

PART III. OTHER
DZIAŁ III. RÓŻNE

SUPERIOR MESENTERIC ARTERY SYNDROME – DIAGNOSTIC DIFFICULTIES

ZESPÓŁ TĘTNICY KREZKOWEJ GÓRNEJ – TRUDNOŚCI DIAGNOSTYCZNE

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- A. Study design/planning
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- B. Data collection/entry
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- C. Data analysis/statistics
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- D. Data interpretation
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Summary

Background. Superior mesenteric artery syndrome (SMAS) is a rare disease caused by the acute angle of branching of the superior mesenteric artery from the aorta.

Material and methods. There were 63 patients (56 women and 7 men) with low body weight, who reported recurrent persistent abdominal pain, nausea, post-prandial vomiting, significant weight loss. All of them had abdominal ultrasonography performed with measurement of the angle of branching of SMA from the aorta. CBC, total bilirubin, AST, ALT, GT, ALP, amylase, lipase, albumins, iron, sodium, potassium, GFR, lipid profile, TSH, urinalysis were ordered. Additionally, esophagogastroduodenoscopy with Hp. test and esophageal impedance measurement in correlation with the reported ailments was performed.

Results. Acid reflux impedance was diagnosed in 10 patients. There were >55 acid reflux episodes per day and a positive reflux sign (SI) for heartburn and nausea. Abnormal impedance recording of acid reflux was diagnosed in 17 patients. They had >21 episodes of non-acid reflux per day. Positive reflux sign (SI) was not confirmed for any non-acid reflux-related symptoms.

Conclusions. It is justified to perform impedance pH monitoring in this group of patients as it allows to modify the therapy. The most important dietary recommendations are weight gain and understanding the cause of the disease.

Keywords: SMAS, laboratory tests, esophageal impedance pH monitoring, gut-brain axis

Streszczenie

Wprowadzenie. Zespół tętnicy krezkowej górnej (ZTKG) (SMAS – ang. superior mesenteric artery syndrome) jest rzadko rozpoznawaną chorobą, a jej przyczyną jest ostry kąt odejścia tętnicy krezkowej górnej od aorty.

Materiał i metody. Wyłoniono 63 pacjentów (56 kobiet i 7 mężczyzn) z niską masą ciała, którzy zgłaszali nawracające uporczywe dolegliwości bólowe w nadbrzuszu, nudności, poposiłkowe wymioty, istotną utratę masy ciała. Wszystkim wykonano ultrasonografię jamy brzusznej z pomiarem kąta odejścia TKG od aorty. Następnie oznaczono morfologię krwi, stężenie bilirubiny całkowitej, AST, ALT, GT, ALP, amylazy, lipazy, albuminy, żelazo, sód, potas, GFR, lipidogram oraz TSH, badanie ogólne moczu oraz wykonano gastrofiberoskopię z testem Hp. i pomiar impedancji przełykowej w korelacji ze zgłaszanymi dolegliwościami.

Wyniki. Nieprawidłowy zapis impedancji w zakresie refluksu kwaśnego rozpoznano u 10 pacjentów. Zarejestrowano >55 epizodów refluksu kwaśnego na dobę oraz dodatni objaw refluksowy (SI) dla zgagi oraz uczucia nudności/mdłości. Nieprawidłowy zapis impedancji w zakresie refluksu niekwaśnego rozpoznano u 17 pacjentów. Obserwowano u nich >21 epizodów refluksu niekwaśnego na dobę. Dla żadnego objawu związanego z refluksem niekwaśnym nie potwierdzono dodatniego objawu refluksowego (SI).

Wnioski. Uzasadnione jest wykonanie impedancji w tej grupie chorych gdyż pozwala na zmodyfikowanie terapii. Najważniejsze zalecenia dietetyczne to przyrost masy ciała i zrozumienie przyczyny choroby.

Słowa kluczowe: SMAS, badania laboratoryjne, impedancja przełykowa, oś trzewno-mózgowa

Tables: 16

Figures: 0

References: 40

Submitted: 2018 March 11

Accepted: 2018 Oct 19

Adamczyk M, Romanowski M, Mędrak-Socha M, Stec-Michalska K. Superior mesenteric artery syndrome - diagnostic difficulties. Health Prob Civil. 2019; 13(4): 296-306. <https://doi.org/10.5114/hpc.2019.81333>

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Introduction

Superior mesenteric artery syndrome (SMAS), also known as Wilkie's Syndrome, is a rare disease caused by the acute angle of branching of the superior mesenteric artery from the aorta. In these narrow forks of both vessels the transverse part of the duodenum passes, and its pressure causes disturbed passage of digestive content. It was first described in 1861 by Carl Von Rokitansky as an anatomical anomaly. A detailed description of 75 clinical cases was presented in 1927 by Dr. P. Wilkie [1-3]. The correct angle of branching of the superior mesenteric artery (TKG) is 35-55 °, the distance between the wall of the superior mesenteric artery and the aortic wall is 10-20 mm. In patients with diagnosed SMAS, the angle of branching of the superior mesenteric artery is below 26 °, the distance between the SMA wall and aortic aorta is 2-8 mm [4-6]. A familial susceptibility to the occurrence of SMAS has been demonstrated [7, 8]. It mainly affects young children and women aged 18-35 years [9]. SMAS should be suspected in individuals who have consciously (dieting) or as a result of a disease rapidly lost weight, including visceral fat which pushes the SMA away from the aorta [10-15]. This applies particularly to people with BMI <18 kg/m² [16, 17]. The acute angle of branching of the SMA (<25°) does not always disturb the passage of digestive content in the transverse part of the duodenum. Studies have shown that SMA has some mobility and only 14% of these patients experience clinical manifestation [18, 19], caused by disturbed intestinal contents passage in the transverse part of duodenum [20]. The ailments usually appear after meals and have a recurring character. Patients complain about abdominal pain, nausea, belching, vomiting, feeling of heartburn. For fear of ailments, they avoid eating meals and the weight loss increases [21-23]. Depending on the severity of symptoms and general condition of the patient, conservative or surgical treatment is considered. Conservative treatment consists of supplementing water-electrolyte deficiencies, recommendation of a rich calorie diet, eating frequent meals in small amounts. After meals the position should be lying on the left side or knee - elbow. This results in gravitational displacement of the SMA from the aorta and reduction of pressure on the duodenum [24]. The aim is to increase body weight. Visceral fat widens the angle between the SMA and the aorta and facilitates the duodenal passage [25]. Surgical treatment is more commonly used in small children or in case of significant cachexia. It consists in the formation of bypassing gastro-intestinal or duodenal intestinal anastomoses [26-28].

Early diagnosis based on subjective examination supported mainly by ultrasound examination of the abdominal cavity, excluding other diseases, is extremely important. Analyses have shown that the majority of patients with SMAS were previously consulted or treated by a psychiatrist with a diagnosis of depression, bulimia, mental anorexia or bipolar disorder [29]. Especially since this syndrome affects young women, who may suffer from menstrual disorders due to weight loss and a decrease in sex hormones. The ailments reported by patients with SMAS are not pathognomonic and can be attributed to functional or organic disorders of the upper gastrointestinal tract. Moreover, literature data show that there is an increased risk of acute pancreatitis or gallbladder stones [30, 31]. It is also worth mentioning that SMAS sometimes co-exists with the nutcracker syndrome, where the left renal vein is pressed through the aorta and the superior mesenteric artery. In this syndrome hematuria, unknown cause proteinuria, atypical abdominal pain located in the left lumbar region and/or the left iliac fossa may be present. They are accompanied by reduced effort tolerance, menstrual disorders in women or varicocele in men [32-34].

Aim of the study

The aim of the study was to identify a group of patients with rarely diagnosed SMAS and then to conduct a detailed analysis of the clinical picture of the disease in terms of differential diagnostics, especially esophageal reflux.

Material and methods

After obtaining permission from the bioethics committee, 63 patients (56 women and 7 men) with low body weight were selected, who reported recurrent abdominal pain, nausea, postprandial vomiting and significant weight loss.

Patients were diagnosed in the Department of Gastroenterology of the Medical University of Lodz, mean hospitalization period 3.69 ± 1.26 days. All of them had abdominal ultrasonography performed with the measurement of the angle of branching of SMA from the aorta. Eventually, 37 patients met the criteria of ZTKG, where the tight angle of TKG's departure from the aorta was determined below 26°. CBC, total bilirubin, AST, ALT, PGD, ALP, amylase, lipase, albumin, iron, sodium, potassium, GFR, lipid profile, TSH, urinalysis were evaluated. Esophagogastroduodenoscopy with urease test for *Helicobacter pylori* and esophageal impedance

were measured in correlation with the reported ailments. The small size of the study group is related to the rare occurrence of SMAS in the population.

Patients before the impedance measurement and gastroscopy for 14 days did not take drugs blocking gastric acid secretion or drugs affecting upper gastrointestinal motility.

The 24-hour esophageal impedance was measured using Sandhill Scientific's ZepHrT™ multi-channel recorder and ComforTEC Z/pH disposable probes from the same manufacturer. This equipment makes it possible to recognize the range and composition of esophageal reflux episodes occurring. The parallel measurement of the reflux pH qualifies the reflux as acidic or non-acidic and the symptoms reported by the patient are qualified as related or unrelated to the reflux episodes. Patients were fasting for 8 hours before the examination. Then, after calibrating the probe in the attached buffers, it was placed through the nasal tube in the stomach and then its position was corrected so that the pH-meter sensor was 5 cm above the lower esophageal sphincter (LES).

The first impedance channel was 3 cm above the LES and the last 17 cm above the LES. Patients were trained in using the recorder to mark meal periods, position of the body and report clinical symptoms. After 24 hours of recording, the probe was removed, and the collected data was analyzed on a computer using BioVIEW Analysis software supplied by the recorder manufacturer. The gastroesophageal reflux incident was considered to be a decrease in impedance of at least 50% in relation to the initial value, in at least two neighboring segments of the probe, and the incident was ascending. Analyzing the pH distribution, acid reflux was considered to be a decrease of the pH of the acid refluxate below 4 for at least 5 seconds, whereas any reflux not accompanied by a pH decrease below 4 was classified as non-acid [35]. The clinical symptom reported by the patient was classified as associated with reflux, i.e. a positive reflux index (index symptom - SI), if in half of the cases it was associated with the occurrence of reflux episode.

The results obtained were compared with standardized standards developed by Shay and his team for a healthy population [36]. According to these standards, the maximum number of episodes allowed should not exceed 73 per day.

Due to the small number of people in the study group, no statistical analysis was carried out with parametric tests.

Results

Characteristics of the studied group of patients

The mean age of women qualified for the study was 31.2 ± 8.2 years and men 28.6 ± 3.4 years. The study group was dominated by young women (92%) in the hormonally active period (two women had irregular menstruations), more than a half of which were under 32 years of age (Table 1). Height, body weight and BMI were analyzed separately for women and men due to the specificity of these variables. The average height of women was 168.3 ± 5.38 cm and that of men was 189.7 ± 2.52 cm. The average body weight of women was 53.2 ± 5.91 kg, of men 64.0 ± 3.61 kg. Despite the natural difference in height and body weight related to the gender difference, the BMI was on average not significantly higher in the group of women 18.6 ± 1.48 kg/m² vs. 17.7 ± 1.68 kg/m² of men. Further analysis of the study was undertaken regardless of the sex of the examined patients. It is worth noting that none of the subjects was characterized by a low height when compared to the Polish population (Table 1).

Table 1. Characteristics of the studied group of patients according to their age, gender, BMI

| Gender | Number of subjects | Current age (years) | Height (cm) | Weight (kg) | BMI kg/m ² |
|--------|--------------------|---------------------|------------------|-----------------|-----------------------|
| Women | 34/91.9% | 31.2 ± 8.2 | 168.3 ± 5.38 | 53.2 ± 5.91 | 18.6 ± 1.68 |
| Men | 3/8.1 % | 28.6 ± 3.4 | 189.7 ± 2.52 | 64.0 ± 3.61 | 17.7 ± 1.68 |

Duration of the disease

Patients reported different duration symptoms; most often up to several years (70%), up to 0.5 years (16%) and 13.5% of patients were not able to specify the duration of the symptoms.

Medical consultations

Due to the ailments, patients were most often consulted by a gastroenterologist (89.2%), followed by an endocrinologist (27%), a gynecologist (21.6%) and a psychiatrist (18.9%).

Weight loss

Nearly half of the subjects reported weight loss up to 5 kg, further 37.8% by 6-10 kg, and 10.8% above 10 kg. Two people (5.4%) did not report weight loss. The time in which weight loss occurred was quite short in the vast majority of patients, up to a maximum of 6 months. Weight loss was most often related to dietary changes (40.5%).

Socio-economic conditions of patients, smoking addiction

From the clinical point of view, an interesting analysis of socioeconomic conditions of the study group was carried out. Characteristics of patients concerning their place of residence, education, economic status (freely determined by the subjects) are presented in Tables 2 and 3. People living in cities accounted for almost 80%. Secondary and higher education was declared by 91.9% of the respondents (Table 2). Based on the questionnaire filled in by patients, 94.5% of the subjects determined their economic situation at a medium and high level (Table 3). Cigarette smoking can have a significant impact on gastric emptying and reflects the level of public awareness of a healthy lifestyle. The vast majority of respondents (81%) denied smoking (Table 4).

Table 2. Characteristics of the studied group of patients by place of residence and education

| | Place of residence | | Education | | | |
|--------------------|--------------------|---------|-----------|------------|-----------|--------|
| | city | village | primary | vocational | secondary | higher |
| Number of subjects | 29 | 8 | 1 | 2 | 15 | 19 |
| Percentage share | 79% | 21% | 2.7 % | 5.4% | 40.5% | 51.4% |

Table 3. Economic status freely determined by patients

| | Economic status | | |
|--------------------|-----------------|--------|--------|
| | Low | Middle | High |
| Number of subjects | 2 | 30 | 5 |
| Percentage share | 5.40% | 81.00% | 13.50% |

Table 4. Frequency of smoking in the studied group of patients

| | Smoking of cigarettes pieces/day | | | Smokers in total |
|--------------------|----------------------------------|-------|----------|----------------------|
| | 0-10 | 10-20 | Above 20 | |
| Number of subjects | 4 | 2 | 1 | 19.00% |
| Percentage share % | 10.80% | 5.40% | 2.70% | |
| | Addiction free | | | Non-smokers in total |
| Number of patients | 30 individuals | | | 81.00% |

*Analysis of laboratory tests**Complete Blood Count*

No significant changes in CBC were noted among the patients studied. Platelet levels in all patients were within normal limits. The analysis of the protein-cell system showed only a slight increase in the percentage of monocytes - $8.42 \pm 1.84\%$ on average (Normal level: 3.0-8.0%) (Table 5).

Table 5. Results of CBC in the tested group

| Variables | Calculated statistical parameters | | | | | |
|-----------------------|-----------------------------------|------|-------------|------|------|-------|
| | min | max | x | Me | SD | v (%) |
| WBC (thous./ μ l) | 4.0 | 10.7 | 5.76 | 5.6 | 1.31 | 22.7 |
| RBC (mln/ μ l) | 3.58 | 5.46 | 4.42 | 4.54 | 0.47 | 10.7 |
| HGB (g/dl) | 11.5 | 17.8 | 13.5 | 13.3 | 1.30 | 9.6 |
| HCT (%) | 33.9 | 50.2 | 39.4 | 39.1 | 3.57 | 9.1 |
| MCV (fl) μ g/dl | 63.0 | 98.1 | 88.5 | 89.3 | 6.42 | 7.2 |
| MCH (pg) | 25.7 | 33.6 | 30.5 | 30.9 | 1.82 | 6.0 |
| MCHC (g/dl) | 32.8 | 35.5 | 34.1 | 34.2 | 0.67 | 1.97 |

| | | | | | | |
|------------------------|-------|-------|--------------|-------|------|------|
| PLT (thous./ μ l) | 130.0 | 329.0 | 232.5 | 327.0 | 42.0 | 18.1 |
| NEUT (thous./ μ l) | 1.82 | 6.0 | 3.22 | 2.94 | 1.09 | 33.7 |
| NEUT (%) | 34.6 | 71.9 | 55.1 | 56.8 | 10.5 | 19.1 |
| LYMPH (thous. μ l) | 1.07 | 4.03 | 1.96 | 1.80 | 0.64 | 32.4 |
| LYMPH (%) | 20.3 | 53.5 | 34.2 | 33.6 | 9.23 | 27.0 |
| MONO (thous./ μ l) | 0.30 | 0.83 | 0.48 | 0.46 | 0.13 | 28.0 |
| MONO (%) | 4.9 | 12.4 | 8.42 | 8.45 | 1.84 | 21.9 |
| EO (thous./ μ l) | 0.01 | 0.35 | 0.105 | 0.080 | 0.08 | 73.4 |
| EO (%) | 0.10 | 7.5 | 1.90 | 1.60 | 1.39 | 72.8 |
| BASO (thous./ μ l) | 0.01 | 0.05 | 0.020 | 0.020 | 0.01 | 50.7 |
| BASO (%) | 0.10 | 0.90 | 0.356 | 0.300 | 0.18 | 51.4 |
| MPV (fl) | 8.7 | 12.4 | 10.4 | 10.3 | 0.96 | 9.2 |

Urinalysis

The specific gravity of urine ranged from 1005 to 1030 mg/dL, averaging 1018.4 ± 7.09 . It was probably due to an insufficient supply of fluids as the reported complaints occurred after both solid and liquid foods. The pH of urine ranged from 5.0 to 8.0, mean 5.91 ± 0.71 (Table 6). Abnormalities: Nitrogen compounds in urine were observed in 8.1% of patients, four patients had leukocyturia >10 in the field of view, abundant mucus, erythrocyturia. Urine cultures were performed and an effective targeted therapy was applied (Table 7).

Table 6. Results of urine tests in the study group

| Variables | Calculated statistical parameters | | | | | |
|------------------|-----------------------------------|------|---------------|------|------|-------|
| | min | max | x | Me | SD | v (%) |
| Specific gravity | 1005 | 1030 | 1018.4 | 1020 | 7.09 | 0.7 |
| Urine pH | 5.0 | 8.0 | 5.91 | 6.0 | 0.71 | 12.1 |

Table 7. Results of urine tests (presence of glucose, bilirubin, etc.)

| Variables | Presence in urine | | | |
|----------------------------|-------------------|------|----|-------|
| | Yes | | No | |
| | n | % | n | % |
| Glucose | - | - | 37 | 100.0 |
| Bilirubin | - | - | 37 | 100.0 |
| Ketone bodies | - | - | 37 | 100.0 |
| Protein | - | - | 37 | 100.0 |
| Nitro compounds | 3 | 8.1 | 34 | 91.9 |
| Blood | 3 | 8.1 | 34 | 91.9 |
| Leukocytes | 6 | 16.2 | 31 | 83.8 |
| Polygonal epithelial cells | 33 | 89.2 | 4 | 10.8 |
| White blood cells | 32 | 86.5 | 5 | 13.5 |
| Red blood cells | 13 | 35.1 | 24 | 64.9 |
| Bacteria | 12 | 32.4 | 25 | 67.6 |
| Mucous | 26 | 70.3 | 11 | 29.7 |

Biochemical blood tests

Serum glucose concentrations were in the range 62-104 mg/dl, mean 90.1 ± 8.22 mg/dl, urea concentration 1-34 mg/dl, mean 23.7 ± 4.79 mg/dl. Creatinine concentration ranged from 0.53 to 0.98 mg/d (mean 0.75 ± 0.12 mg/dl. Albumin concentrations from 4.3 to 5.3 g/dl, mean 4.75 ± 0.26 g/dl. CRP from 0.10 to 24.6 mg/l, averaging 1.85 ± 4.28 mg/l. No decreased serum total protein concentration, mean 7.10 ± 0.43 g/l, total bilirubin concentration 0.68 ± 0.46 μ mol/l was observed. Activity of liver enzymes: AST average values 20.1 ± 7.29 U/l, ALT 16.8 ± 7.53 U/l. Alkaline Phosphatase (ALP) 31 -106 U/l, mean 58.3 ± 19.1 U/l and PGD 4- 306 U/l, mean 26.8 ± 53.3 U/l. Activities of pancreatic enzymes: Serum lipase mean 34.3 ± 9.52 U/l, Serum Amylase 14 to 109 U/l (N to 100U/L), mean 58.5 ± 20.1 U/l. Exceeding the standards of GGTP and amylase was observed in one patient. Serum iron levels in blood between 2 - 181 μ g/dl, mean 98.9 ± 39.1 μ g/dl (N 33-193 μ g/dl). Only one patient

had iron levels decreased to 27 µg/dl (Table 8). Serum potassium ion concentrations ranged from 3.38 to 4.76 mmol/l, mean 4.18 ± 0.32 mmol/l, chlorine 95-108 mmol/l, mean 103.1 ± 2.21 mmol/l, sodium 136-145 mmol/l, mean 141.5 ± 1.95 mmol/l. Average concentrations of the determined ions were within the limits of the norm, except for reduced concentration of potassium ion in one patient to 3.38 mmol/l and chlorine to 95 mmol/l in another patient. GFR was within the norms; 81.8-128.9 ml/min/1.73 m, mean 101.1 ± 16.4 ml/min/1.73 m. TSH was in the range of 1.26 -5.44 µU/ml and the mean was 2.63 ± 1.78 µU/ml. In one of the examined patients the result exceeded the norm - 5.44 µU/ml (N: 0.4-4.0 µU/ml) (Table 9).

Table 8. Results of biochemical tests

| Variables | Calculated statistical parameters | | | | | |
|-------------------------|-----------------------------------|------|--------------|-------|------|-------|
| | min | max | x | Me | SD | v (%) |
| Glucose (mg/dl) | 62 | 104 | 90.1 | 90.5 | 8.22 | 9.1 |
| Urea (mg/dl) | 15 | 34 | 23.7 | 23.0 | 4.79 | 20.2 |
| Creatinine (mg/dl) | 0.53 | 0.98 | 0.75 | 0.74 | 0.12 | 15.6 |
| CRP mg/l) | 0.1 | 24.6 | 1.85 | 0.50 | 4.28 | 231.8 |
| Total protein (g/dl) | 5.99 | 7.80 | 7.10 | 7.11 | 0.43 | 6.1 |
| Total bilirubin (mg/dl) | 0.26 | 2.64 | 0.68 | 0.55 | 0.46 | 67.1 |
| AST (U/l) | 11 | 51 | 20.1 | 19.0 | 7.29 | 36.2 |
| ALT (U/l) | 6 | 36 | 16.8 | 15.0 | 7.53 | 44.9 |
| ALP (U/l) | 31 | 106 | 58.3 | 56.0 | 19.1 | 32.8 |
| GGTP(U/l) | 4 | 306 | 26.8 | 12.5 | 53.3 | 198.9 |
| Albumins (g/dl) | 4.3 | 5.3 | 4.75 | 4.74 | 0.26 | 5.5 |
| Lipase U/l) | 17 | 64 | 34.3 | 34.0 | 9.52 | 27.8 |
| Amylase (U/l) | 14 | 109 | 58.5 | 61.0 | 20.1 | 34.5 |
| Cholesterol (mg/dl) | 113 | 259 | 181.6 | 183.0 | 35.9 | 19.8 |
| LDL (mg/dl) | 55 | 150 | 93.7 | 91.0 | 29.5 | 31.5 |
| HDL (mg/dl) | 38 | 94 | 69.2 | 72.0 | 15.3 | 22.1 |
| TG (mg/dl) | 28 | 168 | 81.2 | 74.0 | 33.7 | 41.5 |
| Iron (µg/dl) | 27 | 181 | 98.9 | 104.0 | 39.1 | 39.5 |

Table 9. Electrolyte, GFR and TSH results

| Variables | Calculated statistical parameters | | | | | |
|--------------------|-----------------------------------|-------|--------------|-------|------|-------|
| | min | max | x | Me | SD | v (%) |
| Potassium (mmol/l) | 3.38 | 4.76 | 4.18 | 4.18 | 0.32 | 7.6 |
| Chlorides (mmol/l) | 95 | 108 | 103.1 | 103.0 | 2.21 | 2.1 |
| Sodium (mmol/l) | 136 | 145 | 141.5 | 141.0 | 1.95 | 1.4 |
| GFR(ml/min/1.73 m) | 81.8 | 128.9 | 101.1 | 105.4 | 16.4 | 16.2 |
| TSH (µU/ml) | 1.26 | 5.44 | 2.63 | 1.74 | 1.78 | 67.7 |

Analysis of the distribution of the measurement of SMA branching angle from the aorta

In more than 75% of the subjects the angle was below 20° and in the remaining ones within the range 21°-26°. The selected group of patients met the criteria for the diagnosis of SMAS (Table 10).

Table 10. Measurements of the angle of branching of the superior mesenteric artery (SMA) from the aorta in the studied group of patients

| | Angle of branching of SMA from the aorta expressed in degrees | | |
|---|---|----------|---------|
| | 7-17 | 16-20 | 21-26 |
| Number of patients/ Percentage share | 14/37.8 % | 14/37.8% | 9/24/3% |

*Analysis of the impedance results**Acid gastroesophageal reflux*

Any decrease of pH<4 in the esophagus lasting over 5 s. was considered to be an episode of acid gastroesophageal reflux. These episodes were registered in 89.1% of patients, but only in 29.7% of patients their number exceeded the cut-off point for the healthy population, which is defined as 50 episodes per day (Table 11).

Table 11. Frequency of acid reflux episodes recorded in 24-hour impedance in patients with SMAS

| Number of acid reflux episodes | Acid reflux episodes in different types of body positioning | | | | | |
|--------------------------------|---|-------|-------|-------|---------|-------|
| | upright | | lying | | overall | |
| | n | % | n | % | n | % |
| 0 | 5 | 13.5 | 9 | 24.3 | 4 | 10.8 |
| 1-20 | 17 | 46.0 | 19 | 51.4 | 8 | 21.6 |
| 21-50 | 8 | 21.6 | 6 | 16.2 | 14 | 37.8 |
| Above 50 | 7 | 18.9 | 3 | 8.1 | 10 | 29.7 |
| In total | 37 | 100.0 | 37 | 100.0 | 37 | 100.0 |

Subsequently, a detailed analysis of the reported ailments during the recording of esophageal impedance in connection with the acid reflux episodes was performed. The highest correlation was observed in the case of heartburn - on average $61.0 \pm 30.7\%$; abdominal pain correlated with acid reflux in $43.8 \pm 24.9\%$, nausea in $55.4 \pm 35.2\%$, belching in $46.2 \pm 24.6\%$ on average. Bloating occurred the least - $34.8 \pm 23.0\%$, gurgling, in $23.5 \pm 13.4\%$ (Table 12). Abnormal acid reflux impedance was diagnosed in 10 patients. There were >55 acid reflux episodes per day and a positive reflux symptom (SI) for heartburn and nausea.

Table 12. Analysis of reported acid reflux-related ailments in patients with SMAS in 24-hour impedance recording

| Confirmed complaints | Calculated statistical parameters (%) | | | | | |
|-----------------------|---------------------------------------|-----|-------------|------|------|-------|
| | min | max | x | Me | SD | v (%) |
| Abdominal pain (n=13) | 13 | 100 | 43.8 | 33.0 | 24.9 | 56.8 |
| Nausea (n=9) | 8 | 100 | 55.4 | 40.0 | 35.2 | 63.5 |
| Belching (n=11) | 14 | 80 | 46.2 | 37.0 | 24.6 | 53.2 |
| Flatulency (n=4) | 13 | 67 | 34.8 | 29.5 | 23.0 | 66.1 |
| Heartburn (n=4) | 27 | 100 | 61.0 | 58.5 | 30.7 | 50.4 |
| Gurgling (n=2) | 14 | 33 | 23.5 | 23.5 | 13.4 | 57.2 |
| Hoarseness (n=1) | 33 | 33 | 33.0 | 33.0 | - | - |
| Cough (n=1) | 12 | 12 | 12.0 | 12.0 | - | - |

Non-acid gastroesophageal reflux

Any episode of regurgitation registered during impedance recording with pH \geq 4 lasting more than 5s was considered to be an acid reflux episode. Non-acid reflux was observed in the vast majority of patients (91.9%). In the upright position, acid reflux occurred in 89.2% of patients and in the lying position in 86.5% (Table 13).

Table 13. Frequency of non-acid reflux episodes recorded in 24-hour impedance in patients with SMAS

| Variable | Non-acid reflux episodes | | | |
|-------------------------------------|--------------------------|------|--------|------|
| | Present | | Absent | |
| Non-acid reflux overall | 34 | 91.9 | 3 | 8.1 |
| Non-acid reflux in upright position | 33 | 89.2 | 4 | 10.8 |
| Non-acid reflux in lying position | 32 | 86.5 | 5 | 13.5 |

A detailed analysis of the number of non-acid reflux episodes showed their occurrence from 1 to 109 episodes, with an average of 26.0 ± 23 episodes (Table 14). In the upright position, 1 to 80 episodes of non-acid reflux were recorded in patients with an average number of such episodes 16.2 ± 16.5 .

Table 14. Characteristics of recorded non-acid reflux episodes in 24-hour impedance in patients with SMAS

| Number of non-acid reflux episodes | Calculated statistical parameters | | | | | |
|------------------------------------|-----------------------------------|-----|-------------|------|------|-------|
| | min | max | x | Me | SD | v (%) |
| Upright position (n=33) | 1 | 80 | 16.2 | 15.0 | 16.5 | 102.0 |
| Lying position (n=32) | 1 | 44 | 10.9 | 8.0 | 9.8 | 89.9 |
| Regardless of the position (n=34) | 1 | 109 | 26.0 | 21.0 | 23.0 | 88.2 |

In the lying position, 1 to 44 episodes of non-acid reflux were recorded, with an average of 10.9 ± 9.8 episodes. The number of registered non-acid reflux episodes varied greatly from patient to patient. The coefficient of variation (calculated as the quotient of standard deviation and mean value) exceeded 100% in the upright position and 90% in the lying position.

The correlation between recorded non-acid reflux and epigastric pain was $17.4 \pm 13.3\%$ on average; with nausea $33.9 \pm 31.7\%$ on average; with belching $20.5 \pm 9.47\%$ on average; and with flatulence 18.7 ± 14.6 on average. The correlation between the symptom reported as heartburn was $29.2 \pm 19.8\%$ on average and cough $17.0 \pm 9.90\%$ on average (Table 15).

Abnormal impedance recording of acid reflux was diagnosed in 17 patients. They had >21 episodes of non-acid reflux per day. No positive reflux signs (SI) were confirmed for any non-acid reflux-related signs.

Table 15. Analysis of complaints reported by patients with SMAS related to non-acid reflux in 24-hour impedance records

| Confirmed complaints | Calculated statistical parameters (%) | | | | | |
|----------------------|---------------------------------------|-----|-------------|------|------|-------|
| | min | max | x | Me | SD | v (%) |
| Pain (n=12) | 5 | 50 | 17.4 | 13.0 | 13.3 | 76.5 |
| Nausea (n=7) | 5 | 100 | 33.9 | 29.0 | 31.7 | 93.6 |
| Belching (n=10) | 8 | 33 | 20.5 | 21.0 | 9.47 | 46.2 |
| Flatulence (n=3) | 5 | 34 | 18.7 | 17.0 | 14.6 | 78.1 |
| Heartburn (n=6) | 8 | 60 | 29.2 | 29.0 | 19.8 | 67.8 |
| Gurgling (n=1) | 29 | 29 | 29.0 | 29.0 | - | - |
| Hoarseness (n=1) | 22 | 22 | 22.0 | 22.0 | - | - |
| Cough (n=2) | 10 | 24 | 17.0 | 17.0 | 9.90 | 58.2 |

Medical Imaging

All patients qualified for the study program had ultrasound and gastroscopy performed. Colonoscopy was previously performed in 29.7% of patients.

In gastroscopy, only one patient had signs of gastritis with *Helicobacter pylori* infection (positive urease test). In the case of other patients, the endoscopic examination was normal. Therefore, it can be assumed that 97.3% of patients did not show any abnormalities in the endoscopic examination. It is worth noting that in CT descriptions in only one out of four individuals, the radiologist pointed out, the narrow angle of the SMA's branching from the aorta.

Treatment used

Depending on the results of laboratory tests, endoscopic tests and impedance measurements, the current treatment was included or modified (Table 16). It was recommended to eat 5-6 small meals which are easily digestible and in some of cases enriched with oral supplements. After a meal, if possible, lying on the left-side should be applied and in case of severe ailments knee-elbow position should be used. In more than half of the patients (51.3%) PPI drugs were used, mainly in patients with acid symptomatic reflux. Prokinetic drugs were recommended in 40.5% of patients, especially in those with dominant non-acid reflux.

Treatment with selective serotonin reuptake inhibitors (SSRI) was applied in 51.3% of patients, most frequently in patients reporting ailments that were not confirmed by the impedance record. In case of *H. pylori* infection, an effective eradication therapy confirmed by a negative urea breath test was applied. All patients were informed in detail about the cause of the ailments, the need to increase their body weight and change their diet. The mere fact of explaining to them the cause of the disease was an important breakthrough in the treatment. In the 6-month observation period, a significant reduction of the ailments in the studied group of patients and an increase in body weight were achieved.

Table 16. Treatment used

| Treatment used | Number of subjects | % |
|-------------------|--------------------|------|
| PPI's | 19 | 51.3 |
| Prokinetic agents | 15 | 40.5 |
| Choleretic agents | 9 | 24.3 |
| SSRI's | 19 | 51.3 |

Discussion

Young patients, especially women with unintended weight loss, who report nausea, vomiting, heartburn, belching should have an abdominal ultrasound examination performed indicating the angle of branching of the superior mesenteric artery. In the studied group of patients, despite significant weight loss, no significant changes in CBC, electrolytes concentration, total protein, albumin and creatinine were found.

Only in one patient an increase in cholestatic enzymes (GGTP, ALP) activity was observed. According to the literature data, this syndrome may lead to impaired bile and pancreatic juice outflow to duodenum [30, 31]. In one of the examined patients elevated TSH concentration of 5.44 $\mu\text{UI/ml}$ was observed (N: 0.4-4.0 $\mu\text{UI/ml}$). This is explained by disturbances in the secretion of hormones on the TRH - TSH axis in patients with low BMI [37].

Analyzing the distribution of the number of registered acid reflux episodes in the group of patients, it was observed that, regardless of the position of the body, only 30% had more than 50 episodes, and every tenth had no acid reflux at all. Out of 37 patients, 32 reported pain, but only 41% of them were confirmed in the study. Nausea was reported by 19 individuals and were justified in less than half of the cases (47.4%). Belching was confirmed in 61.1% of individuals. Flatulence occurred in 11 patients and was confirmed only in 36.4%. Heartburn was confirmed only in every third patient (33.3%). The research also confirmed that cough and hoarseness are not significant ailments in SMAS. Non-acid reflux was observed in the vast majority of patients (91.9%), regardless of body position. It was often related to the feeling of pain in the upper abdomen and the occurrence of belching.

Comparing the distribution of reflux episodes in the study of esophageal impedance with the norms adopted for healthy population [38], it was noted that in patients with diagnosed SMAS, asymptomatic non-acid reflux occurs significantly more frequently (46%).

Conclusions

Superior mesenteric artery syndrome most often occurs in young, educated women with BMI below 20 kg/m^2 , coming from urban agglomerations, without economic problems, most often non-smoking, who observed a significant weight loss in a relatively short period of time.

Laboratory tests are not important in the diagnosis of SMAS, the angle of branching of the SMA from the aorta is the most important factor which helps to estimate the diagnosis of SMAS. Gastroscopy in SMAS is important in differential diagnostics.

24-hour impedance showed an increased number of episodes of asymptomatic non-acid reflux, although no positive reflux signs were confirmed for any of the reported ailments (SI).

Patients who reported ailments not related to reflux episodes were treated with SSRI group drugs with improvement. Since these drugs affect the gut-brain axis, it is possible that in SMAS patients, serotonin secretion may be disturbed on this axis.

It is justified to perform impedance in this group of patients as it allows to modify the therapy.

The most important are dietary recommendations, weight gain and understanding of the essence of the disease.

Disclosures and acknowledgements

The research was financed by a grant from the Medical University of Lodz No: 502-03/5-006-02/502-54-145.

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