

Heart rate variability in patients after cardiac valve surgery

Research article

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Abstract: The aim of study was to analyze heart rate variability (HRV) after different cardiac valve surgery procedures and the prognostic values of these findings. This study included 101 consecutive patients who underwent surgical implantation for an artificial valve. The mean age of the patients was 62 ± 10 years. An aortic valve was implanted in 65 patients. A mitral valve was implanted in 36 patients. HRV was analyzed from 24 hours Holter electrocardiographic (ECG) records. The time from the operation to the recording of Holter ECG and measuring HRV was 3.8 ± 1.4 months. After discharged from stationary cardiac rehabilitation, all involved patients were contacted to provide data on their health in the follow-up period (33 ± 21 months). A total of 46 patients with an implanted artificial valve had decreased overall HRV or standard deviation of all normal R-R intervals (SDNN) < 93 ms. Patients with an implanted artificial mitral valve had a shorter RR interval (817 ± 122 vs. 863 ± 122 ms, $p=0.03$) and lower values of total power (1166 ± 1888 vs. 2802 ± 3601 ms², $p<0.001$) compared to patients with an implanted artificial aortic valve. The results of study show that several months after cardiac surgery, almost half of the patients with an implanted artificial valve have decreased HRV. However, postoperative decreased HRV in those patients have no importance in long-term prediction of mortality rate.

Keywords: Valve • Aortic • Mitral • Surgery • Heart rate

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1. Introduction

In today's modern cardiology and cardiac surgery, dominant valvular heart diseases are aortic stenosis, mitral and aortic regurgitation, while the incidence of mitral stenosis is less common in developed countries [1]. Heart rate variability (HRV) is a physiological phenomenon which shows the impact of the autonomic nervous system on heart activity [2]. In 1996, the Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology published their recommendations for standard measurements of HRV, physiological interpretation and their use in clinical practice [3]. Today in everyday clinical practice HRV is mainly used in risk stratification of manifestation malignant arrhythmia, and sudden death in patients with myocardial infarction (MI) [4]. Previous studies showed that after coronary artery bypass grafting (CABG), HRV becomes significantly

decreased, even more significantly than in patients with MI [5,6]. Furthermore, in clinical practice it was found that a large number of patients with an implanted artificial valve have decreased HRV in the first few months after cardiac valve surgery [7]. In relevant literature there are practically no significant studies which analyzed HRV after surgical implantation of an artificial valve, or their values of predicting long-term mortality rate after cardiac valve surgery.

Therefore, the hypothesis of this study is that cardiac valve surgery procedures significantly decrease HRV, but without clinical prognostic value on long-term mortality.

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Table 1. Differences in primary characteristics of patients with an implanted aortic vs. mitral valve.

Characteristics of patients	Group of patients with artificial aortic valve (N= 65)	Group of patients with artificial mitral valve (N= 36)	<i>p</i>
Age	64 ± 9	58 ± 10	0.004
Sex (Male / Female)	40 / 25	18 / 18	0.25
BMI (kg/m ²)	27.6 ± 3.4	27.1 ± 3.2	0.51
Former smokers / Smokers	5 / 5	2 / 7	0.4
Biological valve	21 (32%)	9 (25%)	0.71
Arterial hypertension	36 (55%)	17 (47%)	0.64
Dyslipidemia	28 (43%)	7 (19%)	0.02
Diabetes mellitus	10 (15%)	2 (6%)	0.57
Previous MI	2 (3%)	4 (11%)	0.81
EF before operation	52 ± 9	51 ± 8	0.45
Total complications after operation	33 (51%)	19 (53%)	0.88
Atrial fibrillation	18 (28%)	11 (31%)	0.74
Infection	13 (20%)	4 (11%)	0.7
Acute renal insufficiency	6 (9%)	2 (6%)	0.84
Pleural effusion	7 (11%)	9 (25%)	0.62
Stroke	1 (2%)	2 (6%)	0.71
Perioperative MI	1 (2%)	0 (0%)	0.67

2. Material and Methods

This study included 101 consecutive patients who underwent surgical implantation of an artificial valve within 6 months of arriving at stationary cardiac rehabilitation. All patients were rehabilitated during the years of 2001 through 2005.

The criteria for involving patients in the study: patients under 75 years old; sinus rhythm; no sinus sick syndrome, atrioventricular block second or third degree; and, no signs of acute heart failure.

The criteria for excluding patients from the study: patient older than 75; persistent or permanent atrial fibrillation; significant sinus rhythm disorders like paroxysmal atrial fibrillation or frequent ventricular ectopic activity; permanent electrostimulation of the heart; simultaneous implantation of artificial aortic and mitral valve; CABG at the same time with an implanted artificial valve; acute heart failure or other acute disease which requires interruption of rehabilitation; chronic disease which can have an impact on HRV variables such as chronic renal insufficiency, etc.

The mean age of patients with an artificial valve was 62 ± 10 years, the median age at 64 years, ranging from 29 to 74 years. There were 58 males (57%) and 43 females (43%). In 65 patients an aortic valve was implanted (64%), and in 36 patients a mitral valve (36%). In 30 patients a biological artificial valve was implanted (30%), while in 71 patients a mechanical artificial valve was implanted (70%).

The reasons that patients underwent cardiac surgery for implantation of an artificial valve were as follows: severe valve stenosis in 34 patients (34%); severe valve regurgitation in 44 patients (43%); mixed dysfunction in view of stenosis and regurgitation in 20 patients (20%); and, subacute endocarditis in 3 patients (3%). Table 1 shows the differences in primary characteristics of the group of patients with an implanted artificial valve - aortic vs. mitral valve.

All involved patients underwent 3 weeks of stationary cardiac rehabilitation (average 19 ± 2 days). The rehabilitation program consisted of regular conditioning on the ergocycle, group exercises under the supervision of a physiotherapist, individual walks, sessions of psychotherapy and diet. During rehabilitation, 24-hours Holter ECG was performed on all patients, and HRV was analyzed from its recordings. Time from the operation to recording Holter ECG and measuring HRV was 3.8 ± 1.4 months, median 3.5 months (ranged 1 - 6 months). All HRV variables were measured through the 23.2-hour period (ranged 21 - 24 hours). Ambulatory ECG recordings were made by 3-channel Medilog Digital Holter recorders FD3, Oxford, with 1024 Hz resolution. A commercial system (Oxford Instruments, with software Excel ECG Replay System – Rel. 8.5) was used. HRV was analyzed by computer and over-read manually. Algorithms for arrhythmia analysis provided a label for each QRS complex. An operator cleaned all recordings from artifacts, reviewed beats and modified them as needed under the supervision of the cardiologist. Only

Table 2. Values of HRV variables in patients with an implanted artificial valve.

HRV variables	Mean value	Standard deviation	Median	Range
Mean RR interval (ms)	847	124	836	602 – 1245
SDNN (ms)	97	30	98	28 – 175
SDNN-i (ms)	36	20	32	15 – 104
SDANN-i (ms)	87	27	88	25 – 160
rMSSD (ms)	29	24	21	7 – 111
pNN50 (%)	5.9	8.7	2.5	0.05 – 47
TP (ms ²)	2174	2103	1706	93 – 10504
ULF (ms ²)	338	652	235	20 – 3032
VLF (ms ²)	1104	1291	683	15 – 7407
LF (ms ²)	320	388	236	44 – 3486
HF (ms ²)	171	271	103	32 – 2412
LF/HF	2.1	1.8	1.6	0.16 – 8.6

Mean RR - mean of R-R intervals for normal beats, SDNN - standard deviation of all normal R-R intervals, SDANN-i - standard deviation of the 5-minute means of R-R intervals, SDNN-i - mean of the 5-minute standard deviations of RR intervals, rMSSD - square root of the mean of the squared successive differences in R-R intervals and pNN50 - percentage of R-R intervals that are at least 50 ms different from the previous interval, TP - Total power (0.0-0.5 Hz), VLF - very low (0.003-0.04 Hz), LF - low (0.04-0.15 Hz) and HF - high (0.15-0.4 Hz) frequency components, LF/HF - low to high frequency ratio.

recordings with less than 15% of ectopic beats were used. Periods with the highest and lowest average R-R intervals, detected from R-R interval histograms, were always validated. The corrected data were processed and HRV was computed. Raw tachogram was used for time domain analysis. The power spectral analysis was computed using fast Fourier transformation. R-R intervals that included ectopic beats were excluded and extrapolated by linear interpolation for the spectral analysis [8]. Most of the variables proposed by the Task Force on the HRV were analyzed [3]. Time domain analysis included: Mean RR - mean of R-R intervals for normal beats; SDNN - standard deviation of all normal R-R intervals; SDANN - standard deviation of the 5-minute means of R-R intervals; SDNN - mean of the 5-minute standard deviations of RR intervals; rMSSD - square root of the mean of the squared successive differences in R-R intervals and pNN50 - percentage of R-R intervals that are at least 50 ms different from the previous interval. Frequency domain analysis covered: TP - Total power (0.0-0.5 Hz), VLF - very low (0.003-0.04 Hz), LF - low (0.04-0.15 Hz) and HF - high (0.15-0.4 Hz) frequency components, with LF/HF - low to high frequency ratio.

Apart from the 24 hours Holter ECG, a complete transthoracic echocardiography was performed during rehabilitation on every patient involved in the study (Aloka ProSound SSD 5500). Also, a symptom limited exercise test was performed on every patient at the beginning and at the end of rehabilitation.

After leaving stationary cardiac rehabilitation, all patients were contacted in writing to provide informatino about their health during the follow-up period. Patients

were required to answer a few questions concerning their health, including those related to their disease after leaving from cardiac rehabilitation. The received data were analyzed to confirm if HRV findings have significance in predicting long-term mortality rate after different cardiac valve surgery procedures.

In the statistical analysis of the obtained results, the commercial system SAS System for Windows, Version 6.12 was used. Normality of distribution of the certain variables was tested with the Kolmogorov-Smirnov test. Values of normal distributed variables are expressed by mean value $\pm$ standard deviation while values of “abnormal” distributed variables are expressed by median with minimum and maximum value. The chi-square test was used to analyze the differences between certain observed proportions. Differences between certain groups of patients were tested by the Mann-Whitney test. A *p*-value less than 0.05 is considered statistically significant.

3. Results

During the 3 weeks of stationary cardiac rehabilitation, the following values of HRV variables were measured (Table 2) in all patients with an implanted artificial valve. Patients with an implanted artificial aortic valve have significantly higher parameters of HRV except pNN50 ($p=0.06$). Table 3 shows the differences in HRV variables between patients with an implanted artificial aortic vs. mitral valve. The cut-off point for normal overall HRV in general cardiology patient population was 93 ms for SDNN [4]. Twenty-two patients with an implanted aortic

Table 3. Differences in HRV between patients with an implanted artificial aortic vs. mitral valve.

HRV variables	Aortic valve	Mitral valve	<i>P</i>
	Mean $\pm$ SD	Mean $\pm$ SD	
	Median	Median	
	Range	Range	
Mean RR interval (ms)	863 $\pm$ 122	817 $\pm$ 122	0.03
	863	815	
	602 – 1245	657 – 1125	
SDNN (ms)	104 $\pm$ 27	84 $\pm$ 31	0.001
	103	80	
	44 – 175	28 – 151	
SDNN-i (ms)	40 $\pm$ 18	28 $\pm$ 20	<0.001
	37	22	
	15 – 90	19 – 104	
SDANN-i (ms)	94 $\pm$ 25	75 $\pm$ 27	0.001
	91	72	
	39 – 160	25 – 144	
rMSSD (ms)	30 $\pm$ 20	27 $\pm$ 28	0.02
	25	16	
	8 – 94	7 – 111	
pNN50 (%)	6.1 $\pm$ 7.3	5.7 $\pm$ 11	0.06
	3.3	1	
	0.05 – 31	0.05 – 47	
TP (ms ²)	2802 $\pm$ 3601	1166 $\pm$ 1888	<0.001
	1657	570	
	131 – 9813	93 – 10504	
ULF (ms ²)	490 $\pm$ 760	206 $\pm$ 432	<0.001
	331	73	
	20 – 3032	27 – 2246	
VLF (ms ²)	1429 $\pm$ 1467	492 $\pm$ 446	<0.001
	986	330	
	86 – 7407	15 – 3854	
LF (ms ²)	424 $\pm$ 548	297 $\pm$ 726	0.002
	269	188	
	44 – 3486	53 – 3036	
HF (ms ²)	254 $\pm$ 332	137 $\pm$ 561	0.02
	117	86	
	32 – 2412	36 – 2012	
LF/HF	2.3 $\pm$ 1.7	1.8 $\pm$ 1.9	0.02
	2.2	1.1	
	0.2 – 8.6	0.16 – 8.4	

valve (34%), and 24 patients with an implanted mitral valve (67%) had value SDNN < 93 ms ($p=0.002$). The mean value of the end-diastolic diameter of left ventricle (LVDd) after cardiac valve surgery in patients with an implanted aortic valve was 5.6 ± 0.82 cm (median 5.6 cm, with a range of 3.8 – 8.4 cm). It was 5.47 ± 0.69 cm (median 5.45 cm, with a range of 4.1 – 7.6 cm) ($p=0.34$) in the group of patients with an implanted mitral valve. In addition, the ejection fraction (EF) of the left ventricle

determined by the Simpson method [9] after surgery in the group of patients with an implanted artificial aortic valve was $59 \pm 9\%$ (median 60%, with a range of 25 – 65%). It was $57 \pm 9\%$ (median 58%, with a range of 33 – 67%), ($p=0.09$) in the group of patients with an implanted artificial mitral.

The mean value achieved on the limited exercise test, which was performed at the end of rehabilitation, in patients with an implanted artificial aortic vs. mitral valve was 101 ± 46 W or 5.3 ± 1.5 metabolic equivalents (METs) vs. 97 ± 44 W or 5.3 ± 1.5 METs, ($p=0.68$ for W and $p=0.87$ for METs).

Average time of follow-up period after leaving stationary cardiac rehabilitation was 33 ± 21 months. Four patients died in the follow-up period, 3 patients from diagnosed MI or sudden death (2 patients with decrease and 1 patient with normal overall HRV), and 1 patient from malignoma.

4. Discussion

The main results of this study showed that several months after cardiac valve surgery almost half of the patients with an implanted artificial valve have decreased HRV. Furthermore, patients with an implanted artificial aortic valve have significantly longer R-R interval or lower sinus frequency, and significantly higher overall HRV referring to patients with an implanted artificial mitral valve. Apart from the fact that patients with an implanted artificial aortic valve were significantly older from the patients with an implanted artificial mitral valve, and it is known that physiologically HRV becomes decreased with age [3,4], there was no differences in all other analyzed patient characteristics such as pre- and postoperative EF and functional capacity.

In addition, the results of this study showed that unlike strong predictive value of decreased HRV in patients with MI [10-12], the findings of decreased HRV in the first months after surgical implantation of an artificial valve have no importance in long-term prediction of mortality rate. Referring to measured values of HRV variables in patients with an implanted artificial valve, excellent patient survival rate was found in the follow-up period on average of almost 3 years (some patients were followed-up with in a period of 6 years).

Reading recent texts on cardiac valve surgery operation techniques [13-16] and speaking with experienced cardiac surgeons about possible reasons for the obtained differences in the results of this study between groups of patients with an implanted artificial aortic vs. mitral valve, we found that in principle, as long as there are no complications, surgical implantation of an artificial

aortic valve lasts shorter than surgical implantation of an artificial mitral valve. Referring to that, the heart arrest, or duration of cardioplegia and hypothermia are shorter during aortic valve surgery than during mitral valve surgery, that certainly can partly explained the obtained differences in results of this study [17,18]. Furthermore, by clamping the aorta, it must be, but very rarely is, separated from the lung artery and during that separation the part of the periaortal nerves can be damaged. Referring to that, implantation of an artificial aortic valve is still less "traumatic" for the heart than implantation of an artificial mitral valve by which the left atrium, and sometimes by trans-septal approach also the right atrium must be incised [13,14]. That also partly explains the reasons for more decreased HRV in patients with an implanted artificial mitral valve.

Unlike patients with coronary artery disease, depending on the type of valvular disease pathophysiological mechanisms are different in patients with valvular disease. Even though the studies on valvular diseases are not numerous, especially studies about surgical corrections of valvular diseases and the impact of that on HRV, Ozdemir *et al.* in their two reports [19,20] on patients with mitral stenosis pointed out the existence of significant autonomic disbalance and assumed increased sympathetic activity in those patients. It is also even more significant that after

percutaneous balloon commissurotomy in those patients [19] pressure in the atria becomes decreased and that leads to improvement of HRV variables and to lowering of the autonomic disbalance.

The main limitation of this study was that HRV was not analysed in patients before cardiac valve surgery. However, the aim of this study was to analyze autonomic heart function after surgical implantation of an artificial valve and the prognostic values of these results, and also the study was performed in the rehabilitation centre in which patients come to in a few weeks or months after cardiac surgery. It would be ideal that the measuring of HRV regularly was possible during the follow-up period or at least at its end to get the information about long-term changes of HRV variables after cardiac valve surgery.

In conclusion, surgical implantation of an artificial valve results in significantly decreased HRV in the first few months after cardiac valve surgery. HRV becomes more significantly decreased in patients with an implanted mitral valve than in patients with an implanted aortic valve. However, postoperative decreased HRV in patients with an implanted artificial valve have no importance in long-term prediction of mortality rate.

References

- [1] Zipes D.P., Libby P., Bonow R.O., Braunwald E., Braunwald's Heart Disease. A textbook of cardiovascular medicine, Elsevier Saunders, Philadelphia, 2005
- [2] Akselrod S., Gordon D., Ubel F.A., Shannon D.C., Barger A.C., Cohen R.J., Power spectrum analysis of heart rate fluctuation: a quantitative probe of beat to beat cardiovascular control, *Science*, 1981, 213, 220-222
- [3] Task Force of The European Society of Cardiology and The North American Society of Pacing and Electrophysiology, Heart rate variability. Standards of measurement, physiological interpretation, and clinical use, *Eur. Heart J.*, 1996, 17, 354-351
- [4] Milicevic G., Lakusic N., Szivovics L., Cerovec D., Majsec M., Different cut-points of decreased heart rate variability for different groups of cardiac patients, *J. Cardiovasc. Risk.*, 2001, 8, 93-102
- [5] Demirel S., Tukek T., Akkaya V., Atilgan D., Ozcan M., Guven O., Heart Rate Variability After Coronary Artery Bypass Grafting, *Am. J. Cardiol.*, 1999, 84, 496-497
- [6] Kuo C.D., Chen G.Y., Lai S.T., Wang Y.Y., Shih C.C., Wang J.H., Sequential Changes in Heart Rate Variability After Coronary Artery Bypass Grafting, *Am. J. Cardiol.*, 1999, 83, 776-779
- [7] Milicevic G., Majsec M., Lakusic N., Istvanovic N., Cerovec D., Utilisation of a Heart Rate Variability in a Routine Practice, *Proceedings of Europace 2001*, Monduzzi Editore, 2001, 359-363
- [8] Lakusic N., Mahovic D., Babic T., Gradual recovery of impaired cardiac autonomic balance within first six months after ischemic cerebral stroke, *Acta Neurol. Belg.*, 2005, 105, 39-42
- [9] Feigenbaum H., Armstrong W.F., Ryan T., Feigenbaum's Echocardiography, Williams & Wilkins, Lippincott, 2005
- [10] Kleiger R.E., Miller J.P., Bigger J.T., Moss A.J. and the Multicenter Post-Infarction Research Group, Decreased heart rate variability and its association with increased mortality after acute myocardial infarction, *Am. J. Cardiol.*, 1987, 59, 256-262
- [11] Quintana M., Storck N., Lindblad L.E., Ericson M., Heart Rate Variability as a means of assessing prognosis after acute myocardial infarction. A 3-year follow-up study, *Eur. Heart J.*, 1997, 18, 789-797

- [12] Vaishnav S., Stevenson R., Marchant B., Lagi K., Ranjadayalan K., Timmis A., Relation Between Heart Rate Variability Early After Acute Myocardial Infarction and Long-Term Mortality, *Am. J. Cardiol.*, 1994, 73, 653-657
- [13] Kouchoukos N.T., Karp R.B., Blackstone E.H., Doty D.B., Hanley F.L., Cardiac surgery, Churchill Livingstone, New York, 2003
- [14] Lukac P., Hjortdal V.E., Pedersen A.K., Mortensen P.T., Jensen H.K., Hansen P.S., Superior transseptal approach to mitral valve is associated with a higher need for pacemaker implantation than the left atrial approach, *Ann. Thorac. Surg.*, 2007, 83, 77-82
- [15] Hung J., Chaput M., Guerrero J.L., Handschumacher M.D., Papakostas L., Sullivan S., et al., Persistent reduction of ischemic mitral regurgitation by papillary muscle repositioning: structural stabilization of the papillary muscle-ventricular wall complex, *Circulation*, 2007, 1259-1263
- [16] Boehm J., Libera P., Will A., Martinoff S., Wildhirt S.M., Partial median "I" sternotomy: minimally invasive alternate approach for aortic valve replacement, *Ann. Thorac. Surg.*, 2007, 84, 1053-1055
- [17] Laitio T.T., Huikuri H.V., Kentala E.S., Maikikallio T.H., Jalonen J.R., Helenius H., et al., Correlation properties and complexity of perioperative RR-interval dynamics in coronary artery bypass surgery patients, *Anesthesiology*, 2000, 93, 69-80
- [18] Hogue C.W., Stein P.K., Apostolidou I., Lappas D.G., Kleiger R.E., Alterations in Temporal Patterns of Heart Rate Variability after Coronary Artery Bypass Surgery, *Anesthesiology*, 1994, 81, 1356-1364
- [19] Ozdemir O., Alyan O., Soylu M., Metin F., Kacmaz F., Demir A.D., et al., Improvement in sympatho-vagal imbalance and heart rate variability in patients with mitral stenosis after percutaneous balloon commissurotomy, *Europace*, 2005, 7, 204-210
- [20] Ozdemir O., Alyan O., Soylu M., Metin F., Demir A.D., Geyik B., et al., Sympathetic over activity in patients with rheumatic mitral stenosis, *Ann. Noninvasive Electrocardiol.*, 2004, 9, 352-357