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Research Article

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ABSTRACT Coronary flow, left ventricular circumference, and left ventricular pressure were observed in the isovolumically contracting, isolated canine heart supported with arterial blood from a donor. Systolic pressure, heart rate, and coronary perfusion pressure were held constant while the coronary bed was progressively embolized with either large (average 865 μ) or small (average 10 μ) polystyrene microspheres. During embolization with large microspheres, coronary flow diminished progressively. After sufficient embolization, decreased ventricular performance was indicated by a rise in end-diastolic pressure. During embolization with small microspheres, coronary flow initially increased, which suggests the effective release of a vasodilator substance. Return of coronary flow to control levels occurred only after the end-diastolic pressure rose, on the average, to above 30 mm Hg. After embolization with both sizes of microspheres, ventricular diastolic pressure-volume relationships showed decreased ventricular compliance. This was attributed, in part, to edema of the ventricular wall and, in part, to focal shortening of the sarcomeres where the circulation was compromised. Embolization with both sizes of microspheres ultimately caused a decrease in ventricular performance, although when the systolic pressure was increased the usual relationship between peak developed wall stress, and end-diastolic pressure showed less of a descending limb than that found in the nonembolized, isolated heart.

It is felt that the data summarized above have bearing on ventricular performance and coronary flow in clinical situations where hearts are perfused through pump oxygenator systems and are thereby subject to embolization from aggregated clumps of platelets and fibrin.

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INTRODUCTION

While observing the performance of an isolated, supported canine heart in this laboratory, it was noted that if the coronary bed were embolized with small quantities of talc granules suspended in saline there was a sustained increase in coronary flow. This increase was observed while coronary perfusion pressure was maintained constant, and while heart rate and peak systolic ventricular pressure, two major determinants of coronary flow (1, 2), were also maintained constant. As one might expect such embolization to block coronary flow, this finding was not expected, and an attempt was made to see if it had been reported previously.

To date, the authors have been unable to find a study in which coronary flow was measured before and after coronary embolization while heart rate, systolic pressure, and coronary perfusion pressure were maintained constant. In one report where coronary flow increased after embolization, both heart rate and systolic pressure varied little from control values (3). Here, however, coronary flow was observed for only 10 min as the authors were primarily interested in reflex effects. Two additional studies reported a significant decrease in coronary vascular resistance after coronary embolization (4, 5). In the latter reports either heart rate or systolic pressure varied considerably throughout the period of observation.

It was decided, therefore, to study the effect of embolization of the coronary bed under controlled circumstances for three reasons. First, in a previous study it was noted that when the support animal in an isolated, supported dog heart preparation was replaced by a mechanical oxygenator there was invariably an increase in coronary flow which heralded a decrease in ventricu-

lar performance (6). Embolization of the coronary bed, although suspected, was never proven in this study. Nevertheless, it was felt that if a decrease in coronary vascular resistance is a reliable precursor of ventricular failure from coronary embolization, it might serve as a sensitive indicator of myocardial damage where the circulation is supported by a mechanical oxygenator and is thereby subject to embolization by aggregates of platelets and fibrin (7–9). Furthermore, when observing the performance of isolated hearts perfused through pump oxygenator systems, a progressive rise in both end-diastolic pressure and coronary flow has been noted (10). As such mechanical oxygenators are currently used during open heart surgery, specifically with coronary perfusion, there is an immediate practical need for an early index of myocardial damage in such situations where the possibility of embolization is high.

Second, in a previous report from this laboratory, only a slight descending limb of ventricular function was noted at high end-diastolic pressures in the healthy left ventricle (11). As others have reported pronounced descending limbs of ventricular performance when the coronary circulation was compromised (12), the question was raised as to what extent coronary embolization might have the same effect, or at least provide a model to study the extent to which such a descending limb might develop in a specifically diseased heart.

Third, in recent years a fairly large body of data has been accumulated which provides strong evidence that ischemic myocardial cells liberate a vasodilator substance and that this mechanism is an intrinsic control of coronary vascular resistance (13–17). If coronary vasodilation after embolization of the coronary bed could be demonstrated under well controlled circumstances, it would tend to support this hypothesis regarding the control of coronary flow.

Accordingly, the effect of coronary embolization on coronary vascular resistance was studied using both large and small emboli. As it was mandatory to control perfusion pressure, heart rate, and systolic pressure, an isolated supported heart preparation was used in which the effects of embolization could be expressed in terms of altered coronary flow.

METHODS

1. The preparation. The preparation used has been described previously in detail and will be described only briefly herein (11). Slight modifications of the original preparation were made to permit a continuous and accurate recording of coronary flow. Fig. 1 is a schematic diagram of the preparation.

As in the previously described preparation, hearts with lungs attached were rapidly excised from heparinized healthy mongrel dogs (11–24 kg) under chloralose (60 mg/kg) and urethane (900 mg/kg) anesthesia and perfused with blood from the femoral artery of a healthy, similarly heparinized and anesthetized, donor dog. As illustrated in Fig. 1, the perfusing blood was directed retrograde into the ascending aorta using two parallel Debakey pumps and a small (20 cc) air chamber to insure a relatively nonpulsatile per-

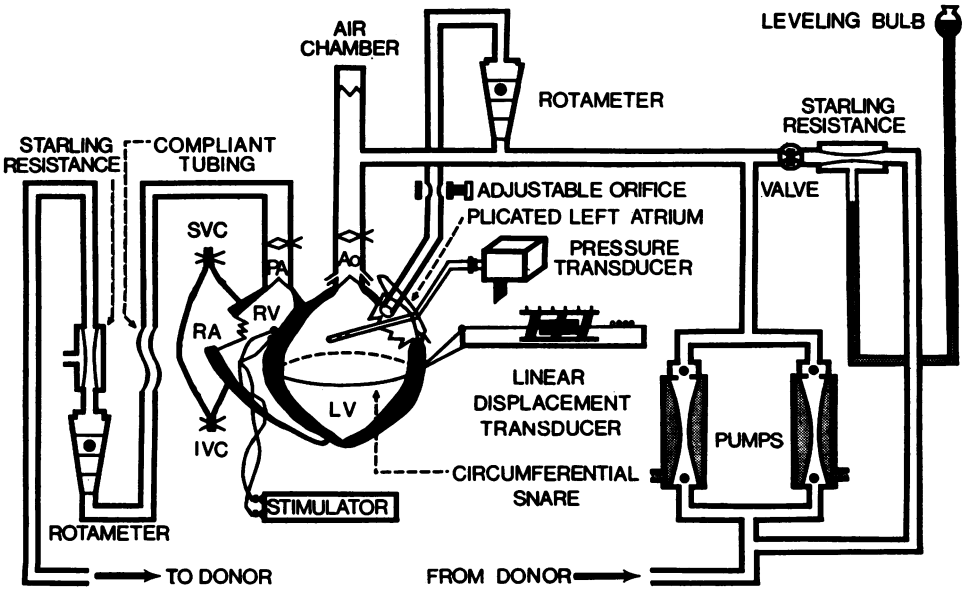

FIGURE 1 Schematic diagram of preparation. Arterial blood is pumped from femoral artery of donor to aorta of isolated heart while perfusion pressure is maintained by Starling resistance. Coronary sinus blood is returned via pulmonary artery to femoral vein of donor. RA = right atrium; LV = left ventricle; RV = right ventricle; Ao = aorta; PA = pulmonary artery; SVC = superior vena cava; IVC = inferior vena cava.

fusion pressure. A Starling resistance was used to maintain the pressure of the perfusing blood constant at approximately 100 mm Hg.

Immediately after the heart was perfused, the pulmonary artery was cannulated and both vena cavae ligated. The coronary venous blood was then directed through the pulmonary artery cannula and through a section of thinly walled, compliant tubing (¾ in. Penrose drain) placed 5 cm below the level of the heart which served to dampen the pulsations of coronary venous flow. From there blood was directed to a rotameter (Fischer & Porter 36-541-22) from which it was returned to the donor after passing through a Starling resistance likewise positioned 5 cm below the level of the heart. In this manner, the rotameter served to record the coronary flow while the coronary sinus pressure was maintained at a constant, slightly negative pressure.

After cannulation of the pulmonary artery, the pericardium was removed and the right atrium opened. A complete heart block was established by ligation and cautery of a section of the bundle of His. Ventricular rate was then controlled by electrical stimulation of the distal portion of the ligated bundle with a pulse generator. Through the right atriotomy, a plastic-coated, stranded, stainless steel wire snare was positioned circumferentially around the outside of the left ventricle and septum at its maximum diameter and maintained in position with loose sutures. The snare was attached, subsequently, to a linear displacement transducer (Hewlett-Packard-Linearsyn 585 DT) thereby allowing the transducer to measure continuously the circumference of the left ventricle. Tension on the snare was carefully adjusted by long elastic bands which allowed the wire to be in close approximation with the external diameter of the left ventricle without perceptibly constricting it.

After closure of the right atriotomy, two catheters were inserted into the left ventricle by way of the pulmonary veins. One was attached to a pressure transducer (Sanborn 267B) for continuous measurement of left ventricular pressure. The other was connected to the output of the perfusing pump via the upper rotameter shown in Fig. 1 and supplied the ventricular cavity with a small flow of blood which it ejected into the aorta.

While perfused as described, the heart contracted at the stimulated rate. As the Starling resistance containing the coronary venous blood was slightly lower than the heart, the right ventricle was kept empty by a continuous negative pressure. The left ventricle, on the other hand, contracted virtually isovolumically, ejecting only the small flow that was allowed through the left ventricular cannula, which was set to deliver less than 1 ml/beat. The peak systolic pressure equaled the perfusion pressure, and the end-diastolic pressure was that which the ventricle required in order to develop the predetermined peak systolic pressure.

Next, individual pulmonary lobes were ligated at the hilus and removed, and the heart was immersed to the level of the coronary ostia in a bath of normal saline maintained at 39°C, which contained electrodes for recording the electrocardiogram. Coronary perfusion pressure was monitored at the level of the coronary ostia with a pressure transducer (Sanborn 267B). The ECG, perfusion pressure, and ventricular pressure were continuously recorded on a Sanborn Polyviso recorder (Sanborn 964).

The surface of the saline in which the heart was immersed provide the reference level for the pressure transducers and was maintained constant by a syphon.

In some experiments in which the hearts were embolized with small microspheres, myocardial oxygen consumption was determined as the product of coronary flow and the arteriovenous oxygen difference of the coronary artery and coronary venous blood. A spectrophotometer (Beckman, model B) was used for the determination of blood oxygen saturation and capacity.

2. Calculation of mean wall stress and internal radius. The formula used for the calculation of left ventricular mean wall stress was:

$$s = \frac{Pr_i^2}{h^2 + 2}$$

as applied to thick walled spheres where s = stress in g/cm²; P = pressure in g/cm²; r_i = ventricular internal radius in cm; h = ventricular wall thickness in cm.

The above formula was considered somewhat more accurate than the formula s = Pr/2h used in a previous study (11), as it included a correction for the thickness of the ventricular wall. Internal radius (r_i) and wall thickness (h) were calculated from measurements made by the circumferential snare described earlier using the following relationships:

$$r_i = \frac{\sqrt[3]{(Cd)^3 - (Ce)^3}}{2\pi}$$

and

$$h = \frac{Cd}{2\pi} - r_i$$

where Cd was the external circumference of the distended ventricle and Ce was the external circumference of the empty ventricle in centimeters.

The assumptions inherent in estimates of stress, calculated as above, have been discussed in detail in a previous publication (11). For reasons described in that report, the method was considered inaccurate at low end-diastolic pressures. In both the present and the previous reports, therefore, greater credence should be placed on estimations of stress at high end-diastolic pressures.

Calculations of internal radius were likewise subject to question at low end-diastolic pressures for the reasons discussed (11). Since the intent of this report is to present data concerning relative rather than absolute changes, values obtained at low end-diastolic pressures have been included.

3. Preparation of the myocardium for cytological study. As subsequently described, a parallel study was made of the myocardial cytology at high end-diastolic pressures using a perfusion fixation technique in both embolized and normal ventricles. For this, as in a previous study, the hearts were arrested with 5% potassium citrate while the ventricles were subjected to an intraventricular pressures of 100 mm Hg, and immediately fixed by perfusion for 30 min with 3.3% gluteraldehyde in 0.05 M phosphate buffer (pH 7.4) while this pressure was maintained at 100 mm Hg (11). Thin blocks of tissue from each heart were removed immediately from the middle of the left ventricular wall at its maximum circumference. These were processed as described previously and ultimately embedded in Araldite. Sections 1 μ thick from the plastic embedded material were then stained with 1% toluidine blue and 0.1% sodium borate in water and examined under oil with a Zeiss brightfield microscope (model RA). Sarcomere lengths were determined from photographs of properly aligned sections by comparison with calibration photographs of a Zeiss ruled grating. Measurements of sarcomere lengths made with this technique compared favorably with those made from electron micrographs of identically prepared material and provided a better selection of sarcomeres for measurement. In four

normal dog hearts distended at 100 mm Hg and perfusate fixed as described above, sarcomere lengths averaged 2.30 μ (±0.12 SD) when measured from electron micrographs (11). In this study, five normal dog hearts were similarly perfusate-fixed at the same pressure and sarcomere lengths averaged 2.30 μ (±0.09 SD) when measured from light micrographs.

RESULTS

1. Embolization with large microspheres. 10 hearts were prepared as described in Methods and stimulated to contact at a constant heart rate (range 80–120 beats/min) while the perfusion pressure and left ventricular systolic pressure were maintained constant at 100 mm Hg (range ±2). For a 10 min control period, coronary flow and left ventricular pressure were monitored while the heart contracted as described above. After the control period, the coronary bed was repeatedly embolized every 5–7 min with 10–20 large polystyrene microspheres averaging 865 μ in diameter (range 750–1200 μ) which were suspended in blood or saline. The emboli were administered until the end-diastolic pressure showed a salient increase. Throughout the period of embolization, ventricular pressure was continuously recorded, and coronary flow was recorded at least every 30 sec.

One such experiment is illustrated in Fig. 2 where the coronary flow progressively decreased as the microspheres accumulated in the coronary bed. Furthermore, after sufficient emboli had been administered there was a relatively abrupt increase in end-diastolic pressure.

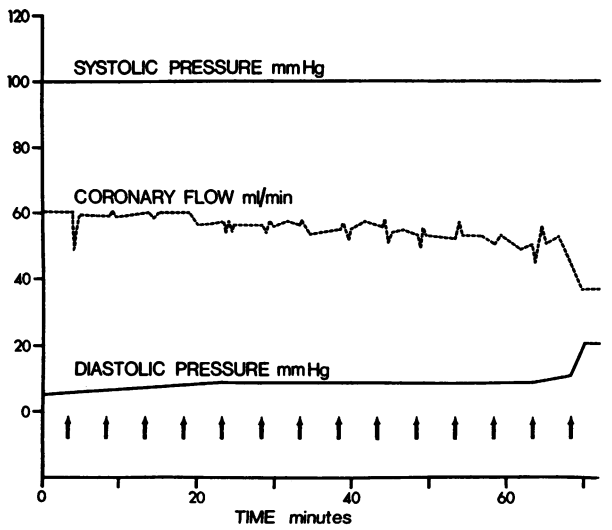

FIGURE 2 Graph of peak left ventricular systolic pressure (solid line), coronary flow (dashed line), and end-diastolic pressure (solid line) against time as coronary bed was embolized with large (average 865 μ) plastic microspheres delivered in increments of 10 at points indicated by arrows. Note progressive decrease in coronary flow.

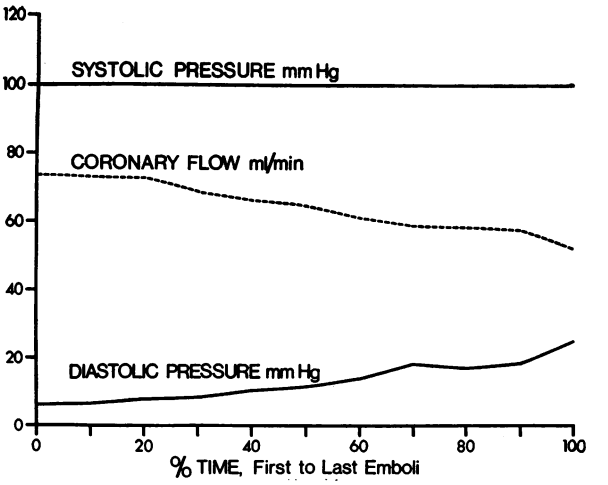

FIGURE 3 Graph of average peak left ventricular systolic pressure (solid line), coronary flow (dashed line), and end-diastolic pressure (solid line) of 10 hearts as coronary bed was embolized with large (average 865 μ) plastic microspheres against per cent of time between administration of first and last increments of emboli. Coronary flow progressively decreased in all 10 hearts.

This pattern was consistently observed in all 10 hearts embolized with large microspheres. Fig. 3 is a composite graph of the data from all 10 hearts and compares average coronary flow and end-diastolic pressure with the per cent of time btween the first and last administration of emboli.

2. Embolization with small microspheres. Nine hearts were again prepared, as described in Methods, and stimulated to contract at a constant heart rate (80–110 beats/min) while the perfusion pressure and left ventricular peak systolic pressure were maintained at a constant 100 mm Hg (range ±2). As before, coronary flow and left ventricular end-diastolic pressure were monitored during a 10 min control period. Next, the coronary bed was repeatedly embolized every 5–7 min with 0.5–1 ml of a 2% suspension of small microspheres averaging 9.95 μ in diameter (range 6–14 μ) suspended in blood or saline. During this period, coronary flow and end-diastolic pressure were carefully monitored. Again, the embolic suspension was administered repeatedly until the end-diastolic pressure showed a significant rise.

The data from one experiment showing the effect of the administration of small emboli are illustrated in Fig. 4. Here it can be noted that there was a progressive increase in coronary flow with administration of the small embolic suspension until a critical amount was accumulated in the coronary bed. At that point there was usually an abrupt decrease in coronary flow concomitant with a sustained increase in left ventricular end-diastolic pressure.

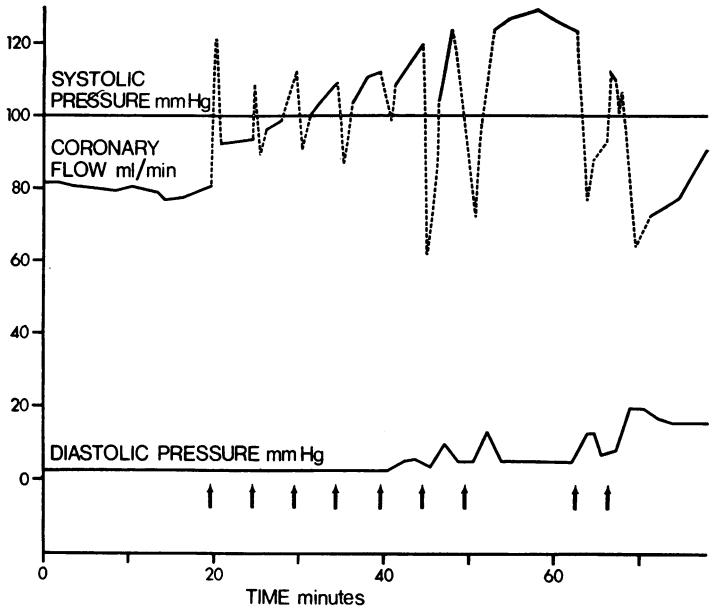

FIGURE 4 Graph of peak left ventricular systolic pressure (solid line), coronary flow (dashed line), and diastolic pressure (solid line) against time as coronary bed was embolized with a suspension of small (average 9.95 μ) plastic microspheres delivered where indicated by arrows. Note progressive rise in coronary flow until end-diastolic pressure shows a sustained increase.

As illustrated in Fig. 4, a rise in coronary flow was invariably seen immediately after each administration of the suspension early during the experiment. However, after the embolic suspension had been administered in sufficient quantities to cause a maximal rise in coronary flow, there was invariably a decrease in coronary flow immediately after further embolization.

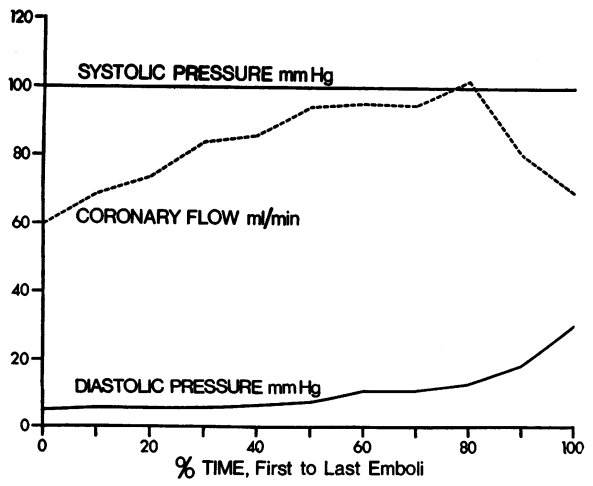

FIGURE 5 Graph of average peak left ventricular systolic pressure (solid line), coronary flow (dashed line), and end-diastolic pressure (solid line) of nine hearts as coronary bed was embolized with small (average 9.95 μ) plastic microspheres against per cent of time between administration of first and last increments of emboli. Note increase in coronary flow which occurred in all hearts and subsequent decrease after rise in end-diastolic pressure.

The gradual increase in coronary flow noted during repeated embolization occurred in all nine hearts so studied. Fig. 5 is a composite graph of the data from all nine hearts and illustrates the average change in coronary flow and end-diastolic pressure during embolization with small microspheres. It should be pointed out that repeated embolization was not necessary to produce a sustained increase in coronary flow. In some experiments where intervals as long as 55 min elapsed between two successive embolizations there was a sustained increase in coronary flow during these intervals.

In eight of the nine experiments in which the coronary bed was embolized with small microspheres, myocardial oxygen consumption was determined before embolization, at or near the point of maximal flow, and also at the end of the experiment when the end-diastolic pressure had markedly increased. The average values for myocardial oxygen consumption before embolization and at the point of maximal flow were 5.02 ($\pm$1.65 SD) and 5.03 ($\pm$1.79 SD) ml/100 g left ventricle per min, respectively, there being no statistically significant difference between the two mean values. When coronary flow was at its maximum after embolization, there was, as might be predicted, an increase in the oxygen content of the coronary sinus blood. For

this reason myocardial oxygen consumption remained at the control levels despite the increase in coronary flow. Myocardial oxygen consumption after the end-diastolic pressure had increased, however, averaged only 3.59 (±1.48 SD) ml/100 g left ventricle per min, a value 29% less than the control, and significantly different ($P < 0.025$).

3. The effect of coronary vasodilators, antihistamines, and autonomic blocking agents on coronary flow after embolization. In five experiments either papavarine (0.25–1.0 mg) or nitroglycerine (0.01–0.12 mg) was administered in a single dose to the coronary artery blood both before embolization and also at the point where maximal flow had been induced by embolization with the small microspheres. Enough of either drug was administered to cause a pronounced increase in coronary flow before embolization. Repetition of this dose at the point of maximal flow was accompanied by a similar, albeit somewhat diminished, effect, which suggests that the coronary bed still retained the ability to react to the vasodilating effect of the drugs after the vasodilation induced by the emboli.

In two experiments each, the following drugs were administered to the preparation before embolization in doses proportional to the weight of the support animal: an antihistamine (promethazine 3.0 mg/kg), atropine (1.0 mg/kg), and propranolol (1.0 mg/kg). In all six experiments the same increase in coronary flow after embolization with small microspheres occurred as that found in those studies where no antihistamines or autonomic blocking agents were administered.

4. Ventricular performance after coronary embolization. In all studies in which the coronary bed was embolized with either large or small microspheres, the end-diastolic pressure ultimately rose indicating a decrease in ventricular performance. Since coronary insufficiency has been shown to produce both a decrease in ventricular performance and a descending limb of ventricular performance at high end-diastolic pressure, an attempt was made to see if coronary embolization would produce a similar descending limb (12).

Accordingly, as in a previous study (11), in 16 hearts embolized with either large or small microspheres, the perfusion pressure was first dropped to approximately 90 mm Hg and subsequently increased to approximately 200 mm Hg, thereby increasing both the developed pressure and the diastolic pressure while both ventricular pressure and ventricular circumference were monitored. From these data left ventricular equatorial mean wall stress was estimated, as described in Methods, and graphs were drawn, which related developed stress with end-diastolic pressure both before embolization and after the emboli had been administered and the end-diastolic pressure had increased.

Fig. 6 is a composite graph from all 16 experiments in which per cent of peak-developed stress is plotted against end-diastolic pressure both before and after embolization. Although it must be remembered that ventricular performance was considerably reduced after embolization, the relationship between developed stress and end-diastolic pressure showed significantly less of a descending limb at 100 mm Hg end-diastolic pressure. The control graph showed a 5.7% decline while that plotted after embolization showed a decline of only 2.7% ($P < 0.005$).

5. Ventricular diastolic pressure-volume relationships after embolization. As shown in Fig. 6, there appeared

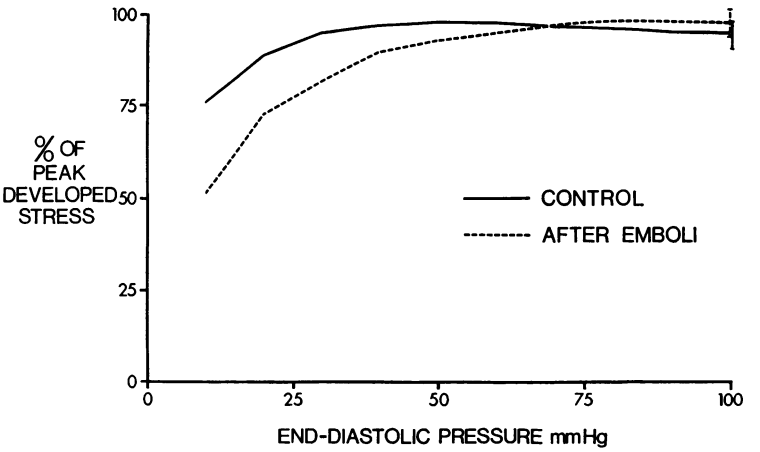

FIGURE 6 Graph of per cent of peak developed stress against end-diastolic pressure in 16 hearts both before and after embolization of the coronary bed. Note diminished limb of ventricular performance at high end-diastolic pressure after embolization. SEM at 100 mm Hg end-diastolic pressure is indicated by brackets.

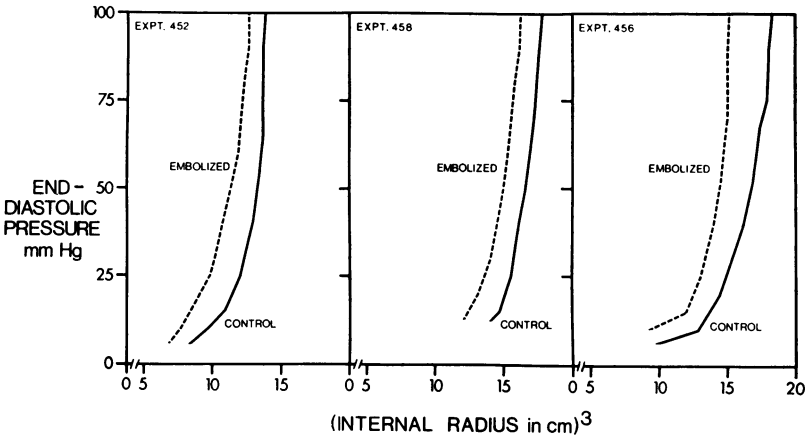

FIGURE 7 Graph of end-diastolic pressure (mm Hg) against cube of end-diastolic internal ventricular radius both before and after embolization in three experiments showing the ventricle to be less distensible after embolization.

to be less of descending limb of ventricular performance at high end-diastolic pressure in embolized hearts when per cent of peak-developed stress was plotted against end-diastolic pressure. The question arose, therefore, whether a given end-diastolic pressure was associated with the same average fiber length in both normal and embolized hearts, or whether the relationship between end-diastolic pressure and fiber length was in some fashion altered by embolization. Accordingly, in five hearts an attempt was made to determine the third power of the internal radius of the left ventricle both before and after embolization as the ventricle was distended from a negative diastolic pressure to an end-diastolic pressure of 100 mm Hg. For reasons discussed in a previous publication, estimates of the internal ventricular radius were considered inaccurate at low end-diastolic pressures, but realistic as the ventricle was distended with high end-diastolic pressures, above 20 mm Hg, where the ventricle tended to assume a more spherical shape.

Fig. 7 is a plot of the third power of the internal radius of the ventricle against end-diastolic pressure in three hearts distended both before and after embolization as described above. In all five hearts there was a smaller internal radius for a given end-diastolic pressure after embolization. Furthermore, when completely evacuated with a negative pressure, all ventricles showed an increase in ventricular circumference averaging 12.2% (range 9–22.2%) after the administration of both large and small microspheres. This implied that embolization cause an increase in the thickness of the ventricular wall that was largely attributed to the formation of edema.

6. Myocardial cytology after coronary embolization. In three hearts the cytology of the ventricular myocardium was examined by high power light microscopy after embolization and was compared with that found in five control hearts that had not been embolized. In both groups the hearts were arrested with 5% potassium citrate and fixed at an intraventricular pressure of 100 mm Hg by perfusion with 3.3% gluteraldehyde in phosphate buffer for 30 min as described in Methods.

Fig. 8 is a photomicrograph of an area of tissue from an embolized heart. Here, stretched sarcomeres can be seen in a well preserved area (right) and contracted sarcomeres in what is presumed to be an infarcted area (left). In both normal and embolized hearts, measurements were made of sarcomere length from properly aligned sections and frequency distribution graphs plotted as illustrated by Fig. 9. Measurements were made on 383 sarcomeres from five normal hearts and 570 sarcomeres from three embolized hearts. The average sarcomere length in the nonembolized hearts was 2.30 μ, and the frequency distribution curve of sarcomere length for those hearts was relatively symmetrical. In contrast, the frequency distribution curve of sarcomere length in embolized hearts indicated two populations, as might be anticipated from Fig. 8, due to the presence of both normally stretched and highly contracted sarcomeres. In the infarcted areas the intercalated discs appeared to be wider and less distinct than those in the normal areas of the light photomicrographs.

DISCUSSION

As described in sections 1 and 2 of the Results, embolization of the coronary bed with small (9.95 μ) microspheres produced an initial vasodilation with an average 70% increase in coronary flow that was not observed when the coronary bed was embolized with the larger (865 μ) particles. Furthermore, this was noted when perfusion pressure, peak systolic ventricular pressure

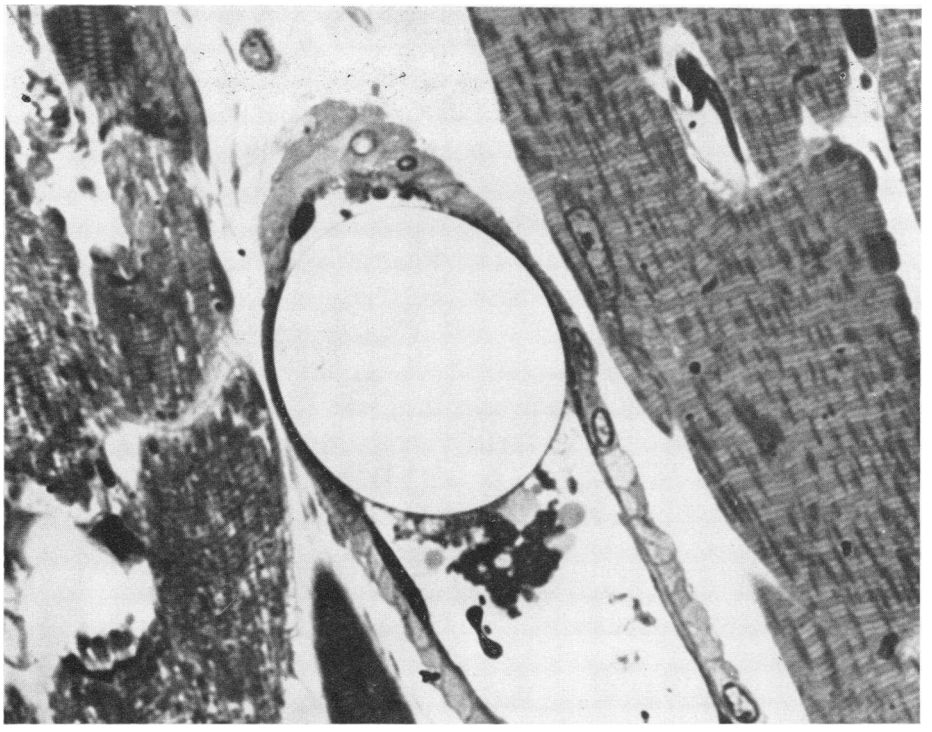

FIGURE 8 High power photomicrograph of an area of ventricular myocardium fixed at a ventricular pressure of 100 mm Hg after embolization with 35 μ plastic microspheres. Note well preserved, extended sarcomeres on right of microsphere in contrast with highly contracted sarcomeres in presumably infarcted area on left. ×1300.

and heart rate were maintained constant, all of these being determinants of coronary flow in the working heart (1, 2).

From the data described in section 3 of the Results, it is doubtful if the coronary vasodilation accompanying embolization with small microspheres was mediated by a neural reflex within the heart. It may be argued that vagal stimulation can cause coronary vasodilation and likewise that both sympathetic stimulation and the administration of sympathetic agents such as epinephrine and norepinephrine are attended by coronary vasodilation (18, 19). However, evidence for the existence of any neural reflex within an isolated heart that would account for the described vasodilation with embolization by small particles has never been well established. Furthermore, the effect was present despite the administration of vagal and β-blocking agents at dose levels sufficient to block any presumptive reflex effects.

In view of the above, it was felt by exclusion of other possibilities that the vasodilation after the administration of such emboli was mediated through some other mechanism probably involving a released substance. This vasodilation persisted despite the administration of an antihistamine making it unlikely that histamine was involved. Furthermore, the vasodilation was noted only after embolization with small emboli and not after embolization with large emboli where, it would be reasonable to assume, any released substance could be trapped within a relatively larger infarcted area and thereby rendered ineffective.

As stated in the Introduction, there has been much recent evidence implicating adenosine as an intrinsic regulator of coronary blood flow (13–17). Accordingly, an attempt was made to see if the coronary arteriovenous difference of adenosine was increased after embolization with small particles. Preliminary results suggested that there may have been an efflux of purine nucleosides from these hearts after embolization. However, as cell death doubtless occurred under these conditions and as the membrane of such cells presumably would become permeable to nucleosides and other substances with cell death, the significance of these preliminary observations was considered questionable.

In all studies, depressed ventricular function was noted after a sufficient amount of either large or small emboli had been administered, as might be anticipated. On the other hand, the loss of a descending limb of ventricular performance at high end-diastolic pressures was an unexpected finding as unequivocal descending limbs were noted by Case, Berglund, and Sarnoff in

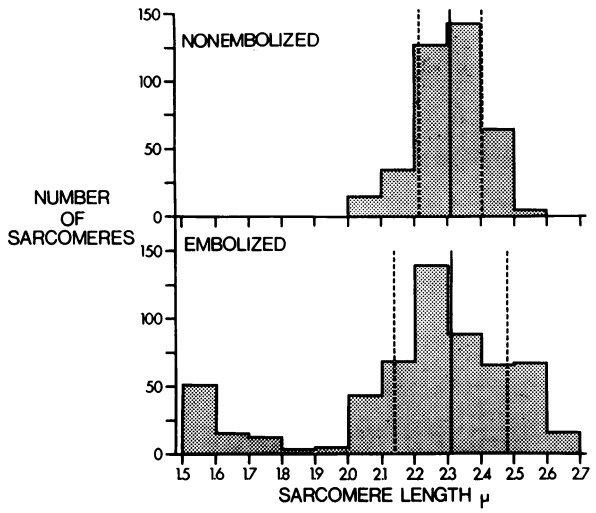

FIGURE 9 Frequency distribution graph of number of sarcomeres against sarcomere length in both normal (top) and embolized (bottom) hearts. Note additional population of highly contracted sarcomeres in embolized hearts not found in normal hearts.

hearts with coronary stenosis (12). An attempt, therefore, was made to see if this could be explained by a change in diastolic pressure-volume relationships resulting from the administration of the emboli. As implied in Fig. 7, at a given end-diastolic pressure ventricular volume was decreased after embolization. If this decrease in volume reflected a decrease in fiber lengths, this could well account for the failure to observe a descending limb at high end-diastolic pressures when developed stress was plotted against end-diastolic pressure. Furthermore, it became evident that with the decrease in ventricular volume at a given end-diastolic pressure there was an increase in the thickness of the ventricular wall that could only be attributed to edema. As edema of the ventricle has been shown to reduce ventricular distensibility, one can attribute reduced distensibility, at least in part, to this cause (20).

Another reason for a decrease in ventricular distensibility after embolization is suggested in Figs. 8 and 9 where there appears to be a large population of super-contracted sarcomeres after embolization and infarction of the ventricle. It must be remembered that these sarcomeres were found to be super-contracted despite fixation at a left ventricular pressure of 100 mm Hg, and therefore could well be effective in reducing the distensibility of the ventricle. In this connection it should also be remembered that the contracted state of striated muscle is the low energy state (21). It would hardly seem surprising, therefore, if the sarcomeres deprived of their source of energy in the embolized and infarcted areas of the myocardium, were found to be super-contracted. Furthermore, super-contraction of sarcomeres oriented at right angles to the equator could well increase the thickness of the ventricular wall at this point and reduce ventricular distensibility even more.

It should be emphasized that the diminished descending limb attributed to a decrease in ventricular distensibility after embolization only describes a stray effect of such embolization. It does not imply, however, that ventricular performance was improved by embolization. Clearly, the opposite was demonstrated. The only implications, then, are that ventricular pressure-volume relationships were so altered after embolization that, with increases in end-diastolic pressures, the ventricle was capable of increasing its developed wall tension until the end-diastolic pressure reached 90 mm Hg.

The increase in coronary flow after coronary embolization with the small microspheres has more immediate practical application. Because this increase was observed long before there was an apparent decrease in ventricular performance it may well serve as an early indicator of myocardial damage from small emboli. As mentioned in the introduction, clinical situations presently exist where hearts are perfused with mechanical oxygenators and where the risk of embolization is high (7–9). By measuring coronary flow when perfusing isolated hearts with blood oxygenated by mechanical oxygenators, the embolic toxicity of such oxygenators may well be determined. Furthermore, it may prove helpful to measure these during open heart surgery in an attempt to evaluate the toxicity of cardiopulmonary bypass on the particular heart involved.

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