HÆMODYNAMIC EFFECTS OF SEVERE AORTIC REGURGITATION*

BY

J. RUSSELL REES†, ELLIS J. EPSTEIN‡, J. MICHAEL CRILEY, AND
RICHARD S. ROSS

From The Wellcome Research Laboratory of the Departments of Medicine and Radiology, The Johns Hopkins University School of Medicine and The Johns Hopkins Hospital, Baltimore, Maryland

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In free aortic regurgitation, the aortic diastolic pressure falls and the left ventricular end-diastolic pressure may rise above normal. In severe cases, these two pressures may equalize. We have recently demonstrated this phenomenon in a patient who, in addition, showed the unusual feature of premature mitral valve closure preceding atrial contraction. A search of the published material showed only 6 other instances in which such early mitral closure was caused by aortic reflux. Review of our catheterization data on nearly 200 patients with aortic disease disclosed no other instance, although there were 7 others in whom aortic and ventricular diastolic pressures equalized: in 2, this occurred constantly at the end of diastole, and in the other 5, equilibration occurred occasionally during long diastolic pauses following premature ventricular contractions. We will first present a detailed report of the single patient (Case 1) in whom equalization of aortic and left ventricular diastolic pressures was associated with premature mitral valve closure, and then review all 8 patients from our series in whom equalization of aortic and left ventricular diastolic pressures was found.

CASE REPORT

C.P. a 40-year-old Negro (Patient 1 in Tables I and II) had had mild hypertension since 1956 with a resting blood pressure of 170/95 mm. Hg. Otherwise, he was well until 1961 when effort dyspnoea commenced, and a chest radiograph showed slight left ventricular enlargement. Thereafter, his exercise tolerance progressively decreased, with increasing lethargy, until November 1962, when he had an attack of acute pulmonary oedema.

Congestive failure was then found and a murmur noted for the first time. His oedema disappeared with treatment, but subsequently he suffered from severe effort breathlessness with recurrent nocturnal dyspnoea and repeated hæmoptyses. Progressive increase in his symptoms led to admission to hospital in January 1963. There was no history of rheumatic fever, venereal infection, or chest trauma.

Physical examination showed a muscular man, afebrile, and comfortable at rest. The jugular venous pressure was normal, the pulse was regular, 80 a minute, and the blood pressure 135/65 mm. Hg. There was moderate left ventricular enlargement and no palpable thrill. On auscultation, the apical first sound was soft. The second sound was loud in the pulmonary area but normal in intensity at the aortic area. There was no ejection sound. An aortic mid-systolic murmur (grade 2/4) and a loud decrescendo diastolic murmur (grade 3/4) were heard. The diastolic murmur extended half-way through diastole and could be heard well at the apex together with a loud third heart sound. There were no residual signs of congestion, and no other significant findings.

A chest radiograph showed cardiac enlargement, mainly left ventricular, with slight dilatation of the ascending aorta. No aortic valve calcification was detected. The electrocardiogram showed sinus rhythm,

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† Present address: The Westminster Hospital, London, S.W.1.

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TABLE I
CLINICAL FEATURES OF 8 CASES OF AORTIC REGURGITATION

Case No.	Age (yr.)	Effort dyspnoea	Paroxysmal dyspnoea	Angina	Aetiology	Associated aortic stenosis	B.P. (mm. Hg)	Apical murmur	Left atrium enlarged on radiograph
1	40	+	+	—	Undetermined	—	135*/65	Mid-diastolic	+
2	42	+	+	—	Lues	—	140/40	Mid-diastolic	+
3	48	+	+	—	Rheumatic	+	115/60	—	+
4	25	—	—	—	Trauma	—	160/45	Presystolic Mid-diastolic Pre-systolic	—
5	46	+	—	+	Congenital bicuspid valve	—	205/70	—	+
6	45	+	+	+	Rheumatic	+	105/65	—	—
7	30	+	+	+	Rheumatic	+	145/55	—	—
8	45	+	—	+	Rheumatic	+	120/60	—	—

* History of previous hypertension.

TABLE II
HÆMODYNAMIC AND CINEANGIOGRAPHIC DATA IN 8 CASES OF AORTIC REGURGITATION

Case No.	Pressure analysis (mm. Hg) above mid right atrium											Aortic valve grad.	Aortic regurgitation on aortic cine-angiogram	Other cine-angiogram	Cineangiogram analysis of LV end-systolic size
	Aorta		Left ventricle			Left atrium									
	Syst./diast	Pulse pressure	Systole	Early diastole	End diastole	a	x	v	y	z	Mean				
1 { Pre-op.	110/55	55	110	2	57	38	18	35	8	35	27	0	+	—	Slight increase
2 { Post-op.	164/82	82	180	0	15	16	3	14	4	14	12	16	+	LV	Normal
3	102/45	57	102	7	45	36	14	20	9	28	18	0	+	—	Much increase
4	76/36	40	130	4	36	36	14	20	9	28	18	55	+	LV LA	Much increase
5	135/36	99	135	0	29	36	14	20	9	28	18	0	+	LV	Much increase
6	181/59	122	187	8	26	32	23	35	17	29	29	0	+	—	Much increase
7	88/55	28	155	12	32	32	23	35	17	29	29	67	+	—	Much increase
8	126/56	70	188	0	17	62	—	—	—	—	—	62	+	—	Slight increase
	115/54	61	200	8	27	85	—	—	—	—	—	85	+	LV	Much increase

LV=Left ventricle

LA=Left atrium

a P-R interval of 0.16 sec., and left ventricular hypertrophy. The antistreptolysin titre and C-reactive protein complement fixation test were normal. Serum tests for syphilis were negative.

Combined left and right heart catheterizations were performed, and sounds were recorded simultaneously with pressures both externally, and internally via the catheter. The results are shown in Table II and Fig. 1A and B.

The left ventricular pressure falls abruptly in early diastole to 5 mm. Hg and then rises rapidly in two stages to equilibrate with the steadily falling aortic pressure. In the first third of diastole left atrial and ventricular pressures are equal (Fig. 1B points b-c). The left ventricular pressure then rises to meet the aortic pressure (Fig. 1B, point d) and thereafter both pressures decline gradually until the onset of systole (Fig. 1B, point e). The left atrial pressure pulse shows a steep y descent following the v peak showing that rapid atrial emptying occurs despite free aortic regurgitation. At point c (Fig. 1B) left ventricular pressure exceeds atrial pressure and reaches much higher levels for the remainder of diastole. At point c this reversed atrio-ventricular pressure gradient causes premature mitral valve closure, limiting atrial emptying to the first third of diastole. This event is marked by a positive wave on the atrial pressure trace. The atrium contracts in late diastole (before point e) after the mitral valve has closed.

Phonocardiography confirmed soft first and normal second sounds at their correct times in the cardiac

FIG. 1A.—Case 1 (C.P.): pre-operative findings. Simultaneous aortic (Ao) and left ventricular (LV) pressure tracings showing equilibration of diastolic pressures in the second half of diastole. Paper speed 75 mm./sec.

FIG. 1B.—Case 1 (C.P.): pre-operative findings. Simultaneous aortic (Ao) and left ventricular (LV) pressure tracings with a superimposed left atrial (LA) pressure tracing. In addition internal and external aortic phonocardiograms are shown. There is a soft 1st sound (1), a normal 2nd sound (2), a third sound (3) at the nadir of the y descent of the atrial trace and an extra sound (X) coinciding with mitral valve closure. An ejection systolic murmur (SM) and a decrescendo diastolic murmur (DM) are also shown. Paper speed 75 mm./sec.

FIG. 2.—Case 1 (C. P.): post-operative findings. Simultaneous aortic (Ao) and left ventricular (LV) pressure tracings with superimposed left atrial (LA) pressure tracings. There is a small systolic gradient across the aortic valve but the unusual diastolic features are no longer present. Paper speed 75 mm./sec.

cycle, together with a third sound coincident with the y point. In addition an extra sound (Fig. 1B-X) was recorded at the time of premature mitral closure. The diastolic murmur continued a little beyond this to end just before equilibration of ventricular and aortic pressures.

The cineangiogram showed slight dilatation of the aortic root and severe aortic regurgitation. Left ventricular filling ceased abruptly in mid-diastole, and there was only a small increase in end-systolic volume suggesting good ventricular function. There was no evidence of mitral regurgitation.

In January 1963 a Starr-Edwards prosthesis was inserted following excision of the damaged valve. Histology of the excised tissue showed non-specific inflammatory changes. The patient made a good recovery and in May 1963 catheterization was repeated, the results of which are shown in Fig. 2 and Table II. The left ventricular diastolic and left atrial pressures are much lower, and the unusual pre-operative hæmodynamic features have gone.

CASE MATERIAL

The clinical data in the 8 cases showing equalization of aortic and left ventricular pressures are given in Table I. C.P. reported above is Case 1. All were men aged between 25 and 48 years. The lesions were considered to be rheumatic in 4, of undetermined ætiology in one, and were respectively luetic, traumatic, and congenital in the remaining 3. Four had calcified aortic valves.

Seven complained of dyspnœa, and one had congestive cardiac failure. All had loud aortic regurgitant murmurs, and 6 had peripheral signs of severe aortic reflux with wide pulse pressures. The diastolic blood pressure ranged from 40 to 70 mm. Hg, and clinical, radiological, and electrocardiographic evidence of left ventricular hypertrophy was present in every case. All were in sinus

rhythm. There were 4 with associated aortic stenosis; 3 had calcified valves with systolic gradients of 62 to 85 mm. Hg across the aortic valve, and one without calcification had a gradient of 55 mm. Hg. None had clinical evidence of mitral stenosis as judged by the absence of a mitral diastolic thrill, mitral valve calcification, and opening snap, although 4 had apical diastolic murmurs thought to be Austin Flint murmurs. Mitral stenosis was excluded by catheter studies, operation, or autopsy (2 cases). Retrograde aortic and left ventricular catheterization was performed in all via the femoral artery using the Seldinger technique. Transseptal left atrial catheterization was done in 3 cases.

Cineradiographic studies of the aortic valve were made with supra-aortic injections of radio-opaque dye, and in some, ventricular and atrial angiograms were also done (Table II). In every case the left ventricle was well opacified by free regurgitation of dye from the aorta. Only Case 2 showed evidence of mild mitral regurgitation.

PRESSURE PULSE ANALYSIS

1. *Aorta.* All the patients had severe aortic regurgitation and showed reduced aortic diastolic pressures (60 mm. Hg or less). An increased pulse pressure was present in all except Cases 3 and 6, who had associated aortic stenosis. Only one failed to show a dicrotic notch in the aortic pressure tracing. An attempt was made to relate the degree of aortic regurgitation to the rate of diastolic decline in aortic pressure following aortic valve closure. Measurements were made in the patients and in 8 normal subjects. There was a wide normal range and overlap between normal subjects and patients. However, the average rate of descent in the diastolic pressure was greater in the patients with aortic regurgitation (92 mm. Hg/sec.) than in the normal subjects (70 mm. Hg/sec.). The rate of decline was not found to be of value in assessing the degree of reflux.

2. *Left Ventricle.* Left ventricular pressure pulse contours followed the aortic during the ejection phase in those without any associated aortic stenosis; the others showed gradients ranging from 55 to 85 mm. Hg. The phase of reduced ejection was unremarkable. The rate of pressure decline in the ventricle following the dicrotic notch was unaffected even in the most severe case, and in none did the early diastolic contours of aortic and left ventricular pressure traces match. Left ventricular end-diastolic pressure was raised in all (17 to 57 mm. Hg), and in association with a reduced aortic diastolic pressure produced the unusual phenomenon, common to the group, of equilibration of aortic and left ventricular end-diastolic pressures. In Case 1 (Fig. 1A) this occurs soon after the middle of diastole and in Cases 2 and 3 (Fig. 3 and 4) at end-diastole. In the others, ventricular premature beats induced during catheterization were followed by long diastolic pauses during which equilibration occurred as shown by Cases 7 and 8 (Fig. 5 and 6).

3. *Left Atrium.* Left atrial pressure tracings were available in 3 cases; all showed raised mean pressures (18 to 29 mm. Hg) with prominent "a" waves. In 2, the "a" waves matched the left ventricular end-diastolic pressure, as illustrated by Case 3 (Fig. 7). In Case 1 the left ventricular end-diastolic pressure greatly exceeded the "a" wave (Fig. 1B). The mean left atrial pressure was lower than the ventricular end-diastolic pressure in all 3 cases. All had a rapid "y" descent despite some increase in the "y" point and thus showed rapid early ventricular filling. The "z" point of the left atrial pressure pulse, measured 0.05 sec. following the Q wave of the electrocardiogram (Braunwald and Frahm, 1961), was substantially higher than the mean left atrial pressure in two of the three.

CINEANGIOGRAPHY ANALYSIS

The details of cine-analysis are shown in Table II. In all cases supra-aortic injection showed regurgitation of large amounts of dye into the left ventricle. Case 2 showed slight mitral regurgitation, but this did not occur in any of the others. From the area opacified in the left anterior oblique cineangiogram, an estimate of end-systolic volume was possible. No attempt at exact quantitation was made. End-systolic volume was slightly increased in 2 and much increased in the others. The increase in the left ventricular diastolic volume was seen to stop abruptly in mid-diastole in Cases 1 and 2.

FIG. 3.—Case 2: equilibration of aortic (Ao) and left ventricular (LV) pressures in late diastole. There is no aortic systolic gradient. Paper speed 75 mm./sec.

FIG. 4.—Case 3: equilibration of aortic (Ao) and left ventricular (LV) pressures in late diastole. There is a large aortic systolic gradient. Paper speed 75 mm./sec.

FIG. 5.—Case 7: simultaneous left ventricular (LV) and aortic (Ao) pressure tracings. There is equilibration of these pressures in the long diastolic pause following the premature contraction (the third ventricular complex). Paper speed 75 mm./sec.

DISCUSSION

Equalization of left ventricular and aortic diastolic pressures in patients with severe aortic reflux was due to both a fall in aortic diastolic pressure and a rise in left ventricular end-diastolic pressure. This is illustrated by pressures at equilibration of 33 to 55 mm. Hg.

The decline in aortic diastolic pressure is determined partly by peripheral run-off and partly by ventricular reflux. It is unlikely that reduced peripheral resistance contributed to the rapid fall in aortic pressure, as peripheral resistance is usually raised in the presence of severe aortic reflux (Sancetta and Kleinerman, 1957). The moderately increased rate of fall in aortic diastolic pressure shown by our patients was probably the result of reflux into the ventricle.

Aortic diastolic pressures did not fall below 33 mm. Hg, and striking increases in left ventricular end-diastolic pressure occurred in all patients before equalization of aortic and ventricular diastolic pressures resulted. Indeed, the first patient (Case 1) who showed this phenomenon best had the highest pressure at equalization, which suggests that an increase in left ventricular diastolic pressure was the critical factor in its development.

End-diastolic pressure in the ventricle depends on the volume load and the myocardial distensibility. In severe aortic regurgitation the volume load is increased because a large portion of the systolic output returns to the ventricle where it must be accommodated together with forward flow from the atrium. In addition, if the ventricle is overburdened and function is impaired, there may be incomplete systolic ejection which contributes further to the diastolic volume load.

There is a limit to the distensibility of the ventricle and as the ventricle becomes too distended small increments in volume produce large increments in pressure. This progressive reduction in

distensibility at large ventricular volumes has been demonstrated by the pressure volume curves of Dodge, Hay, and Sandler (1962). Conditions causing previous ventricular hypertrophy such as aortic stenosis or hypertension increase diastolic stiffness and offer greater resistance to ventricular filling in late diastole.

In early diastole, when most of the aortic reflux occurs, the ventricular cavity is enlarging by intrinsic elastic recoil. Over the range of volume change experienced by the normal left ventricle, it is probable that left ventricular distensibility in our patients was normal. However, with severe aortic reflux, very large left ventricular volumes might occur if resistance to ventricular filling did not at some stage increase. Without this, the left ventricle might form a low resistance run-off limiting forward flow and coronary perfusion. In Case 1 there was probably a sharp reduction in ventricular distensibility beyond a certain point which prevented this occurrence. Reduced left ventricular distensibility may thus be advantageous in limiting the amount of late diastolic regurgitation. Hence, arterial perfusion pressure is maintained, systolic volume loads are reduced, and end-diastolic ventricular pressures are raised, so facilitating ventricular contraction. Some of our patients had clinical features which might have reduced left ventricular distensibility. Case 1 had previously been hypertensive, and Cases 3, 6, 7, and 8 had associated aortic stenosis. Each of the patients described by Wright, Toscano-Barboza, and Brandenburg (1956) and by Kelly, Morrow, and Braunwald (1960) and one described by Meadows, Sharp, and Zacharioudakis (1962) also had aortic stenosis.

However, high left ventricular end-diastolic pressures necessitate a rise in left atrial pressures to maintain ventricular filling. Braunwald and Frahm (1961) have shown that a vigorous left atrial contraction can raise left ventricular end-diastolic pressure to a significantly higher level than mean left atrial pressure. Thus, atrial emptying can continue and the raised left ventricular end-diastolic pressure can be supported with a lower average pulmonary venous pressure. This mechanism is shown by Case 3 (Fig. 7).

In severe aortic reflux when the ventricle is very resistant to distension the diastolic pressure may rise rapidly and exceed left atrial pressure. This results in premature mitral valve closure as seen in Case 1. This phenomenon limits the time available for emptying the atrium, in this case to one-third of the available ventricular diastolic filling period. It protects the lungs from the considerable increases in the left ventricular diastolic pressure, but in Case 1, this advantage was reduced by vigorous atrial contraction against the closed mitral valve, which served only to increase pulmonary venous pressure, and had no effect on ventricular filling.

Premature mitral valve closure in aortic reflux is a rare clinical phenomenon. Single cases have been described by Wright *et al.* (1956), Colvez *et al.* (1959), Dodge, Sandler, and Evans (1960), and

FIG. 6.—Case 8: equilibration of aortic (Ao) and left ventricular (LV) pressures following premature contractions. Paper speed 25 mm./sec.

FIG. 7.—Case 3: simultaneous left atrial (LA) and ventricular (LV) pressure tracings at high sensitivity. Large “a” waves in the atrial tracing match the left ventricular end-diastolic pressure. The end-diastolic pressure at this time was lower than it was earlier (Fig. 4). Paper speed 75 mm./sec.

Kelly *et al.* (1960). Two other cases were reported by Meadows *et al.* (1962). The cause of the aortic disease varied, but three of these patients had a history of bacterial endocarditis. In three, prior aortic stenosis may have been a decisive factor in raising left ventricular diastolic pressure in the same way as proposed for hypertension in our patient.

The effects of severe reflux from aorta to ventricle were studied experimentally in dogs by Welch, Braunwald, and Sarnoff (1957) using an open chest preparation. Progressive increases in reflux raised left ventricular end-diastolic pressure above mean left atrial pressure when the regurgitant volume exceeded one-half to two-thirds of the stroke volume. When mitral regurgitation was added, this difference in diastolic pressure was abolished, and mean left atrial pressure rose as left ventricular end-diastolic pressure fell. They concluded that a competent mitral valve in severe aortic reflux protected the lungs by limiting the rise in the left atrial pressure. It also allowed high left ventricular end-diastolic pressures to develop which produced a more forceful ventricular contraction.

All the reported cases of premature mitral valve closure also had equilibration of aortic and left ventricular diastolic pressures. However, the experiments of Welch *et al.* (1957) showed that left ventricular end-diastolic pressure could exceed left atrial pressure while remaining lower than the diastolic pressure in the aorta.

Colvez *et al.* (1959) from a study of electrocardiograms suggested that premature atrial contraction might occur in aortic regurgitation to prevent premature mitral valve closure. However, none of our patients showed such early atrial activation. Inspection of the pressure tracings in Case 1 suggests that any significant delay in mitral valve closure would have had disastrous effects on the lungs.

Premature closure of the mitral valve in severe aortic regurgitation allows high left ventricular diastolic pressures to develop, thus limiting reflux and enhancing ventricular contraction. It protects the lungs from these high diastolic pressures, but limits the time for atrial emptying, and if sinus rhythm is present, the force of atrial contraction is expended on the lungs.

SUMMARY

Eight patients with severe aortic regurgitation are described who showed equalization of left ventricular and aortic pressure in diastole. In one, this occurred at mid-diastole and in two others at end-diastole. The remaining five showed this phenomenon only during long diastolic pauses following premature systole.

Aortic pressures fell rapidly due to reflux into the ventricle. Left ventricular end-diastolic pressures rose much due to increased diastolic volume loads and reduced ventricular distensibility. Pressures at equalization were 33 to 55 mm. Hg.

Left atrial pressures were measured in three patients who all showed raised mean pressures and large "a" waves. In one, atrial contraction raised left ventricular end-diastolic pressure substantially above mean left atrial pressure. In one, atrial contraction occurred after mitral valve closure.

Premature mitral valve closure occurred in one patient after one-third of the time normally available for ventricular diastolic filling. This resulted from severe aortic reflux combined with rapidly diminishing ventricular distensibility after early diastole. It was thought to limit the degree of reflux and enhance myocardial contraction. It protected the lungs from the extreme rise in left ventricular diastolic pressure, but exposed them to the effects of atrial contraction against the closed mitral valve.

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