Effects of Isometric Exercise on the End-Diastolic Pressure, Volumes, and Function of the Left Ventricle in Man

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SUMMARY Changes induced in left ventricular (LV) hemodynamics by isometric exercise were analyzed in 43 patients: 30 with coronary heart disease (CAD), four with noncoronary heart disease, nine normal. Volumes were angiographically determined and correlated with left ventricular end-diastolic pressure (LVEDP) both at rest and during the fifth minute of 30% sustained handgrip (HNG). All normals and eight with CAD improved LV function during HNG. LVEDP decreased or remained constant, end-diastolic volume (EDV) decreased, end-systolic volume ( ESV) decreased, as ejection fraction (EF) remained constant. None of these eight CAD cases altered their regional LV contraction pattern during HNG.

Twenty-five patients, 21 CAD and four nonCAD, showed diminished LV function during HNG. LVEDP increased, EDV decreased, ESV increased, as EF declined. In these 21 CAD patients, at least one major coronary vessel was narrowed 70% or more and, with but two exceptions, was not supported by adequate collaterals. In 18, new asynergic zones developed in previously normally contracting areas or pre-existing asynergic zones extended during HNG.

SUSTAINED (STATIC) MUSCULAR CONTRACTIONS increase heart rate and blood pressure,1,2 imposing a pressure load and greater oxygen requirement on the left ventricle (LV).3 For these reasons, sustained handgrip contractions (HNG) have been used to evaluate the hemodynamic reserve of patients with heart disease. Although hemodynamic alterations have been well studied,3-7 relatively little is known concerning the volume changes and characteristics of the LV wall motion during HNG.8 The aim of this investigation was to study the pressures, volumes, and wall motion of the LV during HNG in patients with and without heart disease and to correlate observed hemodynamic changes with coronary angiographic findings.

Methods

The material for this study is composed of 43 patients who had good quality left cineventriculograms (LCV) both at rest and during HNG. Nine with recurrent chest pains had no discernable cardiac disorders, 30 had coronary artery disease, and four had other forms of heart disease (two valvular, one hypertensive, and one cardiomyopathy). All were in sinus rhythm. Propranolol treatment had been discontinued at least 48 hours prior to the study with the exception of three patients who received their last oral dose 24, 14, and 8 hours before the study. Two patients had received sublingual nitroglycerin during the half hour preceding resting cineventriculography.

Cardiac catheterization was performed in the fasting state after premedication with 10 mg oral diazepam. Thirty minutes after the completion of coronary angiography a basic protocol was followed to obtain cineventriculograms at rest and repeated during HNG. Fluid-filled catheters were positioned in the LV, main pulmonary artery (PA), and in 26 patients, the brachial artery pressure (BA) was monitored as well. In four patients a Millar micro-tip catheter pressure transducer (#8F PC-481) was used for injection of contrast media and simultaneous measurement of the LV pressure during cineventriculography.

Quantification of the HNG stress was accomplished by means of a special transducer (Statham Precision Readout, Model SC 1000). Using a water-filled rubber bulb and rigid tubing, the force of the isometric contraction could be read in kg on a linear scale. Patients sustained a constant effort by keeping the indicator needle on the readout scale fixed at a given point. The maximum voluntary contraction (MVC) for the left hand of each patient was determined in kg's as described by Lind et al.1

Resting cineventriculography was performed first in 40 cases followed by a period of 20 minutes (or more if needed) to allow LVEDP to return to its preangiographic levels. The patient was then asked to perform HNG with his left hand at 30% of his MVC; a second LCV was then obtained during the fifth minute of exercise prior to the release of HNG. In three normal patients, however, HNG ventriculography was performed first, followed 20 minutes later by resting ventriculography with a right atrial paced heart rate identical to that observed during HNG. Cineventriculograms were filmed at 64 frames/second and recorded on 35 mm film with the patient positioned in a 30° RAO projection and breathing quietly. Forty to 50 cc of meglumine and sodium diatrizoate were injected into the LV at a rate of 14 ml/sec, through a Siemens Contrac 3 (E) power injector. The catheter used for injection of dye was connected by means of a three-way stopcock to a pressure transducer (P23 Db) to facilitate pressure recordings immediately preceding and following contrast injections. During ventriculography the cine pulse signals were recorded together with ECG, PA, and BA pressure pulses at 200 mm/sec paper speed. Rotation of the patient, height of the X-ray table and image intensifier, X-ray settings, amount of contrast media, and rate of injection for each patient were the same during resting and HNG angiograms. Pulmonary artery and BA pressures

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were recorded continuously for one minute before, during, and after left cineventriculography. Recording of LV pressure was interrupted during the injection of contrast media. Left ventricular end-diastolic (LVEDP) and left ventricular systolic (LVSP) pressures were measured immediately prior to this. In three patients, who were studied with a Millar micro-tip catheter, volume-pressure curves for the whole diastole were constructed and data fitted to an exponential equation: $P = be^{kV}$, where $P =$ pressure in mm Hg, $V =$ volume in cc, $e =$ base of the natural log, and $b$ and $K$ were the variables fitted to the data.

Left ventricular volumes were measured from the first three opacified beats. If an extrasystole occurred before adequate visualization of the LV, the LCV was discarded. End-diastolic volume (EDV) was measured from the synchronized frame corresponding to the peak of the R wave in the ECG; end-systolic volume (ESV) was derived from the smallest angiographic silhouette during cardiac contraction. Ejection fraction (EF) was calculated as $\frac{EDV - ESV}{EDV}$. Volumes were measured by the single-plane RAO technique, as described by Kasser and Kennedy. Because the single-plane RAO technique overestimates the LV volumes, the measured volumes were corrected by the formula: corrected volume = measured volume $\times 0.787 + 7.8$ ml.10

Localized abnormalities of LV contraction seen in the resting or HNG LCVs were described in terms introduced by Herman et al.11 Quantification of asynergic areas was achieved in the following fashion: the end-diastolic and end-systolic frames were traced on the same piece of paper. Long axes were drawn from the middle of the aortic valve to the apex and re-aligned so that they coincided. The margins of an asynergic area in the perimeter of the end-systolic tracing were then identified, and the projection of the asynergic area upon the end-systolic axis, expressed as percent of this axis, was used to quantitate the extent of asynergy. Asynergic areas were characterized as anterior or inferior. Apical asynergy was added to the asynergy of the adjusted wall, which in all our cases, was the anterior wall. The degree of asyneresis was indicated by the shortening of the radius of this area expressed as percent of the end-diastolic radius of the same area (fig. 1). Dyskinesis was expressed by the systolic expansion of an area beyond its end-diastolic margins, in mm. No attempt was made to analyze asynchrony in this study. In a few instances, quantification of asyneresis was impossible as there was no clear demarcation between asyneretic and normally contracting segments, and the degree of asyneresis was small.

All patients except one, a patient with mitral stenosis, had selective coronary cineangiography. Coronary artery lesions were quantified as percent obstruction of the diameter of the vessel. Coronary collateral vessels were graded from 0 to 3+ using the following angiographic criteria:

3+ collaterals:
1) The vessel filled by these collaterals beyond its obstructive lesion had the same contrast as the donor vessel.
2) The caliber of the vessel filled by the collaterals was equal to the caliber of the same vessel proximal to obstruction or, in cases where the proximal vessel was not opacified, 1 mm in diameter (using catheter width for correction of the X-ray magnification).
3) There were no significant lesions in the distal vessel and all its branches were opacified.
4) The donor vessel before the origin of the collaterals or the collaterals themselves had no significant obstructive lesions.

2+ collaterals differed from 3+ collaterals in that the contrast in the distal vessel was distinctly fainter than in the donor vessel.

Collaterals were characterized 1+ when:
1) The distal vessel was opacified faintly and erratically without filling of its branches, or had significant obstructive lesions.
2) The donor vessel had significant obstructive lesions before the origin of the collaterals.
3) The collaterals themselves had significant obstructive lesions.

Collaterals were designated ± if only branches of the distal vessel were opacified or the distal vessel itself was opacified very late in a faint, threadlike manner.

**Results**

Handgrip did not evoke angina, dyspnea, or arrhythmias. Mean hemodynamic and volumetric data are presented in table 1. Correlations between LVEDP and volume changes were looked for. Except for a negative correlation between change in ESV and change in EF ($r = -0.88$), no predictively useful relationships were found. One patient who performed a Valsalva maneuver during HNG is presented in figure 5.

**Normal Patients**

During HNG normal patients demonstrated a decline or no change in their LVEDP associated with a decrease of their EDV and no change in their EF. The ESV declined in all but one. All three normals, who were studied with iden-
tical heart rates at rest and during HNG, decreased their ESV. In two the EDV did not increase as EF increased. In the third EDV decreased as EF remained constant (table 1).

**Noncoronary Heart Disease Patients**

Elevation of the LVEDP in these patients was associated with a decrease in EDV. Their ESV increased and EF fell during HNG (table 1).

**Coronary (CAD) Heart Disease Patients**

LVEDP response of the CAD patients during HNG varied. In eight the LVEDP declined 1 to 8 mm Hg and in 21 it increased 1 to 24 mm Hg. CAD patients were separated according to their LVEDP response, into CAD-Group I (decline in LVEDP) and CAD-Group II (elevation of LVEDP). Both groups included patients with angina pectoris (7 in Group I, 18 in Group II), previous myocardial infarctions (4 in Group I, 11 in Group II), congestive heart failure (1 in Group I, 3 in Group II), asynergy in their resting cineventriculograms (4 in Group I, 14 in Group II), large EDV (1 in Group I, 4 in Group II), and LVEDP more than 12 mm Hg (1 in Group I, 10 in Group II). There was no significant difference in resting HR, LVSP, LVEDP, EDV, ESV, and EF between the two groups (table 1). The stress imposed by the isometric exercise, as reflected by the acceleration in HR and augmentation of LVSP, was similar in the two groups (table 1). All CAD-Group II patients had at least one major coronary vessel 70% or more stenotic and in only two patients were the stenotic vessels supported by adequate (2+ or 3+) collaterals. CAD-Group I was not homogeneous; one patient had no significant obstructive disease, two had obstructed vessels supported by 2+ or 3+ collaterals, two had one vessel totally obstructed, and three had 80–95% obstruction in one or more vessels which were unsupported by collaterals.

The changes in EDV, ESV, and EF in CAD-Group I during HNG were similar to the normals (table 1). In CAD-Group II, the EDV decreased, the ESV increased, and EF fell.

The deterioration of LV function in CAD-Group II patients during HNG was segmental in nature, consistent with the appearance of new or the extension of resting asynergy. Only three of the 21 CAD-Group II patients, who elevated their LVEDP during HNG, did not change their contraction pattern (fig. 2).

**Volume-Pressure Relations**

Figure 3 presents data plots from a patient who demonstrated a marked exaggeration of his resting anterior asynergy during HNG. The slight reduction in EDV is associated with an increased ESV and LVEDP. The volume-pressure (V-P) curve during HNG was displaced upward on the pressure axis. The mean diastolic distensibility (change in volume per unit change in pressure, from early to end-diastole) was larger during HNG, 2.7 cc/mm Hg, than at rest, 2.0 cc/mm Hg. The exponential curve during HNG had a higher pressure intercept and a diminished slope. There was also a change in the pattern of the diastolic filling during HNG: the late filling (occurring after the onset of the a wave) was similar at rest (19 cc) and during HNG (21 cc), but the early filling (up to the onset of the a wave) was 65 cc at rest and only 28 cc during HNG. The patient presented in figure 4 had symmetrical contraction at rest, but developed minimal inferior wall asynergy toward the end of systole during HNG, which disappeared during ventricular relaxation and before the opening of the mitral valve. The LVEDP increased 5 mm Hg during HNG but the beginning diastolic pressure did not change. The HNG volume-pressure curve was slightly steeper in the middle and late diastole, and the exponential equation showed basically the same intercept and slightly steeper slope. Early diastolic filling was not diminished. The patient presented in figure 5 probably performed a Valsalva maneuver during the stress of HNG and thus has been excluded from table 1. He elevated his LVEDP a few beats before injection of contrast media and dropped it by the end of the cineventriculogram before releasing HNG. This patient had a total occlusion of his left anterior descending artery with distal filling by collaterals and a symmetrical pattern of LV contraction at rest. During HNG his contraction remained symmetrical, the EDV and

### Table 1. Mean Hemodynamic and Volumetric Values

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**P** = level of significance in the differences between resting values of CAD Group I and CAD Group II.

**Abbreviations**: HR = heart rate; LVSP = left ventricular systolic pressure; LVEDP = left ventricular end-diastolic pressure; EDV = end-diastolic volume; ESV = end-systolic volume; EF = ejection fraction; SV = stroke volume; se = standard error; M = mean; NS = not significant; R = resting; HNG = hand grip.

Normal* = Normal patients whose resting cine-ventriculogram was performed after HNG at a paced heart rate equivalent to that obtained during HNG. CAD Group I = CAD patients who decreased LVEDP during HNG. CAD Group II = CAD patients who increased LVEDP during HNG. Non-CAD = patients with no coronary artery disease.
ESV decreased, the EF increased from 64 to 67% and his early diastolic filling was unaffected. The HNG volume-pressure curve was shifted upward but followed the resting volume-pressure curve. The mean diastolic distensibility did not change and the exponential equation during HNG showed a higher pressure intercept and diminished slope.

**Asynergy (figs. 6–9)**

None of the nine normals, the four non-CAD, and the eight CAD patients who decreased their LVEDP, changed their LV contraction pattern during HNG. Eighteen of the 21 CAD patients who elevated their LVEDP altered their contraction pattern in that they either developed new asynergy in areas normally contracting at rest (8 patients), or exaggerated their pre-existent asynergy (11 patients). Exaggeration consisted of an increase in the size and/or the degree of asynergy. Six of the eight new asynergic areas developed in patients who had normal contraction in their resting cineventriculograms. All new asynergy was in the form of asyneresis (fig. 6).

The relation of the resting asynergy to the degree of coronary artery stenosis and presence of collaterals is given in figure 7. In this and the next figure the number of asynergic areas at rest and their extension during HNG is two greater than the actual number, because the same area was assigned to both the left anterior descending and the left circumflex coronary artery in two patients. In figure 8 it can be seen that all asynergic areas at rest which were supplied by critically narrowed but not totally occluded coronary vessels extended during HNG. Of the eleven areas corresponding to totally occluded vessels, three of the six not supported by collaterals and one of the five supported by adequate collaterals (2+ or 3+) extended during HNG. Figure 9 demonstrates that all new asynergy developed in areas supplied by critically narrowed vessels unsupported by collaterals. None of the six areas which corresponded to totally obstructed vessels that were supported by adequate collaterals and had normal contraction at rest developed new asynergy during HNG.

**Figure 2.** Relations between changes in LVEDP and changes in LV volumes and EF in CAD patients. Each dot from left to right represents a CAD patient. CAD-Group I = CAD patients who decreased their LVEDP during HNG. CAD-Group II = CAD patients who elevated their LVEDP during HNG. No = Patients in CAD-group I who did not develop new or extended pre-existent asynergy during HNG. Asynergy = Patients in CAD-Group II who developed new or extended pre-existent asynergy during HNG. For each patient from the bottom of the figure to the top are depicted: ΔLVEDP = the changes in LVEDP in mm Hg. ΔEDV = change in EDV in cc. ΔESV = the change in ESV in cc. ΔEF = the change in EF, in percent. A negative correlation between ΔESV and ΔEF (τ = −.89) was found; the other correlations were not strong enough to be clinically important.

**Figure 3.** Volume pressure relations in a patient whose asyneresis increased during HNG. Upper panel! Recordings during rest (left) and HNG (right) cine ventriculography. Cine = cine-pulse signals for synchronization. LV press. = left ventricular pressure tracing. Note attenuation to 1.25 mm Hg/mm paper height during HNG. BD = beginning diastolic pressure; d = end of diastasis; respiration = recording of the respiratory movements; RA press. = right atrial pressure. Zero pressure baseline at rest indicated with two short horizontal lines. Lower panel, right: v = end-systolic volume (corresponds to higher pressure). ○ = volume at the point of beginning diastolic pressure (BD in the upper panel). □ = volume at the end of diastasis (D in the upper panel). Δ = end diastolic volume. Open symbols = rest, filled symbols = HNG.
of error must be considered. First, an inadvertent Valsalva maneuver may be performed during HNG, increasing intra-thoracic pressure, thereby increasing LVEDP and reducing LV volume. Second, more widespread areas of asynergy are associated with greater error in measuring EDV. Third, non-simultaneity exists in angiographic measurements of left ventricular diastolic volume-pressure relationships. In our protocol, a delay of three cardiac cycles occurs between the last recorded LVEDP and the first calculated EDV. Fourth, in ventricles with a steep exponential curve relating diastolic pressure to volume, marked elevations in LVEDP may be accompanied by only minimal rises in EDV that may not be easily detected.

To avoid an inadvertent Valsalva maneuver, patients were instructed to breathe quietly, even during ventriculography. LVEDP and PA pressure tracings were recorded for extended periods during and after ventriculography. An inadvertent Valsalva could be detected by the abrupt rise and fall in LVEDP, characteristic of the strain and release phase of the maneuver. Seventeen patients, including eight with CAD, did not elevate LVEDP during HNG. At least 18 of 21 patients increasing LVEDP with HNG simultaneously developed or extended asynergic zones.

The presence of asynergy does increase the error in estimating EDV angiographically and this error becomes greater as left ventricular size exceeds 250 ml. Only four of 21 CAD patients who elevated LVEDP during HNG and showed new or increased areas of asynergy had EDVs exceeding 200 ml, however. Lag time between measurement of LVEDP and EDV could influence pressure-volume curves, through changes in cardiac cycle length or by a direct effect of contrast media on left ventricular volume. No change in heart rate was observed during ventriculography, as has been previously reported. Introduction of opaque dye into the LV during angiography does result in a 10% average in-

Mitril Regurgitation

In four CAD patients mitral regurgitation either increased during HNG or developed de novo. All of these patients increased their LVEDP during HNG.

Discussion

In interpreting hemodynamic and angiographic data obtained during sustained HNG exercise, four major sources of error must be considered. First, an inadvertent Valsalva maneuver may be performed during HNG, increasing intra-thoracic pressure, thereby increasing LVEDP and reducing LV volume. Second, more widespread areas of asynergy are associated with greater error in measuring EDV. Third, non-simultaneity exists in angiographic measurements of left ventricular diastolic volume-pressure relationships. In our protocol, a delay of three cardiac cycles occurs between the last recorded LVEDP and the first calculated EDV. Fourth, in ventricles with a steep exponential curve relating diastolic pressure to volume, marked elevations in LVEDP may be accompanied by only minimal rises in EDV that may not be easily detected.

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crease in LVEDP. Therefore, LVEDP during calculation of EDV was probably slightly higher than that recorded just prior to ventriculography. Comparison of the LVEDP-EDV relationship between patients should remain valid since the directional change in LVEDP was probably similar in all cases.

The exponential curve relating LV diastolic pressure to volume could result in erroneous conclusions when resting ASYNERGY AT REST.

LVEDP is markedly increased and further increments in pressure are associated with minimal, nondetected increments in EDV. In the present study, however, only six of 25 patients who elevated LVEDP with HNG had resting LVEDP exceeding 15 mm Hg.

The present results show that elevations of LVEDP during isometric exercise are not accompanied by an increase in EDV. End-diastolic volume actually declined in most patients who elevated their LVEDP. A rise in LVEDP with a decline in EDV was observed in patients with both coronary and noncoronary heart disease. Similar observations have been made by others. Using thermodilution techniques, Kasparian and Wiener found slight declines in EDV with
significant increases in LVEDP during pacing or exercise provoked angina. With angiographic volume measurements Dwyer and Barry et al. found that elevations in LVEDP were not associated with a rise in EDV during atrial pacing.

The discordant changes in EDV and LVEDP in CAD patients during pacing stress has been ascribed to changes in LV diastolic compliance. Barry et al. constructed compliance curves using coordinate points of LV pressure (beginning and end-diastole) and volume (end-systolic and end-diastolic) and found that during pacing-induced ischemia the log pressure-volume intercept shifts upward and the slope of the curve diminishes. They noted that analogous changes have been observed in tension-length curves of the contracting cat papillary muscle and advanced the hypothesis that during ischemia a portion of the left ventricle does not relax in diastole but remains in a state of sustained contraction which accounts for the elevation of the LV diastolic pressure. Indirect measures of left ventricular diastolic relaxation support this postulation. Maximal rate of decline in LV systolic pressure (peak negative dp/dt) is reduced in coronary heart disease patients during rapid atrial pacing. Diminution in early diastolic LV posterior wall velocity determined by echocardiography has been found during exercise-induced angina pectoris.

Detailed analysis of diastolic volume and pressure in the patient presented in figure 3 supports the hypothesis of incomplete relaxation playing a role in the rise of diastolic pressure during ischemia. Initial diastolic pressure was three times higher during HNG. Pressure during the whole course of diastole remained higher than at rest in spite of slightly smaller volumes. More interestingly the distensibility of the left ventricle (an index of compliance) increased during HNG. This can be explained if we assume that the left ventricle was not completely relaxed in early diastole thereby raising the pressure at that point. As relaxation improves later in diastole the pressure tends to fall, but at the same time ventricular filling occurs and the pressure increases. Viewed in this light, the diastolic pressure at any point will be the net result of two opposing influences, thus changing less for a given change in volume. Furthermore, variations in the temporal relation between relaxation and ventricular filling may influence the apparent distensibility of the ventricle in different ways.

In contrast the CAD patient presented in figure 4 had normal LV contraction at rest. Handgrip stress evoked a late systolic asyneresis of the inferior wall, which subsided during isovolumic relaxation, prior to mitral valve opening. Initial diastolic pressure was unchanged. Diastolic filling prior to left atrial contraction was unaltered. Ventricular filling during left atrial contraction remained undiminished, but ventricular pressure was elevated. Abnormalities of diastolic distensibility were present mainly during late, as opposed to early, diastole. Regional depletion of adenosine triphosphate (ATP) stores in ischemic myocardium has been proposed as a mechanism which might explain sustained contraction or failure of relaxation during diastole. Limited energy stores impede the sarcolemma's sequestration of myoplasmic calcium which mediates relaxation. Elevations in LVEDP observed in CAD patients during HNG might have been related to localized ischemia. Similar elevations seen in non-CAD patients could have been produced by augmented pressure work, which depleted ATP stores to a degree where diastolic relaxation became impaired.

In the normals and some CAD patients LV performance was enhanced during HNG. Greater systolic emptying was achieved from a smaller EDV in the presence of a higher pressure load, even when heart rate was kept constant. Improvement in LV function during HNG has been previously noted by others. The mechanism involved in improvement of the inotropic state of the left ventricle during HNG is not known. It has been postulated that isometric exercise affects the circulation through reflexes triggered from contracting muscles. The efferent limb of this reflex might alter autonomic traffic to the heart causing an increase in contractility. Indeed, there is evidence that both parasympathetic withdrawal and enhanced sympathetic tone to the heart take place during isometric exercise. Increased arterial pressure might also exert a positive inotropic influence upon the left ventricle. It has been shown in isolated, supported heart preparations that when the arterial pressure is increased, the contractility of the left ventricle is augmented (Anrep's effect).

The present results indicate that parallel increases in LVEDP and EDV do not occur in most patients with coronary or other forms of heart disease. Use of conventional LV function curves, where LVEDP is substituted for EDV for characterizing LV performance during HNG may not be justified. LVEDP response during HNG did correlate with angiographic measures of LV performance, however. Patients who did not increase their LVEDP, decreased their end-systolic volume and did not change their ejection fraction. Whereas, in patients who increased their LVEDP, end-systolic volume increased and ejection fraction declined. Therefore, directional changes in LVEDP during HNG can be used to characterize LV response as either normal or abnormal without resorting to separate computations of cardiac output or stroke work. Although none of the normal patients in this study had elevated LVEDP during HNG, slight elevations of LVEDP during isometric stress have been reported in normal patients by others. The data from our CAD patients (fig. 2) suggest that there is an overlap in the LV functional response among patients with mild elevations of LVEDP. Indeed, three CAD patients with elevations of one, three and six mm Hg did not decrease LV.
function appreciably. Yet, eight patients with definite LV dysfunction also had minimal (less than six mm Hg) elevations of LVEDP. If some arbitrary range of pressure rise is selected as “normal response” to HNG, then its sensitivity as an intervention diminishes while its specificity increases. It is quite evident, however, that spurious elevations of LVEDP due to an occult Valsalva maneuver are difficult to detect without careful monitoring of respiratory motion or RA pressure.

In CAD patients, elevations of LVEDP during HNG also implied that at least one major coronary vessel was more than 70% stenosed and unsupported by collaterals and that the myocardial segment supplied by the diseased vessel developed new asynergy or extended pre-existent asynergy. A normal LVEDP response did not rule out critical coronary lesions but did indicate that new or extending asynergic areas did not develop during HNG.

Dwyer and Pasternac et al. showed that asynergy could be a dynamic event in CAD patients. Atrial pacing induced asynergy in previously normally contracting regions or extended the area of previously malcontracting regions. This stress-induced asynergy has been ascribed to disparities between increased metabolic demands associated with tachycardia and limited metabolic supply due to atherosclerotic coronary vessels with limited capacity to increase flow. Isometric exercise in CAD patients also appears to cause or exaggerate segmental wall motion disorders and can be explained on the same basis, an encroachment on coronary reserve. It may also relate to a borderline mechanical weakness in the myocardium which is exposed by the pressure load imposed on the LV during HNG stress. Using radarkymographic video tracking, Ludbrook et al. also demonstrated abnormalities of LV wall motion during handgrip.

One of the main difficulties in evaluating the role of the coronary collaterals in man is the lack of a method of quantification of the collateral flow. The method employed in this study was arteriographic and therefore subject to a number of methodologic limitations; amount and force of injection of contrast media, quality of the cine films, effort made to search for collateral vessels.

Any examination of the protective influence of coronary collaterals on LV function at rest must take into account both the magnitude of collateral tributaries and their recipient vessels. For comparative purposes recipient vessels from homologous sites in the coronary circulation and with equal severity of stenosis should be selected. In the present study, nine of the 11 totally occluded but adequately collateralized vessels were right coronary arteries whereas all six totally occluded but inadequately collateralized vessels were either left circumflex or anterior descending arteries. Therefore, no conclusions about the protective effect of collaterals on LV function at rest could be reached.

Preservation of LV performance during isometric stress might provide a basis for evaluating the functional capacity of collateral flow. In five totally occluded vessels with adequate collaterals but associated with asynergy at rest, only one extended the asynergic zone during HNG. However, in three of six totally occluded vessels without adequate collaterals resting asynergy was also not augmented during HNG. In these instances, restrictions of local myocardial contraction may have been fully expressed at rest.

Coronary perfusion of limited scope, whether via collateral channels or through severely stenosed but non-occluded vessels, did appear to sustain local myocardial contraction. Six occluded coronary arteries with adequate collaterals did provide enough nutrient flow to maintain normal LV wall motion both at rest and during isometric stress. Similarly, in seven of 15 instances subtotal occlusions of 80–99% unaccompanied by adequate collaterals showed normal LV wall motion at rest and during HNG. In the other eight, however, new asynergic zones observed during HNG suggested that occluded vessels with adequate collateral channels may provide a more secure support for myocardial contraction than marked stenosed vessels with limited flow capacity.

References

Myocardial Reperfusion in Acute Experimental Ischemia

Beneficial Effects of Prior Treatment with Steroids

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SUMMARY To test the hypothesis that prior steroid administration may enhance the mechanical and metabolic response to myocardial reperfusion, regional myocardial function (Hg-in-silastic length gauges), transmyocardial lactate balance and K+ difference were measured in 12 control and 13 treated (30 mg/kg methylprednisolone, 30 to 60 min postocclusion) dogs. At three hours of ischemia, systolic shortening in the ischemic segment was greater in treated dogs (40.6% vs. 12%, P < 0.05), while both lactate balance and K+ arteriovenous difference became positive. Lactate balance and K+ difference remained negative in the untreated animals. After three hours of occlusion and one hour of reperfusion, recovery of shortening was significantly greater in the treated animals (75.9 vs. 31.6%, P < 0.05). In addition, while lactate balance remained negative among the control dogs, it further improved in the treated dogs.

Thus, steroid administration during experimental coronary occlusion impedes the progression of ischemia and is additive to reperfusion in reversing ischemic dysfunction.

IT HAS BEEN DEMONSTRATED that myocardial reperfusion is an effective means of reversing mechanical dysfunction due to ischemic injury. However, the routine use of myocardial reperfusion for the treatment of acute myocardial infarction faces two major problems: 1) its effectiveness decreases as the period of ischemia increases, and 2) reperfusion itself may be associated with both hemodynamic deterioration and cell death. Ineffectiveness of reperfusion has been attributed to the fact that after one hour of coronary occlusion, irreversible cellular damage occurs in the infarcted area. Hemodynamic deterioration and death are in large part attributable to intramyocardial hemorrhage and severe ventricular arrhythmias following reperfusion.

Although currently available data are not entirely consistent, the preponderance of evidence suggests that progression of myocardial ischemia to infarction can be substantially delayed by steroid administration. Libby and coworkers have shown that steroid administration decreases the size of an acute myocardial infarction in dogs at 24 hours postocclusion. If the effects of reperfusion are contingent on the degree of cellular injury and if agents exist which do in fact alter the rate of progression of ischemia to infarction, then it could be hypothesized that the administration of steroids shortly after occlusion should influence positively the subsequent effects of reperfusion. The purpose of this study, therefore, was to evaluate this hypothesis.

Methods Studies were carried out in 25 (12 control, 13 treated) healthy mongrel dogs weighing from 22 to 28 kg. The animals received morphine sulfate (2.2 mg/kg, i.m.) 20 minutes prior to anesthesia with chloralose (100 mg/kg i.v.). After endotracheal intubation, respiration was maintained with a Harvard ventilator. A left thoracotomy was performed via the fifth interspace, and the heart was suspended in a pericardial cradle. The left anterior descending coronary artery was isolated for subsequent occlusion at an average of 3.5 cm from its origin. Systemic arterial pressure was continuously monitored with a P23Db pressure transducer (Statham Instruments, Hato Rey, Puerto Rico) by a transfemoral catheter advanced to the thoracic aorta. Left ventricular pressure was recorded by a transducer (Model BT-70, Bio-Tech, Pasadena, California), connected to a 10F catheter inserted in the ventricle through the apex. A large atrial catheter connected to a variable height reservoir was inserted into the left atrium, thus allowing manipulation of preload.

For assessment of regional function, methods previously described in this laboratory were employed. A 1 cm...
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