Early diastolic murmurs in end-stage renal failure

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An early diastolic murmur thought to indicate functional aortic regurgitation was heard in 7 of 74 consecutive patients with end-stage renal failure assessed for chronic intermittent haemodialysis and transplantation. In all 7 cases the murmur was transient and related to episodes of hypertension and fluid overload and disappeared on correction of these factors. In a further 2 patients aortic regurgitation resulted from a structural abnormality of the aortic valve. Thus, an early diastolic murmur is not uncommon in this situation and does not necessarily indicate organic aortic valve disease which might preclude selection for haemodialysis and transplantation.

The causes of aortic regurgitation are many and are well reviewed by Runco and Booth (1963). Functional aortic regurgitation has been described as a rare occurrence in anaemia (Hunter, 1946) and congestive cardiac failure (McKusick, 1958). In hypertension the prevalence of functional aortic regurgitation has been reported as varying from 2 per cent (Paullin *et al.*, 1927) to 9 per cent (Barlow and Kincaid Smith, 1960).

In end-stage renal failure, anaemia is invariable, hypertension is usual, and congestive cardiac failure not uncommon. There might, therefore, be expected to be a high incidence of functional aortic regurgitation in such patients, leading to errors in management, unless this is recognised as such (Matalon *et al.*, 1971). We examined and followed up all patients referred to a Regional Renal Unit for assessment for haemodialysis over a two-year period to assess the incidence of aortic diastolic murmurs.

Results

The 74 patients studied were all those assessed as to their suitability for long-term haemodialysis and transplantation on account of end-stage renal failure. In the course of the study 9 were noted by at least 2 observers to have an early diastolic murmur. Two of these clearly had organic aortic valve disease: 1 had been investigated by cardiac catheterisation and a diagnosis of congenital aortic regurgitation made; the other developed aortic regurgitation in

the course of a staphylococcal septicaemia and died, necropsy revealing bacterial endocarditis involving the aortic valve. In the other 7 patients (see Table for details) the murmur was transient, suggesting that this was caused by functional aortic regurgitation.

A representative history is that of case 4, a 24-year-old man first seen in 1967 complaining of headache. Physical examination showed a blood pressure of 220/130 mmHg, left ventricular hypertrophy, and grade 4 hypertensive retinopathy. He was treated with methyldopa 1 g t.d.s. Twelve months later he was admitted to the renal unit with increasing shortness of breath. He was then found to have a blood pressure of 200/110 mmHg and grade 2 hypertensive retinopathy. Jugular venous pressure was raised 4 cm and there was mild peripheral oedema. On auscultation of the heart there was a soft systolic ejection murmur, a loud aortic valve closure sound, and an early diastolic murmur. Crepitations were heard at both lung bases. The electrocardiogram showed left ventricular hypertrophy, and the chest radiograph showed cardiomegaly and pulmonary oedema. Blood urea was 500 mg/100 ml (83 mmol/l). Peritoneal dialysis was performed and over the next three days he improved considerably: blood pressure fell to 170/100 mmHg, pulmonary and peripheral oedema cleared, and he lost 5 kg in weight; the early diastolic murmur disappeared. He was started on intermittent haemodialysis and methyldopa was continued. He remained well until 6 months later when he again became breathless. He was 5 kg above his estimated ideal weight and his blood pressure was 210/110 mmHg.

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Table Details of patients with end-stage chronic renal failure found to have an early diastolic murmur

Case No.	Age (y)	Sex	Diagnosis	Hb (g/dl)	Lowest recorded BP when murmur present (mmHg)	Highest recorded BP when no murmur present (mmHg)	Evidence of fluid overload
1	27	M	GN	6	160/95	220/140	PD
2	24	M	GN	7	176/110	270/170	P
3	36	F	GN	6	180/120	200/130	P
4	28	F	GN	5	160/90	210/140	PD
5	40	M	VUR	6	160/100	210/115	PD
6	16	F	VUR	6	140/80	160/90	PD
7	23	M	H/T after pregnancy toxæmia	6	170/110	200/150	PD

GN, glomerulonephritis; VUR, vesico-ureteric reflux; H/T, hypertension; P, pulmonary oedema; D, dependent oedema

He had peripheral and pulmonary oedema and again an early diastolic murmur was heard. His dialysis regimen was adjusted and his sodium and water intake restricted. He improved and the early diastolic murmur disappeared. Over the next 2 years he was admitted on 3 occasions, with shortness of breath and clinical and radiological evidence of pulmonary oedema. On each occasion he was well above his estimated ideal weight and a transient early diastolic murmur was heard; his blood pressure on these 3 occasions was 160/90, 210/110, and 180/95 mmHg. Since then he has had a successful renal transplant.

Details of the other patients can be seen in the Table. All were anaemic. All presented with symptoms suggesting fluid overload and were found to have dependent oedema and/or cardiac enlargement with pulmonary oedema on chest x-ray examination. Six were hypertensive at the time the murmur was heard, though in every case a higher blood pressure had been recorded at other times without a murmur being audible. In all cases the murmur disappeared after dialysis. Three patients had forearm arteriovenous shunts when the murmur was first heard (cases 1, 2, and 3). No patient had a history of rheumatic fever. All had negative serological tests for syphilis and sterile blood cultures. Cases 5 and 6 had been hypercalcaemic in the past; band keratopathy and ear drum calcification were present in cases 1, 2, and 3, and case 5 had severe peripheral vascular calcification.

Three patients have had successful transplants and 4 have died, case 3 from myocardial infarction, cases 5 and 6 from uraemia, and case 7 from septicaemia. Necropsy in cases 3 and 5 showed normal aortic valves.

Discussion

The early diastolic murmur in these patients was thought to be the result of aortic regurgitation and to be functional in 7 of the 9. Pulmonary regurgita-

tion was a possible alternative but was unlikely in the absence of any evidence of pulmonary hypertension.

All, except one, of the patients were hypertensive, though each had been seen at other times with a higher blood pressure but no murmur. This confirms the observation of Puchner *et al.* (1960) that functional aortic regurgitation in hypertension is not simply related to the height of the blood pressure. The incidence of functional aortic regurgitation in our patients (9.5%) is higher than in most reported series of hypertensive patients (Paullin *et al.*, 1927; Garvin, 1940; Puchner *et al.*, 1960) though Barlow and Kincaid Smith (1960) found a 9 per cent incidence in their series of 100 patients at the Postgraduate Medical School of London. This also suggests that factors other than hypertension alone were responsible for the aortic regurgitation.

Fluid overload was present in all the patients and the murmur invariably disappeared when this was corrected. However, as commonly occurs in chronic renal failure, dialysis corrected the hypertension and fluid overload simultaneously; it is, therefore, difficult to judge the relative importance of these two factors. It seems likely that fluid overload was the major determinant, since symptoms of cardiac failure with shortness of breath and/or oedema were invariable presenting features and though hypertension was present it was not as severe as on previous occasions when there had been no aortic regurgitation. Anaemia is unlikely to have been an important factor since the murmurs disappeared without a rise in haemoglobin level. It may, however, have made it possible to detect some murmurs that would otherwise have been inaudible, as there is evidence that a low blood viscosity increases the intensity of murmurs (Garb, 1944).

We did not consider the presence of peripheral vascular calcification to be relevant since this is a common finding in end-stage renal failure and no aortic valve calcification was visible on chest x-ray films. It is interesting, however, that no fewer than

3 patients had band keratopathy and ear-drum calcification, which are much less common complications of renal failure.

We conclude that there is a relatively high incidence of aortic regurgitation in patients with end-stage renal failure; this is usually functional, occurring in the presence of fluid overload and hypertension, and is reversible by dialysis.

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