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Assessment of Cardiac Autonomic Regulation and Ventricular Repolarization after Off-Pump Coronary Artery Bypass Grafting

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ABSTRACT

Background. Altered autonomic regulation precipitates cardiac arrhythmias and increases the risk of sudden cardiac death. This risk is further increased by changes in ventricular repolarization. Autonomic regulation is deranged in patients after myocardial on-pump revascularization. We aimed to clarify how off-pump coronary artery bypass grafting (CABG) affects postoperative cardiac autonomic regulation and ventricular repolarization within 4 weeks after CABG.

Methods. Forty-two patients (mean age, 61.9 ± 9.3 years; mean EURO score 2.6 ± 1.9) were electively admitted for off-pump CABG. The electrocardiographic and respiratory waveform recordings were performed in the afternoon in the supine position for 10 minutes. Autonomic modulation was assessed using heart rate variability analysis. Power spectra were computed from 5-minute stable RR intervals using Fourier Transform analysis. Total power of spectra was defined in the range of 0.01 to 0.40 Hz, high-frequency power within 0.15 to 0.40 Hz, and low-frequency power within 0.04 to 0.15 Hz. Normalized power was defined as a ratio of power in each band/total power. The high- and low-frequency power as well as their normalized values indicated cardiac vagal and sympathetic modulation, respectively. Ventricular repolarization was assessed using QT interval, QT interval variability, and QT-RR interdependence analysis. QT intervals were determined from the beginning of the 5-minute segments. QT interval variability was evaluated by a T-wave template-matching algorithm. Pearson correlation between length of RR and QT interval was applied to study QT-RR characteristics. The results were tested for significance using the Fisher exact test, nonpaired *t* test, and analysis of variance; a $P < .05$ was considered significant.

Results. The frequency of arrhythmic events and heart rate increased from the fourth to the seventh postoperative day and returned to preoperative levels 4 weeks after CABG. Heart rate variability measures indicating autonomic modulation remained depressed even 4 weeks after the procedure. QT variability index increased from –1.2 ± 0.5 to –0.8 ± 0.4 on the fourth day after the operation ($P < .05$) and returned to –1.0 ± 0.5 4 weeks after CABG (P = not significant). QT-RR correlation decreased from 0.41 to 0.23 ($P < .05$) and remained significantly impaired as long as 4 weeks after CABG.

Conclusions. Observed faster heart rates until 1 week after off-pump CABG imply excessive adrenergic activation, which is comparable to on-pump CABG procedure rates. The results indicate profound autonomic derangement and loss of rate-dependent regulation after off-pump CABG even 4 weeks after operation. Restituted repolarization as assessed by QT variability index 4 weeks postoperatively corresponded with decreased frequency of rhythm disturbances 4 weeks after CABG. The loss of coupling between QT and RR intervals shows increased electrical instability postoperatively, which may serve as an additional promoter for postoperative arrhythmias, especially at higher heart rates.

INTRODUCTION

Substantial numbers of patients are threatened after coronary artery bypass grafting (CABG) by cardiac arrhythmias, which can cause sudden cardiac death [Scharf 2001]. Some of the proposed factors indicating predisposition to arrhythmias include electrolyte disturbances, pericardial effusion, ischemia and perioperative myocardial infarction, cardiopulmonary bypass (CPB) with reperfusion after cessation of CPB, trauma from cannulation and pulmonary vein venting, varying catecholamine states, changed sympathovagal interaction [Chung 2000], and altered repolarization [Bonnemeier 2001].

Cardiac electrical properties and structural remodeling are established pro-arrhythmic factors, whilst the ability of the cardiac autonomic nervous system to precipitate and promote arrhythmias has not been widely recognized. Beating heart CABG (off-pump) without CPB might be associated with a lower rate of postoperative complications including myocardial

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infarction, acute lung and renal failure, and postoperative arrhythmia than conventional CABG (on-pump) [Angelini 2002], but guidelines referring patients to the optimal technique of myocardial revascularization were obviously lacking until now. Nevertheless, off-pump CABG has been recommended recently as a safe alternative to the conventional procedure using CPB provided there exist sufficient surgical expertise and facilitated exposition by stabilizers [Puskas 2004].

Autonomic derangement has deleterious effects on the heart [Armour 1999]. Frequency domain (spectral) methodologies have been used during the last decade to infer information on the functional state of cardiac autonomic modulation and control of heart rate using noninvasive advanced computer analyses of high-quality electrocardiographic recordings [Special Report 1996; Furlan 2001]. By means of heart rate variability parameters such as total power, high-frequency power, low-frequency power, and their normalized counterparts, it is possible to quantify cardiac autonomic neural regulation and determine the levels of sympathetic and parasympathetic modulation of the heart [Special Report 1996; Goldberger 2001; Zaza 2001; Verrier 2004].

Several studies have shown that there exists a profound reduction of various heart rate variability parameters in a number of disease states such as myocardial infarction, coronary artery disease, congestive heart failure, cardiac transplantation, and different atrial and ventricular tachyarrhythmias [Special Report 1996; Hogue 1998; Lombardi 2001]. Reduced heart rate variability indicates cardiac autonomic dysfunction and is related to increased mortality, higher occurrence of sudden death, and malignant arrhythmias [Special Report 1996; Filipovic 2003]. Heart rate variability is markedly reduced after on-pump CABG [Niemela 1992; Kuo 1999]. However, the information about the profile of heart rate variability changes and postoperative sympathovagal interaction after beating heart CABG is incomplete [Kalisnik 2002].

Increased inhomogeneity of ventricular repolarization is responsible for the development of arrhythmic events including sudden cardiac death in coronary heart disease, after myocardial infarction, in congestive heart failure, and in hyperthrophic cardiomyopathy [Verrier 2004]. Prolonged QT interval on the surface electrocardiogram indicates a higher risk for sudden cardiac death after myocardial infarction [Bonnemeier 2001]. Because conventional measurements of QT interval have limited value, some recent studies substituted QT interval measurement with the assessment of QT variability [Berger 1997; Atiga 1998] or by directly studying QT-RR relationship [Faber 2003].

In the present study, we used spectral analysis of heart rate variability to evaluate cardiac autonomic parasympathetic and sympathetic modulation, described their time course, and assessed ventricular repolarization and dynamic adaptation of repolarization to heart rate after off-pump CABG.

MATERIALS AND METHODS

Patients

There were 42 patients with stable isolated coronary artery disease enrolled in the study. The study was approved by the Slovenian State Medical Ethics Committee and all the patients gave written informed consent prior to participation. Inclusion criteria were normal preoperative medical examination and laboratory findings and planning of elective isolated off-pump CABG procedure. Exclusion criteria were diabetes mellitus with late neurological impairment, severely impaired ejection fraction below 40%, coexisting valvular disease, permanent pacemaker, atrial fibrillation/undulation or any rhythm other than sinus confirmed by electrocardiographic recordings, kidney and/or liver disease, thyroid or systemic disease, malignancies, new myocardial infarction within 6 months or postoperative myocardial infarction, and the need for inotropic support, intra-aortic balloon pump, or endotracheal intubation lasting more than 24 hours after operation. Preoperative beta-blocker and calcium channel blocker medication was continued postoperatively. After CABG, we excluded 8 patients due to sustained atrial fibrillation and/or other arrhythmia or technical failure at the time of the recording (5 patients), conversion to on-pump operation (1 patient), acute stroke (1 patient), and respiratory failure with subsequent lethal pneumonia (1 patient). Finally, electrocardiographic recordings from 34 patients were considered for further analyses of heart rate variability and QT interval/variability characteristics. Clinical and preoperative data are presented in Table 1.

Table 1. Characteristics of Patients*

Age, y	61.9 ± 9.3
Sex, male	85%
Coronary artery disease (1- or 2-vessel)	30%
Previous myocardial infarction	41%
Hypertension	88%
Diabetes mellitus	15%
Dyslipidemia	69%
Percent of left ventricular ejection fraction	57.3 ± 11.7
EURO Score	2.6 ± 1.9
Grafts performed	2.7 ± 0.8
Peak creatine kinase (μg/L)	10.8 ± 13.2
Medication admission/discharge	
Beta-blocker	65%/71% (*P* = .774)
Calcium antagonist	6%/6% (*P* = 1.000)
Nitrates	38%/3% (*P* = .002)
Angiotensin-converting enzyme inhibitor	50%/32% (*P* = .109)

*Numeric variables are reported as mean ± standard deviation; for medication, *P* is added for comparison with admission.

Anesthetic technique consisted of remifentanil infusion at 0.5 to 1 μg/kg per minute combined with propofol infusion at 3 mg/kg per hour. Neuromuscular blockade was achieved by 0.10 to 0.15 mg/kg pancuronium bromide or vecuronium, and the lungs were ventilated to normocapnia with air and oxygen (45%-50%). Heparin was administered at a dose of 100 IU/kg before the start of the first anastomosis to achieve an activated clotting time of 250 to 350 seconds. On completion of all anastomoses, protamine sulphate was given to return the activated clotting time to preoperative levels.

Operative Technique

The exposure and stabilization of the heart were facilitated by the use of a retractor (Guidant, Santa Clara, CA, USA)

and Octopus II stabilizer (Starfish Octopus; Medtronic, MN, USA). Lima stitch was applied when necessary [De Carvalho Lima 2002]. The target vessel was either snared above the anastomotic site with a prolene suture in a soft plastic snugger or opened, and 1.25 to 2.5 mm intraluminal shunts (Guidant) were inserted to achieve a bloodless operative field. Distal anastomoses were performed using a 8.0 or 7.0 prolene suture. Visualization was enhanced by the use of a surgical blower-humidifier (Medtronic).

Postoperative Management, Monitoring, and Definitions

After surgery all patients were transferred to the intensive care unit. The lungs were ventilated with 40% to 60% oxygen with volume-controlled ventilation and a tidal volume of 10 mL/kg with 5-cm H_2O of positive end-expiratory pressure. Adjustments in F_{IO_2} and respiratory rate were made according to routine blood gas analysis to maintain Pa_{O_2} between 80 and 100 mm Hg and Pa_{CO_2} between 35 and 40 mm Hg. Patients were extubated as they met the following criteria: hemodynamic stability, no excessive bleeding (>80 mL/h), normothermia, and consciousness with pain control. Fluid management after surgery consisted of 5% dextrose or normal saline infused at 1 mL/kg per hour, with additional colloid solution, fresh frozen plasma, or concentrated red blood cell transfusion to maintain normovolemia and hematocrit >24%. Potassium and magnesium deficiency was promptly treated as necessary to maintain electrolyte balance within the normal range. Heart rate and rhythm were continuously monitored and displayed on a screen with an automated arrhythmia detector (HP 1205A; Hewlett-Packard, Palo Alto, CA, USA). Twelve-lead electrocardiograms were performed before operation, daily from the fourth to seventh postoperative day, and anytime on the basis of any clinical suspicion of arrhythmia.

Supraventricular rhythm disturbances were documented as atrial premature beats, fibrillation, flutter, or tachycardia, whereby we distinguished sinus tachycardia from atrial ectopic tachycardia by P wave morphology analysis . Ventricular arrhythmias were classified either as complex (estimated more than 30 ventricular ectopic beats/hr, multifocal, and/or repetitive ectopic beats) or simple (unifocal ventricular ectopic beats less than 30/hr) [Huikuri 1990]. The criterion for both supraventricular and ventricular tachycardia was at least 3 abnormal complexes in sequence with a rate exceeding 100/min. Arrhythmia was registered positive if any of the above events appeared.

Clinical diagnostic criteria for perioperative myocardial infarction were new Q waves of >0.04 ms and/or reduction in R waves >25% in ≥2 leads. Arterial hypertension was diagnosed in patients with concurrent antihypertensive therapy and in patients with systolic arterial pressure >160 mm Hg, and/or diastolic arterial pressure >95 mm Hg at admission. Renal failure was defined as serum creatinine >177 μmol/L (= 2 mg/L). Diabetes mellitus was diagnosed if the patient was treated with insulin and/or oral diabetic agents.

Electrocardiographic and Breathing Measurements

Ten-minute simultaneous electrocardiographic and breathing recordings were acquired under resting conditions. The measurements were taken between 3:00 and 6:00 PM in postprandive state, and the subjects were asked not to smoke or drink any caffeinated beverages 24 hours prior to measurements on the preoperative, the fourth, the seventh, and the twenty-eighth day after operation, each time after 10-minute nondormant supine rest in a quiet room at the department. A DEKG 2-channel digital recorder (Intekom, Ljubljana, Slovenia) with the sampling rate of 450 Hz on both channels was used. The electrocardiographic measurements were carried out using self-adhesive Ag-AgCl disk electrodes in bipolar CM5 lead with a resolution of 5 μV. Respiratory waveforms were recorded on the second channel using a custom-designed nose temperature probe (Thermistor 10K3MCD1; Betatherm, Galway, Ireland) with a resolution of 0.03°C.

Analysis of Heart Rate Variability, QT Interval Variability, Respiratory Frequency, and QT-RR Relationship

Both electrocardiographic and respiratory signals were analyzed off-line. Noise from the electrocardiographic signal was reduced by a digital low-pass filter with a cut-off frequency of 40 Hz. Baseline wander was removed by linear correction. Automated computer-based R-wave peak detection algorithm was used to find the RR intervals. Data were manually inspected and 5-minute segments stored for computation of heart rate variability parameters. Irregularities in RR intervals resulting from ectopic beats or sinus pause were replaced by the preceding intervals. A measurement was disregarded if percentage of replacements exceeded 5%. RR intervals were resampled (4 Hz) by linear interpolation. Spectral power analysis was performed with discrete Fourier transform on linearly detrended segments comprising 1200 data points. The sum of spectral components within the frequency range from 0.01 to 0.40 Hz was defined as total power. The areas of spectral peaks in the subranges 0.01 to 0.04 Hz, 0.04 to 0.15 Hz, and 0.15 to 0.40 Hz were defined as very low-frequency power, low-frequency power indicating modulated sympathetic activity, and high-frequency power indicating vagal modulation, respectively [Special Report 1996]. High-frequency power relates to efferent vagus activity and increases in the states of heightened vagal tone; on the other hand, it can be abolished by atropine administration. Conversely, sympathetic activation results in the increase of the low-frequency component and can be abolished by beta-adrenergic blockade [Koh 1994; Eckberg 1997]. Normalized low-frequency power and normalized high-frequency power were defined as power/(total power – very low-frequency power) as previously defined [Special Report 1996]. The average respiratory frequency was determined from the corresponding 5-minute segments. QT intervals were determined from the beginning of the 5-minute segments. Analyses of QT interval were performed only when T-wave amplitude exceeded 0.25 mV, so as to avoid misrecognition error. QT interval variability was evaluated by a T-wave template-matching algorithm previously described in detail [Avbelj 2003]. Time and spectral analysis of QT interval variability was made in the same way as by heart rate variability. A normalized QT variability index was used to assess QT interval variability and its relation to heart rate variability. Normalized QT variability index represented the logarithmic ratio between the QT and heart rate variabilities, each normalized

by the squared mean of the respective time series [Berger 1997]. Thus, greater inhomogeneity of repolarization would be reflected by a QT variability index shift toward more positive values. To assess the QT-RR relationship, Pearson correlation between length of RR and QT interval was computed for each patient's recording. Correlation was chosen rather than slope to make the relationship comparable across subjects and time-periods regardless of differences in variability of heart rate and/or QT interval length.

Statistical Analysis

Descriptive statistics were calculated for all the studied parameters. If heavily right-tailed distributed, heart rate variability parameters were log-transformed to allow for parametric statistical analysis. For the use of beta-blockers and incidence of arrhythmic disturbances, the change in proportion of patients between 2 time-points was tested with exact McNemar's test. Before statistical testing, we applied Fisher's z-transformation to the QT-RR correlations to obtain normal distribution. Repeated-measures analysis of variance (ANOVA) with post-hoc comparisons was used to test the change in heart rate variability parameters, QT interval and corrected QT interval length, and average QT-RR correlation. Statistical analyses were performed using SPSS for Windows 12.0 (SPSS, Chicago, IL, USA). Statistical significance was set at $P < .05$.

RESULTS

Patients

Among 42 patients enrolled, 34 patients (81%) fulfilled clinical and technical criteria for subsequent analyses. The characteristics of patients are presented in Table 1. The early mortality rate was 2.4%, the morbidity (including stroke, postoperative bleeding, acute respiratory, or renal failure) was 4.8%. The number of bypasses was 2.7 ± 0.8. The proportion of patients on beta-blockers did not change postoperatively (Table 1).

Arrhythmia

The arrhythmic events are presented in Table 2. Given that the patients with complex arrhythmias and normal left ventricular ejection fraction after CABG might not be at increased risk for adverse arrhythmic effects [Huikuri 1990], we pooled the data as presented. Arrhythmic disturbances (paroxysms of atrial fibrillation/undulation, atrial or ventricular tachycardia, or premature ectopic beats) occur significantly more frequently on day 4 ($P = .006$ for comparison with preoperative proportion), gradually decline 1 week after operation ($P = .226$), and reach the preoperative level 4 weeks after operation ($P = 1.000$).

HR and the Respiration Rate

The RR interval shortened and the respiration rate increased after CABG ($P < .001$). However, they were not statistically different from preoperative values 4 weeks after the operation (Figure 1, Table 3), whereby there was no significant effect of severity of coronary artery disease, number of bypasses, and the use of beta-blockers. Respiration rate remained elevated on the seventh day and normalized with respect to preoperative values 4 weeks after operation (Table 3).

Table 2. Incidence of Arrhythmic Disturbances before and after Off-Pump Coronary Artery Bypass Grafting*

Before CABG	7 (21%)
After 4 days	17 (50%) ($P = .006$)
Atrial tachycardia	6 (18%)
Atrial premature beats	8 (24%)
Ventricular premature beats	7 (21%)
After 1 week	12 (35%) ($P = .226$)
Atrial tachycardia	3 (9%)
Atrial premature beats	4 (12%)
Ventricular premature beats	6 (18%)
After 4 weeks	6 (18%) ($P = 1.000$)
Atrial tachycardia	0 (0%)
Atrial premature beats	2 (6%)
Ventricular premature beats	4 (12%)

*Where added, *P* refers to comparison with preoperative proportion.

Time Course of Heart Rate Variability after CABG

After operation, heart rate variability declined significantly in all frequency bands (Table 3). Spectral indices expressed in absolute powers remained depressed consistently on the seventh day and also 4 weeks after operation ($P < .001$; Figures 1-3). With regard to the normalized low-frequency power, high-frequency power-power, and the low-frequency power-to-high-frequency power ratio, no significant changes could be observed on each respective day as compared with the preoperative levels (Table 3). Hence, there was no restoration of heart rate variability indices even 4 weeks after the CABG procedure.

QT Interval, QT Interval Variability, and QT-RR Relationship after CABG

No significant change over time was found either in QT or QTc length (ANOVA $P = .355$ and .678, respectively). The descriptive statistics are listed in Table 3. QT variability index significantly increased after CABG and elevated levels per-

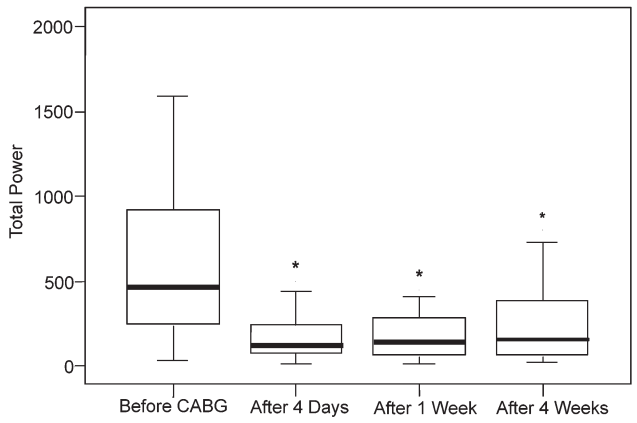

Figure 1. Total power (ms^2) of RR intervals before and after off-pump coronary artery bypass grafting. *$P < .05$ for comparison with preoperative level.

Table 3. RR and QT Parameters after Off-Pump Coronary Artery Bypass Grafting *

	Day 1 Preoperatively	Day 4 Postoperatively	Week 1 Postoperatively	Week 4 Postoperatively
Mean RR interval, ms	978 ± 133	761 ± 121†	852 ± 137†	910 ± 151
Respiratory rate	17.3 ± 4.3	21.1 ± 4.3†	21.8 ± 3.1†	18.9 ± 2.8
Low-frequency power, ms^2	254 ± 473	49 ± 50†	37 ± 36†	100 ± 116†
High-frequency power, ms^2	218 ± 441	32 ± 32†	52 ± 86†	91 ± 180†
Total power, ms^2	727 ± 1028	167 ± 127†	193 ± 186†	288 ± 328†
Mean QT interval, ms	318 ± 40	291 ± 51	310 ± 43	315 ± 55
Corrected mean QT interval, ms	322 ± 34	331 ± 39	335 ± 35	330 ± 39
QT variability index	−1.2 ± 0.5	−0.8 ± 0.4†	−0.8 ± 0.7†	−1.0 ± 0.5

*All values expressed as mean ± standard deviation.

†P <.05 for comparison with preoperative level.

sisted through the fourth and seventh postoperative day. However, 4 weeks after the off-pump procedure QT variability index statistically did not differ from preoperative values (Table 3). The correlation between the length of the QT interval and the length of the R-R interval changed significantly over time (ANOVA P = .025; P <.05 for quadratic contrasts). It dropped significantly after the operation (P <.05 for comparison with day 4, week 1, and week 4 after operation) and then showed a slight but insignificant trend toward the preoperative value as illustrated in Figure 4.

DISCUSSION

Increased sympathetic tone and/or decreased parasympathetic tone reflect faster heart rates, which have been associated with a higher risk for sudden and nonsudden cardiac death [Abildstrom 2003]. Faster heart rates until 1 week after off-pump CABG in the present study imply excessive adrenergic activation, which is comparable to the on-pump CABG procedure [Kalisnik 2002; Niemela 1996]. Accordingly, the incidence of arrhythmic disturbances in our study was significantly higher in the first week after the procedure than 4 weeks after CABG, when heart rate normalized and the arrhythmia incidence returned to preoperative level.

The previous studies of heart rate variability after CABG showed reduction of total power, low-frequency power, and high-frequency power indicating profound autonomic derangement after cardiac operations and attributed it to reduced vagal modulation with no or partial restoration after on-pump CABG [Niemela 1996; Kuo 1999]. The absolute high-frequency power and low-frequency power proved better indicators of sympathovagal modulation than normalized high-frequency power and low-frequency power in the setting of excessive adrenergic tone [Goldberger 1997], so we used absolute measures of total power, high-frequency power, and low-frequency power to better depict the changes in autonomic nervous modulation after operation. Moreover, low-frequency power/high-frequency power ratio, normalized high-frequency power, and normalized low-frequency power did not differ on any day, suggesting that they should be interpreted with caution in the setting of increased adrenergic tone. We pointed out in the previous study that impaired autonomic regulation exists 1 week after any type of CABG [Kalisnik 2002]. However, markedly reduced total power, high-frequency, and low-frequency absolute powers after CABG in the latest study show profound autonomic derangement even 4 weeks after the off-pump procedure. The results showing markedly reduced heart rate variability

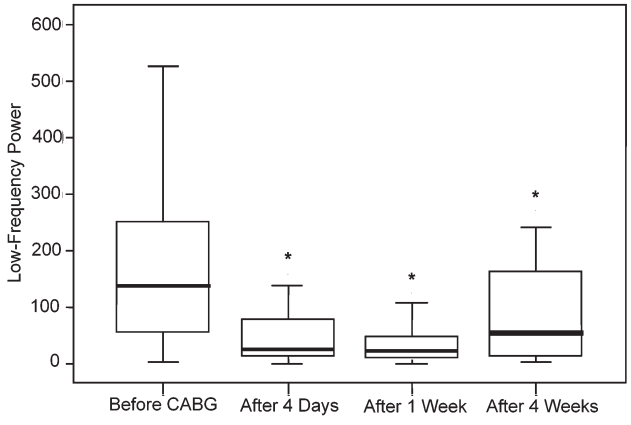

Figure 2. Low-frequency power (ms^2) of RR intervals before and after off-pump coronary artery bypass grafting. *P <.05 for comparison with preoperative level.

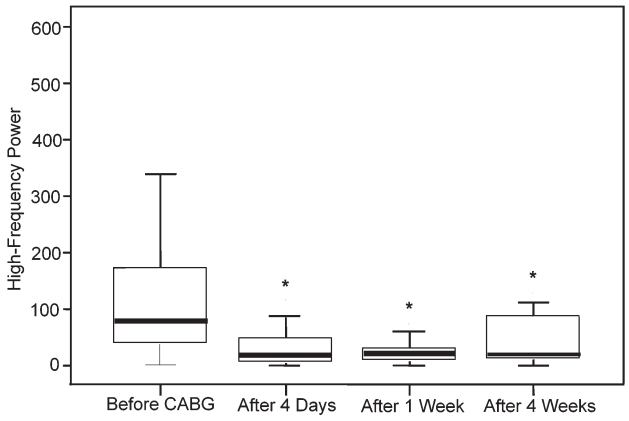

Figure 3. High-frequency power (ms^2) of RR intervals before and after off-pump coronary artery bypass grafting. *P <.05 for comparison with preoperative level.

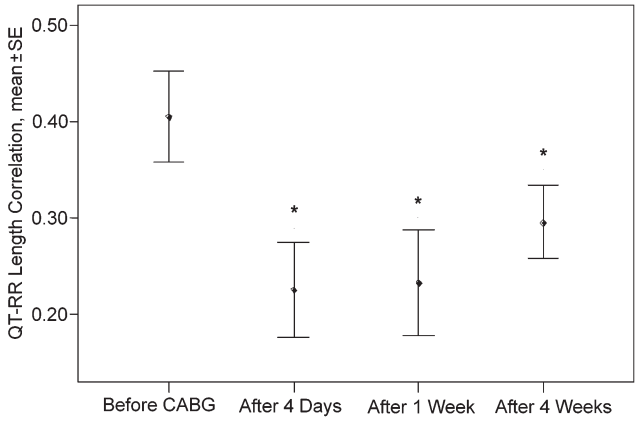

Figure 4. QT-RR correlation before and after off-pump coronary artery bypass grafting. *P <.05 for comparison with preoperative level.

even after off-pump CABG further imply that inadequate intraoperative myocardial protection during cardiac arrest or central nervous system microembolisms due to CPB might not be major determinants of the observed cardiac autonomic derangement, as has been previously postulated [Niemela 1996; Kuo 1999]. The results demonstrate that the systemic response of the organism to the invasive procedure and myocardial revascularization itself in the early phase is similar to the adrenergic activation after on-pump CABG and is not compensated for on the level of local cardiac autonomic modulation regardless of the CABG technique applied [Kalisnik 2004].

However, recent observations of heart rate variability attenuation after CABG in spite of documented viable myocardium with recovery of left ventricular function even 6 months after CABG [Wiggers 2002] and of incomplete restoration of heart rate variability as long as 6 months after percutaneous transluminal coronary angioplasty despite the complete revascularization and anatomical preservation of the autonomic nerve fibers do suggest that the observed autonomic derangement comes neither from permanently impaired cardiac function after operation nor from anatomical dissection at surgery [Wennerblom 2000] and thus further veil the exact underlying mechanism.

Increased QT interval variability in patients with coronary artery disease or dilated cardiomyopathy could identify those at increased risk of sudden death [Berger 1997; Atiga 1998]. Recent studies of dynamic assessment of QT-RR relationship revealed less tight coupling between QT and RR interval in diseased hearts. The observed decreased electrical integrity with limited adaptation of repolarization to changing heart rates has been proposed consequently as an additional pathological factor for enhanced arrhythmic risk in patients with severe chronic heart failure, coronary artery disease, dilated myocardiopathy, or unstable angina pectoris [Faber 2003]. Off- and on-pump coronary revascularization may affect QT interval, either directly by influencing the electrophysiological milieu or indirectly by interference with cardiac autonomic nervous control [Bonnemeier 2001; Verrier 2004]. In this study, QT interval variability increased after the operation and remained elevated until the seventh postoperative day indicating ventricular repolarization lability, whereby we observed a higher incidence of rhythm disturbances on the fourth and seventh postoperative days. Four weeks after CABG, the QT variability index returned to preoperative levels, and the incidence of rhythm disturbances also decreased. To further explore the dynamic aspect of QT variation in relation to heart rate, we performed a QT-RR interdependence analysis. The results show that the CABG procedure has a destabilizing effect on ventricular repolarization as manifested by increased uncoupling between RR and QT interval and consequently impaired rate dependent QT interval adaptation, which persists even 4 weeks after CABG. It is interesting to note that we observed an increased electrical instability also in this group of patients who were operated off-pump, suggesting that the direct effect of the CPB might not be the cause of the observed derangement. Consequently, increased electrical instability after any type of CABG might be an additional previously unreported mechanism potentially leading to postoperative arrhythmias, especially at higher and/or rapidly changing heart rates.

It remains to be answered whether the observed effects are direct or indirect consequences of myocardial revascularization and reperfusion of the ischemic myocardium regardless of the technique, increased adrenergic response, or any other factor not defined. Finally, the issue of (ir)reversibility of impaired QT/RR coupling after CABG longer-term also remains unanswered.

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