Cardiac Autonomic Innervation Following Coronary Artery Bypass Grafting Evaluated by High Resolution Heart Rate Variability

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Abstract

Objective of this preliminary study is to propose a method to assess the status of autonomic nervous regulation and adaptation reserves of the body in patients with multivessel coronary artery disease (MCAD) in the preoperative and early postoperative period after CABG. A modified Indicator of the Activity of Regulatory Systems (IARS) has been used, whose value is determined by the estimated 5 HRV indices: heart rate (HR), standard deviation of examined normal RR interval (SDNN), geometrical HRV index, low frequency (LF) and very low frequency (VLF) bands of total HRV spectrum.

The results show: i. Significantly higher sympathetic tone towards the parasympathetic contour preoperative ($p < 0.001$) and postoperative ($p < 0.0001$), and this prevalence increases postoperative; ii. Parasympathetic tone is moderately suppressed preoperative and to a greater extend postoperative ($p < 0.05$); iii. Compared to the moderate stress of the regulatory systems preoperative (IASR = 4.07), in the early postoperative period, they are in a state of high tone (IASR = 5.36; $p < 0.05$), with increased activity of renin-angiotensin-aldosterone system to provide a higher adaptability of the organism.

1. Introduction

Surgical revascularization is the most commonly performed cardiac intervention. An important point in patients with coronary artery disease (CAD) is the decision about the type of revascularization - coronary artery bypass grafting (CABG) or percutaneous coronary intervention (PCI). Publications in literature are showing the benefits of CABG versus the PCI in terms of late mortality [1]. Surgical treatment is recommended most often when two or more branches (vascular systems) are affected and there are no contraindications for surgery [2]. Usually in patients with FC III-IV of NYHA conservative treatment is insufficient. The decision for surgical revascularization determines the currently growing interest in methods for finding informative features for cardiac surgery indication, prognosis and follow-up of the intervention. The ability of the vegetative nervous system (VNS) to respond to myocardial ischemia by increased activity of the efferent and afferent contours, is bringing it out to a forefront research in this aspect. Current goals are: to form a diagnosis of violations in the regulation of the sinoatrial node in patients with CAD for surgical treatment, tracking the dynamics of the condition of the patients postoperative, and to determine the risk of complications in cardiac surgery intervention. An opinion has been formed that the assessment of cardiac autonomic regulation may be an independent marker of success of the cardiac surgery [3-5]

Indicators of heart rate variability (HRV) are used to assess the state of the mechanisms regulating the physiological functions of the body, including: the total activity of the regulatory contours; the neuro-humoral cardiac regulation; and the autonomic balance - the ratio between the sympathetic and parasympathetic part of the autonomic nervous system (ANS). According to many authors, HRV is an integral indicator of the functional state of the cardiovascular system and the body as a whole [4,6,7].

Statistical (time) and spectral (frequency) indices are used in the analysis of HRV. More rarely complex quantitative indicators for an overall assessment of the variability are applied.

The index of total variability in the time domain (standard deviation of normal-to-normal RR intervals – SDNN) and the total spectral power (TP) have their independent significance for the overall assessment of HRV. Sets of indices or a complex indicator for the tone of the VNS contours are needed to assess their individual regulatory activity.

The evaluation of the activity of the parasympathetic part of the VNS is of great importance to the analysis of the functional status of patients with CAD. The parasympathetic activity defines the functional reserve of the body with coronary disease; it characterizes changes

after non-invasive and invasive treatment of the disease [8,9].

The severity functional state of the cardiovascular system in patients with CAD, indicated for cardiac surgery decision, directed us in this preliminary study to find a comprehensive method for assessing the state of the autonomic nervous system and adaptation reserves of the body in patients with CAD before and immediately after CABG.

2. Materials

Rest ECG of 14 CABG patients with MCAD (2-4 coronary arteries shunting) was recorded before the intervention and on 3 to 7 days following. All patients were in sinus rhythm pre- and postoperative. Each recording contains the conventional 12 leads. All ECGs have been digitized at 1000 samples per second, with 16 bit resolution over a range of ±16.384 mV. The recordings were typically about fifteen minutes in length.

Using our software package for computing time and frequency variables of HRV we evaluated indices: i. from RR-tachogram - average HR, average RR interval, SDNN, mean deviation, median, HRV index; ii. from dRR-tachogram (the difference of the RR intervals between subsequent heart beats) – average, standard deviation, mean deviation, pNN50%, RMS; iii. from spectrum – VLF%, LF%, HF%, LF/HF and geometrical HRV index. For spectral analysis we use FFT and Hanning spectral window.

3. Methods

The increased physiological stress in patients with MCAD and the severity of intraoperative period suggest significantly altered autonomic regulation of the cardiovascular system and the adaptive ability of the organism [10,11]. We assessed a number of complex indices and tools for integrated assessment of cardiac autonomic control. The so called Indicator of the Activity of Regulatory Systems (IARS), proposed by Bayevskiy [6], is appropriate for the purpose of this study in our opinion, performing the appropriate modification of the participating in the indicator indices. IARS has been used successfully in individuals at increased functional stress or patients with severe damage on the cardiovascular system.

IARS is calculated in point scale by special algorithm that takes into account five statistical and spectral indicators of HRV: HR, SDNN, index of tension of regulatory systems, LF and VLF. We replaced the index of tension of regulatory systems with the more commonly used generic, in physiological terms, geometric indicator - HRV index, and determined for him interval estimates based on data from our previous studies in patients with CAD.

Point-scores for the 5 indicators are determined based on the following algorithm: in the range of the average value of the indicator M ± standard error of the mean – (0 points); in the range M ± SD - zone of moderate deviations from the norm (respectively + or - 1 point); outside the range M ± SD - zone of marked deviations from the norm (respectively + or - 2 points). The possible conclusions based on the assessment of each parameter are given in the 4th column of Table 1. Based on this algorithm and the data available for the patients' contingent, we identified the relevant thresholds for the 5 indicators - column 2 in Table 1.

Table 1. Thresholds for the 5 indicators. ST – sympathetic tone; PST – parasympathetic tone; VC - vasomotor center

Variable	Range	Score	Physiological evaluation
HR (bpm)	≥ 101	+2	Manifested tachycardia
	81÷100	+1	Moderate tachycardia
	61÷80	0	Normocardia
	51÷60	-1	Moderate bradycardia
	≤ 50	-2	Manifested bradycardia
SDNN (ms)	≤ 30	+2	Very high ST
	31÷40	+1	High ST
	41÷80	0	Normal activity of RS
	81÷110	-1	High PST
	≥ 111	-2	Very high PST
HRV Index	≤ 2	+2	Very high ST
	2.1÷6.0	+1	High ST
	6.1÷10.0	0	Normal ST
	10.1÷12.0	-1	Low ST
	≥12.1	-2	Very low ST
LF (%)	≥ 51	+2	Very high activity of VC
	41÷50	+1	High activity of VC
	16÷40	0	Normal activity of VC
	11÷15	-1	Low activity of VC
	≤ 10	-2	Very low activity of VC
VLF (%)	≥ 41	+2	Very high ST; hyper adaptability
	31÷40	+1	High ST; high adaptability
	16÷30	0	Normal ST
	11÷15	-1	Low ST; energy deficit
	≤ 10	-2	Very low ST; lack of functional reserve

The share of the summary '+IARS' and summary '-IARS' in the total IARS (calculated as the sum of the

absolute values of the two units) respectively, points to the predominance of sympathetic or parasympathetic contour of the autonomic nervous regulation. Based on the IARS estimates, the tone of the regulatory systems (RS) is assessed - Table. 2.

Table 2. Tone of the regulatory systems (RS), based on the IARS estimates.

Range of IARS	Evaluation of activity of RS
1-2	Normal (optimal activity of RS)
3-4	Moderately increased tone of RS. The adaptation are necessary functional reserve
5-6	Highly increased tone of RS. Increased activity of renin-angiotensin-aldosterone system.
7-8	Hyperactivity of RS. Failure of adaptation mechanisms. Lack of functional reserve for support of hyperactivity of RS
9-10	Exhausted RS, adaptation collapse

4. Results

Estimates of the tone of regulatory systems and the autonomous balance as IARS values for each patient before and in the early period after CABG are presented in Table. 3 and 4, and Figures 1 and 2.

Table 3. Evaluation of IARS preoperative.

Patient №	+ IARS	- IARS	IARS	Physiological evaluation of RS tone
1	3	0	3	Moderately increased
2	4	2	6	Highly increased
3	1	3	4	Moderately increased
4	2	2	4	Moderately increased
5	5	0	5	Highly increased
6	3	0	3	Moderately increased
7	2	2	4	Moderately increased
8	3	0	3	Moderately increased
9	3	0	3	Moderately increased
10	3	1	4	Moderately increased
11	4	0	4	Moderately increased
12	6	0	6	Highly increased
13	3	1	4	Moderately increased
14	3	1	4	Moderately increased

Table 4. Evaluation of IARS postoperative (3-7 days).

Patient №	+ IARS	- IARS	IARS	Physiological evaluation of RS tone
1	7	0	7	Hyperactivity
2	5	0	5	Highly increased
3	5	0	5	Highly increased
4	6	0	6	Highly increased
5	3	2	5	Highly increased
6	6	0	6	Highly increased
7	4	0	4	Moderately increased
8	5	0	5	Highly increased
9	7	0	7	Hyperactivity
10	4	0	4	Moderately increased
11	7	0	7	Hyperactivity
12	6	0	6	Highly increased
13	5	0	5	Highly increased
14	3	0	3	Moderately increased

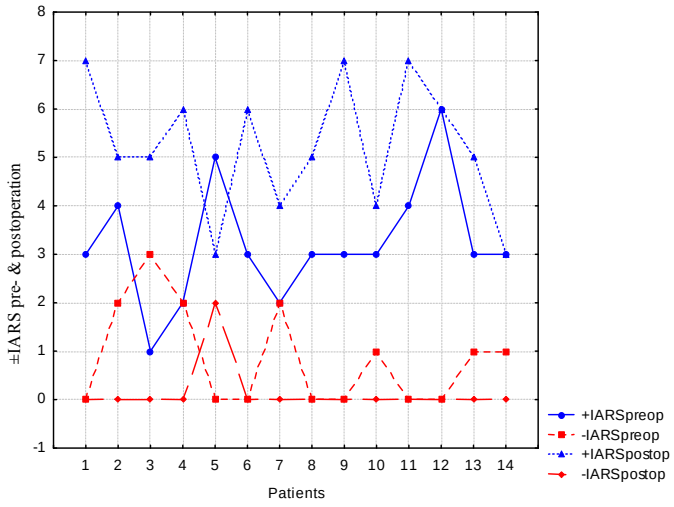

Figure 1. +IARS and –IARS pre- and postoperative

Table 5 shows the comparison between the total score of IARS, sympathetic +IARS and parasympathetic -IARS parts of the indicator, pre- and postoperative.

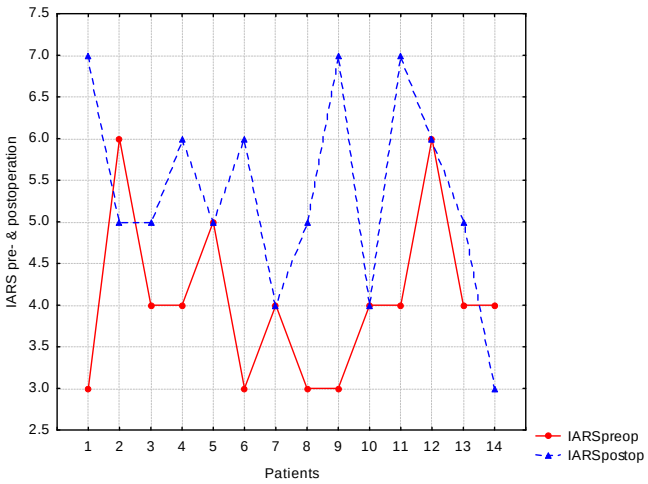

Figure 2. IARS pre- and postoperative.

Table 5. Comparison between the total score of IARS, +IARS and -IARS elements, pre- and postoperative.

Variable 1	Variable 2	Mean 1	Mean 2	p <
+IASR preop	+IASR postop	3.21	5.21	0.001
-IASR preop	-IASR postop	.86	0.14	0.05
+IASR preop	-IASR preop	3.21	0.86	0.001
+IASR postop	-IASR postop	5.21	0.14	0.00001
IASR preop	IASR postop	4.07	5.36	0.05

5. Discussions and conclussion

There is an obvious transition from moderate RS tone preoperative to highly increased RS in the early postoperative period. In 3 patients with moderate RS tone preoperative, RS activity becomes highly increased in the early postoperative period. In 5 patients the increase of the RS tone is from moderately to highly increase. In 3 patients with moderately increased tone and another 3 patients with highly increased RS preoperative tone, the RS values do not change postoperative.

The results in Table 5 show: 1. Significant higher sympathetic versus parasympathetic tone contours pre and postoperative, and this dominance increases postoperative; 2. The parasympathetic tone is strongly suppressed preoperative and at even greater extend postoperative; 3. In the early postoperative period RS are in highly increased state of, with an increased activity of sympatico-adrenal and pituitary-adrenal systems to provide a higher adaptability of the organism.

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