Effects of Intraaortic Balloon Counterpulsation on the Severity of Myocardial Ischemic Injury following Acute Coronary Occlusion

Counterpulsation and Myocardial Injury

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SUMMARY

The effects of intraaortic balloon counterpulsation (IABC) on the magnitude and severity of myocardial ischemic injury were studied in 19 dogs following acute coronary occlusion and in two patients with cardiogenic shock. In the experimental group, epicardial electrocardiograms were taken from 10–14 sites on the anterior surface of the left ventricle following occlusion of the left anterior descending coronary artery or its apical branch. The average S-T-segment elevation (ST) was used as an index of the magnitude of myocardial ischemic injury. In six dogs, two successive 20-min occlusions were performed, and IABC was started prior to the second occlusion. ST 15 min following occlusion decreased from 3.3 ± 0.9 mv after the control occlusion to 1.4 ± 0.4 mv (P < 0.01) after the occlusion with IABC. In three dogs in which the occlusion was maintained and IABC initiated 30 min later, ST decreased from 1.2 to 0.6 mv. In six dogs in which IABC was started 3 hours after occlusion, it induced a reduction of ST from 4.2 ± 1.1 to 2.8 ± 1.0 mv (P < 0.01). In four dogs, ischemic injury was augmented by isoproterenol infusion (0.25 μg/kg/min), and while continuing the infusion IABC was initiated. It reduced ST from 8.0 ± 1.9 to 5.7 ± 1.8 mv (P < 0.05). Thus, IABC reduced the magnitude and extent of myocardial ischemic injury after experimental coronary occlusion, both when IABC was employed prior to, and 3 hours following, coronary occlusion. IABC was also effective in reducing myocardial ischemic injury which had been increased by isoproterenol infusion. Employing a noninvasive technic, which utilizes 35 electrodes on the thorax, the effects of IABC were examined in two patients with cardiogenic shock associated with acute myocardial infarction. Preliminary observations in these patients confirmed the experimental results indicating that IABC reduced myocardial ischemic injury.

Additional Indexing Words:
Epicardial electrocardiograms
Acute myocardial infarction
Cardiogenic shock
S-T-segment elevation
Mechanical circulatory assistance
Myocardial oxygen consumption

Intraaortic balloon counterpulsation (IABC) is potentially useful in the treatment of patients with cardiogenic shock resulting from acute myocardial infarction.¹⁻⁶

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Received September 7, 1971; revision accepted for publication November 5, 1971.
Recently, we have utilized a reproducible electrocardiographic technic for measuring alterations in the extent of ischemic injury following coronary ligation in experimental animals. With this technic it is possible to compare the extent and severity of ischemic injury following successive coronary occlusions in the same dog and thereby to determine the influence of various hemodynamic and pharmacologic interventions on the size of the injured zone. The present investigation was designed to determine the effect of IABC on the magnitude and severity of ischemic injury following experimentally performed coronary occlusions. Subsequently, we developed a noninvasive technic to monitor changes in electrocardiographic injury using multiple chest leads in dogs and patients. This method enabled us to study the alteration in ischemic injury in patients in whom IABC was performed.

Methods

Experimental studies were carried out in 19 dogs, anesthetized with sodium thiamylal (25 mg/kg). A left thoracotomy was performed through the fifth intercostal space, and the heart was suspended in a pericardial cradle. The left anterior descending coronary artery or one or two of its branches were dissected free from the adjacent tissue and occluded intermittently or permanently with a Schwartz intracranial clamp. Pressure in the aortic arch, proximal to the balloon, was monitored through a catheter introduced into the left carotid artery, and the distal aortic pressure was measured through a catheter introduced into the left femoral artery. The left jugular vein was used for administration of drugs.

A catheter-mounted intraaortic balloon, 20 cm long and 1.1 cm in diameter, was introduced through the right femoral artery and positioned so that its tip was located immediately distal to the aortic arch at the origin of the left subclavian artery. The balloon was inflated with 8–10 cc of helium using the model IABP-7 counterpulse pump, as described elsewhere. Accurate synchronization of balloon inflation and deflation was based on the arterial pressure waveform proximal to the balloon. The area of acute myocardial ischemic injury was characterized by the area of S-T-segment elevation obtained by epicardial electrocardiography, as previously described.

Briefly, the technic consists of recording unipolar leads from the epicardium using a saline-soaked cotton wick exploring electrode. Ten to 14 sites on the anterior surface of the left ventricle were arbitrarily chosen for recordings at the onset of the experiment. These sites were selected so that some were within and others distant from the distribution of the occluded coronary artery. Thus, there were always sites whose blood supply was not affected by the occlusion and served as internal controls, while other sites were in areas whose blood supply could be reduced by the occlusion. The use of each dog as its own control allows this arbitrary selection of sites. S-T-segment elevations of more than 2 mv were taken to indicate myocardial injury, and the number of sites with this degree of S-T elevation (NST) defined the area of injury, while the average S-T-segment elevation (ST) was taken as an estimate of its severity. It has been shown previously that ischemic injury, defined by S-T-segment elevation 15 min following coronary occlusion, reliably predicts the area of myocardial necrosis, as reflected by myocardial creatine phosphokinase (CPK) depletion and by histologic observation. These animals were divided into three groups:

Group 1. In six dogs, two 20-min occlusions were performed, separated by a 60-min interval, which permitted the return of all parameters to control levels. The first occlusion was done without any other intervention. IABC was begun 5 min before and continued throughout the second occlusion. Epicardial recordings were made before each occlusion and every 5 min thereafter. In each animal, the ST and NST during the first and second occlusions were compared at each of these time intervals. The ST and NST 15 min following occlusion in the two groups were compared using the paired t test.

Group 2. In nine dogs, the coronary occlusion was maintained continuously; 30 min (three dogs) or 3 hours (six dogs) later IABC was started, and the effects of this intervention on ST and NST were determined.

Group 3. In four dogs, coronary occlusion was maintained continuously as in group 2. However, 2 hours after occlusion, the extent and severity of ischemic injury were increased by the intravenous administration of isoproterenol (0.25 µg/kg/min). IABC was started 3 hours after occlusion, i.e., 1 hour after the onset of isoproterenol, and while the infusion of this drug was continued the effects of IABC on the augmented area of ischemic injury were analyzed.

Patients. Two patients with acute myocardial

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*Circulation, Volume XLV, June 1972*
infarction who had developed cardiogenic shock were treated by IABC. IABC was performed employing a helium-inflated, 40-cc, three-chamber, intraaortic balloon (Avco) introduced through a femoral artery cutdown using the Kantrowitz technic. Otherwise, the technic employed was identical with that used in experimental animals. In these patients, preliminary evaluation of this therapy by the thoracic mapping technic was done as follows: the indices of magnitude and extent of myocardial ischemic injury were \( \Sigma ST \) (sum of S-T-segment elevation) and NST (number of sites with S-T-segment elevation exceeding 0.1 mv) calculated from records obtained with an electrode blanket positioned on the patient's chest, as described previously. In brief, this blanket consists of 35 electrodes (Hewlett-Packard model 14057) arranged in five horizontal rows, marked from A (top) to E (bottom), of 7 leads each, marked from 1 (extreme right) to 7 (extreme left). The distance between vertical columns 1 and 2 was 7 cm and between all of the other adjacent columns, 4.5 cm. The distance between the horizontal rows was 4 cm. Thus, when the top right electrode (A1) is placed in the second intercostal space on the right parasternal line, the lower left electrode (E7) is at or near the sixth intercostal space at the left midaxillary line. The electrodes were connected to a switch box which was in turn connected to the V lead of the electrocardiograph. Recordings were made every 2–4 hours during the first 48 hours after the patient's admission to the hospital and every 6 or 8 hours thereafter. When therapy with IABC was instituted, maps were taken more frequently.

**Results**

**Group 1.** In each of the six dogs in which intermittent occlusions were performed, \( \overline{ST} \) and NST 15 min after occlusion were smaller when coronary occlusion was carried out during IABC. Mean \( \overline{ST} \) and NST decreased significantly (fig.1). A representative experiment is shown in figure 2. At any time interval following coronary occlusion, IABC was associated with a reduced \( \overline{ST} \) (fig. 2, left) and NST (fig. 2, right), indicating that the area of injury following occlusion in the presence of IABC was much smaller when compared to that existing after occlusion alone. This decrease was always accompanied by a corresponding diminution in the area of visible cyanosis which develops after an occlusion.

**Group 2.** In the three dogs in which IABC was started 30 min after occlusion, the \( \overline{ST} \) decreased from an average of 1.2 to 0.6 mv within 15 min while the average NST decreased from 3.3 to 1.6; these changes were

![Figure 1](http://circ.ahajournals.org/doi/abs/10.1161/01.CIR.45.6.1152)

Figure 1.

The influence of counterpulsation (CNP) on average S-T-segment elevation (\( \overline{ST} \) left panel) and on the number of sites which showed abnormal S-T-segment elevation (NST right panel). Each line represents one animal, and the values of \( \overline{ST} \) and NST are shown in open triangles during the control occlusion and in closed triangles during occlusion with counterpulsation. The mean values for the group are represented as squares connected by the interrupted lines. Brackets represent standard errors of the mean. Mean \( \overline{ST} \) decreased from 3.3 ± 0.8 to 1.4 ± 0.4 mv (P > 0.01), and mean NST decreased from 7.8 ± 1.7 to 4.0 ± 1.5 (P < 0.025.)
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Figure 2

(Left panel) Average S-T-segment elevation (ST) during occlusion alone (closed circles) and during occlusion with counterpulsation (open circles). (Right panel) Schematic representation of the heart with circles indicating sites where epicardial electrocardiograms were obtained.

The area of ischemic injury after occlusion alone (S-T > 2 mV) is depicted by the striped area and during occlusion with counterpulsation by the stippled area. Note the reduction of the injured zone by counterpulsation. LA = left atrial appendage; LAD = left anterior descending coronary artery.

In all six dogs in which IABC was started 3 hours after coronary occlusion there was a decrease in ST (fig. 4, left) and in NST (fig. 4, right), when these indices were compared just before and 15 min after the IABC began. The average ST decreased from 4.2 ± 1.1 to 2.8 ± 1.0 mV (P < 0.01), and the average NST fell from 6.5 ± 1.0 to 3.7 ± 1.4 (P < 0.01), while mean arterial pressure and heart rate did not change significantly (from 108 ± 5 to 110 ± 6 mm Hg and from 157 ± 11 to 154 ± 10 beats/min).

Group 3. In the four dogs in this group, isoproterenol increased the severity and extent of myocardial ischemic injury, raising ST from 6.0 ± 1.7 mV and NST from 9.0 ± 0.7, 2 hours following occlusion, to 8.0 ± 1.0 and 9.3 ± 0.6, respectively, 1 hour later. IABC was started 3 hours after occlusion. Under these circumstances, ST and NST decreased in all cases (fig.

Figure 3

An example of the effect of counterpulsation (IABC) on the average S-T-segment elevation (ST) when coronary occlusion was maintained.
The effects of IABC 3 hours after coronary occlusion

4). Average $\overline{ST}$ decreased from $8.0 \pm 1.9$ to $5.7 \pm 1.8$ mV ($P < 0.05$) and average NST from $9.3 \pm 0.6$ to $7.5 \pm 0.9$ ($P < 0.05$) while mean arterial pressure and heart rate did not change significantly from $124 \pm 7$ to $129 \pm 13$ mm Hg and from $177 \pm 6$ to $178 \pm 6$ beats/min. An example is illustrated in figure 5.

When all 10 dogs in which IABC started 3 hours following occlusion are considered as a group, i.e., six in group 2 and four in group 3, the $\overline{ST}$ and NST were stable prior to the onset of IABC; the average $\overline{ST}$ at 2.5 hours after occlusion was $5.8 \pm 1.2$ mV, and after 3 hours it was $5.7 \pm 1.1$ mV (ns) while NST was $7.4 \pm 0.7$ and $7.6 \pm 0.8$, respectively. With 15 min of IABC the average $\overline{ST}$ fell to $4.0 \pm 1.0$ mV ($P < 0.01$), and 30 min later it was $3.7 \pm 1.0$ mV; similarly, NST was $5.2 \pm 1.1$ ($P < 0.01$) and $5.4 \pm 0.9$ ($P < 0.01$) at these two times.

Clinical Observations. Results in patients treated with IABC were similar to those obtained experimentally (decrease in $\Sigma ST$ and NST with IABC). In one of the patients (W.W.), when the IABC was interrupted for 15 min the effect of this intervention could be clearly demonstrated: $\Sigma ST$ and NST rose when IABC was interrupted and fell again when it was resumed. The resumption of IABC also increased mean aortic pressure and lowered pulmonary artery wedge pressure (fig. 6). This patient maintained a reasonable hemodynamic state during the IABC (cardiac index 2.61 liters/min/m²; peak arterial pressure during counterpulsation 90 mm Hg; urinary output 35 ml/hr). Coronary cineangiography disclosed three-vessel disease, and a double saphenous vein-coronary artery bypass was performed. The patient expired 12 hours after operation.

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The second patient (S.A.) showed a clinical picture of cardiogenic shock following successive extensions of an acute anteroseptal infarction laterally, inferiorly, and finally lateroposteriorly. IABC was initiated, and 30 min later his ischemic injury was found to have decreased strikingly. ST on the lateral wall fell by 35%, and his ischemic injury of the posterior wall represented by S-T-segment depressions in the right-sided leads decreased by 80% (fig. 7). After institution of IABC the patient's hemodynamic state also improved: cardiac index 2.6 l/min/m²; peak arterial during counterpulsation 100 mm Hg; urinary output 25 ml/hr. IABC was continued intermittently for 3 weeks when gram-negative septicemia supervened, with deterioration of the hemodynamic condition and death 1 month following the acute myocardial infarction.

Discussion
IABC produces favorable hemodynamic alterations similar to those of other counterpulsation modalities,12-16 and because of its relative simplicity this technic has recently been applied in the treatment of patients with cardiogenic shock.1,3,5,6 In view of this application and its potential theoretical advantages in improving the relation between myocardial oxygen supply and demand, we examined the effects of IABC on the size of the zone of ischemic injury following coronary occlusion. Under the conditions of these experiments IABC significantly decreased the extent and magnitude of ischemic injury following coronary occlusion. The results of Goldfarb et al.17 tended to show less histologic deterioration after coronary occlusion following counterpulsation. However, their method did not allow quantification of the effects. Nachlas and Siedband15 and Sugg et al.,18 using the Nitro Blue method,19 compared infarct size of control and counterpulsed dogs subjected to coronary ligation. The inherent disadvantage of this approach is that variations in coronary arterial distribution in different animals result in a wide range of infarct size, even when the site of coronary artery occlusion is constant, making it difficult to prove significant modification in infarct size following an intervention. Another problem inherent in these methods is that several hours elapse between the coronary occlusion
and the recognition of the infarct. During this time interval, hemodynamic alterations, such as the development of arterial hypotension and tachyarrhythmias, may profoundly affect the size of the infarct. Therefore, the shorter this time interval, the less the likelihood that such hemodynamic alterations might alter the size of the infarct.

Because of the disadvantages of the earlier methods, as outlined above, we selected the epicardial electrocardiographic techniques for estimating the magnitude of ischemic injury. This method has been demonstrated to be highly reproducible, permits the use of each dog as its own control (thus obviating the problem of variations in distribution of coronary vessels), and allows measurements of the injured area within minutes after occlusion. The reliability of this method has been substantiated by biochemical, histologic, ultrastructural, and histochemical studies.

The results of the present investigation show clearly that IABC exerts a beneficial effect on the size of the zone of ischemic

**Figure 6**

An example of the effects of IABC on a hypotensive patient (W. W.). \( \Sigma ST = \text{sum of S-T-segment elevations (1 mm = 0.1 mv)}; \) NST = number of sites that showed S-T-segment elevation higher than 0.1 mv; PA wedge pressure = pulmonary artery wedge pressure recorded through a Swan-Ganz catheter; \( \bar{AP} = \text{mean pressure in the ascending aorta; shaded bars represent periods of IABC.} \)
Figure 7

Electrocardiograms of the 35 sites on the chest in a patient (S. A.) before (A) and during (B) IABC. The extreme upper left electrode (A1) was located at the second intercostal space at the parasternal line, and the extreme lower right electrode (E7) in the sixth intercostal space on the midaxillary line. (A) Before IABC. Note marked S-T-segment depression in the right columns (myocardial ischemic injury from the acute "true" posterior wall infarction) and marked S-T-segment elevation on the left columns (myocardial ischemic injury of the lateral wall). (B) After IABC. Note the decrease in S-T depression in the right columns (less ischemic injury of the "true" posterior wall) and a reduction in S-T-segment elevation in the left columns (less ischemic injury of the lateral wall).

injury. This effect was not only apparent when IABC was begun prior to coronary occlusion, as described above, but was also observed in all 13 dogs in which IABC was started up to 3 hours following coronary occlusion. These observations demonstrate that IABC effectively decreases myocardial injury even several hours after occlusion and suggests its usefulness in the clinical situation for reducing infarct size. This decrease in myocardial ischemic injury was observed in normotensive dogs and implies that even under these conditions there is a substantial improvement in oxygen supply in relation to the oxygen requirements of the myocardium; this might result from reductions of myocardial oxygen needs, from increasing total coronary diastolic flow, and/or from augmenting coronary collateral flow to the ischemic zone. Therefore, these data suggest the potential usefulness of
this technic not only for the treatment of patients with cardiogenic shock but also for normotensive patients with acute myocardial infarction in an effort to decrease myocardial injury.

The findings of this investigation imply that IABC might be useful in a number of clinical situations involving patients with acute myocardial infarction. Thus, the reduced ischemic injury observed in dogs in group 1, after pretreatment with IABC, suggests consideration of the clinical use of this therapeutic approach in patients with the clinical syndrome of impending myocardial infarction. The effect of IABC in combination with isoproterenol on myocardial injury is also of interest since this drug has been commonly used in cardiogenic shock, but has been shown experimentally to increase the severity and extent of myocardial ischemia and necrosis following coronary occlusion. The results of the present study show that such injury increased by isoproterenol can be reduced by concurrent IABC; thus, the valuable positive inotropic effects of the drug could be employed in appropriate patients while the disadvantageous effects resulting from the augmented oxygen needs can be counteracted by IABC.

The preliminary observations in two patients tend to confirm the experimental results in the clinical situation. IABC not only improved the hemodynamic state, as has been previously demonstrated, but also reduced myocardial ischemic injury. In addition, temporary interruption of IABC increased myocardial ischemic injury and was associated with deterioration of the hemodynamic state (fig. 6).

In conclusion, IABC significantly reduced the magnitude and extent of acute myocardial ischemic injury when used as pretreatment or up to 3 hours after coronary occlusion in normotensive animals. This might be expected from the decrease in myocardial oxygen consumption and increase in coronary blood flow which were induced. It was also shown that when IABC is combined with a positive inotropic drug, such as isoproterenol, the increase in ischemic injury caused by the drug's positive inotropic action could be reversed.

Acknowledgment

The authors wish to acknowledge the skill and technical assistance of Mr. Anthony E. Murphy, Jr., and Mrs. Beverly Kelly.

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Circulation. 1972;45:1150-1159
doi: 10.1161/01.CIR.45.6.1150
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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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:
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