THE INITIAL SYTOLIC TIME INTERVAL (ISTI) IS A VALID ALTERNATIVE FOR THE PRE-EJECTION PERIOD IN A WIDE RANGE OF LABORATORY AND AMBULATORY CONDITIONS

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Introduction

Hyperactivity of the sympathetic nervous system (SNS) may be paramount to the detrimental effects of stress on cardiovascular health. The Pre-Ejection Period (PEP) is the golden standard to measure SNS activity during naturalistic conditions. PEP measurement heavily relies on the accurate detection of ECG and ICG landmarks that are difficult to detect due to lapses in beat-to-beat signal quality for instance introduced by movement. Large scale epidemiological studies would benefit from a measure that relies on landmarks in ECG and ICG that are less sensitive to noise and do not show rater dependency. This study evaluates whether the more easily detected Initial Systolic Time Interval (ISTI) can be used as a valid alternative for PEP.

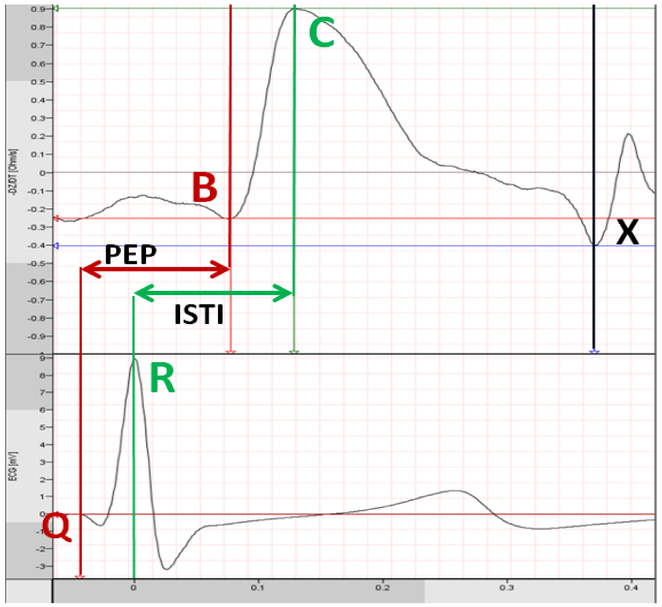

Figure 1. *The Impedance Cardiogram (TOP) represents the mechanical activity of the heart and indicates the opening of the aortic valve (B-point) and the moment of maximum velocity of aortic blood flow (C-point). The Electrocardiogram (BOTTOM) represents the electrical activity of the heart and indicates the onset of the electrical activity through the heart (Q-point) and the peak of electrical activity (R-point). PEP is defined as the Q-point to B-point interval and ISTI is defined as the interval from the R-point to the C-point. X represents the closing of aortic valves.*

Materials and methods

Ninety-one subjects participated in a 90 minute *laboratory experiment* in which a variety of often employed physical and mental stressors were presented and 31 further subjects participated in a structured 2 hour *ambulatory recording* in which they partook in natural activities that induced large variation in posture and physical activity (Table 1). The ICG and ECG signals were continuously recorded with the Biopac data acquisition system (lab study) and with the VU Ambulatory Monitoring System (ambulatory study). Four landmarks were automatically scored in the electrocardiogram (ECG) and impedance cardiogram (ICG) and rigorously checked by interactive inspection of two independent raters: QRS-onset, R-peak, B-point, and C-point (dZ/dt-min) (Figure 1).

The statistical analyses were identical for the ambulatory and laboratory study. For both laboratory and ambulatory protocols a repeated measures ANOVA was used to test for the effect of condition on IBI and PEP to verify successful manipulation of autonomic tone within subjects. Pre-planned contrasts compared the pre-test resting baseline levels of the variables to the levels obtained in the experimental condition. Intraclass correlations correlation coefficients (ICCs) based on a random effects model (absolute agreement) were computed between PEP and ISTI scored by rater 1 and rater 2 separately for each of the conditions across all subjects (per-condition inter rater reliability) and for each of the subjects across all conditions (per-subject inter rater reliability). Finally, multilevel analysis was used to test the validity of using the ISTI as a replacement for PEP (Blackwell, de Leon, & Miller, 2006) allowing a random intercept and slope.

Experimental conditions	IBI Mean (SD)	Δ IBI	real PEP Mean (SD)	Δ real PEP	ISTI Mean (SD)	Δ ISTI
Resting Baseline	845 (111)	NA	107 (18)	NA	127 (17)	NA
Paced breathing (BF32)	803 (114)	-42*	101 (18)	-6*	121 (17)	-6*
Paced breathing (BF20)	805 (112)	-40*	105 (17)	-2*	123 (17)	-4*
Paced breathing (BF12)	803 (104	-42*	105 (17)	-2*	126 (16)	-1
Paced breathing (BF6)	825 (93)	-20*	107 (18)	0	127 (16)	0
Paced talking (Words)	780 (106)	-65*	109 (18)	2	128 (18)	1
Paced talking (Numbers)	757 (97)	-88*	107 (21)	0	123 (19)	-4*
Stroop color word conflict	758 (97)	-87*	104 (19)	-3*	121 (19)	-6*
Serial subtraction	748 (101)	-97*	104 (20)	-3*	120 (19)	-7*
Orthostasis (Sitting)	859 (108)	14	108 (18)	1	128 (16)	1
Orthostasis (Lying down)	963 (126)	117*	95 (19)	-12*	121 (21)	-6
Orthostasis (Standing)	723 (83)	-123*	117 (16)	10*	138 (16)	11*
Humoristic movie	875 (123)	29*	108 (17)	1	124 (17)	-3
Cold pressor	836 (117)	-9	110 (19)	3	126 (17)	-1
Handgrip	840 (119)	-5	112 (17)	5*	128 (17)	1
Bicycle ergometer (Baseline)	833 (109)	NA	115 (17)	NA	133 (17)	NA
Bicycle ergometer (50W/60cpm)	598 (78)	-235*	77 (20)	-38*	94 (19)	-39*
Bicycle ergometer (100W/60cpm)	504 (80)	-329*	66 (17)	-49*	82 (180)	-51*
Bicycle ergometer (Recovery)	715 (116)	211*	90 (25)	24*	118 (22)	36*

Experimental conditions	IBI Mean (SD)	Δ IBI	real PEP Mean (SD)	Δ real PEP	ISTI Mean (SD)	Δ ISTI
Baseline sitting	784 (98)	NA	112 (17)	NA	118(19)	NA
Standing 1	674 (84)	-110*	117 (16)	5*	123 (17)	5*
Lying down 1	900 (117)	114*	108 (21)	-4	120 (19)	2
Sitting 1	787 (97)	3	113 (17)	1	122 (18)	4*
Lying down 2	899 (120)	115*	114 (25)	2	127 (19)	9*
Standing 2	691 (79)	-92*	119 (14)	7*	125 (18)	8*
Sitting 2	808 (105)	24*	117 (13)	5*	123 (15)	5*
Tone Avoidance Task	755 (99)	-29*	110 (15)	-2	115 (17)	-2
Walking outside	597 (65)	-187*	86 (13)	-36*	88 (16)	-30*
Walking & Talking	587 (69)	-197*	85 (11)	-37*	87 (13)	-31*
Staircase Climbing	430 (43)	-354*	66 (9)	-46*	61 (14)	-57*
Staircase Climbing Recovery	642 (124)	-142*	80 (16)	-32*	82 (15)	-36*
Bicycle ergometer (50W/60cpm)	557 (124)	-227*	88 (18)	-24*	90 (17)	-28*
Bicycle ergometer (100W/60cpm)	463 (76)	-321*	73 (14)	-39*	75 (19)	-43*
Bicycle ergometer (150W/60cpm)	397 (48)	-387*	63 (12)	-49*	57 (15)	-61*
Bicycle ergometer recovery	505 (86)	-279*	79 (19)	-33*	77 (23)	-41*
Treadmill walking (5km/h)	511 (83)	-273*	80 (14)	-32*	78 (19)	-40*
Treadmill walking (6km/h)	486 (77)	-298*	76 (13)	-36*	79 (17)	-39*
Treadmill walking (8km/h)	400 (51)	-384*	72 (19)	-40*	67 (26)	-51*

Table 1 and 2. *Means (SD) and delta scores for all experimental conditions of the laboratory study (LEFT) and ambulatory study (RIGHT). * = significant at p <.002*

Results

Interrater Reliability

The C-point gained a higher per condition interrater reliability score than the B-point in both the laboratory (.99 vs .92) and ambulatory (.85 vs .74) study. The lower per-condition interrater reliability for the B-point compared to C-spoint was confirmed in a lower per-subject interrater reliability (e.g. correlating PEP of rater 1 with PEP of rater 2 across all conditions for each subject).

The C-point gained a higher per subject interrater reliability score than the B-point in both the laboratory (1.00 vs .92) and ambulatory (.92 vs .85) study.

The relation of PEP to ISTI

Within and between-subject variation in the PEP was largely captured by the within and between-subject variation in the ISTI. Multilevel results showed that ISTI explains 75.6 % of the variance in laboratory PEP and 81.2% in the ambulatory PEP.

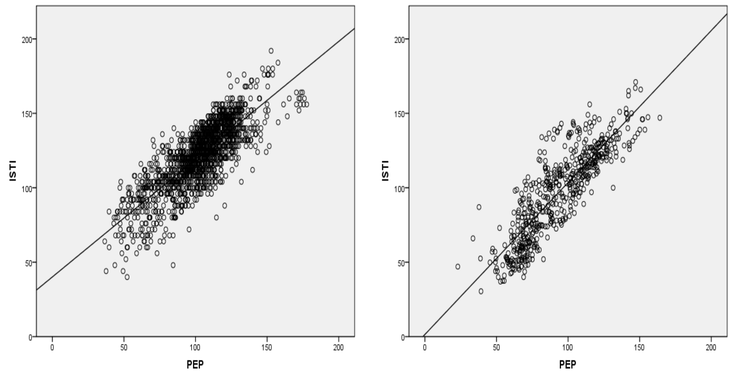

Figure 2. *Scatter plots of the relationship between PEP and ISTI for the laboratory study (LEFT) and the ambulatory study (RIGHT). Note that these plots contain both within and between subject variance.*

- The C-point is more reliably detected than the B-point.
- ISTI and PEP are highly correlated within and between subjects.
- This was found in laboratory as well as ambulatory situations.

We conclude that ISTI is a good alternative for the PEP to index cardiac sympathetic activity in large scale data collections in epidemiological or ambulatory monitoring studies.

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