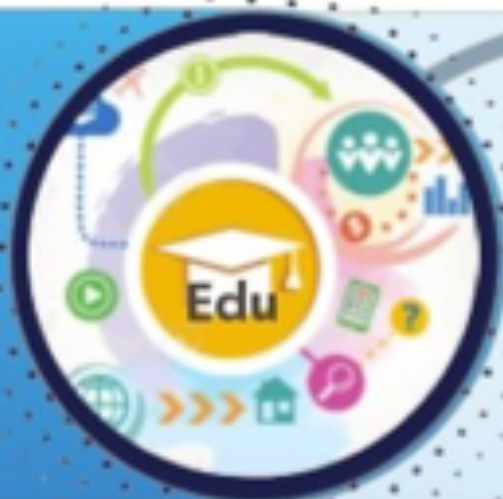


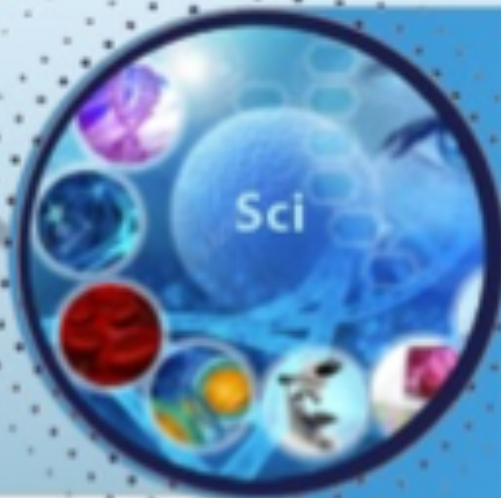


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# Problems of Early Pathogenetic Diagnosis of Biliary Reflux after Bariatric Surgery

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## ABSTRACT

Many studies devoted to the analysis of the long-term results of bypass surgeries provide contradictory information about the advantages of one or another method in the treatment of obesity and concomitant comorbid conditions. Moreover, in studies devoted to the analysis of the effectiveness of weight loss, remission of type 2 diabetes mellitus, many authors tend to give preference to mini-gastric bypass. As for some studies, some studies report a higher incidence of gastroenteroanastomosis ulcers in the long-term postoperative period after Roux-en-Y gastric bypass. At the same time, in the vast majority of studies, the assessment of biliary reflux is formed by analyzing clinical symptoms using various scales, questionnaires and endoscopic data, and only in three studies a morphological study was performed. This makes this scientific direction extremely promising for identifying risk groups after mini-gastric bypass and making timely decisions on revision interventions.

**Keywords:** gastric bypass surgery, bariatric surgery, postoperative complications

Making a clinical diagnosis of biliary reflux after bypass surgery is difficult unless the patient has regurgitation of biliopancreatic secretions and/or vomiting bile, especially during the night. Other symptoms may include bloating, heartburn, nausea, belching, epigastric pain, or signs of bile aspiration (due to bile vomiting).

Fibrogastroscopy is the first instrumental method of examination of patients who have clinical signs of biliary

reflux. Although not very sensitive, this test allows visual documentation of the presence of bile in the lumen of the gastric stump and/or esophagus and can be used to identify some pathological changes observed in the mucous membrane of the stomach and esophagus (gastritis, erosions, acute ulcers, esophagitis, Barrett's esophagus, or suspected tumor).

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The next method for determining the reflux of biliary-pancreatic secretion is pH-metry. However, measuring the pH level of the esophagus is not a reliable method and cannot provide an accurate diagnosis of alkaline reflux, due to the presence of many associated artifacts leading to non-specific results.

Fiber-optic spectrophotometry, in combination with pH monitoring, is considered by a number of authors to be the most accurate method for diagnosing biliary reflux. However, due to methodological limitations, the spectrometric method was not sufficiently developed and was replaced by pH impedancemetry, which experts consider to be a more reliable and suitable method [19].

Multichannel intraluminal impedance monitoring allows for the analysis of changes in electrical resistance and the detection of all virtual episodes of reflux (liquid, gas, or both). In combination with pH monitoring, pH impedancemetry can be used to characterize all reflux episodes, both acidic and alkaline [18].

To date, only one study has been conducted using systematic monitoring of pH impedance, manometry, and upper endoscopy [13].

The study included 15 patients with preoperative reflux symptoms who underwent mini-gastric bypass. At 1 year after mini-gastric bypass surgery, no cases of esophageal-gastric junction dysfunction were detected, but at the same time, intragastric pressure decreased significantly from 15 to 9.5 ( $p < 0.01$ ), the gastroesophageal pressure gradient decreased from 10.3 to 6.4 ( $p < 0.01$ ), and the number of gastroesophageal reflux events decreased from 41 to 7 ( $p < 0.01$ ). However, no endoscopic signs of lesions of the gastric and/or esophageal mucosa secondary to possible biliary reflux were found [3, 4].

Regardless of these results, the small number of patients studied, as well as the short follow-up periods, do not allow us to draw definitive conclusions.

The most informative method for diagnosing biliary reflux is the determination of morphological changes in the gastric mucosa. Due to the stereotypical nature of changes in the gastric mucosa, it became possible to develop a biliary reflux index (BRI) based on histological data.

This index was introduced by G.M. Sobala et al. in 1993 on the basis of biopsy data of the antrum of the stomach or the distal part of the gastric stump. The pathologist, who was "blinded," that is, had no idea of the clinical data of the patients, evaluated each sample of stomach tissue according to the aforementioned BRI system.

The index is derived based on the presence and severity of some histological parameters: edema in the lamina propria of the gastric mucosa (designated as E in the formula below), intestinal metaplasia (IM), chronic inflammation (CI in the formula below) and colonization of *Helicobacter pylori* (H.p.) in the stomach.

Each histological parameter is assigned a score from 0 to 3 by the pathologist, which corresponds to the levels: no parameter, mild, moderate or high degree of presence, respectively.

The formula for determining the biliary reflux index was derived based on a stepwise logistic regression analysis:

$$BRI = (7 \times E) + (3 \times IM) + (4 \times CI) - (6 \times H.p.)$$

According to Sobala et al., a BRI above 14 indicates biliary reflux (which corresponds to a bile acid level greater than 1 mmol/L, i.e., above the upper limit of physiological normal) with 70% sensitivity and 85% specificity.

Based on these data, as well as on the fact that other methods of diagnosing duodenal gastric reflux, primarily 24-hour pH-metry, do not currently have high accuracy, this index is used by a number of authors as a diagnostic criterion in clinical trials [9, 11, 14].

In 2019, B. Keleidari et al. was the first in Europe to use the biliary reflux index (BRI) in their comparative study to diagnose biliary reflux in bariatric patients who underwent mini-gastric bypass and Roux-en-Y gastric bypass surgery [10].

At the same time, in 2019, Khitaryan A.G. and co-authors published the results of a study on a comparative analysis of the pathomorphological aspects of the development of biliary reflux after minigastric bypass with the formation of manual and instrumental gastroenteroanastomosis, where the BRI index was also used to assess the severity of biliary reflux for screening patients at high risk of complications.

The authors concluded that the formation of a manual anastomosis in the studied group of patients is more functional, as it allows to reduce the frequency of endoscopic and histological signs of biliary reflux compared to hardware anastomosis.

Reflux gastritis is considered the most common post-resection complication. Dyspeptic symptoms such as epigastric pain, heartburn, nausea, bile belching due to reflux gastritis worsen the quality of life of patients after surgery.

Researchers from the Isfahan Medical University (Iran), led by Behrouz Keleidari, were among the first to conduct a study to compare the incidence of biliary re-

flux in obese patients after minigastric bypass and Roux-en-Y gastric bypass.

The study was conducted from November 2015 to June 2017; It involved obese patients who underwent Roux-en-Y gastric bypass grafting (the length of the small ventricle was 7–10 cm, the length of the biliary loop was 120–150 cm, the length of the alimentary loop was 50–70 cm) and minigastric bypass grafting (the length of the small ventricle was 18–22 cm, the anastomosis was applied at a distance of 150–200 cm from the Treitz ligament). All subjects were determined for baseline weight, height, body mass index, fasting blood glucose, lipid profile, and endoscopic fibrogastroduodenoscopy with biopsy of the small ventricular wall.

The presence of biliary reflux was assessed by several parameters: anamnesticly – whether there was heartburn, bile vomiting; according to endoscopic data – the presence of gastritis, bile in the small ventricle, changes in the mucous membrane; histological criteria for the presence of reflux. The bile reflux index was calculated using the Sydney rating system.

The results of 122 patients included in the study were obtained: 58 patients in the Roux-en-Y gastric bypass group and 64 patients in the minigastric bypass group. Although body mass index decreased significantly in both study groups ( $p < 0.001$ ), the decrease was still more pronounced in the Roux-en-Y gastric bypass group ( $p = 0.007$ ). The mean fasting blood glucose and lipid profile in each group decreased significantly after 12 months of follow-up ( $p < 0.01$ ).

The history of biliary reflux according to endoscopy and the incidence of postoperative complications in the two groups did not differ significantly. No statistically significant difference was found. The results of this study showed that minigastric bypass surgery is as safe as Roux-en-Y gastric bypass, especially in the presence of postoperative biliary reflux.

Based on the findings, minigastric bypass was shown to have a similar effect to Roux-en-Y gastric bypass in terms of overall weight loss, reduction in mean fasting blood glucose, and changes in lipid profile.

The authors recommend minigastric bypass grafting as a safe and effective bariatric surgery with no increased risk of biliary reflux in patients in the postoperative period, and also advise in the future to conduct studies with larger sample sizes and longer follow-up periods.

The main role in damage to the mucous membrane of the gastric stump is played by bile acids, which are part of the duodenal contents that enter the stomach. In addition, a necessary condition for the development of gastritis is the presence of hydrochloric acid in gastric juice.

Bile acids, which have detergent properties, cause solubilization of lipids of the membranes of the surface epithelium. This effect depends on the concentration, level of conjugation and hydroxylation of bile acids, as well as on the acidity of gastric juice. At low pH values, only taurine conjugates damage the mucous membrane, and other bile acids precipitate under such conditions. In contrast, at high pH, unconjugated and hydroxyl bile acids have great damaging properties.

A sharp decrease in the hydrophobicity of surfactant phospholipids of the outer membrane of epithelial cells under the influence of bile salts was proved under experimental conditions in vitro. A certain role in epithelial damage is also played by lysolecithin, which is formed during the hydrolysis of lecithin by pancreatic phospholipase A [15].

The morphological characteristics of reflux gastritis are quite characteristic and well studied. The gastric folds are high papillomatous, sometimes deformed with small thickenings and "adhesions", sometimes they can resemble the villi of the small intestine. The pits deepen and acquire a bizarre "corkscrew-like" shape. The integumentary epithelium is flattened, with basophilic cytoplasm saturated with RNA and reduced mucus content.

Sometimes the nuclei of the integumentary-pitted epithelium are located at different levels, there are hyperchromic, wrinkled or vesicular nuclei. Changes in the stroma are reduced to edema of the lamina propria, dilation and fullness of blood vessels, thickening of their walls, and proliferation and branching of the muscular plate. Mononuclear infiltration is weakly or moderately pronounced, concentrated in the interfoveal zones, and sometimes an admixture of neutrophils is found. The infiltrate is dominated by plasma cells, lymphocytes and fibroblasts are less common.

IgA is found only in single cells at the tops of the rollers and in somewhat larger numbers in the pit epithelium. There are quite a lot of IgG-producing cells in the plasma cyte population. Plasma cells containing IgE as well as labrocytes are almost always detected [5].

The glands of the gastric stump mucosa acquire a pyloric appearance as a result of the replacement of specialized glandulocytes with mucus-producing cells such as cervical mucocytes [8].

A histological marker of duodeno-gastric reflux in the mucous membrane of the gastric stump is subnuclear vacuolization of the foveal epithelium, which can be detected several years after resection. Vacuoles appear optically empty and do not contain mucoid.

The incidence of this sign is highest after gastric resection according to Billroth-2 (87.5%), less common

after Billroth-1 surgery (15.9%), and extremely rare after vagotomy in combination with pyloroplasty (2.1%) [6].

Often in the mucous membrane of the gastric stump, you can find foci of intestinal metaplasia, occupying one or more rollers and gastric pits. Both columnar and goblet cells are found in such areas, and their ultrastructural characteristics do not bear full resemblance to typical enterocytes and goblet exocrinocytes [1].

The development of reflux gastritis seems to depend on a number of conditions:

Intragastric level of bile acids in gastric juice. According to Lopez P.P., et al., the concentration of bile acids in gastric juice was 830  $\mu\text{M}/\text{h}$  in patients undergoing gastric resection with Billroth-2 gastrojejunostomosis, 18  $\mu\text{M}/\text{hour}$  in patients after cholecystectomy, and 8  $\mu\text{M}/\text{hour}$  in patients with mild symptoms of dyspepsia [12].

High-quality composition of bile acids. It is believed that both conjugated and unconjugated bile acids have a damaging effect in the gastric stump, and the share of the latter can be up to 25% [7].

If unbound bile acids are an absolute pathogen, then the damaging effect of conjugated bile acids is associated with a high pH level in the gastric stump.

It is known that in an unoperated stomach under conditions of normal acidity of gastric juice, conjugated bile acids precipitate and their pathogenic action is limited [2].

Duration of exposure to the mucous membrane. The experiment proved the complete reversibility of changes in the gastric stump mucosa after the elimination of duodenal gastric reflux, the action of which caused reflux gastritis for 6 months [11].

A number of authors note a favorable effect on the clinical manifestations and morphological changes of the gastric stump mucosa in operated patients with reflux gastritis after surgical treatment aimed at eliminating duodenal gastric reflux [14,18].

### CONCLUSION:

Thus, attention is drawn to the scarcity of comparative studies of the immediate and long-term results of obesity treatment using Roux-en-Y gastric bypass and mini-gastric bypass. In the analysis of intraoperative outcomes, there are no statistical differences in the development of intraoperative complications, although early postoperative complications in the Clavien-Dindo analysis tend to develop more frequently after Roux-en-Y gastric bypass, these differences are statistically insignificant in a number of studies.

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**Bariatrik operatsiyadan so'ng biliar refluksning  
erta patogenetik diagnostikasi muammolari**  
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**Toshkent tibbiyot akademiyasi**

**АБСТРАКТ**

Bypass operatsiyalarining uzoq muddatli natijalarini tahlil qilishga bag'ishlangan ko'plab tadqiqotlar semizlik va bir-biriga mos koorbid holatlarni davolashda bir yoki boshqa usulning afzalliklari to'g'risida bir-biriga zid ma'lumotlarni taqdim etadi. Bundan tashqari, vazn yo'qotish samaradorligini tahlil qilish, 2-tip qandli diabetning remissiyasiga bag'ishlangan tadqiqotlarda ko'plab mualliflar mini-gastrik bypassga ustunlik berishga moyildirlar. Ba'zi tadqiqotlarga kelsak, ba'zi tadqiqotlarda Roux-en-Y gastrik bypassidan keyingi uzoq muddatli postoperativ davrda gastroenteroanomoz yaralari ko'p uchraydi. Shu bilan birga, tadqiqotlarning katta qismida biliar refluksni baholash klinik belgilarni turli tarozilar, so'rovnomalar va endoskopik ma'lumotlar yordamida tahlil qilish orqali shakllanadi va faqat uchta tadqiqotda morfologik tadqiqot amalga oshirildi. Bu esa ushbu ilmiy yo'nalishni mini-gastrik bypassdan so'ng xavf guruhlari ni aniqlash va o'zgartirish aralashuvlari bo'yicha o'z vaqtida qaror qabul qilish uchun nihoyatda va'da beradi.

**Tayanch iboralar:** gastrik bypass xirurgiyasi, bariatrik xirurgiya, operatsiyadan keyingi asoratlar

**Проблемы ранней патогенетической диагностики  
желчного рефлюкса после бариатрических  
операций**

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**АБСТРАКТ**

Во многих исследованиях, посвященных анализу отдаленных результатов шунтирующих операций, даются противоречивые сведения о преимуществах того или иного метода в лечении ожирения и сопутствующих коморбидных состояний. Более того, в исследованиях, посвященных анализу эффективности снижения веса, ремиссии сахарного диабета 2 типа, многие авторы склонны отдавать предпочтение мини-гастрошунтированию. Что касается некоторые исследования сообщают о большей частоте развития язв гастроэнтероанастомоза в отдаленные послеоперационные сроки после гастрошунтирования по Ру. Вместе с тем в абсолютном большинстве исследований оценка билиарного рефлюкса формируется путем анализа клинической симптоматики с использованием различных шкал, опросников и эндоскопическим данным, и лишь в трех работах был произведено морфологическое исследование. Это делает данное научное направление чрезвычайно перспективным для выявления групп риска после мини-гастрошунтирования и своевременного принятия решения о ревизионных вмешательствах.

**Ключевые слова:** шунтирующие операции желудка, бариатрическая хирургия, послеоперационные осложнения