Maximal Rate of Fall of Left Ventricular Pressure in Cardiomyopathy and Constrictive Pericarditis

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SUMMARY

The maximal rate of fall of left ventricular pressure (peak negative dp/dt) was measured in 4 patients with congestive cardiomyopathy (primary myocardial disease), in 5 patients with constrictive pericarditis and in 3 controls. Measurements were made at rest, with leg raising, after a bolus of 6 μg intravenous isoprenaline, and in patients with constrictive pericarditis during pulsus paradoxus. Peak negative dp/dt was 1 810 ± 234 mmHg/sec in controls; it was reduced in patients with constrictive pericarditis (1 337 ± 514 mmHg/sec) and greatly decreased in patients with congestive cardiomyopathy (812 ± 190 mmHg/sec). There was close linear correlation between resting peak positive and peak negative dp/dt and there was little change with leg raising. Isoprenaline caused an increase in peak positive dp/dt, but there was only a small change in peak negative dp/dt. In patients with constrictive pericarditis, peak negative dp/dt varied during pulsus paradoxus: the linear relationship to peak positive dp/dt was maintained throughout the respiratory cycle.

Peak negative dp/dt may be a useful index of myocardial function.


The maximal rate of left ventricular pressure rise has been studied in detail. It is a useful guide for assessing the state of left ventricular contractility, but is influenced by changes in preload, afterload and heart rate. In contrast, there are few studies on the rate of left ventricular relaxation (negative dp/dt). Peak positive and peak negative dp/dt are closely related, but can be dissociated by inotropic stimulation or by changes in afterload: inotropic stimulation causes a greater increase in positive dp/dt, while an increased afterload (e.g. methoxamine infusion) is associated with increased negative dp/dt. Changes in afterload are associated with a fall in stroke volume and an increased left ventricular end-systolic volume: the increased rate of fall of pressure may be related to the increased fibre length at the onset of relaxation. The determinants of the rate of relaxation have not been studied in detail at a molecular level.

We have measured the rate of fall of left ventricular pressure (peak negative dp/dt) in patients with congestive cardiomyopathy and constrictive pericarditis. In congestive cardiomyopathy the left ventricle is large and dilated with poor systolic function, while in constrictive pericarditis the left ventricle is compressed and cavity size reduced, and over-all systolic function is normal or slightly reduced.

PATIENTS

Twelve patients were studied (Table 1).

Group 1 — Congestive Cardiomyopathy

Four patients had congestive cardiomyopathy (primary myocardial disease), the aetiology of which was unknown. The disease was severe in 3 and mild in 1 patient who had responded well to prolonged bed rest and therapy. Two patients had mild additional functional mitral incompetence (regurgitant fraction 20% and 25%), but none had overt pulmonary thrombo-embolism. The patients were receiving digitalis, and this was not discontinued. Informed consent was obtained from each patient before catheterisation.

Group 2 — Constrictive Pericarditis

Five patients with severe constrictive pericarditis were investigated by cardiac catheterisation before operation. The aetiology was tuberculous in 4 and bilharzial in 1. The patients were receiving digitalis and diuretic therapy.

Group 3 — Control Subjects

Three patients presented with disabling chest pain resembling angina pectoris. Cardiac catheterisation and selective coronary angiography showed that they had normal haemodynamics and normal coronary arteries. Their data were compared with those of patients in groups 1 and 2.
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**TABLE I. CLINICAL, HAEMODYNAMIC AND ANGIOGRAPHIC DATA**

As = Asiatic; B = Black; C = Coloured; W = White; EDV = end-diastolic volume; ESV = end-systolic volume; LVEDP = left ventricular end-diastolic pressure; LVdp/dt = 1st derivative of left ventricular pressure; pos. = positive; neg. = negative.
METHODS

Patients were studied in the fasting state. Premedication with 10 mg diazepam and 50 mg pethidine was given 1 hour before study. Routine right and left heart catheterisation was performed, using percutaneous punctures of the femoral vein and artery. Left heart pressure measurements were made using a Statham SF1 micromanometer tipped catheter, right heart pressures were measured with a fluid-filled catheter manometer system and Statham P23 Db bonded strain gauge; the system was carefully debubbled and the frequency response was flat to 20 Hz. Pressure recordings were made on an Electronics for Medicine DR-16 photographic recorder with an electronic analog differentiating circuit which has minimal phase lag and distortion. The mid-chest level was used as the zero reference for pressure measurements. Control measurements of left ventricular pressure and its first derivative were made with the patient in the supine position. The patient's legs were then passively elevated to a height of 60 cm and the measurements were repeated after 3-5 minutes. The patient was allowed to rest supine and recover, and he was then given an intravenous bolus of 6 μg isoprenaline sulphate. Pressure recordings were made at the time of peak tachycardia.

Cardiac output was measured by the indicator dilution method, using 5 mg indocyanine green, a Gilford optical densitometer and Harvard infusion and withdrawal pump sampling at a constant rate of 38 ml/min. The procedure was completed with left ventriculography in the right anterior-oblique position, using a slow injection of 50 ml 76% Urografin. Ventricular volumes and ejection fraction were calculated from the uniplane cine-angiograms according to the method of Greene et al. In patients with angina pectoris, selective coronary angiography was undertaken and this showed normal major coronary arteries.

In 4 patients with constrictive pericarditis, beat-to-beat analysis was made over a respiratory cycle to study the effect of pulsus paradoxus. The mean values over several respiratory cycles were calculated in all the patients, and these values were used for comparison with patients with cardiomyopathy and the control subjects.

The results were analysed using a Wang 700 series programmed calculator and standard statistical methods.

RESULTS

The results are given in Table I. Peak negative dp/dt was $1810 \pm 234$ mmHg/sec in the control subjects. It was reduced in patients with constrictive pericarditis ($1337 \pm 514$ mmHg/sec; $t = 1.46$; NS) and greatly reduced in congestive cardiomyopathy ($812 \pm 190$ mmHg/sec; $t = 6.25$; $P<0.01$) (Fig. 1).

There was close correlation between peak negative dp/dt and peak positive dp/dt (Fig. 2). The maximal rate of pressure fall (peak negative dp/dt) was more rapid than the rate of pressure rise (peak positive dp/dt) in the control subjects and in patients with constrictive pericarditis, but patients with cardiomyopathy had similar values for peak positive and peak negative dp/dt.

![Fig. 1. Peak negative dp/dt in controls (N) and in patients with constrictive pericarditis (CP) and congestive cardiomyopathy (CMO). Resting peak negative dp/dt is reduced in constrictive pericarditis (NS) and greatly reduced in congestive cardiomyopathy ($P<0.01$). There is no change with leg raising, but peak negative dp/dt increases in patients with congestive cardiomyopathy after isoprenaline.](image)

![Fig. 2. Linear relationship between resting peak positive and peak negative dp/dt (peak negative dp/dt = 1.23; peak positive dp/dt = 51.5 ± 368.6; $r = 0.68$, $t = 2.93$, $P<0.05$).](image)

Peak negative dp/dt did not change with leg raising (Fig. 1), but intravenous isoprenaline (6 μg) separated peak positive and peak negative dp/dt. Peak positive dp/dt was greatly increased while the change in peak negative dp/dt was small; this effect was less marked in patients with cardiomyopathy, who had low resting negative dp/dt values (Fig. 3). In these patients peak negative dp/dt also rose, and this confirms the findings of Reale et al.

The effect of changes in preload during pulsus paradoxus is shown in Fig. 4. Inspiration is associated with a fall
in both peak positive and peak negative dp/dt, followed by gradual return to the resting value. Changes in positive and negative dp/dt are closely related to each other at rest, with leg raising and after isoprenaline.

**DISCUSSION**

**Mechanical Aspects**

**Changes in ventricular volume.** Abrupt changes in afterload cause changes in peak negative dp/dt and this may be due to a change in end-systolic volume. The afterload was normal in our patients with constrictive pericarditis and congestive cardiomyopathy, and peak negative dp/dt occurred after aortic valve closure, but extrinsic compression reduces left ventricular volume in constrictive pericarditis and this may explain, in part, the decrease in peak negative dp/dt. On inspiration, left ventricular end-diastolic pressure, stroke output, and probably left ventricular volume decreased, and this may cause the change in peak negative dp/dt during pulsus paradoxus. In contrast, patients with congestive cardiomyopathy have large ventricular volumes, but peak negative dp/dt is greatly decreased. Changes in ventricular volume seem to be less important than changes in contractility in determining the rate of ventricular relaxation in cardiomyopathy.

**The effect of ventricular hypertrophy.** Peak negative dp/dt is reduced in left ventricular pressure overload. Left ventricular wall mass is increased in congestive cardiomyopathy, and hypertrophied myocardial fibres may relax less easily owing to changes in viscosity and inertia. There is also destruction of tissue with inflammation and intra- or intercellular oedema; this may also alter the ability of the ventricle to relax. In constrictive pericarditis the myocardial fibres are atrophied, but we have no data concerning left ventricular muscle or wall mass. Infiltration of the myocardium by fibrous tissue may again impair ventricular relaxation.

**Biochemical Aspects**

**Molecular basis of muscle fibre contraction.** Myocardial depolarisation is associated with the release of calcium (Ca++) from the lateral sacs of the sarcoplasmic reticulum, and Ca++ binding to troponin facilitates interaction of the contractile proteins to form the actomyosin complex. During relaxation Ca++ is taken up by the sarcoplasmic reticulum and re-enters the Ca++ pool in the lateral sacs and subsarcolemmal storage sites. The rate of Ca++ binding to troponin may determine peak positive left ventricular dp/dt.10,22 It is possible that peak negative dp/dt depends in part on Ca++ release from the troponin-tropomyosin complex and its re-uptake by the sarcolemmal system.10,22 In a state of equilibrium it is feasible that Ca++ release and re-uptake, and similarly peak positive and peak negative dp/dt, should be related.

**Changes in inotropicity.** Myocardial contractility is enhanced by increased filling of the intracellular Ca++ pool. Catecholamines increase the rate of Ca++ uptake into intracellular Ca++ storage sites and the rate of Ca++ release from the lateral sacs of the sarcoplasmic reticulum.22 Isoprenaline infusion causes a marked rise in
peak positive dp/dt, but there is little change in peak negative dp/dt: this dissociation may be expected if isoprenaline acts primarily on Ca\textsuperscript{++} influx and release mechanisms.

**Congestive cardiomyopathy.** In cardiac failure from cardiomyopathy in hamsters, the primary defect in the Ca\textsuperscript{++} cycle may be a failure of Ca\textsuperscript{++} re-uptake by the sarcoplasmic reticulum.\textsuperscript{24} It is interesting that peak negative dp/dt was greatly decreased in our patients with cardiomyopathy (Fig. 1), and this change was of greater discriminatory value between normality and abnormality than peak positive dp/dt (Fig. 2). Both peak positive and peak negative dp/dt increased after isoprenaline infusion. It is possible that isoprenaline also affects Ca\textsuperscript{++} re-uptake and that Ca\textsuperscript{++} release, which is probably a passive process down a concentration gradient, may be closely related to Ca\textsuperscript{++} re-uptake, which is most likely an active pumping mechanism.

**Constrictive pericarditis.** In constrictive pericarditis the ventricle is compressed and underloaded, with a reduction in left ventricular end-diastolic volume, stroke index and left ventricular stroke work index. Peak positive dp/dt is normal or slightly reduced.\textsuperscript{30,31} Peak negative dp/dt is also decreased and is closely related to peak positive dp/dt at rest, with leg raising and during pulsus paradoxus. During pulsus paradoxus there is a small change in loading conditions, and this is accompanied by small cyclical changes in peak positive and peak negative dp/dt: the equilibrium of the intracellular Ca\textsuperscript{++} exchange system is presumably not unbalanced.

**REFERENCES**