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ABSTRACT

of the dissertation for the degree of Doctor of Medical Sciences

**IMPROVING THE RESULTS OF OPERATION BASING ON
STUDY OF MORPHOFUNCTIONAL CONDITION OF THE
LIVER AND PANCREAS IN BARIATRIC SURGERY
POST-OPERATIVE PERIOD**

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GENERAL CHARACTERISTIC OF WORK

Actuality of the research and degree of its development.

Excess body mass, as well as obesity, is one of the main pathologies of our modern life. It's logic, because delayed feeling of satiety and sedentary lifestyle comprehend most people, both young and old. In addition, since the disorder in the endocrine system also stimulates the acceleration of hunger, people of this type have to eat more often and include high-calorie foods in their diet. So, due to high calories entering the body on the one hand, and due to stagnation in its consumption the other hand, the body mass of the individual begins to increase because of excessive accumulation of adipose tissue.

The World Health Organization (WHO) called morbid obesity a non-infectious "epidemic" of the late XX and early XXI century, and according to information of 2016, 39% of people over the age of 18 worldwide were overweight. In developed countries, 54% of the population suffer from overweight, 19% suffer from obesity^{1,2}.

According to the WHO Epidemiological Department, the number of people with morbid obesity is expected to redouble in 2025. Still, according to the WHO, morbid obesity is widespread among the population living in the entire geographical area of the Earth, regardless of their economic status. 671 millions people of the world population already have overweight body mass, or rather obesity. Half of them live in 10 countries - USA, Russian Federation, China, India, Brazil, Mexico, Germany, Pakistan and Indonesia³. In

¹ NCD Risk Factor Collaboration (NCD-RisC). Worldwide trends in body mass index, underweight, overweight, and obesity from 1975 to 2016: a pooled analysis of 2416 population-based measurement studies in 128·9 million children, adolescents, and adults //Lancet. 2017. T.390. P.26272642. doi.org/10.1016/S0140-6736(17)32129-3.

² Organisation for Economic Cooperation and Development (OECD). Health at a glance. Paris:2017.

³ Ng M., Fleming T, Robinson M., et al. Global, regional and national prevalence of overweight and obesity in children and adults during 1980-2013: a systematic analysis for the Global Burden of Disease Study 2013. Lancet 2014; 384(9945): 766-781. Doi: 10.1016/S0140-6736(14)60460-8.

addition to having an epidemiological character, morbid obesity is also considered as precursor of a number of diseases in the body in a subclinical state, as well as a risk factor of diseases that cause people to become disabled⁴.

As a result of clinical observations, it was determined that 44% of people with morbid obesity have II type diabetes, 23% have ischemic heart disease, and 80-90% have non-alcoholic steatohepatosis⁵. Morbid obesity is accompanied by metabolic syndrome almost in all patients. For this reason, a number of complications caused by morbid obesity make death danger quite real.

According to the WHO, 700 thousand deaths in the USA and 1 million deaths in Europe are caused by the complications of morbid obesity. It is enough to note that morbid obesity is one of the 5 main causes of death^{6,7}.

The wide spread of morbid obesity among the world population, the negative impact of its complications on human health and at the same time endangering human life have turned the increase of body mass into a social problem as well as a medical one⁸. The increase of body mass together with obesity sharply lowers the quality of life of people, and becomes an important factor that causes

⁴ Самородская И.В., Кондракова Н.В. Сердечно-сосудистые заболевания и ожирение. Возможности бариатрической хирургии. В кн.: Актуальная коморбидная патология. М. 2015, с.53-60.

⁵ Fealy C.E., Nieuwoudt S., Foucher J.A., SceisT A.R. et al. Functional high intensity exercise training ameliorates insulin resistance and cardiometabolic risk factors in type 2 diabetes //Exp. Physiol. 2018, Vol. 103, P.985-994.

⁶ Ройтберг Г.Е. Метаболический синдром. М.: МЕД пресс-информ, 2017, 547 с.

⁷ Hector M. Gonzalez. Metabolic Syndrome and Neurdcdgmntion Among Diverse Middle-Aged and Older Hispanics/Latinos: HCHS/SOL Results //Diabetes Care. 2018, Vol. 41(7), P.1501-1509.

⁸ Крысанова В.С., Журавлева М.В., Сереброва С.Ю. Социальная и экономическая значимость избыточной массы тела и ожирения Российской Федерации. Основные подходы к лечению ожирения. //МРЖ. 2015, №26, с.1534-1537.

loss of work ability and disability⁹.

On the other hand, morbid obesity goes along with a number of diseases, including II type diabetes, arterial hypertension, dyslipidemia, non-alcoholic steatohepatosis, sleep apnea, various types of cancerous growth, gallstone disease, musculoskeletal disorders, dysfunction of erection and overall reproductive health dysfunction and is a high risk factor in the exacerbation of the mentioned diseases¹⁰.

The liver (**hepar**) is one of the main target organ of morbid obesity. Today, non-alcoholic steatohepatosis of the liver is considered as the main comorbidity of morbid obesity. According to the 2014 WHO report, 20-30% of the population living in Western countries, as well as 15-30% of the population of Asian countries, suffer from non-alcoholic liver obesity disease.

One of the main reasons for the wide spread of this pathology among the population is its untimely diagnostocating . As a rule, when in anamnesis liver obesity is detected in people without liability to alcoholism, it is considered as normal condition at first sight. However, over time, this pathology develops from mild steatosis to hard fibrosis and even cirrhosis, and in most cases the latter pathology becomes the main reason of death¹¹.

For this reason, today non-alcoholic liver obesity is considered as the most widespread disease among liver diseases and

⁹ Джафарова А.Г. Качество жизни женщин репродуктивного возраста с избыточной массой тела и ожирением и самооценка ими собственного здоровья. Актуальні проблеми сучасної медицини. Актуальні проблеми сучасної медицини:вісник української медичної стоматологічної академії 2016, № 4 (56), с.101-105.

¹⁰ Cefalu W., Rubino F., Cummings D.E. Metabolic surgery for type 2 diabetes: changing the landscape of diabetes care // Diabetes Care. 2016. Vol. 39. P. 857-860.

¹¹ Драпкина О.М., Ивашкин В.Т.Эпидемиологические особенности неалкогольной жировой болезни печени в России (Результаты открытого многоцентрового проспективного исследования-наблюдения ИЖЕСТ. 01903). //Рос. журнал, гастроэнтерологии, гепатологии, колопроктология. 2014 Т 24. №2. с 32-38.

is considered as a factor that causes chronic liver disease¹².

The fact that morbid obesity results by extremely serious complications and that these complications create a danger to human life has prompted scientists to conduct scientific research for the effective treatment of this pathology¹³.

In the studies, conducted with the aim of providing treatment and prevention of morbid obesity, specialists tried to reduce excess body mass to a normal level by means of various diets, sports, and pharmacological preparations^{14,15,16}. However, despite the widespread promotion and application of these means and tools, they have not proved themselves in practical medicine as a means of treatment. The conservative treatment of morbid obesity, as well as non-alcoholic steatohepatitis of the liver caused by it, did not give the desired results. So, the researchers came to conclusion that bariatric surgery is a more reliable treatment means for reducing the excess body mass and keeping it stable in patients with morbid obesity^{17,18}.

¹² Wiernsperger N. Treatment strategies for fatty liver diseases //Rev. Recent Clin. Trials 2014, Vol.9, N 3, p.185-194.

¹³ Дворецкий Л.В., Ивлева О.В. Ожирение и железodeficit. Еще одна коморбидность? //Архив внутренней медицины 2015, № 5 (25), с.9-16.

¹⁴ Дедов И.И., Мельниченко Г.А., Шестакова М.В., Трошина Е.А. и др. Национальные клинические рекомендации по лечению морбидного ожирения у взрослых //Ожирение и метаболизм 2018. №15(1). с.53-70.

¹⁵ Бирюкова Е.В., Соловьева И.В. Эффективная фармакотерапия ожирения – залог успешного лечения заболеваний, связанных с лишним весом // Эффективная фармакотерапия, 2013, № 19, с.18-26.

¹⁶ Вилар-Гомес Е., Мартинес-Перес Ю., Кальзадила-Бертот Л. и др. Потеря веса в результате изменения образа жизни значительно снижает признаки неалкогольного стеатогепатита. Гастроэнтерологии. 2015, 149 (2), 367-78, e5, Тест E14-5.

¹⁷ Короношин О.В., Торопова Я.Г., Неймарк А.Е. и др. Механизмы влияния бариатрических операций на течение неалкогольной жировой болезни печени //Экспериментальная и клиническая гастроэнтерология, 2017, № 10, С.61-73.

¹⁸ Фишман М.Б., Карев В.Е., Ян. Ван и др. Метаболическая хирургия в коррекции жировой болезни. Вестник хирургии, Санкт-Петербург. 2017, № 1, с. 34-41.

It is the reason that today various surgical operations in the gastrointestinal tract have been proposed. Among these interventions, laparoscopic longitudinal tubular reduction of the stomach is technically easier to perform and does not cause radical changes in the physiology of the digestive tract. However, despite being a popular treatment means among bariatric operations, as well as being able to be performed with minimal changes in the anatomy and physiology of the digestive tract, laparoscopic longitudinal tubular reduction of the stomach can lead to a number of changes in the liver and pancreas in the postoperative period¹⁹.

Certainly, such changes affect negatively the results of laparoscopic longitudinal tubular reduction of the stomach. The main reason for this is that the pathogenesis of complications after laparoscopic longitudinal tubular reduction of the stomach has not yet been clarified fully. It is for this reason that there is a great need to study fully the pathogenesis of the complications that occur after laparoscopic longitudinal tubular reduction of the stomach and affect negatively the results of the surgical operation.

The aim of the research. The main aim of investigation is improving the results of the surgical operation by developing a pathogenetic treatment method and applying it in the clinic basing on the experimental clarification of the complications pathogenesis that appear in the liver and pancreas after the longitudinal tubular reduction of the stomach.

Tasks of the research: According to the object, subject and purpose of the research, in the work the following tasks were set:

1. To study the intensity of free peroxidation of lipids and the condition of the general antioxidant defense system in the liver and pancreas of experimental animals with a model of morbid obesity.

2. To investigate the state of oxidative stress in the liver and pancreas of experimental animals with a model of morbid obesity in

¹⁹ Серкова М.Ю., Бакулин И.Г. Гастроинтестинальные осложнения в позднем послеоперационном периоде после продольной резекции желудка //Экспериментальная и клиническая гастроэнтерология 2019 (вып 170), № 10, с.96-100.

different periods after the longitudinal tubular reduction of the stomach, as well as to study its duration.

3. To study the influence of oxidative stress in the liver tissue on blood markers, characterizing the functional condition of the liver after the longitudinal tubular reduction of the stomach in the experimental animals, in which a model of morbid obesity was created for the experiment.

4. To study the effect of oxidative stress on the mineral exchange and electrolyte balance in the blood, which develops in the liver tissue after the operation of longitudinal tube reduction of the stomach in experimental animals with a morbid obesity model created for the experiment.

5. To define the effect of the body general antioxidant defense system strengthening on the restoration of impaired liver function after the operation of longitudinal tube reduction of the stomach in experimental animals with a model of morbid obesity.

6. To define the role of body general antioxidant defense system strengthening in the recovery of the impaired function of the pancreas after the longitudinal tubular reduction of the stomach in experimental animals with a model of morbid obesity created in the experiment.

7. To study the influence of the body general antioxidant defense system strengthening on the results of the surgical operation in patients who underwent laparoscopic longitudinal tubular reduction of the stomach in the clinic.

8. To define the influence of laparoscopic longitudinal tubular reduction of the stomach, made in the clinic on the diseases accompanying morbid obesity and to improve the results of the operation.

9. To study comparatively the results of laparoscopic cholecystectomy and results of mini-open cholecystectomy performed using our proposed illuminating surgical retractor in patients with morbid obesity.

10. To improve the method of inserting the "Nathanson" liver retractor into the abdominal cavity during laparoscopic operations.

11. To study the effect of joint laparoscopic cholecystectomy

on the results of laparoscopic longitudinal tubular reduction of the stomach.

The object and subject of the research. Experimental studies were conducted on 35 Chinchilla rabbits, in which a model of morbid obesity was created. Based on the obtained results, the pathogenesis of the complications that occurred in the liver and pancreas after the longitudinal tubular reduction of the stomach were investigated.

Clinical studies comprehended 100 patients with morbid obesity who underwent laparoscopic longitudinal tubular reduction of stomach. Patients were divided into 2 groups. 50 patients included in the first group were treated before and after surgery according to the protocol adopted in the clinic, and 50 patients included in the second group were treated additionally antioxidant therapy before and after the surgical operation.

Research methods. In course of the experiments, a model of morbid obesity in "Chinchilla" rabbits was created and biochemical examinations characteristic for liver pathology before and after longitudinal tubular reduction of stomach were performed. For evaluation of oxidative stress markers in the structure of liver and pancreas tissue and of the dynamics of changes in the structure of the liver and pancreas morphological studies were conducted. Based on the obtained results, the use of "Ridutox" ("Glutathione" 600.0 mg) preparation with hepatoprotective and antioxidant effect is justified by scientific principles.

In order to achieve the set aim, the differential diagnosis of the patients with the diagnosis of morbid obesity was carried out and their concomitant diseases were determined. After determining the indication for the operation of the patients, laparoscopic longitudinal tubular reduction of the stomach was performed. The obtained experimental results were statistically analyzed by a programmed method based on modern recommendations.

The main postulates represented for defence:

- The development of oxidative stress in the liver of experimental animals, created as a model of morbid obesity intensifies after the longitudinal tubular reduction of the stomach.

The increase of hydrogen peroxide (H_2O_2) concentration in the tissue, causes particular diffuse changes in the histoarchitectonics of the liver and pancreas by damaging the membrane of hepatocytes.

- Oxidative stress, which develops in liver and pancreas tissue, is the main link in the pathogenesis of the change in the function of the liver and pancreas after the longitudinal tubular reduction of the stomach.

- Oxidative stress in the liver and pancreas continues one month after the longitudinal tubular reduction of the stomach, but its intensity is relatively reduced. The concentration of hydrogen-peroxide (H_2O_2) in the pancreas is kept higher than normal in 100% of the experimental animals, the concentration of diene conjugates (DK) and malondialdehyde (MDA) is higher than normal in 80%.

- Adding of antioxidant drugs to the treatment complex before and after the laparoscopic longitudinal tubular reduction of the stomach regulates the changes in the function of the liver and pancreas and stabilizes common diseases.

- Cirrhosis of the liver in patients with satisfactory liver function and without severe portal hypertension is not an obligatory contraindication for bariatric surgery.

Scientific novelty of the research. In the research its defined for the first time, that:

1. There is a directly proportional relationship between the disturbance of both anatomical structure and physiological function of the stomach and the free peroxidation of lipids.

2. There is an inverse relationship between the anatomical structure and physiological function of the stomach and the general antioxidant defense system.

3. Violation of the anatomical and physiological function of the stomach is a stimulating factor for the development of oxidative stress in the tissue of the liver and pancreas.

4. The level of markers reflecting the functional condition of the liver and the general antioxidant defense system of the body are inversely related to each other.

5. There is a correlative relationship between the intensity of the oxidative stress developed in the liver and pancreas tissue as a

result of the longitudinal tubular reduction of the stomach and the changes in the structure of the liver and pancreas tissue.

6. The importance of antioxidant therapy in order to improve the results of laparoscopic longitudinal tubular reduction of the stomach has been proved on the basis of laboratory and instrumental examinations.

Theoretical and practical significance of the study:

1. Since morbid obesity is a multifactoral disease and is inextricably accompanied by many other metabolic diseases, examination of this disease, preparation of patients for surgery and monitoring of the results of the operation in the postoperative period should be carried out not only by surgeons, but also by specialists of various profiles under surgeons' coordination.

2. In order to improve the results of the surgical operation for the treatment of morbid obesity, antioxidant therapy should be added to the treatment complex of patients both in the preparation for the surgical operation and in the postoperative period.

3. In order to regulate the mineral-electrolyte exchange in the blood by weakening the oxidative stress in the liver, before and after the operation it is important to inject into the patients' body the drug "Ridutox" ("Glutathione" 600.0 mg), which has a hepatoprotective and antioxidant effect.

4. In differ from existing methods, a new method of inserting the "Nathanson" liver retractor into the abdominal cavity without causing trauma was proposed .

Approbation of dissertation and application of results. The materials of the dissertation were published in 35 scientific works, including 18 journal articles and they obtained one International Patent. Materials of research were discussed at the following Scientific Seminars, Conferences and Symposia:

1. The effect of laparoscopic Sleeve Gastrectomy surgeruyon liever condition of the patients with morbid obesity. 5th National&3rd Medi-terreanean Congress for the Surgery of obesity and Metabolic Disorders, Antalya, Turkey. 12-15 October, 2017.

2. IV International Bariatric Metabolic Surgery Congress, Baku. May 18, 2018.

3. The effect of laparoscopic sleeve gastrectomy on nonalcoholic fatty liver disease. 6th National & 5th Mediterranean Congress on Morbid Obesity and Metabolic Disorders (17-20 October 2019).

4. Dynamics of liver and spleen elastography after bariatric surgery. V International Bariatric Metabolic Surgery Congress. Baku. 18 May, 2019.

5. Laparoscopic cholecystectomy in cirrhotic patients with gallbladder disease. Abstracts of the XVIII international congress of surgery and hepatogastroenterology. Baku, 2019.

6. Importance of drainage of abdominal cavity after laparoscopic "Sleeve Gastrectomy" operation. International scientific-practical conference on "Actual Problems of Medicine", dedicated to the 90th anniversary of the Azerbaijan Medical University, Baku. December 19-20, 2020.\

7. Effect of LSG surgery on liver volume and density. III Azerbaijan Diabetes Congress. Baku. 2020. December 25

8. Simultaneous operation - Laparoscopic "Sleeve Gastrectomy" and cholecystectomy operation. International Scientific-Practical Conference on "Actual Problems of Medicine-2021" dedicated to the 100th anniversary of Honored Scientist, professor Tamerlan Aziz oglu Aliyev, Baku. October 6-8, 2021.

9. The influence of laparoscopic sleeve gastrectomy on liver size and its consistency. 7th National & 6th Mediterranean Congress on Morbid Obesity and Metabolic Disorders (22-25 October 2021).

10. Simultaneous operations in patients with morbid obesity. I International Medical Forum. June 18-21. 2022. Azerbaijan. Nakhchivan.

Affiliated institution. Experimental studies on the scientific work were performed at the Scientific Research Center of Azerbaijan Medical University, and clinical studies were performed in the Teaching Surgery Clinic of Azerbaijan Medical University and in the Private Clinic "Baku City Hospital".

Application of research results. The results obtained in the conducted studies are applied in the Teaching Surgery Clinic of Azerbaijan Medical University.

The volume and structure of the dissertation. Dissertation work is posted on 298 pages as a whole. It consists of an introduction, including 25 figures, 33 tables, 2 diagram, 9 chapters, a conclusion, practical recommendations, 360 references include (17 works in Azerbaijani, 122 works in Russian and 221 works in other language). The volume of the dissertation (with the exception of gaps and pictures in the text, tables, graphs, appendices and list of reference) – 406067 characters.

In the **Introduction**, the **actuality** of the subject of the dissertation for modern medical science is justified; the **aim, tasks, object, subject, materials** and **methods** of the conducted researches, the main **postulates**, represented for defence, the **scientific novelty** of the obtained results and their **theoretical-practical importance** for medical science are indicated; **the approbation and application** of the dissertation materials, as well as **information about the organization** where the dissertation work was performed; the **structure** of the work, as a whole and the **volume** of each section separately, the **number of used scientific sources** is indicated; **the brief content of the chapters** is explained.

In the **Chapter I**, a brief analysis (summary) of the available scientific literature on the topic of dissertation work is explained. Here, based on the analysis of works on the modern aspect of morbid obesity, its epidemiological situation, pathogenesis, diagnosis of non-alcoholic hepatic steatoheptosis, which causes its forming, as well as conservative and surgical treatment against it, the relevance of the topic of the dissertation for modern medical science, the importance of its purpose, is justified again.

In **Chapter II** detailed information about the materials and methods used in the research conducted in the dissertation work is provided. Experimental studies were conducted on 35 Chinchilla rabbits (age - 12-24 months, weight between 3-5.0 kg). The experimental animals being placed immobile in special cages, were fed high-calorie foods in a special regime for 1 month in adynamia conditions. As a result a model of morbid obesity was created. According to the aims and tasks of the dissertation, experimental animals were divided into 7 groups, with 5 rabbits in each group.

The experimental animals included in the I group were studied in an intact condition and the results obtained from them were accepted as the norm. In the other 30 experimental animals, longitudinal tubular reduction of stomach was performed. 10 days after the operation, the rabbits included in the II group, 30 days after the operation – rabbits of III group, 3 months after operation the rabbits of IV group, 6 months after operation- the rabbits of V group were excluded from the experiment. In 5 rabbits included in the VI group of experimental animals, the general antioxidant defense system was strengthened during 7 days after the longitudinal tubular reduction of the stomach and the experiments were finished on the 10th day. In the 5 rabbits, i.e. main experimental animals included in the VII group, the antioxidant defense system was strengthened for 7 days after the longitudinal tubular reduction of the stomach and 30 after being kept under control for a day, the experiments were brought to an end.

Oxidative stress markers in the homogenate prepared from the liver and pancreas of experimental animals, as well as ALT, AST, ALP, GGT, LDH in blood, amylase enzymes, AST/ALT ratio (de Ritis coefficient), total protein, albumin, hemoglobin and a number of the amount of minerals, including Cl, P, Ca, K, Fe, Na, was determined.

In order to strengthen the antioxidant defense system, "Ridutox" ("Glutathione" 600.0 mg, 0.2 ml/kg once a day) drug with a hepatoprotective and antioxidant effect was injected into the ear vein of experimental animals from VI-VII groups during 7 days after surgery.

The experiments were carried out in anesthetized conditions in accordance with the decision of the European Bioethics Committee and the Local Bioethics Commission of the Azerbaijan Medical University, adopted in 1982 basing on Helsinki Declaration on the rules about treatment with experimental vertebrate animals. Taking into account the recommendation of B.A. Ananyev (1982), for the purpose of analgesia, "Calypsol" solution was injected into the veins of the experimental animals at a dose of 0.1 ml per 1 kg of weight. After getting complete anesthesia, the surgical site was treated with

an alcoholic solution of chlorhexidine, the abdominal cavity of the animal was opened with an upper middle incision, the stomach was brought to the wound "mouth" and longitudinally resected in groups II-VII. Then the wound area was tightly sealed with 3 layers of sutures. In the post-operative period, 20 ml of liquid with 0.5 ml of vitamin B2 added to 0.9% physiological and 5% glucose solution was transferred to experimental animals. When the experiments ended, all the experimental animals, including the animals of the I group, were anesthetized according to the procedure described above, the liver and pancreas of each were removed from the organism, and a homogenate was prepared from them. At the same time, 5-7 mkm thick sections were prepared from the samples taken from the liver and pancreas using a paraffin block and a microtome. From organs stained with "Van Gieson" and hematoxylin-eosin solution the information about the histological condition of those organs was obtained. The concentration of markers of oxidative stress in the homogenate and general antioxidant defense system of the body was determined.

For determining the concentration of hydrogen peroxide (H_2O_2), which is the first product of free peroxidation of lipids from oxidative stress markers and to study concentration of the last product- malondialdehyde (MDA) the method of T. Askawa, S. Matsushita (1980) was used. To determine the concentration of diene conjugates (intermediate product of free peroxidation of lipids from oxidative stress markers (DC) the modification given in the Ushyama method by I.D.Stalnaya (1997) was used. For this purpose, 1 ml of the liquid part of the prepared homogenate was taken, 0.1 ml of distilled water was added to it, and it was shaken twice. By adding 0.5 ml of ethyl alcohol to the shaken mixture, its optical continuity was measured using a spectrophotometer (233 nm wavelength) and the density of DC was calculated based on the molar ratio.

In order to evaluate the general antioxidant defense system of the organism, surface and internal sulfohydriyl (SH)-protein groups in the homogenate were determined by the method of Ellman (1959), the concentration of total antioxidant activity (TAA) with catalase

was determined by method of E.B. Spektor et al. (1984). The mentioned markers were determined at a wavelength of 232 nm in the USA-made Bio Screen MS-2000 analyzer and Spectro Photometer working in fully automatic mode using reagent sets produced by "Human" company.

Clinical observations were carried out on 100 patients who entered the clinic with the diagnosis of non-alcoholic steatohepatosis of the liver combined with third-degree morbid obesity and were undergone laparoscopic longitudinal tubular reduction of the stomach. 58 of those patients (58%) were at the age between 20-39 years. It is known that this age period is considered as the culmination period of people's working capacity, mental development and creativity. 12 of the patients (21%) who engaged in physical labor noted that they had high physical activity before the onset of morbid obesity and worked tirelessly. After the onset of morbid obesity, more precisely, as the body mass increased, they complained of decreased ability to see, tiredness, heart palpitations and fatigue. 3 of the patients (5%) went on disability pension with the diagnosis of cardiovascular system diseases because they lost their ability to work.

36 of 58 patients (62%) were engaged in mental work, and 8 (14%) were engaged in creative work. Those persons also complained about the limitation of the activity period, the increase in blood pressure when they work a little more, the spontaneous increase in the amount of glucose (blood sugar), short-term and often recurring pains in the chest, especially in the heart area.

10 patients (17%) who were engaged in daily work due to the lack of a permanent place of work complained about the difficulty in their movements and the tendency to lead a sedentary life after the increase in body mass. In addition to morbid obesity, 30% of the observed patients had II type diabetes, 70% had high insulin resistance, 64% had arterial hypertension, 50% had dyslipidemia, 20% had chronic stone cholecystitis. Besides, in 10% patients obstructive respiratory diseases, in 15%- degenerative osteoarthritis, in 12%- ischemic heart disease, in 30%- chronic pancreatitis, in 20%- sleep apnea, and in 50% gastroesophageal reflux disease was observed.

In differ from the information given in the available scientific literature, the patients were taken for surgery only after 5-6 months observations and after using of various methods to reduce the body mass and after stabilization of accompanying diseases. Thus, it was possible to lower their body mass and regulate their metabolism to a certain extent before the operation. Due to the stabilization of insulin resistance, glucose and arterial pressure, it was possible to prevent supposed complications during the operation.

In preparation for surgery, opinion of **A. Fried et al**²⁰. about the regulation of metabolism were taken as basis. The results of the conducted studies have shown that the regulation of metabolism before the surgical operation allows to perform the operation without complications. It is supposed that the disturbance of metabolism disrupts the physiological and biochemical balance at the cellular level. This fact in turn deepens the pathological process existing in extreme conditions (surgical operation) and creates disharmony in the regulatory system of organism - in homeostasis.

Patients were divided into 2 groups by randomization with 50 people in each one. The patients included in the I group were treated according to the traditional rules in the post-surgical period. The patients in the II group before and after surgery to the treatment complex of the preparations with hepatoprotective and antioxidant properties ("Ridutox", "Glutad", "Heptral") were added. Among the patients undergoing laparoscopic longitudinal tubular reduction of the stomach women predominate. (88 patients, i.e. (88%). 8 diseased - (16% of the patients) included in the I group were men, 42 diseased (84% of patients) were women. But in II group 4 diseased (8% of the patients) were men and 46 diseased (92% of patients) were women.

The methodical recommendation prepared jointly by the American Gastroenterological Association, the Liver Disease

²⁰ Fried M., Yumuk V., Pppert J.M., et al. Interdis-ciplinary European Guidelines on Metabolic and Bariatric Surgery. Obesity Surgery 2013, 24 (1), p.42-55.

Association and the College of Gastroenterology in 2012 was used as the basis for the diagnosis of liver non-alcoholic obesity disease. For this purpose, the following diagnostic examinations were performed:

1. Anthropometric measured tests.
2. Ultrasound investigation of the abdominal cavity (U/S).
3. Indirect elastography of liver-ILD.
4. Biochemical tests of blood.

Taking into account the accepted recommendations, patients with a body mass higher than $\geq 40 \text{ kg/m}^2$ were diagnosed as III degree morbid obesity. The diagnosis “non-alcoholic steatohepatosis of the liver” was made basing on the results of U/S (ultrasound).

Table 1

Co-morbidities in patients with III grade morbid obesity and non-alcoholic steatohepatosis undergone laparoscopic longitudinal tubular reduction of the stomach

№	Co-morbidities	Number of patients
1	Type II diabetes	30 (30%)
2	Insulin resistance	70 (70%)
3	Hypertension	64 (64%)
4	Dislipidemie	50 (50%)
5	Chronic stone cholecystitis	20 (20%)
6	Obstructive respiratory diseases	10 (10%)
7	Degenerative osteoarthritis	15 (15%)
8	Ischaemic heart disease	12 (12%)
9	Chronic pancreatitis	30 (30%)
10	Sleep apnoea	20 (20%)
11	Gastroesophageal reflux	50 (50%)

examination of the liver, indirect elastography of the liver and determination of liver biomarkers in the blood. In all patients entered hospital with the diagnosis “III-degree morbid obesity” and “non-alcoholic steatohepatosis of the liver”, i.e. 100%. various co-morbidities were observed.

As its seen from Table 1, non-alcoholic steatohepatosis of the liver, which develops against the background of III degree morbid obesity, was observed together with a number of other diseases. Non-alcoholic steatohepatosis of the liver, which developed against the background of III degree morbid obesity, according to its degrees is represented as follows:

- 1) Morbid obesity of I degree – 10 diseaseds (10% patients)
- 2) Morbid obesity of II degree- - 20 diseaseds (20% of patients)
- 3) Morbid obesity of III degree – 45 diseaseds (45% of patients)
- 4) Morbid obesity of IV - grade - 25 diseaseds (25% of patients)

Table 2 shows the picture obtained by dividing the comorbidities with non-alcoholic steatohepatosis of the liver, which develops on the background of III-degree morbid obesity, according to the degree of severity of steatohepatosis.

During the conducted research, the following norms were strictly followed:

I. Although only patients with a confirmed diagnosis of non-alcoholic steatohepatosis developing on the background of grade III morbid obesity were taken to laparoscopic longitudinal tubular reduction of the stomach, they were excluded from the list of those undergoing surgery and from the study in following cases:

1. The period of ulcer exacerbation in patients with gastric and duodenal ulcers.
2. Pregnancy.
3. Drug addiction.
4. Alcoholism.
5. Hard mental illnesses.
6. Severe and irreversible pathology of vital organs.
7. Infectious cirrhosis of the liver.
8. Anaesthesiological risk.

II. A reasoned selection of criteria with the possibility of monitoring the course of the disease before and after treatment was made.

III. Surgical treatment was carried out under identical rules and conditions, the comparison of study groups was carried out during the same period of time.

Table 2

Distribution of co-morbidities with non-alcoholic hepatic steatohepatosis developing on the background of III-degree morbid obesity according to the degree of severity of steatohepatosis

№	Co-morbides	General number	I degree	II degree	III degree	IV degree
1	Type II diabetes	30	7 (23%)	8 (27%)	7 (23%)	7 (23%)
2	Insulin resistance	70	12 (17%)	13 (18.5%)	30 (43%)	18 (26%)
3	Hypertension	64	10 (16%)	11 (17%)	26 (41%)	17 (26.5%)
4	Dislipidemie	50	8 (16%)	15 (30%)	14 (28%)	14 (28%)
5	Chronic stone cholecystitis	20	5 (25%)	4 (20%)	11 (55%)	-
6	Obstructive respiratory diseases	10	2 (20%)	3 (30%)	5 (50%)	-
7	Degenerative osteoarthritis	15	-	4 (27%)	8 (53%)	3 (20%)
8	Ischaemic heart disease	12	-	4 (33%)	5 (42%)	3 (25%)
9	Chronic pancreatitis	30	9 (30%)	7 (23%)	8 (27%)	3 (10%)
10	Sleep apnoea	20	5 (25%)	3 (15%)	3 (15%)	9 (45%)
11	Gastroesophageal reflux	50	8 (16%)	10 (20%)	24 (48%)	15 (30%)

The statistical analysis of the results obtained in experimental and clinical studies was carried out by taking into account modern theoretical recommendations and using parametric and non-parametric methods. The obtained quantitative indicators satisfactorily corresponded to the graphs of normal distribution laws. It allowed us to process the quantitative indicators of all the parameters obtained from the clinical examinations by variative statistical methods.

In the variation order, numbers that deviated too much from the minimum and maximum limits were excluded from the order. Numbers corresponding to normal distribution curves ($\sigma=3$) were included in statistical calculations. In all cases, the degree of freedom (N) was calculated using the formula $N=[n_1+n_2]-2$. The obtained quantitative indicators corresponded to the curve of the normal distribution law. This fact gave us a reason to work with the quantitative indicators obtained from clinical examinations with the methods of variative statistics.

The average mathematical value of the quantitative indicator of each parameter obtained from clinical examinations, its average mathematical value (\overline{X}), its error ($S\overline{X}$) and the accuracy index were calculated using the formula $C_s = \frac{S\overline{X}}{\overline{X}} \cdot 100$. The difference between a pair of comparable parameters at the confidence level of $P=0.95$ is defined as $P<0,05$, i.e. statistically accepted as strict one.

For statistical analysis of the results obtained from the experiment carried out by the non-parametric method, using the Wilcoxon (Mann-Whitney) U-criterion, Pearson's X_2 -criterion for frequency analysis was applied.

Calculations were carried out on a computer loaded with the program "Statistics 7.0" compiled by Gendel-Marti and others and an EXCEL spreadsheet with the program developed at the "Medical physics and informatics" department of the Azerbaijan Medical University.

Chapters III, IV and V of the dissertation are dedicated to the interpretation and analysis of the results obtained from experimental studies.

Chapter III consists of three paragraphs. This chapter is dedicated to the study of the peculiarities of the intensification of oxidative stress in the liver tissue, to the process of its depression (weakening), and to the changes that occurred in the morphostructure of the liver in experimental animals, in which a morbid obesity model was created.

Concentration of hydroperoxide (H_2O_2), diene conjugates (DC),

malonaldehyde (MDA), surface and intrastuctural SH-protein groups, catalase, total antioxidant activity (TAA) of the organism in the homogenate prepared from the liver tissue of experimental animals in the intact condition (group 1) was established and accepted as a norm.

It has been found that oxidative stress in the liver begins to develop after creating the morbid obesity model in rabbits, and it is further aggravated after gastric bypass surgery. 10 days after longitudinal tubular reduction of stomach in the homogenate prepared from the liver of rabbits included in the II group the concentration of H₂O₂ and MDA (compared with intact stat) increased by 107%, and the concentration of DC increased by 100%.

As a result, the overall antioxidant defense system in the liver tissue is weakened. Thus, the concentration of these markers has decreased significantly compared to the intact state. The density of the surface SH-protein group decreased by 8%, the density of the intra-structural SH-protein group decreased by 14.5%, the density of catalase decreased by 2.4%, and the density of TAA decreased by 20%.

1 month after the operation (in III group rabbits), the intensity of oxidative stress in the liver tissue tended to decrease slightly, probably as a result of activation of the body's compensatory function. For this reason, although the maximum limit of the concentration of H₂O₂ in the homogenate remained stable, the minimum limit compared to the rabbits included in the II group decreased, and remained 97% higher compared to the intact state. Compared to the II group, the minimum limit of DC thickness decreased, but the maximum limit remained stable and was 88% higher compared to the intact state. The concentration of MDA also remained at a high level of 99% compared to the intact state, and the intensity of oxidative stress continued to increase.

In the general antioxidant defense system a positive (some weak), dynamics was observed. In differ from the free peroxidation of lipids, the change to the strengthening of the antioxidant defense system was more noticeable. In this case, although the surface SH-protein group increased compared to that in II group, it could not rise

to the level of the intact state.

The minimum limit of intrastructural SH-protein group concentration remained stable compared to II group, but the maximum limit increased very slightly (0.1 nmol/mg), and such a slight change did not cause a significant changes in the average intrastructural SH-protein group concentration. Compared to group II, the activity of catalase increased to a certain extent, and positive dynamics was observed in the activity of TAA, but the concentration of TAA was still significantly (18%) lower than in the intact state.

The analysis of the distribution of the changes among the experimental animals showed that the concentration of H_2O_2 and MDA in the liver tissue was higher than normal in 100% of them, and the concentration of DC was higher than normal only in 20% of them, and for the concentration of antioxidant defense system markers different results were received.

Thus, referring to the results obtained from experimental animals included in III group, we came to conclusion that even after 1 month of surgery, oxidative stress in the liver tissue still continues. For this reason, despite the weak decrease in the intensity of the free lipid peroxidation process, and the increase in the activity of the antioxidant defense system both factors of oxidative stress significantly differ from the norm. However, the analysis of the concentration of markers of oxidative stress among experimental animals shows that the intensity of oxidative stress occurred in the liver tissue after surgery begins to fade over time, and this fact can be evaluated as the result of the compensatory reaction in organism. However, despite such positive dynamics, oxidative stress continued and free lipid peroxidation, as well as markers of the antioxidant defense system, did not reach normal levels.

Comparing the results obtained 3 months after the operation in the rabbits of the IV group with those of the II and III groups, it was determined that the concentration of H_2O_2 in the homogenate was 15.5% and 11%, respectively, the concentration of DC was 24% and 19%, and the concentration of MDA decreased by 16% and 13%. But the intensity of free lipid peroxidation in the liver remained at a high level compared to the intact state (H_2O_2 -76%, DC-52%, MDA-

72%).

Accordingly, certain positive changes have occurred in the antioxidant defense system also. However, despite such positive dynamics, the markers of the antioxidant defense system in the liver tissue still did not reach normal levels, and oxidative stress continued. Due to the increase in the concentration of catalase in the homogenate, the concentration of H_2O_2 in the liver of rabbits included in IV group significantly decreases.

The obtained results show that, despite the fact that 3 months have passed since the operation, the oxidative stress in the liver has not yet stopped, the changes in the liver have not been completely restored even after 6 months. The intensity of the free lipid peroxidation process has some decreased, but still remained significantly higher than the norm. In accordance with the process of free lipid peroxidation, certain positive changes occurred in the general antioxidant defense system of the organism, but the average concentration of its specific markers was lower than normal.

Thus, the conducted experiments have shown that after the longitudinal tubular reduction of stomach surgery, in the liver oxidative stress begins, and although its intensity decreases within 6 months after the operation, it still cannot reach the normal level (**Table 3**).

In order to weaken the oxidative stress that occurred in the liver of the rabbits in the VI group, the antioxidant defense system of the rabbits was strengthened by injecting 0.2 ml/kg of "Ridutox" (Glutathione 600.0mg) solution once a day into the vein of those rabbits during 7 days. At 10 days after stopping the injection of the solution, the minimum and maximum levels of H_2O_2 and DC in the homogenate were reduced, but exceeded the intact state by 34% and 37%, respectively, and the average concentration of MDA was 29% compared to the level in II group decreased to 49%, but it was still 49% higher than the norm. Although a positive dynamic was observed in the concentration of the surface SH-protein group, it was 5% lower than the normal level; the concentration of the intrastructural SH-protein group increased compared to that in rabbits included in II group, but was 8% lower than the normal limit.

Table 3

Dynamics of oxidative stress in the liver after longitudinal tubular reduction of stomach

№	Groups of experimental animals	Statistical indexes	H ₂ O ₂ c.u.	DC nmol/mq	MDA nmol/mq	Sy-SH nmol / mq	S _D -SH nmol/mq	Catalaze Mkat /l	TAA %
1	1 group	M	2.80	1.90	1.50	34.80	22.80	2.70	20.90
		M	0.07	0.23	0.17	0.22	0.21	0.07	1.16
		σ	0.16	0.52	0.38	0.48	0.47	0.15	2.60
2	2 group	M	5.80	3.80	3.10	32.10	19.50	2.10	16.80
		M	0.19	0.44	0.29	0.84	0.85	0.25	1.46
		σ	0.43	0.99	0.65	1.87	1.89	0.55	3.26
		P<	0.001	0.01	0.01	0.05	0.01	0.05	*
3	3 group	M	5.50	3.60	3.0	32.50	19.80	2.50	17.10
		M	0.24	0.51	0.33	0.84	0.78	0.27	1.41
		σ	0.54	1.14	0.73	1.87	1.75	0.59	3.16
		P<	0.001	0.05	0.01	0.05	0.01	*	*
4	4 group	M	4.90	2.90	2.60	32.90	20.20	2.70	17.40
		M	0.28	0.47	0.30	0.85	0.87	0.30	1.43
		σ	0.63	1.06	0.66	1.91	1.94	0.68	3.20
		P<	0.001	*	0.05	0.05	0.05	*	*
5	5 group	M	3.80	2.20	1.90	33.10	20.40	2.70	18.50
		M	0.45	0.33	0.35	0.82	0.68	0.23	1.66
		σ	1.02	0.73	0.78	1.84	1.53	0.52	3.72
		P<	0.05	*	*	0.05	0.01	*	*

Note: *P>0,05

The concentration of catalase significantly increased (11%) compared to II group; the activity of TAA also increased significantly (18%)

compared to that in II group, but its average concentration ($19.7 \pm 0.53\%$) was 6% less than the norm.

Thus, intravenous injection of "Ridutox" (Glutathione 600.0mg) solution after longitudinal tubular reduction of the stomach significantly weakened the oxidative stress created in the liver by strengthening general antioxidant defense system of organism.

Rabbits in the VII group were injected with 0.2 ml of Ridutox solution into the ear vein once a day during 7 days after the operation of longitudinal tubular reduction of the stomach 30 days after the injection of the solution, the average concentration of DC with H_2O_2 in the homogenate prepared from the liver decreased to the normal level. Although the concentration of MDA decreased compared to that in III group, but it was 9% more than the normal level.

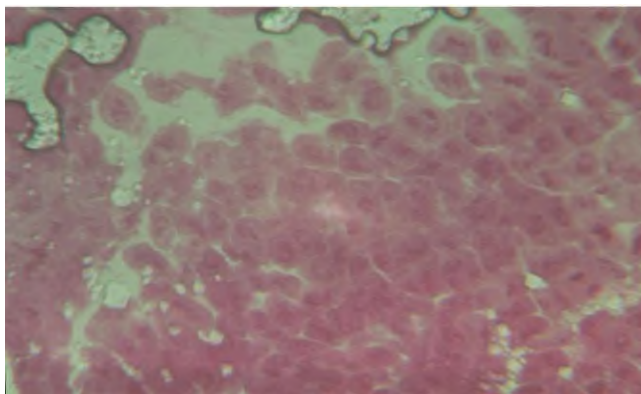
Thus, the results obtained from the experimental animals included in the VII group confirm that the intravenous injection of Ridutox solution suppresses the intensity of free lipid peroxidation in the liver tissue and leads to the strengthening of the general antioxidant defense system. The concentration of the surface SH-protein group rises to almost normal level. Although the concentration of the intrastructural SH-protein group is 1% lower than normal, it increases by 14% compared to III group, and although the concentration of catalase increases by 6% compared to III group, but it remains approximately 3% lower than normal. The average activity of TAA is normal also.

Experimental animals of I group have mild structural changes that may be the result of induced obesity or result of oxidative stress in liver tissue. 10 days after longitudinal tubular reduction of stomach, the structural change in the preparation made from the liver gets a clearer picture, perivascular edema continues to remain, areas infiltrated with mononuclear cells are manifested. 1 month after the operation, although the dystrophic state of the liver tissue continues to remain, in differ from the previous observation period, the liver stroma is slightly thickened, and the postcapillary microvessels and collecting vessels widen.

3 months after surgery, in liver parenchyma and stroma significant changes compared to 1 month are not observed, and this histological

picture is kept during 6 months after surgery. Oxidative stress in the liver during morbid obesity causes certain changes in the histological structure of its parenchyma and stroma, the degree of severity of which corresponds to the intensity of oxidative stress.

This opinion is confirmed by the results obtained in the rabbits included in the VI group. Thus, in the preparation made from the liver of rabbits injected with 0.2 ml/kg of Ridutox (Glutathione 600.0mg) solution once a day during 7 days after the operation, microscopical, no serious changes were detected, only the expansion of postcapillary vessels in the parenchym was seen clearly. Their thickness differs from those included in the I group. Although the dystrophic picture is kept in the liver parenchyma, its angioarchitectonics restore its normal state (**Picture 1**).



Picture 1. A view of the microcirculatory network on the background of dystrophy in the liver parenchyma

Maintenance of the general histoarchitectonics of the liver parenchyma should be also evaluated as a result of strengthening of the body general antioxidant defense system. Thus, the experiments conducted in this chapter show that oxidative stress develops in the liver of rabbits the food ration of which was enriched and movement restricted. The longitudinal tubular reduction of the stomach

increases the oxidative stress that took place. Although its intensity decreases to a certain extent after a certain period of time after the operation, it cannot decrease to the normal level even in 6 months after the operation; in order to strengthen the antioxidant defense system of organism, injecting "Ridutox" (Glutathione 600.0mg) solution into a vein is used. It depresses the oxidative stress in the liver, but it cannot completely liquidated due to the fact that the body has an irritation factor. It means that organism does not fully adapt to the longitudinal tubular reduction of the stomach;

The intensification of free lipid peroxidation, especially the increase in H_2O_2 concentration, damages the membrane of hepatocytes and causes diffuse changes in the histoarchitectonics of the liver. As the strengthening of the antioxidant defense system suppresses oxidative stress, the disturbed histological picture of the liver is partially restored .

Chapter IV consists of three paragraphs. This chapter is dedicated to the experimental study of the condition of oxidative stress in the pancreas after longitudinal tubular reduction of stomach. In the first paragraph of the chapter, the condition of the oxidative stress was studied in the pancreas tissue after the operation on the rabbits of the II-VII groups, taking the condition of the rabbits in the first group as normal.

It was found that 10 days after the surgery, alike in the liver tissue, the antioxidant defense system was significantly weakened in the pancreas tissue and the products of free lipid peroxidation were higher than normal in all the experimental animals. At the same time, the results in the antioxidant defense system were some different for individual rabbits.

30 days after the operation, the intensity of oxidative stress in the pancreas is relatively reduced, but the process still continues. More precisely, as the post-surgery period increases, the intensity of free lipid peroxidation in pancreatic tissue decreases, and the concentration of antioxidant defense system markers increases, albeit weakly. This fact indicates an increase compensatory function in the body. Although the oxidative stress in the pancreatic tissue continued 6 months after the longitudinal tubular reduction of stomach

operation (in the V group of experimental animals), its intensity was significantly weakened compared to the previous observation period.

The state of oxidative stress in the pancreatic tissue of the experimental animals that received antioxidants after the longitudinal tubular reduction of the stomach was also studied with the experiments conducted on the animals of the VI and VII groups. Experimental animals in the VI group 0.2 ml/kg Ridutox (Glutathione 600.0mg) solution was transferred once a day for 7 days starting from the first day after surgery. 10 days after stopping of this drug taking, the animals were removed from the experiment and the concentration of oxidative stress markers was determined in the homogenate prepared from their pancreas. The comparison of the obtained results showed that the concentration of MDA in the pancreas of experimental animals that received "Ridutox" decreased by 12% compared to the II group. However, despite such positive dynamics, the concentration of MDA in the homogenate prepared from the pancreas did not reach the normal level and was 72% higher than it.

As a result of the analysis of the increase in the concentration of free lipid peroxidation products based on the number of experimental animals, it was determined that in 80% of the experimental animals, the concentration both of H2O2 and MDA and in 60% DC concentration was higher than normal. These obtained results show once again that the intensity of free lipid peroxidation has been sharply reduced as a result of the injection of Ridutox solution into the body.

Thus, it was found that strengthening of the body general antioxidant defense system after longitudinal tubular reduction of the stomach sharply reduces the intensity of free peroxidation of lipids in pancreatic tissue, increases the concentration of antioxidant defense system markers, surface and structural SH-protein groups, TAA in pancreatic tissue. But when the strengthening of the antioxidant defense system occurring in the body cannot completely extinguish the oxidative stress caused by the surgical operation in the stomach, the intact level in the pancreas cannot be fully ensured.

In order to check the long-term effects of the "Ridutox" (Glutathione

600.0mg) solution, animals in the VII group were injected with the solution intravenously once a day during 7 days after the longitudinal tubular reduction of the stomach. During the analysis of the results obtained from each experimental animal 30 days after stopping the injection of the solution, it was determined that the concentration of the surface SH-protein group in 80% of them, the intrastructural SH-protein group in 40%, the concentration of catalase in 60%, and its concentration was 100% higher than normal.

Thus, the increased oxidative stress in the pancreas continued for 6 months after the longitudinal tubular reduction of the stomach. Intravenous injection of "Ridutox" (Glutathione 600.0mg) solution depressed oxidative stress and its markers were within normal limits in most experimental animals. However, their average concentration could not reach the level of the intact state.

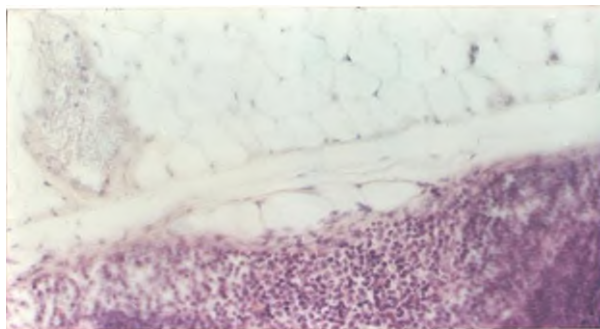
In the micropreparation made from the sample taken from experimental animals of I group, the structure of the pancreas showed some different results from the picture in the intact state. More precisely, the branched blood vessels in the connective tissue that make up the capsule of the pancreas have become somewhat spasmodic. In the parenchyma, on the background of edema, polygonal-shaped, various-sized fibrous tissues and accumulation of fat cells on them, as well as epidermocytes with white protrusions, and secretory epithelial cells secreting enzymes were observed (**Picture 2**).

In the experimental animals of group II, the microscopic picture some changed, they differed from the structure of the pancreas of the animals of the I group as a result of development of intercellular edema and of perivascular connective tissue. So, in the preparations made from the pancreas of the experimental animals of III group, the degenerative changes attracted more attention.

As a result of the activation of the body compensatory function, a slight expansion of the microcirculatory network was observed. However, the large blood-vessels kept their normal structure.

The pancreas of experimental animals in IV group differs from that of experimental animals in groups II-III with more serious structural changes. Although 3 months have passed since the

operation, clearly noticeable pathological processes in exocrine and endocrine cells of the pancreas, blood vessels (especially in the microcirculatory network), and connective tissue structure give reason to evaluate it as the result of oxidative stress. Despite slight disorganization of the connective tissue structure, the collagen fibers in the capsule of the gland retain their integrity.



Picture 2. Microscopic view of a micropreparation made from the pancreas. Accumulation of fatty tissue on blood vessels. Reagent : Hematoxylin-eosin. Magnification: ob.40. ok. 10.

Along with residual degenerative processes, a number of regenerative processes were also observed in the structure of the pancreas of experimental animals in the V group. In the micropreparation made from pancreatic tissue, necrotic areas with small sites, occurred individually indicate that the pathological process still remains. But the microcirculatory network is free from structural changes, there are no coincidences of mucoid swellings in the connective tissue, acinus release, and other marks are evaluated as attributes of regenerative processes.

In the samples taken from the pancreas of experimental animals included in the VI group quite different histological pictures were observed. 10 days after the operation of longitudinal tube reduction of the stomach, in pancreas parenchyme no other pathological signs

were noted, apart from the dystrophy, which was very faintly evident on the background of edema in the parenchyma of the gland. Both the exocrine and endocrine systems of the gland have maintained their normal histoarchitectonics, which is associated with depressing of oxidative stress by injecting Ridutox solution into the vein. Thus, in this chapter, it has been shown that oxidative stress occurs in the pancreas of rabbits with a model of morbid obesity as a result of strengthening the food ration and creating adynamia. As a result of the weakening of the general antioxidant defense system of the body, the longitudinal tubular reduction of the stomach plays a stimulating role in the further intensification of oxidative stress.

Intensified oxidative stress causes structural changes in the tissue due to damage to the membrane of pancreatic cells. This process creates more serious changes as more time after the operation passes and ends with the forming of focal changes in the pancreas. By injecting “Ridutox” solution into the body, strengthening its general antioxidant defense system protects the structure of the pancreas from pathological changes.

Chapter V is dedicated to the biochemical examination of blood after the longitudinal tubular reduction of stomach. This chapter consists of two paragraphs, the changes in the concentration of markers reflecting the functional state of the liver, as well as the amount of minerals and electrolytes in the blood, were studied in detail on experimental animals.

The analysis of the results obtained from the experiments on the study of the changes in the concentration of the markers reflecting the functional state of the liver showed that after the longitudinal tubular reduction of the stomach, there are changes in the functional state of the liver in a pathological direction. As a result of these changes, the concentration of the markers characterizing the function of the liver in the blood increases sharply. In this case, in combination with liver dysfunction, the duration of changes in the concentration of markers, characterizing its function in the blood increases also.

Based on the statistical analysis of the obtained experimental results, it was defined that the injection of “Ridutox” solution into a

vein once a day during 7 days after the operation accelerates the recovery of the impaired function of the liver. This result is also confirmed by the percentage of experimental animals with normal enzyme levels. Thus, the conducted examinations showed that the concentration of γ -glutamyl transferase enzyme, alkaline phosphatase enzyme, amylase and LDH enzyme decreased to normal level in the blood of up to 80% of the tested animals, AST enzyme -in 60%, ALT enzyme - in 40%.

The analysis of the results obtained from the study of the changes in the amount of minerals and electrolytes in the blood after the longitudinal tubular reduction of the stomach showed that the amount of minerals and electrolytes (Cl, P, Ca, K, Fe, Na) in the blood decreased significantly after the operation; it also showed that as time passes, blood levels tended to normalize, but despite this positive dynamic, they did not rise to normal levels after the operation for a long time.

It was found that 30 days after the injection of "Ridutox" solution into the vein of experimental animals, the amount of minerals and electrolytes in the blood, disturbed after operation is gradually restored.

In conclusion of this chapter its shown that the concentration of enzymes (AST, ALT, γ -glutamyl transferase, alkaline phosphatase, amylase, and LDH) in the blood increases due to the disturbance of the functional state of the liver after longitudinal tubular reduction of stomach. In response to this, the balance of minerals and electrolytes (Cl, P, Ca, K, Fe, Na) in the blood is disturbed also. Even 6 months after the operation, the disturbed balance of those indicators (enzymes, minerals and electrolytes) is not restored. Selective intravenous injection of "Ridutox" (Glutathione 600.0mg) solution accelerates the recovery of impaired liver function, as well as the amount of minerals and electrolytes (**Table 4**).

Chapters VI, VII, VIII and IX of the dissertation are dedicated to the interpretation and analysis of the results obtained from clinical observations.

Table 4

The dynamics of changes in the amount of minerals and electrolytes in the blood after longitudinal tubular reduction of the stomach

№	Experimental groups	Statistical indexes	Cl	Ca	P	Na	K	Fe
1	1 group	M	3.3	2.4	1.8	145.2	4.4	30.9
		M	1.30	0.14	0.14	3.38	0.3	0.9
		σ	2.91	0.32	0.32	7.56	0.74	1.94
2	2 group	M	2.9	2.1	1.4	134.6	3.80	27.9
		M	1.23	0.13	0.2	5.11	0.48	1.21
		σ	2.76	0.29	0.44	11.44	1.08	2.71
		P<	*	*	*	*	*	0.05
3	3 group	M	2.7	2.0	1.3	129.6	3.5	25.5
		M	1.21	0.15	0.16	4.20	0.14	0.82
		σ	2.72	0.34	0.36	9.40	0.32	1.84
		P<	*	*	0.05	0.05	0.05	0.01
4	4 group	M	3.10	1.9	1.60	121	3	24.9
		M	0.80	0.1	0.34	6.78	0.09	0.5
		σ	1.79	0.23	0.76	15.17	0.21	1.13
		P<	*	0.05	*	0.05	0.01	0.001
5	5 Group	M	3.1	1.7	1.5	113	3.3	23.1
		M	0.68	0.09	0.3	5.39	0.12	0.58
		σ	1.53	0.21	0.68	12.04	0.26	1.29
		P<	*	0.01	*	0.001	0.05	0.001
6	6 group	M	3.1	2.14	1.6	135	3.98	25.76
		M	0.35	0.21	0.37	5.0	0.14	0.40
		σ	0.79	0.47	0.82	11.18	0.31	0.89
		P<	*	*	*	*	*	0.001
7	7 group	M	3.0	2.3	1.7	142.6	4.2	27.7
		M	0.96	0.17	0.15	3.44	0.12	0.94
		σ	2.15	0.38	0.33	7.70	0.27	2.11
		P<	*	*	*	*	*	0.05

Note: *P>0,05

Chapter VI is dedicated to issues that play an important role in the success of the operation and its satisfactory results, namely, diagnosis of patients, preparation for bariatric surgery and prevention of complications that may arise from the operation. It's noted that, for this purpose, it is preferred to collect accurate anamnesis from the patients before the operation, namely correct information about the dynamics of body mass growth, the presence or absence of genetic obesity, lifestyles, physical activity, nutrition, the measures they have taken against excess body mass and obesity, and about other diseases they are worried should be collected.

Besides, indirect elastography of the liver performed by means of U/S and Fibroscan apparatus, ECG to distinguish the functional state of the liver of patients and concomitant diseases, as well as the use of the HOMA-IR (Homeostasis Model of Insulin Resistance Assessment) test, which is considered as golden standard in the determination of insulin resistance was done. In pre-operation period, the concomitant diseases of the patients were stabilized.

Based on the anamnesis and diagnostic datas collected from the patients, the patients were informed in detail about the operation to be performed, about the results of the operation, the complications that may arise from the operation, about the reduction of body mass in the postoperative period and the nutritional regime. Their written consent to the surgical operation was got, and a protocol about the preparation of the patients for the surgical operation had been done.

Due to the association of morbid obesity with a number of diseases, the anesthesiologist allowed the surgical operation only after careful examining the patients. The main issue here was to assess surgery the probability of occurrence of hypoventilation syndrome, which is characteristic for obesity.

In all the patients under observation, the longitudinal tubular reduction operation was performed laparoscopically in accordance with international standards, in addition, the "stapler" line was sutured with sero-serous sutures, the completeness of the gastric impulse was checked with the "methylene glass" test. Both the operation itself and the post-operation period passed satisfactory, lethality was not noted, the length of stay in the clinic was 2-3 days.

If the patients have concomitant diseases, corresponding anesthesiological and resuscitation measures should be taken to prevent exacerbation of those diseases during the operation.

Alike other authors (Kinjo Y., et al., 2011; Yasumoto A. et al., 2015), "NATHANSON" liver retractor was used to protect the organs of the abdominal cavity from damage. At the same time, in order to avoid complications that may occur during the implementation of that method, the mentioned method of using the retractor has been improved, simplified and made safer. This improved method is simpler, cheaper and technically easier than other existing methods.

Taking into account that patients with morbid obesity are liable to thromboembolism, in order to reduce the risk of thromboembolism, along with compression elastic stockings, pneumo stockings and pharmacological preparations were used. Patients according to their body weight were injected a small molecule anticoagulant (Clexane, Fraxiparine, Arextra) one day before surgery, on the day of surgery and during 10 days after surgery.

The purpose of infusion therapy during the operation was to ensure normal perfusion and hemodynamics in the organs and tissues. When analyzing the results of the operation, it was confirmed once again that the infusion should be carried out during the operation as needed, because overloading the body with too much liquid causes a decrease in the function of the lungs and, as a result, the development of hypoxia.

The fight against surgical infection in the postoperative period is an important issue facing the surgeon as well as the resuscitator, because morbid obesity itself is a factor in the development of surgical infection. In patients with insulin resistance and type II diabetes, the development of infection after surgical operation is more severe, as there are more fertile conditions for the development of surgical infection. For this reason, Ceftriaxone and Ciprofloxacin were used, and the infection that occurred in 15 out of 100 patients in the post-surgical period was quickly eliminated as a result of the introduction of these antibiotics into the body.

20-30 minutes before the end of the surgical operation, 1.2 mg of Haloperidol, 8-10 mg of Dexamethasone, and 4-8 mg of

Ondansetron were injected once. Since haloperidol is antagonistic to D2-dopamine receptors in low doses, by blocking it the number of nausea and vomiting reflexes is reduced. Dexamethasone reduces the forming of prostaglandin and keeps the reduction of endorphin under control.

The results of bariatric surgery for morbid obesity depend on the patient's post-operative care. The early activation plays an important role in the rehabilitation of the patient. All patients were raised and activated in 2-4 hours after surgery. Early activation usually improves lung function and prevents the development of pneumonia in the postoperative period.

In addition, in order to improve breathing movements, to increase the air capacity of the lungs, to prevent lung complications, and strengthen the respiratory muscles, all patients are recommended to perform breathing exercises with the TRI-BALL RABIR TRIFLO breathing simulator during 1 week before surgery, on the day of surgery, and during 10 days after surgery.

Early transition of patients to enteral feeding plays an important role in improving surgical outcomes. On the first day after the operation, making sure that there was no extravasation from the stapler line and after X-ray examination with a water-soluble contrast agent (Urographin 60%) being convicted that the patency of the tubular stomach was satisfactory, the patients were given solid food.

A memory books were distributed to the patients when they were discharged home. In that book the information about proper nutrition of patients, lifestyle and intake of vitamins and trace elements is provided. A special program was prepared to help patients adapt to the inadequate environment created after the operation.

In **Chapter VII** the general characteristics of patients, undergone laparoscopic longitudinal tubular reduction of the stomach is given. It has been pointed out that, as mentioned in chapter II of the dissertation, 100 patients with third-degree morbid obesity were selected from those who were in hospital and included in the study.

Laparoscopic longitudinal tubular reduction of the stomach was performed in all those patients.

Patients were divided into 2 groups with 50 people in each group. 50 patients in the I group undergone laparoscopic longitudinal tubular reduction of the stomach. Most of the patients (46%) were 30-39 years old, 16% were men, 84% were women.

Before the operation, the blood group of all patients was determined and it was defined that 40% of them belonged to I, 34% to II, 18% to III, and 8% to IV blood group.

As a result of the diagnostic examinations performed before the surgical operation, non-alcoholic steatohepatosis was found in all of those patients, type II diabetes -in 22 patients, insulin resistance- in 32 patients, arterial hypertension -in 22 patients, dyslipidemia was found in 45 patients, gallstone disease- in 6 patients, respiratory system disease- in 7 patients, pancreatitis - in 13 patients, reflux esophagitis was found in 47 patients , osteoarthritis- in 11 patients , sleep apnea - in 12 ones, veins varicose of the lower extremities in 4 ones was found.

It was found that among the patients included in the study, reflux esophagitis was in the I place, but among the diseases accompanying morbid obesity dyslipidemia was in II place, and insulin resistance was in III place.

Biochemical examinations of liver markers in the blood showed that before surgery, the concentration of a number of enzymes, including ALT, AST, alkaline phosphatase, and γ -glutamyl transferase enzymes, remained normal in the vast majority of patients.

The concentration of the mentioned enzymes at a normal level at first sight show that, in functional state of the liver of most patients no pathological changes existed. However, the results obtained from instrumental examinations refute this idea. Thus, in U/S, pathological changes in the right and left parts of the liver were not detected only in 1 patient. But the development of hepatitis in the liver tissue was confirmed in the right part of the liver of 49 other patients (98%).

The indirect elastography examination of the liver revealed a

more serious change in the liver tissue. According to the Metavir scale, in 2 patients -F1, in 27 - F2, in 19 patients- F3, and in 2 -F4 degrees were found.

The state of the lipid spectrum in the blood was evaluated basing on the amount of triglycerides and total cholesterol. So, it was determined that lipid metabolism was disturbed in the vast majority of patients, and morbid obesity as well as non-alcoholic steatohepatosis of the liver that rises from it often develops together with the disturbance of the lipid system.

Among the patients in the II group, 4 were men, 46 were women, 7 patients were at the age of 20-29, and the rest 19 patients were 30-39 years old. The age of 10 patients is between 40-49, and 14 patients are older than 50 years. All the patients in this group had a higher than normal body mass index and, alike in the I group, they were diagnosed with III degree morbid obesity.

Alike in the I group, all the patients of the II group had liver steatohepatosis of non-alcoholic origin, type II diabetes was found in 18 people, and high insulin resistance was found in 29 patients. 21 patients were diagnosed with arterial hypertension, 9 patients had gallstone disease, 3 patients had respiratory system disease, 24 patients had chronic pancreatitis, 40 patients had reflux autophagitis. Finally, in 12 patients osteoarthritis, in 7 - apnea, in 3 patients - varicose in veins of the lower extremities, and in 43 patients dyslipidemia was found.

The analysis of the blood markers characterizing the functional state of the liver showed that the majority of the II group of patients who underwent bariatric surgery maintained a normal functional state of the liver. In some patients, liver function was impaired. This result was also confirmed by U/S. As a result of U/S, only in 3 patients any pathological changes in the right and left part of the liver were not observed, but in other 47 people (94%) the development of hepatitis in the liver tissue in the right part of the liver was confirmed (**Picture 3**).



Picture 3. Diagnosis. NAFLD. Sonography of the abdominal cavity: a) Hypertrophy of the right and left parts of the liver; b) Hypertrophy of the left part.

The indirect elastography examination of the liver revealed a more serious change in the liver tissue. According to the Metavir scale, F1 was determined in 5 patients, F2 in 32 patients, and F3 in 13 patients (**Picture 4**).



Picture 4. a) Indirect elastometry of the liver – 22.8 kPa METAVIR- F2-F3.

b) Indirect elastometry of the liver-METAVIR- 37.6 kPa- F4.

Among the patients included in the II group, an increase of insulin resistance was also observed, and all patients had liver steatohepatosis of non-alcoholic origin caused by morbid obesity. 16 patients included in the I and II groups and diagnosed with

cholelithiasis were underwent a simultaneous operation. I.e. laparoscopic longitudinal tubular reduction of the stomach was performed at the same time with laparoscopic cholecystectomy, and in addition, the subhepatic region was drained with No. 16 drainage tube during 2 days.

This additional operation performed in patients with morbid obesity was considered as a more effective operation compared to the mini-open cholecystectomy operation performed using an illuminated surgical retractor and did not have negative influence on the results of the main operation.

Chapter VIII consists of two paragraphs. In this chapter, the results obtained during laparoscopic longitudinal tubular reduction of the stomach are reflected. In patients included in I group, in the first days after the operation of laparoscopic longitudinal tubular reduction of the stomach, the concentration of ALT enzyme in the blood of 100% of patients increased sharply and exceeded the normal limit. This process continued for 6 months and returned to normal level only at the beginning of the 6th month after the operation.

Quite different situation was observed in the concentration of AST enzyme. AST is another marker that reflects the functional state of the liver. Before the surgical operation, the concentration of AST enzyme in the blood of 32 from 50 patients (64%) kept its normal level, (in differ from ALT enzyme), but in 18 people (36%) it was higher than the normal level.

AST enzyme concentration in the blood of 6 patients decreased to its normal level 1 month after the laparoscopic longitudinal tubular reduction of the stomach. As time passed, the number of patients whose concentration of the AST enzyme in the blood decreased to a normal level increased even more.

Basing on the analysis of the results obtained 6 months after the operation of the laparoscopic longitudinal tubular reduction of the stomach, it was determined that the process of lowering the concentration of the AST enzyme in the blood to the normal level continued. So, among 18 patients with a high level of AST enzyme in their blood before surgery, only 2 patients (11%) had a high level of AST enzyme in their blood, other 10 patients (55.5%) had a normal

level.

More precisely, after laparoscopic longitudinal tubular reduction of the stomach, in differ from ALT enzyme, the concentration of AST enzyme in the blood did not increase, but gradually approached the norm. 6 months after the operation, in the blood of 48 patients, and after 1 year in 49 patients AST enzyme concentration was on a normal level.

Thus, the results of the conducted laboratory examinations showed that after the laparoscopic longitudinal tubular reduction of the stomach, in differ form ALT enzyme, the concentration of the AST enzyme in the blood did not increase, but on contrary, got the normal range.

One of the markers reflecting the functional state of the liver is the concentration of alkaline phosphatase enzyme in the blood. The concentration of alkaline phosphatase enzyme in the blood of 46 (92%) of the patients who were observed before the operation kept its normal level. Only in 4 patients (8%) the concentration of mentioned marker in the blood was higher than normal. 1 month after surgery, the concentration of alkaline phosphatase enzyme in the blood of all 4 patients decreased to normal level and remained stable during all observation periods.

The concentration of γ -glutamyl transferase enzyme in the blood was on normal level only in 27 the patients who underwent surgery, in 23 of them it was above the norm. However, after the operation, the concentration of this marker decreased dynamically. Thus, the changes in the function of the liver after laparoscopic longitudinal tubular reduction of the stomach were gradually restored as the postoperative period increased.

The amount of glucose in the blood of 24 (48%) patients included in the study was higher than normal, and in 26 (52%) patients it was within the normal range. The operation significantly reduced the amount of glucose in the blood. So, 6 months after the operation, the amount of glucose in the blood of 17 from the 24 patients with type II diabetes decreased to normal, and in 7 patients the level of glucose remained higher than normal. 1 year after the operation more successful results were obtained, the number of

patients with glucose higher than normal decreased to 3 persons.

Thus, the obtained results showed that the laparoscopic longitudinal tubular reduction of the stomach plays an important role in the treatment of type II diabetes, going along with morbid obesity. Mentioned operation also regulates the disturbance of lipid metabolism in the body, which is one of the main complications arising from morbid obesity, and restores the echostructure of the liver. These positive changes continue even after surgery in most patients.

In the second paragraph of this chapter, an analysis of extinguishing the oxidative stress occurred in the liver and pancreas, its influence on the results of laparoscopic longitudinal tube reduction operation of the stomach is given. It was found that the concentration of ALT enzyme, which is one of the markers reflecting the functional state of the liver, increases in a short period after the operation, but it decreases to the normal level in the following days and remains stable until the end of the observation period.

6 months after the operation, the concentration of alkaline phosphatase enzyme varied between 30.0-98.0 U/l. Accordingly, the average concentration of the alkaline phosphatase enzyme in the blood decreased by 11% compared to the 1 month, and got 55.0 ± 2.0 U/l, and it did not deviate from the norm in the blood of all patients 1 year after the operation. However, although the minimum limit of alkaline phosphatase enzyme concentration in the blood remains stable compared to the 6th month, its maximum limit decreases 18% to 80.0 U/l, and its average concentration also decreased to 48.6 ± 1.7 U/l (**Table 5**). Conducted clinical examinations show that laparoscopic longitudinal tubular reduction of the stomach restores the impaired function of the liver, dynamically reduces the concentration of each of the 4 enzymes that reflect it in a time-dependent manner after the operation, and has a strong positive effect on the regulation of the amount of glucose (blood sugar) and triglycerides in the blood of patients. As its confirmed by the conducted instrumental examinations, this operation plays an important role in the regulation of biochemical and pathological changes in the blood take place because of morbid obesity, in

eliminating the signs of fibrosis observed in the liver, and significantly reduces the degree of obesity.

Table 5

The dynamics of changes in liver enzymes in the blood of patients included in the I and II groups after laparoscopic longitudinal tubular reduction of the stomach

№	Examination period	Group	ALT	AST	QF	γ QT
1	Before operation	I	46.1±3.8	30±1.6	75.5±3.5	43.8±4.4
		II	27.1±1.9	21.5±1.2	71.7±3.5	37.1±4.8
2	1 month after operation	I	35.3±1.4	26.5±1.2	66.0±2.2	35.8±1.6
		II	21.9±0.9	18.1±0.8	61.8±16.1	28.2±2.2
3	6 months after operation after operation	I	25.8±0.7	20.6±0.7	57.4±2.1	31.3±1.3
		II	19.1±0.8	15.5±0.6	55.0±2.0	26.0±1.6
4	12 months after operation	I	22.9±0.6	17.8±0.6	52.4±1.9	28.5±1.3
		II	17.1±0.6	13.7±0.5	48.8±1.7	23.2±1.5

In conclusion of the results obtained from the research conducted in this chapter, it is noted that during morbid obesity in the liver and pancreas oxidative stress is formed. During the operation of laparoscopic longitudinal tubular reduction of the stomach, oxidative stress is induced and becomes more intense due to the effect of the operation and has a negative effect on the results of the operation. The concentration of enzymes in the blood that reflects the functional state of the liver increases, during the U/S and elastography examination a number of pathological conditions in the liver are revealed, the size of the liver remains above normal during the period.

By injecting 4.0 ml of 600.0 mg Ridutox (Glutathione 600.0mg)

solution once a day into the vein of the patient who underwent surgery, it is possible to activate the antioxidant defense system of organism and to extinguish oxidative stress. That's why after the operation of laparoscopic longitudinal tubular reduction of the stomach, in patients whom "Ruditox" drug to the treatment complex (included in I group) was not added some complications were observed. At the same time, compared to this group in patients whom "Ruditox" drug was added to the treatment complex (included in group 2) oxidative stress decreased significantly.

In **Chapter IX**, a comparative analysis of the results obtained from the laparoscopic tubular reduction of the stomach, depending on the state of oxidative stress, was carried out. It has been shown here that in the tissues of the liver and pancreas after laparoscopic longitudinal tube reduction of the stomach oxidative stress occurs.

In order to determine the peculiarities of this issue and guarantee the accuracy of obtained results, the symptoms, listed in protocol, including the severity of the patients' conditions in both groups, were strictly controlled. The treatment of the patients included in the I group in the postoperative period was made according to the traditional rule accepted in the clinic. But in group II patients, before and after surgery to their treatment complex measures to suppress oxidative stress were added.

It became obvious that the oxidative stress developed in the liver and pancreas tissues during the laparoscopic longitudinal tubular reduction of the stomach plays the role of detenuator of the changes in the enzyme system of the liver after the surgical operation. The development of oxidative stress in the liver and pancreas tissue after operation doesn't influence seriously on the increase or decrease of the amount of glucose in the blood. But its extinguishing leads to the regulation of enzymes that reflect the functional state of the liver.

1 year after the operation, there is no significant difference between the groups in terms of number of patients whose blood triglycerides are normal. The depressing of oxidative stress in the tissue of the liver and pancreas after the operation reduces the amount of total cholesterol in the blood relatively much.

In addition to showing the presence of a pathological process in the right part of the liver of patients included in both groups, U/S confirmed the important role of oxidative stress extinguishing in restoring the functional state of the liver. U/S also revealed that the right part of the liver was restored in the majority of patients after laparoscopic longitudinal tubular reduction of the stomach (**Table 6**). The elastography performed on both groups revealed quite positive changes. Thus, in the main majority of both groups of

Table 6
U/S results in patients included in groups 1 and 2 after laparoscopic longitudinal tubular reduction of the stomach

№	Examination period	Groups	Right part mm.	Left part. Mm
1	Before operation	1	141.9±1.5	78±1.0
		2	141.1±1.9	74.7±0.9
2	1 month after operation	1	134.3±1.6	72.6±0.8
		2	132.1±1.5	70.7±0.7
3	6 months after operation	1	131.2±1.4	71.0±0.8
		2	128.7±1.4	69.0±0.7
4	12 months after operation	1	128.9±1.4	69.2±0.8
		2	126.4±1.4	67.8±0.6

patients, fibrotic tissue wasn't seen at all, or its severe form wasn't seen. The observations revealed that the laparoscopic longitudinal tubular reduction of the stomach has a significant positive effect on the degrees of morbid obesity (**Table 7**).

The comparative analysis shows that the depression of oxidative stress after laparoscopic longitudinal tubular reduction of the stomach in patients with III degree morbid obesity improves the results of the operation both distant and close ones.

Table 7

Results of indirect elastography of the liver in patients included in groups I and II after laparoscopic longitudinal tubular reduction of the stomach

№	Examination period	Groups	Elastoraphy indexes				
			F ₀	F ₁	F ₂	F ₃	F ₄
1	Before operation	1-ci	0	4%	54%	38%	4%
		2-ci	0	10%	64%	26%	0
2	6 months after operation	1-ci	44%	46%	8%	2%	-
		2-ci	60%	36%	4%	0	-
3	12 months after operation	1-ci	80%	20%	-	-	-
		2-ci	88%	12%	-	-	-

RESULTS

1. When the motion activity of rabbits belonging to the genus "Chinchilla" is restricted and the food ration is increased, as a result of the increase in their body mass, the free peroxidation process of lipids in the tissues of the liver and pancreas is intensified, but the general antioxidant defense system of the body is weakened. According to the oxidative stress, dystrophic areas are formed in the liver and pancreas [26.29,31,32].
2. In experiment in morbid obesity modeled experimental animals, in 10 days after laparoscopic longitudinal tubular reduction of stomach the concentration of hydrogen-peroxide (H₂O₂) in the liver tissue increased to 107%, the concentration of diene conjugates (DC) increased to 103%, and the concentration of malondealdehyde (MDA) increased to 109% . The concentration of the SH- sulfhydryl protein group and the SH-protein group located inside the cell structure decreased by 8% and 14.5%, respectively, the concentration of total antioxidant activity with catalase decreased by 24% and 20%, respectively. During 3 months, the concentration of free lipid peroxidation products

decreases, the reduction of the markers of the body's antioxidant defense system continues dynamically. Although the process stabilizes relatively in the 6th month, the intensity of free lipid peroxidation is higher than the level in the intact state, and the activity of the antioxidant defense system is at a lower level [26,29,31,32].

3. In experimental animals with morbid obesity, starting from the 10th day of longitudinal tubular reduction of stomach, the amount of chlorine (Cl) in the blood decreased to 12%, the amount of calcium (Ca) -to 13%, the amount of inorganic phosphorus (P) decreased to 12%, sodium (Na) amount decreases to 7%, the amount of potassium (K) decreased to 14%, and the amount of iron (Fe) -to 11%, reaching the most critical level on the 30th day. 3 months after the operation, although the decrease in the amount of chlorine (Cl) in the blood reduced to 4%, and the decrease in the amount of inorganic phosphorus (P) decreased to 15%, calcium (Ca), sodium (Na), potassium (K) and iron (Fe) decrease in quantity becomes more distinct [31,32].
4. In experimental animals with modeled morbid obesity, longitudinal tubular reduction of the stomach further intensifies the oxidative stress that develops in the tissues of the liver and pancreas, and accordingly, a picture, characteristic for pathological changes in the histological structure of both organs , namely the expansion of perivascular, postcapillary and collecting vessels take place.[26,29,31,32].
5. In order to strengthen the general antioxidant defense system of organism after longitudinal tubular reduction surgery in experimental animals with modeled morbid obesity, into the vein of these animals injection of 0.2 ml/kg "Rudutox" ("Glutathione"600.0mg) drug solution (which has a hepatoprotective and antioxidant effect), was added. Although it suppresses oxidative stress by strengthening the general antioxidant defense system, it cannot liquadate it completely, the concentration of markers representing free lipid peroxidation is significantly reduced, but it is higher than the level in the intact state [26,29,32].

6. After longitudinal tubular reduction of the stomach in experimental animals with modeled morbid obesity, the strengthening of the general antioxidant defense system of organism ensures maintenance of the histoarchitectonics of both organs by depressing the oxidative stress that has occurred in the liver and pancreas tissues [26,29].
7. In experimental animals with modeled morbid obesity free peroxidation of lipids in the liver tissue intensifies from the first days after longitudinal tubular reduction surgery and continues with a fairly high intensity even 3 months after surgery. 3 months after the operation, although a certain positive change occurs in the weakened general antioxidant defense system of body, the normal limit is not restored [21,29,31,32].
8. Due to morbid obesity, 3 days after laparoscopic longitudinal tubular reduction of the stomach, the concentration of AST and ALT enzymes rises to a level higher than normal and continues to remain at a high level for 6 months, but the amount of fairly γ -glutamyl transferase enzyme (GGT) decreases dynamically [13,14].
9. As a result of depressing the oxidative stress that develops in the liver tissue by strengthening of general antioxidant defense system in body, 3 days after laparoscopic longitudinal tubular reduction of the stomach, the amount of AST and ALT enzymes in the blood increases. But 1 month after the operation, the concentration of ALT enzyme in the blood of 100% patients, AST enzyme in 98% patients drops to a normal level and remains stable until the end of the observation period [13,14].
10. In patients with morbid obesity, the dynamic development of other diseases, accompanying non-alcoholic hepatic steatohepatosis after laparoscopic longitudinal tubular reduction of the stomach becomes positive [21,33,35].
11. In patients with morbid obesity, laparoscopic cholecystectomy is more optimal than open cholecystectomy, including mini-open cholecystectomy performed using an illuminated surgical retractor [5-7,11,12,22].

12. In patients, who have gallstone disease in addition to morbid obesity, regardless of body weight and age, laparoscopic cholecystectomy combined with laparoscopic longitudinal tubular reduction of the stomach made by an experienced surgical team, is possible, appropriate and undangerous [1,2].

PRACTICAL RECOMMENDATIONS

1. In order to get effective results of bariatric surgery, patients should be prepared for surgery in the following manner during 5 months:
 - a) the diagnosis should be specified and confirmed;
 - b) in order to reduce body mass a special food regime, characteristic for the disease, should be prepared and given patients; it must be ensured that patients adhere to it strictly;
 - c) in order to reduce body mass physical activity should be increased ;
 - d) concomitant diseases, especially type II diabetes, arterial hypertension, ischemic heart disease should be stabilized.
2. In order to depress the oxidative stress that occurred in the liver tissue and pancreas tissue, 4.0 ml of "Glutathione" 600.0 mg of hepatoprotective and antioxidant drug solution should be injected intravenously once a day for 7 days immediately after surgery.
3. In the post-surgical period a memory sheet should be prepared and given the patients with information about the results of the operation, food regime, physical activity, medication intake, their dosage, order and duration. Besides, body weight monitoring, (with indicating the date) should be performed, and coming for a repeat examination must be controlled.

List of published scientific works on the topic of the dissertation:

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