Autonomic Control in Patients Experiencing Atrial Fibrillation After Cardiac Surgery

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Background: *Atrial fibrillation (AF) occurs in 20–40% of patients after open heart surgery and leads to an increased morbidity and prolonged hospital stay. Earlier studies have demonstrated that depressed baroreflex function predicts mortality and major arrhythmic events in patients surviving myocardial infarction. Cardiac surgery per se leads to decreased baroreflex sensitivity (BRS) and heart rate variability (HRV). Hence, the present study was aimed at analyzing the impact of the cardiovascular autonomous system on the development of postsurgical AF.*

Methods and Results: *The study covered 51 patients who consecutively underwent aortic valve replacement, coronary artery bypass surgery, or combined procedures. Noninvasive blood pressure and ECG were recorded the day before and 24 hour after surgery. BRS, linear as well as nonlinear HRV parameters were calculated using established methods. Eighteen patients developed AF during the first postoperative week, while 33 remained in sinus rhythm (SR) throughout the observation period. Patients with postoperative (PostOp) AF exhibited a significantly reduced preoperative (PreOp) BRS in terms of bradycardic and tachycardic regulation (average delayed slope [ms/mmHg]: SR: PreOp: 9.83 $\pm$ 3.26, PostOp: 6.02 $\pm$ 2.29, Pre-Post: $P < 0.001$; AF: PreOp: 7.59 $\pm$ 1.99, PostOp: 6.39 $\pm$ 3.67, Pre-Post: $P < 0.044$; AF vs SR: PreOp: $P < 0.01$, PostOp: ns). In both groups, surgery caused a decrease of BRS and HRV. Analysis of nonlinear dynamics revealed a tendency toward decreased system complexity caused by the operation; this trend was significant in patients remaining in sinus rhythm.*

Conclusions: *Patients experiencing postoperative AF obviously suffer from an impaired BRS before surgery already. These findings may be used to guide prophylactic antiarrhythmic therapy. (PACE 2007; 30: 77–84)*

atrial fibrillation, cardiac surgery, heart rate variability, baroreceptor sensitivity, antiarrhythmic therapy

Introduction

Supraventricular arrhythmias occur with an abundance of 20–40% after open heart surgery despite improvements in anesthesia, surgical technique, and medical therapy.[1] The most common types of arrhythmias are atrial fibrillation (AF) or atrial flutter. While postoperative arrhythmias are seldom life-threatening, they can increase morbidity and the duration of hospitalization with increased health care costs.[2] The pathogenesis of postoperative AF is considered to be multifactorial. One factor is the patient's preoperative status, such as age, reduced left ventricular (LV) function, atrial morphology, and preexisting electrocardiogram (ECG) abnormalities, but also the intraoperative stress, including reperfusion, inflammation, hemostasis, and increased excitotoxicity, plays a role.[3,4] However, the precise contribution of each risk factor, the pathophysiological mechanisms, and the role of the cardiovascular autonomous system in the postoperative patient are still widely unclear.[5–7]

It is well known from earlier studies that the state of the autonomous tone has a major impact on survival and the occurrence of arrhythmias in patients after myocardial infarction[8,9] and is severely altered in patients with dilated cardiomyopathy.[10] Based on these findings, it was demonstrated in a pilot study[11] that a severe imbalance of the vagal and sympathetic response can be observed immediately after an open heart surgery with extracorporeal circulation. It might indicate an increased susceptibility to arrhythmic events. The aim of the study presented here was to analyze the influence of pre- and postoperative cardiovascular autonomous control on the occurrence of postoperative AF.

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Patients and Methods

Fifty-eight patients consecutively undergoing isolated aortocoronary bypass surgery, isolated aortic valve surgery, or combined aortic valve replacement and bypass surgery were included in the study after approval of the local committee of ethics and informed consent. Exclusion criteria were emergency operations, a history of AF or ventricular arrhythmias, and the use of the radial artery as bypass graft, because the contralateral radial artery was used for invasive pressure monitoring.

Induction of general anesthesia was performed in a standardized manner with sufentanil and midazolam. For maintaining narcosis, a continuous infusion of propofol was given; muscle relaxation was achieved by pancuronium. Central venous pressure and pulmonary artery pressure were monitored by a Swan-Ganz catheter, arterial pressure by cannulation of the radial artery. All operations were carried out with a cardiopulmonary bypass (CPB) in a mild hypothermia (32°C–34°C) and pulsatile perfusion mode; cold crystalloid cardioplegia or blood cardioplegia (isolated bypass surgery) was used for cardiac arrest. After declamping, most of the patients needed one countershock to terminate ventricular fibrillation.

The occurrence of atrial fibrillation or of a severe psychosyndrome (first postoperative day), mechanical ventilation (>20 hours after surgery), and the need for inotropic support (>low-dose dopamine 24 hours after surgery) led to *post hoc* exclusion; thus, 51 patients remained for analysis. One week after surgery, the patients were divided into two groups: patients remaining in sinus rhythm (group SR, n = 33) and patients experiencing at least one episode of AF lasting longer than 5 minutes (group AF, n = 18). Demographic and operative data are given in Table I.

Table I.

Preoperative Clinical Data

	PostOp SR	PostOp AF	P-value
N	33 (64%)	18 (36%)	
Age (years)	65.8 ± 16	72.6 ± 8.5	ns
Female	17 (51%)	13 (72%)	ns
Diabetes	5 (15%)	2 (11%)	ns
Valve disease	25 (75%)	12 (67%)	ns
ECC duration > 100 min	14 (42%)	9 (50%)	ns
LVEF < 50%	4 (12%)	5 (27%)	ns
NYHA III/IV	19 (57%)	10 (55%)	ns
Pre-op. β-blockers*	10 (30%)	11 (61%)	ns

PostOp SR = postoperative sinus rhythm; PostOp AF = postoperative atrial fibrillation; ECC = extracorporeal circulation; LVEF = left ventricular ejection fraction; NYHA = New York Heart Association class; ns = not significant.
*Application of β-blockers was continued immediately after extubation.

After 10-minute equilibrations to the environment, noninvasive blood pressure signals were collected from the radial artery by a tonometer (Colin Medical Instruments, San Antonio, TX) at 1,000 Hz. Data were channeled into a bed-side laptop after A/D conversion and stored for analysis. Simultaneously, breathing excursions and a standard ECG were monitored. Data were sampled for a 30-minute period the day before surgery at the hemodynamic laboratory and 24 hours after surgery on the ICU. Care was taken to perform the measurements during the same time of the day for each patient. From the data recorded, the beat-to-beat intervals as well as the beat-to-beat systolic and diastolic values were extracted; premature beats, artifacts, and noise were excluded using an adaptive filter considering the instantaneous variability.[12]

For statistical analysis, the Mann-Whithey U test was applied to find differences of the calculated parameters. To check for the equality of proportions and independence, the χ^2 test was applied.

Analyses

Baroreflex Sensitivity (BRS): Dual Sequence Method (DSM)

Using the DSM, the parameters most relevant to estimating the spontaneous baroreflex (BR) are the coupling slopes of RR intervals (RRI) and systolic blood pressure (SBP) as a measure of sensitivity: BRS = ΔRRI/ΔSBP. The DSM is based on standard sequence methods with several modifications.[13] Two kinds of RRI responses were analyzed: bradycardic (an increase in SBP that causes an increase in the following RRI) and tachycardic fluctuations (a decrease in SBP causes a decrease in RRI). Both types of fluctuations were analyzed in a synchronous and in a 3-interbeat-shifted mode. The bradycardic fluctuations primarily reflect the vagal spontaneous BR.[14,15] Tachycardic fluctuations reflect the delayed responses of the heart rate (shift 3) that result from the beginning slower sympathetic regulation.[16]

The following parameter groups are calculated by DSM: (1) the total numbers of slopes in different sectors within 30 minutes; (2) the percentage of the slopes in relation to the total number of slopes in the different sectors; (3) the numbers of bradycardic and tachycardic slopes; (4) the shift operation from the first (sync mode) to the third

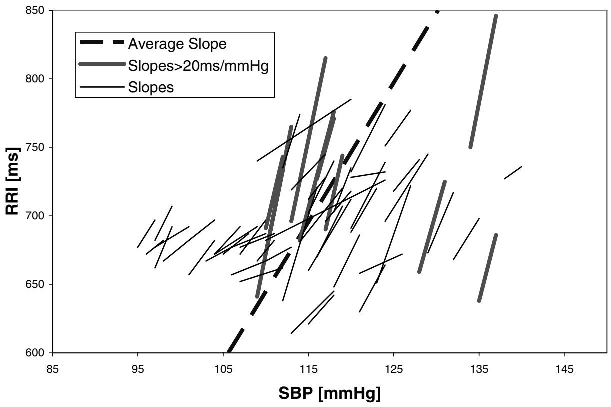

Figure 1. *Schematic representation of the two main baroreflex parameters estimated by the Dual Sequence Method: the average slope (dotted line) of all baroreflex sequences as well as the total number of baroreflex slopes above 20 ms/mmHg (thick lines). The thin lines symbolize all baroreflex slopes below 20 ms/mmHg.*

(shift 3 mode) heartbeat triple; and (5) the average slopes of all fluctuations. DSM parameters are defined as described by Malberg et al.[17] Figure 1 represents a scheme of the two main DSM parameters used in this study: the average baroreflex slope as well as the total number of baroreflex slopes above 20 ms/mmHg.

Heart Rate (HRV)

In line with the suggestions made by the Task Force HRV,[18] the following standard parameters are calculated from the time series: MeanNN (mean value of normal beat-to-beat intervals): this parameter is inversely related to the mean heart rate. SdNN (standard deviation of intervals between two normal R-peaks): it gives an impression of the overall circulatory variability. Rmssd (root mean square of successive RR-intervals): higher values indicate higher vagal activity. Shannon (the Shannon entropy of the histogram): quantification of RR-interval distribution. Apart from the time-domain parameters mentioned above, the HRV analysis focused on high-frequency components (HF, 0.15–0.4 Hz, high values indicate vagal activity) and low-frequency components (LF, 0.04–0.15 Hz, high values indicate sympathetic activity). The following ratios were considered: LFn—the normalized low frequency (LFn = LF/(LF+HF)), HP/P—high frequency normalized to the total power P as well as LP/P—the P-normalized low frequency.

New parameters can be derived from methods of nonlinear dynamics, which describe complex processes and their interrelations. These methods provide additional information about the state of temporal changes in the autonomic tonus.[19,20] Several new measures of nonlinear dynamics as proposed by Wessel et al.,[12] Kurths et al.,[21] and Voss et al.[22] were used. The concept of symbolic dynamics is based on a coarse-graining of dynamics. The difference between the current value (RRI or SBP) and the mean value of the whole series is transformed into an alphabet of four symbols (0; 1; 2; 3). Symbols "0" and "2" reflect small deviation (decrease or increase) from the mean value, whereas "1" and "3" reflect a larger deviation (decrease or increase beyond a predefined limit, for details see Voss et al.[22] Subsequently, the symbol string is transformed to "words" of three successive symbols explaining the nonlinear properties and, thus, the complexity of the system. The Renyi entropy calculated from the distributions of words ("fwrenyi025" – a = 0.25) is a suitable measure of the complexity in the time series ("a" represents a threshold parameter). Higher values of entropy refer to higher complexity in the corresponding time series and lower values to lower ones. A high percentage of words consisting of the symbols "0" and "2" only ("wpsum02") reflect a decreased HRV. The parameter "Forbidden words (FW)" reflects the number of words that never or very rarely occur. A high number of forbidden words is typical of a regular behavior, while very few forbidden words only are found in highly complex time series. When introducing an additional parameter as suggested by Wessel et al.[23,24] six successive symbols of a simplified alphabet, consisting of the symbols "0" or "1" only, were observed. Here, the symbol "0" represents a difference between two successive beats lower than a certain limit (10 ms in our study), whereas "1" represents cases with a difference between two successive beats exceeding this limit: Words consisting of the unique type of symbol "0" only were counted. The parameter "polvar10" depicts the probability of occurrence of the word type "000000" with the limit of 10 ms and detects an intermittently decreased HRV.

Results

Figures 2 and 3 exemplarily show the tracings of systolic and diastolic pressure (first panel) as well as of the RR-intervals (second). Figure 2 represents the preoperative measurements, while the curves in Figure 3 have been recorded postoperatively. Pure visual inspection gives the impression of an overall reduced variability after the surgical procedure.

Clinical Course

All patients included in the study survived the operation and did not suffer from major adverse events in the immediate postoperative course. Eighteen of the 51 patients developed at least one

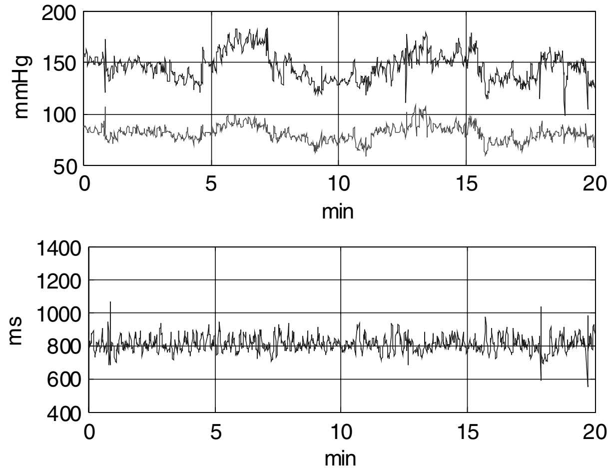

Figure 2. *Tachograms of blood pressure and heart rate in one patient (example), which were recorded preoperatively, first panel: systolic and diastolic blood pressure, second panel: heart rate.*

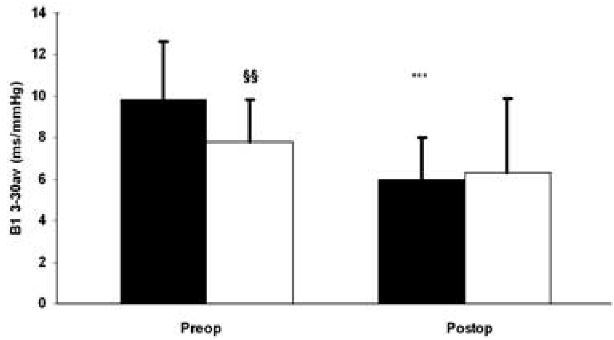

Figure 4. *Baroreflex sensitivity. Average slope of the bradycardic synchronous baroreflex in the range of 3–30 ms/mmHg. Black bars: group SR, white bars: group AF. ***P < 0.001 versus preoperative; P < 0.01 versus group SR.*

episode of AF lasting longer than 5 minutes within the first postoperative week.

Baroreflex Sensitivity

In patients with a postoperative sinus rhythm, the strength of bradycardic and tachycardic regulation (average slope) decreased significantly after surgery. Patients experiencing postoperative AF showed a significant preoperative decrease in BRS compared to patients remaining in SR (Fig. 4).

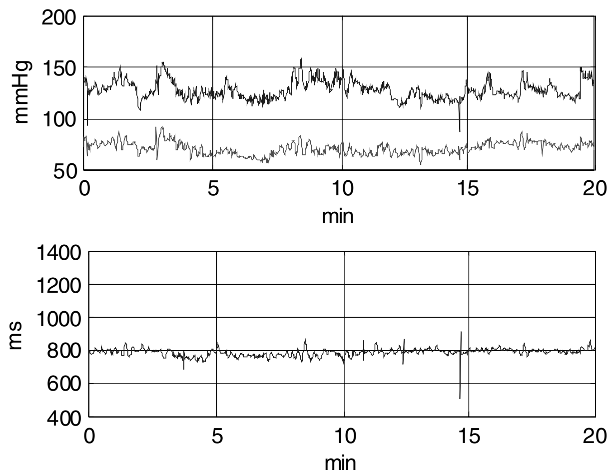

Figure 3. *Tachograms of blood pressure and heart rate in the same patient (Fig. 2), but recorded postoperatively, first panel: systolic and diastolic blood pressure, second panel: heart rate.*

The DSM parameters in Table II show that patients in the AF group had a decreased preoperative bradycardic and tachycardic regulation as compared to patients remaining in sinus rhythm. Postoperatively, there were no differences between the two groups.

Heart Rate Variability

The HRV parameters obtained are presented in Table III. Time-domain intragroup comparison revealed a significant drop of variability parameters due to the surgical intervention in both groups. No differences of time-domain parameters were noticed between groups, neither pre- nor postoperatively. The parameter "Shannon" showed a uniform decrease in both groups (Fig. 5).

As concerns the frequency domain parameters, both groups exhibited a similar behavior. The most obvious difference between pre- and postoperative measurements was a decrease of power in all frequency ranges, which was caused by the operation. Patients experiencing postoperative AF had a tendency to show a reduced power in all ranges before the operation compared to patients remaining in sinus rhythm (SR). Due to the relatively high standard deviations, however, statistical significance was reached for LF/P only.

The nonlinear parameter "Forbidden Words" FW showed a significant increase in patients remaining in sinus rhythm after surgery. In patients with a postoperative AF the trend was not significant. Preoperatively, the AF group had a higher number of forbidden words than the SR group; postoperative analyses did not reveal any intergroup differences.

Regarding the symbolic dynamics, there was a clear and significant trend toward a decreased system complexity after surgery in patients

Table II.

Baroreflex Sensitivity Calculated by the Dual Sequence Method

		SR			AF			SR versus AF	
Range	Parameter	PreOp	PostOp	Pre-Post P-value	PreOp	PostOp	Pre-Post P-value	PreOp P-value	PostOp P-value
Brady sync	av. Slope	9.83 ± 3.26	6.02 ± 2.29	<0.001	7.59 ± 1.99	6.39 ± 3.67	0.044	0.01	ns
	Slope sect	8.84 ± 10.53	3.53 ± 7.12	0.003	3.38 ± 5.40	4.38 ± 9.78	ns	0.04	ns
Brady shift	av. Slope	9.45 ± 3.33	6.11 ± 3.13	<0.001	7.48 ± 1.25	6.32 ± 4.24	ns	0.03	ns
	Slopes sect	9.65 ± 10.42	1.81 ± 6.30	<0.001	2.96 ± 3.55	4.22 ± 12.54	ns	0.02	ns
Tachy sync	av. Slope	9.68 ± 3.36	6.57 ± 2.64	<0.001	7.82 ± 1.97	6.83 ± 3.76	ns	0.03	ns
	Slopes sect	9.99 ± 12.52	3.61 ± 7.59	<0.001	4.76 ± 5.27	5.24 ± 9.66	ns	0.25	ns
Tachy shift	av. Slope	10.17 ± 3.09	7.34 ± 2.64	<0.001	8.09 ± 1.86	8.62 ± 2.81	ns	0.02	ns
	Slopes sect	10.37 ± 12.08	5.02 ± 7.56	0.02	4.69 ± 6.11	7.18 ± 9.83	ns	0.068	ns

PostOp SR = postoperative sinus rhythm; PostOp AF = post-operative atrial fibrillation; Dual sequence method parameters; brady˙sync = synchronous bradycardic slope of the heart rate following an increase in systolic blood pressure; tachy˙shift = delayed (3 beats) tachycardic slope of the heart rate following a decrease in systolic blood pressure (brady˙shift, tachy˙sync resp.); av. Slope = average slope [ms/mmHg]; Slopes sect = number of high BR (range >20 ms/mmHg in [%]) related to the total number of BR events; ns = not significant.

maintaining sinus rhythm. In patients with postoperative AF, only a few parameters showed significant pre- and postoperative differences. While most parameters indicated a trend toward a decreased complexity in AF patients as compared to SR patients, a significant preoperative difference between the groups was observed for the parameters "Forbidden Words" and Fwrenyi025 only. Hence, the difference between the groups cannot be expressed by the pre- or postoperative measurement data *per se*, but by the dynamics from the pre- to the postoperative state.

Table III.

Heart Rate Variability, Selected Time and Frequency Domain as well as Nonlinear Parameters

	SR			AF			SR versus AF	
	PreOp	PostOp	Pre-Post	PreOp	PostOp	Pre-Post	PreOp	PostOp
MeanNN	869.5 ± 134.1	732.2 ± 87.2	P < 0.001	904.0 ± 127.9	747.6 ± 129.9	P < 0.001	ns	ns
SdNN	50.5 ± 38.9	21.3 ± 18.8	P < 0.01	38.4 ± 26.8	25.7 ± 25.9	ns	ns	ns
Rmssd	38.2 ± 41.4	17.9 ± 16.6	P < 0.01	30.2 ± 32.9	24.6 ± 28.5	ns	ns	ns
Shannon	2.10 ± 0.57	1.32 ± 0.50	P < 0.001	1.87 ± 0.57	1.37 ± 0.65	P < 0.01	ns	ns
LFn	0.66 ± 0.16	0.46 ± 0.22	P < 0.01	0.61 ± 0.18	0.36 ± 0.19	P < 0.01	ns	ns
HF/P	0.13 ± 0.1	0.25 ± 0.24	P < 0.01	0.12 ± 0.09	0.34 ± 0.23	P < 0.01	ns	ns
LF/P	0.27 ± 0.15	0.17 ± 0.13	P < 0.01	0.18 ± 0.1	0.15 ± 0.08	ns	P < 0.05	ns
FW	27.3 ± 12.8	40.4 ± 12.6	P < 0.001	34.7 ± 14.5	37.9 ± 15.5	ns	P < 0.05	ns
FWRenyi025	3.4 ± 0.4	2.8 ± 0.5	P < 0.001	3.1 ± 0.5	2.9 ± 0.5	ns	P < 0.05	ns
Wpsum02	0.54 ± 0.3	0.84 ± 0.2	P < 0.001	0.7 ± 0.37	0.8 ± 0.28	ns	ns	ns
Polvar10	0.03 ± 0.08	0.12 ± 0.17	P < 0.01	0.03 ± 0.04	0.10 ± 0.12	P < 0.05	ns	ns

PostOp SR = postoperative sinus rhythm; PostOp AF = postoperative atrial fibrillation, time-domain parameters; meanNN = mean value of a normal-to-normal beat interval; sdNN = standard deviation of the normal-to-normal (NN) intervals; rmssd = root mean square of successive NN-interval differences; frequency domain parameters: LFn, HF/P, LF/P for definition of frequency bands see methods section; nonlinear parameters; FW = forbidden words; FWRreny025i = Renyi distribution of forbidden words; Wpsum02 = percentage of words consisting of the symbols "0" and "2" only; polvar10 = probability of the word type "000000" derived from symbolic dynamics within the special limit of 10 ms; ns = not significant.

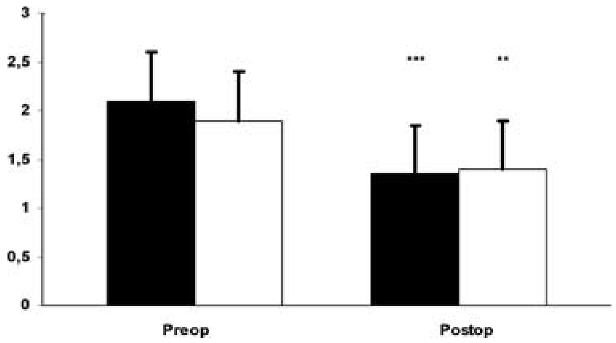

Figure 5. *Shannon entropy. Black bars: group SR, white bars: group AF. **P < 0.01 versus preoperative. ***P < 0.001 versus preoperative.*

Discussion

The analysis of BRS and HRV provides information about the individual risk in cardiac patients and is significantly altered in these patients as compared to healthy volunteers.[9,11] In contrast to several previous studies, a more complex and multiparametric approach, including bradycardic and tachycardic fluctuations of BRS, time and frequency domain analysis of HRV, and nonlinear dynamics of HRV, were used. The combination of these parameters proved to more effectively characterize the functional state of the cardiovascular autonomic system in earlier works.[16,17] AF is the most frequent complication after cardiac surgery and potentially leads to subsequent adverse events like a stroke and to a prolonged hospital stay.[2] Numerous attempts have been made to predict this complication from demographic data, ECG abnormalities, or the atrial size.[3–7] Less attention has been given to the autonomous control of the cardiovascular system.[7]

It was shown in a previous study that heart surgery with ECC leads to a marked alteration of the BRS and HRV, as expressed by time and frequency domain parameters and nonlinear dynamics, respectively.[11] This study only covered patients with isolated CABG surgery, normal LV function, and a mean age of 60 years. As expected, the rate of AF and other postoperative complications was low. Consequently, no correlation analysis of the autonomous function and clinical parameters was performed.

The present study was designed to analyze the impact of the cardiovascular autonomous regulation on the occurrence of postoperative AF. One third of the patients experienced postoperative AF, which was within the expected range. The "classical" demographic and operative parameters putting patients at a higher risk for postoperative AF were not different between the two groups (see Table I).

Baroreflex Sensitivity

In the preoperative DSM analysis, a significantly lower BRS for the bradycardic and tachycardic regulation was found in patients, who later developed postoperative AF. At first sight, these findings seem to sharply contrast with an earlier work published by Chen et al.[25] where the BRS was found to be increased in patients with AF. However, Chen's study covered patients without surgery and paroxysmal AF. Hence, the discrepancies may just reflect the different pathophysiological mechanisms leading to spontaneous or postsurgical AF. Herweg and coworkers[26] even demonstrated that AF can be preceded by either an increase or decrease of the HF component of the power spectrum, indicating that vagal stimulation or depression can cause paroxysmal AF. These data confirm the assumption that the problem of induction of different types of AF in different patients is far from being solved. Our results are partly in agreement with data from patients suffering from recurrent AF after cardioversion[27] or from a recurrence of ventricular arrhythmias,[28] thus demonstrating a decreased BRS as a predictor of the onset of recurring arrhythmias. Patients remaining in SR showed a significant decrease of the strength of regulation in the bradycardic responses, thus closely matching the results of our pilot study. In patients developing postoperative AF, this reduction was not significant. The intergroup differences were no longer evident 24 hours after surgery. This indicates that the occurrence of postsurgical AF is not solely an effect of surgery, but also due to a certain predisposition that exists prior to surgery already. From these data, it can be hypothesized that a higher ability of the autonomous nervous system to react to pressure fluctuations may be protective to overcome the strong arrhythmic stimuli that are obviously generated by the surgical intervention.

Heart Rate Variability

After the operation, the time and frequency domain parameters of HRV showed a strong tendency toward less variability and a predominance of sympathetic regulation. There were no major differences between the two groups, which is in agreement with previous findings by other authors. A reduction of HRV during surgery has already been observed by Souza Neto and coworkers[29] and was attributed to the influences of anesthesia. The postoperative analyses in our patients, however, were done several hours after the application of sedative agents. Hence, a persisting effect of anesthesia is unlikely. These long-term effects that obviously last for months[30] are probably caused by a direct damage of neural fibers during surgery.[31]

In nonlinear dynamics, intragroup comparison between the pre- and postoperative measurements showed a highly significant trend toward a reduced system complexity in patients remaining in SR, while this tendency was weak for patients with AF. Hence, the major difference between both groups in terms of these parameters is manifested by the dynamics of the process during the perioperative setting.

According to the results of nonlinear dynamics, AF patients reveal a higher degree of uniformity in their cardiovascular regulation, which is not disclosed by classical HRV-analysis. For example, high values of the parameter "Forbidden Words" (see Table III) represent a high number of conditions that never appear in the system ("forbidden" conditions), which is a direct indication of uniformity within the cardiovascular system.[22] AF patients obviously show a tendency toward a lower overall dynamic behavior in the preoperative measurements, which may be caused by a smaller regulation power and, therefore, may be less affected by surgery. From these results, it can be hypothesized that mechanisms controlling classical HRV and nonlinear dynamics are at least partly independent of each other. There are only few studies about the nonlinear dynamic behavior of the cardiovascular system following surgery. After an initial reduction of complexity, fast recovery is described as well as persisting low complexity, depending on the parameters chosen.[32] After a look at the results of this study, these conflicting findings may be caused by the variability of initial conditions in the different patients.

Conclusion

In the present study, the BRS and HRV were found to be changed significantly by heart surgery with a cardiopulmonary bypass. This is in very good agreement with the results of a pilot study done in a smaller, more homogeneous patient collective. Furthermore, it was shown that patients experiencing AF after the operation presented a generally lower BRS concerning tachycardic and bradycardic regulation. HRV analyses of time and frequency domain parameters and symbolic dynamics did not reveal any major preoperative differences between the groups. Postoperatively (which means after surgery, but still before the first onset of AF), no differences between the groups could be detected. From these findings, the following conclusions can be drawn: the onset of postoperative AF is not only caused by commonly known clinical risk factors and the influences of the operation, but obviously by the presurgical state of the cardiovascular autonomous system. For the description of complex phenomena in cardiological data, a comprehensive approach, including BRS, classical HRV, and symbolic dynamics, is recommended. In the present study, analysis of HRV alone would have resulted in minor differences between the groups only.

For the future development of a risk stratification tool, the focus will be on the preoperative state of the autonomous regulation. The effects of surgery *per se* seem to equalize any differences between groups. However, the dynamics from pre- to postoperative may play a role, which has to be further elucidated.

This analysis was not done to add another risk factor for postoperative AF, but rather to obtain better insight into the contributing mechanisms. Age, for example, is a very well-known risk factor, but the term "age" is a fuzzy summary of the entity "pathophysiological changes usually related to age"[33]—which, in several patients, may well be present in earlier years, while in others they are absent even later in life. Knowing the variety of clinical risk factors already determined,[34] it was therefore intended to go one step beyond and to analyze not preexisting clinical conditions, but related alterations in the cardiovascular autonomous system.

Limitations

It is clearly not the intention of the present study to prove any causality among altered autonomic function and the occurrence of postoperative AF, which may be impossible within a clinical setting, anyway. We still can hardly speculate if there is causality, or if measurements of autonomic function are only an indicator for forthcoming clinical problems. This study is only intended to be the description of a new phenomenon, which may be of clinical significance in the future.

Further studies with larger patient populations will have to evaluate the predictive value of BRS for post-operative AF and to define a subset of the most suitable parameters and their cut-off points. This information may be used to guide prophylactic antiarrhythmic therapy.

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