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Common carotid intima-media thickness assessment in morbidly obese patients undergoing bariatric surgery

Ocena grubości kompleksu błona środkowa – błona wewnętrzna tętnicy szyjnej wspólnej u pacjentów z otyłością olbrzymią poddawanych operacjom bariatrycznym

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S u m m a r y

Introduction. Obesity is a pathological accumulation of adipose tissue in the organism, and leads to the development of diseases, including cardiovascular diseases.

Aim. The aim of the study was to assess common carotid artery intima-media thickness in morbidly obese patients as well as to study the influence of bariatric surgery on studied parameter.

Material and methods. In all 40 patients we performed: anthropometric, basic laboratory measurement and common carotid artery intima-media thickness, (IMT), (Philips iE 33 system: Andeouver, Massachusetts USA). The protocol was approved by Warsaw Medical University's Bioethics Committee.

Results. Body mass of patients diagnosed with severe obesity changed during the 6-month follow-up post-surgery period (132.03 ± 18.42 vs. 97.46 ± 15.35 kg; p < 0.0001). Fat mass decreased similarly: 49.15 ± 3.83% (OB1) vs. 38.20 ± 5.66% (OB2); (p < 0.0001). Intima-media thickness varied statistically between both groups (OB1, OB2) (0.59 ± 0.11 vs. 0.52 ± 0.011 mm; p < 0.0001), and were within the reference value range (IMT < 0.9 mm). In the control group IMT values were lower than in OB1 (0.59 ± 0.11 vs. 0.42 ± 0.026 mm; p = 0.0001). In OB1 IMT correlated with body mass (r = 0.472; p = 0.002), free fatty mass (r = 0.427, p = 0.0059), fatty mass (r = 0.368, p = 0.019), BMI (r = 0.423; p = 0.006), HbA_1C (r = 0.296; p = 0.063).

Conclusions. Noninvasive assessment of common carotid artery IMT showed unfavorable change in the group of morbidly obese patients in comparison to healthy persons. Weight reduction as a result of bariatric surgery leads to the decrease in IMT as well as beneficial metabolic changes.

Key words: intima-media thickness, obesity, bariatric surgery

S t r e s z c z e n i e

Wstęp. Otyłość definiuje się jako patologiczne nagromadzenie tkanki tłuszczowej w organizmie prowadzące do rozwoju chorób, w tym chorób układu sercowo-naczyniowego.

Cel. Celem badania była ocena grubości kompleksu błona środkowa – błona wewnętrzna tętnicy szyjnej wspólnej (IMT) w grupie pacjentów z otyłością olbrzymią, jak również ocena wpływu chirurgii bariatrycznej na badany parametr.

Materiał i metody. U wszystkich 40 pacjentów wykonano pomiary antropometryczne, oznaczono podstawowe parametry laboratoryjne oraz dokonano oceny IMT (Philips iE 33 system; Andeouver, Massachusetts USA). Protokół badania został zaakceptowany przez Komisję Bioetyczną przy Warszawskim Uniwersytecie Medycznym w Warszawie

Results. Masa ciała pacjentów z otyłością olbrzymią zmieniła się w ciągu 6-miesięcznej obserwacji pooperacyjnej (132,03 ± 18,42 vs. 97,46 ± 15,35 kg; p < 0,0001 ze zmniejszeniem tłuszczowej masy ciała 49,15 ± 3,83% (OB1) vs. 38,20 ± 5,66% (OB2), (p < 0,0001). Grubość kompleksu błona wewnętrzna – błona środkowa różniła się pomiędzy grupami OB1 oraz OB2 (0,59 ± 0,11 vs. 0,52 ± 0,011 mm; p < 0,0001), ale nie przekraczała normy (IMT < 0,9 mm). Wartości IMT w GK były niższe niż w OB1 i wynosiły 0,42 ± 0,026 mm (p = 0,0001). W OB1 IMT korelowała z masą ciała (r = 0,472; p = 0,002), beztłuszczową masą ciała (r = 0,427, p = 0,0059), tłuszczową masą ciała (r = 0,368, p = 0,019), BMI (r = 0,423; p = 0,006), HbA_1C (r = 0,296; p = 0,063).

Wnioski. Nieinwazyjna ocena IMT w grupie pacjentów z otyłością olbrzymią, w porównaniu do grupy osób zdrowych wskazuje na ich niekorzystne zmiany w grupie pacjentek z otyłością olbrzymią, w porównaniu do grupy osób zdrowych. Redukcja masy ciała w wyniku operacji bariatrycznej u pacjentów z otyłością olbrzymią prowadzi do obniżenia IMT oraz do korzystnych zmian metabolicznych

Słowa kluczowe: grubość kompleksu błona środkowa – błona wewnętrzna, otyłość, chirurgia bariatryczna

INTRODUCTION

Obesity as a cardiovascular risk factor

Obesity, according to World Health Organisation definition, is a pathological accumulation of adipose tissue in the organism, and leads to the development of diseases, including cardiovascular diseases (1). Available data on epidemiology of obesity report that obesity occurs in 21.2% men and 22.4% women, in which 0.6% men and 2.2% of women are morbidly obese (2). Moreover, NATPOL study (2011) suggests that number of obese patients in 2035 increases from 22% to 33%, that is from 6.5 mln to more than 9 mln patients. Morbidly obese patients constitutes a group of patients with significantly increased cardiovascular risk. These patients characteristically more frequently suffer from different co-morbidities such as glucose disturbances, hypertension, sleep apnea, venous thromboembolism. Numerous epidemiological studies confirm significant influence of obesity on morbidity and mortality caused by cardiovascular incidents as well as on increase in number of complications caused by cardiac incidents (3). The meta-analysis of 15 studies, conducted in European Heart Journal, including 258 114 patients, showed that increase in waist circumference by 1 cm caused 2% increase in the incidence of cardiovascular diseases. Moreover increase in WHR by 0,01 is related to increase in the cardiovascular risk by 5% (4).

Bariatric surgery

Bariatric surgery is a recognized method of treatment in patients with morbid obesity (5). The indications for surgery in the group of patients are BMI ≥ 40 kg/m^2 or BMI 35-40 kg/m^2 with co-morbidities, whose degree can potentially decrease as a result of weight reduction (metabolic diseases, cardiopulmonary diseases) (5).

Non-invasive assessment of infima-media thickness

According to actual recommendations of European Society of Hypertension and European Society of Cardiology increase in intima-media thickness (IMT) is a subclinical surrogate of morphological abnormalities of arterial walls (6-8). Arterial wall consists of three layers: the intima, media and adventitia (9). Primarily, Pignoli et al. in Circulation in 1986 revealed that assessment of common carotid artery intima-media thickness in ultrasonography correlates with its histopathological assessment (10). On a longitudinal, two-dimensional ultrasound image of the common carotid artery, the anterior and posterior walls of the carotid artery are displayed as two bright white lines. The distance between the leading edge of the first bright line of the far wall (lumen-intima interface) and the leading-edge of the second bright line (media-adventitia interface) indicates the intima-media thickness (10). According to quotabled over european guidelines IMT value more than 0.9 mm indicates abnormality (11). Based on meta-analysis performed by Lorenz et al. in the group of 37 000 patients, increase in IMT by 0,1 mm is related to 10-15% increase in risk of myocardial infarction and 13-18% increase in risk of stroke (11).

Multiple studies enabled us to assess the risk of leading or non-leading to death cardiovascular incidents, based on IMT measurements (12, 13). According to American College of Cardiology Foundation/American Heart Association (2010) recommendations regarding to cardiovascular risk assessment in asymptomatic patients, IMT measurement referred to IIa in the group of patients with intermediate risk (14). Thus, common carotid artery IMT is recognized as a marker of cardiovascular incidents in asymptomatic patients with type 2 diabetes and supporting parameter of cardiovascular risk assessment using Framingham scale (15, 16). Mannheim's consensus authors recommended IMT assessment in all patients with suspected vascular disease (17).

Available data on the influence of antihypertensive treatment on IMT values are equivocal (18). Tropeano et al. in their meta-analysis confirmed significant decrease in IMT in the group of patients undergoing antihypertensive therapy in comparison to the control group undergoing therapy based on placebo: -0.10 (-0.16; -0.04) (18).

AIM

The aim of the study was to assess common carotid artery intima-media thickness in morbidly obese patients. Pararelly, we wanted to compare received results to controls' group results as well as to results in studied group after 6 months bariatric surgery follow-up.

MATERIAL AND METHODS

For the prospective analysis we included 40 patients with severe obesity, admitted to the Department of Internal Medicine and Cardiology for qualification for bariatric surgery procedures (OB1) and reassessed six months after the surgery (OB2). There were 15 healthy women with normal body mass in the control group. They were matched for age and sex with OB1/OB2. In all cases undergoing our study we performed:

physical examination, anthropometric analysis (height, body mass, fat mass, free fatty mass), basic laboratory analysis (morphology, lipidogram, GOT, GPT, creatinine, hsCRP, HbA_1C, fasting glucose, two-hour glucose levels on the OGTT), common carotid artery intima-media thickness (IMT). The patients suffered from hypertension were analyzed during standard treatment according to Eurpean Society of Cardiology guidelines. Angiotensin converting enzyme inhibitors, diuretics and in some cases calcium-antagonists were used. Then, all patients undergone bariatric surgery. All assessments were repeated six months after surgery. The same protocol was performed in the control group.

Common carotid artery intima-media thickness was performed in the morning, after 12 hours at rest, on the base of 3 measurements in both common carotid arteries. The measurements were performed according to accepted protocol using ultrasound Philips iE 33 system (Andeouver, Massachusetts USA) with linear probe (5-7 MHz). All measurements were performed and assessed by one doctor.

For the statistical analysis of the material to describe the quantitative variables, we used standard descriptive statistics. For quantitative variables was tested the hypothesis that the distribution of the features compatibility with a normal distribution (Shapiro-Wilk test, test type graphical QQ). In the case when the distribution of the characteristics was normal, we tested the hypothesis of the equality of the means for the two groups, using the T-test. When comparing the two groups for traits showing deviations from the normal distribution, we used Wilcoxon test for independent samples. By analyzing changes in quantitative parameters during treatment, we used t-test for the characteristics of normal distributions and the Wilcoxon test for the characteristics of the other distributions. Analyzing correlations for quantitative variables, we used Pearson's coefficient for the characteristics of normal distributions and Spearman coefficient for the characteristics of the other distributions. The relationship between qualitative variables was tested in the system of contingency tables using the chi-square test or Fisher's exact test when the expected values in table cells were not sufficiently large (ie. more than 5). By analyzing changes in quality parameters during treatment test, we used the test of symmetry related (McNemar's test). When analyzing the impact of some factors on IMT, we used multivariate generalized linear models (GLM). The GLM models were selected optimal forms: combining function and the distribution of the error. The selection of the optimal model used stepwise variable selection strategy. As a criterion for the selection of model fit assumed statistical minimum AIC (Akaike's Information Criterion). To describe the model fits the data statistics, we used Pearson Chi-Square and pseudo R-Square. The level of statistically significant value of p was < 0.05.

The protocol was approved by Warsaw Medical University's Bioethics Committee on 31.03.2009 (KB/64/2009). The research project was co-financed with funds of Ministry of Science and Higher Education (N N402 490240).

RESULTS

General clinical characteristics of studied groups

The anthropometric results of patients undergoing bariatric surgery as well as control group were presented in table 1.

Incidence of co-morbidities in morbidly obese patients

We recognized hypertension in 38 (95%) patients. At the time of surgery 30 (75%) patients received 2 or more antihypertensive drugs (including angiotensin-converting enzyme inhibitors and diuretics); and 8 (20%) patients only 1 antihypertensive drug (angiotensin-converting enzyme inhibitor). We recognized pre-diabetic state in 11 (27.5%) patients, among them 6 (15%) patients with impaired fasting glucose (IFG), and 7 (17.5%) with impaired glucose tolerance (IGT). We recognized both pre-diabetic states simultaneously in 2 (5%) patients. Patients with type 2 diabetes were excluded from the study. We recognized lipid abnormalities in 22 (55%) patients and moderate sleep apnea in 8 (20%) patients.

Basic biochemical parameters assessment in studied group

In table 2 we presented the results of basic biochemical parameters in studied group.

We compared mean values of lipid parameters in morbidly obese patients and in the control group. We found statistically significantly differences in mean

Table 1. Anthropometric results of patients undergoing bariatric surgery as well as control group.

	Patients before surgery (OB1)	Patients 6-months after surgery (OB2)	Control group (CG)
Body mass (kg)	132.03 ± 18.42	97.46 ± 15.35*	60.73 ± 5.12*
BMI (kg/m²)	47.73 ± 6.18	35.22 ± 5.20*	21.61 ± 1.41*
FAT (%)	49.15 ± 3.83	38.20 ± 5.66*	25.13 ± 4.88*
FFM (kg)	66.78 ± 7.84	59.90 ± 8.92*	45.37 ± 3.7*
BSA M (m²)	2.47 ± 0.20	2.12 ± 0.19*	1.68 ± 0.09*
EBW (kg)	72.34 ± 16.75	37.77 ± 13.97*	

*vs. OB1: $p < 0.0001$

Table 2. Basic biochemical parameters assessment in studied group.

		Patients before surgery (OB1)	Patients 6-months after surgery (OB2)	Control group (CG)
Creatinine (mg/dl)	median, range	0.7; 0.5-1.3	0.80; 0.5-1.0	0.8; 0.6-0.9
Total cholesterol (mg/dl)	mean ± SD	199.15 ± 35.13	189.75 ± 29.64*	184.07 ± 28.68
LDL-cholesterol (mg/dl)	mean ± SD	120.30 ± 31.59	113.25 ± 28.42	102.07 ± 25.32*
HDL-cholesterol (mg/dl)	mean ± SD	52.55 ± 10.97	54.50 ± 9.68	69.53 ± 10.36*
Triglycerides (mg/dl)	median, range	114; 31-255	88.50; 39.00-235.00*	51; 30-203*
hsCRP (mg/l)	median, range	8.80; 1.9-32.02	2.80; 0.4-25.50*	0.60; 0.1-2.40
Fasting glucose (mg/dl)	median, range	89; 67-124	85.00; 66.00-109.00*	90; 81-102
Two-hour glucose levels on the OGTT (mg/dl)	mean ± SD	109.58 ± 31.16	80.20 ± 20.18*	95.27 ± 24.14
HbA_1C (%)	median, range	5.65; 5.20-10.90	5.35; 4.70-6.10*	5.60; 5.30-5.80*

Vs. OB1 p < 0001*; OB1 – before bariatric surgery; OB2 – 6-months after bariatric surgery

Table 3. The results of common carotid intima-media thickness measurements in studied groups.

	Patients before surgery (OB1)	Patients 6-months after surgery (OB2)	Control group (CG)
IMT (mm)	0.59 ± 0.11*	0.52 ± 0.11*	0.42 ± 0.026*

*vs. OB1: p < 0.0001

fasting lipids values (HDL-cholesterol, LDL-cholesterol, triglycerides). In morbidly obese group, we recognized lower mean HDL-cholesterol level (52.55 ± 10.97 vs. 69,53 ± 10.36 mg/dl, $p = 0.005$), and higher mean LDL-cholesterol level (120.30 ± 31.59 vs. 102.07 ± 25.32 mg/dl, $p < 0.0001$). What is more in this studied group, we confirmed higher triglycerides level (124.78 ± 47.70 vs. 63.80 ± 41.02 mg/dl).

Common carotid intima-media thickness measurements in studied groups

The results of common carotid intima-media thickness measurements in studied groups we presented in table 3.

We would like to underline that mean intima-media thickness varied statistically between both groups (OB1, OB2) (0.59 ± 0.11 vs. 0.52 ± 0.011 mm; $p < 0.0001$), and were within the reference value range (IMT < 0.9 mm). In the control group IMT values were lower than in OB1 (0.59 ± 0.11 vs. 0.42 ± 0.026 mm; $p = 0.0001$). We found no patients with IMT value above the upper reference value.

Common carotid IMT correlation with age and serum creatinine in the control group

In the control group, IMT correlated with age ($r = 0.65$; $p = 0.0052$), serum creatinine concentrations ($r = 0.68$; $p = 0.0089$).

The associations between common carotid IMT and body mass parameters in morbidly obese patients

Significant associations with common carotid artery IMT were found for numerous mass parameters. We presented them all in table 4.

The changes in studied parameters just 6 months after bariatric burgery

The associations with common carotid artery IMT changes (Δ IMT) after bariatric surgery were found for chosen anthropometric parameters in morbidly obese patients. We presented them in table 5.

The multidimensional analysis of different parameters on common carotid artery IMT in morbidly obese patients

The influence of chosen parameters on IMT value was studied using generalized linear model (GLM). They used values of chosen parameters in prediction of expected IMT value. We recognized age ($p = 0.0339$) and BSA M ($p = 0.0025$) as important in IMT values prediction, pseudo-R- squared 0.273.

Table 4. The associations between common carotid IMT and body mass parameters in morbidly obese patients.

Parameter: IMT (mm)	r	p
Body mass (kg)	0.472	0.002
FM (kg)	0.368	0.019
BMI (kg/m²)	0.423	0.006
BSA M (m²)	0.442	0.004
HR (1/min)	0.319	0.045

Table 5. The associations with common carotid artery IMT changes (Δ IMT) after bariatric surgery for chosen anthropometric parameters in morbidly obese patients.

Parameter Δ IMT	r	p
Δ BMI	0.328	0.038
Δ body mass	0.371	0.0183
Δ FM	0.308	0.0529

DISCUSSION

In the presented study, we non-invasively assessed the stage of artery remodelling in morbidly obese patients in comparison to the normal-weighted control group, as well as the efficacy of bariatric surgery in decreasing of IMT values.

For the prospective analysis, we included 40 patients with severe obesity (mean age 36.4 ± 9.0 yrs), admitted to the hospital for qualification for bariatric surgery procedures (OB1) and reassessed six months after the surgery (OB2). In the aim of achieving uniformity of the studied group, patients with significant co-morbidities were excluded from the study.

The patients undergoing bariatric surgery did not differ from the control group in their age. Obviously, they differ in BMI (47.73 ± 6.18 kg/m^2 vs. 21.61 ± 1.41 kg/m^2; $p < 0.0001$), body mass (132.03 ± 18.42 kg vs. 60.73 ± 5.12 kg; $p < 0.0001$) and body surface area (2.47 ± 0.20 m^2 vs. 1.68 ± 0.09 m^2; $p < 0.0001$).

Intima-media thickness

A number of studies, among them Grinspoon et al. confirmed the association between body mass index and IMT in the group of 140 young (24-59 yrs), healthy women without recognized cardiac disease. The IMT values were higher in the obese group in comparison to the group with overweight or with normal body mass respectively: 0.69 mm (0.6-0.75 mm) vs. 0.62 mm (0.56-0.68 mm; p = 0.044) vs. 0.59 mm (0.54-0.67 mm; p = 0.016). We observed similar results in our study. Thus, mean IMT values in morbidly obese group were 0.59 ± 0.11 mm, and in the control group 0.42 ± 0.22 mm, respectively.

The up-to-date medical journals highlight that there is no large studies describing IMT associations in morbidly obese groups. Data on parameters influencing IMT changes in this group are poor as well. However, some authors confirmed IMT regression related to weight reduction as a result of bariatric surgery. Sarmento et al. described IMT regression just six months after bariatric sugery (0.73 mm ± 0.12 vs. 0.63 ± 0.12; $p < 0.05$), related to triglycerides and systolic blood pressure changes ($p < 0.05$) (19). Ajzen et al. studied common carotid artery IMT values in the group of 18 patients before bariatric surgery (0.73 ± 0.12 mm) and then 3, 6 (0.63 ± 0.12 mm; $p < 0.05$) and 12 months following surgery. Also, the authors of this study described positive associations between IMT and age (p = 0.002) and triglycerides (p = 0.02) (19).

Similarly, common carotid artery IMT values in our study differ between studied groups: OB1 and OB2 (0.59 ± 0.11 vs. 0.052 ± 0.011 mm; $p < 0.0001$); CG 0.42 ± 0.22 mm, and were within the reference value range (IMT< 0.9 mm). Although we did not describe relations similar to quotabled over study (age, triglycerides), accordingly to Grinspoon et al., we confirmed associations between common carotid IMT and body mass parameters (body mass, free fatty mass, fat mass, BMI).

Our IMT results are mean values of manually taken measurements. Polak et al. paid attention on relation between manual traced-IMT in comparison to edge-traced IMT. The latter used to be lower about 0,19 mm, but similarly related to studied risk factors (20). The METEOR Investigators in Journal of Internal Medicine disagreed any advantage of edge-traced IMT. They underlined similar relations of both methods of measurements with cardiovascular risk factors, measurements repeatability and effects of hypolipidemic therapy. Thus, the authors of the study showed that the method of measurements should be chosen based on logistic and cost procedures only (21).

Main limitations of our study

The present study has certain limitations that need to be taken into account. For the prospective analysis, we included only women, due to a few men assessed for bariatric surgery, all with exclusion criteria, in our department in patients' inclusion period. Moreover, we think that studied group is not very large (40 patients). The number of patients in studied group is in our opinion the result of demanding inclusion criteria (including the extent of obesity, co-morbidities).

Another limitation of this study is the manual way of taking measurements. However, all measurements were taken by one operator. The operator was focused on the present measurement as well as she did not suggest particular results of previous IMT measurements.

CONCLUSIONS

Noninvasive assessment of common carotid artery IMT showed unfavorable changes in the group of morbidly obese patients in comparison to healthy persons. Weight reduction as a result of bariatric surgery leads to the decrease in IMT as well as beneficial metabolic changes.

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