Hemodynamic Effects of Quantitatively Varied Experimental Aortic Regurgitation

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A canine preparation was devised in which aortic regurgitant flow could be acutely produced, metered and controllably varied. Aortic regurgitant flows in excess of the dog's resting cardiac output resulted in a marked decrease of effective cardiac output, a substantial rise of peripheral resistance and left ventricular end-diastolic pressure, and a marked depression of the left ventricular function curve, with little change in the mean left atrial pressure. When mitral regurgitation was added to aortic regurgitation, effective cardiac output, stroke work and left ventricular end-diastolic pressure fell, while left atrial pressure rose.

The purpose of this investigation was to observe the hemodynamic consequences of experimentally induced and quantitatively varied aortic regurgitation and to contrast these findings with those observed to be associated with mitral regurgitation. It was of further interest to examine the interrelationship between mitral and aortic regurgitation with special reference to the protective influence of a competent mitral valve in the presence of aortic reflux.

Method

The general experimental technics of anesthesia, operative procedure, and measurement were essentially the same as those previously described. In these experiments, however, aortico-left ventricular regurgitation was produced, as shown in figure 1, by providing a pathway from the thoracic aorta to a prosthesis sutured into the left ventricular apex by a technic described in detail elsewhere. Of 12 attempts, 11 successful experiments were performed in dogs weighing from 19.5 to 27.0 Kg., averaging 24.7 Kg. A check valve permitted reflux from aorta to left ventricle only during diastole. This regurgitant flow, which will be referred to as aortic regurgitation, was metered by a Potter turbine flow meter in the regurgitant pathway and could be regulated by an externally applied screw-clamp. Total left ventricular output minus coronary flow (effective plus regurgitant flows) was also continuously metered with a second flow meter (fig. 1). In order to superimpose mitral regurgitation upon any given level of aortic regurgitation, a tygon tube with multiple perforations was inserted through the mitral valve by way of the left atrial appendage. This could be withdrawn and replaced at will. Effective cardiac output was calculated as the difference between total left ventricular output and aortic regurgitant flows. Total left ventricular minute work in kilogram meters was calculated as the product of total left ventricular output in liters per minute and mean aortic pressure in centimeters water divided by 100. Effective left ventricular minute work was calculated as the product of effective systemic flow in liters per minute and mean aortic pressure in centimeters water divided by 100. Total peripheral resistance was calculated as the quotient of mean aortic pressure in millimeters mercury and effective cardiac output in liters per minute. The aortic regurgitant pressure gradient was estimated as the difference between mean aortic diastolic pressure, obtained by planimetry, and left ventricular end-diastolic pressure. The regurgitation index was calculated as the product of the duration of diastole and the aortic regurgitant pressure gradient.

Results

Hemodynamic Consequences of Stepped Increases in the Volume of Aortic Regurgitation. The results of 1 of 14 such experiments in 9 dogs are shown in figure 2. As aortic regurgitant flow was increased, effective systemic flow decreased substantially. This was always accompanied by a widening of the pulse pressure and a lower diastolic pressure. Mean pressure usually, but not always, was slightly diminished. Systolic pressure failed to rise in 3 of the 14 experiments of this type, 1 exception is shown in figure 2. Calculated total peripheral resistance rose in 3 of the 14 experiments of this type, 1 exception is shown in figure 2. Calculated total peripheral resistance rose markedly. Left ventricular end-diastolic pressure rose to high levels while mean left atrial pressure exhibited only a slight elevation. Thus, in end-diastole, wide discrepancies between left ventricular and left atrial pressures were observed.

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Effect of Aortic Regurgitation on the Left Ventricular Function Curve. In 9 experiments on 7 dogs ventricular function curves were obtained as described previously by stepwise blood infusion. After each infusion, observations were made with and without a constant amount of aortic regurgitant flow by alternately opening and closing the regurgitant pathway. Figure 3 shows the effective stroke work plotted against left ventricular end-diastolic pressure with and without aortic regurgitation. A marked depression of the effective ventricular function curve was observed in the presence of aortic regurgitation. Figure 4 shows the total left ventricular stroke work done at various filling pressures in the presence of aortic regurgitation as well as the partition of total left ventricular stroke work into effective stroke work and that component of stroke work expended on the regurgitant stroke volume.

Hemodynamic Consequences of Changing Cardiac Output. Stepwise increases in total cardiac output were brought about in 1 experiment by serial infusions, the aortic regurgitant orifice held constant, and observations made on the parameters shown in figure 5. It was observed that, the higher the total stroke volume, the greater was the ratio between effective and total stroke volume. An increase in regurgitant flow did occur, but this was slight even in the presence of an elevation of aortic pressure and the accompanying increase in the aortic regurgitant pressure gradient. That the increase in regurgitant flow was only slight may be explained by the observation that, with the increase in total stroke volume, the diastolic period shortened, and therefore
FIG. 3. Effective left ventricular function curves without (rA.I.) and with an aortic regurgitant flow of 2.6 L./min. (cA.I.). S.W.L.V., left ventricular stroke work in gram meters; L.V.E.D., left ventricular end-diastolic pressure.

FIG. 4. Plot showing the total left ventricular stroke (T.S.W.) and its partition into effective stroke work (E.S.W.) and that component of stroke work expended on the regurgitant stroke volume (A.I.S.W.). Plot was constructed from data obtained during the experiment with aortic regurgitation (cA.I.) shown in figure 3.

Effects of Mitral Regurgitation Superimposed on Aortic Regurgitation. Nine experiments were done in 4 dogs in which the effects on circulatory dynamics of inducing aortic regurgitation were observed and mitral regurgitation then superimposed by means shown in figure 1. The results of 2 such experiments are shown in figure 6. When aortic regurgitation was induced, the previously demonstrated hemodynamic changes occurred. When mitral regurgitation was then added, even though the aortic regurgitant flow was slightly diminished, effective cardiac output fell further from its already depressed level. Simultaneously, left ventricular end-diastolic pressure fell from its high level, while mean left atrial pressure rose from its relatively low level, thus diminishing the discrepancy that had been present between volume is increased in the presence of aortic regurgitation.
**Fig. 6.** Hemodynamic effects of superimposing mitral regurgitation on aortic regurgitation. N.L., no lesion; A.I., aortic regurgitation; A.I. + M.I., after mitral regurgitation was superimposed; T., sum of effective and aortic regurgitant flows; R., aortic regurgitant flow; E., effective flow in L./min.; L.V.E.D.P., left ventricular end-diastolic pressure; L.A.P., mean left atrial pressure; A.P., aortic pressure; M.W., effective minute work in kilogram meters; T.P.R., calculated total peripheral resistance; H.R., constant heart rate 133/min. Dog weight, 25.0 Kg.

them when the mitral valve was competent. The fall in left ventricular end-diastolic pressure with the addition of mitral regurgitation was accompanied, as might be anticipated, by a fall in effective stroke work.

**DISCUSSION**

The large volumes of aortic regurgitant flow that were observed in these experiments do not appear to be unrealistic in terms of the clinical counterpart of this lesion. Braunwald and Morrow (personal communication) observed that when dye was introduced into the aorta at or below the level of the diaphragm in patients with severe aortic insufficiency, it regurgitated to the innominate artery. The studies of clinical aortic regurgitation by the methods of Korner and Shillingford, as well as the suggestion of large aortic regurgitant volumes by Keys et al., would also appear to be consonant with this view. Further, with time for the development of compensatory hypertrophy, it would be expected that the naturally occurring lesion might result in a left ventricle that could endure larger aortic regurgitant volumes than when the lesion is acutely induced as was done in these experiments.

Unlike the results of imposing mitral regurgitation, aortic regurgitation was accompanied by severe depression of the effective left ventricular function curve. In the former lesion, the regurgitant volume is ejected into a low pressure chamber, thus permitting the large stroke volume to be accomplished chiefly as a result of more complete systolic emptying. In contrast, the increased total stroke volume in the presence of aortic regurgitation is ejected into the aorta in which the pressure is high and rises progressively as ejection proceeds. Thus, it appears that the increased stroke volume which is ejected in the presence of aortic regurgitation comes about primarily as a result of increased end-diastolic volume rather than more complete systolic emptying. This finding, namely the elevated left ventricular end-diastolic pressure, may be considered one of the prominent compensatory responses to aortic regurgitation.

The observed increase in calculated peripheral vascular resistance which accompanied the fall in effective cardiac output when aortic regurgitation was acutely induced (fig. 2 and 6) probably represents the activity of baroreceptor regulation in maintaining arterial pressure. Without such a constrictor response, diastolic coronary perfusion pressure would fall to levels even lower than those which were maintained in these experiments. The constrictor response may be construed, therefore, as conferring a protective effect under these experimental conditions. Clinically, since cardiac output at rest is not generally decreased in patients with mild or moderate aortic regurgitation, there is no requirement for an increased peripheral vascular resistance. However, it might be anticipated that, as the severity of the regurgitant lesion progresses, effective cardiac output is depressed because of the ventricle's inability to further compen-
sate. Under such circumstances, increased peripheral vascular resistance may play an increasingly important role in the maintenance of arterial and coronary perfusion pressure. With this in view, it is of interest that the administration of ganglionic blocking agents or spinal anesthesia7 may be hazardous in the patient with severe aortic regurgitation.

Ample confirmation was obtained in these experiments of the observations by Morrow (personal communication) and by Wright et al.8 that occasionally, left ventricular end-diastolic pressure may substantially exceed left atrial pressures in the presence of aortic regurgitation. The experiments shown in figure 6 in which mitral regurgitation was superimposed on aortic regurgitation were designed to elucidate the possible physiologic significance of this phenomenon. First, it is clear that a competent mitral valve must close partially, or completely, well before the onset of ventricular systole, else the late diastolic reverse pressure gradient between ventricle and atrium could not develop. Thus, ventricular filling from the atrium must be completed well before the end of ventricular diastole. Diastolic ventricular pressure continues to rise, however, because of continued aortic reflux, thus accounting for the reversed end-diastolic pressure gradient between ventricle and atrium. Secondly, it was clear that, in the presence of aortic regurgitation, compromising the competence of the mitral valve produced further elevation of left atrial pressure. Simultaneously, the left ventricular end-diastolic pressure fell as shown in figure 6. This decrease in left ventricular end-diastolic pressure (and presumably fiber length) resulted in a further diminution of effective stroke work and effective cardiac output from already depressed levels.

The mitral valve may thus be thought of not only as a secondary resistance to regurgitant flow from the aorta, but also as a means of protecting the pulmonary vascular bed from elevated pressures, while permitting the left ventricle to achieve a higher end-diastolic pressure and volume and thus the discharge of a more adequate stroke volume than would otherwise be the case. Such considerations apply, however, only if the ventricle is on the ascending limb of its ventricular function curve.4 These data also suggest that the inadvertent production or increase of mitral insufficiency in the course of mitral commissurotomy may have more profound consequences in the presence of aortic regurgitation than in its absence. Uricchio and Likoff9 largely attributed the adverse effects of mitral commissurotomy in the presence of aortic stenosis and insufficiency to the aortic stenosis which they thought was functionally intensified by mitral commissurotomy; the above data provide the basis for one possible alternative interpretation.

Berglund10 holds the view, with which the authors concur, that under normal circumstances left atrial pressure is a function of the performance characteristics and working conditions of the left ventricle rather than of left atrial distensibility.11 The premature closure of the mitral valve when aortic regurgitation is present dissociates the ventricular end-diastolic pressure, i.e., the functional determinant of ventricular contraction, from the left atrial pressure. The fact that left atrial pressure is not substantially influenced by changes in ventricular performance (fig. 2) lends further credence to Berglund's view that under usual circumstances when atrium and ventricle are a common chamber at the end of diastole, the pressure in the atrium is a reflection of the ventricle's performance rather than of left atrial distensibility.

**SUMMARY**

Stepwise increases in aortic regurgitation were produced in the open-chest, anesthetized dog, at a constant heart rate until regurgitant flows in excess of the dog's resting stroke volume were observed. A substantial decrease in effective stroke volume occurred. Total peripheral resistance rose markedly. Aortic pulse pressure always widened. The left ventricular function curve was markedly depressed in the presence of aortic regurgitation. The above findings were consistently in contrast to the hemodynamic consequences resulting from similar volumes of mitral regurgitation.

When, at a constant heart rate, aortic regurgitation was induced in the presence of a
competent mitral valve, left ventricular end-diastolic pressure rose to much higher levels than left atrial pressure. The differences could be diminished or almost abolished by inducing concomitant mitral insufficiency. At such times, however, the fall in left ventricular end-diastolic pressure was accompanied by a further diminution in effective stroke volume beyond that which had been produced by the aortic regurgitation alone. Thus, in the presence of aortic regurgitation, a competent mitral valve acts in two ways to protect the circulation. First, it limits the elevation of left atrial and pulmonary capillary pressures. Secondly, it makes possible the high left ventricular end-diastolic pressure, as a result of which a more forceful ventricular contraction occurs, provided the ventricle is still on the ascending limb of its ventricular function curve.

**SUMMARIO IN INTERLINGUA**

In canes anesthesiata e a thorace aperte, augmentos gradate de regurgitation aortic esseva producite sin alteration del frequentia cardiac usque le fluxo regurgitante excedeva le volumine pulsatile del can in stato de reposo. Occurreva un reduction substantial del effective volumine pulsatile. Le resistentia peripheric total cresceva marcatemente. Le pression de pulso aortic se allargava in omne casos. Le curva del function sinistro-ventricular esseva marcamente deprimite in le presentia de regurgitation aortic. Le supra-citata constatazioni esseva uniformemente contrari al consequentias hemodynamic resultante ab simile volumines de regurgitation mitral.

Quando—con constant frequencias cardiac—regurgitation aortic esseva inducide in le presentia de un competent valvula mitral, le presision termino-diastolic sinistro-ventricular cresceva a multo plus alte nivellos que le presision sinistro-atrial. Iste differentia poteva esser reducide o quasi abolite per inducer un concomitante insufficiencia mitral. Tamen, le reducition del pression termino-diastolic sinistro-ventricular esseva alora accompaniate per un diminution additional del effective volumine pulsatile a parte le diminution que habeva essite producide per le regurgitation aortic sol. Assi—in le presentia de regurgitation aortic—un competente valvula mitral age in duo maneras pro proteger le circulation. Primo, illo limita le elevation del pressiones sinistro-atrial e pulmono-capillar. Secundo, illo rende possibile le alte pression termino-diastolic sinistro-ventricular. Como resultato de isto, il occurre un plus forte contraction ventricular, providite que le ventriculo se trova ancora al latere ascendente de su curva de function ventricular.

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