Echo-phonocardiographic Determination of Left Atrial and Left Ventricular Filling Pressures with and Without Mitral Stenosis

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SUMMARY In mitral stenosis (MS) the interval between the second sound and the opening snap (A2-OS) is known to shorten, while the interval between the onset of the QRS and the first sound (Q-M1) lengthens with smaller mitral valve orifice size and higher left atrial pressures. Because M1 and OS are temporally related to the C and E points on the mitral valve echogram, respectively, the ratio of Q-C to A2-E may relate to left atrial pressure in MS and to left ventricular filling pressures (LVFP) in the absence of MS. To test this hypothesis the Q-C/A2-E ratio was measured in 22 patients without MS from simultaneous mitral valve echogram, ECG and phonocardiogram at cardiac catheterization. An excellent correlation between Q-C/A2-E and left ventricular end-diastolic pressure (LVEDP) was observed (r = 0.93; SEE = 2.6 mm Hg; LVEDP range 5-28 mm Hg). The resulting regression equation: LVEDP = 21.6 (Q-C/A2-E) + 1.1, was prospectively evaluated in a second group of 32 patients without MS and with echo-phonocardiograms performed at left-heart catheterization (25 patients) or right-heart catheterization with flow-directed, balloon-tip catheters for measurement of mean pulmonary capillary wedge pressure (PCWP) (seven patients); LVFP ranged from 5-40 mm Hg. Calculated LVFP correlated well with measured LVFP (r = 0.81; SEE = 4 mm Hg). Ten of 11 patients (91%) with LVFP > 14 mm Hg were correctly separated from 19 of 21 patients (90%) with LVFP < 14 mm Hg. In 10 patients, LVFPs were acutely altered by either volume expansion or vasodilators and in all instances, calculated LVFP moved in the same direction as measured LVFP. In addition, the same equation was used to estimate mean PCWP in 22 patients with MS and eight with prosthetic mitral valves. Estimated PCWP correlated well with measured PCWP (r = 0.78; SEE = 4 mm Hg) and correctly separated 18 of 19 patients (95%) with PCWP > 18 mm Hg from nine of 11 patients (87%) with PCWP ≤ 18 mm Hg. Thus, the Q-C/A2-E ratio and left atrial pressure correlate closely. This relationship allows one to closely estimate LVFP in patients with various types of heart disease and to judge severity of MS noninvasively.

IN MITRAL STENOSIS, the interval between the aortic component of the second heart sound (A2) and the opening snap (OS) of the mitral valve frequently shortens, while the interval between the Q wave on the ECG and the mitral component (M1) of the first heart sound lengthens with increasing severity of stenosis.1-2 These changes occur as a result of elevation of left atrial pressures so that it takes less time for the left ventricular pressure declining during isovolumic relaxation to cross left atrial pressure and a longer time for the crossover to occur during isovolumic contraction. Studies relating heart sounds to the mitral valve motion by echocardiography have shown that OS and M1 occur at, or very close to, the time of the E point and the coaptation (or C point) of the mitral valve, respectively.3-5 Because both A2-OS (or A2-E) and Q-M1 (or Q-C) are heart-rate dependent,6 a ratio of one to the other might be expected to change less with heart rate than either interval alone and to relate to the extent of left atrial pressure increase.

The present study was, therefore, designed to explore the relation of the Q-C/A2-E ratio to left ventricular filling pressures in the absence of mitral stenosis, and to left atrial (or pulmonary capillary wedge [PCWP]) pressures in the presence of mitral stenosis.

Patients and Methods

An initial group of 22 patients without mitral stenosis was studied during diagnostic cardiac catheterization. Their ages ranged from 30–64 years. Twenty patients had ischemic heart disease confirmed angiographically and two had idiopathic congestive cardiomyopathy. Echo-phonocardiography was performed in all patients before pressure recordings. Echo-phonocardiographic and hemodynamic measurements were made separately by independent observers. The left ventricular end-diastolic pressure (LVEDP) was measured with fluid-filled catheters at the nadir of the A wave or, when a distinct A wave was not visible, at a point 40 msec after the onset of the electrocardiographic Q wave.

Figure 1 shows an example of the echo-phonocardiographic recordings. All tracings were taken at a paper speed of 100 mm/sec with 10-msec time lines. The ECG was recorded from the limb lead with the best appearing Q wave. The phonocardiogram was recorded from the area that best showed a distinct sec-

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ond heart sound, usually in the fourth intercostal space at the left sternal border, with frequency bands set at medium-frequency range. The mitral valve echo was recorded at the area of greatest amplitude of motion of both leaflets with clear visualization of the C point. The Q-C and A2-E intervals were measured over five to 10 cardiac cycles and averaged. The patient's heart rates ranged from 55–100 beats/min (mean 74.5 beats/min).

Because of the significant relation observed between the Q-C/A2-E ratio and LVEDP in the first group of patients, a second group of 32 patients without mitral stenosis was studied prospectively in an attempt to estimate left ventricular filling pressure from the Q-C/A2-E ratio. Their ages ranged from 40–67 years. There were 24 patients with ischemic heart disease, three with idiopathic congestive cardiomyopathy, two with mild aortic insufficiency (one of whom also had aortic stenosis and mitral regurgitation), one with constrictive pericarditis and two with normal left ventricular function and coronary arteriograms. Their heart rates ranged from 52–130 beats/min (mean 77.3 beats/min). Twenty-five patients were studied during diagnostic cardiac catheterization with a protocol identical to that used for the initial group. Again, the echocardiographic and hemodynamic measurements were made independently by different observers. Seven patients were studied in the coronary care unit during diagnostic catheterization with flow-directed balloon-tip catheters. PCWPs were measured after the echo phonocardiographic recordings by a separate observer.

Left ventricular filling pressures were acutely altered in 10 of the 32 patients to determine the sensitivity of the Q-C/A2-E ratio to these changes. Four patients were studied in the catheterization laboratory — three were studied before and 5 minutes after left ventricular angiography, and one was studied before and 5 minutes after 0.8 mg nitroglycerin sublingually. Six patients were studied in the coronary care unit — three were studied before and 1 minute after straight-leg raising and three before and 10 minutes after vasodilator therapy (one sublingual nitroglycerin, two intravenous nitroprusside).

To assess the relation between the Q-C/A2-E ratio and left atrial pressures in mitral stenosis, echophonocardiograms from 30 patients studied within 48 hours of cardiac catheterization were reviewed. Twenty-two patients had mitral stenosis and eight had prosthetic mitral valves. Measurements of Q-C and A2-E were performed, as shown in figure 2, over five to 10 cardiac cycles at a paper speed of 100 mm/sec and the Q-C/A2-E ratios averaged. The Q-M1 and A2-OS intervals were measured from the phonocardiogram in several cycles and a Q-M1/A2-OS ratio was derived. Results were compared with mean PCWPs measured by independent observers during cardiac catheterization. The patients' heart rates averaged 78 beats/min during echo phonocardiography as well as during catheterization; 13 of the 30 patients were in chronic atrial fibrillation.

All patients who participated in the study gave their informed consent. All comparisons were made using linear regression analysis.

Results

The relation of the Q-C/A2-E ratio to LVEDP in the initial group of 22 patients is shown in figure 3. A highly significant correlation between the two was observed ($r = 0.93$; $\text{SEE} = 2.6 \text{ mm Hg}$). The correlation between each of the components of the ratio and LVEDP was significant ($p < 0.001$), but not as good as the ratio itself (Q-C vs LVEDP, $r = 0.67$; A2-E vs LVEDP, $r = -0.75$). The regression equation LVEDP = 21.6 (Q-C/A2-E) + 1.1 was tested prospectively in the second group of 32 patients.

Figure 4 illustrates the correlation between estimated left ventricular filling pressures using the linear regression equation and directly measured left ventricular filling pressures. The correlation was again significant ($r = 0.81$; $\text{SEE} = 4 \text{ mm Hg}$). Ten of 11 patients (91%) with filling pressures $> 14 \text{ mm Hg}$ were correctly separated from 19 of 21 patients (90%) with filling pressures $< 14 \text{ mm Hg}$.

The sensitivity of the Q-C/A2-E ratio in estimating acute changes in left ventricular filling pressures is shown in figure 5. In all instances, the estimated left ventricular filling pressure was altered in the same direction as the measured filling pressure. The magnitude of the true change in pressure was correctly estimated by the Q-C/A2-E ratio in six patients (ratio of true change to estimated change 1.0–1.4) and underestimated in four (ratio of true change to estimated change $> 2.0$); in no patient was the true change overestimated.

The Q-C/A2-E ratio and mean PCWP correlated well in the 30 patients with left ventricular inflow obstruction ($r = 0.78$). The linear regression equation PCWP = 18.1 (Q-C/A2-E) + 2.45 was similar to the

Figure 1. Simultaneous recording of a phonocardiogram (PCG), electrocardiogram (ECG) and a mitral valve echogram for measurements of A2-E and Q-C intervals. The paper speed is 100 mm/sec and time lines are at 10-msec intervals.
LEFT-SIDED Pressures by Echo-phonocardiography / Palomo et al.

A 0.5 SEC

ECG

PCG

FIGURE 3. Relation of the Q-C/A2-E ratio to left ventricular end-diastolic pressure (LVEDP) in the initial group of 22 patients without mitral stenosis.

equation for estimating left ventricular filling pressures; the absolute values for PCWP derived with both equations were nearly equal. The results were identical when using the Q-M1/A2-OS ratio. Figure 6 illustrates the correlation between estimated PCWPs derived as PCWP = 21.6 (Q-C/A2-E) + 1.1, and measured mean PCWPs in the 30 patients with left ventricular inflow obstruction (r = 0.78; SEE = 4 mm Hg). The equation accurately separated 18 of 19 patients (95%) with PCWP > 18 mm Hg from nine of 11 patients (82%) with PCWP ≤ 18 mm Hg. Thus, a single equation may be applied in the presence or absence of left ventricular inflow obstruction.

Discussion

The results of this investigation indicate that the Q-C/A2-E ratio and left ventricular filling pressures are

FIGURE 2. Simultaneous recording of a phonocardiogram (PCG), electrocardiogram (ECG) and an echocardiogram from a stenotic mitral valve (panel A) and a prosthetic mitral valve (panel B). The A2-E and Q-C intervals are measured, as shown, in several cycles and averaged to obtain a Q-C/A2-E ratio.

FIGURE 4. Correlation between estimated and measured left ventricular filling pressures (LVFP) in a prospective group of 32 patients without mitral stenosis. LVFP (cath) = left ventricular end-diastolic pressure measured during cardiac catheterization; PCW (ccu) = mean pulmonary capillary wedge pressure measured in the coronary care unit.
directly related in patients without mitral stenosis and that the Q-C/A2-E ratio and mean PCWPs are directly related in patients with left ventricular inflow obstruction. Phonocardiographic studies in mitral stenosis have shown an inverse relation between left atrial pressures and the A2-OS interval, and a direct, although weak, correlation between left atrial pressures and Q-M. Because of the influence of heart rate on these intervals, previous investigators developed an index of severity of inflow obstruction by subtracting A2-OS from Q-M (Well's index). In the absence of mitral stenosis, a reduction in the E-to-F slope or a prolongation of the closure time (A-C interval) of the mitral valve echo (corrected for the PR interval) have been associated with elevated left ventricular filling pressures. However, the sensitivity, specificity and predictive values of these findings have been less than optimal. Our results raise new possibilities for the accurate noninvasive assessment of the diastolic pressures on the left side of the heart with and without mitral stenosis.

The rationale for relating the Q-C/A2-E ratio to left atrial pressures is based primarily on the effects of mitral stenosis on these intervals and supported by observations (unpublished) made by us during the course of evaluating left ventricular function with simultaneous left ventricular pressures and echocardiographic dimensions. A shortening of A2-E associated with a lengthening of Q-C in certain patients was noted during an acute elevation in LVEDP brought about by either volume expansion or afterload augmentation (fig. 7). It occurred to us that a ratio of Q-C to A2-E might relate to left ventricular filling pressures and be less affected by heart rate than either interval alone or previously used indexes. The results observed in the initial group of patients demonstrated a very high correlation between Q-C/A2-E and LVEDP and a lower, but statistically significant, correlation between each interval and LVEDP.

These findings are superior to any previous echocardiographic attempt at assessing left atrial or left ventricular filling pressures from mitral valve motion. In addition, the direct response of Q-C/A2-E ratio to acute changes in left ventricular filling pressures in 10 patients is further evidence of the close relation between this ratio and left atrial or left ventricular filling pressures.

To further assess the validity of our present findings, we analyzed data from Proctor et al. who compared the A2-OS and Q-M1 intervals with mean PCWPs (at catheterization) or left atrial pressures (during surgery) in 19 patients with mitral stenosis. We compared the Q-M1/A2-OS ratio derived from their data with the left atrial pressure (or PCWP) and obtained a correlation coefficient of 0.70 with the following regression equation: left atrial pressure = 18.9 (Q-M1/A2-OS) + 2.04. These data are very

**Figure 5.** Left ventricular filling pressures (LVFP), estimated from the Q-C/A2-E ratio, are plotted against measured LVFP in 10 patients during acute changes in LVFP. In all instances, estimated LVFP moved in the same direction as measured LVFP. Abbreviations as in figure 4.

**Figure 6.** Correlation between estimated and measured mean pulmonary capillary wedge pressures (PCW) in 30 patients with left ventricular inflow obstruction.

**Figure 7.** Diagrammatic example from a patient studied during cardiac catheterization with simultaneous left ventricular (LV) pressure and echocardiographic mitral valve motion. In addition, a phonocardiogram (PCG) was recorded from the micromanometer-tip catheter. Panel A was taken at rest and panel B after an infusion of angiotensin resulting in marked increase in end-diastolic pressure. Notice the shortening of A2-E and the lengthening of Q-C from panel A to panel B.
comparable to our own, even though the time between phonocardiographic and hemodynamic observations in Proctor’s study was variable.\textsuperscript{13}

It is somewhat surprising that the Q-C/A\textsubscript{2-E} ratio relates so well to left-sided filling pressures, particularly when one considers the multiple determinants of the components of this ratio. A\textsubscript{2-E} is primarily determined by heart rate,\textsuperscript{6} arterial pressure at the time of aortic valve closure,\textsuperscript{14} 15 rate of isovolumic relaxation,\textsuperscript{14} left atrial pressure at the time of left ventricular-left atrial pressure crossover\textsuperscript{15, 16} and initial diastolic left ventricular filling pressure due to this effect on mitral valve opening velocity.\textsuperscript{8} On the other hand, the Q-C interval is determined by heart rate,\textsuperscript{8} the electromechanical activation period of the left ventricle,\textsuperscript{2, 16} the rate of pressure rise during isovolumic contraction,\textsuperscript{16} the electrocardiographic PR interval\textsuperscript{16} and the left atrial pressure at the time of crossover of left ventricular and left atrial pressures.\textsuperscript{9}

No patients in the present study had severe hypertension, and only two patients had aortic insufficiency, which was mild in both. One patient in the prospective group had a left bundle branch block, and the estimated left ventricular filling pressure (16 mm Hg) compared very well with measured LVEDP (16 mm Hg). However, the accuracy of this technique in a larger group of patients with either severe hypertension, significant aortic insufficiency or intraventricular conduction defects needs to be further evaluated. Excessive prolongation of the PR interval (> 240 msec), which might result in premature closure of the valve, was not present in any of the patients studied.

One might expect that the effects of heart rate on each of the intervals would be cancelled or buffered by using a ratio. The fact that the results were equally good over a wide range of heart rates from 52–110 beats/min gives some support to this hypothesis. However, only one patient had a heart rate above 110 beats/min (130 beats/min), so the accuracy of the ratio at faster rates was not tested. Chronic atrial fibrillation was present in 15 patients (13 with left ventricular inflow obstruction) and did not appear to affect the accuracy of the ratio in estimating the diastolic pressures.

A prolonged isovolumic relaxation time with or without reduced mitral valve opening velocity might result in a normal A\textsubscript{2-E}/Q-C ratio despite significant elevation in left ventricular filling pressure. This potential problem was observed in one patient in the prospective group in whom the Q-C/A\textsubscript{2-E} ratio predicted a left ventricular filling pressure of 10 mm Hg, while the true LVEDP was 20 mm Hg. The A\textsubscript{2-E} interval in this patient was 150 msec, a normal figure; the unusual prolongation was due to lengthening of the interval between the second heart sound and onset of mitral valve opening (95 msec). Even though the Q-C interval was slightly prolonged (65 msec), the Q-C/A\textsubscript{2-E} ratio was, therefore, within normal limits.

Despite the above potential limitations, the results of this investigation indicate that the Q-C/A\textsubscript{2-E} ratio correlates extremely well with measured PCWP and LVEDP in patients with and without left ventricular inflow obstruction, respectively. The ratio is sufficiently sensitive to detect small acute directional changes in left ventricular filling pressures. Finally, this simple, noninvasive technique accurately separates patients with abnormally increased left ventricular filling pressures from normal subjects, thereby suggesting considerable clinical utility.

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