Prediction and monitoring of fluid responsiveness after coronary bypass surgery using the Initial Systolic Time Interval: Preliminary Results

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Abstract. The objective of the study is to develop a non-invasive method to optimize the assessment of cardiac preload and therapeutic fluid administration after coronary artery bypass surgery. Previous studies have reported that the pre-ejection period (PEP), obtained from the electro-cardiogram (ECG) and from the invasively measured arterial pressure P_a, can be used for this assessment as it is dependent on the cardiac preload. The Initial Systolic Time Interval (ISTI), obtained non-invasively by simultaneous measurement of the Electro-CardioGram (ECG) and Impedance CardioGram (ICG), is expected to depend on the cardiac preload as well. 16 patients, admitted to the Intensive Care Unit after coronary artery bypass surgery and presumably hypovolaemic, were measured during administration of 2x250 ml of an isosmotic colloidal fluid solution. The parameters PEP and ISTI were determined before and after fluid administration. Preliminary results show significant relationships between ISTI and CO and between changes in both of these variables before and after fluid administration.

1. Introduction

The objective of this pilot-study is to investigate whether the Initial Systolic Time Interval (ISTI) has the potential to be used as a non-invasive measure to optimize the assessment of cardiac preload and therapeutic volume expansion after coronary artery bypass surgery. Intravenous fluid administration is accepted universally as a treatment for hypotension after cardiac surgery. The accuracy of indices, used to assess preload and predict fluid responsiveness has been questioned [1]. Previous studies have reported that the pre-ejection period (PEP), obtained from the ECG and the intravenously measured arterial pressure P_a, can be used for this assessment as it is dependent on the cardiac preload [2, 3]. The PEP is also regarded as a measure for the time delay between the electrical and mechanical activation of the heart. The Initial Systolic Time Interval (ISTI), obtained non-invasively by simultaneous measurement of the ECG and the Impedance CardioGram (ICG) has been reported to be related to the PEP and proposed as an alternative [4]. Therefore, it is expected to depend on the cardiac preload as well. The registration of ISTI is inexpensive, fast, and easy which makes its use in diagnostics attractive, in clinic as well as in an extramural setting. The measurements are non-invasive and form no burden to the patients. The present study investigates whether the ISTI can be used to predict
responsiveness to fluid administration in patients admitted to the intensive care unit after coronary artery bypass surgery, by comparing ISTI and PEP with the cardiac output (CO) measured by thermodilution.

2. Methods and patients
2.1. ICG and ECG signal registration
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 (0.3 mA r.m.s., 64 kHz) 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 has been described in detail by Meijer et al. [4]. The ECG signal, used for the determination of ISTI, 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. From the time course of this voltage signal the impedance signal is obtained.

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.

The pre-ejection period (PEP), the time from the onset of ventricular depolarization to the beginning of left ventricular ejection, was obtained by simultaneous ECG recording and arterial pressure wave tracing (Pp), obtained from the radial artery, which are commonly monitored in critically ill patients. Cardiac output (CO) was measured in order to establish the effect of volume expansion. The mean of three CO-measurements was used, obtained by a thermodilution technique which is part of the standard clinical practice, using a catheter in the arteria pulmonalis.

2.2. Patients and procedures
16 patients who were administered to the Intensive Care Unit after coronary artery bypass surgery and who were presumed to be hypovolaemic, were measured during intravenous administration of 2x250 ml of a Gelofusine® solution. The patients were considered to be hypovolaemic if either: a) systolic bloodpressure < 110 mmHg, b) CVP < 10 mmHg, c) PCWD < 12 mmHg, d) central or mixed venous SO2 < 70 %, or e) if isotropic or vasopressor drugs were being used. The measurements of CO,
ISTI and PEP were performed at three moments: before infusion, after the first and after the second infusion of 250 ml each. The group of patients consisted of 14 males and 2 females, having an age (mean ± s.d.) of 68 ± 11 years (range 44-84 yrs), height 174 ± 10 cm (range 151-188 cm) and weight 84 ± 15 kg (range 54-125 kg). Reasons for exclusion were an abnormal cardiac rhythm or an artificial pacemaker, relevant alterations in medication, and any medical, ethical or practical drawbacks or objections to perform the measurements. The study was approved by the Ethics Committee of the VU University medical center Amsterdam. All subjects gave informed consent to participate in the test.

3. Results

The mean values (± S.D.) of the three parameters at the three moments are listed in table 1. Cardiac output increased in 7 patients, remained unchanged (change in CO less than 5%) in 6 patients and decreased in 3 patients after the full administration. The mean value of change in cardiac output between moments 1 and 3 was: $\Delta CO_{1-3} = -0.2 ± 0.5 \text{ l/min}$. No significant relationship between CO and PEP and between the changes in CO and PEP were detected. However, a significant relationship between ISTI and CO was found at each of the three moments. These relationships are presented in table 2. Because of the consistency between the observed relationships at the three different moments, the relationship for the pooled data was established. This relationship is presented in the last row of table 2 and in figure 3.

| moment | relationship ISTI-CO | r     | p    |
|---|---|---|---|
| before | ISTI = -13.5*CO + 211 | 0.5453 | < 0.025 |
| after 250 ml | ISTI = -10.1*CO + 201 | 0.4920 | < 0.05 |
| after 500 ml | ISTI = -9.5*CO + 197 | 0.4609 | < 0.05 |
| pooled data | ISTI = -10.7*CO + 202 | 0.4917 | < 0.005 |

The relationship between the absolute and relative change in ISTI and the relative change in CO (%) before and after 500 ml of fluid administration (moment 1 and 3) was also found to be significant: $\Delta ISTI = -0.70*\Delta CO + 6.8 \%$ ($r = 0.5304; \ N = 16; \ p < 0.025$). The relationship between both relative changes between the moments 1 and 2 was found to be similar, however not significant. Between the moments 2 and 3 the effect of fluid administration on all parameters was minimal. The cardiac output did hardly change: $\Delta CO_{2-3} = -0.0 ± 0.3 \text{ l/min}$. 

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Table 1. Mean values (± S.D.) of the Cardiac Output (CO), Pre-Ejection Period (PEP) and Initial Systolic Time Interval (ISTI) at three moments, before and after intravenous administration of 2x250 ml of a Gelofusine® solution in two steps of 250 ml each.

| before infusion | after 250 ml | after 500 ml |
|---|---|---|
| CO (L/min) | 4.7 ± 1.2 | 4.9 ± 1.3 | 4.9 ± 1.3 |
| PEP (ms) | 190 ± 9 | 184 ± 10 | 179 ± 9 |
| ISTI (ms) | 148 ± 30 | 151 ± 28 | 151 ± 26 |
Figure 3. The administration of fluid resulted in a significant correlation between the Initial Systolic Time Interval (ISTI) and the Cardiac Output (CO).

4. Discussion and conclusions

There is a need for parameters that assess preload and predict fluid responsiveness in patients in an intensive care unit. Common methods are invasive and the accuracy has been questioned [1]. In the present study, the use of PEP and ISTI was investigated by comparing these parameters with CO responsiveness. No significant or systematic relationship between PEP and CO and \( \Delta \text{PEP} \) and \( \Delta \text{CO} \) was found. Such relationships have been reported earlier [2, 3]. Probably, this absence originates from the limited nature of this study. The number of patients who responded to the fluid administration was small. The mean response in cardiac output to fluid administration was low and the assessment of CO by thermodilution is of limited accuracy. Moreover, the accuracy of measurement of PEP by means of a catheter in the \textit{arteria radialis} is limited. The time needed for the systolic pressure wave to reach the catheter tip is substantial and will vary between individuals. This suggests that measurement of the PEP is of limited value for the clinical assessment of preload and of the effect of volume expansion.

However, the preliminary results of this pilot study show significant relationships between the ISTI and the cardiac output at any moment during the fluid administration procedure. Further, a significant relationship between \( \Delta \text{ISTI} \) and \( \Delta \text{CO} \) before and after 500 ml of fluid administration was found. This indicates that the ISTI is dependent upon preload via the Frank-Starling mechanism, and that ISTI has the potential to be used as a clinical parameter assessing preload. Future research will clarify the significance and practical usefulness of this non-invasive parameter in monitoring preload and predicting fluid responsiveness.

References

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