Independence of changes in left ventricular diastolic properties of pericardial pressure

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SUMMARY There has been much interest in the published reports as to the extent to which measured left ventricular diastolic properties are affected by the pericardium. In this study observations were made on 24 patients, seven days after cardiopulmonary bypass. Left ventricular dimensions were measured from echocardiographic recordings and left ventricular diastolic pressure assessed from measurements of isovolumic relaxation time. Pericardial pressure was measured directly using a small solid state transducer inserted into the pericardial space at the time of operation. Left ventricular diastolic properties were altered by either isometric handgrip or glyceryl trinitrate administration. Isometric handgrip produced an increase in cavity dimension at end-systole and diastole, with reduction in isovolumic relaxation time, suggesting an increase in left ventricular end-diastolic pressure; glyceryl trinitrate produced the reverse effect, with decreased cavity dimensions and prolongation of isovolumic relaxation time. These changes occurred in the absence of significant changes in pericardial pressure. We therefore conclude that even in the rather unusual conditions of the early postoperative period, when the sensitivity of pericardial pressure to small volume changes might be expected to be increased, substantial changes in left ventricular diastolic properties can occur without detectable alteration in pericardial pressure.

There has been considerable interest concerning the extent to which the pericardium affects measured left ventricular diastolic properties. To date, most observations on this relation have been made on experimental animals and there have been few recorded measurements in man. We have taken advantage of the development of a small solid state transducer (Gaeltec 3EA) to measure pericardial pressure directly in man in the postoperative period after cardiopulmonary bypass. Left ventricular diastolic properties have been altered using isometric stress testing and glyceryl trinitrate administration and associated changes in pericardial pressure measured.

Subjects and methods

Twenty-four patients were studied during the postoperative period after cardiopulmonary bypass for saphenous vein bypass grafting in 18 patients, and for valve replacement in six.

Pericardial pressure was measured with a Gaeltec 3EA solid state transducer. This had an external diameter of 3 mm, low temperature sensitivity, and a

resonant frequency of 50 kHz. The zero drift was low and in the present study was found to be < 2 mmHg in 10 days. It was calibrated in saline at 37°C before insertion and was used in conjunction with a Gaeltec S7 control unit amplifier with an isolated input.

The transducer was inserted into the pericardial space by a separate wound at the end of the operation and was left in situ for up to 10 days. The pericardium was closed once the transducer had been positioned. Previous studies¹ had shown that the site used for transducer placement did not significantly affect the pressure recorded. In all cases the zero for pressure measurement was taken as atmospheric.

Daily recordings of mean and phasic pericardial pressure were recorded. On the seventh postoperative day, simultaneous echo-, phono-, and apex-cardiographic recordings were also made along with standard lead II of the electrocardiogram using Cambridge Instruments Equipment. Echocardiograms were recorded at the level of the tips of the mitral valve leaflets to show the time of separation of anterior and posterior cusps at the start of ventricular filling. Left ventricular cavity size was estimated at this level as the distance between the leading edge of the echoes from the left side of the septum and the endocardium

of the posterior wall. Phonocardiograms were recorded from the left sternal edge, using a medium or high frequency filter in the position where A_2 , the onset of the initial high frequency vibration of the aortic component of the second heart sound, was most obvious. This was definitively identified either from its relation to the dicrotic notch of the indirect carotid pulse, or from the aortic valve echogram. Apexcardiograms were recorded using a transducer of time constant 4 seconds and lower frequency limit of 0.05 Hz. Records were made photographically at a paper speed of 100 mm/s and digitised.²

From these records, the following measurements were made.

(1) DIMENSIONS

From the digitised echocardiogram—end-diastolic (synchronous with the q wave of the electrocardiogram) and minimum cavity dimension.

(2) TIME INTERVALS

(a) Isovolumic relaxation time—the interval between A_2 and the onset of mitral valve opening. This interval has previously been shown to bear strong and negative correlation with left ventricular end-diastolic pressure.³

(b) A_2 to the O point of the apexcardiogram. This interval has been studied in the past as isovolumic relaxation time⁴ but can be more usefully regarded as a measure of the time taken by the left ventricular pressure to fall to its minimum value at the end of ejection. Like true isovolumic relaxation time ((a) above) this interval is strongly and negatively correlated with left ventricular end-diastolic pressure.³

(c) O point to the peak of the f wave (rapid filling wave in early diastole) of the apexcardiogram.

(3) RELATIVE AMPLITUDE OF F WAVE OF APEXCARDIOGRAM EXPRESSED AS PERCENTAGE OF TOTAL AMPLITUDE

The timing and relative amplitude of the f wave relate to both the duration of the isovolumic relaxation time and the end-diastolic pressure, a high end-diastolic pressure being associated with an earlier f wave of increased relative amplitude.³

After completing control measurements, the patients performed isometric handgrip by squeezing a sphygmomanometer bulb at 30% of the maximum force they could generate for three to five minutes until the onset of fatigue. Recordings of pericardial pressure and echo-, phono-, and apexcardiograms were made during the last 30 seconds of effort. After 20 minutes rest, control measurements were repeated and the patients took two 0.5 mg glyceryl trinitrate tablets sublingually over an interval of five minutes. Measurements of pericardial pressure and echo-,

phono-, and apexcardiographic recordings were repeated at two, five, 10, and 20 minutes; those coinciding with the maximum heart rate response were noted. Changes in measured diastolic properties were correlated with changes in pericardial pressure.

This study had the approval of the Ethics Committee of the National Heart and Chest Hospitals.

Results

(1) PERICARDIAL PRESSURE

MEASUREMENTS—MEAN AND PHASIC

During the first 24 hours after operation, the mean pericardial pressure was in the range of 2 to 5 mmHg. After this time there was a consistent fall in mean pressure to less than 3 mmHg, the average value by the seventh postoperative day being 2 ± 1 mmHg (mean ± 1 SD) (Fig. 1). Phasic waveforms varied with mean pericardial pressure, so that when pressure was low, the overall amplitude of the waveform was small. Regardless of amplitude, however, the highest values in the cardiac cycle were always recorded during isovolumic contraction, reaching a peak which coincided with ejection. Pericardial pressure then fell and was at its lowest during late ejection or isovolumic relaxation, increasing again during ventricular filling (Fig. 2).

In individual patients, measurements of pericardial pressure were closely linked to clinical status, for example high pericardial pressures were found to correlate with the presence of postoperative tamponade.

(2) EFFECTS OF GLYCERYL TRINITRATE AND ISOMETRIC EXERCISE

(a) Heart rate, arterial pressure, and cavity dimensions

Well documented changes³ in heart rate and arterial pressure were produced by glyceryl trinitrate administration and isometric exercise. Glyceryl trinitrate produced an increase in heart rate (mean increase: + 5 beats/min) and decrease in systolic (– 11 mmHg) and diastolic (– 3 mmHg) arterial pressure. Isometric exercise caused an increase in both heart rate (+ 15 beats/min) and systolic (+ 28 mmHg) and diastolic (+ 15 mmHg) pressure.

After administration of glyceryl trinitrate cavity dimensions fell at end-systole (mean decrease = 0.9 mm, $p < 0.001$) and end-diastole (mean decrease = 2.9 mm, $p < 0.001$) (Table 1). Isometric stress caused an increase in cavity dimension at end-systole (+ 1.0 mm, $p < 0.001$) and end-diastole (+ 1.8 mm, $p < 0.001$) (Table 1).

(b) Diastolic time intervals (Table 2)

Glyceryl trinitrate prolonged isovolumic relaxation time from 82 ± 6 ms to 112 ± 8 ms ($p < 0.01$), A_2 -O point

Fig. 1 Mean pericardial pressure at varying time intervals after cardiopulmonary bypass. Results shown are mean $\pm$ 1 SD.

Fig. 2 Phasic waveform of pericardial pressure with superimposed left ventricular pressure trace.

interval from 138 ± 18 ms to 153 ± 10 ms ($p < 0.05$), and O-f wave interval from 76 ± 8 ms to 85 ± 3 ms ($p < 0.05$); the relative amplitude of the f wave fell from 24 ± 9 to $11 \pm 6\%$ ($p < 0.02$). Isometric stress caused isovolumic relaxation time to shorten from 86 ± 8 ms to 69 ± 5 ms ($p < 0.01$); A_2 -O point and O-f intervals tended to shorten but these changes did not reach statistical significance.

(c) Pericardial pressure

Under control conditions, mean pericardial pressure

on the seventh postoperative day was 2 ± 1 mmHg (Fig. 1). After glyceryl trinitrate administration or isometric stress testing, there were no significant changes in pressure recorded, values being 1 ± 1 and 2 ± 1 mmHg, respectively (Table 2). The amplitude of phasic changes in pericardial pressure was not affected.

Discussion

Left ventricular diastolic pressures have considerable physiological significance and are frequently used to document the presence of disease or as a basis for clinical decision making. Their rigorous determination, however, presents difficulties, since the zero reference is usually taken as the pressure at mid-thorax, sternal angle, or of the atmosphere, so that pressure differences across the myocardium are not, in fact, measured. Whether this technical limitation is of clinical or physiological significance remains uncertain, though when contradictory findings arise in the course of experiment, the fundamentals on which such measurements are based must be carefully examined. For this reason we have determined pericardial pressure directly in patients after open heart surgery. The method, described in detail elsewhere,¹ involves the positioning of a solid state transducer immediately behind the posterior left ventricular wall, its exact position being unimportant. Mean and phasic traces derived by this method are similar to those previously reported from animals,⁵⁻⁷ and in individual patients they have been found to correlate with the presence or absence of postoperative tamponade. In the present study, measurements were made seven days after operation. A possible limitation of the method is that it is applicable only to patients who have undergone open heart surgery, and who are

Table 1 *Effect of isometric handgrip and glyceryl trinitrate administration on cavity dimensions at end-systole (ESD) and end-diastole (EDD)*

Case No.	Isometric exercise				Glyceryl trinitrate			
	EDD (mm)		ESD (mm)		EDD (mm)		ESD (mm)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	58	60	46	47	59	56	46	46
2	51	52	40	42	51	50	40	39
3	40	41	33	35	39	37	32	31
4	43	44	31	32	43	40	30	30
5	43	43	32	33	44	40	32	30
6	42	43	31	32	42	40	29	27
7	41	44	33	33	41	39	32	32
8	48	49	35	36	47	42	35	35
9	38	42	28	30	38	34	27	26
10	39	42	31	32	39	37	30	30
11	38	41	31	31	38	35	31	30
12	34	36	26	27	33	30	24	22
13	41	42	28	29	40	38	28	28
14	46	47	32	33	46	41	33	31
15	50	52	39	39	50	46	40	40
16	48	50	40	42	48	45	38	36
17	39	39	32	33	39	36	30	30
18	50	51	37	38	51	47	38	37
19	43	45	30	32	43	42	31	30
20	41	43	32	33	41	39	32	31
21	40	42	32	32	40	39	31	30
22	46	49	36	38	47	42	36	34
23	46	48	36	37	46	43	37	36
24	40	44	31	31	39	37	30	30
Mean increase	1.83 mm		1.04 mm		2.88 mm		0.90 mm	
Mean decrease								
Significance	p<0.001		p<0.001		p<0.001		p<0.001	

Table 2 *Effect of isometric handgrip and glyceryl trinitrate administration on isovolumic relaxation time and on pericardial pressure*

		Control	Change
Glyceryl trinitrate	Isovolumic relaxation time (ms)	82 ± 6	+ 30 ± 5 (p<0.01)
	Pericardial pressure (mmHg)	2 ± 1	- 1 ± 1 (NS)
Isometric handgrip	Isovolumic relaxation time (ms)	86 ± 8	- 17 ± 7 (p<0.01)
	Pericardial pressure (mmHg)	2 ± 1	0 ± 1 (NS)

thus more likely than normal subjects to have left ventricular disease. In addition, the pericardium, having recently been subject to surgical trauma, is likely to be oedematous and hyperaemic, so that it is likely to be stiffer than normal, and the compliance of the pericardial space reduced.

In spite of these considerations, pericardial pressure seven days after operation was low, and was unaffected by changes in left ventricular cavity size induced by glyceryl trinitrate or isometric handgrip. These latter were large, amounting to approximately 10% of transverse dimension, which might be expected to correspond to volume changes between 25 and 30%. Since glyceryl trinitrate is normally held to act by reducing venous return, right ventricular cavity size is also likely to have fallen. Similarly, after

isometric handgrip, left atrial and hence pulmonary artery pressure can both be presumed to have risen, so that right ventricular volume changes were in the same direction as those of the left. We conclude, therefore, that even in the rather unusual conditions of the early postoperative period when the sensitivity of pericardial pressure to small volume changes might be expected to be increased, substantial changes in cardiac chamber size can occur without detectable alteration in pericardial pressure.

In spite of this, however, changes in left ventricular diastolic pressure could be shown. Glyceryl trinitrate caused arterial pressure to fall and yet isovolumic relaxation time was prolonged, suggesting a significant fall in left atrial and left ventricular end-diastolic pressure,³ while exactly the reverse occurred

during isometric handgrip. Thus, these two manoeuvres both caused well defined changes in left ventricular diastolic behaviour, suggesting significant changes in both end-diastolic pressure and volume.

There has been much interest in the published reports as to the extent to which measured left ventricular diastolic properties are affected by the pericardium. Holt's early work⁸ suggested an effect of the pericardium on the diastolic pressure-volume relations of the ventricle, which were significantly shifted when the pericardium was removed. Similarly, volume loading of the heart with the pericardium intact in dogs shifts the entire left ventricular pressure volume curve upwards, primarily because of a rise in intrapericardial pressure.⁹ Nitroprusside infusion in the presence of such acute cardiac distension displaces the curve downwards again as pericardial pressure falls. These acute shifts are abolished after removal of the pericardium. By contrast, Mann *et al.*¹⁰ noted that when patients with ischaemic heart disease were paced, the increase in left ventricular end-diastolic pressure in the left ventricle was greater than that in the right. This finding is incompatible with the idea that the increase in left ventricular end-diastolic pressure is solely the result of mechanical coupling between the two ventricles, mediated by an intact pericardium. Similarly, Ludbrook *et al.*¹¹ noted that administration of glyceryl trinitrate shifted the pressure-volume curve downwards in a group of patients with ischaemic heart disease. Since right ventricular pressures and left ventricular end-diastolic volumes were not significantly increased in any of their patients, it seems unlikely that pericardial restriction played any significant part in the displacement of the pressure-volume curves. Our results are wholly compatible with these. Major changes in left ventricular cavity size, and probably in left ventricular end-diastolic pressure occurred in the absence of any significant change in pericardial pressure. Clearly, these observations do not exclude such an increase in individual cases as a mechanism of impairment of left ventricular filling; indeed, it forms the basis of the haemodynamic disturbance of pericardial tamponade. It is uncommon, however, closely related to the presence of pericardial disease, and does not appear to operate in the majority of cases. We conclude, therefore, that changes in left ventricular diastolic function measured invasively by others, and non-invasively by ourselves cannot be routinely ascribed to such external influences. Rather, it seems that primary changes in the passive properties of the left ventricle can be

induced by drugs or other manoeuvres in patients with heart disease. The exact nature of these changes remains obscure, though their clinical and theoretical significance is profound. With their existence more firmly established, further studies of their underlying mechanism seem justified.

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