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Cardiac Tamponade and Pericardial Effusion: Respiratory Variation in Transvalvular Flow Velocities Studied by Doppler Echocardiography

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Cardiac tamponade has been associated with an abnormally increased respiratory variation in transvalvular blood flow velocities. To determine whether this finding is consistently present in cardiac tamponade, seven patients were studied prospectively with Doppler echocardiography before and after pericardiocentesis and the results were compared with those found in 20 normal adults and 14 asymptomatic patients with pericardial effusion who did not have definite clinical evidence of tamponade. Doppler ultrasound evaluation included measurement of mitral, tricuspid, aortic, pulmonary and central venous flow velocities, as well as left ventricular ejection and isovolumic relaxation times during inspiration, expiration and apnea.

In the patients with severe cardiac tamponade, respiratory variation in transvalvular flow velocities and left ventricular ejection and isovolumic relaxation times were markedly increased compared with values in normal subjects and those obtained after pericardiocentesis. In the 14 asymptomatic patients with pericardial effusion but without overt tamponade, 7 showed respiratory variation in flow velocity similar to that of normal subjects. The other seven patients demonstrated increased respiratory change compared with normal, but less than that in the patients with tamponade. Clinical and hemodynamic data in this latter group suggest that these patients may represent an intermediate stage of pericardial effusion with an element of hemodynamic compromise.

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Two-dimensional echocardiography is a sensitive technique for recognizing pericardial effusion. Although several studies (1–4) have described M-mode and two-dimensional echocardiographic findings suggestive of cardiac tamponade, the assessment of hemodynamic compromise remains difficult (5). Recently, preliminary reports (6–9) using Doppler ultrasound have described an exaggerated respiratory variation in transvalvular blood flow velocities in patients with cardiac tamponade. The purpose of this study was to determine whether the increased respiratory changes reported in patients with cardiac tamponade are consistently present, and whether these differ significantly from respiratory changes in patients with pericardial effusion but without tamponade.

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Methods

Study patients. Twenty-one patients with pericardial effusion, aged 22 to 77 years (mean 49), underwent complete M-mode, two-dimensional and Doppler echocardiographic examination. The cause of the effusion was malignancy in five patients, postcardiac surgery in six, postmyocardial infarction in one, postelectrophysiologic study in one, postcardiac transplantation in seven and chronic renal failure in one. Seven patients were judged by clinical criteria to have severe life-threatening cardiac tamponade and underwent emergency pericardiocentesis. Of the remaining 14 patients, 5 underwent elective pericardiocentesis within 12 h of echocardiography, 3 for therapeutic and 2 for diagnostic reasons. The seven patients who underwent emergency pericardiocentesis for severe cardiac tamponade and the five other patients who underwent elective pericardiocentesis had repeat Doppler ultrasound examination immediately after the procedure. Twenty healthy adult volunteers aged 26 to 60 years (mean 45) also underwent complete echocardiographic examination and served as a control group.

Echocardiography. Two-dimensional and M-mode echocardiograms were obtained using a Hewlett-Packard model 77020AC imaging system with a 2.5 or 3.5 MHz transducer.

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Wall thickness, chamber sizes and percent fractional shortening were calculated in standard fashion from parasternal (10) and apical views and the recordings were analyzed for the presence of diastolic right atrial or ventricular collapse (1–4). Doppler ultrasound recordings were made using an Irex Exemplar ultrasonograph with a transducer frequency of 2.5 MHz for imaging and 2.0 for Doppler tracings. Doppler ultrasound recordings were made with simultaneous electrocardiogram, phonocardiogram and respiration recording at paper speeds of 50 mm/s for velocity analysis, and at 100 mm/s for the measurement of isovolumic relaxation and ejection times. Onset of "inspiration" and "expiration" was referred to the signal from a nasal thermistor recording; the approximate timing of thermistor response having been previously determined by recording respiration simultaneously with pulmonary wedge pressure.

Blood flow velocities across all four cardiac valves were recorded with pulsed wave Doppler ultrasound during both normal respiration and 5 to 10 s of end-tidal volume apnea. Mitral and tricuspid flow velocities were obtained with the sample volume placed between the leaflets to record maximal velocity of anterograde flow. All variables were measured and averaged for three beats of apnea, and three first inspiratory and expiratory beats on consecutive respiratory cycles. The variables measured were the left ventricular isovolumic relaxation time (interval from aortic closure on the phonocardiogram to the start of mitral flow), left ventricular ejection time, aortic and pulmonary artery flow velocities and integrals and peak velocity of mitral and tricuspid flow in both early diastole and at atrial contraction and their total diastolic velocity integrals. Because of individual variation in flow velocities, the percent change of expiratory compared with inspiratory values was also calculated for all variables in each subject. Figure 1 illustrates the measurement of mitral flow velocities and left ventricular isovolumic relaxation time from a normal subject and shows the respiratory timing of these measurements.

Superior vena cava pulsed wave Doppler ultrasound recordings were obtained from a supraclavicular window at a sampling depth of 5.5 to 7.0 cm. Hepatic vein recordings were obtained using a subcostal view with the sample volume in the right superior hepatic vein 1.0 to 2.0 cm proximal to its junction with the inferior vena cava. Venous flow velocity recordings were analyzed for peak velocity and duration of forward and reverse flow during systole and diastole; these intervals were defined by tricuspid opening and closure on tricuspid flow velocity recordings. Changes in these velocities and flow duration with inspiration and at the onset of expiration were also noted.

Patient groups. The subjects were initially classified into four groups: 1) patients with severe cardiac tamponade requiring emergency pericardiocentesis, 2) the same patients after pericardiocentesis, 3) patients with effusion but without marked hemodynamic compromise, and 4) normal adults. Of the 14 patients with effusion but without marked hemodynamic compromise, 7 showed respiratory variation in transvalvular flow velocities as well as in left ventricular isovolumic relaxation and ejection intervals that were similar to those in normal subjects whereas the other 7 had increased variation that was intermediate between that of patients with severe tamponade and normal subjects. To assess the clinical importance of these findings, these patients with effusion were classified into two groups: one with (effusion-variation) (n = 8) and one without (effusion-no variation) (n = 7) increased respiratory variation in ejection times and flow velocities; clinical and hemodynamic findings were examined separately. After pericardiocentesis, one patient in the tamponade group continued to have increased pericardial pressure and some increase in respiratory variation in flow velocities; postprocedure Doppler ultrasound variables were included in the effusion-variation group for analysis.

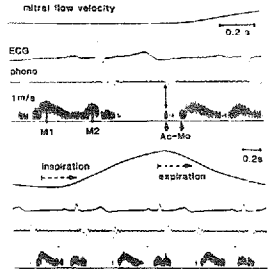

Figure 1. Normal mitral flow velocity patterns. Upper panel shows a pulsed wave mitral flow velocity recording together with respiration (top line), electrocardiogram (ECG) and phonocardiogram (phono) with measurement of peak velocity in early diastole (M1), velocity at atrial contraction (M2) and the interval from aortic valve closure to mitral valve opening (Ac-Mo) (left ventricular isovolumic relaxation time). Lower panel shows mitral flow velocity recorded together with respiration, ECG and phonocardiogram. Doppler ultrasound variables were measured during apnea and for the first beat after the onset of inspiration and expiration as shown. Inspiration was assumed to begin 300 to 400 ms before the upward deflection registered by the nasal thermistor.

Hemodynamics. All seven patients in the tamponade group and four of the five other patients who underwent pericardiocentesis had right heart and pericardial pressures measured before and after the procedure. The remaining patient had only pericardial pressure measured. In addition, three cardiac transplant patients with effusion had right heart pressures measured within 12 h of echocardiographic study at the time of cardiac biopsy for routine rejection surveil-

Table 1. Left Ventricular Isovolumic Relaxation and Ejection Times and Peak Velocities of Mitral, Tricuspid, Aortic and Pulmonary Flow During Apnea, Inspiration and Expiration

Patient Group	Heart Rate (beats/min)	Phase of Resp	IVRT (ms)	M_1 (cm/s)	M_2 (cm/s)	T_1 (cm/s)	T_2 (cm/s)	LVET (ms)	Ao (cm/s)	PA (cm/s)
Normal	65 ± 11*	Apnea	69 ± 12	83 ± 18	61 ± 14	56 ± 11	40 ± 5	300 ± 19	113 ± 8	87 ± 12
(n = 20)		Exp	72 ± 14	85 ± 18	59 ± 17	56 ± 9	39 ± 6	305† ± 20	113 ± 9	86 ± 12
		Insp	74 ± 15	82 ± 17	58 ± 16	64 ± 10	44 ± 6	295 ± 20	109 ± 9	90 ± 13
Tamponade	111 ± 18	Apnea	84 ± 8	59 ± 14	60 ± 21	35 ± 12‡	48 ± 7	199 ± 29§	95 ± 21	86 ± 15
(n = 7)		Exp	64 ± 20	68 ± 19	64 ± 23	30 ± 9‡	39 ± 11	212 ± 30§	107 ± 26	75 ± 21
		Insp	117 ± 39†	39 ± 12‡	49 ± 21	60 ± 6	61 ± 16	168 ± 28§	80 ± 22	101 ± 13
Post-tap	101 ± 10	Apnea	71 ± 8	75 ± 11	66 ± 14	52 ± 11	45 ± 6	229 ± 30‡	114 ± 29	77 ± 18
(n = 6)		Exp	67 ± 16	77 ± 13	67 ± 14	50 ± 8	43 ± 4	225 ± 29‡	107 ± 23	86 ± 19
		Insp	69 ± 15	71 ± 12‖	65 ± 14	60 ± 9	54 ± 8	214 ± 33¶	103 ± 22	98 ± 12
Effusion-variation	95 ± 15	Apnea	94 ± 17	59 ± 10**	64 ± 25	39 ± 10	38 ± 14	234 ± 23‡	85 ± 19	68 ± 8
(n = 8)		Exp	77 ± 19	79 ± 25	73 ± 23	35 ± 13‡	39 ± 14	234 ± 26‡	110 ± 30	58 ± 14
		Insp	102 ± 29	55 ± 23	64 ± 24	60 ± 19	49 ± 12	212 ± 26**	93 ± 27	87 ± 22
Effusion-no variation	87 ± 18	Apnea	63 ± 21‖	96 ± 33	57 ± 38	46 ± 9	41 ± 12	273 ± 43	155 ± 87	97 ± 31
(n = 7)		Exp	67 ± 25	98 ± 35	58 ± 33	48 ± 9	39 ± 11	275 ± 42	153 ± 79	98 ± 30
		Insp	69 ± 24	93 ± 33	56 ± 33	61 ± 11	48 ± 18	268 ± 40	149 ± 78	104 ± 30

*p < 0.05 vs. all other groups; †p < 0.05 tamponade vs. normal, post-tap and effusion-no variation; ‡p < 0.05 vs. normal only; §p < 0.05 tamponade vs. normal and effusion-no variation; ‖p < 0.05 effusion-variation vs. effusion-no variation; ¶p < 0.05 post-tap vs. normal and effusion-no variation; **p < 0.05 effusion-variation vs. normal and effusion-no variation. Ao = aortic flow velocity; Effusion-variation = patients with increased respiratory variation in flow velocities and time intervals; Effusion-no variation = patients without increased respiratory variation in flow velocities and time intervals; Exp = expiration; Insp = inspiration; IVRT = left ventricular isovolumic relaxation time; LVET = left ventricular ejection time; M_1,T_1 = mitral and tricuspid flow velocities in early diastole; M_2,T_2 = mitral and tricuspid flow velocities at atrial contraction; n = number of patients; PA = pulmonary artery flow velocity; Post-tap = after pericardiocentesis; Resp = respiration. Values are mean ± 1 standard deviation.

lance. Cardiac and pericardial pressures were measured using fluid-filled catheters attached to manifold micromanometers (Gould P-50).

Statistical analysis. All values are expressed as mean ± 1 standard deviation. Differences between group means for Doppler ultrasound variables were assessed using an analysis of variance. When the F statistic was significant, Scheffe's test was used to determine which group differed from the others. In the patients with cardiac tamponade, pre- and postpericardiocentesis pressures were assessed using a paired t test.

Results

Left ventricular isovolumic relaxation time and mitral and tricuspid flow velocities (Tables 1 and 2). Patients in the tamponade group had an inspiratory increase in isovolumic relaxation time of 85 ± 14%, a decrease in early mitral flow

Table 2. Percent Change From First Beat of Expiration to First Beat of Inspiration in Left Ventricular Isovolumic Relaxation and Ejection Times and Peak Velocities of Mitral, Tricuspid, Aortic and Pulmonary Flow

Patient Group	IVRT (ms)	M_1 (cm/s)	M_2 (cm/s)	T_1 (cm/s)	T_2 (cm/s)	LVET (ms)	Ao (cm/s)	PA (cm/s)
Normal (n = 20)	2 ± 3	−4 ± 4	−2 ± 6	14 ± 9	11 ± 10	−3 ± 3	−4 ± 2	5 ± 4
Tamponade (n = 7)	85 ± 14*	−43 ± 9*	−25 ± 12*	85 ± 53†	58 ± 25*	−21 ± 3*	−26 ± 6*	40 ± 25‡
Post-tap (n = 6)	4 ± 4	−8 ± 9	−4 ± 4	22 ± 15	25 ± 12	−5 ± 3	−4 ± 4	13 ± 14
Effusion-variation (n = 8)	32 ± 11§	−31 ± 9§	−12 ± 12	74 ± 42‖	28 ± 20	−9 ± 3¶	−17 ± 9§	49 ± 38§
Effusion-no variation (n = 7)	3 ± 5	−5 ± 4	−5 ± 7	32 ± 17	21 ± 13	−2 ± 2	−4 ± 3	6 ± 7

*p < 0.05 vs. all other groups; †p < 0.05 tamponade vs. normal, post-tap and effusion-no variation; ‡p < 0.05 tamponade vs. normal and effusion-no variation; §p < 0.05 effusion-variation vs. effusion-no variation; ‖p < 0.05 vs. normals only; ¶p < 0.05 effusion-variation vs. normal and effusion-no variation. Abbreviations as in Table 1. Values are mean ± one standard deviation.

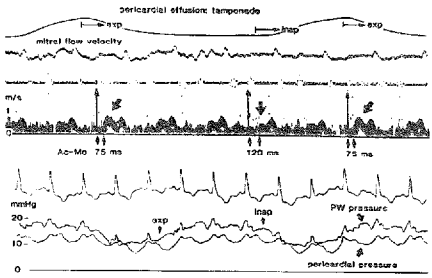

Figure 2. Patient with severe cardiac tamponade. Upper panel shows a pulsed wave mitral flow velocity recording together with simultaneous respiration, electrocardiogram (ECG) and phonocardiogram in a patient with cardiac tamponade. Note the decrease in early mitral flow velocity (**second large arrow**) on the *first* beat of inspiration (insp) compared with the preceding beat recorded during apnea and the increase on the *first* beat of expiration (exp) (**first and third large arrows**). Also note the marked difference in the left ventricular isovolumic relaxation time (Ac-Mo interval) associated with these beats as shown by the **smaller arrows**. In the lower **panel** phasic pulmonary wedge (PW) and pericardial pressures are shown with the ECG in the same patient but are not simultaneous with the flow velocity recordings. The respiratory variation in pulmonary wedge pressure is larger than that in pericardial pressure. This results in a reduced pulmonary wedge-pericardial pressure gradient with inspiration and an increased gradient with expiration.

velocity of 43 ± 9% and a decrease in mitral flow velocity at atrial contraction of 25 ± 12% compared with that at expiration. In contrast, the mean change in these values after pericardiocentesis and in normal subjects was <10%. At the same time that mitral flow velocity was decreasing, the patients in the tamponade group had an inspiratory increase in early tricuspid flow velocity of 85 ± 53% and an increase in velocity at atrial contraction of 58 ± 25% whereas, after pericardiocentesis, in the same patients and in normal subjects, the mean change in these values was <25%.

In all patients in the tamponade group, the timing and pattern of the maximal respiratory variation in flow velocities and left ventricular isovolumic relaxation time was characteristic (Fig. 2). In all patients the largest decrease in early mitral flow velocity and largest increase in isovolumic relaxation time compared with the other beats occurred on the *first* beat after the onset of inspiration when referenced to the nasal thermistor recording. Conversely, opposite changes were seen on the first beat after the onset of expiration. Tricuspid flow velocity showed reciprocal changes with a marked increase on the first beat after the onset of inspiration and a decrease on the first beat after the onset of expiration compared with other beats. After pericardiocentesis and in normal subjects, the respiratory variation in mitral flow velocities and isovolumic relaxation time was minimal (Table 2) and, although tricuspid flow velocity increased with inspiration, the percent increase compared with expiration was smaller, an increased velocity was usually seen on all inspiratory beats and there was no decrease in velocity at the onset of expiration compared with apnea (Fig. 3).

Patients in the effusion-variation group had respiratory changes in the isovolumic relaxation time and early diastolic mitral and tricuspid flow velocity that were intermediate between those of patients in the tamponade group and the normal group (Tables 1 and 2). In contrast, in the effusion-no variation group, the respiratory changes in isovolumic relaxation time and mitral and tricuspid flow velocities were similar to normal values.

Table 3 shows the respiratory variation in mitral and tricuspid flow velocity integrals and the percent change in these values from expiration to inspiration in all patient groups. In general, the changes in flow velocity integrals paralleled the changes seen in flow velocity with the largest respiratory variation in patients in the tamponade group. After pericardiocentesis and in the effusion-no variation group, there was much less respiratory variation whereas intermediate values were seen in the effusion-variation group.

Left ventricular ejection time and aortic and pulmonary blood flow velocity (Tables 1 and 2). In patients in the tamponade group, the mean decrease in left ventricular ejection time of 21 ± 3% and aortic flow velocity of 26 ± 6% from expiration to inspiration was significantly larger than the <5% mean change seen after pericardiocentesis, in patients in the effusion-no variation group and in normal subjects. The effusion-variation group had percent changes that were intermediate in value. Mean inspiratory pulmonary flow velocity increased 40 ± 25% compared with expiratory values in the patients in the tamponade group; this change decreased to 13 ± 14% after pericardiocentesis. Patients in the effusion-variation group had an inspiratory increase in pulmonary velocity that was similar to that of patients in the tamponade group, whereas normal subjects and patients in the effusion-no variation group showed significantly less increase. The inspiratory decrease in aortic flow velocity observed in the patients in the tamponade group occurred on the second beat of inspiration. After pericardiocentesis, aortic flow velocity was increased and the inspiratory decrease in velocity was markedly less.

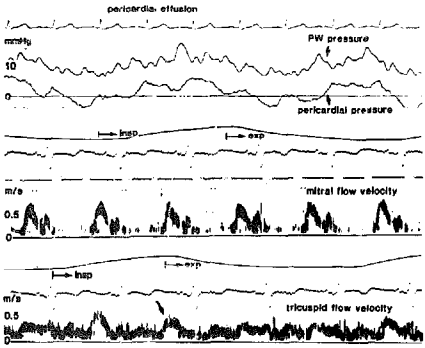

Figure 3. Pulsed wave mitral and tricuspid flow velocity recordings and pericardial and pulmonary wedge pressure in a patient with a large pericardial effusion that is without hemodynamic effect. In the **middle panel**, note the normal minimal respiratory (insp) variation in the mitral flow velocity recording. In the **lower panel**, early tricuspid flow velocity is seen to increase normally with inspiration and does not show a decrease in velocity on the first expiratory (exp) beat (**arrow**). In the **upper panel**, pericardial and pulmonary wedge (PW) pressures are within normal limits and "track" each other during the respiratory cycle in both phase and amplitude.

Superior vena cava and hepatic vein flow velocity recordings. In all normal subjects, systolic velocity in the venous recordings was greater than diastolic velocity during all phases of respiration, and a small flow reversal at atrial contraction was usually seen. In the majority of subjects, both systolic and diastolic velocities increased with inspiration, although in a few normal subjects the increase was minimal or a slight decrease was observed, usually on the second or third beat of inspiration. At the onset of expiration there was no decrease in diastolic velocity compared with that during apnea.

Six of seven patients in the cardiac tamponade group had superior vena cava recordings adequate for analysis. During apnea, five patients showed a marked predominance of

Table 3. Mitral, Tricuspid, Aortic and Pulmonary Flow Velocity Integrals During Apnea, Inspiration and Expiration and the Percent Change From Expiration to Inspiration

Patient Group	Phase of Resp	M_1 (cm)	M_2 (cm)	M_1+M_2 (cm)	T_1 (cm)	T_2 (cm)	T_1+T_2 (cm)	Ao (cm)	PA (cm)
Tamponade	Apnea	5.6 ± 1.3	5.6 ± 2.3	10.7 ± 1.8	4.2 ± 2.7	4.1 ± 1.5	8.2 ± 1.6	14.7 ± 6.1	12.3 ± 3.2
(n = 7)	Exp	8.0 ± 2.2	6.2 ± 2.8	13.3 ± 2.6	3.1 ± 2.3	3.6 ± 1.5	6.7 ± 0.7	16.3 ± 6.3	10.6 ± 3.3
	Insp	3.8 ± 1.0	4.8 ± 2.6	8.1 ± 2.0	8.1 ± 3.7	7.3 ± 2.8	14.1 ± 3.0	11.1 ± 5.8	14.9 ± 3.2
	Exp–Insp	−52 ± 10*	−28 ± 22	39 ± 8*	305 ± 36*	113 ± 38*	113 ± 48*	−35 ± 11*	45 ± 27
Post-tap	Apnea	7.6 ± 0.8	6.1 ± 2.0	13.5 ± 1.3	5.3 ± 0.5	3.4 ± 1.0	9.2 ± 1.3	15.5 ± 1.8	11.8 ± 1.4
(n = 6)	Exp	7.9 ± 0.5	5.9 ± 1.6	14.1 ± 1.6	5.2 ± 0.9	3.6 ± 0.4	9.1 ± 1.1	16.0 ± 1.9	11.9 ± 1.7
	Insp	7.4 ± 0.7	5.5 ± 2.1	12.7 ± 1.9	7.7 ± 0.4	4.7 ± 1.0	12.2 ± 1.3	14.0 ± 2.0	14.4 ± 3.8
	Exp–Insp	−7 ± 6	−11 ± 8	−10 ± 6	50 ± 32	25 ± 17	35 ± 20	−12 ± 5	6 ± 7
Effusion-variation	Apnea	6.4 ± 2.7	5.4 ± 1.5	11.3 ± 3.2	6.5 ± 3.8	2.9 ± 1.3	7.9 ± 2.0	14.4 ± 5.3	10.3 ± 1.7
(n = 8)	Exp	7.5 ± 3.1	5.5 ± 1.7	12.9 ± 3.9	5.0 ± 4.3	2.9 ± 1.5	6.5 ± 2.7	15.8 ± 5.8	8.0 ± 2.0
	Insp	4.6 ± 2.4	5.0 ± 1.4	9.2 ± 3.2	8.6 ± 5.1	4.9 ± 2.8	12.2 ± 5.1	11.7 ± 5.2	15.1 ± 4.3
	Exp–Insp	−43 ± 12†	0 ± 17	−29 ± 9†	200 ± 297	59 ± 28	91 ± 29†	−27 ± 12†	75 ± 74
Effusion-no variation	Apnea	15.0 ± 3.7	5.5 ± 2.7	18.8 ± 6.8	9.2 ± 1.6	3.6 ± 1.9	12.1 ± 2.9	27.4 ± 14.9	17.8 ± 6.7
(n = 7)	Exp	15.5 ± 3.9	5.7 ± 3.0	19.5 ± 7.5	8.9 ± 1.7	3.5 ± 1.9	12.2 ± 3.0	28.4 ± 16.4	17.9 ± 6.6
	Insp	14.6 ± 4.0	5.5 ± 2.9	18.5 ± 6.7	10.8 ± 0.9	4.5 ± 2.8	15.4 ± 3.4	26.2 ± 13.7	19.9 ± 7.4
	Exp–Insp	−6 ± 9	−5 ± 6	−4 ± 7	24 ± 18	22 ± 15	27 ± 10	−7 ± 7	11 ± 6

*$p < 0.05$ tamponade vs. post-tap and effusion-no variation; †$p < 0.05$ effusion-variation vs. post-tap and effusion-no variation patients. Ao = aortic flow velocity integral; Exp-Insp = percentage change from the first beat of expiration compared with the first beat of inspiration; M_1,T_1 = mitral and tricuspid flow velocity integrals in early diastole; M_2,T_2 = mitral and tricuspid flow velocity integrals at atrial contraction; M_1+M_2,T_1+T_2 = total mitral and tricuspid flow velocity integrals; PA = pulmonary artery flow velocity integral. Other abbreviations as in Table 1. Values are mean ± one standard deviation. Statistics are given *only* for Exp-Insp percentage change.

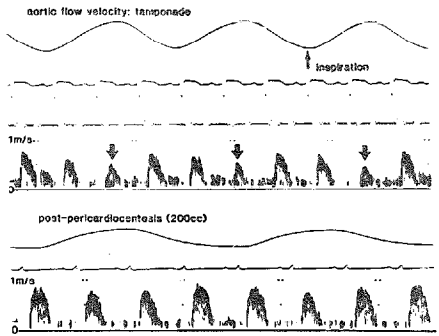

Figure 4. Aortic flow velocity recorded from the suprasternal notch before and after pericardiocentesis in a patient with cardiac tamponade. In the upper panel, before pericardiocentesis, there is a marked decrease in peak flow velocity and flow velocity duration (left ventricular ejection time) on the second beat following the onset of inspiration (large arrows). In the lower panel, after removal of 290 ml of pericardial fluid, aortic flow velocity is increased and the inspiratory reduction in flow velocity is less.

systolic forward flow with a lower velocity and shorter duration of diastolic filling that was followed by flow reversal in late diastole or at atrial contraction (Fig. 4). The remaining patient had a larger diastolic than systolic velocity. With the first beat of inspiration, all patients showed only minimal increases in systolic and diastolic flow velocities that were less than the inspiratory increases observed in most normal subjects. On subsequent beats of inspiration variable patterns were seen; some patients continued to show small increases in velocity compared with that during apnea, although most showed decreases in velocity. On the first beat after the onset of expiration, all patients in the tamponade group showed a decrease, disappearance or reversal in diastolic and sometimes systolic flow velocity, as compared with recordings during apnea. This decrease corresponded in time to the marked decrease seen in early diastolic tricuspid flow velocity at the onset of expiration.

After pericardiocentesis, all patients showed increased forward flow velocities in the superior vena cava during apnea. In the six patients who had a larger systolic than diastolic flow velocity before pericardiocentesis, all increased their diastolic flow velocity to more than their systolic velocity (Fig. 5). The remaining patient showed the opposite change. With inspiration, six of the seven patients increased their forward flow velocities, usually to a much larger extent as compared with before the procedure. The remaining patient, who was hypovolemic and had a mean right atrial pressure of 2 mm Hg after fluid removal, showed an inspiratory decrease in velocity. After pericardiocentesis, the decrease in diastolic velocity at the onset of expiration was no longer seen in any patient.

In superior vena cava recordings from patients with effusion but without severe tamponade, no consistent patterns in the relation between systolic and diastolic velocities were seen. However, with inspiration, all patients had a greater increase in forward flow velocities than that of the patients with tamponade, and none had a decrease or disappearance in diastolic velocity at the onset of expiration compared with apnea.

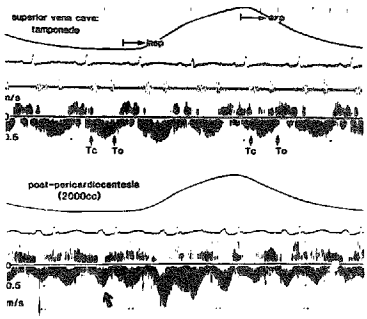

Figure 5. Superior vena cava flow velocity recordings before and after pericardiocentesis in a patient with cardiac tamponade. Flow below the zero reference line is toward the heart. In the upper panel, note that during tamponade there is a predominance of systolic (Tc–To intervals) forward flow velocity as compared with diastolic velocity and a relative lack of increase in velocity with inspiration. In the lower panel, after pericardiocentesis, diastolic flow velocity (note ECG and arrow) has increased and the relatively larger increase in both systolic and diastolic velocities with inspiration is apparent. insp = onset of inspiration; exp = onset of expiration; Tc = tricuspid closure; To = tricuspid opening.

Hepatic vein flow velocity recordings adequate for analysis were obtained in 6 of 20 normal subjects. Qualitatively, the flow velocity contours were similar to those seen in the superior vena cava but peak velocities were usually lower; all patients had increases in forward flow velocities throughout inspiration, flow reversals at atrial contraction were more prominent, and flow reversals at end systole were sometimes observed.

Four patients in the tamponade group had adequate hepatic vein recordings. The flow velocity contours were also similar to those from the superior vena cava in each patients. However, with inspiration, all four patients showed larger percent increases in velocity in the hepatic vein as compared with the superior vena cava, and the increases continued throughout inspiration. Conversely, more prominent reversals were seen at the onset of expiration.

Two-dimensional echocardiographic findings, hemodynamics and clinical follow-up. Of the seven patients in the tamponade group, three had diastolic right atrial and right ventricular collapse, one had right atrial collapse only and three had neither finding. Of the eight patients in the effusion-variation group, two had both right atrial and right ventricular diastolic collapse and six had neither finding. After pericardiocentesis, the diastolic right heart collapse present disappeared in all cases. In the seven patients in the effusion-no variation group, no diastolic right atrial or ventricular collapse was observed.

Table 4 shows mean values for heart rate, systolic blood pressure, pulsus paradoxus and estimated central venous pressure in all patient groups and pericardial and right heart pressures in patients who had a pericardiocentesis or right heart catheterization. In the patients with tamponade, the mean pulsus paradoxus was 29 ± 5 mm Hg and all had equalization (≤2 mm Hg) of right ventricular end-diastolic and mean pericardial, right atrial and pulmonary wedge pressures. In addition, all of these patients had less respiratory variation in pericardial pressure (mean 7 ± 1 mm Hg) than in pulmonary wedge pressure (mean 17 ± 2 mm Hg) (Fig. 2). After pericardiocentesis, respiratory variation in pericardial pressure increased in all patients (mean 12 ± 4 mm Hg). In five of the seven patients in the tamponade group, the mean pericardial pressure was <4 mm Hg after pericardiocentesis. In the other two patients, pericardial pressure remained elevated; one patient had a mean right atrial pressure of 12 mm Hg and pericardial pressure of 7 mm Hg and the other had a mean right atrial pressure of 16 mm Hg and pericardial pressure of 8 mm Hg. The former patient continued to have some increase in respiratory variation in flow velocities after pericardiocentesis. Two patients in the tamponade group died from their malignancy during their hospitalization; the others were discharged home.

In the seven patients in the effusion-variation group, the mean pulsus paradoxus was 13 ± 6 mm Hg. In the three patients in this group who had a pericardiocentesis, the mean pericardial pressures were 4, 7 and 11 mm Hg, respectively. None of these patients had diastolic equalization of pressures. All patients in the group were discharged home from the hospital.

In the seven patients in the effusion-no variation group, the mean pulsus paradoxus was 6 ± 3 mm Hg. In two patients who underwent diagnostic pericardiocentesis, the mean pericardial pressure was 0 and 1 mm Hg, respectively. The respiratory variation in pericardial and pulmonary wedge pressure in these two patients was approximately equal. Three additional patients, all cardiac transplant recipients, had right heart catheterization in association with cardiac biopsy for rejection surveillance. None of these patients had elevation or equalization of diastolic pressures. All patients in the group were discharged home from the hospital.

Discussion

This study confirms that, compared with normal subjects, patients with pulsus paradoxus and severe cardiac tamponade have a marked increase in respiratory variation in transvalvular flow velocities, flow velocity integrals and left ventricular ejection and isovolumic relaxation times. In addition, some patients with pericardial effusion but without overt hemodynamic compromise also had increased respiratory variation in these variables. After pericardiocentesis and normalization of pericardial pressure, the increased respiratory variation disappeared.

Correlation of Doppler echocardiographic and hemodynamic findings. In all patients with severe tamponade, the marked respiratory variation in transvalvular flow velocities was associated with elevation and diastolic equilibration of cardiac and pericardial pressures. In the patients in the effusion-variation group, the increased pericardial and diastolic pressures, which decreased after pericardiocentesis, suggest that they also had an element of hemodynamic compromise. Compared with normal subjects, these patients had increased respiratory variation in both left ventricular isovolumic and ejection times and in *early* mitral and tricuspid flow velocity. The lack of respiratory variation in velocity at atrial contraction compared with the patients with tamponade probably reflects the less severe hemodynamic compromise and a better ability to maintain ventricular filling with atrial systole despite an increase in pericardial pressure. In patients whose pericardial pressure decreased to normal after pericardiocentesis, the increased respiratory variation in intervals of flow velocities disappeared.

Mechanism of increased respiratory changes in tamponade. Although the mechanism of increased respiratory changes in ventricular filling and ejection in patients in the tamponade and effusion-variation groups is unknown, our data support theories implicating a changing relation between intracardiac diastolic and intrathoracic pressures with respiration as a key element (11–13). In this study, the tamponade group demonstrated less respiratory variation in pericardial (mean

Table 4. Heart Rate, Systolic Blood Pressure, Pulsus Paradoxus, Estimated Central Venous Pressure and Hemodynamic Data in 21 Patients With Pericardial Effusion

	Tamponade n = 7	Post-Tap n = 6	Effusion-Variation (n)	Effusion-No Variation (n)
Heart rate (beats/min)	111 ± 18	101 ± 10	95 ± 15 (8)	87 ± 18 (7)
Systolic blood pressure (mm Hg)	118 ± 23	130 ± 5	122 ± 23 (8)	150 ± 37 (7)
Pulsus paradoxus (mm Hg)	20 ± 5*	7 ± 1	13 ± 6 (8)	6 ± 3 (7)
Central venous pressure (mm Hg)	15 ± 6	7 ± 5	9 ± 3 (8)	7 ± 2 (8)
Mean right atrial pressure (mm Hg)	17 ± 6*	7 ± 5	11 ± 4 (4)	8 ± 1 (4)
Pulmonary artery systolic pressure (mm Hg)	35 ± 10	33 ± 10	30 ± 4 (4)	35 ± 7 (4)
Mean pulmonary wedge pressure (mm Hg)	15 ± 5	11 ± 6	16 ± 7 (4)	15 ± 3 (4)
Mean pericardial pressure (mm Hg)	15 ± 6*	3 ± 3	7 ± 4 (4)	0 ± 1 (2)
Maximal change in pericardial pressure with respiration (mm Hg)	7 ± 1*	12 ± 4	9 ± 3 (4)	9 ± 4 (2)
Maximal change in pulmonary wedge pressure with respiration (mm Hg)	17 ± 2	16 ± 4	16 ± 5 (4)	13 ± 2 (2)
Difference in maximal change between pulmonary wedge and pericardial pressures (mm Hg)	11 ± 2*	4 ± 1	7 ± 0 (4)	1 (1)

*$p < 0.05$ tamponade vs. post-tap. Abbreviations as in Table 1. Numbers in parentheses = number of patients in each category. Values are mean ± 1 standard deviation. Statistical analysis includes only tamponade and post-tap groups.

7 ± 1 mm Hg) than in pulmonary wedge pressure (mean 17 ± 2 mm Hg) (Fig. 2 and 6). This resulted in a constantly varying difference between the two pressures throughout the respiratory cycle. Assuming that the pericardial pressure and pressure contour in diastole approximate those of the left ventricle in severe cardiac tamponade (11–13), inspiration would result in a larger decrease in pulmonary wedge pressure than in left ventricular pressure. A reduction in the pulmonary venous to left ventricular diastolic pressure gradient with inspiration would result in a later mitral valve opening, longer isovolumic relaxation time and decreased early mitral flow velocity compared with findings at expiration or during apnea. Reddy (12) proposed that in cardiac tamponade the maximal and minimal pressure differences between the pulmonary veins and left ventricle are largest at the onset of inspiration and expiration because rapid equilibration of venous, ventricular and pericardial pressures occurs on subsequent beats. However, simultaneous pressure recordings in two patients in the tamponade group appeared also to demonstrate a slight respiratory phase delay in pericardial as compared with pulmonary wedge pressure. With either mechanism, the largest variation in mitral and tricuspid flow velocity in early diastole would occur, and was consistently observed in the patients with tamponade, on the *first* beat of thermistor-indicated inspiration and expiration (Fig. 2 and 6).

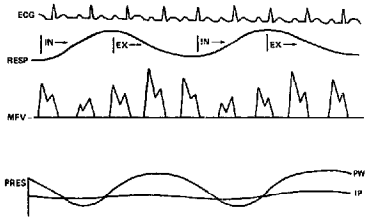

Figure 6. Schematic diagram of the relation between mitral flow velocity and pulmonary wedge and pericardial pressures during the respiratory cycle constructed from data in one patient with severe cardiac tamponade. In the **upper panel** are the electrocardiogram (ECG), respiratory phase as determined by a nasal thermistor (RESP) and the mitral flow velocity (MFV) tracings. Onset of inspiration (IN) and expiration (EX) for a thermistor like the one used in this study are marked. In the **lower panel**, simultaneous pulmonary wedge (PW) and intrapericardial (IP) pressure (PRES) are depicted. With inspiration, pulmonary wedge pressure decreases more than pericardial pressure with a resultant reduced pressure gradient from the pulmonary venous circulation to the left ventricle (as approximated by pericardial pressure). This results in a marked reduction in peak early mitral flow velocity as shown. After the onset of expiration, the opposite changes occur and the larger pressure gradient results in an increased peak early mitral flow velocity (see text for discussion).

Relation to pulsus paradoxus. An inspiratory decrease in the normal pressure gradient from the pulmonary veins to the left ventricle in cardiac tamponade was an early observation (14), which has subsequently been supported by study in animals (15) and later described in other patients with tamponade (11,13,16,17). In an experimental study investigating pulsus paradoxus in cardiac tamponade, Shabetai et al. (18) presented evidence that an increase in right heart filling with inspiration is the key factor that prevents a normal inspiratory decrease in pericardial pressure. However, whether an inspiratory increase in right heart filling or

the inspiratory decrease in left heart inflow gradient is the initiating mechanism in the generation of pulsus paradoxus remains unresolved. The immediate inspiratory decrease in left heart filling after a period of apnea seen in the patients in this study is inconsistent with theories linking pulsus paradoxus with respiratory effects on right heart filling delayed by the transit through the pulmonary circulation.

In the patients in whom increased variation in flow velocities disappeared after pericardiocentesis, the respiratory amplitude and phase of pericardial and pulmonary wedge pressure became approximately equal. In normal subjects and in the effusion-no variation group, minimal changes were seen in the left ventricular isovolumic relaxation time with respiration. This suggests that the respiratory variation in diastolic left ventricular and pulmonary wedge pressures were approximately equal and also "tracked" each other in both phase and amplitude in these subjects.

The maximal decrease in left ventricular ejection time and aortic flow velocity in the patients with tamponade was seen on the second inspiratory beat (Fig. 4). This was the beat immediately after the lowest mitral velocity and demonstrates the close temporal relation between ventricular filling and ejection dynamics.

Central venous flow velocities. As previously reported (19,20), superior vena cava flow velocity contours reflect right atrial pressure contours and generally show a reciprocal relation between pressure and flow. In this study, six of seven patients with cardiac tamponade had a larger systolic flow velocity as compared with diastolic flow velocity (Fig. 5). After pericardiocentesis, in patients in the effusion-no variation group and in normal subjects the central venous flow velocities were usually biomodal, with more equal systolic and diastolic forward flow velocities. Systolic predominance of venous return in patients with tamponade is well recognized (21). The one patient in the tamponade group with larger diastolic than systolic forward flow velocity had prior cardiac radiation, suggesting that the physiology of venous return may reflect not only the presence of cardiac tamponade but also coexistent cardiac disease.

In the patients with tamponade, a characteristic decrease or loss of the diastolic venous flow velocity occurred shortly after the onset of expiration. This corresponded in time to the maximal decrease in tricuspid flow velocity and probably occurred as a result of impedance to right ventricular filling. Increased flow reversals in the superior vena cava and hepatic veins were also observed in most patients at the onset of expiration and are probably due to the same mechanism.

Comparison with other studies. In previous studies using M-mode and two-dimensional echocardiography, an exaggerated inspiratory decline in mitral valve area and left ventricular dimension, with reciprocal inspiratory expansion of the right ventricle, were reported in patients with cardiac tamponade (1,22,23). More recently, increased respiratory variation in transvalvular blood flow velocity and flow velocity intervals in patients with tamponade, which markedly diminished after pericardiocentesis, were reported (6–9). However, the brief description of methods and results in these preliminary reports prohibits a direct comparison with this study. Marked respiratory changes in central venous and transvalvular flow velocities with identical timing characteristics have also been reported preliminarily in patients with constrictive pericarditis (24,25).

Our study describes a group of patients with pericardial effusion who have respiratory variation in ejection time and transvalvular flow velocities that are intermediate between patients with severe tamponade and normal subjects. Although we are unaware of any previous Doppler ultrasound studies in similar patients, Wayne et al. (26) reported that some patients with effusion who did not have clinical signs of cardiac tamponade have abnormally increased inspiratory reductions in echocardiographic left ventricular dimensions that correlate directly with exaggerated respiratory changes in left ventricular ejection time. Spodick et al. (27) also reported increased respiratory variation in left ventricular ejection time in patients with effusion but without evidence of tamponade. These investigators hypothesized that the condition of these patients may represent an intermediate state between normal and overt tamponade, wherein the pericardial effusion is causing a mild hemodynamic effect. In this framework, cardiac tamponade is viewed as a continuum from effusion with minimal hemodynamic effect to effusion with life-threatening hemodynamic compromise.

Our study did not attempt to compared the sensitivity of two-dimensional (1–4,28) and Doppler echocardiographic findings suggestive of hemodynamic compromise in patients with pericardial effusion. However, all patients with diastolic right heart collapse had equalization or near equalization of diastolic pressures and underwent therapeutic pericardiocentesis. Three patients in the tamponade group did not have diastolic wall motion abnormalities but did have increased respiratory flow velocity variation. The reason for the absence of right heart collapse in these latter patients is unclear but possible causes are the etiology of the effusion, coexistent cardiac disease or the postcardiac surgery state (4,11,29,30).

Other conditions with increased respiratory flow velocity variation. Increased respiratory variation in both transvalvular flow velocity and left ventricular diameter has been reported in patients with chronic obstructive pulmonary disease (31). However, in these patients the lowest mitral flow velocity usually occurs later during inspiration, and tricuspid flow velocity does not usually fall below apnea values on expiration as it does in patients with tamponade. Patients with constrictive pericarditis may show respiratory flow velocity changes similar to those of patients with tamponade (22,23), and constrictive pericarditis might be difficult to distinguish if an effusion causing a hemodynamic

effect was also present. However, a predominantly unimodal systolic central venous flow velocity pattern would be expected only in tamponade and might provide a differential Doppler echocardiographic feature. Other conditions that may show increased respiratory variation in flow velocities include severe tricuspid regurgitation and right ventricular infarction. In these conditions the flow velocity variation with respiration resembles that seen in patients with obstructive pulmonary disease.

Study limitations. A limitation of this study was that a complete hemodynamic evaluation was not available in all patients. Therefore, separation of the patients without measured pressures into groups based on presence or lack of respiratory flow velocity and left ventricular ejection time variation may seem arbitrary. However, previous studies (11,26,27,32) have shown that normal subjects have little respiratory variation in left ventricular ejection time. By inference, patients with variation have altered ejection dynamics and pressures. The hemodynamic findings in the patients in the effusion-variation group who underwent pericardiocentesis support this conclusion. Conversely, it is unlikely that the patients in the effusion-variation group not undergoing pericardiocentesis had severe hemodynamic compromise because all were discharged uneventfully from the hospital without undergoing invasive procedures.

In this study, the patients with severe cardiac tamponade consistently showed the largest variation in tricuspid and mitral flow velocities on the *first* beat after the onset of inspiration and expiration as determined by nasal thermistor recording. However, because pulmonary wedge and intracardiac pressures were not recorded simultaneously with flow velocities, the precise relation between pressure and velocity changes could not be established; other types of respiratory monitors may show slightly different timing characteristics. The use of fluid-filled catheters may also introduce some delay and artifact into the pressure recordings. These issues require further investigation, and Figure 6 should be used only as a schematic diagram.

All the patients in this study with cardiac tamponade had pulsus paradoxus. The absence of pulsus paradoxus has been reported in patients with tamponade and coexistent cardiac abnormalities (11,29,30). Whether such patients, and others with unusual types of cardiac tamponade (such as localized compression by clot), would show respiratory flow velocity variation needs further investigation. Patients with effusion after cardiac surgery are another important group requiring further study. We have observed one such patient with tamponade who was on a ventilator and whose respiratory variation in mitral and tricuspid flow velocities was opposite in timing to that of spontaneously breathing patients. Similar findings were reported in an experimental animal model of tamponade (33).

Inadequate Doppler ultrasound recordings for analysis of respiratory variation may be seen in patients with rapid heart rates or first degree atrioventricular block whose atrial contraction comes so early after mitral valve opening that mitral flow is unimodal. In patients with arrhythmias, transvalvular flow velocities may vary independently of respiration, making interpretation difficult or impossible.

Doppler ultrasound methods. In most patients, the largest early mitral and tricuspid flow velocities were obtained with the sample volume between the leaflet tips. Positions far back in the orifice or beyond the leaflet tips in the ventricle may result in lower velocities being recorded. The movement of the Doppler sample volume relative to the heart with respiration should also be observed because excessive cardiac movement could result in spurious changes in flow velocity, although such changes would not be accompanied by respiratory alterations in left ventricular ejection and isovolumic relaxation times.

Clinical implications. This study suggests that Doppler ultrasound recordings, like two-dimensional echocardiography, may help identify which patients with pericardial effusion have an element of hemodynamic compromise. In patients with pulsus paradoxus, the presence of increased respiratory variation in left ventricular isovolumic relaxation and ejection times, as well as mitral and tricuspid flow velocity both in early diastole and at atrial contraction, suggests significant hemodynamic compromise regardless of the size of effusion or two-dimensional echographic findings. Patients with effusion and respiratory variation in mitral and tricuspid flow velocity in early diastole but not at atrial contraction probably also have an element of hemodynamic compromise, regardless of clinical findings, and should be watched carefully. The sensitivity of these Doppler ultrasound findings compared with two-dimensional echocardiographic findings of diastolic right heart collapse in identifying patients with, or at risk for, life-threatening hemodynamic compromise will require further investigation.

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