Beat-to-Beat Evaluation of Systolic Time Intervals during Bicycle Exercise Using Impedance Cardiography

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1Health Science Center, Toyohashi University of Technology, Toyohashi, 441-8580,
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ONO, T., MIYAMURA, M., YASUDA, Y., ITO, T., SAITO, T., ISHIGURO, T., YOSHIZAWA, M. and YAMBE, T. Beat-to-Beat Evaluation of Systolic Time Intervals during Bicycle Exercise Using Impedance Cardiography. Tohoku J. Exp. Med., 2004, 203 (1), 17-29 —— In order to elucidate the beat-to-beat changes of the systolic time intervals (STI) during exercise, we proposed new techniques relating to an adaptive filter and detection algorithms for B- and X-points in the impedance cardiograph (ICG). Six male subjects underwent a ramp bicycle exercise up to maximum intensity during which an ECG, ICG and phonocardiogram (PCG) were continuously measured. Following the application of an adaptive filter, the scaled Fourier linear combiner (SFLC), to the first derivative (dZ/dt) of the base impedance (∆Z) and PCG waveforms, the B- and X-points were automatically determined. For the B-point detection we used three criteria: the zero-crossing point (Bzero), the 15% response point (B15%) of the negative peak of the dZ/dt (dZ/dtmin) and a new algorithm (Bnew). The X-point was separately determined by using the ICG and PCG waveforms. It was found that the shape of the dZ/dt waveform directly affected the determination of the B- and X-points. The B-points determined using Bzero and B15% criteria were sometimes unstable caused by the location of a notch preceding the dZ/dtmin compared to the Bnew. The time difference between the X-points measured by the ICG and PCG was mostly within ± 20 milliseconds but statistically significant. Although a wide variation was seen in R-R intervals, the STI were more stable. The relationships between HR and STI from rest to maximal exercise showed a gentle curvilinear relationship. It is suggested that the STI can be obtained precisely on a beat-to-beat basis by using the adaptive filter and detection algorithms for the inflection points of the ICG even during maximum exercise. ——— left ventricular ejection time; pre-ejection period; total systolic interval; impedance cardiography; ramp exercise

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The systolic time intervals (STI): the left ventricular ejection time (LVET), pre-ejection period (PEP), total systolic interval (TSI) etc., had been used for the evaluation of the contractility of the myocardium, and/or the diagnosis of cardiovascular disorders. Previously, these parameters had been mainly determined by using the electrocardiogram (ECG), phonocardiogram (PCG) and carotid pulse tracing; however, carotid pulse tracing was often thought to be difficult due to movement artefacts, especially during exercise (Pigott and Spodick 1971; Wolfe et al. 1978). The impedance cardiograph (ICG) that was firstly proposed by Kubicek et al. (1966, 1970) for the measurement of stroke volume (SV) and cardiac output (Q̇), had been also used for the measurement of LVET, PEP and other parameters relating to the cardiac cycle (Lababidi et al. 1970; Máttar et al. 1991). However, controversy remains on how to determine these parameters from the ICG. For example, Kubicek et al. (1966) had first introduced a method in determining the LVET from the zero-crossing or a deflection point just preceding the maximum negative peak (dZ/dt_{min}) of the dZ/dt waveform (B-point), to the positive peak of the dZ/dt waveform in the region of the second heart sounds (X-point). Thereafter, they revised the algorithm for the determination of B-point from the zero crossing point to the 15% response point of the dZ/dt_{min} (Kubicek et al. 1970). Although the reason for this modification has not been clarified yet, the latter criterion might be introduced to avoid misjudgements due to noise around the base line rather than physiological means. Furthermore, as mentioned by Kubicek et al. (1966), a small notch preceding the dZ/dt_{min} would be a lead for the B-point, but its detection might bring about many misjudgements due to noise around the base line rather than physiological means. Therefore, it may be summarized that the determination of the aortic valve opening by using the ICG is still obscure.

Moreover, the thoracic electrical impedance includes the signals derived not only by cardiovascular movements, but also by respiration, body movement, or other sources. These various origins of the impedance signals may bring about misjudgements for detecting B-, X- and/or other points. Several types of filters: a high pass filter and a band pass filter had been used for the elimination of noises outside of the known frequency band. However, the frequency band of respiration and body movements sometimes overlapped with the frequency band derived by cardiovascular events. Barros et al. (1995) proposed an adaptive filter that can selectively pass the frequency components synchronous with R-R interval in ECG. This technique may allow the elimination of noises and reduce inaccuracies of the inflection points in the dZ/dt waveform (Ono et al. 2004). In the present study, we firstly aimed, therefore, to examine the reliability for the determination of the so-called B- and X-points by different criteria by using an adaptive filter and detection algorithms on the dZ/dt waveform.

However, the changes of LVET and PEP against heart rate (HR) during exercise had been evaluated by different protocols such as carotid pulse tracing, echo ultrasound or ICG, showing an inverse linear relationship between them (Van der Hoeven et al. 1977; Miyamoto et al. 1983). These relationships were obtained only for a small number of subjects and/or small experimental situations, probably due to the methodological limitation. The technique noted above permits a continuous and beat-to-beat measurement of the
LVET, PEP, and TSI even during exercise. The second purpose of the present study was to evaluate the beat-to-beat relationships between LVET and HR, between PEP and HR, and between TSI and HR during a ramp bicycle exercise, from unloaded to maximal intensity on different subjects.

**Materials and Methods**

**Subjects**

After obtaining their informed consent, six healthy male students voluntarily participated in this study. Average values and standard deviations (±SD) of age, height and body weight were 20.5±1.4 years, 170.8±2.3 cm, and 62.8±6.1 kg, respectively. Each subject had been familiarized with all measurement devices and the experimental procedure before the study. The Human Subjects Review Committee at the Toyohashi University of Technology approved all experimental procedures.

**Experimental procedure**

The subjects underwent a ramp bicycle exercise up to a maximum intensity level using an automated electro-magnetic bicycle ergometer designed in our laboratory (Ito et al. 1996). The ergometer system consisted of a bicycle ergometer (Aerobike300, Combi, Tokyo), a photo-sensor, a torque meter, a power supply and a microcomputer. The power output of the ergometer was controlled by the PID feedback control theory with a frequency of 50 Hz. Following an unloaded pedalling on the ergometer for 2 minutes, the power output was automatically increased in a linear fashion by an incremental rate of 20 W min⁻¹.

During an unloaded and a ramp exercise, an electrocardiogram (ECG), a phonocardiogram (PCG) and an impedance cardiograph (ICG) were continuously measured. The ECG and PCG were obtained with a standard bipolar lead from the chest using a bioamplifier (AC-601G, Nihon Kohden, Tokyo) and a PCG unit (AS-601H, Nihon Kohden), respectively. The transthoracic impedance was also measured using a standard ICG unit (AI-601G, Nihon Kohden) with disposable spot electrodes. Four electrically connected spot electrodes were placed around the base of the neck and four electrodes placed around the thorax at the level of the xiphoid as the inner voltage electrodes. An upper current electrode was set at the central forehead and another lower current one at the lateral side of the lower ribcage. The impedance signals: basic thoracic impedance (Z₀) and its relative change (ΔZ), ECG and PCG were continuously recorded on a digital data recorder (MD-120TE, TEAC, Tokyo) at a sampling frequency of 200 Hz for subsequent analyses.

**Data analyses**

The dZ/dt signal was obtained from the first differentiation of the ΔZ, and then the adaptive filter, the scaled Fourier linear combiner (SFLC), was applied. The algorithm of the SFLC was based on the hypothesis that the required signal can be expressed as a sum of sine and cosine curves in a Fourier series in a period of T determined as each R-R interval in ECG. The basic algorithm of this filter had been previously reported by Barros et al. (1995).

In the ECG waveform, the positions of the onset of the Q wave, R spike, and the end of the T wave were determined by using a low pass filter and a peak detection algorithm. The HR was calculated from each R-R interval (RRI). For the detection of the B-point, we used three criteria. Firstly, the zero crossing point of the dZ/dt waveform just before the dZ/dtₘᵢₙ (Bₒ indicated as 1 in Fig. 1). Secondly, the 15% response point of the dZ/dtₘᵢₙ (B₁₅% indicated as 3 in Fig. 1) from the baseline, and thirdly, a new algorithm for the determination of the intersection between the zero-line and the regression line calculated from the 40% to 80% data of the descending curve of the dZ/dtₘᵢₙ (Bnew indicated as 2 in Fig. 1). The Bnew algorithm was produced in order to search a notch located between zero and the dZ/dtₘᵢₙ in the waveform. The X-point was separately determined as the peak of the upward deflection of the dZ/dt waveform located around the end of T wave.
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(XICG), and the onset of the second heart sound in the rectified and filtered PCG waveform (XPCG). The time intervals from Q to B-point, from B- to X-points, and from Q to X-point were determined as the preejection period (PEP), left ventricular ejection time (LVET) and total systolic interval (TSI), respectively. Time resolution of each variable was every 5 milliseconds depending on a sampling frequency.

Statistical analysis

The beat-to-beat values of the STI, determined using different criteria, were compared with each other by means of the paired t-test and the Wilcoxon signed-ranks test. The statistical significance was set at 0.05. The relationships be-

Fig. 1. Schematic presentation for the determination of the B-point using different criteria: 1) the zero crossing point of the dZ/dt waveform just before the dZ/dt_{min} (B_{zero}), 2) the 15% response point of the dZ/dt_{min} (B_{15%}), and 3) a new algorithm for detecting the cross-point between the 0-line and the regression line which was calculated from the 40 to 80% response of the descending limb of the dZ/dt_{min} (B_{new}). The horizontal line shows the zero value of the dZ/dt.

Fig. 2. A typical example of A: ECG, B: dZ/dt and C: PCG waveforms before and after the treatment of the SFLC. As shown in the figure, it seems in the filtered dZ/dt waveform that a small vibration and a slow wave around the base line could be mostly eliminated by the SFLC. Furthermore, the rectified and filtered PCG waveform could also be detected at the onset of the second heart sound.
between HR and PEP, between HR and LVET, and between HR and TSI were fitted by a linear equation and an exponential equation using the least squares method. A coefficient of determination ($r^2$) was also calculated as the degree of conformity of the fitted curve.

**RESULTS**

Fig. 2 shows a typical example of the data for ECG, $dZ/dt$ and PCG waveforms with and without filter. As in the figure, it seems in the filtered $dZ/dt$ waveform that small vibrations could be mostly eliminated and the inflection points could be clearly determined through filtering compared to the raw $dZ/dt$ waveform. Moreover, the rectified and filtered PCG waveform also made it possible to ascertain the onset of the second heart sound more easily.

Fig. 3 indicates typical patterns of the $dZ/dt$ waveform on the determination of the B-point. The patterns could be roughly divided into three by the appearance or location of a notch preceding the $dZ/dt_{\min}$. In the left panel a clear notch did not appear from zero to the $dZ/dt_{\min}$, and in this case, the B-points usually appeared in the order of $B_{\text{zero}}$, $B_{\text{new}}$, and $B_{15\%}$ (Pattern A). In the middle, the notch was located between the zero-line and the 15% response of the $dZ/dt_{\min}$. In this case, the B-points were detected in the order of $B_{\text{zero}}$, $B_{\text{new}}$, and $B_{15\%}$ (Pattern B). In the right panel, the notch appeared below the 15% response of the $dZ/dt_{\min}$. In this case, the B-point was generally detected in the order of $B_{\text{zero}}$, $B_{15\%}$ and $B_{\text{new}}$ (Pattern C). The patterns of the $dZ/dt$ waveform varied among subjects and the phase of exercise, but it came together in the form of pattern A during mild to heavy exercise because a clear notch tended to disappear in this period.

Time differences among PEP determined by different criteria for B-point are shown in Fig. 4. Data indicated the values of (PEP$_{\text{zero}}$–PEP$_{\text{new}}$) and (PEP$_{15\%}$–PEP$_{\text{new}}$). The differences in (PEP$_{15\%}$–PEP$_{\text{new}}$) were almost within ± 5 milliseconds in four subjects (HA, OO, YA and YO), but were much more varied in two subjects (OH and TN). These differences between PEP$_{15\%}$ and PEP$_{\text{new}}$ were significant ($p<0.001$) in all subjects. The changes in (PEP$_{\text{zero}}$–PEP$_{\text{new}}$) were generally larger than those in (PEP$_{15\%}$–PEP$_{\text{new}}$), and significant differences were seen between PEP$_{15\%}$ and PEP$_{\text{new}}$ in all subjects.

Fig. 5 shows the differences between the TSI$_{\text{ICG}}$ calculated from Q to X$_{\text{ICG}}$ and the TSI$_{\text{PCG}}$ from Q to X$_{\text{PCG}}$ in each subject. The differences between TSI$_{\text{ICG}}$ and TSI$_{\text{PCG}}$ were varied among subjects: the mean values of TSI$_{\text{ICG}}$ were significantly shorter than those of TSI$_{\text{PCG}}$ in five of six subjects, but longer in one subject.

Time courses of the changes in RRI, TSI estimated from Q to X$_{\text{ICG}}$, LVET measured from B$_{\text{new}}$ to X$_{\text{ICG}}$, and PEP$_{\text{new}}$ from a sitting rest for 30 seconds to unloaded exercise for 2 minutes and followed by a ramp exercise on six subjects, are illustrated in Fig. 6. All these parameters...
Fig. 4. Time courses of the PEP measured using different criteria on the six subjects. Data indicates the difference between PEP_{zero} to PEP_{new} (a solid line) and between PEP_{15%} and PEP_{new} (a dotted line). The mean values and ±s.d. of the (PEP_{zero}−PEP_{new}) and the (PEP_{15%}−PEP_{new}) in each subject are as follows. A: Subj. HA, PEP_{zero}−PEP_{new}: −4.94±2.46 milliseconds, p<0.001, and PEP_{15%}−PEP_{new}: 0.50±2.26 milliseconds, p<0.001. B: Subj. OH, PEP_{zero}−PEP_{new}: −17.62±18.14 milliseconds, p<0.001, and PEP_{15%}−PEP_{new}: −4.56±7.71 milliseconds, p<0.001. C: Subj. OO, PEP_{zero}−PEP_{new}: −3.54±2.93 milliseconds, p<0.001, and PEP_{15%}−PEP_{new}: 1.26±2.20 milliseconds, p<0.001. D: Subj. TN, PEP_{zero}−PEP_{new}: −22.46±11.69 milliseconds, p<0.001, and PEP_{15%}−PEP_{new}: −5.49±5.59 milliseconds, p<0.001. E: Subj. YA, PEP_{zero}−PEP_{new}: −9.92±7.76 milliseconds, p<0.001, and PEP_{15%}−PEP_{new}: 0.84±3.13 milliseconds, p<0.001. F: Subj. YO, PEP_{zero}−PEP_{new}: −4.00±3.13 milliseconds, p<0.001, and PEP_{15%}−PEP_{new}: 1.14±2.14 milliseconds, p<0.001. All these differences are statistically significant both by the paired t-test and the Wilcoxon signed-ranks test.
gradually decreased according to the increase of exercise intensity. The RRI seemed to fluctuate largely, from rest to light intensity of exercise, but it dropped under moderate and strenuous exercise. The pattern of changes in the TSI and LVET were quite similar to each other, but the pattern of the PEP clearly differed from those in the TSI and LVET.

Fig. 7 illustrates the beat-to-beat changes of the TSI, LVET, and PEP against the changes of HR and the fitted curves using an exponential equation among them. All data are the same as

Fig. 5. Beat-to-beat differences between the total systolic intervals detected by ICG (TSI\textsubscript{ICG}) and by PCG (TSI\textsubscript{PCG}) from rest to maximal exercise in each subject. The mean value and ±S.D. in each subject are as follows. A: Subj. HA, TSI\textsubscript{ICG}−TSI\textsubscript{PCG}: −1.54±6.88 milliseconds, \(p<0.001\). B: Subj. OH, TSI\textsubscript{ICG}−TSI\textsubscript{PCG}: −4.92±7.26 milliseconds, \(p<0.001\). C: Subj. OO, TSI\textsubscript{ICG}−TSI\textsubscript{PCG}: −8.90±4.51 milliseconds, \(p<0.001\). D: Subj. TN, TSI\textsubscript{ICG}−TSI\textsubscript{PCG}: −4.44±6.18 milliseconds, \(p<0.001\). E: Subj. YA, TSI\textsubscript{ICG}−TSI\textsubscript{PCG}: 4.81±8.77 milliseconds, \(p<0.001\). F: Subj. YO, TSI\textsubscript{ICG}−TSI\textsubscript{PCG}: −6.47±4.92 milliseconds, \(p<0.001\). All these differences are statistically significant both by the paired \(t\)-test and the Wilcoxon signed-ranks test.
in Fig. 6. The mean values of the coefficient of determination ($r^2$) regressed by an exponential equation between HR and TSI, between HR and LVET and between HR and PEP were 0.966, 0.914 and 0.858; these were higher than those regressed by a linear equation: 0.963, 0.912 and 0.839, respectively. However, a significant difference was not observed between them. Furthermore, a wide variation was observed between HR and STI especially in the lower range of the HR.

**DISCUSSION**

To our knowledge there are few studies that show the beat-to-beat changes of the STI (such as the LVET and PEP), with respect to the changes of HR (from rest to maximal intensity), during ramp exercise. Perhaps this is due to methodological difficulties. In the present study, we demonstrated the beat-to-beat changes of the STI from rest to maximal exercise by using an adaptive filtering technique and algorithms for the B-
Fig. 7. The changes of the PEP, LVET and TSI against HR from rest to maximal exercise. The exponential equations and the coefficients of determination of the fitted curve in each subject are as follows. A: Subj. HA, PEP: $y=141.3e^{-0.0063x}$, $r^2=0.911$, LVET: $y=356.8e^{-0.0041x}$, $r^2=0.963$, TSI: $y=494.9e^{-0.0046x}$, $r^2=0.984$. B: Subj. OH, PEP: $y=165.3e^{-0.0114x}$, $r^2=0.877$, LVET: $y=332.9e^{-0.0026x}$, $r^2=0.788$, TSI: $y=470.4e^{-0.0046x}$, $r=0.935$. C: Subj. OO, PEP: $y=253.2e^{-0.0108x}$, $r^2=0.939$, LVET: $y=326.7e^{-0.0055x}$, $r^2=0.927$, TSI: $y=543.6e^{-0.0054x}$, $r^2=0.991$. D: Subj. TN, PEP: $y=114.5e^{-0.0063x}$, $r^2=0.727$, LVET: $y=385.3e^{-0.0053x}$, $r^2=0.936$, TSI: $y=501.5e^{-0.0057x}$, $r^2=0.957$. E: Subj. YA, PEP: $y=113.2e^{-0.0033x}$, $r^2=0.772$, LVET: $y=316.1e^{-0.0032x}$, $r^2=0.905$, TSI: $y=426.1e^{-0.0037x}$, $r^2=0.954$. F: Subj. YO, PEP: $y=162.8e^{-0.0072x}$, $r^2=0.924$, LVET: $y=285.3e^{-0.0033x}$, $r^2=0.952$, TSI: $y=437.4e^{-0.0043x}$, $r^2=0.975$. 
and X-points detection in the dZ/dt waveform, and eventually clarified a gentle curvilinear relationship between HR and STI.

Filtering performance

As shown in Fig. 2, the raw dZ/dt waveform is noisy and it is often difficult to detect the inflection points of the waveform especially during exercise. In the present study, we used an adaptive filter, a scaled Fourier linear combiner (SFLC) to eliminate the noises (Barros et al. 1995; Ono et al. 2004). This filter was designed to eliminate noises asynchronous with the frequency of R-R interval. It was found, that by using the SFLC, the waveform of the dZ/dt became clear and the inflection points of the waveform could be determined more easily and precisely. Furthermore, the application of this technique also made it possible to determine the onset of the second heart sound in PCG more easily. It suggests from the above results that the SFLC must be a superior tool for the elimination of noises and thereby for the determination of the deflection points in the dZ/dt and PCG waveforms.

Validity for the determination of B- and X-points from the dZ/dt waveform

When evaluating the STI from ICG waveform, controversy remains especially on how to determine the B-point in the ICG. Kubicek et al. (1966) first introduced the determination of the B-point, which corresponded to the opening of the aortic valve, as the crossing point of the dZ/dt waveform with the base line (Bzero). Thereafter, they revised this criterion to the 15% response point (B15%) of the negative peak of the dZ/dt waveform (dZ/dtmin) from the baseline instead of the Bzero, probably in order to avoid any misinterpretations from the noises around the base line (Kubicek et al. 1970). Up to now, most of the studies attempting to determine the B-point by ICG have been via the Bzero method, and little research has been conducted employing the B15% method (Miyamoto et al. 1981, 1988). Alternatively, Kubicek et al. (1966) noticed in their first study that a small notch preceding the dZ/dtmin would be the true B-point. However, this small notch might be ambiguous or disappear in the dZ/dt waveform especially during exercise (Sherwood et al. 1990; Fahrenberg et al. 1997). Wang et al. (1995) proposed the time-frequency distribution technique to determine the B- and X-points which involved finding a peak or inflexion point of the waveform, but this technique was not widely accepted because of the methodological difficulties. Due to the above reasons, the criterion for the detection of the notch might not be used for the measurement of the B-point. In the present study, we have proposed a new algorithm whose purpose is to detect a notch by using an extrapolation technique on the downslope of the dZ/dtmin from 40 to 80%. We firstly attempted to examine the effect of different criteria: Bzero B15% and Bnew methods on the determination of PEP and relating problems.

Present results showed that the order of appearance of each B-point, detected by different criteria, varied depending on the shape of the dZ/dt waveform, and the appearance of each B-point could be divided into three typical patterns as illustrated in Fig. 3. In pattern A, each B-point appeared closely and the time differences were almost within ± 5 milliseconds (Subjects HA, OO and YO). In pattern B, the B15% and Bnew appeared closely as in the pattern A, but the Bzero sometimes differed largely from the other ones as observed in the subjects TN, YA and OH. In these subjects, the Bzero sometimes appeared preceding the Q-wave, and this might be unreasonable if one takes into consideration the physiological mechanism of the aortic valve opening, followed by the depolarization of the left ventricle. In pattern C, which was observed in subjects TN and OH, large differences ranging from 10 to 20 milliseconds were often observed between B15% and Bnew. From the above results it can be summarized that the conventional methods often provided unstable data due to the appearance or location of a notch, but the new method proposed here could provide more stable data as opposed to the conventional
methods. This is also proved indirectly by the smooth change of the PEP during exercise as shown in Fig. 6. However, in this present study, we were unable to identify the location of the true B-point that coincided with the aortic valve opening because we did not directly measure the aortic valve movement. Furthermore, we used the linear extrapolation technique on the data from the 40 to 80% response of the $dZ/dt_{\text{min}}$ based on the hypothesis that $dZ/dt$ waveform changed approximately in a linear fashion for this portion as in Fig. 1, and the notch did not exceed the 40% response of the $dZ/dt_{\text{min}}$. However, we could see a few exceptions in the results because the descending limb of the $dZ/dt_{\text{min}}$ from 40 to 80% did show a curvilinear change rather than a linear fashion. Further improvements, therefore, should be required for a more accurate and valid determination of the B-point in the ICG.

Previous studies have shown that the X-point corresponding to the closure of the aortic valve was accredited the maximum positive peak of the $dZ/dt$ waveform following the $dZ/dt_{\text{min}}$ ($X_{\text{ICG}}$). This coincides with the onset of the second heart sound in PCG ($X_{\text{PCG}}$) (Kubicek et al. 1970; Lababidi et al. 1970; Miles and Gotshall 1989; Ono et al. 2004). However, the coincidence between $X_{\text{ICG}}$ and $X_{\text{PCG}}$ has not been investigated, especially during exercise, because PCG waveform is also noisy and often ambiguous when identifying the $X_{\text{PCG}}$ similar to that in the $dZ/dt$ waveform. In the present study, we applied the same filtering technique on the rectified PCG waveform and, because of this, the $X_{\text{PCG}}$ could be detected more clearly (Fig. 2). As in Fig. 6, the time differences between TSI, measured by the $X_{\text{ICG}}$ and $X_{\text{PCG}}$, were mostly within $\pm$ 20 milliseconds, but a significant difference was found in all subjects. In the five subjects: OH, OO, TN, HA and YO, the appearance of the $X_{\text{ICG}}$ was significantly faster than that of $X_{\text{PCG}}$, and in contrast to this, the $X_{\text{ICG}}$ was significantly delayed compared to the $X_{\text{PCG}}$ in the subject YA. Although the real reasons for this discrepancy cannot be resolved here, some possible reasons can be put forward. Firstly, the misjudgment of the $X_{\text{ICG}}$ may be of concern because the $dZ/dt$ waveform corresponding to the end of T-wave in the ECG sometimes showed a near plateau or made double peaks rather than making a clear peak. In these cases, inaccuracies might have occurred. Secondly, previous studies that showed a good agreement between $X_{\text{ICG}}$ and $X_{\text{PCG}}$, had measured the X-points only for a few beats and only at rest (Lababidi et al. 1970; Miles and Gotshall 1989). The present study here demonstrated that the difference between TSI$_{\text{ICG}}$ and TSI$_{\text{PCG}}$ fluctuated greatly at rest and during low-intensity exercise, but it was inhibited during mild to heavy exercise. It suggests, therefore, that the exercise intensity may modulate the appearance of the X-point. Further experiments will need to be conducted in order to resolve this problem.

**Time courses of RRI, TSI, LVET and PEP from unloaded to ramp exercise**

It has been well demonstrated that the time course of RRI during ramp exercise shows a curvilinear relationship with the increase of work rate or work time. As shown in Fig. 6, the present results also confirmed a curvilinear relationship between RRI and work time. The time courses of the TSI and LVET were similar to each other, but the fluctuation in each variable was much attenuated compared to that in RRI. The PEP seemed to be stable and did not show clear fluctuations.

**Relationships HR versus TSI, PEP and LVET**

A number of studies using different apparatuses including ICG, carotid pulse tracing or echo ultrasound, reported an inverse relationship between HR and STI mainly between HR and LVET (Van der Hoeven et al. 1977; Vanfraechem 1979; Miyamoto et al. 1983; Mátter et al. 1991). However, those relationships were measured only for several degrees of exercise intensity. In the present study, we demonstrated the beat-to-beat relationship between HR and STI from rest to maximal intensity during a ramp exercise, and observed a gentle curvilinear relationship between them. Therefore, an exponential equa-
tion was used to describe the relationship between HR and STI, but insignificant differences in the coefficients of determination \( (r^2) \) between the exponential and linear equations were observed. Therefore, the results obtained by the present study and the previous ones are thought to be essentially similar.

It has been clarified that the relationship between HR and TSI, obtained both at rest and during exercise, are modulated by several factors. These include body posture (Miyamoto et al. 1983; Smith et al. 1989), physical training (Vanhees et al. 1984; Krzemiński et al. 1989), aging and cardiovascular diseases (Van der Hoeven et al. 1977; Máttar et al. 1991; Thomas and Crowther 1993). For example, Miyamoto et al. (1983) reported that the regression line between HR and LVET shifted downward, but the regression line between HR and PEP was shifted upward by the postural change from supine to upright. Krzemiński et al. (1989) noted that endurance training shifted the HR-LVET relationship downward. Van der Hoeven et al. (1977) reported a significant change between HR and STI in patients with coronary insufficiencies compared to healthy individuals. Since it is possible to provide the beat-to-beat changes of the STI and HR, not only at rest but also during heavy exercise, the techniques proposed in the present study may have strong advantages for the evaluation of cardiovascular fitness or the diagnosis of cardiovascular dysfunctions.

**Conclusion**

In conclusion, it became possible to measure the STI on a beat-to-beat basis, not only at rest but also during heavy exercise. This was carried out by using an adaptive filtering technique and detection algorithms for the inflection points of the dZ/dt waveform in an ICG. The present technique may contribute to detailed and precise analyses of the relationships between HR and STI being modulated by aging, endurance training, and the degree of cardiovascular disorders.

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