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PhD Thesis Booklet

Head of Doctoral School: Lajos Bogár MD, DSc

Programme Leader: András Vereczkei MD, DSc

Thesis Supervisor: Sándor Márton MD, PhD

New considerations in the field of invasive bariatrics

Miklós Siptár, MD

University of Pécs Medical School

Department of Anesthesiology and Intensive Care

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1. LIST OF ABBREVIATIONS

BMI: Body Mass Index, DM II: 2-es típusú Diabetes Mellitus, FiO2: Fraction of Inspired Oxygen, FEV 1: Forced expiratory volume in the first second, FVC: Forced Vital Capacity, HDL: High Density Lypoprotein, LSG: Laparoscopic Sleeve Gastrectomy, PaO2: Partial Arterial Blood Oxygen Pressure, PEEP: Positive end-expiratory pressure, SpO2: Arterial Haemoglobin Oxygen Saturation, TLC: Total Lung Capacity

2. INTRODUCTION

Obesity is a major public health problem of our time, both globally and in our country, and given current trends, we must prepare for a further worsening of the situation, which will place a significant and growing burden on both the health systems and the financial resources of societies.

The aetiology of obesity is typically multifactorial, i.e. attributable to several factors. In terms of non-inherited factors, the development of obesity is due to a persistently positive energy balance in the vast majority of cases, but a number of obesity-related genes have been described.

In the discussion of obesity, it is essential to introduce the concept of BMI, which is the ratio of body weight in kilograms divided by the square of height in metres. If the BMI is less than 18.5 kg/m², the patient is abnormally thin, between 18.5 and 24.9 kg/m², the patient is of normal weight, between 25 and 29.9 kg/m², the patient is overweight, and above 30 kg/m², the patient is obese. Within this range, between 30 and 34.9 kg/m² is Class I obesity, between 35 and 39.9 kg/m² is Class II obesity and above 40 kg/m² is Class III obesity.

There are two basic patterns of adipose tissue gain. The classical view is that women tend to have what is known as gynoid obesity, also known as peripheral, subcutaneous, gluteofemoral or pear-type obesity, while android (or central, or visceral, or abdominal or apple) obesity is more common in men. In android-type obesity, the excess adipose tissue is much more likely to be in the visceral organ walls, and this adipose tissue is hormonally active and is responsible for a good proportion of the known comorbidities associated with obesity, whereas gynoid-type obesity is associated with far fewer negative consequences for patient health, according to the available data.

Primary obesity develops when a patient persistently takes in more calories than they burn. In secondary obesity, obesity develops as a complication of some disease, most commonly hypothyroidism.

Obesity is a disease in itself, but it also significantly increases the incidence of other diseases, such as heart disease, stroke, type 2 diabetes mellitus (DM II), certain types of cancer, a number of metabolic diseases, sleep apnoea syndrome, certain orthopaedic disorders, gastroenterological problems, a number of urological-reproductive problems, certain mental disorders and psychological problems. In addition, obese patients are significantly more likely to suffer from acute conditions such as polytrauma, extensive burns or sepsis, and are at higher risk of perioperative complications.

There are basically two treatment options for obesity, conservative and surgical. Two of the most important elements of the conservative approach are reducing calorie intake and increasing physical activity, while pharmacological treatment is a fashionable and emerging area. Surgical intervention may be justified if conservative methods fail, unless secondary obesity-causing disease is confirmed. Today, several types of bariatric surgery are in use. These are now performed almost exclusively by laparoscopic surgery. Initially, laparoscopic gastric banding was a promising option, but it was later shown to have a temporary effect, a poor side-effect profile and a high complication rate. Modern surgery includes LSG, bypass surgery and a combination of the two, omega loop bypass or minibypass surgery. Other procedures include gastroscopic surgery, like gastric balloon insertion (which has poor long-term results and is therefore in decline) and endoscopic gastric bypass, which reduce the volume of the antrum by insertion of internal sutures.

The basic indications for bariatric surgery are BMI over 35 kg/m^2 with comorbidities or BMI over 40 kg/m^2 without comorbidities. However, surgery can be performed at lower BMI if appropriate, so as not to wait for comorbidities to develop. It cannot be stressed enough that surgery alone will not solve the patient's problem, but merely add to the effects of the lifestyle changes that are already necessary. These operations are now almost exclusively performed laparoscopically.

3. OBJECTIVES

3.1 Objectives of our study on the impact of PEEP on intraoperative and early postoperative gas exchange

Patients with morbid obesity have a much higher risk of perioperative morbidity and mortality compared to the normal weight population. Performing surgery laparoscopically significantly reduces the perioperative risk, but intraoperative administration of anaesthesia and patient management make the anaesthesiologist's task more difficult, especially with regard to intraoperative ventilation of the patient. PEEP is widely used intraoperatively, not only for obese patients, and not only for anaesthesia in laparoscopic surgery, because of its many positive effects. However, the use of PEEP is also known to have adverse effects and cannot be considered a completely side-effect-free therapeutic procedure. Despite the extensive use of PEEP, there are few data on its effects on postoperative gas exchange, particularly in the early postoperative period. The question therefore arises, does the use of intraoperative PEEP improve gas exchange in the early postoperative period, and if so, how long-lasting is the effect?

3.2 Objectives of our study on the effect of laparoscopic gastric sleeve surgery in morbidly obese patients

Our aim was, on the one hand, to investigate whether the degree of obesity influences physiological parameters, the prevalence of comorbidities and their severity, with particular reference to cardiac and pulmonary comorbidities of major anaesthetic relevance, by analysing preoperative and postoperative data from our patient population undergoing LSG surgery, with a one-year follow-up. We also wanted to know whether LSG is effective in terms of weight loss, what complication rates should be expected and how our results compare with international results.

4. MATERIALS AND METHODS

4.1 Materials and methods of our study on the impact of PEEP on intraoperative and early postoperative gas exchange

To address the question of the potential positive effect of PEEP on intraoperative and early postoperative arterial partial arterial oxygen pressure (hereafter PaO2) in obese patients undergoing laparoscopic surgery, we designed a prospective, randomized clinical trial. Patients undergoing laparoscopic gastric banding surgery were divided into two groups by block randomization, with 30-30 patients in each group. The two groups showed no significant difference in demographics, comorbidity and lung function parameters, as shown in Table 1. Our data were used as median and interquartile range. Mann Whitney U test was used for statistical analysis.

	Group I	**Group II**	**p=**
Gender (male/female)	12/18	14/16	0,69
Age (years))	47 (34-57)	39 (22-53)	0,29
BMI (m/kg²)	52 (37-65)	45 (35-55)	0,49
Duration of surgery (min)	148 (106-250)	129 (75-210)	0,48
FEV 1 (L)	2,94 (1,82-4,43)	2,91 (2,36-3,53)	0,15
FVC (L)	3,67 (2,74-4,81	3,76 (2,50-4,45)	0,21
Complience (L/vízcm)	1,67 (1,2-2,3)	1,50 (1,3-1,9)	0.55
Hypertension	17/13	14/16	0,75
Ischemic heart disease	16/12	18/12	0,77
Heart failure	10/20	12/18	0,66
Diabetes mellitus type II	16/14	18/12	0,74
Sleep apnea syndrome	17/13	15/15	0,75

Table 1: Demographic and pulmonary function test data and prevalence of comorbidities in the two groups

All patients underwent laparoscopic gastric banding surgery for morbid obesity, each surgery was performed by the same surgeon. The patients' body weight index was above 35 m/kg² in all cases. Anaesthesia was administered in a standard way. Patients were divided into two groups after envelope randomization. Patients in the first group (Group 1, n=30) were ventilated with 10 water centimetres of PEEP, while patients in the second group (Group 2, n=30) were ventilated without PEEP (0 water centimetres of end-expiratory pressure). The nature of our study was a prospective, randomised clinical trial.

Blood gas samples were taken through an arterial cannula before surgery and preoxygenation (t0), after preoxygenation (t1) and every 20 min during surgery (t2, t3, t4, t5, t6, t7). Blood gas samples were also taken after discharge from the operating room and every four hours (tp1, tp2, tp3, tp4, tp5). We sought to answer the question whether a significant difference in PaO2 values between the samples of the two groups could be demonstrated, and whether and how long the effect of PEEP on intraoperative gas exchange and oxygenation could be improved in the postoperative period.

Power analysis performed prior to the study included sixty patients to ensure a statistically validated $p \leq 0.05$ difference. Due to the distribution of the sample, traditional parametric tests were not feasible and therefore non-parametric tests were used. Our data were used as median and interquartile range. Mann Whitney U test was used for statistical analysis.

4.2 Materials and methods of our study on the effect of laparoscopic gastric sleeve surgery in morbidly obese patients

Based on the principles of the Declaration of Helsinki, after obtaining the approval of the University of Pécs Clinical Centre Ethics Committee and with proper registration of our study, we analysed data from 151 patients (89 women and 62 men) who underwent LSG surgery in 2021 and 2022. As part of the preoperative check-up, we assessed the patients' preoperative health status, BMI, body fat percentage by bioimpedance, and recorded any co-morbidities, using cardiac ultrasound, respiratory function and laboratory tests. All operations were performed by the same surgeon. The effectiveness of the procedure was assessed six months and one year after the surgery. Data analysis was performed using IBM Statistic program version 20.0, while one-sample T test, Pearson's correlation analysis was used for statistical analysis. Data are presented as median and standard deviation, and $p<0.05$ was considered statistically significant.

5. RESULTS

5.1 Results of our study on the impact of PEEP on intraoperative and early postoperative gas exchange

We can conclude that, after reviewing and analysing the results of the blood gas semples obtained during gastric banding surgery and the early postoperative period in obese patients with a BMI above 35 kg/m², we found no statistically validated difference in Pa02 between the results of the group ventilated with PEEP and the group ventilated without PEEP, neither during surgery nor when analysing the blood gas samples taken after surgery ($p<0.05$). However, our results (as shown by the t1 values in Figure 1) emphasize the positive effect of preoxygenation, which increases the time available for intubation and reduces the risk of hypoxemia, as shown by the t2 result. Intraoperative PaO2 values are demonstrated in Figure 1, while PaO2 values for the first 24 hours postoperatively are demonstrated in Figure 2.

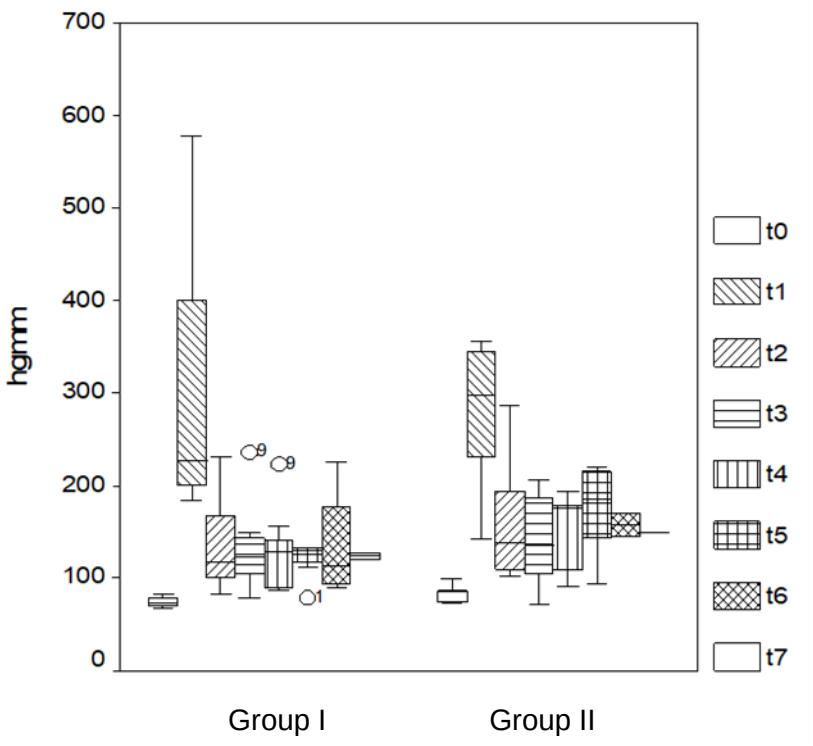

Figure 1: Arterial oxygen tension values during surgery in the two groups
Abbreviations: t0: partial arterial oxygen tension (PaO2) before preoxygenation, t1: PaO2 after preoxygenation, t2: PaO2 after surgery 20. t3: PaO2 at 30 min of surgery, t4: PaO2 at 40 min of surgery, t5: PaO2 at 50 min of surgery, t6: PaO2 at 60 min of surgery, t7: PaO2 at 70 min of surgery.

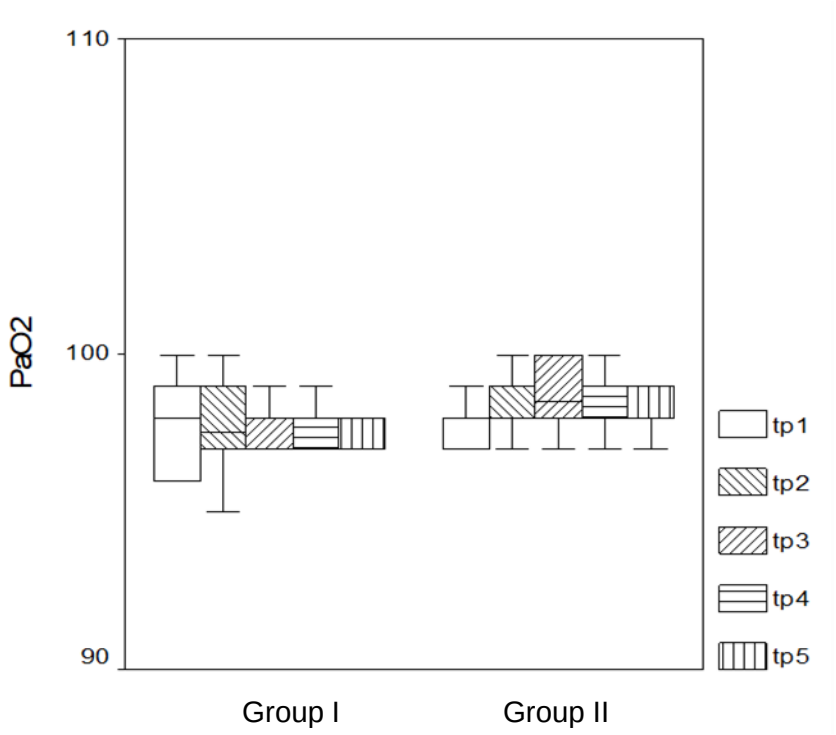

Figure 2: Arterial oxygen tension values in the two groups in the first postoperative 24 hours Abbreviations: tp1:PaO2 4 hours after opus, tp2:PaO2 8 hours after opus, tp3: PaO2 12 hours after opus , tp4: Pa02 16 hours after opus tp5:PaO2 24 hours after opus

5.2 Results of our study on the effect of laparoscopic gastric sleeve surgery in morbidly obese patients

Demographic data of the patients are summarized in Table 2. It should be highlighted that with a BMI above 45kg/m2, the mean age of the patients is 39.5 years, suggesting that these patients suffer from very severe obesity at a young age. Table 3 shows the results of the patients' preoperative cardiac ultrasound and respiratory function tests. Contrary to our expectations, echocardiography results did not confirm the abnormal values we expected, such as dilated right or left ventricle, elevated right ventricular pressure, reduced ejection fraction. The same was observed for respiratory function tests, the values did not indicate the expected restrictive or mixed ventilation disturbances, the measured parameters were within the physiological range appropriate for age. Our preoperative laboratory values are summarized in Table 4, here we found higher values for blood lipids, total cholesterol and LDL. Among the typical co-morbidities, hypertension was the most frequent, affecting 51.7% of patients, while the prevalence of DM II was much lower than expected, only 13.8%. Looking at the morbidity and mortality data of our patient population, we can say that there

were no deaths in the early postoperative period during our one-year study. A morbidity data are also favourable, with 4 cases of major morbidity. One case required reoperation for peritonitis and sepsis due to suture failure. After the reoperation, the patient was admitted to the ICU. Presumably the reason of suture failure was a gross dietary errors in the early postoperative period. 2 reoperations was needed for haemorrhage. One case of pneumonia in the early postoperative period, which responded well to the antibiotic treatment. The effectiveness of the surgery was demonstrated in Figure 3. The mean BMI of the study patient population decreased by 26.9% during the first six months, with an overall reduction of 35.4% by the end of the first year. The figures also show that the weight loss of patients in the first six months was higher than in the secod six months period. Using a single-sample T test, BMI values calculated at six months and one year after surgery were significantly lower than baseline BMI values ($p<0.001$), and the same was observed for changes in body fat percentage at similar time points ($p<0.001$). We also examined the changes in BMI by sex and found no difference between the two groups (Figure 3). Pearson's correlation analysis was performed, which to our surprise found no statistically valid correlation between baseline BMI and age ($p=0.07$).

	Minimum	Maximum	Median	Std. deviation
Age (years)	18	70	41,25	12,09
Height (cm)	146	201	172,93	9,875
Body weight (kg)	83	247	139,46	35,22
BMI	32,3	76	44,9	10,01
Body fat (%)	37,8	80	52,	10,01
Ideal body weight (kg)	49.7	81	65,97	11,05

Table 2: Preoperative demographics of patients. Data are shown as minimum, maximum, median and standard deviation.

Abbreviations: BMI: Body Mass Index, cm: centimetre, kg: kilogram

	Minimum	Maximum	Median	Std. deviation
EF (%)	50,00	74,00	59,89	5,99
RV diameter (mm)	19	44	29,5	4,26
LV diameter (mm)	43	63	51	4,48
E/A	0,44	5,00	1,28	0,73
FVC %	60	121	91,4	17,74
FEV1 %	44,00	119,5	97,5	17,70
PEF %	58	101	77,5	18,45
Tiffaneu index	47	99,6	78,12	7,89

Table 3: Results of cardiac ultrasound and respiratory function tests. Data are shown as minimum, maximum, median and standard deviation.
Abbreviations: EF: ejection fraction, E/A: early to atrial filling velocity ratio, RV: right ventricle, LV: left ventricle, FVC: Forced Vital Capacity, FEV1: Forced expiratory volume in the first second, PEF: Peak Expiratory Flow

	Minimum	Maximum	Median	Std. Deviation
Total cholesterol (mmol/l)	2,8	7,9	5,6	1,036
LDL (mmol/l)	1,22	5,37	3,21	0,92
HDL (mmol/l)	0,8	2,0	1,35	0,31
Triglycerides (mmol/l)	0,79	4,67	2,12	0,922
Blood sugar (mmol/l)	4	8,5	5,82	1,46
HgbA1c (%)	4,8	9,7	6,08	1,26
morning Cortisol (nmol/l)	118	577	322	122,03
TSH (mIU/l)	0,22	4,26	2,18	1,129

Table 4. Laboratory values measured before surgery. Data are shown as minimum, maximum, median and standard deviation.
Abbreviations: LDL: low-density lipoprotein, HDL: high-density lipoprotein, TSH: thyroid-stimulating hormone, HgbA1c: hemoglobin A1c

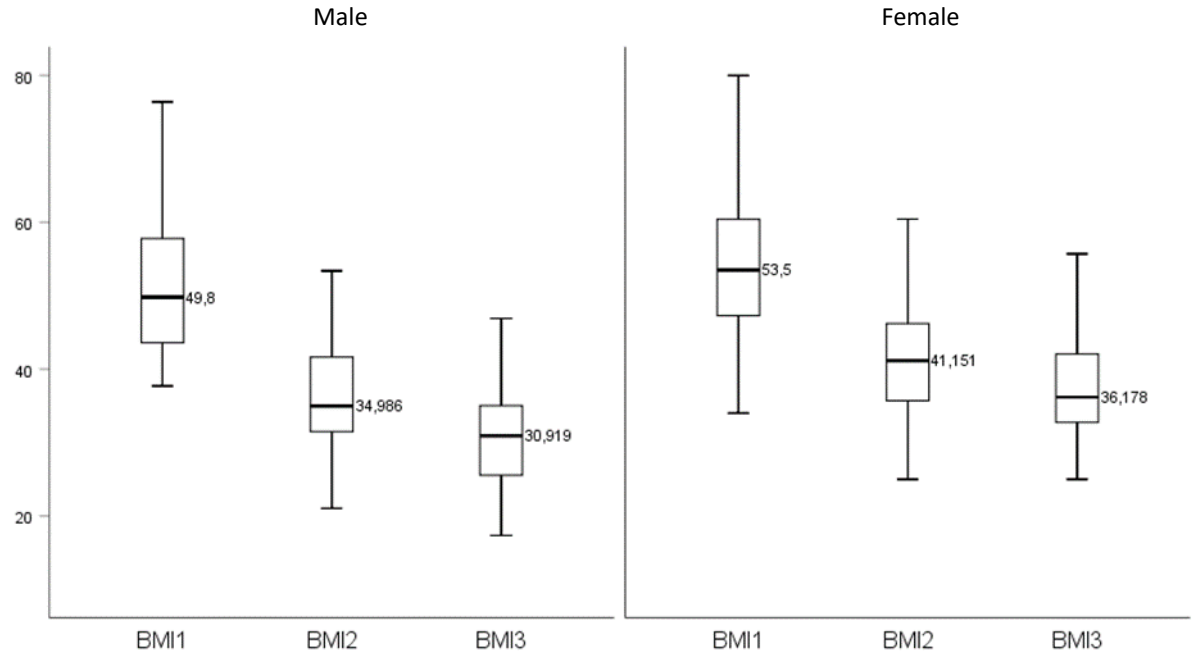

Figure 3: Changes in the average BMI value of the patients, broken down by gender, six months and one year after surgery. The data were represented as a "box plot", median, interquartile, minimum-maximum

Abbreviations: BMI 1: BMI value calculated before surgery, BMI 2: BMI value calculated six months after surgery, BMI 3: BMI value calculated one year after surgery

6. DISCUSSION

6.1 Discussion of our study on the impact of PEEP on intraoperative and early postoperative gas exchange

In our clinical study, we sought the answer to the question of whether PEEP applied during intraoperative positive pressure ventilation of morbidly obese patients has a beneficial effect on intraoperative and early postoperative oxygen supply, arterial oxygen partial pressure (PaO2) and arterial oxygen saturation (SpO2). According to our study, contrary to our expectations, PEEP does not affect oxygenation during surgery or in the 24 hours after it.

The reason for this is still unknown. One of the possible explanations for this phenomenon may be the hypoxic pulmonary vasoconstriction (HPV). The higher PEEP used in laparoscopic surgeries reduces the extent of pulmonary atelectasis caused by elevated abdominal pressure due to pneumoperitoneum and higher diaphragm accommodation. However, due to HPV in these areas, it is possible that the importance of the shunt circulation caused by atelectasis is much smaller than previously assumed. Consequently, either the opening of these atelectasis lung areas by PEEP has no significant effect on oxygen uptake, or PEEP has little role in opening the atelectasis lung areas, rather it is responsible for maintaining the opening of already opened lung areas. In short, a possible explanation for this phenomenon could be that the effectiveness of HPV has been underestimated so far.

In addition to the underestimation of the effect of HPV, another explanation of the phenomenon can be given if we assume that PEEP plays a role in keeping the atelectasis lung areas open after opening, rather than in opening them. It would be interesting to repeat the experiment in such a way that both the group ventilated with PEEP and without PEEP is divided into 2 more subgroups, and after induction of anesthesia manual alveolar recruitment is performed in one subgroup and not in the other.

It is also possible that in obese patients, PEEP is less effective than in patients with a normal BMI in terms of alveolar opening. Therefore, it would be interesting to conduct the study by comparing obese and normal BMI groups, for example in connection with laparoscopic cholecystectomy or other laparoscopic surgery.

Many questions therefore arise regarding the possibility of continuing the research.

6.2 Discussion of our study on the effect of laparoscopic gastric sleeve surgery in morbidly obese patients

In terms of comparison with international data, we can say that the 35% reduction in BMI we experienced at the end of our one-year follow-up is essentially the same as the result of a similar study at the Hebrew University of Jerusalem, where 33.5% reduction in BMI was observed at the end of the one-year period. Regarding our morbidity and mortality data, our previously described complication rate corresponds to a severe morbidity of 2.6%, without mortality, which also correlates with the literature data (based on the data of 3983 LSG operations analyzed in the study by Singhal et al., the mortality was 0.1%, the the frequency of serious complications (Clavien–Dindo 3-4) was 2.1%). The results of our studies show, on the one hand, that laparoscopic gastric bypass surgery is effective in terms of reducing the patients' body weight in a period of six months and one year, but we could expect to judge the durability of the effect in the case of a five-year follow-up, where patients must maintain lifestyle changes and diet in order to avoid repeated weight gain. For this, ideally, the patient will also receive help later on, which is ideally implemented within the framework of multidisciplinary cooperation. The dietitian continues to help the patient with nutritional advice to avoid possible weight gain. Cooperation with an internist or family doctor is also important, who treats existing co-morbidities and newly developing ones. The role of the physiotherapist should also be emphasized, who develops individualized therapy in order to improve physical condition, taking into account possible co-morbidities. The low average age of the patients (41 years) is important, as well as the fact that comorbidities typically associated with obesity, apart from high blood pressure, which occurred in 51.7%, did not develop in a significant proportion, surprisingly even the second most frequently detected DM II was only confirmed in 13,8%. The conclusion can be drawn from the above that, in the case of patients undergoing surgery, the lack of multimorbidity, the normal laboratory parameters, the respiratory function and heart ultrasound findings without significant deviations from physiology, and the partially resulting low morbidity and mortality data that correlate with international data are presumably largely due to the young age of the patients. Based on these, it may be advisable to direct some of the patients who do not exhaust the classical indication range of bariatric surgery towards the operative solution, based on our results, it seems that it is not worth waiting for the appearance of comorbidities, especially multimorbidity. By performing operations on young patients who are essentially healthy apart from their obesity, we can give back several years spent in a better quality of life. In addition, the perioperative

risk could also be reduced, since younger patients with fewer comorbidities would be operated. Our young, obese patients, who are still about to have children, can face fewer problems during conception after significant weight loss, and in the case of women, maternal and fetal risks are also reduced during pregnancy. Unfortunately, the surgical intervention is not financed by the state. It would be necessary to change this, because based on our current knowledge, conservative treatment is not a suitable alternative for this group of patients.

7. CONCLUSIONS

7.1. Conclusions of our study on the impact of PEEP on intraoperative and early postoperative gas exchange

Based on our present study, the intraoperative PEEP value of 10 cm of water did not favorably affect intraoperative or early postoperative oxygen supply. Given that the use of PEEP cannot be considered a therapeutic procedure without side effects, it is advisable to use it with due caution and evaluate its role in a complex manner, taking into account other mechanical ventilation parameters, and apply it tailored to the patient.

At the same time, our results clearly demonstrate the effectiveness of preoxygenation in patients with a BMI over 35 kg/m^2. Thus, in the case of these patients, careful preoxygenation can definitely be recommended, since desaturation occurs later due to the filled oxygen stores in the event of a possible difficulty in securing the airway, and the anesthesiologist has more time to overcome the difficulty before the patient suffers hypoxic damage.

7.2. Conclusions of our study on the effect of laparoscopic gastric sleeve surgery in morbidly obese patients

The data of our follow-up study after one year clearly show that LGS is an effective weight loss procedure in the short term. In order to establish the durability of the effect, we plan to extend the follow-up examination to (at least) five years. Based on the study, we believe that in case of ineffectiveness of conservative treatment, it is worthwhile to direct the treatment of patients towards surgical care as soon as possible, in order to reduce the perioperative risk and the number of years spent in poor quality of life, and to prevent the subsequent development or further deterioration of co-morbidities.

8. ASCERTAINMENTS

8.1. Ascertainments of our study on the impact of PEEP on intraoperative and early postoperative gas exchange

Based on our present study, the intraoperative PEEP value of 10 cm of water in obese patients with a BMI over 35 kg/m² did not favorably affect the body's intraoperative or early postoperative oxygen supply. Consequently, in the case of intraoperative low arterial oxygen saturation and low arterial partial oxygen pressure, it is not necessarily a good idea to try to improve gas exchange simply by increasing PEEP. At the same time, our study clearly confirmed the effectiveness of preoxygenation, so it can definitely be recommended for patients who, for any reason, have difficulty in securing the airway.

8.2. Ascertainments of our study on the effect of laparoscopic gastric sleeve surgery in morbidly obese patients

Based on our present study, LSG is an effective weight loss procedure in the short term, which can be performed with a low morbidity and mortality rate in young patients who are not yet affected by multimorbidity.

9. ACKNOWLEDGEMENTS

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10. LIST OF PUBLICATIONS

Miklós Siptár, Krisztina Tóth, Lívia Szélig, Alexandra Csongor, Zsombor Márton, Ferenc Molnár, Lajos Bogár, Sándor Márton. Effect of positive end-expiratory pressure applied during general surgical anaesthesia on intraoperative and postoperative gas exchange in extremely obese patients. Romanian Journal of Anaesthesia and Intensive Care, forthcoming
IF: 0,00

Miklós Siptár, György Tizedes, Bálint Nagy, Szilárd Rendeki, Sándor Márton. Intraoperative gastroscopy during laparoscopic sleeve gastrectomy after gastric band surgery with unrecognized hiatal hernia - a case report. Signa Vitae. 2023 vol.19(5), 254-257. DOI:10.22514/sv.2023.093
IF: 1,1

Miklós Siptár, Krisztina Tóth, Alexandra Csongor, Zsuzsanna Németh, Ferenc Molnár, György Tizedes, Zsombor Márton, Sándor Márton. Efficacy of laparoscopic sleeve gastrectomy on morbidly obese patients. (Kórosan elhízott betegeken végzett laparoszkópos csőgyomor képzés hatásának vizsgálata.) Orv. Hetil. 2023; 164(44): 1744–1749. DOI: 10.1556/650.2023.32918 . [Hungarian]
IF: 0,6

Miklós Siptár, Natália Tóth, Krisztina Tóth, Zsuzsanna Németh, Ferenc Molnár. The effect of gastric sleeve surgery on the comorbidities of morbidly obese patients. (Gastric sleeve műtétek hatása a kórosan elhízott betegek társbetegségeire.) Aneszteziológia és Intenzív Terápia, forthcoming[Hungarian]
IF: 0,00

Total Impact Factors: 1.7