CHARACTERIZATION OF URAEMIC CARDIOMYOPATHY BY LEFT HEART CATHETERIZATION WITH SERIAL ANALYSIS OF PRESSURE-VOLUME RELATIONS AND MYOCARDIAL O_2 CONSUMPTION

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Summary

Twenty-nine patients on maintenance haemodialysis were studied by serial computer-assisted pressure-volume relations of the left ventricle (LV) during rest and stress. Beta-adrenergic stimulation resulted in an increase in LV contractility but due to increased myocardial oxygen consumption LV-efficiency was unchanged. Alpha-adrenergic stimulation depressed LV contractility in 41 per cent of haemodialysis patients. Both catecholamines induced an excessive increase in LV-end diastolic pressure indicating an impaired diastolic compliance.

Introduction

Abnormalities of left ventricular (LV) function in patients on haemodialysis have been described, the existence of a specific uraemic cardiomyopathy, however, remains controversial.

Echocardiographic screening in 131 patients on haemodialysis revealed LV hypertrophy in 57 per cent without a pattern of a *dilated* cardiomyopathy. However, concentric hypertrophy was found in 58 of 131 patients, and asymmetric hypertrophy (septum-posterior wall-ratio >1.4) in 17 of 131 of all the patients studied.

In the presence of LV hypertrophy, we found a depressed response to inotropic stimulation with calcium [1], while disturbances of beta-adrenergic response of the heart in uraemia has been reported by other investigators. The purpose of the present study was to establish the basic abnormality (loading condition versus contractile state) of LV function in uraemia by analysing pressure-volume relations under beta-stimulation and afterload increase.

Patients and methods

Conventional cardiac catheterization including LV angiography and coronary angiography was performed in 29 patients on haemodialysis who were prospective recipients of kidney transplants.

Coronary angiography revealed coronary artery disease in seven of 29 patients. Using a high fidelity micromanometer-tipped catheter and technetium-99-scintigraphy we analysed (computer assisted) alterations of pressure-volume relations and myocardial oxygen consumption (MVO_2-ET) in both the resting state and during pharmacological interventions. The computer-based data represent the mean of 300 cardiac cycles during each intervention.

An altered afterload (mean increase: 40mmHg) was obtained by intravenous injection of phenylephrine, beta-adrenergic stimulation by infusion of dobutamine (10μg/kg b.w./min).

Results

The major differences between baseline haemodynamic data of the 29 haemodialysis patients and 10 healthy control subjects were: elevated LV end-diastolic pressure (16.6 vs 8.9mmHg, $p<0.01$), increased LV muscle mass (231 vs 93g/m^2, $p<0.001$), augmented cardiac index (4.1 vs 3.4L/min/m^2, $p<0.01$) and LV stroke work index (61 vs 50g · m/m^2, $p<0.05$). Both groups could not be differentiated by mean values of ejection fraction (65% vs 66%) or dP/dt_{max} (2190 vs 2140mmHg/sec).

In haemodialysis patients without coronary artery disease beta-stimulation resulted in an augmentation of the ejection fraction (64% vs 72%, $p<0.001$), while in the presence of coronary artery disease no change was observed. Enhancement in contractility was accompanied by a further increase in LV filling pressure (16.6 vs 22mmHg, $p<0.001$).

Afterload increase induced depressed contractility in 41 per cent of the patients *without* coronary artery disease and in all patients *with* coronary artery disease. Neither dobutamine nor phenylephrine resulted in an increase of LV-efficiency since these interventions caused an increase in myocardial oxygen consumption (phenylephrine: 7.9 vs 10.8ml/min/100g, $p<0.001$; and dobutamine: 7.9 vs 9.0ml/min/100g, $p<0.01$).

The baseline data identified an impaired LV diastolic compliance in 19 of 29 patients (diastolic pressure-volume loops, elastic stiffness constant). During overload stress, however, a further reduction of LV diastolic distensibility (higher diastolic pressure at any volume) was observed in all patients.

Comment

Traditional indices of LV function (ejection fraction, dP/dt_{max}, etc) cannot discriminate between changes in loading conditions and changes in myocardial contractility. However, the end-systolic pressure-volume relation, as obtained with serial computer-assisted pressure-volume measurements is independent of cardiac preload and afterload. When we analyse our data, the controversy of the existence of a *specific* uraemic cardiomyopathy appears to be a question of definition. According to invasive data of Ikram et al [2] we were unable to identify haemodynamic characteristics of a *dilated* cardiomyopathy in patients on haemodialysis. Uraemic cardiomyopathy is characterized by an increased LV

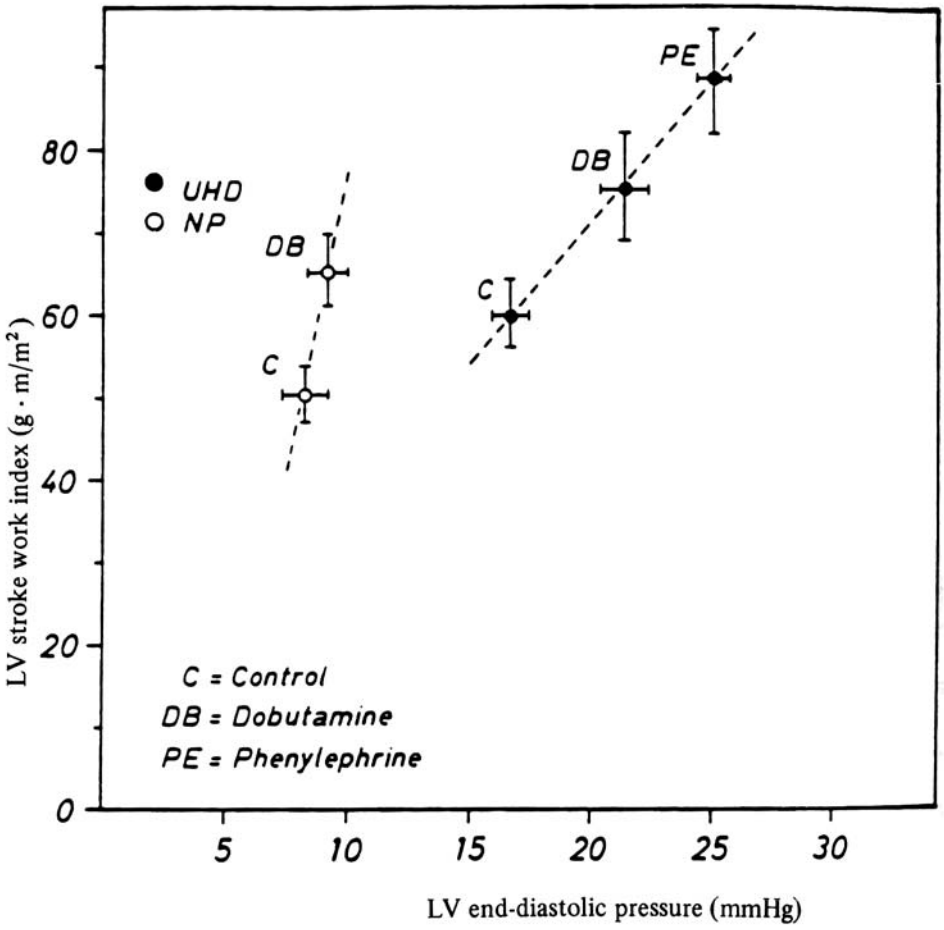

Figure 1. Relationship between LV stroke work index and LV end-diastolic volume. Compared to normal persons (NP) in uraemic heart disease (UHD) stroke work index increases simultaneously with LV diastolic pressure during adrenergic stress

muscle mass, stroke work index, normal chamber volume, preserved systolic function but impaired diastolic compliance (similar to hypertrophic cardiomyopathy). However, a hyperdynamic contractile state – a typical feature in hypertrophic cardiomyopathy – was not observed (Figure 1).

In conclusion, beta and alpha adrenergic responsiveness is preserved in uraemia but depends on the contractile reserves and/or severity of diastolic dysfunction. Serial LV pressure-volume relations identify latent systolic dysfunction in these patients.

The clinical implications are that patients with impaired diastolic compliance would neither tolerate rapid volume removal during haemodialysis, reduction of peripheral vascular resistance, nor inotropic drug treatment (digitalis, catecholamines). On the other hand, in the presence of a reduced diastolic distensibility,

volume overload during the dialysis-free interval may easily result in pulmonary congestion. A third consequence of our invasive study is the necessity for establishing a precise concept of the cardiological status of the patient before starting renal replacement therapy.

References

1 Kramer W, Wizemann V, Thormann J et al. *Klin Wochenschr 1985; 63:* 272
2 Ikram H, Lynn KL, Bailey RR, Little PJ. *Kidney Int 1983; 24:* 371