Influence of heart rate increase on uncorrected pre-ejection period/left ventricular ejection time (PEP/LVET) ratio in normal individuals

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In 26 normal volunteers, increase in heart rate from mean 73.94±1.97 to 103.61±2.72/min, by either intravenous atropine administration or rapid right atrial pacing, produced definite changes in the uncorrected systolic time intervals. As expected, total electromechanical systole (QS₂) and left ventricular ejection time (LVET) were shortened, while the pre-ejection period (PEP) was unaffected. There was a consistent and significant increase of the PEP/LVET ratio (P<0.001). It is postulated that when this ratio is taken to express left ventricular contractility, it should probably be corrected for heart rate. Appropriate regression equations for such a correction were calculated (PEP/LVET=0.249+0.0168 HR).

Measurement of the systolic time intervals of the left ventricle as reported by Weissler, Harris, and Schoenfeld (1968, 1969) is currently being applied widely for the evaluation of cardiac function. The advantages and reliability of this method, as well as reservations about its validity, have been already discussed in numerous publications (Aronow, Bowyer, and Kaplan, 1971; McConahay, Martin, and Cheitlin, 1972; Parker and Just, 1974). Weissler and co-workers (1969) have particularly stressed the use of the pre-ejection period/left ventricular ejection time (PEP/LVET) ratio as a very sensitive index of ventricular function. According to these investigators this ratio offers the additional advantage of being self-corrected for sex and heart rates from 50 to 110/min. Most authors have subsequently adhered to this principle, and have used the PEP/LVET ratio in its uncorrected form (McConahay et al., 1972; Timmis et al., 1975). However, it becomes apparent from Weissler’s own regression equations and additional investigators’ reports that the PEP and the external isovolumic contraction time (EICT) are only minimally affected by changes in heart rate (Goldstein, DeGroot, and Leonard, 1961; Harris, Schoenfeld, and Weissler, 1967; Talley, Meyer, and McNay, 1971), while the LVET is altered to a considerable degree (Wallace et al., 1963). Therefore, changes in heart rate would be expected to yield a larger PEP/LVET ratio.

We investigated whether correction of this ratio for heart rate is justified. Some authors have already corrected this ratio, using Weissler’s equations (Strangfeld et al., 1973; Frishman et al., 1975), but as far as we know no detailed data have been given on the behaviour of this ratio with heart rate changes.

Subjects and methods

Twenty-six subjects were included in this study. Most were house physicians, and hospital personnel. In two patients STI intervals were measured during the process of rapid right atrial pacing for the investigation of atypical chest pain (both tests proved negative). Ages ranged from 17 to 38 years (mean 27.1). All were considered free from any cardiac abnormality by history, clinical examination, resting and exercise electrocardiograms (sub-maximal test: 85% of predicted maximal heart rate), and evaluation of heart size and motion by image intensifier fluoroscopy. The electrocardiogram (usually lead II), carotid pulse tracing, and phonocardio-gram were recorded on a Hewlett-Packard 4578A photographic multichannel recorder. Thus, the heart rate, total electromechanical systole (QS₂), and left ventricular ejection time (LVET) were

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### TABLE  
*Systolic time intervals before and after the production of tachycardia*

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<th>Q₂ (ms)</th>
<th>LVET (ms)</th>
<th>PEP (ms)</th>
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**Mean:** 73-94 97-0 289-66 107-16 0-370 0-331 103-61 359-08 252-23 106-85 0-426 0-349 27:1

**SEM:** ±1-97 ±2-72 ±3-99 ±1-75 ±0-0071 ±0-0047 ±2-72 ±5-79 ±5-09 ±3-26 ±0-0143 ±0-007 5 (548-29) (412-41) (136-73) ±5-20 ±3-09 ±1-61 ±3-2 ±2-84 ±0-28 5 (424-23) (148-28) 5

**Significance:**

### Abbreviations:
- **HR:** Heart rate
- **Q₂:** Heart rate
- **LVET:** LVET index
- **PEP:** PEP index
- **PEPI:** PEPI/LVETI
- **LVET + PEP/LVETI:** LVET index
- **QS₂:** QS₂ index
- **QS₂ + 2-1:** QS₂ index
- **LVET + 1-7:** LVET index
- **PEP + 0-4:** PEPI/LVETI

The systolic time intervals were measured at the highest rate achieved. In 2 subjects, in whom rapid right atrial pacing was performed, they were measured at basal heart rate levels and at 111-1 and 109-0 beats/min, 2 minutes after these heart rates had been reached (Table).

Before and after the production of tachycardia, the QS₂ index (QS₂), PEP index (PEP), and LVET index (LVETI) were calculated according to the regression equations of Weissler et al. (1969)

**Males:**
- QS₂ = QS₂ + 2-1 heart rate
- LVET = LVET + 1-7 heart rate
- PEPI = PEPI + 0-4 heart rate

**Females:**
- QS₂ = QS₂ + 2-0 heart rate
- LVET = LVET + 1-6 heart rate
- PEPI = PEPI + 0-4 heart rate

**Calculated,** as proposed by Weissler et al. (1968, 1969). The PEP was estimated by subtracting the LVET from the QS₂. All measurements were performed between 8:00 and 9:00 a.m. at the fasting state and supine position.

Paper speed was 100 mm/s. Ten to fifteen consecutive heart beats were measured to the closest 5 ms and averaged. Care was taken to start and finish measuring at the same respiratory phase, as estimated by direct observation of the patient and manual marking of the inspiration phase on the chart paper. The arterial blood pressure was measured by a cuff sphygmomanometer immediately after recording the systolic time intervals.

The nature and purpose of this study was explained to all participants and informed consent was obtained.

After the initial basal study, atropine was given intravenously in 0-5 mg increments every 3 minutes to 24 subjects, until a heart rate around 110/min or a total dose of 1-5 mg was reached. The systolic time intervals were measured at the highest rate achieved.
Influence of heart rate increase

The PEP/LVET ratio increased consistently and significantly (Table, Fig. 1). The PEP1/LVET1 was also found to increase with heart rate. However, the percentage change in each patient was significantly smaller in the PEP1/LVET1 ratio than in the PEP/LVET ratio (P < 0.001, Table).

The PEP/LVET or the PEP1/LVET1 ratio in the 26 subjects were not related to heart rate at rest (r = 0.168, P > 0.10, and r = 0.043, P > 0.10, respectively). They were not significantly related to the heart rate after tachycardia, either (r = 0.336, P > 0.05 and r = 0.102, P > 0.10, respectively). However, when all 52 heart rate measurements (before and after tachycardia) were pooled the PEP/LVET ratio was significantly correlated to heart rate (r = 0.508, P < 0.01 Fig. 2).

When the PEP1/LVET1 ratio was used, there was no correlation of the 52 measurements to heart rate (r = 0.267, P > 0.05, Fig. 3).

From the correlation of PEP/LVET to the total of 52 heart rate measurements the following regression equation was calculated:

PEP/LVET: 0.249 + 0.00168 HR

The arterial blood pressure was normal in all subjects, and did not appreciably change with the increase in heart rate.

Discussion

From our findings we cannot reach any conclusions as to whether the PEP/LVET should always be corrected for heart rate or not. However, we are puzzled by certain discrepancies in the published reports. It has been shown that the PEP is only minimally affected by changes in the heart rate (Harris et al., 1967; Talley et al., 1971); our findings are similar.

The PEP is significantly correlated with dP/dt max and the ejection fraction (Aronow et al., 1971, McConahay et al., 1972; Ahmed et al., 1972); a weaker but still quite satisfactory correlation has also been found with the stroke volume (Weissler et al., 1968, 1969; Ahmed et al., 1972).

The stroke volume is affected considerably by tachycardia (Weissler, Peeler, and Roehll, 1961; Stein et al., 1966; Benchimol and Liggett, 1966). It is probable that the PEP is prevented from lengthening during the tachycardia-induced decrease in stroke volume by a compensatory shortening through the increased contractility associated with tachycardia (Vatner and Braunwald, 1974; Schwarz, Thormann, and Winkler, 1975; Roy, Sowton, and DiLuzio, 1975).

The ejection fraction does not significantly change with tachycardia in dogs (Bristow et al.,

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29.66 0.054 0.016 +14.08 +4.78 ±1.24
±2.27 ±0.0078 ±0.0038

P < 0.001 P < 0.001 P < 0.001

After the PEP/LVET ratio was calculated, a PEP1/LVET1 ratio was also estimated. The values of both ratios before and after the production of tachycardia were compared by the paired t test.

The PEP/LVET and the PEP1/LVET1 ratio were correlated to heart rate either before the production of tachycardia (26 correlations), or after its production (26 correlations). Moreover, these ratios were correlated with heart rate both at rest and at tachycardia (52 correlations), by the regression analysis test.

Results

Under basal conditions the systolic time interval values in our subjects were within the accepted normal range (Table). With increase of the basal heart rate from 79.94 ± 1.97 to 103.61 ± 2.72/min, there was a consistent shortening of the QS2 and LVET, while the PEP did not appreciably change.
1963) or humans (Krayenbuehl et al., 1975).

There is agreement among the various authors about the profound effects of heart rate changes on the LVET. When rate corrected, this interval correlates well with the stroke volume and ejection fraction, but less well with the dP/dt (McConahay et al., 1972).

The uncorrected PEP/LVET (and its reverse analogue, the LVET/EICT) ratio has been found to correlate better with the ejection fraction and dP/dt than the corrected LVET, PEP, or EICT alone (Garrard, Weisler, and Dodge, 1970; Aronow et al., 1971; McConahay et al., 1972). If this ratio is used as an expression of stroke volume, then it should probably not be rate-corrected. However, if it is taken as an index of cardiac contractility, or the ejection fraction, it should be rate-corrected, especially when serial measurements are carried out in the same individual after pharmacological or physiological interventions. Otherwise, any drug or man-

**FIG. 1** Increase of the uncorrected PEP/LVET ratio over the basal values with the occurrence tachycardia in the 26 patients used in the present study.

**FIG. 2** Significant correlation of the uncorrected PEP/LVET ratio with 52 heart rate measurements (26 patients, studied at basal conditions and after production of tachycardia).
Weissler's equations and those of Fabian, Epstein, and Coulshed (1972) were calculated from studies performed on a group of 121 men and 90 women with normal cardiac function, under basal conditions. Thus, these equations may not be appropriate for correcting the STI in serially studied individuals. On the other hand, Layton et al. (1973) and Lindquist, Spangler, and Blount (1973) used regression equations based on serial measurements.

In most of our subjects tachycardia was produced by atropine. This drug has been widely used to this purpose by Weissler's group (Harris et al., 1967), who consider it free of any inotropic action. Similarly, Kosowsky et al. (1966) found no differences in the haemodynamic measurements between atropine and right atrial pacing-induced tachycardia.

We have no haemodynamic or angiographic studies to support our findings. However, such studies have been carried out in detail by others, as already discussed, and there is no reason why these data should not apply for the individuals presented in our report. It is self-evident that these conclusions are valid as long as tachycardia does not produce ischaemia, which would alter both the haemodynamic parameters and the systolic time interval values.

References


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Influence of heart rate increase on uncorrected pre-ejection period/left ventricular ejection time (PEP/LVET) ratio in normal individuals.

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