The Cardiac Pre-ejection Period:

A Correlate of Peak Ascending Aortic Blood-flow Acceleration

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The relationship between peak ascending aortic blood-flow acceleration and the cardiac pre-ejection period (PEP) was studied in five chronically prepared dogs. Acceleration was measured as the first derivative of the signal from a flow probe placed around the aortic root. PEP was derived indirectly by subtracting left ventricular ejection time (obtained from a central arterial pressure signal) from the total active electromechanical time (the Q-S$_2$ interval measured from the ECG and heart sounds). Resulting values of PEP were inverted and squared so that they shared a common time unit with acceleration-time^{-2}. Comparison of 1/PEP^2 and peak acceleration produced correlation coefficients from 0.74 to 0.96. A linear relationship between these two measurements was maintained over a sixfold change in the inotropic state of the heart. The quotient 1/PEP^2 appears to be an easily obtainable, potentially noninvasive expression of the myocardial contractile state. (Key words: Patient monitoring; Inotropy; Pre-ejection period; Blood flow acceleration.)

IN RECENT YEARS several promising indices for evaluating myocardial function have been proposed. Among these are the initial ventricular impulse,[1] the maximum positive slope of the left ventricular pressure curve and its combination with isometric pressures,[2] the isometric

time–tension index,[3] and blood-flow acceleration.[4] All of these measurements involve invasive techniques potentially hazardous to patients. The purpose of this study was to investigate the relationship between peak ascending aortic blood-flow acceleration and the cardiac pre-ejection period, an interval that can be obtained indirectly by noninvasive means.[5]

Methods

Five mongrel dogs with chronically implanted, pulsed, ultrasonic ascending aortic-flow probes were studied. Indwelling polyvinyl catheters in the aortic arch and a central vein were used for pressure measurements and sampling. All wires and catheters were brought out through the dorsum of the neck. Experiments were conducted at least ten days after the final surgical procedures, when the dogs appeared fully recovered from the implantation operation and had returned to normal activity. No clinically observable infections occurred. Anesthesia was induced with methohexital, 12.5 mg/kg. Pulmonary ventilation was controlled at approximately 1½ times the normal minute volume through an endotracheal tube with a mixture of nitrous oxide, 70 per cent, and oxygen, 30 per cent, with supplemental graded doses of halothane ranging from 0.3 to 3.0 per cent. In every instance, a steady state of anesthesia was demonstrated by equilibrium between end-tidal and inspired gas concentrations. A constant infusion of succinylcholine abolished electromyographic interference. The electrocardiogram was a standard lead 1. Pressures were measured by Statham P-23 Db transducers. Heart sounds were recorded from a Biocom 1010B microphone placed on the chest wall or with an AEL model 204 esophageal microphone. Signals from the electrocardiogram

FIG. 1. The method of indirect calculation of the cardiac pre-ejection period is illustrated. The pulse waveform may be recorded transcutaneously from various peripheral arterial sites.
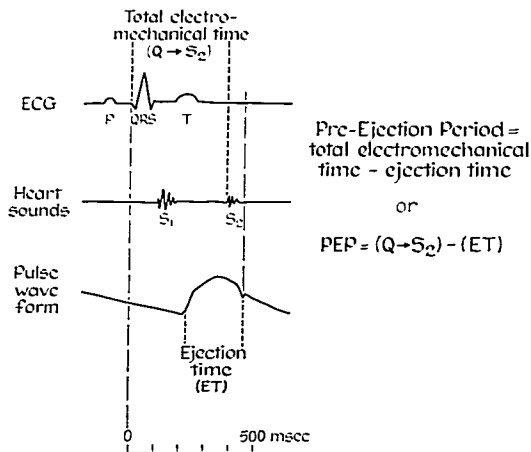
and phonocardiogram, aortic pressure (pulse waveform), and flow-probe signals were recorded with a Beckman model R Dynograph and transferred simultaneously to an Ampex FR-1300 magnetic FM recorder. Data used in analysis were played from tape onto a Clevite-Brush Mark 200 Rectilinear Recorder at 100 mm/sec.

Dye-dilution cardiac output determinations were made using indocyanine green during various stable states of myocardial excitation or depression, and the actual cardiac output values were computed by the forward triangulation method. Two to seven dye-dilution curves were obtained during each animal experiment. Calibration of the flow probes was accomplished *in vivo* by simultaneous comparison of the beat-to-beat stroke volume (the integrated ascending aortic-flow signal) with the calculated dye-dilution cardiac output values. The first derivative of the flow signal (acceleration) was obtained electronically on a Beckman EASE 2000 series analog computer. The differentiator was calibrated daily with known voltages from a triangular waveform generator.

The cardiac pre-ejection period was derived indirectly in the following manner: the interval from the Q-wave of the ECG through the

first high-frequency component of the second heart sound constituted the total active electromechanical time of the ventricle. Left ventricular ejection time was measured from the onset of the upstroke through the dicrotic notch on a pulse waveform—in these experiments, the aortic pressure tracing. The pre-ejection period (PEP) was calculated by subtracting the left ventricular ejection time from the total active electromechanical time. This indirect approach to the measurement of the pre-ejection period was unaffected by pulse-wave transmission delay, and is illustrated in figure 1. All measurements of PEP were done manually on rectilinear paper tracings at a speed of 100 mm/sec.

In order to compare the pre-ejection period with ascending aortic blood-flow acceleration, the pre-ejection period was inverted and squared so that its units coincided with those of acceleration. During each drug response, a representative $1/PEP^2$ was derived from ten consecutive heart beats. These values were compared with the mean peak acceleration value over the same ten cardiac cycles. Measurements were obtained during apnea and under stable circulatory conditions. Figure 2 is a representative sample of the data output necessary for comparison of indirect $1/PEP^2$
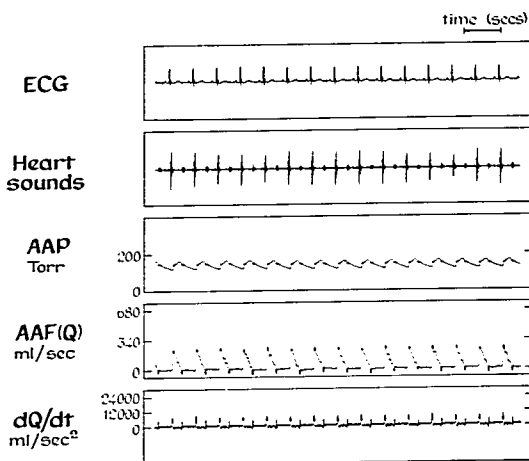
time (secs)

ECG

Heart
sounds

AAP
Torr   200
              0

AAF(Q)   o80
ml/sec   320
              0

dQ/dt   24000
ml/sec²   12000
              0

Fig. 2. These tracings
show the data output
necessary during an ani-
mal experiment. AAP =
ascending aortic pressure
(the pulse waveform),
AAF = ascending aortic
flow, dQ/dt = blood flow
acceleration. The record-
ing was taken from a
dog during halothane-
induced myocardial de-
pression.

Record From Dog Receiving 1.5% Halothane

with peak ascending aortic blood-flow accele-
ration. In the bottom tracing peak accelera-
tion is the maximum amplitude of the first
positive deflection during each cardiac cycle.

Final correlations, t tests and probability
values were calculated on an IBM 360 com-
puter using a standard statistical program. In
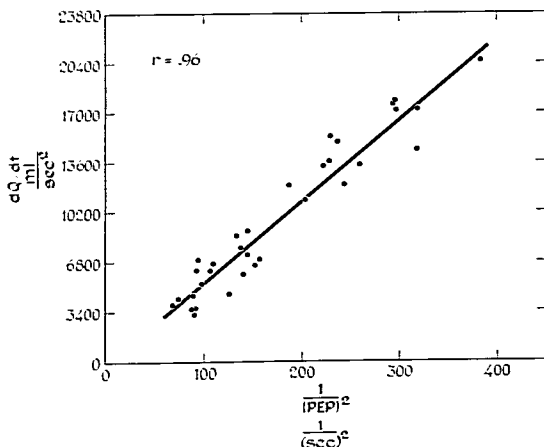addition, computer plot programs were uti-

$r = .96$

Fig. 3. This scatter-
gram plots peak blood
flow acceleration on the
ordinate against indi-
rectly derived 1/PEP² on
the abcissa. A compari-
son of 33 separate ino-
tropic states is repre-
sented in this graph of
data from experiment 6
in table 1. In each ex-
periment, computer plot
programs were utilized
to produce similar scat-
tergrams.

lized to produce scattergrams similar to figure 3 for each experiment.

The inotropic state of the heart was changed with graded doses of isoproterenol, propranolol, calcium gluconate, sodium citrate, epinephrine, and halothane. In addition, heart rate was augmented with atropine, afterload was altered with phenylephrine and amyl nitrate introduced by inhalation, and a rapid saline infusion was used to increase preload. Generally, the changes in inotropy produced in any one animal were sixfold.

Results

Correlation coefficients between peak blood-flow acceleration and $1/PEP^2$ ranged from 0.74 to 0.96 (table 1). P values were less than 0.001 in five of seven of the experimental runs. Experiments with less significant results were done early in the series when fewer individual alterations in inotropic state were obtained.

A scattergram which plots peak blood-flow acceleration against $1/PEP^2$ in one dog is shown in figure 3. The best-fit line was drawn from an equation calculated by computer program. The correlation coefficient in this case was 0.96. Thirty-three pairs of data points were compared, representing 330 heart beats analyzed, since each point was the mean of ten cardiac cycles.

Discussion

In this study a reproducible, linear relationship between $1/PEP^2$ and peak ascending aortic blood-flow acceleration was demonstrated.

Noble et al.[4] found that the maximum acceleration of blood ejected from the left ventricle is a remarkably sensitive indicator of myocardial ischemia. It reflects the depression of coronary blood flow in conscious dogs earlier, and to a greater degree, than peak ascending aortic flow, stroke volume (cardiac output), or left atrial pressure. Unfortunately, measurement of blood-flow acceleration entails major invasive surgery and does not lend itself to patient monitoring.

Systolic time intervals may be obtained noninvasively by measuring the arterial pulse waveform superficially from a convenient source, such as the carotid or brachial artery.[5] Metzger et al.[6] and Bush et al.[7] have shown

TABLE 1. Comparison and Statistical Evaluation of the Relationship between Peak Blood-flow Acceleration and $1/PEP^2$ *

Experiment	N	Correlation Coefficient	t	P
1	5	0.95	5.3	<0.02
2	14	0.83	5.1	<0.001
3	9	0.74	2.9	<0.05
4	16	0.87	6.5	<0.001
5	31	0.94	14.3	<0.001
6	33	0.96	18.4	<0.001
7	20	0.82	6.1	<0.001

* Correlation coefficients, t-test values, and P values were calculated on a digital computer using standard statistical programs. N represents the number of steady-state conditions analyzed during each experimental run.

excellent correlations between the externally derived (noninvasive) intervals and direct measurements using end-catheter micromanometers. In our study the pulse waveform was obtained from a central aortic catheter so that blood pressure and arterial blood gases could be measured directly. The use of such a technique in this work should not reflect on the potentially noninvasive character of $1/PEP^2$.

Clinical uses of the cardiac pre-ejection period have been studied by several authors. Weissler et al.[8] found that the pre-ejection period was prolonged in patients with overt heart failure, and this prolongation correlated well with reduced cardiac output. Diamant and Killip[9] observed a significant lengthening of the pre-ejection period in serial studies of patients undergoing acute myocardial infarction. In volunteer subjects, Harris et al.[10] showed that beta-adrenergic stimulation by isoproterenol, epinephrine, and moderate doses of nonepinephrine shortened the pre-ejection period, while beta-adrenergic blockade by propranolol lengthened it.

However, certain investigations have shown the pre-ejection period to be influenced by changes in preload or afterload; that is, lengthening by increased arterload and shortening by increased preload.[10-12] Conversely, Noble[13] observed that changes in ventricular preload and output impedance caused little variation in peak blood-flow acceleration.

In comparing the pre-ejection period and blood-flow acceleration, no specific analysis of

the effects of heart loading was made in our study, yet the high correlation coefficients between the two measurements would seem to preclude any great variation caused by preload or afterload. An augmentation of left ventricular dp/dt with increasing left ventricular afterload in dogs has been described by Wallace *et al.*[14] Our measurements were made during steady-state conditions in dogs with intact sympathetic nervous systems; during this time the rate of rise of ventricular pressure in the isovolumic phase may have increased sufficiently in response to an increased afterload (via phenylephrine) so that any prolongation of the pre-ejection period was minimized. Shortening of the interval by increasing preload may have been too subtle for detection with our statistical techniques.

A few technical difficulties arise in the use of the pre-ejection period as a monitor of myocardial function. Systolic heart murmurs may diffuse the second heart sound so that the Q-S_2 interval becomes indistinct. During operations the use of electrocautery obliterates the ECG. Finally, the external transducing of the arterial pulse is susceptible to muscle artifacts and gross displacement of sensors by vigorous movements of the patient.

In spite of these problems, the cardiac pre-ejection period, particularly its inverse square ($1/PEP^2$), appears to be a good indicator of ventricular functions, and it is applicable as a noninvasive, beat-to-beat monitor in the operating room or intensive care unit, and in clinical studies.

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