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Assessment of Nonlinear Heart Rate Dynamics after Beating-Heart Revascularization

Jus Ksela, MD,[1] Piotr Suwalski, MD, PhD,[2] Jurij Matija Kalisnik, MD, PhD,[3] Viktor Avbelj, PhD,[4] Grzegorz Suwalski, MD,[2] Borut Gersak, MD, PhD[3]

[1]Department of Cardiac Surgery, University Clinical Centre Maribor, Maribor, Slovenia; [2]Department of Cardiac Surgery, 1st Chair of Cardiology, Medical University of Warsaw, Warsaw, Poland; [3]Department of Cardiovascular Surgery, University Medical Centre Ljubljana, Ljubljana, Slovenia; [4]Department of Communication Systems, Jozef Stefan Institute, Ljubljana, Slovenia

ABSTRACT

Background: Advanced nonlinear methods of measuring heart rate variability (HRV) derived from the mathematics of complex dynamics and fractal geometry have provided new insights into the abnormalities of heart rate behavior in various pathologic conditions. These methods have provided additional prognostic information compared with traditional HRV measures and clearly have complemented the conventional linear methods. Knowledge about the behavior of complex cardiac dynamics indices after different cardiac procedures is very limited, however. We aimed to clarify how nonlinear heart rate dynamics are affected by beating-heart revascularization (off-pump coronary artery bypass graft [CABG] surgery) within the first week after the procedure.

Methods: Included in the study were 66 patients who had isolated stable multivessel coronary artery disease and were in normal sinus rhythm. The patients were on chronic β-blocker therapy and were scheduled for off-pump CABG. We performed 15-minute high-resolution electrocardiographic recordings preoperatively and on the third and seventh postoperative days to assess linear and nonlinear heart rate dynamics. Frequency-domain measurements, detrended fluctuation analysis (DFA) with short-term (≤11 beats, $\alpha 1$) and long-term (>11 beats, $\alpha 2$) correlation properties of RR-intervals, and fractal dimension (FD) measurements (average, high, and low) were made. Arrhythmia was monitored preoperatively with 24-hour Holter recordings, postoperatively by continuous monitoring for the first 4 days after the procedure, and subsequently by clinical monitoring; 24-hour Holter recordings were obtained again on the seventh postoperative day. We used the paired-samples Student t test, the Mann-Whitney U test, and the Fisher exact test for statistical analyses. Differences in arrhythmia occurrence before and after the procedure were tested with the Wilcoxon signed rank test and the McNemar test. A P level <.05 was considered statistically significant.

Results: Values for all frequency-domain parameters decreased significantly after off-pump CABG ($P < .001$). Values for the $\alpha 1$ and high FD parameters decreased significantly after the procedure ($P = .028$ and .001, respectively), whereas $\alpha 2$ increased significantly ($P = .023$). DFA $\alpha 1$ was significantly lower in patients with postoperative atrial fibrillation than in patients remaining in sinus rhythm (mean ± SD, 0.79 ± 0.32 versus 1.13 ± 0.45 [$P = .003$] on the third postoperative day; 0.89 ± 0.31 versus 1.22 ± 0.34 [$P < .001$] on the seventh postoperative day), whereas low and average FDs were significantly higher (1.84 ± 0.16 versus 1.68 ± 0.19 [$P = .003$] on the third postoperative day and 1.77 ± 0.18 versus 1.66 ± 0.17 [$P = .01$] on the seventh postoperative day for the low FD; 1.83 ± 0.09 versus 1.76 ± 0.10 [$P = .011$] on the third postoperative day and 1.80 ± 0.11 versus 1.73 ± 0.10 [$P = .014$] on the seventh postoperative day for the average FD). The low FD was significantly higher on the third postoperative day in patients with postoperative deterioration of ventricular ectopy than in patients with improved ventricular ectopy (1.74 ± 0.17 versus 1.48 ± 0.08, [$P = .03$]).

Conclusion: The decreases in $\alpha 1$, average FD, and high FD indicate that a profound decay of cardiac complexity and fractal correlation can be observed after off-pump CABG. Furthermore, a more extensive impairment of nonlinear indices was observed in patients who developed postoperative arrhythmias than in those who remained in stable sinus rhythm. Our findings suggest that the postoperative hyperadrenergic setting acts as a preliminary condition in which both reduced and enhanced vagal activity may predispose patients to arrhythmia, indicating that postoperative rhythm disturbances are an end point associated with divergent autonomic substrates.

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Correspondence: Jurij Matija Kalisnik, MD, PhD, University Medical Centre, Department of Cardiovascular Surgery, Zaloska 7, Ljubljana, SI-1525, Slovenia; 00386-1-522-4941; fax: 00386-1-522-2583 (e-mail: jurij-matija.kalisnik@mf.uni-lj.si, jmkalisnik@gmail.com).

INTRODUCTION

Heart rhythms exhibit extraordinary complexity, characterized by self-similar dynamics with correlations over multiple time scales that defy analysis by conventional mathematical and biostatistical methodologies [Saeed 2005]. Consequently, traditional time- and frequency-domain methods of linear heart rate variability (HRV) analysis that measure

Table 1. Patients' Clinical Data*

Age, y	63.5 ± 9.8
Men/women, n	43/23
Coronary artery disease, n	
2-Vessel	20 (30%)
3-Vessel	46 (70%)
Previous myocardial infarction, n	33 (55%)
Hypertension, n	60 (91%)
Diabetes mellitus, n	19 (29%)
Dyslipidemia, n	66 (100%)
LVEF, %	55.3 ± 9.8
LA, cm	4.0 ± 0.5
EuroSCORE	2.9 ± 2.6
No. of grafts performed	2.5 ± 0.9
β-Blocker therapy at admission/discharge, n	66 (100%)/62 (100%)

*Data for numerical variables are reported as the mean ± SD. LVEF indicates left ventricular ejection fraction; LA, left atrium diameter.

only the overall magnitude of RR-interval fluctuations around its mean value lack the ability to detect elusive but important changes in HRV [Huikuri 2003; Beckers 2006; Krstacic 2007]. Therefore, nonlinear HRV methods based on fractal geometry and complex dynamics have lately been used as a new approach for evaluating subtle fluctuations in heart rate that are not evident with conventional linear analysis [Signorini 2004; Saeed 2005]. Compared with linear indices, nonlinear parameters have been shown to be superior for predicting benign and malignant arrhythmias, sudden cardiac death, and mortality after myocardial infarction [Mäkikallio 1997, 2001; Tapanainen 2002; Jokinen 2003; Shin 2006].

The profile of changes in nonlinear parameters that occur after different cardiac procedures, such as coronary artery bypass graft (CABG) surgery, is incomplete [Wu 2005; Bauernschmitt 2007]. In our previous studies with linear HRV parameters, we were able to show that autonomic regulation is profoundly deranged after CABG surgery, with or without the use of cardiopulmonary bypass [Kalisnik 2006, 2007]. Our aim in the present study was to clarify the complexity of RR-interval dynamics after off-pump CABG and to associate newer nonlinear HRV parameters of cardiac sympathetic and parasympathetic alteration with clinical outcomes following the procedure.

MATERIALS AND METHODS

The protocol of the study was approved by the National Medical Ethics Committee of Slovenia and by the Ethics Committee of the Medical University of Warsaw, Warsaw, Poland. Written informed consent was obtained from each patient prior to measurements.

Patients

The study included 66 consecutive patients (43 men) who had stable multivessel coronary disease, sinus rhythm prior to operation, and chronic therapy with β-blockers, and who underwent off-pump CABG at the Medical Academy in Warsaw, Poland. Exclusion criteria were coexisting valvular disease, any rhythm other than sinus rhythm (as confirmed by 24-hour Holter electrocardiographic [ECG] recordings), a permanent pacemaker, diabetes mellitus with late neurologic impairment, and a new myocardial infarction within 1 month before the procedure.

Operation and Postoperative Monitoring

All preoperative medication, including β-blockers, was routinely omitted on the day of surgery. A standardized anesthetic technique with fentanyl, midazolam, propofol, and pancuronium was used. All patients underwent isolated elective off-pump CABG in a standardized manner, as described elsewhere [Kalisnik 2007]. Intraoperative monitoring included invasive measurement of radial artery blood pressure and central venous pressure, continuous ECG leads II and V_5 with ST-segment monitoring, pulse oximetry, capnometry, and urine output. After the surgical procedure, patients were transferred to the intensive care unit. Preoperative β-blocker medication was continued postoperatively and was guided by hemodynamic criteria during the first 3 days.

To detect any arrhythmia occurrence, we obtained 24-hour Holter recordings 1 day before surgery. Postoperatively, heart rate and rhythm were monitored continuously and displayed on a screen with an automated arrhythmia detector for the first 4 days after the operation. Subsequently, clinical observations were performed. In all cases of clinical suspicion of arrhythmia occurrence, an ECG was recorded, and continuous monitoring was restarted. On the seventh postoperative day, 24-hour Holter recordings were obtained again. Atrial fibrillation (AF), atrial flutter, and supraventricular tachycardia (SVT) were considered as arrhythmic events if they lasted more than 30 seconds. Ventricular-rhythm disturbances were classified as simple (Lown I-II) or complex (Lown III-V), as sustained or nonsustained ventricular tachycardia, and as ventricular fibrillation. Intraoperative and postoperative data, including complications and adverse events, were recorded. The clinical diagnostic criteria for perioperative myocardial infarction were as described previously [Kalisnik 2007].

ECG Recordings

Studies evaluating nonlinear dynamics have mostly been done with 24-hour ECG (long-term) measurements; however, recent reports have indicated that results obtained from

Table 2. Preoperative and Postoperative Arrhythmias*

Arrhythmias	Preoperatively, n	Postoperatively, n	*P*
AF	0	27	<.001
AFL	0	1	<.001
SVT (<30 s)	4	4	1.000
SVT (>30 s)	0	1	<.001
Lown I-II	30	14	.022†
Lown III-V	36	48	

*AF indicates atrial fibrillation; AFL, atrial flutter; SVT (<30 s), supraventricular tachycardia lasting less than 30 seconds; SVT (>30s), SVT lasting more than 30 seconds; Lown I-II, ventricular ectopic activity Lown I and II; Lown III-V, ventricular ectopic activity Lown III to V.

†Wilcoxon signed rank test for comparison of pre- and postoperative ventricular ectopy in all patients.

10- to 15-minute (short-term) recordings reliably and reproducibly reflect information provided by long-term data sets in patients with angina pectoris and previous myocardial infarction [Perkiömäki 2001; Krstacic 2007]. In our study, nonlinear parameters were evaluated from 15-minute high-resolution recordings.

Fifteen-minute ECG recordings were obtained from each patient on the day before the operation and on the third and seventh postoperative days by means of a DEKG 1-channel digital recorder (Intekom, Ljubljana, Slovenia) with a sampling frequency of 1000 Hz. All measurements were taken after the patient had undergone a 10-minute supine equilibration period in a quiet room, each time in the afternoon and at least 2 hours after the last meal. Patients were asked not to smoke or to drink any caffeinated beverages 24 hours prior to measurements.

Analysis of HRV

All ECG recordings were scanned with the HolCard 24W analyzing system (Aspel, Cracow, Poland). The ECG wave complex was automatically classified and later manually verified as normal sinus rhythm, atrial or ventricular premature beats, or artifacts by comparison with adjacent QRS morphologic features. After eliminating all abnormal beats (including 1 beat succeeding a premature beat), we applied a moving-average window filter to eliminate outliers. After this step, only recordings with >95% pure sinus beats were included in the analysis.

Frequency-domain HRV analysis. We used fast Fourier transform analysis to estimate the power spectrum of HRV from 5-minute stable RR intervals. The sum of spectral components within the frequency range of 0.01 to 0.40 Hz was defined as total power (TP). The areas of spectral peaks in the subranges of 0.04 to 0.15 Hz were defined as low-frequency power (LF), indicating modulated sympathetic activity, and areas of spectral peaks in the subranges of 0.15 to 0.40 Hz were defined as high-frequency power (HF), indicating vagal modulation. The ratio of LF and HF (LF/HF ratio), indicating sympathovagal balance, was calculated [ESC/NASPE 1996].

Nonlinear HRV analysis. The same preedited RR-interval time series used for frequency-domain analyses was also used for detrended fluctuation analysis (DFA) and for calculating the fractal dimension (FD).

DFA is a modified root-mean-square analysis of a random walk used to quantify fractal-like scaling properties of the RR-interval data. In our study, the short-term (≤11 beats) scaling exponent α1 and the long-term (>11 beats) scaling exponent α2 were calculated separately with freely available software (http://www.physionet.org) [Peng 1995; Goldberger 2000]. Today, α1 is considered the most powerful predictor of life-threatening arrhythmias, mortality after myocardial infarction, and sudden cardiac death, whereas the specific physiological process attributable to α2 changes remains unrecognized. Earlier studies determined α1 to be clearly related to vagal activity, whereas α2 is more related to sympathetic modulation [Beckers 2006].

FD is the exponent of the number of self-similar windows with a certain magnification into which an RR data set may be broken and is regarded as an indicator of cardiac system complexity. Nowadays, many algorithms are available for determining the FD of a heart rate signal. In the present work, we implemented an algorithm proposed by Higuchi. This algorithm is supposedly superior to others, particularly with shorter data sets [Kikuchi 2005]. Analyses were performed with software developed by Acharya et al [2005]. Besides the average FD for all windows sizes, low FD for short window sizes (≤9 beats) and high FD for long window sizes (≥9 beats) were calculated separately from the ECG recordings. Whereas average FD, which is decreased in various cardiac abnormalities compared with the healthy population, shows a clear relation to parasympathetic activity, the physiological explanation for the low FD and high FD components is much less defined [Acharya 2005]. In previous studies, both were related to the development of the fetal autonomic nervous system during pregnancy [Kikuchi 2005].

Table 3. Linear and Nonlinear Parameters of Heart Rate Variability before and after Off-Pump Coronary Artery Bypass Grafting*

				P		
	Preoperatively	Postoperative Day 3	Postoperative Day 7	Time Effect	Postoperative Day 3	Postoperative Day 7 versus Postoperative Day 3
TP	577.4 ± 362.9	263.2 ± 178.3	298.9 ± 194.0	<.001	<.001	.436
HF	195.2 ± 165.6	69.7 ± 65.8	84.5 ± 82.0	<.001	<.001	.520
LF	164.2 ± 103.7	62.0 ± 46.1	72.4 ± 47.9	<.001	<.001	.306
LF/HF	0.9 ± 0.3	1.1 ± 0.7	1.2 ± 0.7	.007	.043	.311
α1	1.19 ± 0.22	1.05 ± 0.44	1.16 ± 0.33	.029	.028	.048
α2	0.93 ± 0.12	0.98 ± 0.15	1.00 ± 0.13	.009	.023	.414
Low FD	1.71 ± 0.10	1.72 ± 0.19	1.67 ± 0.17	.088	NA	NA
High FD	1.92 ± 0.06	1.88 ± 0.09	1.87 ± 0.09	<.001	.001	.434
Average FD	1.81 ± 0.06	1.78 ± 0.10	1.74 ± 0.10	<.001	.066	.023

*Data for numerical variables are reported as the mean ± SD. TP indicates total power; HF, high-frequency power; LF, low-frequency power; LF/HF, ratio of LF to HF; α1, detrended fluctuation analysis (DFA) short-term scaling exponent; α2, DFA long-term scaling exponent; FD, fractal dimension; NA, not applicable.

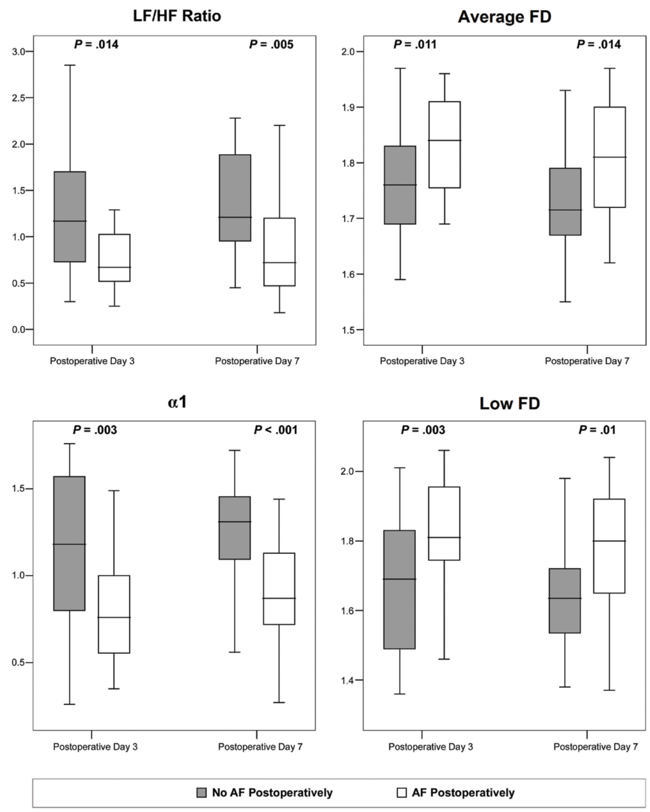

Figure 1. Time course of the ratio of low-frequency power to high-frequency power (LF/HF), detrended fluctuation analysis α1, average fractal dimension (FD), and low FD parameters in patients with and without atrial fibrillation (AF) after off-pump coronary artery bypass graft surgery. Horizontal lines denote the median, boxes denote first and third quartiles, and T-bars denote first and ninth deciles.

Statistical Analysis

The paired-samples Student *t* test or the Mann-Whitney *U* test was used for statistical analyses of numerical variables, and the Fisher exact test was used for categorical variables. Differences in arrhythmia occurrence before and after the procedure were tested with the Wilcoxon signed rank test for ordinal values (Lown class), and the McNemar test was used for dichotomous variables. Analyses were performed with the SPSS for Windows 14.0.2 software package (SPSS, Chicago, IL, USA). Statistical significance was set at a *P* level of <.05.

RESULTS

Of the 66 patients included in the study, 54 patients fulfilled the clinical and technical criteria for subsequent analyses.

Clinical Course

Table 1 summarizes the clinical characteristics of the patients. Early postoperative mortality was 4.4%. One patient died from a massive perioperative myocardial infarction, and 2 patients died for noncardiac reasons. Early postoperative morbidity without any late consequences (including transitory ischemic attack, postoperative bleeding, or early hemodynamic instability) was 9%. Conversion from off-pump to on-pump surgery was unavoidable in 1 patient because of hemodynamic instability. We excluded the recordings of 12 patients from final analyses: the patients who died, the patient who underwent conversion to an on-pump procedure, and 8 patients whose preoperative or postoperative recordings contained >5% ectopic beats and measurement artifacts.

Arrhythmias

All patients presented with stable sinus rhythm preoperatively (Table 1). Pre- and postoperatively, 4 patients had paroxysms of SVT shorter than 30 seconds that were not included in the arrhythmia analysis. Within the first week after their procedures, 27 patients developed at least one episode of AF, 1 patient developed an episode of atrial flutter, and 1 patient had an episode of SVT; all of the episodes lasted longer than 30 seconds. Patients with postoperative AF were older ($P < .001$), had a higher operative risk according to EuroSCORE assessment ($P < .001$), and a higher incidence of 2-vessel disease ($P = .014$). No other clinical parameters correlated significantly with the occurrence of postoperative AF. Ventricular arrhythmias, as represented by a score based on the Lown classification, were more complex and occurred significantly more frequently after the procedure ($P = .022$, Wilcoxon signed rank test; Table 2). No significant differences in clinical variables

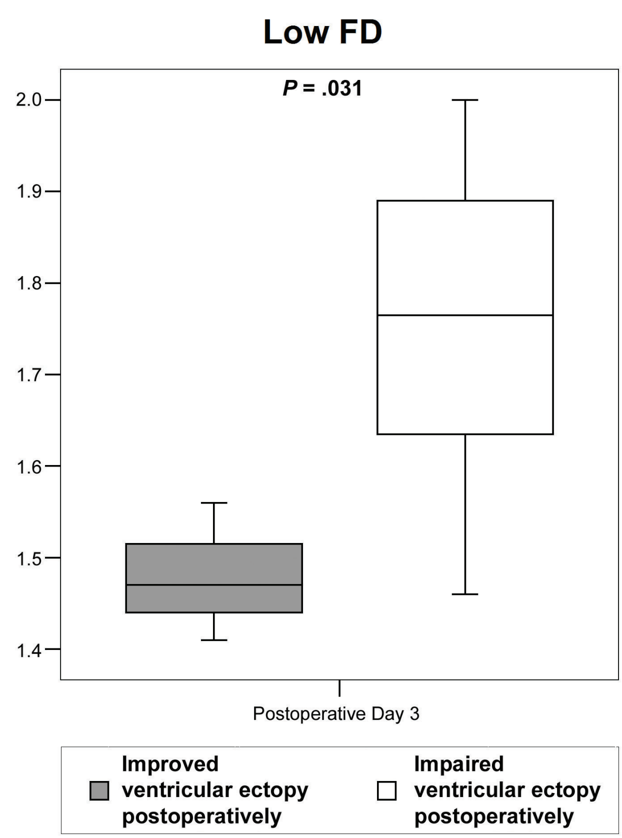

Figure 2. Values for the low fractal dimension (FD) parameter on the third postoperative day in patients with impaired and improved ventricular ectopy after off-pump coronary artery bypass graft surgery. Horizontal lines denote the median, boxes denote first and third quartiles, and T-bars denote first and ninth deciles.

Table 4. Postoperative Values for Linear and Nonlinear Heart Rate Variability Parameters in Patients with Postoperative Atrial Fibrillation (AF)*

	Postoperative Day 3		Postoperative Day 7	
	AF	No AF	AF	No AF
TP	289.6 ± 240.1	249.7 ± 138.6	301.1 ± 211.4	297.5 ± 185.9
HF	85.0 ± 81.9	61.8 ± 55.5	93.5 ± 81.5	79.1 ± 83.1
LF	61.6 ± 60.3	62.2 ± 37.7	62.4 ± 47.5	78.3 ± 47.8
LF/HF	0.8 ± 0.5	1.3 ± 0.7†	0.9 ± 0.6	1.4 ± 0.7†
α1	0.79 ± 0.32	1.13 ± 0.45†	0.89 ± 0.33	1.22 ± 0.34†
α2	1.01 ± 0.11	0.98 ± 0.17	0.99 ± 0.16	1.00 ± 0.13
Low FD	1.84 ± 0.16	1.68 ± 0.19†	1.77 ± 0.18	1.66 ± 0.17†
High FD	1.88 ± 0.10	1.87 ± 0.09	1.88 ± 0.08	1.86 ± 0.09
Average FD	1.83 ± 0.09	1.76 ± 0.10†	1.80 ± 0.11	1.73 ± 0.10†

*Data for numerical variables are reported as the mean ± SD. AF indicates group of patients with postoperative atrial fibrillation; No AF, group of patients with postoperative stable sinus rhythm. Other abbreviations are expanded in the footnote to Table 3.

†$P < .05$ for comparison between groups.

were observed between the groups of patients with postoperative improvement (from Lown III-V to Lown I-II) and those with impairment of ventricular ectopy (from Lown I-II to Lown III-V). Only the incidence of postoperative AF and deterioration from simple to complex ventricular-rhythm disturbances was high enough to enable a valid calculation.

Time Course of HRV after Off-Pump CABG

The linear HRV parameters TP, HF, and LF significantly declined on the third day after the procedure ($P < .001$) and remained unchanged until the seventh postoperative day (P = .306-.520), whereas the LF/HF ratio increased significantly on the third postoperative day ($P = .043$) and remained unchanged until the seventh day ($P = .311$; Table 3).

DFA α1 declined significantly on the third postoperative day ($P = .028$) and then showed a marginally significant increase toward preoperative values on the seventh postoperative day ($P = .048$; Table 3). DFA α2 increased significantly on the third postoperative day ($P = .023$) and remained elevated through the seventh postoperative day ($P = .414$). FD analysis showed a significant decline in the high FD on the third postoperative day ($P = .001$), and the high FD remained impaired in the first postoperative week ($P = .434$; Table 3). The average FD showed an insignificant decrease on the third postoperative day ($P = .066$) but later decreased significantly on the seventh postoperative day ($P = .023$). The low FD index showed an insignificant increase early after the operation and a decrease on the seventh postoperative day (P for time effect = .088).

Correlation between Linear and Nonlinear HRV Parameters and Postoperative Arrhythmias

The group of patients with postoperative AF had significantly lower LF/HF ratios on the third and seventh postoperative days ($P = .014$ and .005, respectively), significantly lower α1 values ($P = .003$, and $P < .001$), and significantly higher values of the low FD ($P = 0.003$ and 0.010) and the average FD (P = 0.011 and 0.014), compared with the group of patients who remained in stable sinus rhythm (Table 4, Figure 1).

Patients who deteriorated from simple (Lown I-II) to complex (Lown III-V) ventricular arrhythmias had significantly higher values for the low FD on the third postoperative day ($P = .031$) than patients who showed an improvement in their ventricular arrhythmia (from Lown III-V to Lown I-II; Table 5, Figure 2). No significant intergroup differences were observed for linear and DFA indices (P = .113-.951).

DISCUSSION

The analysis of HRV provides valuable information about the functional state of the autonomic system in various cardiac patients, including individuals after beating-heart revascularization. Several authors have observed intensely altered values in conventional linear parameters after on- and off-pump CABG [Wu 2005; Bauernschmitt 2007; Kalisnik 2007], but no study has yet described nonlinear cardiac dynamics following beating-heart surgery.

We used a linear analysis of HRV indices to compare our findings with previous studies that reported on HRV changes following off-pump CABG and to assure the comparability of our study population to groups of patients from earlier studies. Since the absolute values of HF and LF proved more accurate for describing sympathovagal activity than normalized powers in the setting of excessive adrenergic tone, absolute measures of TP, LF, HF, and the LF/HF ratio were useful for depicting changes in autonomic modulation following operation. In the current trial, the frequency-domain analysis showed a significant postoperative decline in the values of linear parameters in all selected frequency bands, as well as a reduction in the LF/HF ratio, indicating a strong tendency toward less variability and a predominance of sympathetic regulation after off-pump CABG. This finding is in agreement with the findings of our previous study, which revealed profound autonomic derangement with increased sympathet-

Table 5. Postoperative Values of Linear and Nonlinear HRV Parameters in Patients with Postoperative Ventricular Ectopy*

	Postoperative Day 3		Postoperative Day 7	
	Impaired Ventricular Ectopy	Improved Ventricular Ectopy	Impaired Ventricular Ectopy	Improved Ventricular Ectopy
TP	235.4 ± 154.8	204.3 ± 6.4	230.2 ± 96.9	312.0 ± 211.1
HF	65.2 ± 66.3	39.7 ± 3.5	57.6 ± 46.5	97.3 ± 60.7
LF	51.1 ± 35.5	64.7 ± 20.5	59.5 ± 21.5	77.5 ± 63.4
LF/HF	1.0 ± 0.6	1.7 ± 0.6	1.3 ± 0.8	0.83 ± 0.45
α1	1.03 ± 0.40	1.50 ± 0.10	1.23 ± 0.31	1.05 ± 0.38
α2	1.01 ± 0.17	1.04 ± 0.20	1.01 ± 0.12	0.97 ± 0.13
Low FD	1.74 ± 0.17	1.48 ± 0.08†	1.63 ± 0.17	1.77 ± 0.17
High FD	1.86 ± 0.09	1.84 ± 0.14	1.87 ± 0.09	1.87 ± 0.07
Average FD	1.78 ± 0.11	1.65 ± 0.07	1.72 ± 0.10	1.79 ± 0.12

*Data for numerical variables are reported as the mean SD. Impaired ventricular ectopy indicates the group of patients deteriorating from simple (Lown I-II) to complex (Lown III-V) ventricular arrhythmias; improved ventricular ectopy, patients improving from complex (Lown III-V) to simple (Lown I-II) ventricular arrhythmias. Other abbreviations are expanded in the footnote to Table 3.

†$P < .05$ for comparison between groups.

ic modulation and reduced vagal modulation, even 4 weeks after the off-pump procedure [Kalisnik 2006, 2007].

Heart rhythm is generated by a complex self-regulating system and has a fractal organization characterized by fractal dynamics. A breakdown of cardiac fractal geometry into excessive order or uncorrelated randomness leads to a less adaptable system that is characteristic of aging and different disease states [Saeed 2005]. The postoperative derangement of nonlinear indices shows distinctly that a profound breakdown of cardiac fractal organization with no or partial restoration during the first week occurs after beating-heart revascularization. Because vagal pathways play a dominant role in the generation of complex cardiac dynamics, the majority of nonlinear indices, such as α1 and the average FD, are predominantly under the influence of vagal activity [Beckers 2006]. The postoperative decline in the α1, high FD, and average FD parameters clearly indicates that reduced cardiac complexity accompanies a decrease in vagal tone after off-pump CABG. Furthermore, a significant postoperative increase in α2, a marker of sympathetic modulation, clearly shows that a substantial increase in sympathetic modulation can be observed after off-pump CABG.

The pathogenesis of postoperative arrhythmias is multifactorial and is far from being fully elucidated [Echahidi 2008]. Several causative mechanisms have been proposed, however, including the inflammatory response, excessive production of catecholamines, and a profoundly deranged autonomic system after the procedure, with this last mechanism being one of the most important factors [Hogue 1998; Echahidi 2008]. The usually applied time- and frequency-domain HRV methods describe only strong periodic phenomena of the RR data sets and have limited ability to distinguish between patients who develop postoperative arrhythmias and those who remain in sinus rhythm [Hogue 1998; Amar 2003]. In this aspect, our observations are consistent with previous reports; that is, none of the conventional frequency-domain parameters in our study, except the LF/HF ratio, was significantly changed in patients who had postoperative AF or deterioration of ventricular ectopic activity, clearly demonstrating that conventional HRV analysis lacks the ability to elucidate the state of the cardiac autonomic system in arrhythmic patients after their procedures.

Hogue et al [1998] suggested that 2 different autonomic patterns might underlie AF after CABG, one of heightened vagal tone and one of adrenergic predominance. A lower LF/HF ratio in patients with postoperative AF is consistent with vagal resurgence, indicating that some of the AF episodes in our patients might be the consequence of concomitant sympathetic and vagal augmentation; however, a more accurate insight into the autonomic status of arrhythmic patients is not possible with the use of linear parameters.

Patients who developed postoperative AF had consistently lower values for the α1 parameter after their procedures than those who remained in stable sinus rhythm, indicating that the former individuals had lower vagal activity in the early postoperative period. This result is in accord with the findings of Dimmer et al and Hogue et al, who showed that vagal withdrawal and increase in sympathetic tone might be the primary triggers of postoperative AF [Dimmer 1998; Hogue 1998].

More controversial is the interpretation of the average FD and low FD parameters. The LF and low FD parameters show similar changes during fetal development of the autonomic nervous system during the first and second trimesters [Kikuchi 2005; David 2006], suggesting that the low FD mirrors the sympathetic activity or that it better describes sympathetic modulation in hyperadrenergic settings. Consistently higher postoperative values of the low FD in patients with postoperative AF might therefore indicate that significantly higher sympathetic modulation exists in the majority of AF patients, a conclusion that clearly enhances our assumption that increased sympathetic activity and reduced parasympathetic activity constitute the most important underlying mechanism of postoperative AF in our group. Higher postoperative values of the average FD, a marker of vagal activity, complement the conventional linear methods in identifying individuals with concurrent activation of both autonomic limbs.

Less remarkable differences in the postoperative status of autonomic regulation were observed in patients who deteriorated from simple (Lown I-II) to complex (Lown III-V) ventricular arrhythmias; however, the higher values for the low FD suggest that patients with higher sympathetic activity following their procedures are prone to ventricular ectopy, which is in agreement with previous studies showing that ventricular arrhythmias are more dependent on sympathetic modulation [Hogue 1998].

One of the limitations of the present study is that it applies only to patients with isolated coronary artery disease, normal left ventricular function, a mean age of approximately 60 years, and isolated off-pump CABG surgery. In addition, our sample group was relatively small. Future studies with larger patient populations that include older individuals with poor left ventricular function, who are at the highest risk for postoperative arrhythmia, will have to evaluate the value of nonlinear HRV parameters.

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