both mitral regurgitation and ventricular aneurysms result in an increase in end-diastolic volume and a decrease in stroke volume and cardiac output. A ventricular septal defect may also decrease stroke volume and cardiac output. The sum total of these additional hemodynamic burdens may be to produce a "low output state" and cardiogenic shock or severe and at times medically refractory left ventricular failure. Of clinical importance is the fact that the murmur of mitral regurgitation bears no relationship to the actual severity of the MR and that severe mitral regurgitation may be present *even in the total absence of any apical murmur*. Likewise a ventricular aneurysm may be present and there may not be a single physical sign that aids in its identification. One must have a high index of suspicion as regards the presence of acute mitral regurgitation and ventricular aneurysm in any certain clinical situation of acute myocardial infarction.

EXTENSION OF PREVIOUS MYOCARDIAL INFARCTION

There is some interesting recent experimental work by Doctors Maroko, Braunwald, and their associates demonstrating that in anesthetized dogs with a ligation around their left anterior descending coronary artery there is a relationship between epicardial ST segment elevation and subsequent myocardial creatine phosphokinase depletion. These investigators have used this relationship to demonstrate that isuprel, digitalis (in the nonfailing heart), rapid pacing, and hypotension appear to extend the area of myocardial ischemia during acute coronary occlusion in the dog while propranolol and intraaortic balloon counterpulsation reduce the area of injury. Figures 11-13 demonstrate some of the previous observations of Maroko *et al*. There is now additional experimental evidence that steroids, hyaluronidase, and hyperosmolar agents (mannitol) also appear to reduce the area of myocardial injury in experimental coronary insufficiency. This is a research area that is currently receiving a great deal of attention in cardiology as the implications of the use of agents that may either reduce or

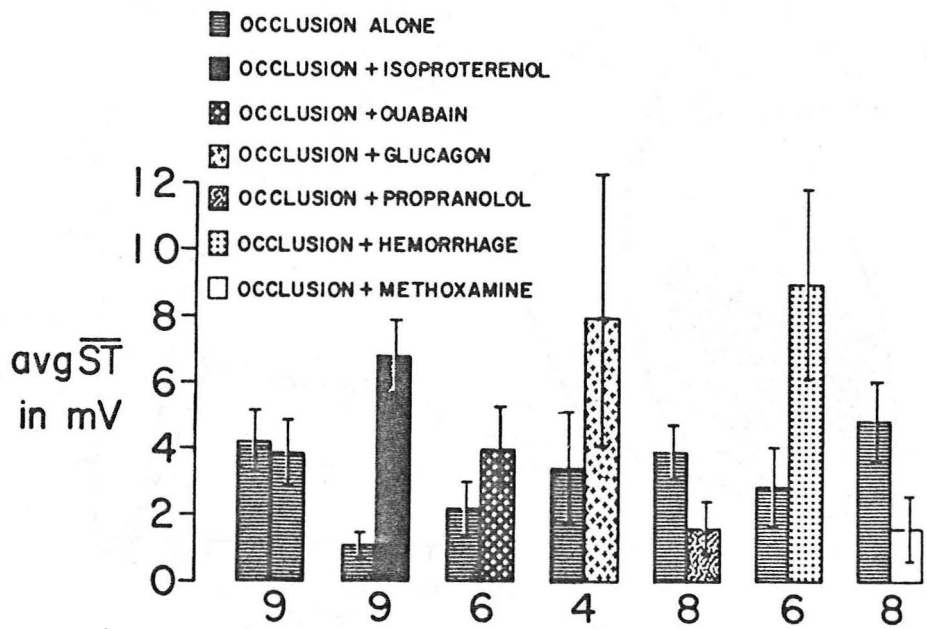
extend the area of myocardial ischemia during coronary occlusion are obvious.

Figure 11



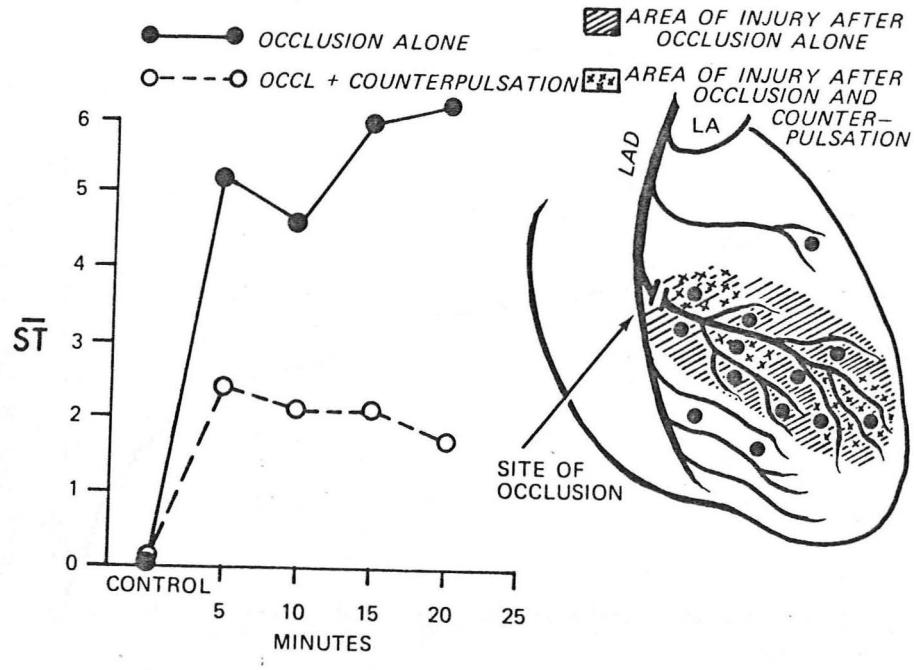
Legend: The above figure demonstrates the increase in epicardial ST segment elevation associated with coronary occlusion and the administration of isoproterenol.

Figure 12



Legend: The above figure demonstrates the epicardial ST segment changes that occur in experimental coronary occlusion associated with the administration of some commonly used agents in clinical cardiology.

Figure 13



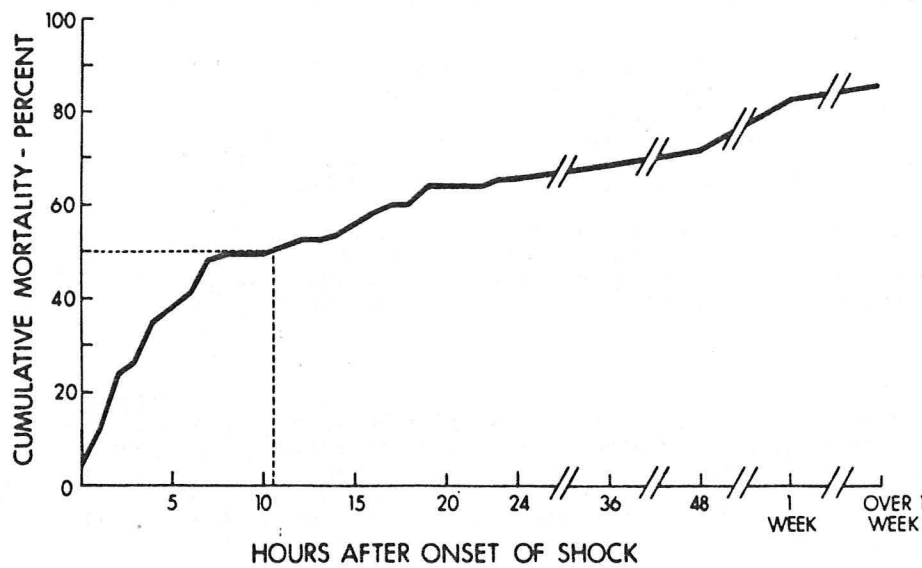
Legend: The above figure shows that aortic counterpulsation reduces epicardial ST segment elevation that occurs with coronary occlusion.

TREATMENT OF CARDIOGENIC SHOCK

True cardiogenic shock treated by medical means alone is generally relatively rapidly lethal. In the series of Killip and his associates of 73 patients in cardiogenic shock 7% of the patients were dead within one hour of its onset, 40% in 6 hours, and 65% in 24 hours (Fig. 14). Eighty-six per cent of patients eventually died of shock or of its complications. These survival statistics

for patients in cardiogenic shock are representative of other studies present in the literature.

Figure 14



Legend: The cumulative mortality from the time of onset of cardiogenic shock.

TREATMENT OF CARDIOGENIC SHOCK USING MEDICAL MEANS

1. Volume Expansion

In caring for patients with cardiogenic shock one must be certain that the left ventricular filling pressure is adequate in or-

der to be sure that the left ventricle is working at its peak performance on the ventricular function curve utilizing the Frank-Starling mechanism. If left-sided filling pressure is less than 15 mm Hg, cautious fluid challenge should be the first form of therapy employed. The type of fluid recommended by different investigators for intravascular volume expansion has varied but the different suggested methods are listed in Table 13.

Table 13

Volume Expansion in Patients in Cardiogenic Shock

1. Nixon and his associates have recommended infusions of dextrose solutions as initial therapy.
2. Allen *et al.* found hypovolemia in 20% of patients with cardiogenic shock and also advocated initial dextrose therapy for volume expansion.
3. Gunnar and Loeb have advocated the use of dextran infusion.
4. Cohn and his associates have also suggested that dextran be used as the volume expander.
5. Sanders and his associates have used salt-poor albumin to provide volume expansion for patients in cardiogenic shock.

Summary

The measurement of left ventricular filling pressure in patients in "cardiogenic shock" and subsequent volume expansion in appropriate patients using an agent that remains predominantly within vascular spaces are of crucial importance. This maneuver may restore reasonably normal blood pressure to a previously hypotensive patient.

Pressor Agents

In general pure vasoconstrictors like methoxamine, neosynephrine, and angiotensin are not of much value in patients in cardiogenic shock and may do some harm. The pure vasoconstrictors increase afterload and ventricular work. Since they generally lack an independent inotropic effect the ventricle dilates, wall tension increases, oxygen demands increase, and the ventricle may then perform at an even greater mechanical disadvantage.

Norepinephrine

Agent with both alpha and beta-adrenergic stimulatory effects. Shubin and Weil treated 10 patients in cardiogenic shock with this agent and found an increase in cardiac output and arterial pres-

sure. They stated, however, that when the systolic arterial pressure was elevated above 90 mm Hg there was a decrease in cardiac output and a marked increase in systemic vascular resistance. Gunnar and Loeb reported on the use of norepinephrine in 33 patients in shock with acute myocardial infarction, all except one of which had a control mean arterial pressure of less than 75 mm Hg. The administration of norepinephrine to these patients increased cardiac output 18%, arterial pressure increased 43%, and systemic vascular resistance increased 37%. Laks and his associates have demonstrated in the intact dog that at low infusion rates norepinephrine increases cardiac output with little effect on systemic vascular resistance. Mueller and her associates have demonstrated that *l*-norepinephrine infusions (12-40 µg/min) changed cardiac index insignificantly but increased arterial pressure and total coronary blood flow by an average of 28% ($p < 0.01$) while concomitantly improving myocardial metabolism. The latter was assessed by studying myocardial lactate production in these patients. In Mueller's studies *l*-norepinephrine appeared to be superior to isoproterenol.

Isoproterenol

Isoproterenol is a potent activator of beta-receptors thereby producing marked inotropic and chronotropic changes. This results in increases in the force and rate of cardiac contraction but also increased myocardial oxygen consumption. Isoproterenol has been used with success in the treatment of shock related to sepsis and trauma and in cardiogenic shock following cardiac surgery. Its usefulness in cardiogenic shock following acute myocardial infarction has been less clear cut, however. Gunnar and Loeb compared isoproterenol infusion in amounts of 1-7 µg/min in 13 patients with cardiogenic shock to an infusion of norepinephrine. None of the patients given isoproterenol demonstrated clinical improvement and there was "rapid deterioration" in 4 patients on switching from norepinephrine to isoproterenol. This deterioration was reversed in one patient by reinstituting norepinephrine. Mueller and her associates have shown that isoproterenol increased myocardial lactate production in patients in cardiogenic shock. This occurred despite an increase in total coronary blood flow. The mechanism of metabolic deterioration in the face of an increased total coronary blood flow may be a "coronary steal syndrome" in which blood is actually diverted away from ischemic areas by virtue of the fact that isoproterenol reduces coronary vascular resistance and improves blood flow to uninvolved areas of myocardium. Bing *et al.* have also shown that isoproterenol enhances peak tension development in ischemic muscle but that deterioration occurs more rapidly than in ischemic muscle not exposed to isoproterenol. This increased rate of deterioration could be slowed but not reversed by the addition of glucose. The

authors proposed that isoproterenol caused depletion of high-energy stores. Thus isoproterenol appears not only to divert blood from the ischemic areas but enhances myocardial deterioration in the ischemic area.

Dopamine

This agent is a precursor of norepinephrine and activates both beta and alpha-adrenergic receptors. It also dilates renal and mesenteric vessels independent of its effects on adrenergic receptors. When compared to norepinephrine and isoproterenol, dopamine increases cardiac output more than norepinephrine and less than isoproterenol and increases arterial pressure more than isoproterenol and less than norepinephrine. Dopamine may precipitate ventricular arrhythmias so careful ECG monitoring is indicated. Dopamine appears to increase LVEDP in patients with cardiogenic shock while increasing cardiac output.

Digitalis

In an experimental model of cardiogenic shock Cronin and Zsotér showed that digitalis resulted in an increase in cardiac output, an increase in blood pressure, and a very significant increase in stroke volume with a fall in LVEDP. Gunnar and Loeb, however, have described the acute effects of digitalis in a group of patients in cardiogenic shock and they found that there was no significant change in cardiac output, arterial pressure, CVP, and systemic vascular resistance. Some patients improved but others deteriorated. There remains a real question as to the absolute efficacy of acute digitalization in patients in cardiogenic shock.

Glucagon

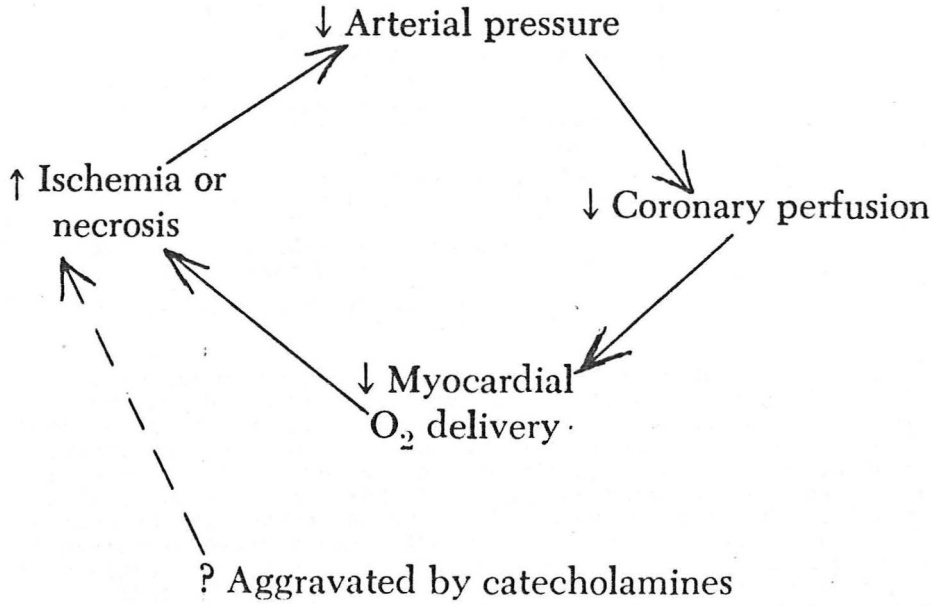
This agent has been shown to increase cardiac output, LV dp/dt, and heart rate in man and experimental animals without preexisting heart disease and in man with acutely developing heart failure. Its value in patients with long-standing heart failure and in experimental animal preparations with chronic heart failure remains uncertain. Gold, Armstrong, and their associates were unable to show any significant inotropic effect in patients with chronic congestive heart failure and in right ventricular papillary muscles obtained from cats that had chronic pulmonary artery banding performed. Diamond *et al.* treated 10 patients with acute myocardial infarction (9 had associated LV failure) and noted increases in heart rate, cardiac output, and arterial pressure. Suffice it to say that glucagon's value in cardiogenic shock remains to be clearly established.

Glucagon acts by activating the adenyl cyclase system which converts adenosine triphosphate to cyclic AMP which itself appears to activate the contractile mechanism. Catecholamines apparently activate adenyl cyclase through a different receptor.

MECHANICAL CIRCULATORY ASSISTANCE

Despite the use of maximal medical regimens the mortality in cardiogenic shock following acute myocardial infarction has remained at approximately 90%. Predominantly for this reason other means of treating cardiogenic shock have been recently developed. A review of Figure 15 helps one to recognize and understand the vicious cycle of cardiogenic shock. From this figure it should be apparent that one wants to develop methods of treatment for cardiogenic shock that increase coronary perfusion pressure and reduce left ventricular work.

Figure 15



Legend: The vicious cycle of cardiogenic shock.

Mechanical circulatory assist devices have been the most recent form of therapy employed to treat cardiogenic shock. The types of devices that have been used for circulatory support are listed in Table 14.

Table 14

Types of Mechanical Circulatory Assist Devices

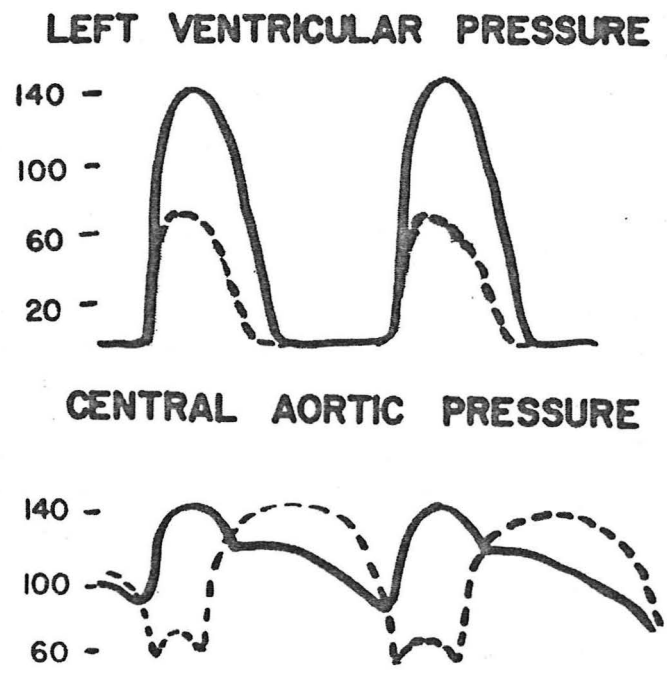
1. Decreased preload
   a. Venoarterial pumping (total cardiopulmonary bypass)
   b. Left atrial-arterial bypass
      1) Closed transseptal cannulation
      2) DeBakey pump
   c. Left ventricular-arterial bypass
      1) Closed transarterial left ventricular cannulation*
      2) Left ventricle-aorta bypass pump
2. Decreased afterload
   a. Counterpulsation
      1) Arterioarterial pumping*
      2) Intraaortic balloon pump*
      3) External regional pressure variation*
   b. Body acceleration synchronous with heart beat (Bash)*
3. Direct cardiac compression
   a. Anstadt cup*

* Devices currently in clinical use.

The various mechanical circulatory assist devices have been developed on the basis that they would: 1) decrease preload, 2) decrease afterload, or 3) provide direct cardiac compression. Those devices that decrease preload and afterload act to reduce left ventricular diastolic volume thus resulting in a decrease in intramyocardial tension and a reduction in myocardial oxygen requirements. Decreased preload may be accomplished by shunting of blood away from the left ventricle. The cardiopulmonary bypass machine is the classical means of decreasing preload. Afterload may be diminished through counterpulsation. With counterpulsation at the beginning of diastole balloon inflation increases diastolic arterial pressure and promotes runoff of blood to the periphery and back toward the coronary arteries. The balloon is deflated just prior to the onset of the next ventricular systole (using the ECG as a signal) so that the left ventricle ejects its contents into an aorta relatively emptied of blood by the previous balloon systole.

Therefore, peak left ventricular systolic pressure is lowered (Fig. 16). Counterpulsation then acts to increase diastolic perfusion pressure and coronary blood flow and reduces left ventricular work.

Figure 16



Legend: Effect of counterpulsation on left ventricular (top) and aortic pressures (bottom). Solid line is control pressure. Dotted line shows counterpulsation pressure. Systolic pressure falls in both while aortic diastolic pressure increases.

Figure 17 demonstrates the balloon catheter used for counterpulsation. This is inserted into the femoral artery and positioned under fluoroscopy in the descending aorta just distal to

the origin of the left subclavian artery. It is connected to a nearby console with portable helium tanks and balloon inflation is triggered from the portable console by the T wave of the ECG and deflation is signaled by the P wave of the ECG.

Figure 17

Legend: Balloon catheter used in aortic counterpulsation.

The current clinical indications for mechanical circulatory assistance are shown in Table 15.

Table 15

Indications and Contraindications for Mechanical Circulatory Assistance (Sanders et al.*)*

Current
1. Cardiogenic shock secondary to:
   a. Acute myocardial infarction
   b. Myocardial depression following cardiac surgery
2. Acute heart failure refractory to medical therapy
3. Recurrent life-threatening ventricular arrhythmias unresponsive to pharmacologic agents
4. Severe three-vessel chronic coronary disease

Potential
1. Circulatory support of patients prior to total cardiac replacement
2. Anginal syndromes (unstable, "preinfarction")
3. Acute myocardial infarction (? reduces infarct size)

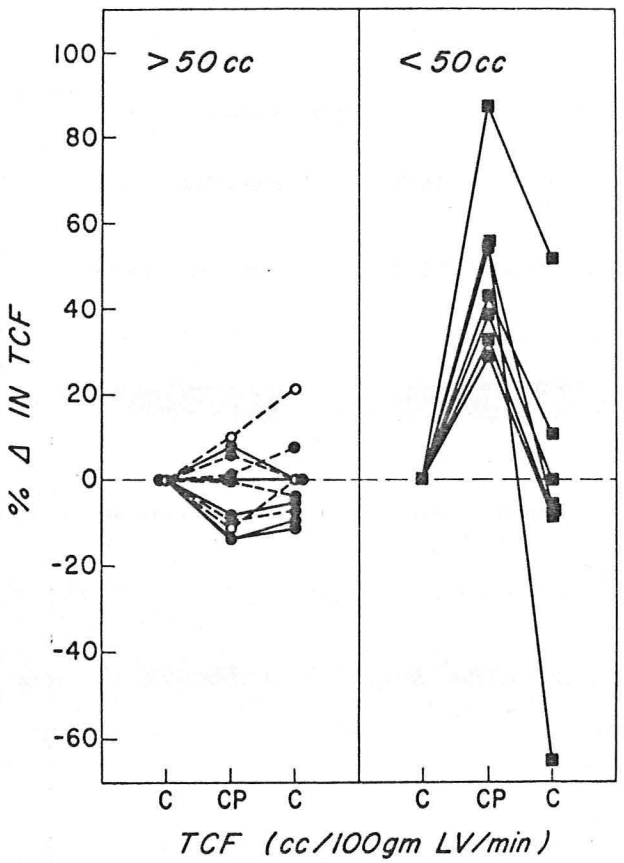
Contraindications

1. Irreversible brain damage
2. Chronic endstage heart disease (cardiomyopathy)
3. Severe associated disease
4. Incompetent aortic valve

All of the assist devices currently available may only be used temporarily. Important in the use of these assist devices is the premise that either 1) mechanical circulatory assist devices will reverse myocardial injury by increasing collateral coronary flow to marginally perfused areas thereby subsequently returning the left ventricle to a level of function sufficient to support the circulation or 2) MCA will sustain hemodynamic situation until a more definitive procedure can be performed (*i.e.*, in some instances myocardial revascularization).

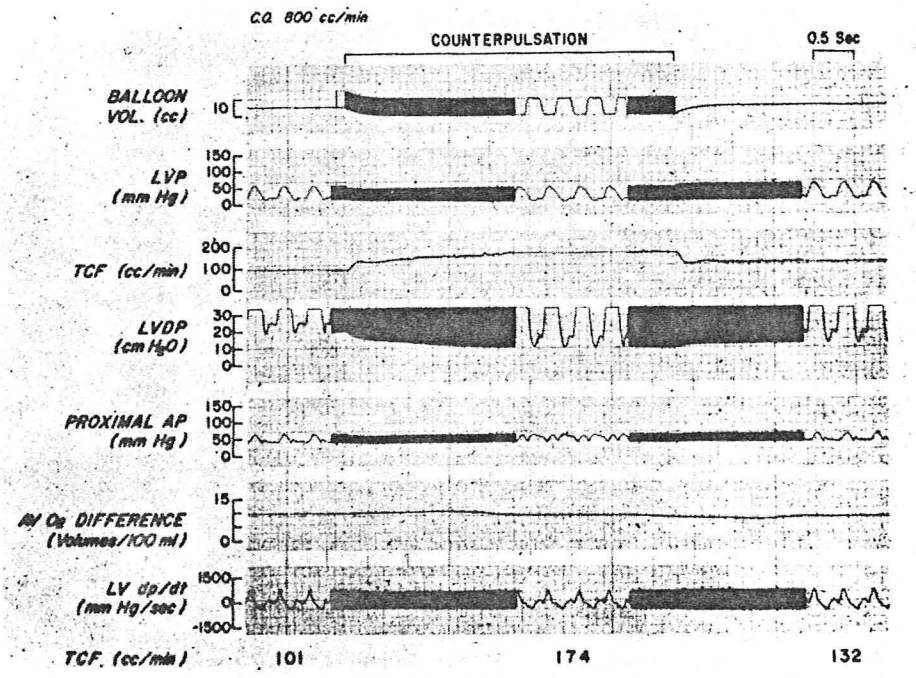
The most commonly used MCA device presently is the intraaortic balloon (IABP). Measurements of coronary blood flow have generally shown increases in flow in flow-limited situations. Powell and his associates found in experimental animals that IABP had no effect on coronary flow but decreased MVO_2 slightly in normotensive animals. However, in hypotensive animals with coronary blood flows of less than 50 ml/min IABP produced significant increases in coronary flow and MVO_2. These results are shown in Figure 18. Figure 19 also demonstrates some of the data obtained by Powell *et al.* in their studies of IABP in acute coronary insufficiency in dogs.

Figure 18



Legend: Note the increase in total coronary flow produced by IABP in animals with coronary flows < 50 ml/min.

Figure 19



Legend: Influence of IABP on various LV parameters generally demonstrating a beneficial effect on LV performance.

INTRAAORTIC BALLOON PUMP (IABP)

This approach was originally described by Moulopoulos and associates in 1962. As described above it employs a nonocclusive catheter-balloon system inserted retrograde through a femoral artery into the descending thoracic aorta just distal to the left subclavian artery. Helium is used to inflate the balloon and as described earlier phasing of the balloon is accomplished by an ex-

ternal console using the ECG to trigger inflation and deflation. Kantrowitz and his associates were the first to apply the polyurethane balloon in the treatment of cardiogenic shock. In their report of 30 patients that were treated IABP reversed the shock syndrome in 25 and a survival rate of 45% was described in patients whose shock developed immediately following myocardial infarction. In some of these patients balloon assist was continued for as long as 8 days. Experience in treating a group of patients with cardiogenic shock employing a balloon with 3 segments has recently been reported by Sanders and his associates at the Massachusetts General Hospital. This balloon is made of avcothane. A reduction in platelet counts was noted in some patients but low molecular weight dextran and heparin were used in all of these patients in a successful attempt to prevent clinically apparent emboli and marked thrombocytopenia. Average duration of shock prior to IABP was 14 hours in 31 patients and 3-9 days in the remainder. IABP reversed the shock state in 31 patients and resulted in an average increase of 700 ml and 8 mm Hg in cardiac index and arterial pressure and a decrease of 4 mm Hg in the pulmonary wedge pressure (Table 16). In these patients pulmonary capillary wedge pressures were maintained at approximately 18 mm Hg to try to maximize the effect of the Frank-Starling mechanism. Average arterial pO_2 rose from 65 to 127 and signs of pulmonary vascular congestion diminished. Five of the first 26 patients treated with IABP were "long-term survivors".

Table 16

The Hemodynamic Effect of IABP in 31 Patients in Cardiogenic Shock (Sanders et al.*)*

Parameter	Balloon On	Balloon Off
1. Pulmonary artery wedge pressure (mm Hg)	18	22
2. Mean arterial pressure (mm Hg)	72	64
3. Peak systolic arterial pressure (mm Hg)	68	78
4. Peak diastolic arterial pressure (mm Hg)	95	55
5. Cardiac index	2.5	1.7
6. Arterial pO_2 (mm Hg)	127	65

The series of patients with cardiogenic shock treated at the MGH is now much larger (in excess of 70 patients). While it has been possible to reverse the shock state in many of the patients it has been difficult to discontinue IABP in some patients and long-term survivors in patients subsequently weaned from balloon

support and not further treated by other means have been few in number. Table 17 demonstrates survival rates in patients treated with IABP alone at the MGH and elsewhere.

Table 17

IABP Treatment of Cardiogenic Shock

Study Group	Patient (No)	Survival > 2 Months (No)	Mortality (%)
1. Cooperative investigators	87	14	83.9
2. Massachusetts General Hospital	31	7	77.4
Total	118	21	82.2

Since January 1972 we have supported 9 patients in cardiogenic shock with IABP. Prior to beginning IABP in these 9 patients it had been impossible to stabilize their blood pressures with pressor agents and volume infusion. Table 18 describes the clinical details of these patients.

Table 18

Patients in Cardiogenic Shock Supported With the Avco Intraaortic Balloon Pump at Parkland Hospital

#	Name	Age	Sex	Diagnosis	On Balloon
1	RS	58	Male	Cardiogenic shock, alcoholism	40 hr
2	IR	71	Female	Cardiogenic shock, acute MI	21 hr
3	WH	45	Male	Cardiogenic shock, alcoholism	4 d, 8 hr
4	LC	43	Male	Severe CHF, CAD	9 d
5	WJ	62	Male	CAD, acute MI	29 hr
6	GL	45	Male	Cardiogenic shock, acute MI	6 d
7	WR	57	Male	Cardiogenic shock, acute MI	10 d
8	JA	51	Male	Cardiogenic shock, acute MI	2 hr
9	WT	61	Male	Cardiogenic shock, acute MI	24 hr

In the above group of 9 patients treated at PMH only 2 survived more than 2 months but the shock state was reversible in 6 of the 9. One of the two patients that survived has since died

of another apparently unrelated problem. The present survivor (GL) is asymptomatic and virtually unlimited in what he is capable of doing.

EXTERNAL NONINVASIVE SYSTEMS TO PROVIDE COUNTERPULSATION

There is currently a great deal of interest in the evaluation of "external body suits" that may be capable of providing circulatory assistance in a noninvasive manner. These systems provide a negative pressure of up to 50 mm Hg to the limbs during ventricular systole thus encouraging the flow of arterial blood into the extremities, lowering central aortic pressure, and aiding in left ventricular emptying. Positive pressure (up to 200 mm Hg) is applied to the limbs during diastole; this positive pressure has a combined effect of producing counterpulsation in the arterial circulation and forcing venous blood back to the heart during diastole. Dennis *et al.* were the first to apply this principle in experimental animals. Soroff and associates extended the technique to man utilizing a device consisting of two large heater-filled sleeves placed about the legs and encased in an airtight seal. Pressure variation synchronized with an electrocardiogram is provided by the rapid movement of water in and out of the sleeves. Cohen, Mitchell, and Mullins here have evaluated a newer, more portable sequenced external pulsation in experimental animals and the results from all of these above studies have been encouraging. A sizable experience in patients in cardiogenic shock has not yet been obtained with these external suits but efforts to obtain information in this area are now being made.

ROLE OF CARDIAC SURGERY (MYOCARDIAL REVASCULARIZATION AND/OR INFARCTECTOMY) IN ASSOCIATION WITH IABP

The persistently high mortality (80%) in patients with cardiogenic shock treated with IABP suggested that MCA would have to be combined with another possibly more definitive procedure in the majority of these patients. Such a procedure might be acute myocardial revascularization (saphenous vein or internal mammary bypass grafts), myocardial resection, or both. The following criteria have been used at the Massachusetts General Hospital to decide when to perform coronary angiography and consider surgical intervention in patients on IABP. Those patients that 1) do not show significant hemodynamic improvement within 12-24 hours on a therapeutic program of IABP and/or pressor agents (levophed), 2) demonstrate increasing pressor requirements despite IABP, 3) show marked dependence on IABP after 24 hours, or 4) demonstrate hemodynamic deterioration after being previously weaned from IABP are taken to

the cardiac catheterization laboratory where coronary arteriograms and a left ventricular angiogram are obtained on IABP. Those patients showing suitable distal coronary vessels for coronary artery bypass graft surgery and/or an area of resectable dyskinetic myocardium are taken from the catheterization laboratory to the operating room for necessary cardiac surgery. IABP is continued throughout this period of time. Only one patient out of a total of more than 35 has died following the cardiac catheterization procedure and that was the first patient studied in this manner.

The results of combined IABP and coronary revascularization are shown in Table 19.

Table 19

Survival in Cardiogenic Shock (MGH Series)

	Patient No	Survival > 2 Months	Mortality
1. IABP alone	31	7	77.4
2. IABP and surgery (after failure to maintain pressure when IABP was withdrawn)	29	7	75.8
3. Total	60	14	76.5

Poor operative results with coronary artery bypass graft surgery can be expected in patients in cardiogenic shock that 1) have ejection fractions (SV/EDV) below 25%, 2) have multiple ventricular areas of avascularity and akinesis, and/or 3) have diffuse severe obstructive disease involving all three coronary arteries without good distal vessels beyond the obstruction.

Intraaortic counterpulsation (and other MCA devices) either alone or in combination with acute myocardial revascularization and/or ventricular resection does salvage for relatively long-term survival some patients who would otherwise die with cardiogenic shock in the setting of acute myocardial infarction. The MCA devices also commonly reverse the shock-like state but many patients remain dependent on their use and additional definitive measures (most of which are not yet available) are necessary. One may hope that the further development of newer circulatory assist devices that may function in ambulatory patients over long periods of time and/or the conquering of the immunological problems associated with cardiac transplantation will make further inroads into our ability to salvage such desperately ill patients.

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