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# Reduction of 24-h blood pressure variability in extreme obese patients 10 days and 6 months after bariatric surgery depending on pre-existing hypertension

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BACKGROUND

Bariatric surgery is considered as a first line treatment in extreme obese patients to achieve a reduction in health risks. However, after surgical procedure obese patients with normal blood pressure (BP) levels still present residual risk, which may be partly related to lack of correction of BP profile and variability.

*Aim:* To evaluate short (10 days) and mid-term (6 months) changes of mean values, profile and variability of BP after bariatric surgery in extremely obese patients with and without hypertension.

*Materials & methods:* A follow-up of cross-sectional study was conducted in 90 obese patients (aged 41.7 ± 11.3, BMI = 46.7 ± 5.7 kg/m2), who met the eligibility criteria and underwent bariatric surgery. Each patient underwent 24-h ambulatory BP monitoring with profile and variability estimation before, 10 days and 6 months after the intervention.

*Results:* Sixty-seven (74.4%) patients had hypertension. Significant decrease from baseline in mean values of systolic and diastolic BP in 10 days ($p < .005$) and 6 months ($p < .005$) follow-up were observed only in patients with hypertension. Moreover, only hypertensive subjects revealed significant reduction ($p < 0,05$) from baseline in 24-h systolic and diastolic BP weighted standard deviation and average real variability after surgical procedure. No changes were found in dipping status.

*Conclusions:* Bariatric surgery not only decreased BP levels, but also contributed to reduction in BP variability in early period after intervention mainly in patients with pre-existing hypertension.

## 1. Introduction

According to World Health Organization in 2014 about 13% of the World's adult population (over 600 million) were obese [1]. The recently published data from 19,2 million adult participants in 186 countries of 21 regions of the world, revealed that age-standardised prevalence of obesity increased from 3.2% in 1975 to 10.8% in 2014 in men, and from 6.4% to 14.9% in women [2]. Moreover, 2.3% of the world's men and 5.0% of women were severely obese (body mass index [BMI] $\geq 35\ kg/m^2$). If increasing trends of obesity continue, by 2025, global obesity prevalence will reach 18% in men and 21% in women, but severe obesity will surpass 6% in men and 9% in women [2].

Overweight and obesity represent a major risk factor for cardiovascular (CV) diseases, stroke, hypertension, hyperlipidemia, type 2 diabetes, osteoarthritis, sleep apnea, cancer and death [3–5]. Disability due to obesity related diseases leads to serious public health threats [4].

*Abbreviations and symbols:* %EBMIL, percent Excess BMI loss; %TWL, percent Total Weight loss; ABPM, ambulatory blood pressure monitoring; ARV, average real variability; BMI, body mass index; BP, blood pressure; BPV, blood pressure variability; CV, cardiovascular; DBP, diastolic blood pressure; HbA1C, glycated haemoglobin; HDL, high-density lipoprotein; HOMA, homeostatic model assessment; HR, heart rate; hsCRP, high sensitivity C-reactive protein; IR, insulin resistance; LDL, low-density lipoprotein; ND, night dipping; OBP, office blood pressure measurements; RYGB, Roux-en Y Bypass; SBP, systolic blood pressure; SD, standard deviation; SG, Sleeve Gastrectomy; wSD, weighted standard deviation

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Epidemiological studies have revealed especially increased risk of morbidity and death in those with severe or morbid (BMI ≥ 40 kg/m$^2$) obesity [3–5].

The last European and American guidelines on the management of obesity emphasize realistic weight loss to achieve a reduction in health risks [6,7]. Significant clinical benefits may be achieved even by modest weight loss (i.e. 5–10% of initial body weight), but greater (20% or more) weight loss should be considered for those with greater degrees of obesity (BMI ≥35 kg/m$^2$). The most effective treatment method for morbid obesity in terms of long-term weight loss, improvements of co-morbidities, quality of life and decrease of overall mortality is bariatric surgery [8–11]. Cochrane Database Systematic Reviews revealed that surgery resulted in greater improvement in weight loss outcomes and weight-associated comorbidities compared with non-surgical interventions, regardless of the type of procedures used [12].

Weight loss, regardless of the treatment procedure, has been associated with favourable changes in CV risk factors. Recently published results of long-term post-operative observation indicate that the favourable effect, both in terms of weight reduction and reduction of risk of developing, or remission of diabetes mellitus, hypertension or dyslipidaemia persisted for 12 years [10].

Effects of bariatric surgery on resolution of hypertension and improvement in office blood pressure (BP) measurements are well established [10,11,13–15]. Blood pressure reduction reduces cardiovascular risk by the extent proportional to risk level. However, among hypertensive patients, BP-lowering treatment induces greater absolute risk reductions the higher the CV risk level, but a higher risk level is also associated with higher residual risk, as was shown in meta-analysis of Thomopoulos C et al. [17]. From a pathophysiological point of view, residual risk may be partly related to nonreversible alterations of cardiovascular structures and functions among hypertensives, but also lack of correction of “nonclassic” risk factors, such as BP profile and variability of 24-h BP (BPV). Obesity, inter alia due to increase in sympathetic activity was related to high BPV in spectral analysis [16], visit-to visit BPV [18] and to increased standard deviation (SD) index of ambulatory blood pressure monitoring (ABPM) readings [19–21].

To the best of our knowledge, little is known about the alterations of the BPV among extremely obese patients after bariatric surgery [22–24]. What is more, no study assessed the profile and blood pressure variability (BPV) in a short period after bariatric surgery. The aim of our study was to evaluate changes of mean values, profile and variability of BP in ABPM performed in short (10 days) and mid-term (6 months) time after bariatric surgery in extremely obese patients with and without hypertension.

## 2. Methods

### 2.1. General study design and population

This is a prospective cohort study examining the effectiveness of bariatric surgery on alteration of parameters of blood pressure monitoring in patients with and without hypertension. Experimental protocol was approved by the local Ethics Committee at the Medical College of Jagiellonian University (number: KBET/155/B/2011) and conformed to the guidelines set forth by the Declaration of Helsinki. Study was performed from July 2012 to October 2015 with follow up duration to December 2015.

Subjects were recruited into the study from among patients with severe obesity who met the eligibility criteria for bariatric surgery (age 18–60 years old, BMI ≥40.0 kg/m$^2$ or with BMI in [35.0–39.9] kg/m$^2$ and at least one co-morbidity) [9]. Exclusion criteria were: pregnancy or breast-feeding, current participation in an obesity-related clinical trial, and presence of clinical contraindications to bariatric surgery. Two months prior to planned surgery, all eligible patients underwent preoperative evaluation at the Department of Internal Medicine and Geriatrics, University Hospital, Krakow, Poland. Each participant provided written informed consent before inclusion into the study. Baseline assessment included demographic data (i.e sex, age), detailed medical history, medication use, history of smoking, sleep disturbances, and physical examination. In case of specific medical problems, the participant was consulted by the appropriate specialist. The qualification for the type of procedure was performed at the Department of General Surgery, Jagiellonian University, Medical College, Krakow, Poland. Surgical techniques for SG and RYGB were standardised and described in our previous study [25]. Patients were treated in accordance with enhanced recovery after surgery (ERAS) pathway [26]. Anthropometric parameters, blood pressure measurement and laboratory data were collected before surgery and at 10 days and further 6 months after surgery.

### 2.2. Anthropometric parameters and weight loss

Body weight was measured to the nearest 0.1 kg and height to the nearest 1 cm. BMI was calculated as weight in kilograms divided by height squared in meters (kg/m$^2$). Waist circumference was measured in the supine position halfway between the lower rib margin and the iliac crest.

Both absolute and relative changes of BMI from baseline and Percent Total Weight Loss (%TWL) were analysed [27].

### 2.3. Blood pressure measurement

We measured standard office blood pressures (OBP) with standardised mercury sphygmomanometer furnished with a cuff of appropriate size, according to the ESH guidelines [28]. The measurements were taken after at least 5 min of rest, with the right arm supported at the heart level. A set of three measurements, one minute apart, was taken. The mean of the second and third measurements was registered as systolic (SBP) and diastolic (DBP) office blood pressure values.

We performed the ABPM using the automated SpaceLabs 90,207 oscillometric device (SpaceLabs Inc., Redmond, Washington, USA) according to the current European Society Hypertension (ESH) practice guidelines [29]. All recordings were performed during hospitalisation before and during follow-up, on non-dominant arm, with appropriately matched cuff-size. The devices were pre-programmed to measure BP every 20 min during day and every 30 min during night. Awake and asleep periods were defined in fixed narrow intervals, excluding transition periods, which ranged from 8 AM to 10 PM and from 12 PM to 6 AM, respectively. > 70% of successful readings were required for the recording to be valid. Based on the recordings we computed: the average 24-h, day and night systolic (S) and diastolic (D) blood pressure and average heart rate (HR). BP variability were computed as weighted 24 h standard deviation (wSD), where average of day and night SD values were corrected for the number of hours included in each of these subperiods [30]. Moreover, average real variability (ARV) was calculated using the average of the absolute difference between adjacent blood pressure values, according the formula proposed by Mena L. et al. [31].

### 2.4. Laboratory assessment

Blood samples were obtained before surgery, 10 days, and 6 months after surgery. Blood samples obtained from participants in the morning (from 6 AM to 8 AM), after an overnight fasting were used to determine blood count, serum glucose, HbA1C, and lipid profile (i.e., total cholesterol, triglycerides, and low and high lipoprotein cholesterol), high sensitivity assay of C-reactive protein (hsCRP) according to established methods. Because of strong impact of postoperative factors on inflammatory parameters, we did not assess hs-CRP 10 days post procedure.

Deep frozen sera were stored at −80 °C until analysed for: insulin,

**Table 1**
Parameters of ambulatory blood pressure monitoring and heart rate before, 10 days and 6 months after the surgery. Entire group. Data as means ± SD.

| Variable | Baseline | 10 days after surgery | 6 months after surgery |
|---|---|---|---|
| 24 h SBP/DBP (mmHg) | 122.18 ± 10.75 /69.73 ± 6.94 | 114.68 ± 9.69 ($p_b$ = 0.0004) /65.4 ± 1.03 ($p_b$ = 0.0027) | 114.51 ± 9.9 ($p_b$ = 0.0003) /67.91 ± 6.93 |
| wSD SBP/DBP (mmHg) | 13.04 ± 2.55 /12.16 ± 1.71 | 11.72 ± 0.35 ($p_b$ = 0.005) /10.6 ± 1.94 ($p_b$ = 0.0004) | 11.57 ± 2.57 ($p_b$ = 0.0137) /10.33 ± 2.23 ($p_b$ = 0.0001) |
| Day-time SBP/DBP (mmHg) | 125.0 ± 10.63 /73.32 ± 6.85 | 118.04 ± 10.18 ($p_b$ = 0.0001) /68.74 ± 6.57($p_b$ = 0.0004) | 118.28 ± 11.55 ($p_b$ = 0.0002) /71.46 ± 7.83 |
| Night-time SBP/DBP (mmHg) | 117.56 ± 13.01 /62.24 ± 9.19 | 108.91 ± 11,2 ($p_b$ = 0.0152) /59.45 ± 7.02 | 107.28 ± 10.14 ($p_b$ = 0.0025) /61.15 ± 7.46 |
| wSD day –time SBP/DBP (mmHg) | 11.3 ± 3.29 /10.68 ± 2.02 | 10.76 ± 2.34/9.88 ± 2.04 | 9.96 ± 3.17 /8.71 ± 2.81 ($p_b$ = 0.0002) |
| wSD night –time SBP/DBP (mmHg) | 10.97 ± 3.16 /9.87 ± 2.8 | 9.16 ± 2.86 ($p_b$ = 0.0065) /8.15 ± 0.44 ($p_b$ = 0.095) | 8.76 ± 2.62 ($p_b$ = 0.002) /8.29 ± 0.44 |
| ARV SBP/DBP (mmHg) | 10.14 ± 2.5 /10.03 ± 2.04 | 9.62 ± 1.76 /8.87 ± 1.39 ($p_b$ = 0.0012) | 8.63 ± 1.1($p_b$ = 0.0006) ($p_{10}$ = 0.03) /7.85 ± 1.42($p_b$ = 0.0012) ($p_{10}$ = 0.0042) |
| 24 h HR(bpm) | 74.73 ± 8.51 | 69.74 ± 9.60 ($p_b$ = 0.0017) | 65.19 ± 7.25 ($p_b$ = 0.0001) ($p_{10}$ = 0.0045) |

SBP- systolic blood pressure, DBP- diastolic blood pressure, wSD- weighted standard deviation.
ARV- average real variability, HR- heart rate; $p_b$- p value vs. baseline; $p_{10}$- *p* values vs. 10 days.

leptin, adiponectin. Insulin (μIU/ml) was measured with an enzyme immunoassay (DRG Insulin ELISA Kit, DRG), leptin (pg/ml) and adiponectin (ng/ml) with the enzyme immunoassay technique (Quantikine ELISA, Human Leptin, Human Total Adiponectin/Acrp30, R&D Systems).

### 2.5. Comorbid conditions

According to the American Society for Metabolic and Bariatric Surgery outcome reporting standards, we also analysed selected comorbid conditions [27]. Hypertension was considered present if self-reported, if BP values were above thresholds for hypertension diagnosis based on initial ABPM or if patients were taking antihypertensive drugs. Dyslipidemia was considered present if self-reported, if the patient was currently taking lipid lowering therapy or if any of the following biochemical data were present: total cholesterol of 5.0 mmol/L or greater, low-density lipoprotein (LDL) of 3.0 mmol/L or greater, high-density lipoprotein (HDL) < 1.0 mmol/L for men and < 1.2 mmol/L for women, or triglycerides of 1.7 mmol/L or greater [32]. Type 2 diabetes and prediabetes were considered present if self-reported, if HbA1c was 6.5% or greater or if patients were currently taking antidiabetic medications and if HbA1c was between 5.7 and 6.4% for prediabetes [33] Insulin resistance was estimated using the homeostasis model (HOMA-IR), which is calculated using the formula: (fasting plasma insulin concentration [mIU/ml] x fasting glucose concentration [mmol/l])/ 22.5 [34].

Improvement in comorbidity was defined as any reduction in medication use. Comorbidity resolution was defined as complete cessation of treatment during follow-up.

### 2.6. Statistical analysis

Statistical analyses were performed with STATISTICA version 12 PL (StatSoft Inc) software. Differences in BP parameters from baseline to follow up in whole studied population and separately in groups according to diagnosis of hypertension, were analysed using general linear models for repeated measurements. Tukey's post hoc test was used in all analysis. Spearman correlation coefficients were calculated between studied variables in the whole studied population and separately in the hypertensive and non-hypertensive participants. A *p* value of < 0.05 was considered statistically significant.

## 3. Results

Study population consisted of 90 subjects. Forty percent (40%) were men. Mean ( ± SD) age was 41.7 ± 11.3 years. Sixty-seven (74.4%) had hypertension, with mean duration of 6.2 years. Antihypertensive medications were used by 52 patients (57.7%), including ACE inhibitors (36.7%), beta blockers (35.6%), thiazide and thiazide-like diuretics (22.2%), calcium channel blockers (14.4%), angiotensin II receptor antagonists (11.1%) and loop diuretics (11.1%). Other classes of antihypertensive drugs were used occasionally (alpha-2 adrenergic receptor agonists- 3.3%, aldosterone receptor antagonists- 5.6%, vasodilators- 1.1%, centrally acting α2 adrenergic agonists-1.1%).

Lipid disorders were present in 77 (85.5%) patients, type 2 diabetes in 20 (22.2%) and prediabetes in 27 (20%) subjects. Obstructive sleep apnea was diagnosed in 11 (12.2%) persons. History of smoking was found in 52 (57.8%) persons among whom 33 (36.7%) were current smokers.

Mean body weight before intervention was 137.3 ± 24.5 kg, body mass index (BMI)- 46.7 ± 5.7 kg/m2 and waist circumference- 134.3 ± 15.8 cm.

All patients met eligibility criteria for bariatric surgery. Thirty-seven (41.1%) patients underwent RYGB and the others SG.

Absolute values of body weight and other anthropological measurements diminished significantly during follow-up. Patients weight loss after 6 months was 35.4 ± 9.98 kg on average and %TWL- 25.9 ± 5.8%. BMI decreased to 35.2 ± 5.1 kg/m2 after 6 months (there was no change in BMI 10 days after intervention) and %EBMIL was 55.5%.

BP values diminished significantly in both OBP and ABPM at 10 days and half a year from intervention. Remission of hypertension was visible after half a year in 41.7% of patients and improvement defined as reduction in hypertensive drugs in 6% of subjects.

Office systolic and diastolic BP values decreased from 136.14 ± 15.53/88.12 ± 10.45 mmHg before surgery to 126.85 ± 16.35/83.78 ± 8,9 mmHg after 10 days and to 120.36 ± 12.26/80.4 ± 8.72 mmHg after 6 months from intervention.

All patients had performed ABPM before surgery. ABPM was repeated in 72 persons (44 in sleeve gastrectomy group and 28 in by-pass group) after 10 days and in 43 after 6 months (19 in sleeve gastrectomy group and 24 in by-pass group) from intervention.

Significant reductions of mean values of SBP and DBP in ABPM during 24 h, day and night occurred (Table 1). Additionally, there was a

**Table 2**
Mean values, dipping, variability of blood pressure and heart rate before, 10 days and 6 months after the surgery in the groups with and without hypertension.

| Variable | Hypertension ($n$ = 67) | Without hypertension ($n$ = 23) |
|---|---|---|
| 24 h SBP/DBP | | |
| Baseline | 123.73 ± 10.95 /70.29 ± 7.1 | 114.46 ± 5.27 /66.92 ± 5.84 |
| 10 days post procedure | 116.11 ± 9.74 ($p_b$ =0.0004) /65.82 ± 6.28 ($p_b$ = 0.0025) | 107.53 ± 5.73 /63.30 ± 5.46 |
| 6 months post procedure | 115.75 ± 9.38 ($p_b$ = 0.0003) /68.69 ± 6.31 | 108.32 ± 10.95 /64.03 ± 9.14 |
| 24 h HR | | |
| Baseline | 73.82 ± 8.77 | 79.26 ± 5.54 |
| 10 days post procedure | 67.61 ± 8.77 ($p_b$ = 0.0005) | 79.26 ± 5.54 |
| 6 months post procedure | 63.75 ± 8.69 ($p_b$ = 0.0001) | 80.41 ± 6.58 |
| Day-time SBP/DBP | | |
| Baseline | 125.96 ± 10.63 /73.32 ± 6.85 | 118.82 ± 5.79 /71.14 ± 5.73 |
| 10 days post procedure | 118.04 ± 10,18 ($p_b$ = 0.0003) /68.74 ± 6.57 | 112.87 ± 5.67 /67.82 ± 7.48 |
| 6 months post procedure | 118.28 ± 11.55 ($p_b$ = 0.0004) /71.46 ± 7.83 | 112.99 ± 13.4 /68.30 ± 10.81 |
| Night-time SBP/DBP | | |
| Baseline | 114.55 ± 13.01 /62.24 ± 9.19 | 105.97 ± 6.46 /59.58 ± 5.33 |
| 10 days post procedure | 108.91 ± 11.2 ($p_b$ = 0.037) /59.45 ± 7.02 | 99.90 ± 8.31 /56.87 ± 1.95 |
| 6 months | 107.28 ± 10.14 ($p_b$ = 0.0063) /61.15 ± 7.46 | 99.88 ± 9.11 /56.18 ± 6.45 |
| ND | | |
| Baseline | 8.86 ± 8.14 | 25.91 ± 36.58 |
| 10 days post procedure | 7.10 ± 7.21 | 12.0 ± 5.33 |
| 6 months post procedure | 8.75 ± 7.49 | 12.09 ± 4.28 |
| wSD SBP/DBP | | |
| Baseline | 13.37 ± 2.6 /12.16 ± 1.71 | 12.56 ± 2.55 /11.37 ± 1.89 |
| 10 days post procedure | 11.52 ± 2.09 ($p_b$ = 0.0283) /10.6 ± 1.94 ($p_b$ = 0.0004) | 10.72 ± 2.01 /10.04 ± 1.83 |
| 6 months post procedure | 11.73 ± 2.66 ($p_b$ = 0.0133) /10.33 ± 2.23 ($p_b$ = 0.0001) | 10.28 ± 2.1 /8.79 ± 1.8 |
| Day-time wSD SBP/DBP | | |
| Baseline | 11.30 ± 3.29 /10.68 ± 2.02 | 9.08 ± 2.38 /10.3 ± 1.42 |
| 10 days post procedure | 10.76 ± 2.34 /9.88 ± 2.04 | 10.53 ± 1.71 /10.95 ± 0.78 |
| 6 months post procedure | 9.96 ± 3.17 /8.71 ± 2.81 | 9.04 ± 1.80 /8.81 ± 0.79 |
| Night-time wSD SBP/DBP | | |
| Baseline | 10.97 ± 3.16 /9.87 ± 2.8 | 10.69 ± 2.23 /9.4 ± 1.69 |
| 10 days post procedure | 9.16 ± 2.86 ($p_b$ = 0.0034) /8.15 ± 2.58 ($p_b$ = 0.00375) | 11.27 ± 3.30 /8.73 ± 4.58 |
| 6 months post procedure | 8.76 ± 2.62 ($p_b$ = 0.0017) /8.29 ± 2.57 ($p_b$ = 0.194) | 9.83 ± 2.19 /8.73 ± 2.67 |
| AVR SBP/DBP | | |
| Baseline | 10.31 ± 2.57 /10.08 ± 2.11 | 9.27 ± 2.13 /9.80 ± 1.83 |
| 10 days post procedure | 9.60 ± 1.79 /8.88 ± 1.42 ($p_b$ = 0.004) | 9.73 ± 1.77 /8.87 ± 1.34 |
| 6 months post procedure | 8.69 ± 1.04 ($p_b$ = 0.0013) /7.80 ± 1.37 ($p_b$ = 0.0001) ($p_{10}$ = 0.0108) | 8.32 ± 1.41 /8.06 ± 1.77 |

SBP– systolic blood pressure, DBP-diastolic blood pressure, ND- night dipping, wSD- weighted standard deviation, ARV- average real variability, HR-heart rate; $p_b$- $p$ value vs. baseline; $p_{10}$- $p$ values vs. 10 days.

reduction from baseline in 24 h SBP and DBP weighed SD both before the surgery and at the end of follow-up. ARV of DBP significantly decreased in 10 days after intervention. Reductions of SBP and DBP ARV were achieved after 6 months. In subgroup analysis, significant changes of mean values and variability of BP, regarding 24 h period, were observed only in patients with hypertension (Tables 2 and 3). Moreover, we noted that mean 24 h heart rate (HR) decreased both 10 days and six months after surgery.

Serum levels of glucose, HbA1c, total cholesterol, LDL cholesterol and hsCRP diminished after 6 months from intervention (Table 4). Moreover, leptin and insulin levels decreased significantly after 10 days from intervention, with further fall after 6 months. We found a reduction in insulin resistance expressed as HOMA-IR score. Level of adiponectin and HDL cholesterol increased considerably after half a year. A similar trend was observed in hypertensive and non-hypertensive patients groups (data not shown).

Some parameters of ABPM correlated significantly with BMI, hsCRP, insulin and leptin levels at baseline. We observed significant positive correlations between BMI and night-time wSD DBP ($r = 0.35$, $p < .05$), ARV SBP ($r = 0.33$, $p < .05$) ARV DBP ($r = 0.31$, $p < .05$). HsCRP correlated positively with night-time wSD SBP ($r = 0.30$, $p < .05$) and night-time wSD DBP ($r = 0.29$, $p < .05$). Positive correlations were also detected between insulin levels and SBP24 h ($r = 0.32$, $p < .05$), day-time SBP ($r = 0.28$, $p < .05$), night-time SBP ($r = 0.37$, $p < .05$). Leptin levels correlated positively with wSD DBP24 h ($r = 0.23$, $p < .05$), day-time wSD DBP ($r = 0.29$, $p < .05$), ARV DBP ($r = 0.23$, $p < .05$) and also negatively with DBP values in 24 h ($r = -0.27$, $p < .05$), day-time ($r = -0.25$, $p < .05$) and night-time ($r = -0.26$, $p < .05$). After 6 months of follow-up, significant correlations were observed only between night-time DBP and leptin level ($r = -0.32$, $p < .05$) and between ARV DBP and BMI ($r = 0.42$, $p < .05$).

## 4. Discussion

The novel finding of our study, is that in extremely obese subjects who underwent bariatric surgery both blood pressure level and blood pressure variability decrease significantly already after ten days postoperatively, and the decrease remains sustained after six months of follow-up. The statistically important differences were found mainly in group with hypertension. Decrease in blood pressure values was confirmed in all 24 h, day-time and night-time periods. Blood pressure variability, expressed as weighted standard deviation and average real variability, was also constantly reduced in the follow-up. There was no change in dipping status. After 6 months, remission or improvement of hypertension was observed in approximately 50% of patients. In parallel with the decrease in BP values we also observed improvements of metabolic hormones levels (decrease of insulin and leptin levels and increase of adiponectin concentration) and reduction of inflammation (expressed as hsCRP level). Relationships between of ABPM parameters with BMI, hsCRP, insulin and leptin levels at baseline almost completely disappeared during follow-up.

Bariatric surgery was demonstrated to have advantage over non-surgical treatment in reduction of BP levels and resolution of hypertension in obese subjects. Last Schiavon et al. one year observation, exhibit that bariatric surgery is more efficient in reduction of the total number of antihypertensive medications and hypertension resolution comparing to medical therapy alone [11]. The meta-analysis of prospective interventional studies evaluating the 12–24 months impact of bariatric surgery on cardiovascular risk factors, showed significant hypertension risk reduction of 48% and BMI reduction of 5 after surgery corresponded with hypertension reduction of 27% [35]. Our study showed comparable results 6 months after surgical procedure. Longer than 24 months observations revealed that hypertension risk get nadir earlier than diabetes and hyperlipidaemia, when BMI decrease up of 10 units [36]. What is more, the reduction in the risk of hypertension

**Table 3**
Changes in laboratory parameters 10 days and 6 months after bariatric surgery. Entire population.

| Variable | Baseline | 10 days | 6 months |
|---|---|---|---|
| BMI | 46.7 ± 5.7 | 46.4 ± 10.2 ($p_b$ = 0.0013) | 35.2 ± 5.1 ($p_b$ = 0.0001) ($p_{10}$ = 0.0001) |
| Weight [kg] | 137.2 ± 24.5 | 130 ± 25.3 ($p_b$ = 0.0014) | 102.23 ± 29.94 ($p_b$ = 0.0001) ($p_{10}$ = 0.0001) |
| Glucose [mmol/l] | 5.76 ± 1.62 | 5.37 ± 0.87 | 4.81 ± 0.92 ($p_b$ = 0.0001) ($p_{10}$ = 0.0063) |
| HbA1c [%] | 6.09 ± 1.14 | 5.83 ± 0.93 | 5.32 ± 0.5 ($p_b$ = 0.0001) ($p_{10}$ = 0.0002) |
| Total cholesterol [mmol/l] | 5.25 ± 1.0 | 4.96 ± 0.89 | 4.59 ± 1.23 ($p_b$ = 0.0001) ($p_{10}$ = 0.0235) |
| HDL cholesterol [mmol/l] | 1.1 ± 0.3 | 0.82 ± 0.03 ($p_b$ = 0.0001) | 1.2 ± 0.26 ($p_b$ = 0.0103) ($p_{10}$ = 0.0001) |
| LDL cholesterol [mmol/l] | 3.18 ± 0.96 | 3.28 ± 0.91 | 2.83 ± 1.13 ($p_b$ = 0.0128) ($p_{10}$ = 0.0012) |
| Triglycerides [mmol/l] | 2.0 ± 0.98 | 1.86 ± 0.75 | 1.22 ± 0.42 |
| hsCRP [mg/l] | 7.1 ± 2.5 | Not tested | 4.2 ± 7.75 ($p_b$ = 0.0213) |
| Adiponectin [pg/ml] | 4285 ± 1934 | 4753 ± 2159 | 6794 ± 2930 ($p_b$ = 0.0001) ($p_{10}$ = 0.0001) |
| Leptin [pg/ml] | 58,552 ± 27,864 | 42,544 ± 24,518 ($p_b$ = 0.0001) | 18,601 ± 13,191 ($p_b$ = 0.0001) ($p_{10}$ = 0.0001) |
| Insulin [μIU/ml] | 29.37 ± 13.09 | 23.24 ± 1.77 ($p_b$ = 0.0026) | 18.85 ± 11.08 ($p_b$ = 0.0001) ($p_{10}$ = 0.0418) |
| HOMA-IR score | 7.89 ± 5.89 | 5.84 ± 3.93 ($p_b$ = 0.0247) | 4.5 ± 4.64 ($p_b$ =0.0002) |

HbA1c- glycated hemogl)bin HDL-high-density lipoproteins, LDL- low-density lipoprotein hsCRP – high-sensitivity C-reactive protein, HOMA - homeostatic model assessment, IR- insulin resistance; $p_b$- *p* value vs. baseline; $p_{10}$- *p* values vs. 10 days.

reached a plateau about 20 months after surgery, whereas the reduction in the risk of type 2 diabetes and hyperlipidemia continued beyond that period. However, in comparison to conservative interventions, bariatric surgery played a preponderant role in SBP reduction, but presented diminished effect on decreasing of DBP [37]. Moreover, effects were dependent on the initial grade of obesity and time of the follow-up. In the meta-analysis of 57 articles, focused only on the influence of bariatric surgery on the improvement or resolution of hypertension, Wilhelm et al. revealed that hypertension resolved in 50% and improved in 63.7% and this improvement remained significant after 1 year period of follow-up [15]. In one of the largest prospective studies on bariatric surgery, the Swedish Obese Subjects (SOS) Intervention Study, results of surgically treated patients were compared with the effects in the control group after traditional obesity management up to 10 years follow-up [38]. Unadjusted SBP decreased about 9 ± 1 mmHg and DBP 6 ± 3 mmHg in the intervention group during the first 6 months but had relapsed to control values at last examination. Adjustments for the sex, age, weight, height, and BP, smoking, alcohol intake, and current BP medications did not change these patterns. In the SOS study, much of the improvement in blood pressure observed in the surgical group at 2 years was lost at 10-year follow up [14]. However these data have recently been contested by results of 12 years of follow-up which demonstrated persistent, clinically important decrease of blood pressure and disease remission [10]. In our study office systolic and diastolic BP reduction was even greater after 6 months from intervention, and the significant drop about 10/8 mmHg was already noticed 10 days after surgery. Ahmed et al. exhibited similar observations after 1 week and half a year from surgery [39]. However, in patients with diabetes no significant effect of bariatric procedures on BP was observed, in comparison to the clinical approach [40].

Over recent years, several articles documented the effects of bariatric surgery on the ABPM parameters. Van de Borne et al., obtained 7 mmHg fall in diurnal SBP and 8 mmHg in nocturnal SBP, with no difference in DBP, 4 months after restrictive gastric surgery [24]. Half a year after surgery, we observed similar results with a decrease of 6 mmHg in day-time SBP and about 7 mmHg in night-time SBP and with no significant reduction in DBP versus baseline. Careaga et al. evaluated one-year effect of surgical weight loss on ABPM patterns in patients with and without hypertension [22]. They showed greater decrease of BP among patients with hypertension than in the normotensive group as in our study, after just half a year. In our study population, decrement of BP showed already after 10 days postsurgically. BP lowering effect of bariatric surgery was already observed one day after the intervention, as was shown by Pedersen et al. [41]. Moreover, similarly as in our research, they revealed decrease of BP in both hypertensive and normotensive patients 10 days after surgery.

Our study showed that bariatric surgery was connected with significant improvement in BPV expressed as weighted SD and AVR. DBP AVR decreased after 10 days and other short-term BPV parameters significantly decline after 6 months. There is first report of effects of bariatric surgery on short term BPV. According to the available knowledge, obesity is connected with higher BPV [42]. Obesity has been related to high BPV in spectral analysis [43], altered visit-to visit BPV [17] and increased SD index of ABPM readings [17,21,44]. It is well documented that higher short term BPV and impaired day-night pattern are related with more frequent target organ damage and higher risk of severe CV events, independently of mean BP values [44–49]. Moreover, elevated nocturnal short-term BPV in obese patients doubled the risk of all- causes mortality in comparison with non- obese subjects [40]. Obesity was considered to prompt pathological non-dipper pattern, but some studies did not confirmed such relationship [50]. Current studies concentrated mainly on the effect of bariatric surgery on night-day BP variations, as nocturnal BP is considered to have higher predictive value than diurnal BP [51]. Several studies confirmed improvements in dipper status and circadian BP rhythm after bariatric surgery. Czupryniak et al., in 8 obese, hypertensive patients with impaired circadian BP variation showed decrease in 24-h systolic BP and restoration of the circadian BP rhythm 8 weeks after gastric by-pass surgery [23]. Van de Borne et al. reported significantly decreased nocturnal BP after 4 months of follow-up in 28 morbidly obese, normotensive individuals who underwent gastric restrictive surgery [24]. Norstrand et al. revealed pre-eminence of gastric- bypass surgery over lifestyle intervention in lowering of night-time BP and improvement in night-to-day ratio after 1 year follow up [52]. In our study, in 6 months' time, nocturnal SBP decrease was similar (about 7 mmHg) in sleeve gastrectomy and gastric bypass group and we did not observe significant improvement in dipping status of study population. However, our patients with hypertension were effectively treated before intervention, only part of them presented impaired circadian BP rhythm, and ABPMs were performed during hospital stay, what might influence the circadian patterns. However, as showed Careaga et al. percentage of non dipping patterns remained significantly high in patients with and without hypertension and the prevalence of nocturnal hypertension remained significantly high in hypertensive patients one year after surgical intervention [22].

In our study, especially pronounced changes in BP and BPV were observed in hypertensive group, what might indicate that morbidly obese patients with hypertension could particularly benefit from bariatric surgery. Changes in BPV as well as BP levels were already visible in a short period after operation, before achieving significant weight loss. Postsurgical modulations in adipokines secretion seem to be intimately involved with not only cardiovascular risk reduction, but also

regulation of blood pressure levels [53]. We observed correlations of BPV parameters with BMI, leptin concentration and the marker of inflammation in extremely obese patient, similarly as Abramson et al. showed in healthy adults [42]. We also revealed concomitant decrease in leptin and insulin levels, with significant increase in adiponectin. Insulin resistance and hyperleptinemia, besides an activation of the sympathetic nervous system, the arterial-pressure control mechanism of diuresis and natriuresis, activation of tissue and circulating renin angiotensin system, inflammation and endothelial dysfunction are considered as mechanisms through which obesity is associated with hypertension [54]. Bariatric surgery was effective in achieving insulin resistance normalization and remission of diabetes [54,55]. In our study, several parameters of ABPM in baseline correlated with BMI, hsCRP and levels of insulin and leptin, both in hypertensive and normotensive subjects. However, those relationships were not detected after surgery, which may confirm significance of hormonal postsurgical changes in modulation of blood pressure levels.

Moreover, gastrointestinal peptides variations after bariatric surgery may be involved in blood pressure regulation. It's changes were observed soon after surgery (ghrelin, leptin), whereas others were maintained long term (glucagon-like peptide 1, peptide YY, ghrelin, leptin), [53]. Intravenous administration of ghrelin decrease blood pressure level and supress sympathetic nervous system activity [56]. There are also reports considering reductions in systolic blood pressure and endothelial amelioration after taking GLP-1 receptor agonists in patients with diabetes [57].

As obesity is associated with the increased risk of hypertension, hyperlipidemia, diabetes and other co-morbidities, guidelines recommend assessment and active treatment of CVD risk factors and other obesity-related medical conditions, regardless of weight loss efforts [6,7]. Bariatric surgery causes reduction of cardiovascular risk in extreme obese patients, starting to be relevant in very short time after operation. Besides of changes in laboratory parameters, BP and BPV, decrease in heart rate in short and long time after intervention was observed. That finding might indicate on diminish of sympathetic nervous system activation and increase in sensitivity of arterial and cardiopulmonary reflexes.

Our results should be considered in the context of their limitations. All BP measurements were performed in hospital environment. That could influence on BP values and dipping status. However, to avoid discrepancy between subsequent measurements we carried out all the tests in the same environment. Information about sleep apnoea were collected only by questionnaire, and we did not perform polysomnography to verify diagnosis. In our study, we did not measure changes in life style such as food composition and salt consumption. Loss of weight could also contribute to more intensive physical activity. Differences in life style could have impact on blood pressure diversity. Forty seven of our patients were lost to follow-up, which was connected with the fact that most of them dwelled in other localities, returned to professional activities, and refused additional hospital assessment after surgery.

In conclusion our study showed that bariatric surgery is contributed to reduction in blood pressure and blood pressure variability in early period after intervention mainly in patients with pre-existing hypertension.

## Conflict of interest

The authors declare no conflict of interest.

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