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# Autonomic balance and impedance cardiography analysis in patients undergoing leg revascularization

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## ABSTRACT

**Introduction:** Changes in autonomic nervous system (ANS) balance associated with endovascular interventions may potentially cause haemodynamic abnormalities that lead to periprocedural cardiovascular complications. This study aimed to determine the relationships between changes in ANS balance and impedance cardiography (ICG) parameters after endovascular leg revascularization.

**Material and methods:** Before the procedure, and 1, 3 and 5h after the intervention, 5-min examinations of both ANS balance and ICG parameters were performed using a Task Force Monitor in 42 patients undergoing endovascular leg revascularization.

**Results:** When compared to patients with intermittent claudication, individuals with chronic limb-threatening ischaemia had a significantly shorter R-R interval and lower stroke volume (SV) and left ventricle ejection time (LVET) at the beginning of the study. During the 5h after endovascular leg revascularization, significant fluctuations were noted in the following: heart rate, frequency-domain parameters of heart rate variability, baroreflex effectiveness indices, and ICG parameters, such as total peripheral resistance, SV, LVET, and ejection rate. The deltas of ANS parameters correlated with the deltas of ICG parameters in the respective periods of measurement.

**Conclusions:** Dynamic fluctuations in ICG and ANS parameters that occurred in patients who had undergone endovascular leg revascularization might potentially affect the risk of the occurrence of a cardiovascular event in the periprocedural period. The correlations between the ANS and ICG parameters suggest that haemodynamic oscillations after endovascular leg revascularization are mediated by changes in ANS activity, most probably through a sympathoexcitatory effect of the procedure related to changes in skeletal muscle perfusion.

**Key words:** peripheral artery disease, chronic lower limb ischaemia, impedance cardiography, heart rate variability, endovascular revascularization

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## Introduction

It is recognized that endovascular procedures are associated with a periprocedural risk of a cardiovascular event, including periprocedural death, of 1–5% [1, 2]. A potential explanation of such a high prevalence of severe complications in patients undergoing minimally invasive leg revascularization is the coexistence of factors such as multisite atherosclerosis, cardiac failure, haemodynamic changes related to the procedure (e.g., massive bleeding or acute kidney insufficiency), as well as reperfusion syndrome and a systemic toxic effect of metabolic products washed out from the leg regions that were ischaemic before the procedure [3, 4]. These substances may, in turn, increase vascular permeability and provoke changes in circulating blood volume, induce acute inflammatory reaction and endothelial dysfunction, and can lead to acute fluctuations in the balance of autonomic nervous system (ANS) activity.

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In this study, the authors tested the hypothesis that a periprocedural imbalance in ANS activity provokes systemic changes in haemodynamic cardiac function that are measurable using impedance cardiography (ICG) in patients undergoing leg revascularizing procedures. The abnormalities mentioned above might be a potential substrate for arrhythmia and form the basis for the occurrence of cardiac and limb-vascular adverse events. This hypothesis, which considers nervous and metabolic feedback in cardiac and limb ischaemia, is supported, on the one hand, by (a) numerous publications showing an imbalance in ANS activity as a predictor of the occurrence of a major adverse cardiovascular event [5]; (b) a report of ANS activity as a potential cause of leg artery spasm [6]; and (c) the fact that a rest heart rate, one of important ANS balance parameters, determined a walking distance in patients with vascular-type claudication [7]; and, on the other, that ANS balance not only influences the course of cardiovascular diseases, including leg ischaemia but (d) may also be impaired by feedback relating to the severity of leg ischaemia and the revascularization procedure. The last association between leg ischaemia and ANS activity might be mediated through (I) remote feedback in the autonomic control of the heart rate, cardiopulmonary baroreflex, and peripheral vasodilatation reserve resulting from skeletal muscle reperfusion after prolonged lower limb ischaemia and the activation of muscle mechano-, chemo- and metaboreceptors (i.e. sympathoexcitatory effect, norepinephrine overflow) [3, 8–17]; and (II) changes to the filling of leg veins in the standing position (venoarteriolar reflex) due to increased leg perfusion after the procedure, which may, in turn, impair an orthostatic response [18, 19], which was improved after successful endovascular revascularization of the femoropopliteal level of leg arteries [20]. Moreover, in patients with chronic limb-threatening ischaemia (CLTI), ANS imbalance may also potentially be affected by: (III) leg pain severity; (IV) the sympathoexcitatory effect of inflammatory processes secondary to the wound or infection [3, 11]; (V) peripheral ischaemic neuropathy [21]; and (VI) lumbar sympathectomy [6] and spinal cord stimulation [22], which are recognized as therapeutic methods for CLTI patients with the non-reconstructable peripheral arterial disease [23].

Based on the above-mentioned data showing potentially clinically important cross-talk between chronic leg ischaemia and reperfusion, and the dynamic fluctuations of the ANS and the haemodynamic function of the cardiovascular system after the endovascular intervention, this study was conducted to determine the relationship between periprocedural changes in ANS balance and ICG parameters after endovascular leg revascularization in relation to the severity of the leg ischaemia. To the best of the author's knowledge, this is the first study concerning such analyses.

## Material and methods

### Patients

The authors enrolled 42 patients in the study who were undergoing superficial femoral artery (SFA) stenting due to chronic lower extremity ischaemia. The inclusion criteria were as follows: a) diagnosis of chronic leg ischaemia causing both life-limiting walking distance (intermittent claudication [IC] — category 3 according to the Rutherford classification, n = 32) or with resting leg pain without leg necrosis (CLTI — category 4 according to the Rutherford classification, n = 10); b) low ankle-brachial index (ABI) (< 0.7); c) occlusion or significant narrowing of the SFA found in Doppler ultrasonography (DUS) with at least a three-fold acceleration of peak systolic velocity; d) qualification for scheduled endovascular treatment of the femoropopliteal vascular region; and e) informed consent for participation in the study. Patients with diabetes mellitus, alcohol addiction, a history of stroke or neuropathy, or who had received chemotherapy were excluded from the study due to the potential coexistence of toxic autonomic neuropathy. The severity of angiographic lesions of the femoropopliteal vascular region in all patients undergoing SFA stenting was classified as C or D according to the Trans-Atlantic Inter-Society Consensus II (TASC-II) classification [24]. All patients were medicated in accordance with actual clinical recommendations, for all comorbidities, including cardiovascular conditions, and pain management [2, 24]. None of the drugs or their doses were modified during the 2 weeks prior to the study. After endovascular leg revascularization, all patients remained in a horizontal position with pressure dressings to achieve haemostasis in the site of the vascular access for 12h. All patients were enrolled in the study between August 2015 and March 2016.

### Methods/study design

The following assessments were undertaken for each of the patients enrolled in the study prior to percutaneous leg revascularization: medical history (including cardiovascular comorbidity); physical examination; height (cm), body weight (kg) and body mass index (BMI, kg/m$^2$); and ABI, DUS, and blood samples for biochemical analysis. Prior to endovascular leg revascularization, and 1, 3, and 5h after the intervention, 5-min examinations of both ANS balance and ICG parameters were performed in a patient's horizontal position using a Task Force Monitor® (Schiller, Switzerland).

The Task Force Monitor provided a noninvasive, continuous beat-to-beat measurement and high-resolution six-channel ECG of the following: R-R interval (RRI, ms), which is the distance between successive R waves; heart rate (HR/beats per min); continuous

noninvasive arterial blood pressure (CNABP, mmHg), with a determination of systolic (SBP, mmHg) and diastolic (DBP, mmHg) blood pressure; pulse pressure (PP, which is the difference between SBP and DBP, mmHg); and mean arterial pressure (MAP, mmHg). CNABP measurements were automatically corrected with reference to measurements made using the Korotkoff method and fully synchronized for the early detection of rapid and short-term changes in a continuous noninvasive examination of cardiac output (CO = SV * HR, L/min), and the other haemodynamic parameters of ICG examination, such as: left ventricular ejection time (LVET, ms); pre-ejection period (PEP, ms); stroke volume (SV, mL); stroke index (SI = SV / body surface area [BSA]); cardiac index (CI = CO / BSA); total peripheral resistance (TPR, dyn × s/cm$^5$ or Mpa × s/m$^3$); TPR index (TPRI = TPR / BSA); thoracic fluid content (TFC, 1/ohm); index of contractility (IC); acceleration index (ACI); systolic time ratio (STR = PEP / LVET, %); ejection rate (ER = LVER / RRI, %); left ventricular work index (LVWI, mmHg × l/(min × m$^2$); mean systolic ejection rate (MSER = SV/LVET, ml/s); rapid ejection period (REP, ms); end diastolic index (EDI); RZ interval = time (in ms) between the ECG R peak and the dZ/dt Z peak; power spectral density (PSD), and Heather Index (HI). The following parameters of ANS balance were also analysed: heart rate variability (HRV), blood pressure variability (BPV) and baroreceptor sensitivity (BRS). In addition, baroreceptor effectiveness indices (BEI) were assessed: "down-BEI" is the ratio of down-events that occurred to down-ramps that were detected (diminishing sequences of baroreceptors); "up-BEI" is the ratio of up-events that occurred to up-ramps detected; and "total-BEI" is the ratio of all total-events that occurred to total-ramps detected. The following parameters of frequency-domain measures of HRV were obtained: low-frequency power (LF); the relative power of the low-frequency band (0.04–0.15 Hz) in normal units (LFnu); high-frequency power (HF); the relative power of the high-frequency band (0.15–0.4 Hz) in normal units (HFnu); and the ratio of LF to HF power (LF/HF).

Body surface area was calculated using the following formula:

$$BSA\ (m^2) = 0.01666667 \times height^{0.5} \times body\ mass^{0.5}$$

### Outcomes measured

The outcomes measured were changes in the values of parameters of ANS function (RRI, HR, SBP, DBP, MAP and PP); parameters of frequency-domain HRV and BP variability: LF, HF, LFnu-RRI, HFnu-RRI, ramp count (RC), and event count (EC); slope (ms/mmHg): minimum, maximum, mean and standard deviation (SD); and parameters of BEI and ICG (SV, SI, CO, CI, TPR, TPRI, LVET, PEP and ER) before and 1, 3, and 5 h after an endovascular leg revascularization procedure.

### Bioethics Committee

The investigation was conducted in compliance with the Declaration of Helsinki for medical research, after receiving permission from local Bioethical Committee No. 532/2015, given on June 16, 2015. Each patient signed a written consent form to participate in the study.

### Statistics

Statistical analysis was conducted using the licensed version of the statistical software STATISTICA version 13.1 (data analysis software system) developed by TIBCO Software Inc. (2017). The normal distribution of the study variables was checked using the Kolmogorov-Smirnov test. The statistical significance level was set at a p-value of $< 0.05$. The results were presented as the mean ± SD, or n, %. The statistical significance of differences between groups was verified using the t-Student test, the Mann-Whitney U-test and the two-paired Chi$^2$ test, as well as two-factorial ANOVA with four repetitions.

The sample size was calculated with the assumption that the parameters studied would change after endovascular intervention by at least 10% with a 25% SD in comparison to baseline values. In the use of two-paired ANOVA with four repetitions, the authors assumed an alpha of 0.05 and a beta of 0.15 (with a power of analysis of at least 85%). To ensure this (statistical power), a total sample size of 37 patients was required to analyse the group effect, 34 patients for the time (repetition) effect and 67 patients for the interaction effect.

## Results

None of the patients studied experienced a periprocedural cardiovascular event. Compared to IC patients, patients with CLTI had lower blood glucose concentration in a fasting state and lower ABI values prior to the intervention, with similar values for the other clinical characteristics, possibly acting as confounding factors (Tab. 1). At the beginning of the study, compared to IC patients, individuals with CLTI had significantly lower RRI, SV and LVET, as well as a higher HR (Tab. 2). One hour after endovascular leg revascularization, a statistically significant decrease was found in RRI, and baroreflex sensitivity (such as down-BEI), as well as in some ICG parameters (TPR, TPRI, LVET, and RZ). Moreover, a significant increase was observed in measurements taken 1 h after the procedure for HR, SV, CO, CI and ER (Tab. 3). Three hours after the

**Table 1.** Clinical characteristics of patients according to the severity of leg ischaemia before the procedure

| Feature | IC (N = 32) | CLTI (N = 10) | P-value |
|---|---|---|---|
| Age (years) | 63.3 ± 7.8 | 65.0 ± 7.4 | 0.56 |
| Male gender (n, %) | 24 (75%) | 7 (70%) | 0.75 |
| BMI (kg/m$^2$) | 27.0 ± 4.4 | 24.4 ± 4.4 | 0.11 |
| Smoking habit (in the past, currently; n, %) | 16 (50%)<br>16 (50%) | 5 (50%)<br>5 (50%) | 0.99 |
| Hypertension (n, %) | 20 (62.5%) | 8 (80%) | 0.31 |
| Beta-blockers (n, %) | 20 (62.5%) | 8 (80%) | 0.31 |
| Leukocytes (g/L) | 7.7 ± 1.6 | 7.5 ± 3.1 | 0.82 |
| LDL cholesterol (mg/dL) | 121.8 ± 47.4 | 116.0 ± 4.4 | 0.74 |
| Triglycerides (mg/dL) | 144.6 ± 63.2 | 102.8 ± 26.6 | 0.06 |
| CRP (mg/dL) | 12.0 ± 9.7 | 7.8 ± 13.7 | 0.77 |
| Glucose (mg/dL) | 102.9 ± 16.2 | 91.5 ± 8.3 | 0.04 |
| Creatinine (mg/dL) | 0.83 ± 0.22 | 0.8 ± 0.2 | 0.80 |
| Target artery occlusion (n, %) | 27 (84.4%) | 8 (80%) | 0.75 |
| TASC-II (C or D; n, %) | 26 (81.3%) | 10 (100%) | 0.14 |
| Use of DEB (n, %) | 2 (6.3%) | 2 (20%) | 0.20 |
| ABI before procedure | 0.5 ± 0.3 | 0.3 ± 0.1 | 0.03 |
| ABI after procedure | 0.9 ± 0.3 | 0.9 ± 0.1 | 0.65 |
| Number of stents used (n) | 1.4 ± 0.6 | 1.8 ± 0.6 | 0.09 |
| The sum of stents used (length, mm) | 189.6 ± ± 117.4 | 250.9 ± ± 114.9 | 0.16 |

ABI — ankle-brachial index; ASA — aspirin; BMI — body mass index; CLO — clopidogrel; CLTI — chronic limb-threatening ischaemia; CRP — C-reactive protein; DEB — drug-eluting balloon; IC — intermittent claudication; LDL — low-density lipoprotein; TASC-II — Trans-Atlantic Inter-Society Consensus II

endovascular procedure, the results for the majority of the parameters studied had returned to their initial values (Tab. 3). The percentage deltas between the current and preceding measurements were greatest in the second examination period (i.e., between 3h and 1h after intervention) and reached the highest values concerning: TPR, PPRI, PDS-RRI, up-BEI, down-BEI, total-BEI and HF-SBP (data not presented). For the whole study group, significant changes between the baseline values and the measurements taken 1, 3, and 5h after percutaneous intervention in ANOVA analysis with four repetitions were found concerning RRI ($p < 0.001$), HR ($p = 0.028$), TPR ($p = 0.041$), TPRI ($p = 0.036$), LVET ($p = 0.013$), ER ($p = 0.005$) and down-BEI ($p = 0.022$) (Fig. 1). It was surprising that no significant effect was found of beta-blockers or other pharmacotherapy for chronic use on the ANS and ICG parameters studied.

We found some statistically significant correlations between the percentage deltas of ANS and ICG parameters (Tab. 4). The strongest correlations were noted between ΔLF-RRI and ΔSI, ΔCI, ΔEDI; between ΔRRI and ΔLVWI, ΔER; and between ΔDBP and ΔTPRI (Tab. 4). The R-values of those correlations amounted to 0.41–0.91, demonstrating that changes in ANS activity parameters explained 17–83% of the variations in ICG parameters.

## Discussion

The present investigation confirmed the study hypothesis that lower limb endovascular revascularization induces dynamic fluctuations in ANS activity which, in turn, cause cardio-dynamic disturbances that are possible to determine in ICG. To the best of the authors' knowledge, they are the first authors to investigate this phenomenon. The conclusions are supported through the observation of significant changes in the deltas of parameters between the respective measurements and baseline values during the first 5h after the intervention (Tab. 2–3, Fig. 1), as well as through finding strong correlations between parameters of ANS and ICG (Tab. 4). Moreover, it was found that at the baseline, individuals with CLTI had greater sympathetic ANS activity, expressed by higher HR and lower ICG parameters, such as SV and LVET, than IC patients (Tab. 2), which may be a potential mechanism leading to increased myocardial oxygen demand and could explain the high cardiovascular 1-year mortality among CLTI patients [1, 2, 23–25].

We also revealed that endovascular leg revascularization induced an increase in HR, SV, and, consequently, CO and CI, which was counteracted by decreased LVET, TPR and TPRI in the 1h period after revascularization. Three hours after the endovascular procedure, the results for the majority of the parameters mentioned had returned to their initial values (Tab. 3, Fig. 1). Despite the patients remaining in a horizontal position following the intervention, dynamic oscillations in BRS were also noted (Tab. 3, Fig. 1). Similar to the frequency-domain parameters of HRV (e.g. ΔLF, ΔHF, ΔLF-RRI, ΔHF-RRI), those dynamic fluctuations in BRS (e.g. ΔHF-SBP, ΔT-BEI) correlated strongly with the haemodynamic alterations after leg revascularization found in ICG (Tab. 4).

The present study outcomes cannot be compared to those of other studies due to the lack of similar investigations. Only Husmann et al. [20] revealed a long-term favourable effect of successful femoropopliteal angioplasty on orthostatic, venoarteriolar response determined by laser Doppler flowmetry, but without assessment of changes in the autonomic nervous system and ICG parameters. However, the results obtained in this study may have potential clinical importance because they show that even the minimally invasive technique of leg revascularization may produce significant changes

**Table 2.** Selected baseline Task Force Monitor parameters of patients divided in relation to the severity of leg ischaemia prior to intervention

| Parameter | IC(N = 32) | CLTI(N = 10) | P-value |
|---|---|---|---|
| RRI (ms) | 982.6 ± 138.4 | 873.9 ± 141.9 | 0.047 |
| HR (beats/min) | 62.8 ± 9.5 | 71.1 ± 11.7 | 0.04 |
| SV (mL) | 75.8 ± 20.8 | 60.7 ± 13.7 | 0.049 |
| SI (mL/m$^2$) | 40.3 ± 9.4 | 36.2 ± 11.5 | 0.28 |
| CO (L/min) | 4.7 ± 1.3 | 4.3 ± 0.8 | 0.34 |
| CI (L/min/m$^2$) | 2.5 ± 0.6 | 2.5 ± 0.8 | 0.92 |
| TPR (Mpa × s/m$^3$) | 1643.6 ± 464.1 | 1817.6 ± 520.1 | 0.34 |
| TPRI (Mpa × s/m) | 3075.0 ± 866.4 | 3162.7 ± 1088.0 | 0.80 |
| LVET (ms) | 317.2 ± 15.0 | 304.6 ± 19.1 | 0.044 |
| ER (%) | 33.0 ± 4.2 | 35.8 ± 4.8 | 0.10 |
| RZ intervals (ms) | 187.8 ± 17.4 | 193.1 ± 21.5 | 0.45 |
| LF-RRI | 903.3 ± 2606.1 | 1062.5 ± 1787.6 | 0.87 |
| PSD RRI | 3183.8 ± 10352.7 | 2491.2 ± 3589.6 | 0.85 |
| LF HF RRI | 1.9 ± 1.8 | 1.3 ± 0.9 | 0.31 |
| LF HF | 0.9 ± 0.7 | 0.7 ± 0.6 | 0.48 |
| LF HF DBP | 2.8 ± 1.8 | 2.2 ± 1.6 | 0.34 |
| Up-BEI (%) | 48.9 ± 20.6 | 46.7 ± 19.4 | 0.78 |
| Down-BEI (%) | 45.4 ± 16.5 | 51.3 ± 18.6 | 0.37 |
| Total-BEI (%) | 46.3 ± 16.5 | 48.4 ± 17.8 | 0.74 |

BEI — baroreceptor effectiveness index; CI — cardiac index; CLTI — chronic limb-threatening ischaemia; CO — cardiac output; DBP — diastolic blood pressure; ER — ejection rate; HF — high-frequency power of frequency-domain measures of heart rate variability; HR — heart rate; IC — intermittent claudication; LF — low-frequency power of frequency-domain measures of heart rate variability; LVET — left ventricular ejection time; PSD = power spectral density; RRI — R-R interval; RZ interval — time (in ms) between ECG R peak and dZ/dt Z peak; SI — stroke index; SV — stroke volume; TPR — total peripheral resistance; TPRI — total peripheral resistance index

**Table 3.** Dynamics of Task Force Monitor parameters for the respective measurements

| Parameter | Before procedure | 1h after the procedure | 3h after the procedure | 5h after the procedure |
|---|---|---|---|---|
| RRI (ms) | 957.5 ± 144.9 | 875.2 ± 126.2 * | 951.9 ± 164.2 + | 925.9 ± 181.1 |
| HR (beats/min) | 64.7 ± 10.5 | 71.0 ± 10.6 * | 67.4 ± 15.4 | 70.4 ± 20.3 |
| SV (mL) | 72.4 ± 20.3 | 78.5 ± 33.7 * | 67.1 ± 14.2 + | 77.4 ± 41.7 |
| SI (mL/m$^2$) | 39.4 ± 9.9 | 42.8 ± 17.2 | 36.7 ± 7.9 + | 42.6 ± 23.5 |
| CO (L/min) | 4.6 ± 1.2 | 5.5 ± 2.6 * | 4.4 ± 0.9 + | 6.0 ± 6.8 |
| CI (L/min/m$^2$) | 2.5 ± 0.6 | 3.0 ± 1.4 * | 2.4 ± 0.5 + | 3.3 ± 3.7 |
| TPR (Mpa × s/m$^3$) | 1683.8 ± 476.3 | 1458.9 ± 521.8 * | 1774.1 ± 559.0 + | 1612.7 ± 553.1 |
| TPRI (Mpa × s/m) | 3095.2 ± 907.5 | 2677.9 ± 986.7 * | 3262.4 ± 1078.6 + | 2937.6 ± 977.6 |
| LVET (ms) | 314.3 ± 16.7 | 303.5 ± 17.4 * | 309.2 ± 24.0 | 303.5 ± 30.9 |
| ER (%) | 33.6 ± 4.4 | 35.5 ± 3.9 * | 33.6 ± 4.6 + | 34.0 ± 5.3 |
| RZ intervals (ms) | 189.0 ± 18.2 | 181.9 ± 20.1 * | 190.3 ± 18.7 + | 186.6 ± 26.3 |
| LF-RRI | 941.0 ± 2415.6 | 674.0 ± 1356.2 | 1470.1 ± 2907.1 + | 1241.2 ± 2113.7 |
| PSD RRI | 3019.7 ± 9164.3 | 2214.4 ± 4421.7 | 5118.0 ± 10355.4 + | 3492.5 ± 5956.1 |
| LF HF | 0.9 ± 0.7 | 0.9 ± 0.6 | 0.8 ± 0.6 | 1.0 ± 0.7 |
| LF HF DBP | 2.7 ± 1.8 | 3.0 ± 2.5 | 2.7 ± 2.4 + | 2.4 ± 2.0 |
| Up-BEI (%) | 48.4 ± 20.1 | 43.1 ± 17.9 | 52.2 ± 17.2 + | 45.3 ± 21.7 |
| Down-BEI (%) | 46.8 ± 16.9 | 38.8 ± 15.0 * | 49.5 ± 19.5 + | 47.9 ± 21.8 |
| Total-BEI (%) | 46.8 ± 16.2 | 41.0 ± 14.7 | 50.3 ± 15.5 + | 47.2 ± 18.8 |

BEI — baroreceptor effectiveness index; CI — cardiac index; CO — cardiac output; DBP — diastolic blood pressure; ER — ejection rate; HF — high-frequency power of frequency-domain measures of heart rate variability; HR — heart rate; LF — low-frequency power of frequency-domain measures of heart rate variability; LVET — left ventricular ejection time; PSD — power spectral density; RRI — R-R interval; RZ interval — time (in ms) between ECG R peak and dZ/dt Z peak; SI — stroke index; SV — stroke volume; TPR — total peripheral resistance; TPRI — total peripheral resistance index. Statistically significant differences the lowest significant difference post hoc test: * — $p < 0.05$ between the initial measurement and the preceding measurement; + — $p < 0.05$ between the second measurement (3h after the procedure) and the preceding measurement; # — $p < 0.05$ between the third measurement (5h after the procedure) and the preceding measurement

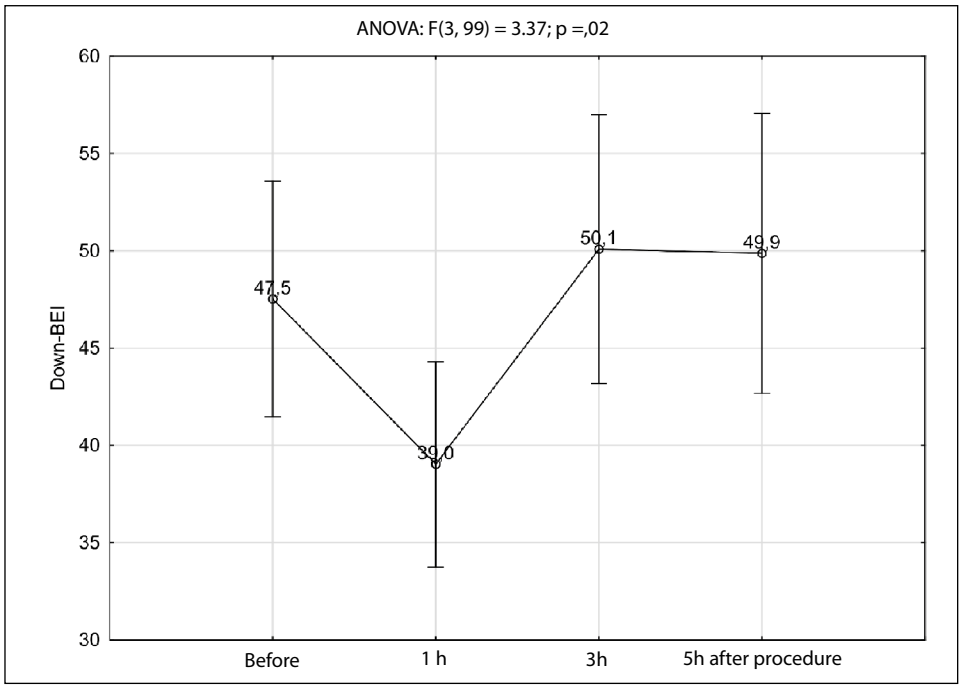


**Figure 1.** Changes in down-BEI, one of the baroreceptor effectiveness index (BEI) parameters, in the periprocedural period

**Table 4.** Correlations between selected percentage deltas of mean ANS and impedance cardiography parameters between 5-min measurements 1 h after the procedure and before the intervention

| | **Δ SI** | **Δ CI** | **Δ TPRI** | **Δ EDI** | **Δ IC** | **Δ LVWI** | **Δ PEP** | **Δ ER** | **Δ MSER** | **Δ REP** | **Δ HI** |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Δ RRI | 0.30; p = 0.14 | 0.02; p = 0.92 | –0.22; p = 0.30 | 0.30; p = 0.14 | 0.28; p = 0.17 | 0.78; p < 0.01 | 0.42; p = 0.04 | –0.91; p < 0.01 | 0.22; p = 0.29 | 0.01; p = 0.99 | 0.25; p = 0.24 |
| Δ SBP | –0.14; p = 0.051 | –0.13; p = 0.54 | 0.38; p = 0.06 | –0.15; p = 0.48 | –0.13; p = 0.53 | –0.09; p = 0.68 | –0.13; p = 0.54 | 0.06; p = 0.77 | –0.13; p = 0.53 | 0.01; p = 0.96 | –0.14; p = 0.50 |
| Δ DBP | –0.41; p = 0.04 | –0.31; p = 0.13 | 0.79; p < 0.01 | –0.39; p = 0.06 | –0.41; p = 0.04 | –0.53; p < 0.01 | 0.21; p = 0.32 | 0.32; p = 0.12 | –0.38; p = 0.06 | –0.47; p = 0.02 | –0.41; p = 0.04 |
| Δ LF | –0.05; p = 0.81 | –0.02; p = 0.93 | 0.03; p = 0.88 | –0.04; p = 0.84 | –0.05; p = 0.83 | –0.33; p = 0.11 | –0.07; p = 0.76 | 0.04; p = 0.87 | –0.02; p = 0.93 | –0.10; p = 0.64 | –0.01; p = 0.97 |
| Δ HF | 0.03; p = 0.91 | –0.03; p = 0.90 | –0.13; p = 0.53 | 0.01; p = 0.99 | 0.03; p = 0.91 | 0.35; p = 0.09 | –0.16; p = 0.44 | –0.13; p = 0.55 | –0.01; p = 0.97 | 0.12; p = 0.56 | –0.01; p = 0.97 |
| Δ LF RRI | 0.75; p < 0.01 | 0.69; p < 0.01 | –0.41; p = 0.04 | 0.76; p < 0.01 | 0.73; p < 0.01 | 0.29; p = 0.17 | 0.01; p = 0.98 | –0.25; p = 0.24 | 0.75; p < 0.01 | 0.14; p = 0.51 | 0.73; p < 0.01 |
| Δ HF RRI | 0.45; p = 0.02 | 0.43; p = 0.03 | –0.38; p = 0.06 | 0.46; p = 0.02 | 0.47; p = 0.02 | 0.49; 0.01 | –0.10; p = 0.64 | –0.14; p = 0.50 | 0.45; p = 0.02 | 0.18; p = 0.38 | 0.44; p = 0.03 |
| Δ LF SBP | –0.15; p = 0.48 | –0.25; p = 0.23 | 0.46; p = 0.02 | –0.12; p = 0.56 | –0.14; p = 0.49 | –0.04; p = 0.85 | 0.48; p = 0.02 | –0.46; p = 0.02 | –0.16; p = 0.44 | –0.23; p = 0.26 | –0.16; p = 0.44 |
| Δ HF SBP | –0.14; p = 0.51 | –0.20; p = 0.35 | 0.49; p = 0.01 | –0.12; p = 0.58 | –0.13; p = 0.53 | –0.16; p = 0.46 | 0.42; p = 0.04 | –0.34; p = 0.10 | –0.14; p = 0.51 | –0.29; p = 0.17 | –0.14; p = 0.52 |
| Δ Total BEI | –0.08; p = 0 .70 | –0.20; p = 0.34 | 0.14; p = 0.52 | –0.06; p = 0.77 | –0.12; p = 0.58 | 0.27; p = 0.19 | 0.47; p = 0.02 | –0.46; p = 0.2 | –0.12; p = 0.58 | –0.15; p = 0.46 | –0.16; p = 0.44 |

Δ — calculated according to the formula: Δ = 100 × (values obtained 1h after intervention – initial measurement)/value obtained during initial measurement; BEI — baroreceptor effectiveness index; CI — cardiac index; DBP — diastolic blood pressure; EDI — end-diastolic index; ER — ejection rate; HF — high-frequency power of frequency-domain measures of heart rate variability; HI — Heather Index; IC — intermittent claudication; LF — low-frequency power of frequency-domain measures of heart rate variability; LVWI — left ventricular work index; MSER — mean systolic ejection rate; PEP — pre-ejection period; REP — rapid ejection period; RRI — R-R interval; SBP — systolic blood pressure; SI — stroke index; TPRI — total peripheral resistance index

in chronotropic (RRI, HR), dromotropic (ER, RZ), and inotropic heart function (SV, CO, LVET), as well as dynamic fluctuations in peripheral vascular resistance (TPR, TPRI) (Tab. 3, Fig. 1). These reactions may lead to changes in cardiac oxygen demand and may be a potential substrate of periprocedural arrhythmia and the occurrence of acute cardiovascular events during the initial period after leg revascularization [3, 8–17, 23–25]. At least in regard to RZ intervals, the present results resembled other research in which ANS changes were observed as being related to effort [10, 25–27].

In the present study, 17–83% of the variations in ICG that occurred during the early postprocedural period were explained by accompanying dynamic changes in ANS activity events (Tab. 4). As presented in the introduction, the changes in ANS activity during the periprocedural period are most likely to be evoked through activation of central (cardiopulmonary baroreflex) [29] and peripheral sympathetic ANS afferents by stimulation of mechanical (flow-mediated shear stress after vessel opening) and chemical (e.g., inflammatory mediators and reactive oxygen species) receptors located in the skeletal muscles [3, 14, 25–28]. The relatively high SD observed in the respective ANS and ICG parameters (Tab. 2), as well as their deltas and SDs between the respective measurements and the baseline values (data not presented), showed individual variation in skeletal muscle adaptation to ischaemia and reperfusion (ischaemic preconditioning), probably related to genetic and metabolic factors, as well as to individual differences in adherence to recommendations of exercise training before the endovascular intervention [25–30]. As a method of ischaemic preconditioning for IC patients, walking training prepares skeletal muscles for reperfusion and decreases sympathetic activation in response to ischaemia [3, 28–30]. This observation shows the value of walking training before leg revascularization as it may potentially reduce periprocedural sympathetic activation and the associated risk of cardiovascular events.

The present study has some limitations, which were related mainly to the small study population. However, despite this limitation, statistically significant differences between study groups were obtained.

## Conclusions

In patients who had undergone endovascular leg revascularization, dynamic fluctuations in ICG and ANS parameters occurred that might potentially affect the risk of the occurrence of a cardiovascular event in the periprocedural period. Correlations between ANS and ICG parameters suggest that haemodynamic oscillations after endovascular leg revascularization are mediated by changes in ANS activity, most probably through a sympathoexcitatory effect of the procedure related to changes in skeletal muscle perfusion.

Conflict of interest: *None.*

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