Lack of Recovery of Baroreflex Function in Hypertensive Patients after Heart Surgery

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Abstract

Baroreflex sensitivity (BRS) and heart rate variability (HRV) have significant influence on the patients' prognosis after cardiovascular events. The following study was performed to assess differences in the response of the autonomic regulation in hypertensive and normotensive patients undergoing cardiac surgery with heart-lung machine. 166 consecutive patients were enrolled in a prospective study; 102 of them were hypertensive according to the criteria of the WHO. Cardiovascular signals were recorded the day before, 24h after surgery and one week after surgery. SDNN steeply declined in Hypertensives 24h after the operation (46.5 vs. 24.5ms, p<10-7), the decline in Normotensives was less pronounced (52 vs. 30.8ms, p<0.01).The mean number of bradycardic fluctuations of BRS decreased in both groups at 24h, then there was recovery in Normotensives after one week, but not in Hypertensives. While the response to surgery is similar in normotensive and hypertensive patients, there obviously is a decreased ability to recover in Hypertensives.

1. Introduction

While the pathogenesis of essential hypertension is still widely unclear, data from the Framingham study suggest a correlation of decreased HRV and the development of hypertension [1]. Likewise, an association of BRS and hypertension was described in the older population [2]. From earlier studies we know, that cardiovascular autonomic function declines following heart surgery with a tendency to recover within 3-6 months [3]. The following prospective study was performed to analyse differences in the autonomic response to heart surgery between hypertensive and normotensive patients.

2. Methods

166 consecutive patients undergoing various types of open heart surgey were prospectively enrolled; 102 of them were hypertensive according to the WHO-criteria (systolic blood pressure above 140 mmHg, diastolic above 90 mmHg, or antihypertensive medication for more than 6 months). The mean age of our patients was 68 +/- 13 years.

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 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 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 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 (see tachograms in figure 1); premature beats, artifacts and noise were excluded using an adaptive filter considering the instantaneous variability .

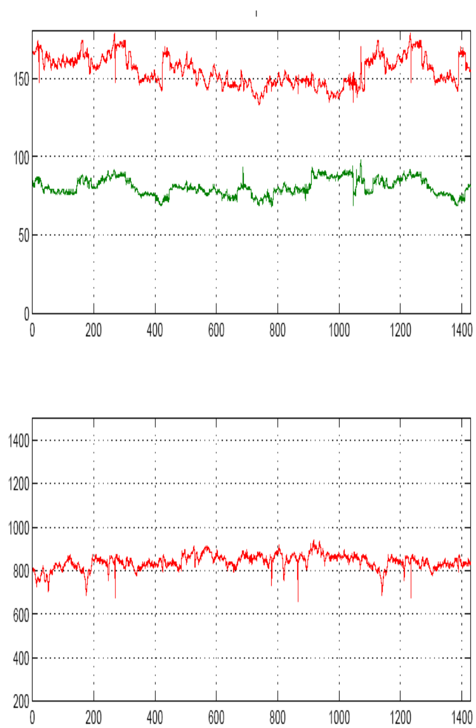

Figure 1: Tachograms of blood pressure (upper panel) and heart rate (lower panel)

For statistical analysis the Mann-Whithey-U test was applied to find differences within the calculated parameters.

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 [4].

Heart rate variability (HRV)

Respecting the suggestions 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): 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): 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 [5]. Several new measures of non-linear dynamics in order to distinguish different types of heart rate dynamics as proposed by Kurths [6] 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 [7]. 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

Time and frequency domain parameters of heart rate variability showed comparable dynamics in normotensive and hypertensive patients (Fig.1,2): there was a pronounced decline 24h after surgery and partial recovery seven days after surgery.

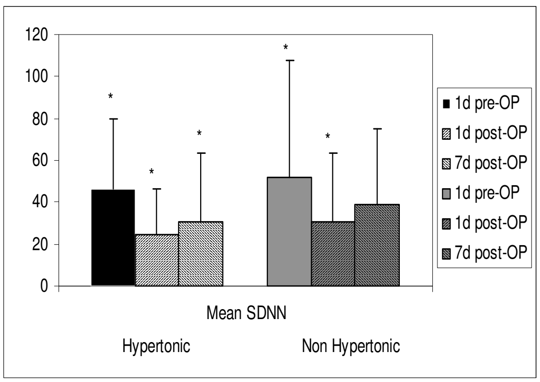

Figure 2: Mean SDNN. *: $p<0.05$ vs. 1d pre-OP #: $p<0.05$ vs. 2d post-OP. §:$p<0.05$ same time

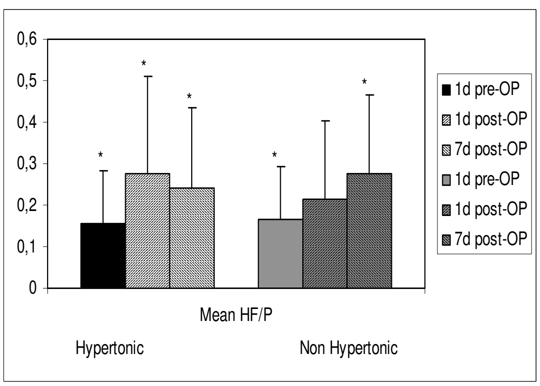

Figure 3: HF/P (see Fig.2 for further legends)

Baroreflex sensitivity showed a different behaviour throughout the postoperative course. Regarding the number of bradycardic regulations, there was a marked reduction in both groups 24h after surgery. After 7d partial recovery was observed in normotensive patients, while the values remained unchanged in hypertensives. The same, but less pronounced, was true for the average strength of regulation (Fig. 4,5).

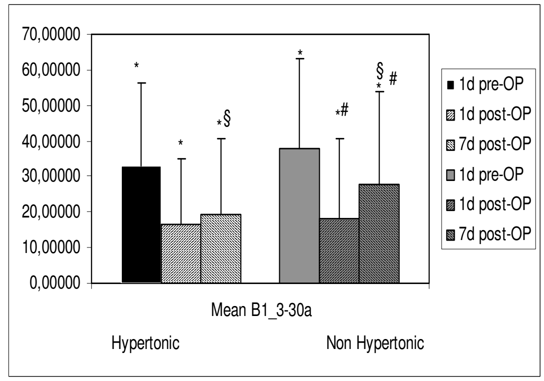

Fig. 4: Bradycardic BRS (number). See Fig.2 for further legends

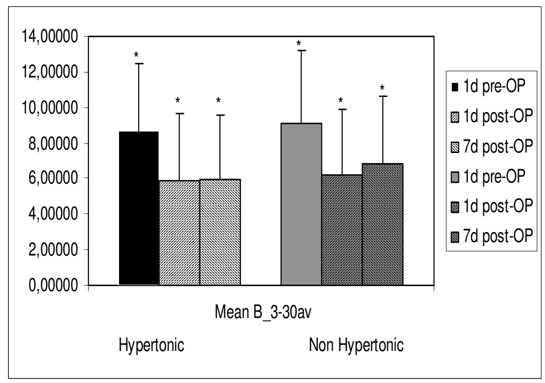

Fig. 5: Bradycardic BRS (strength). See Fig.2 for further legends

For the tachycardic regulation, values for number and strength of regulation were more or less unchanged one day after surgery, but were significantly decreased one week after the operation; this drop was more pronounced in the hypertensive group (Fig. 6).

As a representative parameter of the nonlinear dynamics analyses, WPSUM02 was chosen as a parameter describing reduced variability (the higher the value, the lower overall variability, see "Methods"). There is an increase in both groups, being more pronounced in hypertensive patients. In addition, in hypertensive patients there seems to be no tendency to recovery (Fig. 7). The same tendency is true for the parameter "Forbidden words" (data not shown).

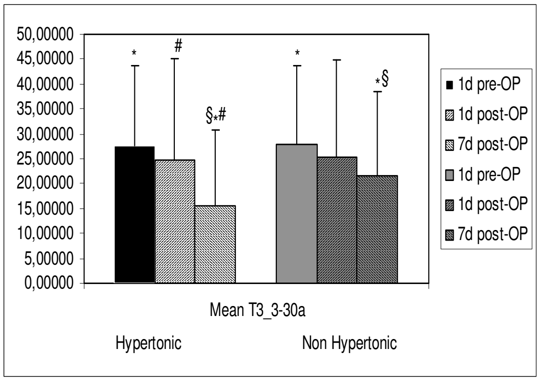

Fig. 6: Tachycardic BRS (number). See Fig.2 for further legends

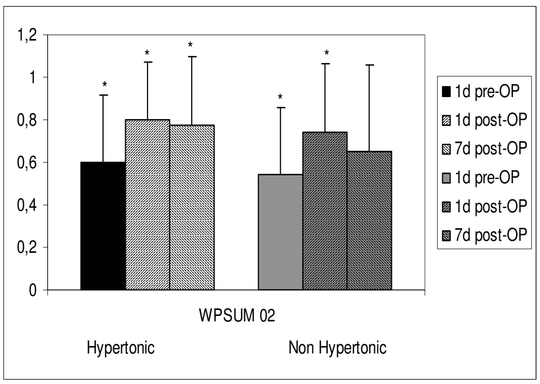

Fig. 7: Symbolic dynamics: WPSUM_02. See Fig.2 for further legends

4. Discussion and conclusions

Although there still is a lack of knowledge concerning the pathogenesis of essential hypertension, a correlation to reduced baroreflex sensitivity and heart rate variability seems possible [1,2]. 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 [3,8]. Therefore the aim of our study was to assess differences of autonomic regulation among normotensive and hypertensive patients in response to cardiac surgery.

We did not find major differences in the preoperative values, and we did not expect that, because our “control” group also suffered from cardiovascular diseases and therefore altered regulation can be assumed. The analysis of HRV-parameters did not disclose any major variations among the groups during the postoperative course.

Baroreflex sensitivity, however, was markedly reduced in hypertensives one week after surgery. This may explain the increased risk of patients with hypertension after cardiac surgery [9]. Ongoing research is required for further clarification of the pathophysiology of this phenomenon and to establish strategies to restore autonomic function.

Acknowledgements

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