Relationship between Systolic Time Intervals and Heart Rate during Atrial or Ventricular Pacing in Normal Subjects

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SUMMARY

Systolic time intervals (STI) are regarded as good indices of cardiac performance in many heart diseases. It must be considered, however, that they are temporally related to the cardiac contraction cycle and, therefore, may be modified by heart rate changes. Thus, it is necessary to define the possible relationship between STI and heart rate changes. In this study, changes in heart rate were induced by atrial and ventricular pacing. Tachycardia caused a proportional decrease of left ventricular ejection time (LVET) ($y=275.142-1.0025 x$, $r=0.76$, $p<0.001$ for atrial pacing and $y=298.28-0.691 x$, $r=-0.75$, $p<0.001$ for ventricular pacing, respectively), but did not modify the pre-ejection period (PEP) and the isometric contraction time (ICT) and the electromechanical interval (QS_1).

These results demonstrate that while LVET must be corrected for the changes in heart rate, no correction of PEP and ICT is necessary.

Additional Indexing Words:

Heart performance Polygraphic tracings
Atrial contribution to systole

SYSTOLIC time intervals (STI), defined many years ago,¹⁾⁻³⁾ have received new attention over the past few years for the correlations which have been made with more direct parameters of myocardial performance.⁴⁾⁻¹⁰⁾ STI are temporally related to the cardiac contraction cycle and, therefore, it would be important to ascertain the relationship, if any, between STI and heart rate. Actually, it has been demonstrated that there is an inverse relationship, both at rest and during atrial pacing, between left ventricular ejection time (LVET), which is strictly correlated to the stroke volume, and heart rate.^{9),11)} On the contrary the influence of heart rate on pre-ejection period (PEP) and on isometric contraction time (ICT) is not completely

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understood. In fact, some investigators support the hypothesis that, at rest, PEP changes when heart rate varies, because it is affected by the autonomic nervous activity.⁵⁾ Moreover, Wiggers²⁾ in the dog and Orenskov¹²⁾ in man demonstrated that heart rate increments induce significant decrease of ICT, while, on the contrary, Harris et al¹³⁾ failed to observe any significant change in ICT in 3 normal subjects during atrial pacing.

This study was undertaken in order to define the relationship between STI and heart rate during tachycardia induced by atrial and ventricular pacing that causes well known hemodynamic changes.^{14)–20)}

METHODS

The study was performed in 21 normal subjects of either sex, whose age ranged from 20 to 50 years. Twelve were studied during atrial pacing and the remaining during ventricular pacing. The studies were performed in the postabsorptive state after a 12–14 hr fast. Right heart catheterization was performed with a n° 5F bipolar electrode catheter, inserted percutaneously into a brachial vein and then positioned at the lateral wall of the right atrium or ventricle for atrial and ventricular pacing, respectively. A photographic multichannel polygraph (Electronics for Medicine DR8) was used to record simultaneously ECG, phonocardiogram, and carotid arterial pulse tracing at a paper speed of 100 mm/sec, while the subject was lying on an examination bed in the supine position. The mean values of 5 cardiac cycles were evaluated for the following parameters:

- left ventricular ejection time (LVET), measured from the beginning of the upstroke to the onset of the dicrotic notch of the carotid pulse;
- electromechanical systole (QS_2), recorded as the interval from the onset of QRS complex to the first high frequency vibration of the second heart sound;
- pre-ejection period (PEP), calculated by subtracting the ejection time from the electromechanical systole (QS_2 –LVET);
- isovolumetric contraction time (ICT), obtained by subtracting the electromechanical interval from PEP (PEP – QS_1);
- electromechanical interval (QS_1), measured from the onset of the QRS complex in the ECG to the onset of ventricular contraction;
- PEP/LVET ratio.

All these parameters were first recorded at rest. Then, heart rate was gradually increased by atrial or ventricular pacing starting from a rate of 5–10 beats/min above the resting level. Lead II of ECG was continuously monitored. Subsequent rate increases were in increments of approximately 20 beats/min until the rate of 150 beats/min was reached. STI were recorded 2 min after each increment.

Data were presented as mean $\pm$ 1 SE. Statistical analysis was performed by the Student's *t* test for unpaired samples and by the regression analysis.

RESULTS

The basal mean values of STI in the group of subjects who underwent

the atrial pacing were not statistically different from those obtained in the group in which ventricular pacing was performed (Table I).

During atrial and ventricular pacing, LVET showed an inverse correlation with heart rate ($y=275.14-1.0025x$, $r=-.76$, $p<0.001$ for atrial pacing and $y=298.28-0.691x$, $r=-.75$, $p<0.001$ for ventricular pacing). These 2 regression equations were significantly different with regard to both the slope ($p<0.001$) and the intercept ($p<0.005$) (Fig. 1).

No relationship was found between heart rate and PEP, ICT, and QS_1 during both types of electrostimulations. These parameters did not show any statistically significant change from the rest value during atrial pacing. In contrast, during ventricular pacing, PEP and QS_1 increased soon after the beginning of electrostimulation from the basal values of 98.3 ± 4.5 and 65.5 ± 4.2 msec, respectively, to 151.1 ± 4.1 and 118.3 ± 3.3 msec. Then, no change in PEP and QS_1 was observed with further increments of heart rate.

Table I. Basal Values of Heart Rate and STI of the Subjects Who Underwent Atrial Pacing (Group 1) and Ventricular Pacing

	H.R. (beats/min)	LVET (msec)	PEP (msec)	ICT (msec)	QS_1 (msec)	PEP/LVET
Group 1 (n=12)	78.4 ± 4.5	297.9 ± 6.7	97.6 ± 3.2	36 ± 1.8	60 ± 2.3	0.328 ± 0.013
Group 2 (n=9)	72.1 ± 5.4	291.1 ± 8.4	98.3 ± 4.5	33.8 ± 2	65.5 ± 4.2	0.314 ± 0.018
	n.s.	n.s.	n.s.	n.s.	n.s.	n.s.

Each value represents mean $\pm$ SE. Statistical comparison has been performed between corresponding values of the 2 groups using t test for unpaired observations. n=number of subjects.

Fig. 1. Relationship between heart rate and LVET during atrial pacing (a.p., n=12) and ventricular pacing (v.p., n=9). Each point represents mean. Dashed lines represent the period before the beginning of the electrostimulation.

Fig. 2. Relationship between PEP, QS₁, ICT, and heart rate during atrial pacing (■—■) (n=12) and ventricular pacing (▲—▲) (n=9). Each point represents mean. Symbols as in Fig. 1.

Fig. 3. Relationship between PEP/LVET ratio and heart rate during atrial pacing (a.p) (n=12) and ventricular pacing (v.p) (n=9). Each point represents mean. Symbols as in Fig. 1.

Furthermore, ICT was not modified by ventricular pacing (Fig. 2).

Finally, the PEP/LVET ratio showed a direct correlation with heart rate during both types of electrostimulations ($y=0.20+0.001x$, $p<0.001$ for atrial pacing; $y=0.43+0.002x$, $p<0.001$ for ventricular pacing). These 2 regression equations were different with regard to both the slope ($p<0.01$) and the intercept ($p<0.001$) (Fig. 3).

DISCUSSION

The absence of statistically significant differences in the rest values of STI between the subjects studied with atrial pacing and those in whom ventri-

cular pacing was performed insures that the changes in STI following pacing are exclusively due to the 2 different ways of cardiac electrostimulation.

LVET, an index strictly related to stroke volume, shows during atrial and ventricular pacing a linear inverse correlation with heart rate, in agreement with the hemodynamic finding that stroke volume progressively decreases when heart rate increases.

The highly significant difference between the 2 LVET regression equations obtained during atrial and ventricular pacing, respectively, could probably mean that the stroke volume during ventricular pacing is smaller than during atrial pacing because in the former the hemodynamic contribution of the atrial systole to the ventricular filling, and then to the stroke volume, is minimal. This observation tends to support the hypothesis that the contribution of the atrial systole to the cardiac function is not negligible according to the reports of previous authors.^{21), 22)} Moreover, the finding that during atrial pacing at high heart rate LVET tends to approach the values obtained during ventricular pacing suggests that the effectiveness of the atrial contribution decreases as heart rate increases, thus confirming the hypothesis of Benchimol et al²¹⁾ that a properly timed atrial systole improves cardiac function significantly.

It is of interest in the current study that QS_1 , PEP, and ICT do not show any relationship with heart rate because they are not modified during the 2 types of cardiac stimulation. In fact, the initial increments of QS_1 and PEP during ventricular pacing are probably due to the ventricular anomalous depolarization produced by this way of electrostimulation.²³⁾ Such a behaviour of PEP and ICT during pacing-induced tachycardia suggests that these parameters are not affected by heart rate changes. On the other hand, this conclusion seems to be in contrast with the common opinion that PEP and ICT are reliable indices of myocardial contractility, by virtue of the close correlation found between these 2 parameters and the invasive indices of the left ventricular performance.¹⁰⁾ In fact, it has been demonstrated in normal subjects and in isolated myocardial tissue that the pacing-induced increment in heart rate produces an increase of Vmax and dp/dt max.^{18), 24)} This contrast, however, may be explained by the fact that PEP and ICT are influenced by the myocardial contractility itself (as expressed by the Vmax and the dp/dt max) as well as by the ventricular end-diastolic pressure (pre-load) and the aortic diastolic pressure (after-load). In other words, PEP and ICT can be considered as a cathetus of a right angled triangle in which the hypotenuse is the dp/dt and the other cathetus the difference between aortic diastolic pressure and ventricular end-diastolic pressure, according to Metzger's hypothesis.⁷⁾ Therefore, one can easily understand that PEP and

ICT may not vary if the increment of the dp/dt is associated with a decrement of ventricular end-diastolic pressure as it occurs during cardiac pacing.

Finally, the PEP/LVET ratio reflects essentially, during atrial and ventricular pacing, the LVET behaviour, since PEP does not vary with heart rate increments.

In conclusion, this study confirms that pacing-induced tachycardia causes a progressive reduction in LVET, so that it is necessary to correct LVET for heart rate. On the contrary, PEP and ICT are not modified by heart rate changes probably because they are not indices of myocardial contractility *sensu strictu*, but they also depend on other parameters such as ventricular end-diastolic pressure and aortic diastolic pressure.

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