Relationship between the Initial Systolic Time Interval and RR-interval during an exercise stimulus measured with Impedance Cardiography

Femke Hoekstra¹, Esther Habers¹, Thomas W J Janssen¹³, Rudolf M Verdaasdonk² and Jan H Meijer²

¹ VU University Amsterdam, Faculty of Human Movement Sciences, Amsterdam, the Netherlands
² VU University Medical Center, Dept. of Physics and Medical Technology, Amsterdam, the Netherlands
³ Rehabilitation Center Amsterdam, Amsterdam, the Netherlands

E-mail: jh.meijer@vumc.nl

Abstract. The Initial Systolic Time Interval (ISTI), obtained from the electrocardiogram and impedance cardiogram, is considered to be a measure for the time delay between the electrical and mechanical activity of the heart and reflects an active period of the heart cycle. The relationship between ISTI and the total heart cycle (RR-interval) was studied in three groups of young, healthy volunteers: low, moderately and highly trained subjects. The three groups were exposed to an exercise stimulus on a cycle ergometer with an increasing work load to increase the heart rate. ISTI was decreased with decreasing RR-interval. However, the relative proportion of ISTI, ISTI/RR, was found to increase with decreasing RR-interval. This relationship was found to be inversely proportional. The rate of this increase in ISTI/RR was significantly higher in highly trained subjects. Also, over the whole range of heart rates ISTI was longer in these subjects. It is concluded that ISTI can be used to evaluate cardiac performance during physical exercise non-invasively and in an extramural setting.

1. Introduction

When measuring the electrical impedance of the human thorax, a variation synchronous with the heart activity is observed. The time derivative of this variation is called the Impedance CardioGram (ICG). The ICG-signal represents the mechanical activity of the heart cycle, while the widely used ElectroCardioGram (ECG) represents the electrical activity of the heart cycle. The Initial Systolic Time Interval (ISTI), obtained from simultaneous recordings of the ECG and ICG, can be considered as a measure for the time delay between the electrical and mechanical activity of the heart and reflects an early active period of the heart cycle [1]. Measurement of the ISTI is attractive because it is fast and easy to obtain. Moreover, the ISTI can be measured non-invasively and is not restricted to hospital settings.

The effect of exertion on the ISTI has not been studied explicitly so far. In the present study the relationship between ISTI and RR-interval was investigated by exposing young healthy subjects to an exercise stimulus. The dependence of the relative proportion of ISTI/RR on the RR-interval was studied as well.
Further, it has been reported that long term physical exercise can induce physiological changes of the heart of elite athletes. These adaptations to training can cause an ‘Athlete’s heart’, which is structural and electrical different from a ‘normal’ heart [2]. Abnormalities in the ECG of these athletes are commonly reported [2] and sometimes associated with a pathological condition [3]. It is possible that these physiological changes also lead to differences in ISTI. Therefore, the ISTI-RR relationships were studied in highly, moderately and low trained subjects to detect possible differences between these groups.

2. Methods

2.1. ICG and ECG recordings

ICG recordings were made using the method described by Meijer et al. [1] (see figure 1). A typical example of a simultaneous recording of the ICG and ECG signal is shown in figure 2. The Initial Systolic Time Interval (ISTI) is the time interval between the R-peak in the ECG and C-wave in the ICG signal, which is depicted in the figure.

Figure 1. Electrode configuration: A small electrical current (i) of 0.3 mA r.m.s. (64 kHz) is applied between the outer two electrodes. The inner pair of electrodes measure the subsequent electrical voltage difference (V) over the heart. The Impedance CardioGram (ICG) is obtained from the time course of this voltage signal.

Figure 2. A typical example of simultaneous registration of an Impedance CardioGram (ICG) and an ElectroCardioGram (ECG) (arbitrary units). The Initial Systolic Time Interval (ISTI) is the time interval between the R-peak in the ECG and the C-wave in the ICG signal, which are indicated in the figure.

2.2. Subjects

Twenty young, healthy subjects participated in this study (table 1). The group consisted of 9 males and 11 females with an age (mean ± S.D.) of 21 ± 2 years, a height of 178 ± 10 cm and a body mass of 67 ± 9 kg. Based on the level of exercise, the subject group was divided into three groups: low trained (<4 hrs/wk of exercise, N=7), moderately trained (4 – 10 hrs/wk of exercise, N=7) and highly trained subjects (>10 hrs/wk of exercise, N=6). Most of the highly trained subjects were endurance athletes.

| Age (years)     | 21 ± 2 | 22 ± 3 | 21 ± 1 | 22 ± 3 |
|-----------------|--------|--------|--------|--------|
| Male(m)/Female(f) | 9m/11f | 3m/4f  | 2m/5f  | 4m/2f  |
| Height (cm)     | 178 ± 10 | 173 ± 12 | 176 ± 5 | 186 ± 6 |
| Body mass (kg)  | 67 ± 9 | 64 ± 10 | 65 ± 7 | 72 ± 6 |

Table 1. Subjects’ characteristics (mean ± S.D.). The groups did not differ in gender, age and weight. The highly trained group was significantly (p<0.05) taller than the other two groups.
The moderately trained subjects were recreational or at a regional level active in their sport. The highly trained subjects were active at a national or international level. Unpaired t-tests showed that the groups did not differ in gender, age and body mass. However, the highly trained subjects were significantly taller than the other two groups. The study was approved by the ethics committee of the Faculty of Human Movement Sciences of the VU University Amsterdam. Prior to participation subjects signed an informed consent after being informed about the protocol.

2.3. Procedure
A questionnaire assessed the daily physical activity of the subjects and their participation in sports. Before measurement, the subjects rested in supine position during ten minutes. Subsequently, they performed an exercise test on a cycle ergometer with an increasing work load to increase heart rate. The exercise stimulus consisted of 5 or 6 blocks of 3 minutes cycling with an individually adapted, increasing work load. To prevent disturbances caused by movement, ECG and ICG recordings were made during a one-minute break after each block. During the last block of cycling all subjects exercised with an intensity of at least 80% of the maximal heart rate.

2.4. Analysis
The first 15 cardiac cycles after each block of exercise were used to determine the RR-intervals and the corresponding values of ISTI. Periods with too much noise to determine the ISTI were omitted. The relationship between ISTI and RR-interval was established using linear regression analysis according to equation 1:

\[ \text{ISTI} = a + b \cdot \text{RR} \]  
(1)

The relationship between the ISTI/RR and the RR-interval was observed to be inversely proportional. Equation 2 was used to describe this relationship and to establish the parameters by regression analysis:

\[ \frac{\text{ISTI}}{\text{RR}} = \frac{a}{\text{RR}} + b \]  
(2)

To illustrate differences between the groups at high and low exertion, the individual values of ISTI were calculated from the individual relationships at an RR-interval of 350 ms and 600 ms: ISTI(350) and ISTI(600). Unpaired t-tests were used to detect the differences between the groups in the values of the parameters mentioned above. All statistics was run on SPSS 15.0 for Windows.

3. Results
3.1. ISTI, ISTI/RR and RR-interval
The ISTI decreased significantly in all subjects with a decrease in RR-interval caused by exercise. A typical example of this relationship is shown in figure 3. However, ISTI/RR increases with a decrease in RR-interval. Figure 4 presents a typical example of the relationship between ISTI/RR and RR-interval. No differences were found in the mean values of the coefficients a and b when determined according to equation 1 or 2.

![Figure 3](image1.png)

**Figure 3.** A typical example of the relationship between ISTI and RR-interval. ISTI decreases with decreasing RR-interval caused by exercise.

![Figure 4](image2.png)

**Figure 4.** The same subject as in figure 3. The relative proportion of ISTI (ISTI/RR) increases with decreasing RR-interval.
3.2. Differences between groups
The constant a in the equations 1 and 2 was significantly higher in highly trained subjects than that in the other groups (table 2). No differences between the groups were observed in the coefficients b. Over the whole range of heart rates, ISTI was longer in the highly trained subjects, which is illustrated by significantly higher values for ISTI(350) and ISTI(600) in this group. No differences were found between the low and moderately trained subjects.

Table 2. Mean values (± S.D.) of coefficients a (in s) and b and the mean (± S.D.) ISTI (in ms) at an RR-interval of 350 and 600 ms. The a, ISTI(350) and ISTI(600) were significantly different in highly trained subjects compared with less trained subjects.

| Group  | a (± S.D.) | b (± S.D.) | ISTI(350) (± S.D.) | ISTI(600) (± S.D.) |
|--------|-----------|-----------|-------------------|-------------------|
| low    | 0.06 ± 0.03* | 0.09 ± 0.03 | 90 ± 23*          | 112 ± 20*         |
| moderate | 0.06 ± 0.03* | 0.08 ± 0.02 | 89 ± 23*          | 108 ± 20*         |
| high   | 0.10 ± 0.02 | 0.06 ± 0.04 | 119 ± 14          | 133 ± 14          |

*Significantly different (p<0.05) from highly trained subjects

Consistent with the observed differences in length, significant correlations (p<0.05) were found between the subjects’ height and respectively the coefficients a, ISTI(350) and ISTI(600).

4. Discussion and conclusions
The positive linear relationship between the ISTI and RR-interval demonstrates that with a decrease in the RR-interval, also the ISTI is shortened. The inverse proportional relationship between the ISTI/RR and RR-interval shows that with a decrease in RR-interval, this active phase decreases less than the total cardiac cycle. The observed linear relationship between ISTI and RR-interval is in agreement with Boudoulas et al. [4], who reported linear relationships between the electrical systole versus the heart rate and the electromechanical systole versus the heart rate. Also, it has been reported in early literature that the Preejection Period (PEP), a parameter analogous to the ISTI [1], was shortened with increased heart rate [5].

The coefficients a and the values of ISTI(350) and ISTI(600) are significantly higher in highly trained subjects than in the other groups, indicating that ISTI is longer in this highly trained group at the same length of the cardiac cycle, and that ISTI acquires a longer proportion of this cycle when the cardiac cycle shortens. This finding is consistent with the results of Fardy et al. [5]. They reported that during exercise the PEP was significantly longer in former athletes compared to non-athletes. Also, during exercise the PEP was significantly longer in subjects who were more physical active [5]. However, since the highly trained subjects were taller than the other two groups, it cannot be excluded that the observed difference is influenced by a difference in height.

The longer ISTI and the higher rate of increase of ISTI/RR in highly trained subjects indicate that the time delay between electrical and mechanical activity is longer in highly trained subjects and responds differently to an exercise stimulus as compared to less trained subjects. This may reflect a more efficient use of the heart muscle. Further research is necessary to elucidate these observations. It can be concluded that the ISTI is an attractive measure that can be used to evaluate cardiac performance during physical exercise non-invasively and in an extramural setting. The measurement can be performed fast and easily, not only in sport settings, but also in clinical applications.

References
[1] Meijer J H, Boesveldt S, Elbertse E and Berendse HW 2008 Physiol. Meas. 29 S383-S391
[2] Fagard R 2003 Heart 89 1455-1461
[3] Lauschk J, Maisch B 2009 Clin. Res. Cardioiol. 98 80-88
[4] Boudoulas H, Geleris P, Lewis R P and Rittgers S E 1981 Chest 80 613-617
[5] Fardy P S, Maresh C M and Abbott R D 1976 Med Sci Sports 8 26-30