Role of heart-rate variability in preoperative assessment of physiological reserves in patients undergoing major abdominal surgery

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Background: Major abdominal surgery (MAS) is associated with increased morbidity and mortality. The main objective of our study was to evaluate the predictive value of heart-rate variability (HRV) concerning development of postoperative complications in patients undergoing MAS. The secondary objectives were to identify the relationship of HRV and use of vasoactive drugs during anesthesia, intensive care unit length of stay (ICU-LOS), and hospital length of stay (H-LOS).

Patients and methods: Sixty-five patients scheduled for elective MAS were enrolled in a prospective, single-center, observational study. HRV was measured by spectral analysis (SA) preoperatively during orthostatic load. Patients were divided according to cardiac autonomic reactivity (CAR; n=23) and non-cardiac autonomic reactivity (NCAR; n=30).

Results: The final analysis included 53 patients. No significant difference was observed between the two groups regarding type of surgery, use of minimally invasive techniques or epidural catheter, duration of surgery and anesthesia, or the amount of fluid administered intraoperatively. The NCAR group had significantly greater intraoperative blood loss than the CAR group (541.7±541.9 mL vs 269.6±174.3 mL, p<0.05). In the NCAR group, vasoactive drugs were used during anesthesia more frequently (n=21 vs n=4; $p<0.001$), and more patients had at least one postoperative complication compared to the CAR group (n=19 vs n=4; $p<0.01$). Furthermore, the NCAR group had more serious complications (Clavien–Dindo ≥ Grade III n=6 vs n=0; $p<0.05$) and a greater number of complications than the CAR group (n=57 vs n=5; $p<0.001$). Significant differences were found for two specific subgroups of complications: hypotension requiring vasoactive drugs (NCAR: n=10 vs CAR: n=0; $p<0.01$) and ileus (NCAR: n=11 vs CAR: n=2; $p<0.05$). Moreover, significant differences were found in the ICU-LOS (NCAR: 5.7±3.5 days vs CAR: 2.6±0.7 days; $p<0.0001$) and H-LOS (NCAR: 12.2±5.6 days vs CAR: 7.2±1.7 days; $p<0.0001$).

Conclusion: Preoperative HRV assessment during orthostatic load is objective and useful for identifying patients with low autonomic physiological reserves and high risk of poor postoperative course.

Keywords: heart-rate variability, spectral analysis, orthostatic load, autonomic dysfunction, major abdominal surgery, postoperative complications

Introduction

A fundamental feature of a healthy organism is continuous communication between vital organs through the autonomic nervous system (ANS).¹ The ANS is composed of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS) and plays a crucial role in maintaining homeostasis in response to internal and external stimuli.² Surgical trauma leads to tissue injury and activates inflammatory...
pathways. The organism responds with complex reactions, leading to structural and functional repair of injured tissues. However, dysregulation of the inflammatory response may aggravate local tissue damage, leading to shock, multiple organ dysfunction syndrome (MODS), and death. Under physiological conditions, the pro-inflammatory response is balanced by an anti-inflammatory response, including the cholinergic anti-inflammatory pathway of the vagus nerve.

In addition, anesthetics influence cardiovascular homeostasis, and pre-existing autonomic dysfunction (AD) can lead to hemodynamic instability during anesthesia. Persisting autonomic regulation represents adequate physiological reserves and better reactivity to various insults during the perioperative course.

Analysis of heart-rate variability (HRV) – the oscillation of intervals between consecutive heart beats – is an accepted noninvasive method of evaluating the autonomic influence on heart activity. The human organism is a nonlinear biological system characterized by so-called oscillation phenomena. The oscillations originate from a neurally mediated organ interaction. The disturbance in variations of oscillations may show the beginning of, or advanced, deterioration of organ systems. HRV is an objective method for possibly evaluating this phenomenon. In our study, we used spectral analysis of HRV, which is a linear method, that simplified the biosignal of HRV. However, some autonomic challenges, such as orthostatic load or the Valsalva maneuver, can improve the sensitivity of ANS assessment and better reflect the real autonomic physiological reserves of patients.

AD represented by reduced HRV is widely accepted as an independent adverse prognostic factor in various pathological conditions (eg, myocardial infarction, coronary artery disease, congestive heart failure, diabetes mellitus, MODS). AD may negatively influence the perioperative course due to hemodynamic instability during anesthesia, thus increasing postoperative morbidity and mortality. The link between low HRV and worse surgical outcome has been confirmed by several studies. Nevertheless, routine assessment of HRV by anesthesiologists is still rare.

The main goal of our study was to investigate the relationship between spectral analysis of HRV during orthostatic load with postsurgical outcome in patients scheduled for elective major abdominal surgery (MAS). The primary endpoint was the occurrence of postoperative complications, according to the Clavien–Dindo classification.

Secondary endpoints were evaluation of HRV as a predictor of the need for vasoactive drugs during anesthesia, intensive care length of stay (ICU-LOS), and hospital length of stay (H-LOS).

Materials and methods
This prospective observational study was approved by the Institutional Ethics Committee of the University Hospital Ostrava (ref no 606/2014) and registered at ClinicalTrials.gov (Identifier NCT02375412). Written informed consent was signed by all enrolled patients. The study was conducted between February 2015 and December 2016 at University Hospital Ostrava, Czech Republic. We enrolled 65 patients scheduled for elective MAS. The exclusion criteria were: emergency or acute surgery, absence of sinus rhythm, American Society of Anesthesiologists (ASA) physical status I, and age <18 years. Standard baseline demographic and clinical data were collected before surgery.

HRV was measured in a quiet, mildly illuminated room, at room temperature 22°C–24°C, between 14:00 and 17:00 the day before the surgery. Short-term spectral analysis of HRV was conducted according to Task Force recommendations using a DiANS PF8 diagnostic system (Olomouc, Czech Republic). The R-R intervals on the electrocardiogram were recorded with a sampling rate of 1,000 Hz, and the acquired data were automatically filtered in order to eliminate ectopic beats or artifacts using the recognition algorithm, as verified manually. The intervals were analyzed using modified fast Fourier transformation (FFT). Recordings were obtained in three consecutive positions (supine-1, standing, and supine-2), each lasting 300 seconds. The first supine position (supine-1) was an adaptive one, the active standing position (standing) represents autonomic load, and another supine position (supine-2) is the final position for an overall evaluation of the spectral parameters of HRV. The final results were displayed in the form of a three-dimensional chart of HRV patterns. This HRV analysis allowed a visual overview of HRV dynamics and improved the evaluation of cardiac autonomic reactivity.

In addition to the visual representation, the following parameters of frequency (spectral) domain were calculated in every position: (1) spectral power of low frequency (LF; 0.05–0.15 Hz), reflecting a combination of sympathetic and parasympathetic effects on cardiac autonomic tone; (2) spectral power of high frequency (HF; 0.15–0.4 Hz) corresponding exclusively to parasympathetic tone; (3) total spectral power (TP; 0.05–0.4 Hz), representing the main outcome variables in both frequency bands (LF + HF); and (4) the LF to HF ratio (LF/HF), representing the index of sympathovagal interaction. Spectral indexes were expressed both in absolute values (ms²) and natural logarithm (ln). For the final evaluation of HRV, we used the TP from the supine-2 position. Patients were divided into two
groups: cardiac autonomic reactivity (CAR), characterized by a calculated TP (supine-2) $\geq 200$ ms$^2$ and a chart with peaks of spectral energy in a particular frequency band (Figure 1), and non-cardiac autonomic reactivity (NCAR), characterized by TP $< 200$ ms$^2$ and a plain chart due to a reduction in overall spectral power (Figure 2).

Anesthetic and surgical techniques were carried out in a standardized manner. Surgical procedures were undertaken under general anesthesia (GA) or a combination of general and epidural anesthesia. GA was induced by the administration of sufentanil, propofol, and cis-atracurium. Sevoflurane in an oxygen/air mixture was added to maintain balanced anesthesia. Mechanical ventilation was standardized (6–8 mL/kg predicted body weight, PEEP 5–7 cm H$_2$O). Anesthesia management (ie, use of balanced crystalloids, blood products, and vasoactive drugs) was left to the discretion of the anesthesiologist. Intraoperative data such as the duration of the procedure, fluid intake, output, and the use of vasoactive drugs were recorded. All patients were transferred to the ICU after the surgical procedure.

Figure 1 Typical three-dimensional chart of a spectral analysis of heart-rate variability during orthostatic load in the cardiac autonomic reactivity group. Notes: Standing augmented the low-frequency power (0.05–0.15 Hz) and reduced the high-frequency power (0.15–0.4 Hz) in T2 due to baroreceptor unloading and reduced vagal activity. High-frequency power was augmented in the repeated supine position in T3. The frequency of fluctuations in R-R intervals (Hz) is given on the x-axis; power spectral density (PSD; ms$^2$/Hz) on the y-axis; and time (s) on the z-axis. T1: supine-1, T2: standing, T3: supine-2.

Figure 2 Typical plain three-dimensional chart of a spectral analysis of heart-rate variability during orthostatic load in the non-cardiac autonomic reactivity group. Notes: The frequency of fluctuations in R-R intervals (Hz) is given on the x-axis; power spectral density (PSD; ms$^2$/Hz) on the y-axis; and time (s) on the z-axis. T1: supine-1, T2: standing, T3: supine-3.
Complications were defined as any postoperative process that was not part of normal recovery during the postoperative period. These complications were classified according to the Clavien–Dindo classification. Grades I and II are defined as any deviation from the normal postoperative course without need for surgical, endoscopic, or radiological intervention (Grade I), with Grade II including a need for pharmacological treatment; Grade III requires a surgical, endoscopic, or radiological intervention without (Grade IIIa) or with GA (Grade IIIb); Grade IV includes single-organ failure requiring ICU care (Grade IVa) or multiple organ failure (Grade IVb); and Grade V is characterized by the patient’s death. We recorded the most severe grade of complications for each patient according to recommendations. Moreover, the complications were divided into two subgroups: minor (Grade I and Grade II) and major (Grade ≥ III). All complications encountered in our study were recorded.

### Statistical analysis
For numerical data, the arithmetic mean ± standard deviation (SD) was computed. Categorical data were summarized by absolute count and relative frequency (%). Differences between the CAR and NCAR were assessed using the t-test (numerical data) or Fisher exact test (categorical data). All statistical analyses, figures, and tables were created by a certified statistician (co-author MB) using R software (version 3.3.3). The level of significance was defined as $p \leq 0.05$.

### Results
Sixty-five patients were screened for the study. We excluded 12 patients from further analysis due to cancellation of the operative procedures (n=2), technically inadequate recordings (artifacts or excessive ectopic beats, n=7), and missing data during the postoperative period (n=3). Therefore, the final study population comprised 53 patients; see the CONSORT flow diagram (Figure 3). No significant differences were found between groups with regard to demographic characteristics. We found some significant differences in medical history between the CAR and NCAR (myocardial infarction: n=0 vs n=6, $p<0.05$; diabetes mellitus: n=1 vs n=11, $p<0.01$; and hyperlipidemia: n=4 vs n=18, $p<0.01$, respectively). These differences in comorbidities were reflected by differences in chronic medications between the CAR and NCAR (per oral antidiabetics: n=0 vs
n=7, p<0.05; statins: n=3 vs n=14, p<0.05, respectively). We also found that a significantly greater proportion of patients in the CAR had ASA II than the NCAR (78% vs 47%, p<0.05; Table 1).

Cardiac autonomic reactivity during orthostatic load was observed in 23 patients (CAR) and a reduced autonomic response was observed in 30 patients (NCAR). Significant differences were found between study groups in all calculated spectral power indices of HRV expressed in absolute values (ms²) and natural logarithm (LN) values in all three measurement positions during orthostatic load (p<0.0001). The LF/HF ratio was significantly different in only supine-1 (p<0.05; Table 2).

### Table 1 Patient characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CAR</th>
<th>NCAR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Demographic data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of patients</td>
<td>23</td>
<td>30</td>
<td></td>
</tr>
<tr>
<td>Age, years</td>
<td>64.8±8.4</td>
<td>69.1±8.2</td>
<td>NS*</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>16/7</td>
<td>22/8</td>
<td>NS</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>80.4±13.3</td>
<td>81.5±11.2</td>
<td>NS</td>
</tr>
<tr>
<td>Height, cm</td>
<td>172.3±8.4</td>
<td>172.2±8.6</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>27.0±3.5</td>
<td>27.1±3.6</td>
<td>NS</td>
</tr>
<tr>
<td>BSA, m²</td>
<td>1.9±0.2</td>
<td>2.0±0.2</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Medical conditions</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>14 (61)</td>
<td>25 (83)</td>
<td>NS</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>2 (9)</td>
<td>8 (27)</td>
<td>NS</td>
</tr>
<tr>
<td>Chronic heart failure</td>
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<td>2 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>History of MI</td>
<td>0 (0)</td>
<td>6 (20)</td>
<td>0.0303</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>3 (13)</td>
<td>3 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>1 (4)</td>
<td>11 (37)</td>
<td>0.0071</td>
</tr>
<tr>
<td>Chronic renal failure</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>NS</td>
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<tr>
<td>COPD</td>
<td>1 (4)</td>
<td>5 (17)</td>
<td>NS</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>4 (17)</td>
<td>18 (60)</td>
<td>0.0022</td>
</tr>
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<td><strong>Medication</strong></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>B-adrenergic blockers</td>
<td>10 (43)</td>
<td>12 (40)</td>
<td>NS</td>
</tr>
<tr>
<td>ACE inhibitors</td>
<td>7 (30)</td>
<td>11 (37)</td>
<td>NS</td>
</tr>
<tr>
<td>ARBs</td>
<td>1 (4)</td>
<td>6 (20)</td>
<td>NS</td>
</tr>
<tr>
<td>CCBs</td>
<td>4 (17)</td>
<td>12 (40)</td>
<td>NS</td>
</tr>
<tr>
<td>Diuretics</td>
<td>5 (22)</td>
<td>8 (27)</td>
<td>NS</td>
</tr>
<tr>
<td>Aspirin</td>
<td>3 (13)</td>
<td>8 (27)</td>
<td>NS</td>
</tr>
<tr>
<td>Anticoagulants</td>
<td>1 (4)</td>
<td>5 (17)</td>
<td>NS</td>
</tr>
<tr>
<td>Oral antidiabetics</td>
<td>0 (0)</td>
<td>7 (23)</td>
<td>0.0148</td>
</tr>
<tr>
<td>Insulin</td>
<td>0 (0)</td>
<td>4 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Statins</td>
<td>3 (13)</td>
<td>14 (47)</td>
<td>0.0163</td>
</tr>
</tbody>
</table>

**Notes:** Data are presented as mean ± standard deviation. *p>0.05.

**Abbreviations:** NS, not significant; CAR, cardiac autonomic reactivity; NCAR, non-cardiac autonomic reactivity; BMI, body mass index; BSA, body surface area; MI, myocardial infarction; COPD, chronic obstructive pulmonary disease; ACE, angiotensin-converting enzyme; ARBs, angiotensin II receptor blockers; CCBs, calcium channel blockers; ASA, American Association of Anesthesiologists physical status classification system.

With regarding intraoperative characteristics, no difference was observed between groups for the type of surgery, use of minimally invasive techniques, use of an epidural catheter, amount of intraoperative fluids, and duration of surgery and anesthesia. However, we found significant differences in blood loss (269.6±174.3 mL vs 541.7±541.9 mL, p<0.05) and the use of at least one vasoactive drug (n=4 vs n=11, p=0.001; Table 3) between the CAR and NCAR, respectively.

The number of patients with at least one complication was significantly lower in the CAR than the NCAR (n=4 vs n=19, p=0.001) group. In addition, significant differences were found in Clavien–Dindo classification Grade II (CAR, n=2 vs NCAR, n=12, p<0.05) and Grade ≥ III (CAR, n=0 vs NCAR, n=6; p<0.05; Table 4). Analyzing the frequency of particular types of complications, we found a significant difference in the occurrence of hypotension requiring vasoactive drugs (CAR, n=0 vs NCAR, n=10, p<0.05) as well as ileus (CAR, n=2 vs NCAR, n=11, p<0.05). Finally, the overall number of complications was significantly lower in the CAR than the NCAR group (n=5 vs n=57, p<0.001, Table 5).

### Table 2 Intergroup comparison of parameters in a frequency domain analysis of heart-rate variability during orthostatic load (supine-1-standing-supine-2)

<table>
<thead>
<tr>
<th>Spectral power</th>
<th>CAR</th>
<th>NCAR</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Supine-1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Power LF, ms²</td>
<td>243.4±140.7</td>
<td>59.0±39.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Power LF, ln(ms²)</td>
<td>5.3±0.6</td>
<td>3.7±1.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Power HF, ms²</td>
<td>183.5±106.4</td>
<td>32.6±20.3</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Power HF, ln(ms²)</td>
<td>5.1±0.6</td>
<td>3.2±0.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total power, ms²</td>
<td>426.9±233.8</td>
<td>91±53.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total power, ln(ms²)</td>
<td>5.9±0.5</td>
<td>4.3±0.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LF/HF</td>
<td>1.4±0.6</td>
<td>2.2±1.8</td>
<td>0.0361</td>
</tr>
<tr>
<td>Standing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Power LF, ms²</td>
<td>259.1±145.4</td>
<td>51.7±39.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Power LF, ln(ms²)</td>
<td>5.4±0.6</td>
<td>3.7±1.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Power HF, ms²</td>
<td>93.4±42.4</td>
<td>21.2±19.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Power HF, ln(ms²)</td>
<td>4.4±0.5</td>
<td>2.7±0.9</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total power, ms²</td>
<td>352.5±166.3</td>
<td>72.9±53.0</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Total power, ln(ms²)</td>
<td>5.8±0.5</td>
<td>4.1±0.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LF/HF</td>
<td>3.2±2.0</td>
<td>3.9±3.5</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Notes:** Data are presented as mean ± standard deviation. *p>0.05.

**Abbreviations:** CAR, cardiac autonomic reactivity; HF, high frequency; LF, low frequency; NCAR, non-cardiac autonomic reactivity; NS, not significant.
Concerning outcomes, ICU-LOS and H-LOS were significantly lower in the CAR than the NCAR group (2.6±0.7 days vs 5.7±3.5 days \( p<0.0001 \) and 7.2±1.7 days vs 12.2±5.6 \( p<0.0001 \), respectively; Table 4).

### Discussion

Our study used a dynamic autonomic test (orthostatic load) for preoperative assessment of HRV to identify patients with reduced autonomic physiological reserves undergoing elective MAS. Our findings clearly show a higher occurrence of postoperative complications, higher hemodynamic instability during anesthesia, and prolonged ICU-LOS and H-LOS in patients with low autonomic reserves (NCAR). Therefore, we confirmed that patients with AD are at risk of an adverse intraoperative and postoperative course.

The NCAR patients had a plain spectral analysis for HRV without reactivity during orthostatic load, and all of their calculated parameters were reduced. The reduction in HRV parameters was similar to the identification of diabetic cardiovascular autonomic neuropathy (CAN).

CAN is an accepted risk factor for intraoperative hemodynamic instability and increased occurrence of postoperative cardiovascular events, including sudden death. CAN is a complication not only of diabetes mellitus, but also of other comorbidities, including chronic coronary disease, chronic heart failure, hypertension, and chronic obstructive pulmonary disease. Neurological and psychiatric disorders have some degree of AD. In our study, the NCAR group comprised patients with more chronic comorbidities than in the CAR group. We found that AD reflected both the number and severity of illnesses in the CAR group. These findings were confirmed by an assessment of ASA; the NCAR group comprised more patients with ASA III and IV than the CAR group, which comprised predominantly ASA II patients.

During anesthesia, the NCAR group had a significantly greater need for vasoactive drugs to adequately maintain blood pressure. NCAR and CAR were similar in regard to intraoperative characteristics (ie, amount of administered fluids, type of surgery, use of minimally invasive technique, etc.).

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**Table 3** Intraoperative characteristics

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>CAR</th>
<th>NCAR</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of surgery</td>
<td></td>
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</tr>
<tr>
<td>Colon resection</td>
<td>13 (57)</td>
<td>14 (47)</td>
<td>NS*</td>
</tr>
<tr>
<td>Low anterior resection</td>
<td>10 (43)</td>
<td>16 (53)</td>
<td>NS</td>
</tr>
<tr>
<td>Minimally invasive technique</td>
<td>17 (74)</td>
<td>20 (67)</td>
<td>NS</td>
</tr>
<tr>
<td>Epidural catheter</td>
<td>20 (87)</td>
<td>22 (73)</td>
<td>NS</td>
</tr>
<tr>
<td>Blood loss, mL</td>
<td>269.6±14.3</td>
<td>541.7±541.9</td>
<td>0.0140</td>
</tr>
<tr>
<td>PRBCs</td>
<td>0 (0)</td>
<td>5 (17)</td>
<td>NS</td>
</tr>
<tr>
<td>FFP</td>
<td>0 (0)</td>
<td>5 (17)</td>
<td>NS</td>
</tr>
<tr>
<td>Intraoperative fluids, mL</td>
<td>2.269.6±439.1</td>
<td>2.256.7±598.1</td>
<td>NS</td>
</tr>
<tr>
<td>Urine output, mL</td>
<td>489.1±245.9</td>
<td>516.0±242.6</td>
<td>NS</td>
</tr>
<tr>
<td>At least one vasoactive drug</td>
<td>4 (17)</td>
<td>21 (70)</td>
<td>0.0002</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>3 (13)</td>
<td>9 (30)</td>
<td>NS</td>
</tr>
<tr>
<td>Noradrenalin</td>
<td>2 (9)</td>
<td>20 (67)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Duration of surgery, minutes</td>
<td>189.6±63.5</td>
<td>191.7±59.5</td>
<td>NS</td>
</tr>
<tr>
<td>Duration of anesthesia, minutes</td>
<td>211.5±64.8</td>
<td>213.3±60.1</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Notes:** Data are presented as mean ± standard deviation or n (%). *p<0.05.

**Abbreviations:** CAR, cardiac autonomic reactivity; FFP, fresh frozen plasma; NCAR, non-cardiac autonomic reactivity; NS, not significant; PRBCs, packed red blood cells.

**Table 4** Postoperative complications according to the Clavien–Dindo classification and length of stay

<table>
<thead>
<tr>
<th>Classification</th>
<th>CAR</th>
<th>NCAR</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Minor (I–II)</td>
<td>4 (17)</td>
<td>13 (43)</td>
<td>NS*</td>
</tr>
<tr>
<td>I</td>
<td>2 (9)</td>
<td>1 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>II</td>
<td>2 (9)</td>
<td>12 (40)</td>
<td>0.0129</td>
</tr>
<tr>
<td>Major (≥III)</td>
<td>0 (0)</td>
<td>6 (20)</td>
<td>0.0303</td>
</tr>
<tr>
<td>III</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>NS</td>
</tr>
<tr>
<td>IIb</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>IVa</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>IVb</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>V</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>At least one complication</td>
<td>4 (17)</td>
<td>19 (63)</td>
<td>0.0001</td>
</tr>
<tr>
<td>ICU-LOS, days</td>
<td>2.6±0.7</td>
<td>5.7±3.5</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>H-LOS, days</td>
<td>7.2±1.7</td>
<td>12.2±5.6</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Notes:** Data are presented as mean ± standard deviation or n (%). *p<0.05.

**Abbreviations:** CAR, cardiac autonomic reactivity; ICU-LOS, intensive care length of stay; H-LOS, hospital length of stay; NS, not significant.

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**Table 5** Complications encountered in the study

<table>
<thead>
<tr>
<th>Complications</th>
<th>CAR</th>
<th>NCAR</th>
<th>( p )-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lung</td>
<td>0 (0)</td>
<td>3 (10)</td>
<td>NS*</td>
</tr>
<tr>
<td>Abdominal</td>
<td>0 (0)</td>
<td>3 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Urinary tract</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>Central venous catheter</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>Wound</td>
<td>1 (4)</td>
<td>3 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arrhythmia</td>
<td>1 (4)</td>
<td>4 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Hypotension requiring vasoactive drugs</td>
<td>0 (0)</td>
<td>10 (33)</td>
<td>0.0029</td>
</tr>
<tr>
<td>Heart failure</td>
<td>0 (0)</td>
<td>1 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>Respiratory failure requiring intubation</td>
<td>0 (0)</td>
<td>3 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Acute kidney injury</td>
<td>0 (0)</td>
<td>4 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ileus</td>
<td>2 (9)</td>
<td>11 (37)</td>
<td>0.0252</td>
</tr>
<tr>
<td>Gastrointestinal bleeding</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>Leak anastomosis</td>
<td>0 (0)</td>
<td>3 (10)</td>
<td>NS</td>
</tr>
<tr>
<td>Delirium</td>
<td>1 (4)</td>
<td>5 (17)</td>
<td>NS</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>Death</td>
<td>0 (0)</td>
<td>2 (7)</td>
<td>NS</td>
</tr>
<tr>
<td>Total number of complications</td>
<td>5</td>
<td>57</td>
<td>0.0006</td>
</tr>
</tbody>
</table>

**Notes:** Data are presented as n (%). *p<0.05.

**Abbreviations:** CAR, cardiac autonomic reactivity; NCAR, non-cardiac autonomic reactivity; NS, not significant.
and overall morbidity. 20,21,25–27,42 Various measurements to evaluate ANS (triangular index, fractal scaling exponent α1, BRS) were used, but all studies confirmed the significant influence of ANS on cardiovascular homeostasis.

Postoperative ileus increases postoperative morbidity and is a cause of prolonged hospital stay after MAS. The complex pathophysiology of postoperative ileus involves several factors, including the degree of surgical trauma. However, AD is also an important factor in its development. 43 In our study, NCAR patients had extremely reduced HF power (dominantly parasympathetic vagal activity) and LF power (sympathetic and parasympathetic influence). The reduced parasympathetic and sympathetic parts of the ANS represent serious AD, the main reason for impaired gastrointestinal motility in NCAR.

We found significantly longer ICU-LOS and H-LOS in NCAR patients. These results are related to higher grade complications according to the Clavien–Dindo classification (grade ≥ III) in NCAR – that is, the number of reoperations and organ failures. This finding is consistent with another study in which decreased HRV was found to be a predictor of prolonged ICU stay in patients after coronary artery bypass grafting (CABG) surgery and abdominal aortic surgery. 18,19,24,25 However, variable parameters used for HRV assessment and time of own measurement (fractal scaling exponent α1, very low frequency [VLF] measurement during 24 h, preoperative and postoperative measurements) were also used in these studies.

HRV was identified as a powerful predictor of long-term mortality, with LF/HF ratio <2 and postoperative elevation of serum troponin I levels being independent predictors of 1-year mortality in patients undergoing major non-cardiac surgery. 22 The same authors investigated 2-year mortality and found that LF/HF ratio <2 remained an independent predictor of mortality together with a history of heart congestion and age >70 years. 23 These findings suggest that HRV measurement reflects physiological reserves necessary for recovery after hospital discharge. We evaluated LF/HF in the present study, but our values were different and we did not find significant differences in the LF/HF ratio between our study groups (except the supine-1 adaptive position). These findings may be due to different measurement methods. Our LF/HF ratios were calculated from measurements made during orthostatic load, which influenced the particular frequency band depending on the specific position. Moreover, our measurements were performed the day before surgery. Filipovic et al used LF/HF from a supine position immediately before induction of GA. Measurement in only one static
position and psychological stress before surgery could have significantly influenced the LF and HF values.\textsuperscript{12,13}

In clinical research of HRV, various methods of analysis (time-domain analysis, geometric analysis, frequency-domain analysis, and entropy or fractal analysis), indexes, and units (absolute, logarithmic, standard units) have been used. Moreover, differences are present in the time and duration of measurements. No normative HRV values are currently, generally, accepted.\textsuperscript{14,15} As HRV is a very sensitive biosignal, high interindividual (age, gender, psychological stress during measurement, etc.) and intraindividual (circadian rhythm, food intake, smoking, etc.) variability can be obtained.\textsuperscript{16–18} Most chronic diseases manifest some degree of autonomic dysfunction.\textsuperscript{8,10–17} In addition, HRV measurements are influenced by the use of chronic medication.\textsuperscript{6,10} The use of some autonomic challenge (ie, the Valsalva maneuver or orthostatic load) can improve HRV measurement and better reflect the real degree of autonomic physiological reserves, in contrast to measurements under static conditions.\textsuperscript{10,11} In our study, we used orthostatic load which can help us identify patients without autonomic reactivity (NCAR) among elderly patients with comorbidities scheduled for MAS. NCAR was characterized by a plain chart of HRV patterns without reactivity in particular positions and low TP in the supine-2 position (TP < 200 ms\textsuperscript{2}). We used TP because it represents overall HRV, and we used TP from the supine-2 position because it showed the real status of autonomic regulation, especially due to uncovered vagal activity, which can be suppressed by psychological stress during evaluation in the supine-1 position. Moreover, vagal activity is reflexively augmented after laying down from standing to the supine-2 position. As a global parameter of HRV in the supine-2 position, TP can be considered acceptable for quick determination of the real autonomic physiological reserves of patients.

This study has a few possible limitations: the small sample size and its being performed at a single center.

**Conclusion**

Preoperative assessment of autonomic physiological reserves based on HRV is important for the early identification of patients at high risk for the development of intraoperative and postoperative complications. This has the potential to influence perioperative clinical decision-making and eventually improve outcome. We suggest that standardized measurement of HRV during autonomic challenge be performed by anesthesiologists as routine perioperative practice. However, further research in the field is needed.

**Acknowledgments**

The authors thank Dr Rudolf Metelka and Professor Jaroslav Opavský from University Hospital Olomouc for advice on HRV measurement.

Michal Burda acknowledges partial support by the NPU II project LQ1602 “IT4Innovations excellence in science” provided by the Ministry of Education Youth and Sport, Czech Republic.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**


