Dynamic response of the Initial Systolic Time Interval to a breathing stimulus measured with impedance cardiography

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Dynamic Response of the Initial Systolic Time Interval to a Breathing Stimulus measured with Impedance Cardiography

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Abstract. The Initial Systolic Time Interval (ISTI) is a measure for the time delay between the electrical and mechanical activity of the heart. The present study reports about the dynamic response of ISTI to a Valsalva manoeuvre. This response was investigated in 22 young healthy volunteers, having different levels of training in sports. The time course of the ISTI during the Valsalva manoeuvre was found to follow a distinct pattern and to be analogous to the course of the Pre-Ejection Period (PEP), also obtained from ECG and ICG signals, reported earlier. The recordings show a definite influence of the Frank-Starling mechanism and are to some extent consistent with reports on the time course of sympathetic activation. The highly trained subjects showed an ISTI that was systematically longer at all moments of the manoeuvre.

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). During the last decades several studies have demonstrated that the *amplitude* of the ICG-signal is too complicated to make a simple physiological model interpretation as cardiac stroke volume [1]. An interesting aspect of the ICG-signal, however, can be found in the *time relationships*, especially when this signal is compared to the Electro CardioGram (ECG). Regardless of the multiple sources of the signal, the ICG reflects the mechanical aspects of the cardiac cycle [2], while the ECG reflects the electrical aspects of the cardiac activity. Therefore, by recording both signals simultaneously, the time difference between electrical and mechanical events in the cardiac cycle can be evaluated in various (patho-) physiological conditions.

The Initial Systolic Time Interval (ISTI), obtained by simultaneous recordings of the ECG and the ICG, has been proposed as a measure for the time delay between the electrical and mechanical activation of the heart [3]. The use of the ISTI in clinical and other diagnostics is attractive because the registration is inexpensive, fast and easy. The measurements are non-invasive, form no burden to the subjects and are not restricted to a hospital environment. However, so far little is known about the behaviour of the ISTI under various circumstances. Theoretically, the ISTI depends on three factors: the preload of the heart by way of the Frank-Starling mechanism, the autonomic nervous control, and the afterload of the heart caused by the peripheral resistance. There is a need for observational research to reveal the behaviour of the ISTI under different circumstances. The present study reports about the dynamic response of ISTI to a Valsalva manoeuvre, which is used in clinical practice to provide measures of cardiovascular autonomic nervous function [4]. In the present study, this response of ISTI to a Valsalva manoeuvre was investigated in a group of 22 young, healthy volunteers, consisting of individuals who were trained at various levels in sports.

2. Methods and subjects

2.1. ICG and ECG signal recordings

ICG recordings were made using a four-electrode system on the left side of the body (figure 1). The outer two electrodes applied a small electrical current through the thorax. The inner two electrodes continuously measured the subsequent electrical voltage difference over the heart, from which the impedance was calculated. The measurement was described in detail by Meijer et al. [3]. The ECG signal was derived simultaneously from the two inner electrodes.

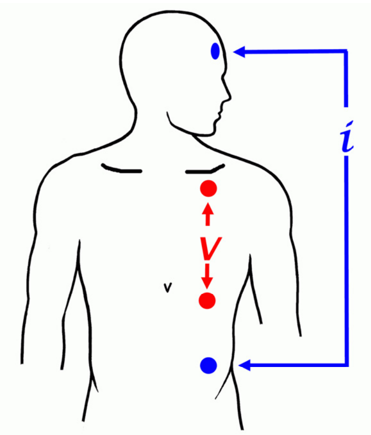

Figure 1. Electrode configuration: A small AC current (0.3 mA, 64 kHz) is applied to the thorax by means of the two outer electrodes. The two inner electrodes measure the subsequent electrical voltage difference over the heart. The impedance recording is obtained from the time course of this voltage signal. The ECG-signal is obtained from the two inner electrodes.

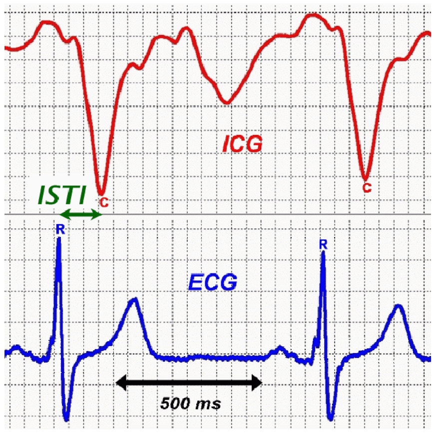

Figure 2. A typical example of simultaneous registration of an Impedance CardioGram (ICG) and an ElectroCardioGram (ECG) (arbitrary units). The marker points R in the ECG and C in the ICG are indicated. From these points the Initial Systolic Time Interval (*ISTI*) is determined, which can be considered as a measure of the time lag between the electrical and mechanical activity of the heart.

Figure 2 shows a typical example of a simultaneous recording of an ICG and an ECG. The ICG-signal is the first time-derivative of the impedance variations across the heart. The R- and C- points, which are used for the determination of the Initial Systolic Time Interval (ISTI), are indicated.

2.2. Subjects

Twenty-two young healthy volunteers (11 males and 11 females), with an age (mean ± s.d.) of 21 ± 2 years (range 19-28 yrs), a height of 180 ± 10 cm (range 158-197 cm) and a weight 68 ± 8 kg (range 50-81 kg) participated in this study. Subjects using medication were excluded from the study, which was approved by the Ethics Committee of the Faculty of Human Movement Sciences of the VU University Amsterdam. All subjects gave informed consent to participate in the test. Based upon their level of training, the group was stratified in three subgroups: highly active sportive (>10 hrs/wk of exercise , N=7) moderately active (4-10 hrs/wk of exercise, N=7) and low active subjects (<4 hrs/wk of exercise , N=8).

2.3. Procedure
After ten minutes of supine rest, the manoeuvre was performed in a sitting position at an expiratory pressure of 40 mmHg during 20s. An analogue manometer provided visual feedback to the subjects. Closure of the glottis was prevented by a small leak in the mouthpiece. ECG and ICG recordings were made from at least 20s before, during and until at least 30s after the manoeuvre. From these recordings the RR-interval and ISTI were calculated off-line and plotted against time.

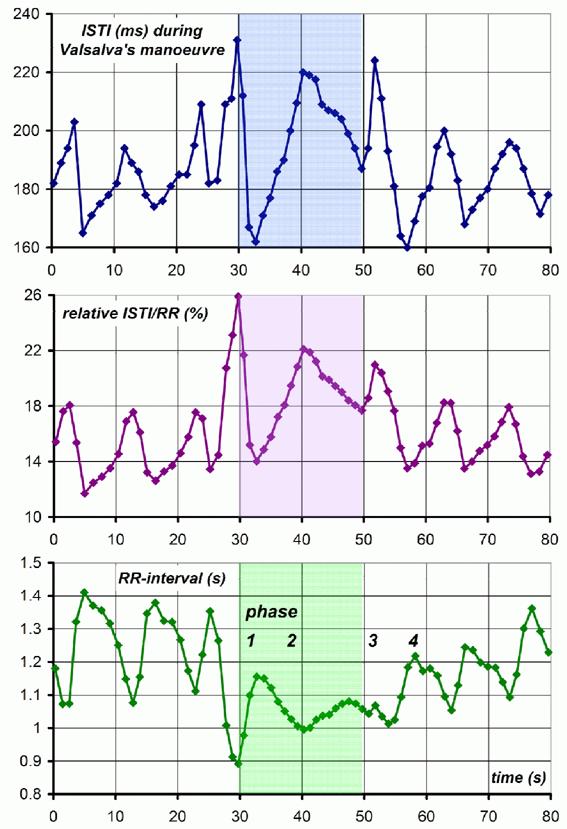

Figure 3. A typical example of the time course of the ISTI (top graph) and the RR-interval (bottom graph) during a Valsalva manoeuvre. The points represent the values of one heart beat and are plotted on the moment of the first R-top in the ECG of a cycle. The time course of ISTI/RR, which represents the proportion of RR occupied by ISTI, is shown in the middle. The successive phases of the Valsalva's manoeuvre are indicated in the lower graph. Before the manoeuvre, the ISTI showed a pattern synchronous with breathing. At the onset of the manoeuvre, there frequently was an increase in ISTI. In phase 1 a sharp decrease in ISTI occurred in all of the subjects. In early phase 2 the ISTI increased in all of the subjects, up to or above the pre-Valsalva level, followed by a decrease in late phase 2. At the relief of pressure, in phase 3, there was a sharp decrease in ISTI, frequently preceded by a sharp increase. In phase 4 no specific dissimilarity in the course of ISTI with the pre-Valsalva period was observed.

3. Results
The time course of the parameters during the Valsalva manoeuvre is described in terms of the standard phases 1 to 4 [5, 6, 7]. A typical example of the time course of the ISTI and the RR-interval is shown in figure 3. In the middle the relative proportion of ISTI, ISTI/RR is expressed as a percentage of the RR-interval. The specific observations are mentioned in the caption of the figure. Based on these observations, five reference moments were selected that were present in the course of the ISTI in each subject: the onset, the sharp minimum in phase 1, the maximum in phase 2a, the minimum in phase 2b and the minimum in phase 3. The mean value (values ± S.D.) of the ISTI was calculated in each group of subjects and is presented in table 1.

Table 1. Mean ISTI (± S.D.) (ms) at five reference moments during the manoeuvre in the three groups of subjects. All maximum values differed from the minimum values in each group (all $p < 0.005$). The mean ISTI of the highly trained subjects was longer than that in the other two groups at all reference moments (all $p < 0.025$).

training level group	onset	minimum phase 1	maximum phase 2a	minimum phase 2b	minimum phase 3	N
low	146 ± 13	108 ± 19	143 ± 16	112 ± 20	116 ± 21	7
moderate	142 ± 13	102 ± 15	139 ± 10	115 ± 17	104 ± 17	7
high	184 ± 25	141 ± 26	187 ± 22	157 ± 28	151 ± 37	8

All minimum values of ISTI differed significantly from the maximum values in each group of subjects (paired t-test, all $p < 0.005$). The mean of ISTI in the highly trained group was significantly longer than that in the other two groups at all reference moments (unpaired t-test, all $p < 0.025$). No significant difference was found between the low and moderately trained groups at any of the reference moments (unpaired t-test, all $p > 0.1$).

4. Discussion and conclusions

The time course of the ISTI before and after the Valsalva manoeuvre showed a cyclic pattern, originating from breathing. It is concluded that also the maxima of ISTI at the onset and just after the Valsalva manoeuvre, present in most subjects, are the consequences of taking a breath. Variations in these maxima are thought to be due to variations in the depth of the breath. Very significant is the sharp decrease in ISTI in phase 1. This occurs within 1-2 heartbeats after the onset of the Valsalva's manoeuvre. This response is too fast to originate from a sympathetic influence. It is the consequence of an extra volume of blood that is pushed out of the lungs towards the heart by the high pressure inside the thorax. This clearly demonstrates the influence of the Frank-Starling mechanism on the ISTI. The cyclic breathing pattern before and after the manoeuvre can be attributed to the same mechanism. The sharp decrease in ISTI at the end of phase 3/early phase 4 can also be attributed to the increased preload of the heart originating from the decrease in pressure inside the thorax, although sympathetic influence cannot be excluded. It coincides with a period of high sympathetic activity [5, 6, 7]. The decrease of ISTI in phase 2b cannot be attributed to preload, because of the low venous return in this phase. It corresponds with a high level of sympathetic activity in this phase [5, 6, 7]. Therefore, ISTI is influenced by at least two factors: preload and sympathetic control.

The time course of the ISTI during the Valsalva manoeuvre was similar to the course of the Pre-Ejection Period (PEP), also obtained from the ICG and ECG, reported by Ermishkin et al. [8]. The course of the PEP showed a comparable pattern of maxima and minima. This means that PEP and ISTI are expected to measure similar (patho-)physiological factors. The only difference observed in this study, is that ISTI was not systematically shorter in phase 4 than during the pre-Valsalva period as was reported for the PEP [8]. Measurement of the PEP has a disadvantage that it is based on points in the recordings (Q- and B-points) that are difficult to trace and that are strongly susceptible to noise, especially in a hospital environment. This makes automated processing of the PEP almost impossible. Recording of the ISTI is considered to be a good alternative.

The long ISTI observed in highly trained subjects during the whole manoeuvre demonstrates a difference in functioning of the heart in these subjects. Further research is needed to elucidate the significance of this observation.

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