DELAYED RECOVERY OF CARDIOVASCULAR AUTONOMIC FUNCTION AFTER MITRAL VALVE SURGERY

Evidence for Direct Trauma?

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Keywords: Biosignal processing, Baroreflex response, surgery.

Abstract: Baroreflex Sensivity (BRS) and heart rate variability (HRV) have significant influence on the patients' prognosis after cardiovascular events. The following study was performed to assess the differences in the postoperative recovery of the autonomic regulation after mitral valve (MV) surgery and aortic valve (AV) surgery with heart-lung machine. 43 consecutive male patients were enrolled in a prospective study; 26 underwent isolated aortic valve surgery and 17 isolated mitral valve surgery. Blood pressure, ECG and respiratory rate were recorded the day before, 24h after surgery and one week after surgery. BRS was calculated according to the Dual Sequence Method, time and frequency parameters of HRV were calculated using standard methods. There were no major differences between the two groups in the preoperative values. At 24 h a comparable depression of HRV and BRS in both groups was observed, while at 7 days there was partial recovery in AV-patients, which was absent in MV-patients: p (AV vs. MV)<0,001. While the response of the autonomic system to surgery is similar in AV- and MV-patients, there obviously is a decreased ability to recover in MV-patients, probably attributing to traumatic lesions of the autonomic nervous system by opening the atria. Ongoing research is required for further clarification of the pathophysiology of this phenomenon and to establish strategies to restore autonomic function.

1 INTRODUCTION

The well-known depression of cardiovascular autonomic function following cardiac surgery is related to a variety of reasons like anaesthesia and the use of the heart-lung-machine (Brown et al., 2003), (Bauernschmitt et al., 2004). The role of direct surgical trauma to the autonomic nerves (AN) is still unclear. The following study was performed comparing patients with isolated aortic valve replacement (AV, the surgical trauma to AN is considered to be low) or isolated mitral valve surgery (MV, high surgical trauma to AN is expected). With regard to the hypothesis that there is a traumatic lesion of the cardiovascular autonomic nervous system by opening the atria we observe the postoperative recovery of AV- and MV-patients.

2 METHODS

43 consecutive male patients were analysed. 26 of them underwent aortic valve surgery and 17 of them mitral valve surgery. The mean age of AV-patients was 63 +/- 13 years and the mean age of MV-patients 59 +/- 12 years. Patients with concomitant coronary heart disease were excluded for the known effects of atherosclerosis. Perioperative medication was standardized.

Anaesthesia was standardized; induction was performed 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 cardiopulmonary bypass (CPB) in mild hypothermia (32-34°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.

After 10-min equilibrations to the environment, non-invasive blood pressure signals were collected

Bauernschmitt R., Retzlaff B., Wessel N., Malberg H., Brockmann G., Uhl C. and Lange R. (2008).
DELAYED RECOVERY OF CARDIOVASCULAR AUTONOMIC FUNCTION AFTER MITRAL VALVE SURGERY - Evidence for Direct Trauma?.
In *Proceedings of the First International Conference on Bio-inspired Systems and Signal Processing*, pages 504-507
DOI: 10.5220/0001064705040507

from the radial artery by a tonometer (Colin Medical Instruments) at 1000 Hz. Data were channelled 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-min period the day before surgery, 24h and seven days after surgery on the ICU. Care was taken to perform the measurements during the same time of the day in each patient. From the recorded data 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.

Baroreflex Sensitivity (BRS): Dual Sequence Method (DSM). Using the DSM, the most relevant parameters for estimating the spontaneous baroreflex (BR) are the slopes as a measure of sensitivity. The DSM is based on standard sequence methods with several modifications: Two kinds of BBI responses were analyzed: bradycardic (an increase in systolic blood pressure (SBP)) that causes an increase in the following beat-to-beat-intervals (BBI) and tachycardic fluctuations (a decrease in SBP causes a decrease in BBI). Both types of fluctuations were analyzed both in a synchronous and in a 3-interbeat-shifted mode. The bradycardic fluctuations primarily represent the vagal spontaneous BR analysis of the tachycardic fluctuations represent the delayed responses of heart rate (shift 3) assigned to the beginning slower sympathetic regulation. The following parameter groups are calculated by DSM: (1) the total numbers of slopes in different sectors within 30 min; (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 (shift 3 mode) heartbeat triple; and (5) the average slopes of all fluctuations. DSM parameters are defined as described by Malberg et al (European Heart Journal, 1996).

Heart rate Variability (HRV). Respecting the suggestions by the Task Force HRV (Malberg et al., 2003), the following standard parameters are calculated from the time series: MeanNN (mean value of normal beat-to-beat intervals): Is inversely related to mean heart rate. sdNN (standard deviation of intervals between two normal R-peaks): Gives an impression of the overall circulatory variability. Rmssd (root mean square of successive RR-intervals):

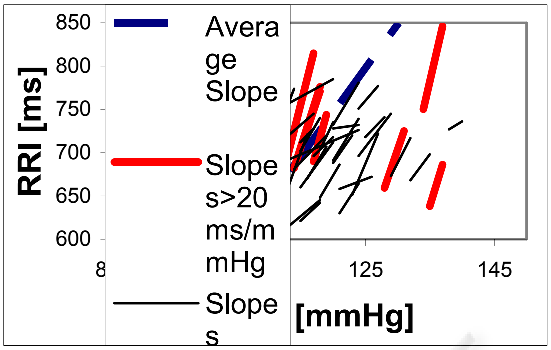

Figure 1: Schematic representation of the two main baroreflex parameters estimated by the Dual Sequence Method: the average slope (dotted line) of all baroreflex sequences as well as the total number of baroreflex slopes above 20 ms/mmHg (thick lines). The thin lines symbolize all baroreflex slopes below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

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 - the to the total power P normalized high frequency as well as LP/P - the P-normalized low frequency.

Nonlinear Dynamics. 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 and temporal changes in the autonomic tonus. Several new measures of non-linear dynamics in order to distinguish different types of heart rate dynamics as proposed by Kurths were used. The concept of symbolic dynamics is based on a coarse-graining of dynamics. The difference between the current value (BBI or systolic blood pressure) 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 low deviation (decrease or increase) from mean value, whereas '1' and '3' reflect a stronger deviation (decrease or increase over a predefined limit, for details see Voss et al. 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 for the complexity in the time series ('a' represents a threshold parameter). Higher values of entropy refers to higher complexity in the corresponding time series and lower values to lower ones. A high percentage of words consisting only of the symbols '0' and '2' ('wpsum02') reflects decreased HRV. The parameter 'Forbidden words (FW)' reflects the number of words which never or very rarely occur. A high number of forbidden words are typical for regular behaviour, while in highly complex time series, only very few forbidden words are found.

3 RESULTS

There were no major differences among the two groups preoperatively. At 24h after surgery, both groups showed a comparable depression of HRV and BRS. One week after surgery, however, marked differences were present: SDNN 15+/-6 (MV) vs. 42+/-33 (AV); p<0.001 (Fig. 1).

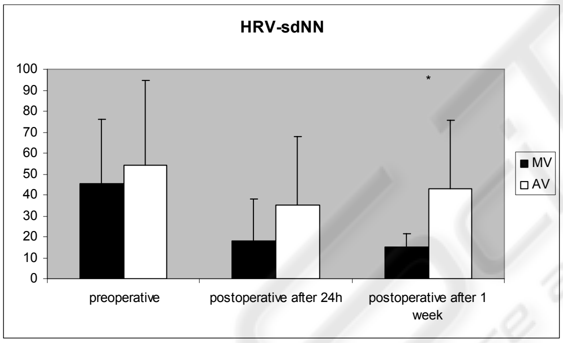

Figure 2: HRV-sdNN, heart rate variability - standard deviation of beat to beat intervals.

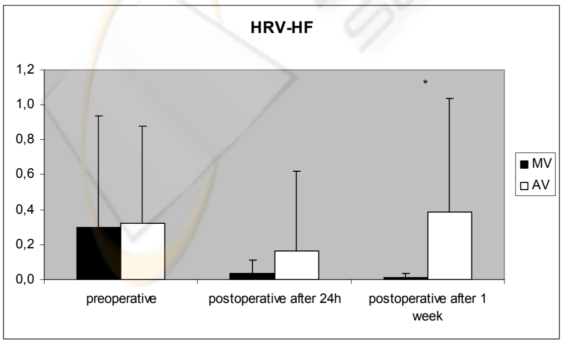

Figure 3: HRV-HF: heart rate variability – high frequency (indicator for parasympathetic regulation).

Similar kinetics were found for the High- and Low-Frequency components of HRV (HF 0.01+/-0.02 (MV) vs. 0.38+/- 0.64 (AV); p<0.02 (Fig. 2, 3).

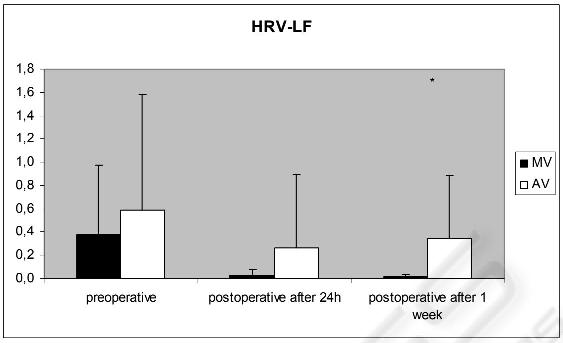

Figure 4: HRV, low-frequency.

Regarding the nonlinear parameters, there was a significant depression present already 24h after surgery with mitral patients more suppressed than aortic patients, these alterations being even more distinct after one week (Fig. 4).

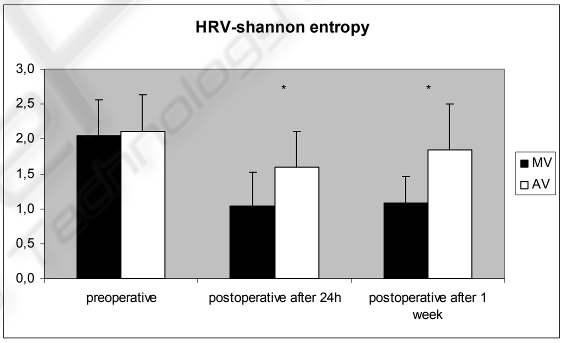

Figure 5: HRV, Shannon-entropy.

The baroreflex was impacted in a similar way for both the number and strength of regulations (BRS bradycardic 4.5+/-1.2 (MV) vs. 7.3+/-2.7 (AV); p<0.001 (Fig. 5, 6).

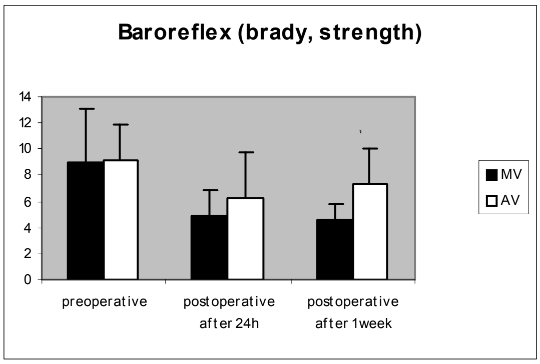

Figure 6: BRS, strength of bradycardic regulations.

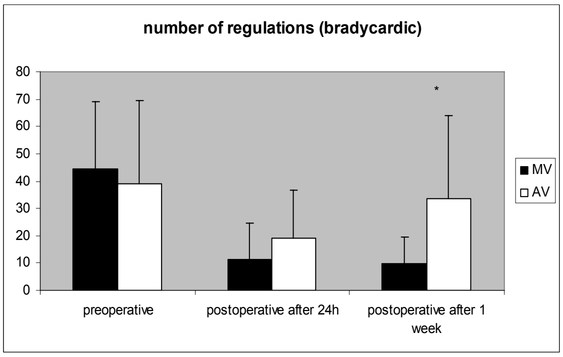

Figure 7: BRS, number of bradycardic regulations.

For the tachcardic part of the baroreflex, however, the differences among aortic and mitral patients failed significance after one week ($p<0.08$, data not shown).

4 DISCUSSION AND CONCLUSIONS

The last decade witnessed a strong increase in basic knowledge of the cardiovascular autonomic system. However, as far as alterations in the cardiac patient and in patients undergoing open heart surgery are concerned, we are still at the very start.

Meanwhile it is well known, that cardiac surgery leads to an early depression of autonomic function, and that there is potential for recovery after a certain time frame. The mechanisms for both phenomena are quite unclear, so the aim of the present study was to shed light on the precise role of direct surgical trauma. In contrast to earlier studies, where different preoperative conditions and different surgical procedures were mixed up, we focussed on patients with isolated aortic valve disease and isolated mitral valve disease, thus excluding the well known influences of atherosclerosis on cardiovascular autonomic function. On the other hand, the operative procedures done in these patients offer two entirely distinct entities of surgical trauma: while for aortic valve replacement the heart is left more or less untouched and the valve is approached by an incision in the anterior aspect of the ascending aorta only, in mitral valve operations, both the caval veins are extensively dissected, and the heart is opened by an incision right posterior to the interatrial groove, where an abundance of autonomic nerve endings are supposed to be.

The similar depression in both groups observed at 24h may reflect the effects of standardized anesthesia and perioperative treatment being comparable in all patients. While AV-patients showed a clear tendency to recover after one week, no recovery was recorded in MV-patients. In our opinion, this is a strong indicator of higher surgical trauma to AN, if the atria are dissected. Recovery of autonomic fibres is possible, even in heart transplant patients, as described earlier, so the next step will be investigating time and frequency parameters and baroreflex sensivity after six months to give evidence of the hypothesis of direct surgical trauma.

Summarizing, we were able to demonstrate for the first time, that direct surgical trauma can be one of the major mechanisms leading to depression of cardiovascular autonomic function. The diversity of results in earlier studies may be caused by the case-mix of patients, comprising different initial conditions as well as different extents of trauma.

ACKNOWLEDGEMENTS

This study was supported by grants from the Deutsche Forschungsgemeinschaft (DFG BA 1581/4-1, BR 1303/8-1, KU 837/20-1).

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