ISSN 2786-5584 PRINT
ISSN 2786-5592 ONLINE

Ukrainian
Peer-Reviewed Scientific
and Practical Medical Journal

GENERAL SURGERY

1 (16) | 2026

ЗАГАЛЬНА ХІРУРГІЯ

Treatment tactics for patients with borderline resectable and locally advanced pancreatic cancer

Endoscopic transluminal interventions in the management of acute infected necrotizing pancreatitis

Acute skeletal muscle loss in surgically treated patients with severe infected necrotizing pancreatitis

Ukraine NOW ua

WWW.GENERALSURGERY.COM.UA

VIT-A-POL PUBLISHING COMPANY

ISSN 2786-5584 PRINT
ISSN 2786-5592 ONLINE
DOI 10.30978/GS

Bogomolets National Medical University
Національний медичний університет імені О. О. Богомольця

Ukrainian
Peer-Reviewed Scientific and Practical Medical Journal

1 (16) | 2026

GENERAL SURGERY

ЗАГАЛЬНА ХІРУРГІЯ

Український рецензований науковий спеціалізований медичний журнал

Founded in May 2021
Qpuarterly journal

Заснований у травні 2021 року
Виходить 4 рази на рік

The journal is registered as a professional edition of scientific research in the field of medicine and approved as a «B» list journal by the Ministry of Education and Science of Ukraine Order of the Ministry of Education and Science of Ukraine No 1166 as of December 23, 2022, Appendix 3

Журнал включено до Переліку наукових фахових видань України з медичних наук. Категорія «Б»
Наказ МОН України № 1166 від 23.12.2022 р., Додаток 3

Indexed in | Журнал зареєстрований та індексується в наукометричних базах і каталогах

BASE, Open AIRE, CrossRef, Vernadsky National Library of Ukraine, Google Scholar, OUCI, Scilit, WorldCat, Ulrich's Periodicals Directory

Kyiv | VIT-A-POL LLC | 2026

Founders
Bogomolets National Medical University
VIT-A-POL limited liability company

State registration
Register of entities in the field of media. Media ID R30-03941
Decision of the National Council of Ukraine on Television and Radio Broadcasting No 1440 dated April 25, 2024

Approved for printing by the Academic Council of Bogomolets National Medical University
Protocol No 10 signed March 24, 2026

Publishing
VIT-A-POL limited liability company
USREOU code 23720292
Certificate of publishing business entity
DK No 4757 granted August 5, 2014

Editorial office and publisher address
Office 3, 19a Academician St. Yefremov, Kyiv, 03179
Tel. +38096 70-21-152. E-mail: vitapol3@gmail.com

Project manager Bernyk O. M.
Translation and editing Sachuk O. V.
Design Mamchych V. S.

Signed for printing March 30, 2026. Circulation 400 copies

Printed
Pro Format Ltd.
USREOU code 41438677
45b, Kubanska Ukrayiny str., off. 16, 02166, Kyiv
Certificate of publishing business entity
DK No 5942 granted January 11, 2018

Printed on acid-free paper

Healthcare professionals are the intended audience for this journal

Засновники
Національний медичний університет імені О. О. Богомольця
Товариство з обмеженою відповідальністю «ВІТ-А-ПОЛ»

Державна реєстрація
Реєстр суб'єктів у сфері медіа. Ідентифікатор медіа R30-03941
Рішення Національної ради України з питань телебачення і радіомовлення № 1440 від 25.04.2024 р.

Рекомендовано Вченою радою
Національного медичного університету імені О. О. Богомольця
Протокол № 10 від 24.03.2026 р.

Видавець
Товариство з обмеженою відповідальністю «ВІТ-А-ПОЛ»
Код ЄДРПОУ 23720292
Свідоцтво суб'єкта видавничої справи
ДК № 4757 від 05.08.2014 р.

Адреса редакції та видавця
03179, м. Київ, вул. Академіка Єфремова, 19а, оф. 3
Тел. 096-70-21-152. E-mail: vitapol3@gmail.com

Менеджер проєкту Берник О. М.
Переклад та редагування тексту Сачук О. В.
Комп'ютерна верстка Мамчич В. С.

Підписано до друку 30.03.2026 р. Наклад 400 прим. Ум. др. арк. 8,84

Друк
Товариство з обмеженою відповідальністю «Про Формат»
Код ЄДРПОУ 41438677
Свідоцтво суб'єкта видавничої справи
ДК № 5942 від 11.01.2018 р.
02166, Київ, вул. Кубанської України, 45б, оф.16

Надруковано на безкислотному папері

Видання призначено для фахівців у галузі охорони здоров'я

BIOGRAPHIES

БІОГРАФІЇ

ОРИГІНАЛЬНІ ДОСЛІДЖЕННЯ

ОРИГІНАЛЬНІ ДОСЛІДЖЕННЯ

ОГЛЯДИ

REVIEWS

UDC 617(092)
DOI http://doi.org/10.30978/GS-2026-1-5

ISSN 2786-5584 PRINT
ISSN 2786-5592 ONLINE

Yosyp Hryhorovych Turovets – a life devoted to surgery

This article reviews the life and professional achievements of Yosyp Hryhorovych Turovets (1899–1987), an outstanding surgeon, scientist, and educator. It traces his path from a childhood in a peasant family in Volhynia to his professorship at the Kyiv Medical Institute. It highlights his academic training, clinical residency, and early medical practice, where his organisational skills became apparent. The article examines his wartime service in evacuation hospitals, participation in military campaigns, and research on gunshot wounds to blood vessels and joints. It notes his contributions to military field surgery, traumatology, reconstructive techniques, and the invention of a unique traumatological device. The article also discusses his post-war scientific and teaching activities, departmental leadership, training of scientific personnel, implementation of innovative surgical methods, and production of educational films. It emphasises his role in introducing the term «herniology» and advancing hernia surgery. The article concludes by recognising Turovets' significant impact on Ukrainian and global medicine, clinical science, and medical education.

Yosyp Hryhorovych Turovets was born on 1 April 1899 in the village of Nemylnia, Gulsk (Rogachiv) volost, Novograd-Volynskyi district, Volyn province (now Zhytomyr region) into a peasant family. He spent his childhood and youth in poverty, working hard on his native land. He attended a rural school and finished the Zhytomyr Educational Seminary in 1920. The challenging living conditions and the hard labour of peasants fostered in him a sense of prudence, kindness, and empathy, inspiring him to pursue a career in medicine and devote his life to improving public health in his homeland and throughout the world. In 1921, Yosyp Hryhorovych enrolled in the medical faculty of the Kyiv Medical Institute, graduating in 1926, and completed medical training at the Kyiv Clinical Military Hospital by 1928.

In 1928, Y. H. Turovets began a clinical residency in the Department of Propaedeutic Surgery at the Kyiv Medical Institute, which he completed in 1931. He then served as chief physician and surgeon at the district hospital in Velykyi Tokmak, Dnipropetrovsk Oblast until 1934. During this period, Yosyp Hryhorovych demonstrated strong organisational skills and talent by establishing and equipping an X-ray room, operating theatre, surgical department, and other hospital departments, significantly raising the hospital's surgical standards and making it the best district hospital and surgical facility in the region.

In September 1934, Yosyp Hryhorovych was appointed assistant professor of the Department of Propaedeutic Surgery at the Kyiv Medical Institute. In 1937, he defended his thesis on «Surgery for colon cancer».

From 1939, Y. H. Turovets was a senior resident at the surgical clinic of the Kyiv Military Hospital. He was a student of S. T. Novitsky, who later headed the Department of Operative Surgery at the Kyiv Medical Institute.

From September 1939 to August 1940, Yosyp HryHorovych took part in the Polish and Finnish wars. In June 1940, a conference on military field surgery was held in Kyiv, during which a wide range of issues was discussed. Kyiv surgeon Y. H. Turovets shared his experience of working in an evacuation hospital during recent military conflicts, outlining requirements for the treatment of gunshot wounds.

As a result of the conference discussions, an official ban was instituted on the immediate application

of primary sutures after the initial surgical treatment of gunshot wounds.

In June 1941, Yosyp Hryhorovych was drafted into the army once again, serving until January 1946. According to personal records from the command and management staff of the Kyiv Military Hospital dated July 1941, Y. H. Turovets held the position of resident physician and was classified as a military doctor of the 2nd rank at that time.

From June 1941 to May 1943, Yosyp Hryhorovych served as head of the surgical department at the Kyiv Military Hospital. After the hospital's evacuation to Tomsk, he supervised the training of military surgeons. In addition to serving as the head of the hospital department, he held the position of associate professor in the Department of Surgery at the Tomsk Medical Institute. In May 1942, Y. H. Turovets was sent to the front, where he served as the chief surgeon of the triage hospital and as an inspector-surgeon on the Southwestern, Stalingrad, Southern, and 4th Ukrainian fronts. During World War II, Major Turovets, as head of the trauma department at the Kyiv Military Hospital, collected extensive material on hip joint injuries and the surgical treatment of gunshot wounds to blood vessels. He noted that unfavourable outcomes in cases of gunshot wounds to blood vessels were associated with delays in receiving qualified medical assistance. In 1942, Yosyp Hryhorovych published an article in the journal «Surgery» entitled «Gunshot wounds to blood vessels». This work was later cited by the famous American surgeon Michael E. DeBakey in his 1946 article, «Battle injuries of the arteries in World War II», in Annals of Surgery.

According to the characteristics and review of the commander of military unit N 11956 dated 06.03.1951, Y. H. Turovets demonstrated exceptional qualifications as a surgeon, teacher, and scientist on the fronts of World War II. While serving on the front lines, he developed new techniques and addressed challenges in treating gunshot wounds to blood vessels and other injuries. He also designed an original, universal trauma traction device that was widely used in hospitals.

By integrating practical surgical and organisational responsibilities with extensive teaching, Yosyp Hryhorovych mentored many young doctors, who subsequently became leading surgeons.

In the post-war period, Y. H. Turovets worked as a senior researcher at the Institute of Blood Transfusion and Emergency Surgery in Kyiv. From 1950, he was an associate professor in the Department of Faculty Surgery at the Kyiv Medical Institute, headed by Prof. A. P. Krymov. In 1951, Yosyp Hryhorovych defended his doctoral dissertation entitled «Acute purulent complications of gunshot wounds to the hip joint». In 1953, he became a professor of the Department of Faculty Surgery at the Kyiv Medical Institute, serving as its head from 1954 to 1955. From 1956 to 1976, Prof. Turovets headed the Department of Surgery of the Sanitary and Hygienic Faculty at the Kyiv Medical Institute.

Yosyp Hryhorovych established a creative and friendly atmosphere within the department and clinic, characterised by professionalism, work discipline, ethical standards, unity, mutual support, and assistance among staff. He consistently demonstrated respect and care toward colleagues, students, and patients, generously sharing his knowledge and dedicating significant time to mentoring the next generation of medical professionals, particularly in surgery. Y. H. Turovets devoted special attention to clinical residents and young doctors, who regularly accompanied him during patient rounds, examinations, consultations, and surgical procedures. He often assisted them by performing some stages of surgical interventions, reflecting his excellence as a surgeon, teacher, and scientist. He was distinguished by his high erudition and exceptional technical proficiency in surgeries involving the abdominal cavity, chest, skull, thyroid gland, major blood vessels, and hematopoietic organs.

Yosyp Hryhorovych introduced novel approaches to the surgical treatment of stomach and duodenal ulcers, varicose veins of the lower extremities, gallbladder and intestinal diseases, and hernias. He also played a significant role in establishing modern anaesthesiology and advancing thyroid surgery.

Prof. Y. H. Turovets delivered lectures that incorporated the latest scientific achievements. In 1963, he released a full-length educational film titled «Alloplasty of Abdominal Hernias».

Between 1964 and 1966, several more educational films were produced, including «Necrosis», «Sclerotherapy of Varicose Veins of the Lower Extremities», and «Surgical Treatment of Goitre». These films were shown during lectures on corresponding surgical topics.

Yosyp Hryhorovych assembled a productive scientific team. Their planned research addressed important areas: potential anaesthesia in surgery, treatment of portal hypertension, surgical treatment of goitre, thrombophlebitis and its treatment, and prevention and treatment of paraproctitis. Over the years, the staff authored about 200 scientific papers.

Regular methodological meetings were conducted to discuss and approve methodological developments for each topic. Methodological guidelines for patient care and clinical training were established, and a comprehensive list of required clinical studies

for students was defined. Extensive teaching materials, including tables, slides, and diafilms, were produced for demonstrations in lectures and practical classes, which also featured patient demonstrations. Additional sources such as visual aids, a museum of macro preparations, and a biochemical laboratory were also created.

The international community of herniologists recognises Y. H. Turovets for introducing the term «herniology». He was the first to use this term in his 1965 article «Problems of Modern Herniology» in the journal «Clinical Surgery», where he described the current state of anterior abdominal wall hernia treatment. Under his supervision, five candidate dissertations and one doctoral dissertation were defended.

From 1976 to 1982, Yosyp Hryhorovych served as a professor-consultant. By that time, his wife had died, and they had no children. He spent his last years living modestly, alone, practically in oblivion.

Y. H. Turovets died in 1987 and was buried in Berkovtsy Cemetery.

References

1. Національний медичний університет імені О. О. Богомольця. 160 років Національному медичному університету імені О. О. Богомольця (1841-2001]) Гончарук ЄГ, редактор. Київ: Століття; 2001. 368 с. ISBN: 966-95952-2-3.
2. Іоффе ОЮ, Діброва ЮА, Цюра ЮП, Стеценко ОП, Тарасюк ТВ, та ін. Від минулого до майбутнього крізь сучасність. Історія кафедри загальної хірургії № 2. Київ: Медпринт; 2024. 312 с.

Y. P. Tsyura, M. S. Kryvopustov
Bogomolets National Medical University

Йосип Григорович Туровець — життя, присвячене хірургії

Ю. П. Цюра, М. С. Кривопустов

Національний медичний університет імені О. О. Богомольця, Київ

Стаття присвячена видатному хірургу, ученому й педагогу Йосипу Григоровичу Туровцю (1899—1987). Простежено його шлях від дитинства в селянській родині на Волині до професора Київського медичного інституту. Висвітлено роки навчання, клінічної ординатури та ранньої лікарської практики, де виявилися його організаторські здібності. Значну увагу приділено воєнному періоду: роботі в евакогоспіталях, участі в бойових кампаніях, науковому аналізу вогнепальних поранень судин і суглобів. Відзначено внесок Туровця в розвиток військово-польової хірургії, травматології та реконструктивних методик, а також створення оригінального травматологічного апарата. Представлено його науково-педагогічну діяльність у повоєнні роки, керівництво кафедрами, підготовку наукових кадрів, розробку нових хірургічних підходів і створення навчальних фільмів. Висвітлено роль ученого у впровадженні терміна «герніологія» та розвитку хірургії гриж. Зроблено висновок про вагомий внесок Й.Г. Туровця в українську і світову медицину, клінічну науку та медичну освіту.

UDC 616.37-007.253-039.71-089.168:616.37+616.342]-089.87
DOI http://doi.org/10.30978/GS-2026-1-8

ISSN 2786-5584 print
ISSN 2786-5592 online

Treatment tactics for patients with borderline resectable and locally advanced pancreatic cancer

V. M. Kopchak[1], L. O. Pererva[1], O. V. Duvalko[1], V. V. Khanenko[1], V. I. Trachuk[1], V. Y. Bondar[1], Z. Y. Holobor[2]

[1] O. O. Shalimov National Center of Surgery and Transplantology of NAMS of Ukraine, Kyiv
[2] Bogomolets National Medical University, Kyiv

✉ Pererva Liudmyla: liudmylapererva@gmail.com

V. M. Kopchak, http://orcid.org/0000-0003-0134-7500
L. O. Pererva, http://orcid.org/0000-0002-4030-1030
O. V. Duvalko, http://orcid.org/0000-0001-7423-916X
V. V. Khanenko, http://orcid.org/0000-0003-4548-0039
V. I. Trachuk, http://orcid.org/0000-0002-7663-7011
V. Y. Bondar, http://orcid.org/0009-0008-8684-8243
Z. Y. Holobor, http://orcid.org/0009-0000-0912-4606

Objective – to evaluate the outcomes of extended pancreatic resections in the treatment of patients with borderline resectable and locally advanced pancreatic cancer and to identify strategies for improving the effectiveness of these procedures.

Materials and methods. Between 2010 and 2023, a total of 874 pancreatic resections were performed for patients with pancreatic adenocarcinoma: 142 distal pancreatosplenectomies (16.2%), 706 pancreaticoduodenectomies (80.8%), and 26 total pancreatectomies (3.0%). The cohort included 388 females (44.4%) and 486 males (55.6%), with a mean age of 57.7 ± 10.5 years (range: 22–81). Extended pancreatic resections were conducted in 202 (23.1%) patients, comprising 130 extended pancreaticoduodenectomies (64.4%), 58 extended distal pancreatosplenectomies (28.7%), and 14 extended total pancreatectomies (6.9%). A total of 144 (71.3%) patients underwent pancreatic resections with venous resections, 13 (6.4%) with arterial resections, 3 (1.5%) with combined vascular resections, and 42 (20.8%) with resections of adjacent organs.

Results. Postoperative complications were observed in 248 patients (36.9%) in the standard resection group and in 84 patients (41.6%) in the extended resection group ($\chi^2 = 1.4$; $p = 0.22$), with no statistically significant difference. The mortality rate was 2.6%, with 23 deaths: 16 (2.4%) after standard pancreatic resections and 7 (3.5%) after extended pancreatic resections, indicating no statistically significant difference ($\chi^2 = 0.71$; $p = 0.39$). Implementation of a personalized treatment algorithm increased the median survival of patients with borderline resectable and locally advanced pancreatic head cancer from 19 to 28 months ($\chi^2 = 1.7$; $p = 0.18$) and the five-year survival from 22% to 28.5%. For patients with pancreatic cancer of the body and tail, median survival increased from 22 to 36 months ($\chi^2 = 1.78$; $p = 0.18$) and five-year survival from 24% to 34% ($\chi^2 = 1.78$; $p = 0.18$).

Conclusions. The results suggest that morbidity and mortality after extended pancreatic resections are comparable to those observed after standard pancreatic resections. Extended resections are feasible and can increase the number of patients eligible for radical surgery. Implementation of the developed treatment algorithm was associated with improved median survival in patients with borderline resectable and locally advanced pancreatic cancer.

Keywords
extended pancreatic resections, pancreatic cancer, borderline resectable pancreatic cancer, locally advanced pancreatic cancer, venous resections, arterial resections.

ARTICLE • Received 2026-01-26 • Received in revised form 2026-03-03 • Published 2026-03-31

Despite advancements in diagnostic and surgical techniques, pancreatic ductal adenocarcinoma (PDAC) remains the fourth leading cause of cancer-related mortality in Europe and the United States, with a persistently low five-year survival rate [12, 18]. Expert projections suggest that pancreatic cancer may become the second leading cause of cancer-related death worldwide within the next decade [20].

The incidence of pancreatic cancer in Ukraine is rising. At the time of diagnosis, only 10–25 % of patients with pancreatic adenocarcinoma have resectable tumours. Approximately 60 % of patients globally present with tumour extension to adjacent organs and vessels. Locoregional progression and early systemic dissemination of malignant pancreatic tumours frequently result in local invasion of major vessels and adjacent organs, thereby limiting resectability [13, 17, 19]. Advances in surgical techniques and systemic chemotherapy have broadened the indications for pancreatic resection to include borderline resectable and locally advanced tumours. Consequently, extended pancreatic resections involving adjacent organs and vessels often represent the only radical treatment option to improve survival in this patient population [2, 9, 11, 22, 23].

Postoperative complication rates after pancreatic resections are among the highest in abdominal surgery, ranging from 30 % to 60 % [20]. The risk associated with extended pancreatic resections, particularly those involving arterial resection, remains substantial. Nevertheless, recent evidence suggests that survival outcomes after extended resections with venous and arterial reconstruction surpass those achieved with palliative surgery and chemotherapy [4, 5, 10, 16]. Therefore, ongoing refinement of surgical techniques and the development of strategies to reduce complications are essential to improve long-term outcomes in patients undergoing extended pancreatic resections for malignant tumours.

Materials and methods

Between 2010 and 2023, a total of 874 pancreatic resections were performed for patients with malignant pancreatic tumours: 142 distal pancreatosplenectomies (16.2 %), 706 pancreaticoduodenectomies (80.8 %), and 26 total pancreatectomies (3.0 %). The cohort included 486 males (55.6 %) and 388 females (44.4 %), with a mean age of 57.7 ± 10.5 years (range: 22–81). Extended pancreatic resections were conducted in 202 (23.1 %) patients, comprising 130 extended pancreaticoduodenectomies (64.4 %), 58 extended distal pancreatosplenectomies (28.7 %), and 14 extended total pancreatectomies (6.9 %).

All patients underwent a planned preoperative examination, which included computed tomography of the chest and abdominal organs with intravenous contrast no later than 4 weeks before determining the treatment tactics and MRI with DWI mode in patients with suspected metastatic liver damage and distant metastases. A blood test for the oncological marker CA 19–9 was mandatory. Using preoperative examination data, the anatomical resectability of the tumour was assessed. The diagnosis was confirmed by morphological examination of the specimens.

Among patients undergoing extended pancreatic resections, 144 (71.3 %) had venous resections, 13 (6.4 %) arterial resections, 3 (1.5 %) combined vascular resections, and 42 (20.8 %) resections of adjacent organs.

Venous resection types were defined based on the International Study Group of Pancreatic Surgery (ISGPS) classification. Tangential venous resection with venorrhaphy (type A) was performed in 64 patients. Tangential venous resection with patch venoplasty (type B) was conducted in 3 patients. Segmental resection with end-to-end venous anastomosis (type C) was performed in 74 patients. Segmental resection, including venoplasty with either an autologous vein or a prosthetic graft (type D) was conducted in 3 patients, with autologous vein grafts used in 2 cases and a prosthetic graft in 1 case.

Arterial resections were performed in 16 patients with borderline resectable or locally advanced pancreatic tumours that exhibited arterial vessel invasion. Among these, 4 patients underwent extended pancreaticoduodenectomy with arterial resection: 1 patient had pancreaticoduodenectomy with segmental resection of the left hepatic artery, 2 patients had pancreaticoduodenectomy with resection of the right hepatic artery, and 1 patient had pancreaticoduodenectomy with resection of the common hepatic artery. In all cases, end-to-end arterial anastomosis was performed. Extended distal pancreatosplenectomy with arterial vessel resection was performed in 11 patients. Of these, 9 patients underwent a modified Appleby operation, with one patient also requiring resection of the portosplenomesenteric confluence (Fig. 1). In 2 patients, combined resections (arterial resections with additional resection of the affected organs) were performed: 1 patient underwent distal pancreatic resection (posterior radical antegrade modular pancreatosplenectomy [RAMPS posterior]) with resection of the left gastric artery and left crus of the diaphragm, while another patient underwent distal subtotal pancreatosplenectomy with resection of the portosplenomesenteric confluence, colonic mesentery, and common hepatic artery.

Extended total pancreatectomies were performed in 14 patients (6.9 %). Among these, one case involved combined arterial-venous resection, specifically the portosplenomesenteric confluence, with resection and reconstruction of the right hepatic artery, which originated from the superior mesenteric artery as a separate trunk. 13 cases involved extended total pancreatectomy with only venous resections. Of these, one included resection of the

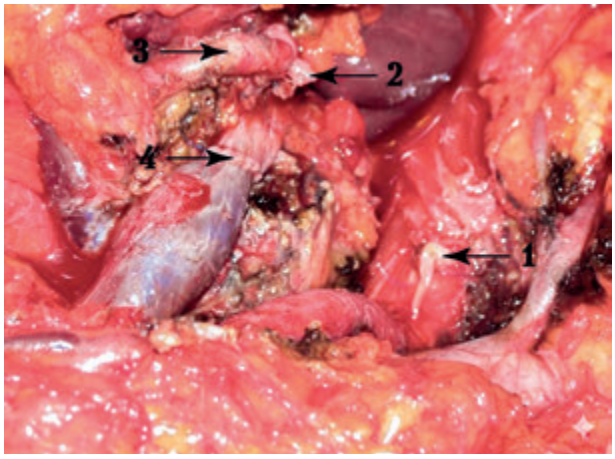

Figure 1. **Intraoperative photo. Modified Appleby operation with additional resection of the portosplenomesenteric confluence:** 1 – stump of the celiac trunk, 2 – stump of the common hepatic artery, 3 – gastroduodenal artery, 4 – end-to-end venous anastomosis

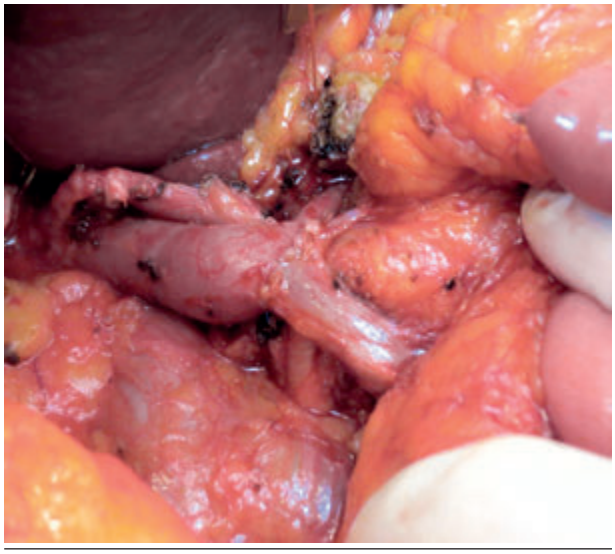

Figure 2. **Intraoperative photo. Pancreaticoduodenal resection with resection of the portosplenomesenteric confluence and end-to-end venous anastomosis, with wedge-shaped resection of the portal vein, and the extension of the incision to the splenic vein confluence**

portosplenomesenteric confluence and the inferior vena cava, and another involved total pancreatectomy with nephrectomy.

Postoperative complications were assessed according to the International Study Group of Pancreatic Surgery (ISGPS) guidelines. Mortality was defined as death occurring in the hospital after surgery.

Specific surgical complications included pancreatic fistula, as defined by the revised criteria of the International Study Group of Pancreatic Fistula [1], as well as postpancreatectomy bleeding and delayed gastric emptying.

Risk factors for postoperative complications were identified, and targeted preventive measures were developed to reduce their incidence.

To minimize intraoperative blood loss during both standard and extended pancreaticoduodenectomy, the inferior pancreaticoduodenal artery was ligated at the initial stage of mobilization of the pancreaticoduodenal complex, when technically feasible. This approach reduced intraoperative blood loss.

In cases of venous invasion, the surgical team employed venous reconstruction techniques. These techniques enabled the reconstruction of venous vessels and the safe formation of venous anastomoses without the use of prosthetic venous grafts. For pancreatic head tumours invading the portal vein, a specific pancreatic head resection method (patent No 95976) was used. This technique involves wedge-shaped resection of the portal vein, extending the incision beyond the splenic vein confluence, and forming a venous anastomosis between the proximal and distal segments of the splenic vein (Fig. 2).

The criteria used to compare standard and extended surgical interventions included complication rate, operative time, blood loss, length of hospital stay, and mortality.

The collected data were digitized and compiled into a unified database. Mathematical methods were used to identify risk factors for postoperative complications. Relationships between factors and complication frequency were analysed using contingency tables and the chi-square test. The Spearman rank correlation coefficient (ρ) was calculated to determine associations between two variables. Differences in mean values were evaluated using the Mann–Whitney test. Long-term treatment outcomes were assessed by calculating actuarial five-year survival rates with the Kaplan–Meier method. All statistical analyses were conducted using MS Excel and Statistica 5.0 software.

Since 2018, new tactical approaches and perioperative management strategies have been implemented to prevent postoperative pancreatic fistula and other complications.

Sarcopenia was detected in patients by computed tomography during preoperative planning. Patients diagnosed with sarcopenia received specialized nutrition to improve their sarcopenic profile. A prerehabilitation programme was implemented. Nutritional status was evaluated with active nutritional support before surgery. Postoperative pancreatic fistula was identified as a primary source of severe postoperative complications. During pancreaticoduodenectomy, the risk of postoperative pancreatic fistula was assessed intraoperatively in all patients using the modified Callery–Kopchak scale

Table 1. **Modified Pancreatic Fistula Risk Scale (M.Callery — V.Kopchak)**

Risk factor	Points
Pathology	
Pancreatic adenocarcinoma or pancreatitis	0
Adenocarcinoma of the major duodenal papilla, distal part of the common bile duct, duodenum, cystic tumours, neuroendocrine tumours	1
Pancreatic duct diameter, mm	
≥ 5	0
4	1
3	2
2	3
≤ 1	4
Intraoperative blood loss, ml	
≤ 400	0
401–700	1
701–1000	2
> 1000	3
Pancreatic fibrosis, %	
< 15	2
15–30	1
> 30	0

(Table 1). Appropriate surgical techniques were used to prevent postoperative pancreatic fistula, including various pancreaticojejunostomy methods.

For high-risk patients (7–10 points) at the reconstructive stage after pancreaticoduodenectomy, pancreaticojejunal anastomosis with external drainage of the main pancreatic duct was performed. In moderate-risk patients (4–6 points), pancreaticojejunal anastomosis with invagination was conducted. Preliminary data indicate that this approach was associated with the lowest incidence of postoperative pancreatic fistulas. In low-risk patients (0–3 points), the choice of anastomosis was determined by the surgeon. To minimize postoperative blood loss, ligation of the inferior pancreaticoduodenal artery was implemented during the initial stage of pancreaticoduodenectomy, resulting in a significant reduction in intraoperative blood loss from 450.7 ± 184.3 ml to 356.25 ± 197.4 ml (p = 0.003).

All patients diagnosed with malignant tumours in the left anatomical segment of the pancreas underwent radical antegrade modular pancreatosplenectomy.

The results of extended pancreatic resections, median survival, and five-year survival rates were compared between two periods: 2010–2017 and 2018–2023, the latter reflecting the implementation of newly developed methods and algorithms. The patient groups were comparable with respect to comorbidities, disease stage, and the number of extended pancreatic resection variants performed.

Results

Table 2 presents data on postoperative complications after standard and extended pancreatic resections.

Postoperative complications were observed in 248 patients (36.9 %) in the standard resection group and in 84 patients (41.6 %) in the extended pancreatic resection group; this difference was not statistically significant ($\chi^2 = 1.4$; p = 0.22). A total of 23 patients (2.6 %) died: 7 (3.5 %) after extended pancreatic resections and 16 (2.4 %) after standard pancreatic resections. Patients who underwent extended pancreatic resections had higher mortality, though the difference was not statistically significant ($\chi^2 = 0.71$; p = 0.39).

Table 2. **Comparative characteristics of standard and extended pancreatic resections**

Parameter	Pancreatoduodenectomy		Distal pancreatosplenectomy		Total pancreatectomy	
Resection	**Standard (n = 576)**	**Extended (n = 130)**	**Standard (n = 84)**	**Extended (n = 58)**	**Standard (n = 12)**	**Extended (n = 14)**
Operative time, min	366 ± 78	387 ± 72	253 ± 60	305 ± 71	361 ± 78	396 ± 56
p	0.03 (U = 6515)		0.0006 (U = 343.0)		0.56 (U = 19)	
Blood loss, ml	420 ± 229	627 ± 556	513 ± 333	610 ± 330	649 ± 460	950 ± 459
p	0.10 (U = 6462)		0.32 (U = 1617)		0.26 (U = 15)	
Complication rate	164 (28.4 %)	38 (29.2 %)	18 (21.4 %)	17 (29.3 %)	45 (41.7 %)	6 (42.8 %)
p	0.10 ($\chi^2 = 0.26$)		0.30 ($\chi^2 = 1.1$)		0.50 ($\chi^2 = 0.3$)	
Length of hospital stay, days	18.7 ± 13.7	20.4 ± 11.7	13.6 ± 6.9	20.5 ± 14.4	16.0 ± 5.3	12.0 ± 7.4
p	0.87 (U = 8660)		0.25 (U = 755.0)		0.19 (U = 16.5)	

Complications were reported in 64 patients (44.4 %) after venous resections, a rate higher than that observed after standard resections (248 patients, 36.9 %). However, this difference was not statistically significant ($\chi^2 = 2.8$; $p = 0.09$). In the venous resection group, 5 patients (3.5 %) died. This group had higher mortality, though not statistically significant ($\chi^2 = 0.56$; $p = 0.45$), compared to the standard resection group (16 patients, 2.4 %). Thus, no statistically significant difference in the incidence of complications or mortality was identified between extended pancreatic resections with venous resections and standard resections.

A total of 11 patients (68.7 %) who underwent arterial resections had a higher complication rate than that observed after standard pancreatic resections; this difference was statistically significant ($\chi^2 = 6.3$; $p = 0.01$). The arterial resection group had higher (1 patient, 6.2 %), though not statistically significant ($\chi^2 = 1.68$; $p = 0.2$), mortality compared to the standard resection group (2.4 %, 16 patients).

No statistically significant difference in the incidence of complications or mortality was observed between extended pancreatic resections involving resection of adjacent organs and standard resections.

The most clinically significant complications are pancreatic fistula, post-pancreatectomy haemorrhage, and delayed gastric emptying.

Pancreatic fistula occurred in 27 patients (13.4 %) after extended resections and in 87 patients (12.9 %) after standard resections; this difference was not statistically significant ($\chi^2 = 0.02$; $p = 0.8$). Post-pancreatectomy haemorrhage was observed in 17 patients (8.4 %) and 39 patients (5.8 %), respectively; this difference was not statistically significant ($\chi^2 = 1.76$; $p = 0.2$). Gastrostasis developed in 9 patients (4.5 %) and 23 patients (3.4 %), respectively; this difference was not statistically significant ($\chi^2 = 0.4$; $p = 0.5$). Therefore, no statistically significant difference was found in the overall or specific rates of postoperative complications, including pancreatic fistula, post-pancreatectomy haemorrhage, and delayed gastric emptying, between standard and extended resections. Extended resections are feasible when performed in specialized centres with substantial experience in these surgical procedures.

A comparison was conducted regarding the incidence of clinically significant postoperative pancreatic fistula (grades B and C), total complications, and mortality after pancreaticoduodenectomy in 280 patients treated between 2018 and 2023 and 426 patients treated between 2010 and 2017. The patient groups were comparable with respect to comorbidities, the number of extended pancreaticoduodenectomies performed, and disease stage.

Implementation of the newly developed method for preventing postoperative pancreatic fistula resulted in a significant reduction in its incidence in the main group (31 cases, 11.1 %), which is nearly half the rate observed in the comparison group (91 cases, 21.8 %; $\chi^2 = 12.5$; $p = 0.0004$).

A statistically significant reduction in the total complication rate was observed, decreasing from 43.7 % to 27.1 % ($\chi^2 = 19.7$; $p = 0.0001$). However, a reduction in the mortality rate from 2.1 % (9 of 426 patients in the comparison group) to 1.4 % (4 of 280 patients in the main group) was not statistically significant ($\chi^2 = 0.4$; $p = 0.5$).

Comparison of extended pancreatic resections across the two periods demonstrated a statistically significant reduction in postoperative complications in the main group from 46.1 % to 28.6 % ($\chi^2 = 6.64$; $p = 0.009$), whereas a decrease in mortality from 4.8 % to 2.0 % was not statistically significant ($\chi^2 = 1.15$; $p = 0.28$).

The implementation of a personalized diagnostic and treatment algorithm, which incorporated a comprehensive approach, differentiated treatment strategies based on risk factors for postoperative complications, and targeted preventive measures, resulted in an increase in median survival for patients with locally advanced pancreatic head tumours from 19 to 28 months ($\chi^2 = 1.7$; $p = 0.18$) and five-year survival from 22 % to 28.5 %. For patients with malignant tumours of the body and tail of the pancreas, median survival increased from 22 to 36 months ($\chi^2 = 1.78$; $p = 0.18$), and the five-year survival rate improved from 24 % to 34 % ($\chi^2 = 1.78$; $p = 0.18$).

Discussion

Recent advances in polychemotherapy and the development of new surgical techniques, including extended pancreatic resections with venous and arterial resections and reconstructions, have enabled patients with initially unresectable pancreatic tumours to become candidates for surgical intervention at high-volume pancreatic surgery centres [1, 4, 5, 10, 15, 16, 22, 24].

Retrospective analyses by international authors indicate that extended pancreatic resections are associated with significantly longer operative times and increased blood loss [8, 24]. However, the rates of postoperative complications and mortality are comparable to those observed with standard techniques [8, 20, 24].

The present study indicates longer operative time, though not statistically significant, for extended pancreaticoduodenectomy and extended distal pancreaticosplenectomy compared to standard

resections. No statistically significant differences were observed in blood loss, length of hospital stay, complication rates, or mortality.

Multiple studies have demonstrated no significant difference in long-term survival, postoperative complications, or mortality between patients with and without venous resection [1, 7, 15, 20]. The present findings are consistent with these results. The venous resection group had higher mortality, though not statistically significant, compared to the standard resection group. Resection of affected major venous vessels did not have a statistically significant impact on postoperative complication rates or mortality compared to standard resections.

An increased incidence of complications and mortality after arterial resections and reconstructions has been observed both in high-volume pancreatic surgery centres and in the present study.

Historically, arterial resections in pancreatic cancer surgery were considered inappropriate due to the high risk of postoperative complications and mortality associated with extended pancreatic resections involving arterial vessels. However, recent studies have demonstrated significant survival benefits for patients undergoing these procedures compared with those receiving palliative operations, with a median survival of 6–8 months [4, 9, 10, 13, 16]. In the present study, the arterial resection group (6.2 %) had higher mortality, though not statistically significant ($\chi^2 = 1.68$; $p = 0.2$), compared to the standard resection group (2.4 %).

Following two pancreaticoduodenal resections with right hepatic artery resection, patients survived for 18 and 31 months, respectively. In the present study, a patient who underwent distal resection (RAMPS posterior with resection of the left gastric artery and left crus of the diaphragm) survived for 12 months without recurrence. Another patient who underwent a modified Appleby operation (distal subtotal pancreatic resection with resection of the celiac trunk) with portosplenomesenteric confluence resection and end-to-end anastomosis survived for 14 months without recurrence.

Postoperative pancreatic fistula is among the most serious complications of pancreatic surgery and can precipitate other life-threatening conditions [1]. Risk assessment for postoperative pancreatic fistula is a critical initial step in pancreatic surgery to prevent its occurrence and mitigate adverse outcomes. An ideal method of pancreaticojejunal anastomosis that completely prevents fistula formation has not yet been established. One preventive approach involves pancreaticojejunal anastomosis with external drainage of the main pancreatic duct. However, studies have not consistently demonstrated the benefits of main pancreatic duct stenting [14]. B. L. Ecker and M. T. McMillan reported that stent use reduces the incidence of clinically significant postoperative pancreatic fistulas [6]. Y. Dai et al. found that stent implantation may benefit patients with a non-dilated pancreatic duct or those with a main pancreatic duct stent and external drainage [3]. Ying Sun et al., in an analysis of 20 randomized controlled trials (1117 patients after pancreaticoduodenectomy with pancreaticojejunostomy), found that only external, not internal, stents were significantly associated with reduced incidence of clinically significant grade B and C pancreatic fistulas compared to no stents. Additionally, stenting in patients with a main pancreatic duct diameter ≤ 3 mm, but not in those with a diameter > 3 mm, was associated with a significantly reduced incidence of clinically significant grade B and C pancreatic fistula compared to no stent [21]. In the present study, pancreaticojejunostomy with main pancreatic duct stenting and external drainage significantly reduced the incidence of postoperative pancreatic fistulas of grade B and C, as well as overall postoperative complications and mortality. Surgical tactics to reduce postoperative pancreatic fistulas and other complications should be continually refined for both standard and extended pancreatic resections.

In the context of modern multidisciplinary management of malignant pancreatic tumours, radical extended pancreatic resection with venous and arterial resections is justified and should be performed in specialized expert centres.

Conclusions

The rates of total postoperative complications, postoperative pancreatic fistula, gastrostasis, postpancreatectomy haemorrhage, and mortality after extended pancreatic resections are comparable to those observed after standard resections. Extended pancreatic resections are feasible and oncologically justified. Their implementation increases the number of radical surgical interventions, without a statistically significant increase in complication or mortality rates.

By implementing surgical tactics to prevent postoperative pancreatic fistulas and other complications, the incidence of postoperative complications in patients undergoing extended pancreatic resections was reduced from 46.1 % to 28.6 %, and mortality decreased from 4.8 % to 2.0 %.

The implementation of a personalized diagnostic and treatment algorithm, which incorporated a comprehensive approach, differentiated treatment strategies based on risk factors for postoperative

complications, and targeted preventive measures, resulted in an increase in median survival for patients with locally advanced pancreatic head tumours from 19 to 28 months ($\chi^2 = 1.7$; $p = 0.18$) and five-year survival from 22 % to 28.5 %. For patients with malignant tumours of the body and tail of the pancreas, median survival increased from 22 to 36 months ($\chi^2 = 1.78$; $p = 0.18$), and the five-year survival rate improved from 24 % to 34 % ($\chi^2 = 1.78$; $p = 0.18$).

Acknowledgements

The authors express their sincere gratitude to the leadership of our center, as well as to the staff of the Department of Pancreatic and Bile Duct Surgery and the Department of Anaesthesiology.

Declaration of interests

The authors declare no conflict of interest.

Funding. This work was funded by the authors..

Authors contributions

Conception and design — V. M. Kopchak, L. O. Pererva; data acquisition, analysis and interpretation of data, statistical data processing, drafting the article — L. O. Pererva, O. V. Duvalko, V. V. Khanenko, V. I. Trachuk, V. Y. Bondar, Z. Y. Holobor.

References

1. Bassi C, Marchegiani G, Dervenis C, et al.; International Study Group on Pancreatic Surgery (ISGPS). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. Surgery. 2017 Mar;161(3):584-591. doi: 10.1016/j.surg.2016.11.014. Epub 2016 Dec 28. Erratum in: Surgery. 2024 Sep;176(3):988-989. doi: 10.1016/j.surg.2024.05.043. PMID: 28040257.
2. Cillo U, Perri G, Bassi D, Pellegrini R, et al. Pancreatectomy with venous resection and peritoneal patch reconstruction: bridging transplantation and pancreatic surgery to combine the advantages of tangential and segmental resections. HPB (Oxford). 2025 Oct;27(10):1318-1327. doi: 10.1016/j.hpb.2025.07.010. Epub 2025 Jul 12. PMID: 40717005.
3. Dai Y, Lu X, Jiang L, Lu Z, Jiang K, Miao Y, Wei J. The impact of pancreatic duct stent placement on the clinically relevant postoperative pancreatic fistula rate for high-risk anastomoses: a systematic review and meta-analysis. BMC Gastroenterol. 2025 Feb 25;25(1):116. doi: 10.1186/s12876-025-03700-w. PMID: 40000944; PMCID: PMC11852884.
4. Del Chiaro M, Rangelova E, Halimi A, et al. Pancreatectomy with arterial resection is superior to palliation in patients with borderline resectable or locally advanced pancreatic cancer. HPB (Oxford). 2019 Feb;21(2):219-225. doi: 10.1016/j.hpb.2018.07.017. Epub 2018 Aug 6. PMID: 30093144.
5. Ducreux M, Cuhna AS, Caramella C, et al.; ESMO Guidelines Committee. Cancer of the pancreas: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol. 2015 Sep;26 Suppl 5:v56-68. doi: 10.1093/annonc/mdv295. Erratum in: Ann Oncol. 2017 Jul 1;28(suppl_4):iv167-iv168. doi: 10.1093/annonc/mdx258. PMID: 26314780.
6. Ecker BL, McMillan MT, et al. Characterization and Optimal Management of High-risk Pancreatic Anastomoses During Pancreatoduodenectomy. Ann Surg. 2018 Apr;267(4):608-616. doi: 10.1097/SLA.0000000000002327. PMID: 28594741.
7. Hackert T, Klaiber U, Hinz U, Strunk S, Loos M, Strobel O, Berchtold C, Kulu Y, Mehrabi A, Müller-Stich BP, Schneider M, Büchler MW. Portal Vein Resection in Pancreatic Cancer Surgery: Risk of Thrombosis and Radicality Determine Survival. Ann Surg. 2023 Jun 1;277(6):e1291-e1298. doi: 10.1097/SLA.0000000000005444. Epub 2022 Jul 6. PMID: 35793384.
8. Hartwig W, Gluth A, Hinz U, Koliogiannis D, Strobel O, Hackert T, Werner J, Büchler MW. Outcomes after extended pancreatectomy in patients with borderline resectable and locally advanced pancreatic cancer. Br J Surg. 2016 Nov;103(12):1683-1694. doi: 10.1002/bjs.10221. Epub 2016 Sep 30. PMID: 27686238.
9. Hartwig W, Vollmer CM, Fingerhut A, Yeo CJ, Neoptolemos JP, Adham M, Andrén-Sandberg A, Asbun HJ, Bassi C, Bockhorn M, Charnley R, Conlon KC, Dervenis C, Fernandez-Cruz L, Friess H, Gouma DJ, Imrie CW, Lillemoe KD, Milićević MN, Montorsi M, Shrikhande SV, Vashist YK, Izbicki JR, Büchler MW; International Study Group on Pancreatic Surgery. Extended pancreatectomy in pancreatic ductal adenocarcinoma: definition and consensus of the International Study Group for Pancreatic Surgery (ISGPS). Surgery. 2014 Jul;156(1):1-14. doi: 10.1016/j.surg.2014.02.009. Epub 2014 Feb 20. PMID: 24856668.
10. Hirose Y, Oba A, Inoue Y, Maekawa A, Kobayashi K, Omiya K, Takahashi A, Ono Y, Sato T, Ito H, Mie T, Sasaki T, Ozaka M, Sasahira N, Wakai T, Takahashi Y. Arterial resection and divestment in pancreatic cancer surgery in the era of multidisciplinary treatment: decadal comparative study. BJS Open. 2025 Mar 4;9(2):zraf026. doi: 10.1093/bjsopen/zraf026. PMID: 40244877; PMCID: PMC12005265.
11. Hoffman D, Ganjouei AA, Hernandez FR, et al. Graft choice in pancreatectomy with vascular resection: equivalent safety in selected patients. J Gastrointest Surg. 2024 Nov;28(11):1799-1804. doi: 10.1016/j.gassur.2024.08.016. Epub 2024 Aug 22. PMID: 39181231.
12. Kaiser J, Hackert T, Büchler MW. Extended Pancreatectomy: Does It Have a Role in the Contemporary Management of Pancreatic Adenocarcinoma? Dig Surg. 2017;34(6):441-446. doi: 10.1159/000478539. Epub 2017 Jul 13. PMID: 28700995.
13. Kasumova GG, Conway WC, Tseng JF. The Role of Venous and Arterial Resection in Pancreatic Cancer Surgery. Ann Surg Oncol. 2018 Jan;25(1):51-58. doi: 10.1245/s10434-016-5676-3. Epub 2016 Nov 23. PMID: 27882472.
14. Kawaida H, Kono H, Hosomura N, et al. Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery. World J Gastroenterol. 2019 Jul 28;25(28):3722-3737. doi: 10.3748/wjg.v25.i28.3722. PMID: 31391768; PMCID: PMC6676555.
15. Libia A, Marchese T, D'Ugo S, et al. Use of Vascular Shunt at the Time of Pancreatectomy with Venous Resection: A Systematic Review. Cancers (Basel). 2024 Jun 27;16(13):2361. doi: 10.3390/cancers16132361. PMID: 39001423; PMCID: PMC11240683.
16. Małczak P, Sierżęga M, Stefura T, et al. Arterial resections in pancreatic cancer – Systematic review and meta-analysis. HPB (Oxford). 2020 Jul;22(7):961-968. doi: 10.1016/j.hpb.2020.04.005. Epub 2020 Apr 30. PMID: 32360186.
17. Miao Y, Cai B, Lu Z. Technical options in surgery for artery-involving pancreatic cancer: Invasion depth matters. Surg Open Sci. 2023 Mar 3;12:55-61. doi: 10.1016/j.sopen.2023.03.001. PMID: 36936450; PMCID: PMC10020102.
18. Mizrahi JD, Surana R, Valle JW, Shroff RT. Pancreatic cancer. Lancet. 2020 Jun 27;395(10242):2008-2020. doi: 10.1016/S0140-6736(20)30974-0. PMID: 32593337.
19. Sinn M, Bahra M, Denecke T, Travis S, Pelzer U, Riess H. Perioperative treatment options in resectable pancreatic cancer – how to improve long-term survival. World J Gastrointest Oncol. 2016 Mar 15;8(3):248-57. doi: 10.4251/wjgo.v8.i3.248. PMID: 26989460; PMCID: PMC4789610.
20. Strobel O, Neoptolemos J, Jäger D, Büchler MW. Optimizing the outcomes of pancreatic cancer surgery. Nat Rev Clin Oncol. 2019 Jan;16(1):11-26. doi: 10.1038/s41571-018-0112-1. PMID: 30341417.
21. Sun Y, Li Y, Liu Z, Peng T, Wang C, Wu H, Gou S. Stent placement for the prevention of clinically-relevant postoperative pancreatic fistula following pancreaticojejunostomy: A systematic review and meta-analysis. Am J Surg. 2024 Aug;234:122-128. doi: 10.1016/j.amjsurg.2024.04.002. Epub 2024 Apr 3. PMID: 38594142.
22. Takaori K, Bassi C, Biankin A, et al.; IAP/EPC study group on the clinical managements of pancreatic cancer. International Association of Pancreatology (IAP)/European Pancreatic Club (EPC) consensus review of guidelines for the treatment of pancreatic cancer. Pancreatology. 2016 Jan-Feb;16(1):14-27. doi: 10.1016/j.pan.2015.10.013. Epub 2015 Nov 12. PMID: 26699808.

23. Tinguely P, Hidalgo Salinas C, Staubli SM, Raptis DA, Fusai GK; Pancreasgroup.org Chief Investigator; Pancreasgroup.org Scientific Committee collaborators; Pancreasgroup.org Management Committee collaborators; Pancreasgroup.org Country Leaders; all Pancreasgroup.org collaborators. Analysis of Short-Term Outcomes in Pancreatic Surgery with Vascular Resection from a Prospective Multicenter Global Study. Ann Surg Oncol. 2025 Aug 26;32(12):8870-80. doi: 10.1245/s10434-025-17911-8. Epub ahead of print. Erratum in: Ann Surg Oncol. 2025 Sep 7. doi: 10.1245/s10434-025-18348-9. PMID: 40858955; PMCID: PMC12534231.

24. Wang X, Demir IE, Schorn S, Jäger C, Scheufele F, Friess H, Ceyhan GO. Venous resection during pancreatectomy for pancreatic cancer: a systematic review. Transl Gastroenterol Hepatol. 2019 Jun 19;4:46. doi: 10.21037/tgh.2019.06.01. PMID: 31304423; PMCID: PMC6624360.

Наша тактика лікування хворих з гранично-резектабельними та місцево поширеними пухлинами підшлункової залози

В. М. Копчак [1], Л. О. Перерва [1], О. В. Дувалко [1], В. В. Ханенко [1], В. І. Трачук [1], В. Ю. Бондар [1], З. Ю. Голобор [2]

[1] Національний науковий центр хірургії та трансплантології імені О. О. Шалімова НАМН України, Київ

[2] Національний медичний університет імені О. О. Богомольця, Київ

Мета — оцінити результати виконання розширених резекцій підшлункової залози у хворих із гранично-резектабельними та місцево поширеними пухлинами підшлункової залози.

Матеріали та методи. У 2010—2023 рр. виконано 874 радикальних резекції підшлункової залози в пацієнтів з аденокарциномою підшлункової залози. Серед хворих чоловіків було 486 (55,6%), жінок — 388 (44,4%). Середній вік становив — (57,7±10,5) року (від 22 до 81 року). Дистальні панкреатоспленектомії виконані в 142 (16,2%) хворих, панкреатодуоденектомії — у 706 (80,8%), тотальні панкреатектомії — у 26 (3,0%) хворих. Розширені резекції підшлункової залози проведені 202 (23,1%) хворим: розширені панкреатодуоденектомії — 130 (64,4%), розширені дистальні панкреатоспленектомії — 58 (28,7%), розширені тотальні панкреатектомії — 14 (6,9%), розширені резекції підшлункової залози з резекцією венозних судин — 144 (71,3%), з резекцією артеріальних судин — 13 (6,4%), з комбінованою артеріовенозною резекцією — 3 (1,5%), з резекцією суміжних органів — 42 (20,8%).

Результати. Післяопераційні ускладнення виникли в 248 (36,9%) хворих після стандартних резекцій підшлункової залози та у 84 (41,6%) хворих після розширених резекцій ($\chi^2=1,4$; $p=0,22$). Померли 23 (2,6%) пацієнти: після розширених резекцій — 7 (3,5%), після стандартних резекцій підшлункової залози — 16 (2,4%), вірогідної різниці за рівнем летальності не виявлено ($\chi^2=0,71$; $p=0,39$). Розроблена нами персоніфікована лікувальна тактика дала змогу збільшити медіану виживаності пацієнтів із гранично-резектабельними та місцево поширеними пухлинами голівки підшлункової залози з 19 до 28 міс ($\chi^2=1,7$ $p=0,18$) та 5-річну виживаність — з 22,0 до 28,5%, медіану виживаності у хворих зі злоякісними пухлинами тіла й хвоста підшлункової залози — з 22 до 36 міс ($\chi^2=1,78$ $p=0,18$) та 5-річну виживаність — з 24 до 34% ($\chi^2=1,78$ $p=0,18$).

Висновки. Рівень післяопераційних ускладнень і летальність після розширених резекцій підшлункової залози порівнянні з такими після стандартних резекцій. Розширені резекції є можливими. Їхнє виконання може збільшити кількість радикально прооперованих хворих. Завдяки застосуванню розробленої нами лікувальної тактики підвищилася медіана виживаності хворих із гранично-резектабельними та місцево поширеними злоякісними пухлинами підшлункової залози.

Ключові слова: розширені резекції підшлункової залози, злоякісні пухлини підшлункової залози, місцево поширені пухлини, венозні резекції, артеріальні резекції.

FOR CITATION

Kopchak VM, Pererva LO, Duvalko OV, Khanenko VV, Trachuk VI, Bondar VY, Holobor ZY. Treatment tactics for patients with borderline resectable and locally advanced pancreatic cancer. General Surgery (Ukraine). 2026;(1);8-15. http://doi.org/10.30978/GS-2026-1-8.

UDC 616.74-007.23:616.37-002.4-089;616.073.43
DOI http://doi.org/10.30978/GS-2026-1-16

ISSN 2786-5584 print
ISSN 2786-5592 online

Acute skeletal muscle loss in surgically treated patients with severe infected necrotizing pancreatitis: a longitudinal ultrasound study

V. Teterina

Bogomolets National Medical University, Kyiv

✉ Viktoriia Teterina: dr.teterina@nmu.ua

V. Teterina, http://orcid.org/0000-0001-8250-7646

Objective – to evaluate perioperative changes in ultrasound-derived parameters of peripheral muscle mass, using the cross-sectional area of the rectus femoris muscle as a representative measure, in patients undergoing surgery for severe acute pancreatitis complicated by infected necrosis. Additionally, changes in handgrip strength were assessed, and the association between ultrasound findings and computed tomography–derived muscle mass indices was analyzed.

Materials and methods. This prospective observational study was conducted at two clinical centers and included 28 patients aged 19–59 years who underwent surgery for infected necrotizing pancreatitis. The median length of hospital stay was 49 (39–59) days. Serial measurements of the cross-sectional area (CSA) of the rectus femoris muscle were obtained using a portable ultrasound device equipped with a wireless high-frequency linear transducer, and handgrip strength was assessed with a dynamometer at three clinically defined time points (T1–T3). Serial measurements were obtained at clinically defined time points reflecting the perioperative course of severe acute pancreatitis: the first examination was performed on day 8 (6–10) of hospitalization, and the second on day 29 (26–31). In a subgroup of 17 patients with available paired computed tomography (CT) scans, skeletal muscle area (SMA) at the L3 vertebral level was assessed, and the association between changes in ultrasound parameters and CT-derived measurements was analyzed using Spearman's rank correlation coefficient. Linear mixed-effects models were applied to evaluate the longitudinal dynamics of skeletal muscle parameters.

Results. A statistically significant progressive decrease in CSA of the rectus femoris muscle ($p < 0.001$) was observed during hospitalization. The total relative reduction in CSA between T1 and T3 was 20.5 %. Modeling the length of hospital stay as a continuous variable confirmed an independent association between CSA decline and time ($\beta = -0.025$ cm^2/day; $p < 0.001$). The reduction in handgrip strength was even more pronounced ($p < 0.001$), with a total relative decrease of 36.7 % between T1 and T3. In the subgroup of patients with paired CT scans, ultrasound-derived changes in CSA demonstrated a moderate positive correlation with changes in skeletal muscle area (SMA) at the L3 vertebral level ($\rho = 0.65$; $p = 0.005$), supporting the concordance between the two assessment methods.

Conclusions. Patients who underwent surgery for infected necrotizing pancreatitis demonstrated progressive deterioration in both morphological and functional skeletal muscle parameters during hospitalization. A more pronounced decline in muscle strength compared with ultrasound-derived measures of muscle mass may reflect asynchronous functional and morphological changes in skeletal muscle in the context of severe acute pancreatitis complicated by infected necrosis. These findings support the clinical utility of a combined morphological and functional assessment of muscle status for the timely identification of acute secondary sarcopenia and optimizing nutritional and rehabilitation interventions in this patient population.

Keywords
skeletal muscle wasting, acute sarcopenia, muscle ultrasound, severe acute pancreatitis, infected pancreatic necrosis, critical illness, catabolism.

ARTICLE • Received 2026-01-05 • Received in revised form 2026-02-13 • Published 2026-03-31

Acute pancreatitis is a common condition with a variable clinical course; in some patients, it is complicated by persistent organ failure and infected pancreatic or peripancreatic necrosis [4], necessitating intensive care and prolonged hospitalization. Severe disease is associated with a pronounced systemic inflammatory response, hypercatabolism, immobilization, and impaired nutritional status, creating conditions for rapid skeletal muscle loss. In critically ill patients, acute muscle wasting may develop as early as the first week of illness and can reach substantial levels [8, 19].

Sarcopenia, as confirmed by computed tomography (CT), is increasingly recognized as a predictor of adverse clinical outcomes in patients with acute pancreatitis [3, 7]. Despite growing interest in assessing skeletal muscle parameters in critically ill patients, data on muscle mass dynamics during the clinical course of infected necrotizing pancreatitis remain limited, particularly prospective studies evaluating muscle parameters serially in patients undergoing surgery for this condition.

Ultrasound (US) is considered an accessible, reliable, and effective tool for the serial assessment of skeletal muscle morphology in critically ill patients [16, 17]; however, its clinical application and the correlation of ultrasound-derived findings with functional muscle parameters in this surgical cohort have not been sufficiently investigated. Consequently, there is increasing interest in combining imaging and functional approaches to assess skeletal muscle status, allowing for more comprehensive characterization of sarcopenia and longitudinal monitoring of structural and functional changes without additional radiation exposure or substantial increases in resource utilization.

Objective – to evaluate perioperative changes in ultrasound-derived parameters of peripheral muscle mass, using the cross-sectional area of the rectus femoris muscle as a representative measure, in patients undergoing surgery for severe acute pancreatitis complicated by infected necrosis. Additionally, changes in handgrip strength were assessed, and the association between ultrasound findings and computed tomography–derived muscle mass indices was analyzed.

Materials and methods

Study Design

The study employed a prospective observational design. Patients were consecutively recruited from the surgical departments of two hospitals serving as clinical teaching sites of Bogomolets National Medical University between November 2024 and December 2025. All patients were screened throughout the study period; however, only those fulfilling the predefined criteria for the present observational analysis were included. The present analysis was restricted to patients managed under standard care; individuals receiving protocolized nutritional interventions during the same recruitment period were not included.

The primary endpoint was the change in rectus femoris cross-sectional area across time points T1–T3, including assessment of the overall effect of time and pairwise comparisons between observation points. Secondary endpoints included changes in handgrip strength and the association between ultrasound-derived rectus femoris cross-sectional area and computed tomography–derived skeletal muscle area at the L3 vertebral level.

The study included 28 patients aged 19–59 years diagnosed with severe acute pancreatitis according to the Revised Atlanta Classification, defined by the presence of persistent organ failure lasting more than 48 hours, often accompanied by local complications [1]. Additional inclusion criteria comprised the presence of pancreatic or peripancreatic necrosis with subsequent infection, surgical intervention during hospitalization as part of a step-up approach [23], and the availability of serial ultrasound measurements of rectus femoris cross-sectional area at predefined clinically relevant time points.

The age range of 19–59 years was selected to minimize the influence of age-related sarcopenia and to reduce sample heterogeneity when assessing secondary muscle mass loss associated with severe acute pancreatitis.

The study excluded patients aged <18 or ≥ 60 years, those with acute pancreatitis not meeting the criteria for severe disease according to the Revised Atlanta Classification, patients without confirmed infected necrosis or managed non-operatively, and those with missing or technically unfeasible serial ultrasound measurements of the rectus femoris muscle.

The sample size was determined by the number of eligible patients identified during the enrollment period, taking into account the relative rarity of severe acute pancreatitis complicated by infected necrosis requiring surgical treatment, as well as the feasibility of performing serial measurements. Eligibility criteria were defined in accordance with the objectives of the present observational analysis.

Clinical management

Management followed a step-up approach in accordance with contemporary principles for the treatment of infected necrotizing pancreatitis. Initial

Table 1. **Baseline characteristics of the study population (n = 28)**

Variable	Total group (n = 28)
Demographic characteristics	
Age, years	44.5 [36–52]
Male Female	18 (64.3 %) 10 (35.7 %)
Body mass index at admission, kg/m^2	30.5 [23.1–32.2]
Clinical characteristics	
Etiology of pancreatitis	
Alcoholic	17 (60.7 %)
Alimentary	9 (32.1 %)
Biliary	2 (7.1 %)
Admission to intensive care unit	28 (100 %)
Disease severity	
APACHE II score at admission	14.5 [13–17.5]
Respiratory failure	22 (78.6 %)
Renal failure	8 (28.6 %)
Cardiovascular failure	12 (42.9 %)
Multiple organ failure (≥ 2)	13 (46.4 %)
Laboratory markers	
C-reactive protein at admission, mg/L	172.5 [156.5–194]
Hospital course	
Length of hospital stay, days	49 [39–59]
In-hospital mortality	9 (32.1 %)
Nutritional parameters	
Body weight at admission, kg	86.2 [66.2–103.1]
Change in body weight, kg	–13.0 [–19.0 ... –8.4]
Nutritional support	
Enteral nutrition	20 (71.4 %)
Parenteral nutrition	8 (28.6 %)
Availability of data	
Complete CSA measurements (T1–T3)	26 (92.9 %)
Complete handgrip strength measurements (T1–T3)	26 (92.9 %)
Paired CT scans for validation	17 (60.7 %)
Timing of ultrasound examinations	
Days from admission to US T1	8 [6–10]
Days from admission to US T2	29 [26–31]

Note. Categorical variables are presented as the number of cases and percentage, while quantitative indicators are presented as median [IQR].

treatment consisted of conservative management, including intensive supportive care and close clinical and radiological monitoring. Patients received organ support when required, infection control with appropriate antimicrobial therapy, and source control of infected necrosis.

Nutritional support was provided according to clinical tolerance, with a preference for enteral nutrition when feasible. Management followed a step-up approach. Initial treatment consisted of conservative management, including intensive supportive care and close clinical and radiological monitoring. The decision to proceed with surgical intervention was made during the disease course in the presence of infected pancreatic or peripancreatic necrosis. Whenever feasible, surgical intervention was deferred until the development of walled-off necrosis, typically 3–4 weeks after disease onset. The timing of surgery was determined based on the patient's clinical condition and computed tomography (CT) findings [11]. Minimally invasive interventions, including percutaneous drainage, were applied when clinically indicated as part of the step-up strategy; however, all patients ultimately required open surgical necrosectomy due to disease progression or insufficient response to initial interventions. Baseline patient characteristics, indicators of disease severity and progression, and details of nutritional support are summarized in Table 1.

Ultrasound muscle assessment

All ultrasound measurements were performed by a single investigator using a standardized protocol, with subsequent random spot-checks conducted by a senior specialist blinded to the results of other instrumental examinations. Ultrasound examinations were carried out using a Sonostar Uprobe-L6C wireless linear transducer. A dedicated musculoskeletal preset with an operating frequency of 7.5–10 MHz was used for skeletal muscle assessment, depending on image quality. Scan depth was adjusted to the minimum level required for complete visualization of the rectus femoris cross-sectional area (typically 100 mm). Additional imaging parameters included an overall gain of 60 dB, a dynamic range of 50 dB, and spatial compounding enabled. The mechanical index (MI) and thermal index for soft tissue (TIS) were 0.9 and 0.2, respectively. Ultrasound acquisition settings were kept constant across serial measurements for each patient.

Participants were examined in the supine position with lower limb muscles relaxed. To maintain methodological consistency and enable reliable comparison of serial measurements, all assessments were performed on the right thigh. A transverse

image of the rectus femoris muscle was acquired at a standardized anatomical landmark located in the mid-thigh region, defined as the midpoint between the anterior superior iliac spine and the superior border of the patella.

Ultrasound assessment was performed in B-mode using a transverse scanning plane with minimal transducer pressure applied to the skin. At each time point, three consecutive measurements of rectus femoris cross-sectional area were obtained, and the mean value was used for statistical analysis. The validity and reproducibility of ultrasound-based assessment of rectus femoris cross-sectional area have been demonstrated in previous studies [6, 21]. The primary ultrasound outcome measure was rectus femoris cross-sectional area (cm^2).

Handgrip strength assessment

Handgrip strength was measured using a calibrated digital dynamometer (CAMRY EH-101; CAMRY Electronic Co., Ltd., China) with a maximum capacity of 90 kg. Measurements were recorded in kilograms from the dominant hand. Device settings were standardized and remained unchanged across serial assessments for each patient. Grip strength testing was performed with the patient seated, the shoulder in a neutral position, the elbow flexed at approximately 90°, and the forearm and wrist in a neutral position [20]. At each time point, three consecutive trials were conducted with brief rest intervals, and the highest value was used for statistical analysis.

Computed tomography

In a subgroup of 17 patients with available paired contrast-enhanced CT examinations, obtained for clinical indications related to the management of necrotizing pancreatitis and performed at corresponding time points (T1 and T2), skeletal muscle mass was assessed on a single axial image at the mid-vertebral level of the third lumbar vertebra (L3) [17].

Image analysis was conducted using the web-based version of CoreSlicer software (version 1.0), applying semi-automated tissue segmentation followed by manual correction. Skeletal muscle area (SMA) was quantified in cm^2 using a predefined attenuation range of –29 to +150 Hounsfield units (HU) [18]. Segmentation was performed by a single investigator and subsequently reviewed by a senior specialist who conducted an independent assessment and was blinded to the ultrasound measurement results.

For body composition analysis, images from the native (non-contrast) CT phase were used to ensure standardized tissue attenuation assessment. CT examinations and corresponding ultrasound measurements obtained at time points T1 and T2 were treated as paired observations, provided that the interval between the two procedures did not exceed 48 hours.

Measurement time points

The first measurement time point (T1) included an ultrasound examination performed after clinical stabilization of the patient's condition during the early course of hospitalization. A corresponding CT examination was obtained within the same clinical period. The median time from hospital admission to T1 was 8 days (IQR 6–10).

The second measurement time point (T2) corresponded to the later stage of hospitalization, when repeat ultrasound and follow-up CT examinations were performed as part of ongoing clinical assessment and surgical decision-making. The median time from hospital admission to T2 was 29 days (IQR 26–31).

The third measurement time point (T3) consisted of an ultrasound examination performed after surgical intervention during the late stage of hospitalization. In patients who were discharged, T3 corresponded to the period of clinical stabilization prior to discharge; in patients who died during hospitalization, it represented the late phase of the disease course. Thus, T3 reflected the final observation time point during the hospital stay. Computed tomography was not performed at this time point.

Analysis of the association between ultrasound and CT-derived parameters was therefore restricted to time points T1 and T2, for which paired measurements were available.

Statistical analysis

Continuous variables were summarized as mean and standard deviation or median (interquartile range), depending on data distribution, while categorical variables were presented as absolute and relative frequencies. All statistical tests were two-sided, and p-values < 0.05 were considered statistically significant. Statistical analyses were performed using IBM SPSS Statistics software (version 31.0).

Longitudinal changes in rectus femoris cross-sectional area were analyzed using linear mixed-effects models. Model parameters were estimated by restricted maximum likelihood (REML). Time was included as a categorical fixed effect with predefined measurement points (T1–T3), while a random intercept for each patient was incorporated to account for interindividual variability. The correlation between repeated measurements was modeled using a Toeplitz covariance structure, selected based on information criteria (Akaike information

criterion (AIC) and Bayesian information criterion (BIC)) and model convergence stability.

The overall effect of time was evaluated using a Type III fixed-effects test. When a significant overall time effect was detected, pairwise comparisons between measurement points were performed with Bonferroni adjustment. Estimated marginal means with corresponding 95 % confidence intervals were reported to facilitate the interpretation of longitudinal effects. To assess the robustness of the results, time was additionally modeled as a continuous variable, defined as the number of days from the start of hospitalization to the corresponding measurement. The linear effect of time was evaluated by estimating the coefficient β, which represents the change in CSA per unit time, along with its 95 % confidence interval and p-value.

Longitudinal changes in handgrip strength were analyzed using linear mixed-effects models with time included as a categorical fixed effect (T1–T3). A random intercept for each patient was incorporated to account for interindividual variability, and the correlation between repeated measurements was modeled using a Toeplitz covariance structure. The overall effect of time was evaluated using a Type III fixed-effects test. When a statistically significant time effect was observed, pairwise comparisons between measurement points were performed with Bonferroni adjustment. Results were reported as estimated marginal means with corresponding 95 % confidence intervals.

In the subgroup of patients with available paired CT and ultrasound measurements, the association between ultrasound-derived changes in rectus femoris cross-sectional area and CT-derived changes in skeletal muscle area at the L3 vertebral level was evaluated using correlation analysis. Spearman's rank correlation coefficient (ρ) was used to quantify the strength of the association.

Model convergence was evaluated based on the presence or absence of algorithm warnings and the stability of parameter estimates. Model assumptions were assessed through residual diagnostics, including inspection of histograms, Q–Q plots, and residuals plotted against model-predicted values. Potentially influential observations were examined by reviewing individual longitudinal trajectories and residual distributions, as well as by identifying values that exerted disproportionate influence on fixed-effect estimates.

Results

Sample characteristics

The study cohort comprised 28 patients aged 19–59 years with severe acute pancreatitis complicated by infected necrosis who underwent surgical intervention during hospitalization. Surgical treatment was performed during the interval between the second and third ultrasound assessment time points. The median time from hospital admission to the first ultrasound examination was 8 days (IQR 6–10), and to the second examination was 29 days (IQR 26–31).

Preliminary results

A statistically significant progressive decrease in rectus femoris cross-sectional area was observed over time (Type III fixed-effects test: $F(2, 31.06) = 87.90$; $p < 0.001$). The estimated marginal means (EMMs) of CSA were 4.825 cm^2 (95 % CI 4.399–5.251) at T1, 4.196 cm^2 (95 % CI 3.770–4.623) at T2, and 3.836 cm^2 (95 % CI 3.409–4.263) at T3.

The absolute difference was –0.629 cm^2 (95 % CI –0.732 to –0.526; $p < 0.001$) between T1 and T2, –0.360 cm^2 (95 % CI –0.467 to –0.253; $p < 0.001$) between T2 and T3, and –0.989 cm^2 (95 % CI –1.150 to –0.828; $p < 0.001$) between T1 and T3. The relative reduction in CSA was 13.0 % between T1 and T2 and 8.6 % between T2 and T3, resulting in a total reduction of 20.5 % between T1 and T3.

Sensitivity analysis of results

Additional modeling of time from hospital admission as a continuous variable confirmed an independent association between duration of hospitalization and a decrease in rectus femoris CSA ($\beta = -0.025$ cm^2/day; 95 % CI –0.030 to –0.020; $p < 0.001$).

Secondary outcomes

A statistically significant effect of time on handgrip strength was observed (Type III fixed-effects test: $F(2, 29.96) = 445.01$; $p < 0.001$). Estimated marginal means were 24.5 kg (95 % CI 21.1–27.8) at T1, 20.0 kg (95 % CI 16.6–23.4) at T2, and 15.5 kg (95 % CI 12.1–18.9) at T3.

The absolute difference in handgrip strength was –4.5 kg between T1 and T2, –4.5 kg between T2 and T3, and –9.0 kg between T1 and T3 (all $p < 0.001$). The relative reduction was 18.4 % between T1 and T2 and 22.5 % between T2 and T3, resulting in a total reduction of 36.7 % between T1 and T3.

Association between ultrasound and CT parameters

In the subgroup of patients with paired CT examinations ($n = 17$), ultrasound-derived changes in rectus femoris CSA showed a moderate positive correlation with CT-derived changes in skeletal muscle area at the L3 vertebral level ($\rho = 0.65$; $p = 0.005$). The median relative reduction in CSA was 14.8 % (IQR 8.9–17.4 %), whereas the median relative reduction in SMA was 18.7 % (IQR 14.1–20.8 %).

Discussion

This study demonstrated a significant reduction in rectus femoris cross-sectional area, assessed by ultrasound, in patients who underwent surgical treatment for severe acute pancreatitis complicated by infected necrosis. During hospitalization, rectus femoris CSA decreased by 20.5 % from baseline, whereas handgrip strength showed a more pronounced decline of 36.7 %.

Considering the magnitude of these changes, the findings should be interpreted in the context of established mechanisms of muscle catabolism in critically ill patients. The results suggest the persistence of a hypercatabolic state despite individualized nutritional support based on patient tolerance throughout the perioperative period, with no evidence of stabilization by the time of hospital discharge. Such progressive reductions in muscle mass and strength may reflect the sustained impact of systemic inflammation, prolonged immobilization, and postoperative metabolic stress.

Comparable patterns have been reported in patients with sepsis and multiple organ dysfunction, in whom rapid declines in muscle thickness or cross-sectional area occur from the early days of intensive care unit admission [19, 22]. However, most available studies involve heterogeneous critically ill populations and do not specifically address the contribution of surgical intervention. In contrast, perioperative changes in skeletal muscle status among patients with severe acute pancreatitis complicated by infected necrosis remain insufficiently investigated.

The discrepancy between the magnitude of structural and functional changes warrants particular attention. These findings suggest that functional impairment is not solely attributable to reductions in muscle mass but may also reflect additional pathophysiological mechanisms. A similar dissociation between morphological and functional parameters has been described in critically ill patients and has been linked to the development of intensive care unit–acquired myopathy and polyneuropathy [9].

In this context, declines in muscle strength may also reflect alterations in muscle quality, impaired neuromuscular transmission, and reduced contractile function of muscle fibers. In the present cohort, further deterioration in handgrip strength was observed at later stages of follow-up, despite less pronounced changes in morphological parameters. This pattern may indicate a dynamic interplay between catabolic processes, neuromuscular dysfunction, and immobilization across different clinical phases of severe acute pancreatitis.

It is important to emphasize that the observed structural and functional changes developed over a relatively short period of hospitalization (median 49 [39–59] days), which is consistent with current understanding of the potential for rapid-onset acute secondary sarcopenia in the context of severe acute illness. Notably, there is currently no consensus in the literature regarding the time frame within which sarcopenia can be attributed to an acute event; reported intervals range from 28 days to 6 months from the onset of the acute pathological process [5].

A distinctive finding in the present cohort of patients with infected necrotizing pancreatitis was that substantial muscle mass loss had already occurred prior to surgical intervention, indicating that surgery was performed in the setting of an established muscle deficit. Subsequent assessments demonstrated further deterioration of these parameters during the postoperative period. Thus, the perioperative course in patients with infected necrotizing pancreatitis appears to be characterized by the combined impact of surgical stress and a persistent hypercatabolic state, which may adversely affect recovery of functional capacity and prolong the rehabilitation process.

In cohorts of patients with acute pancreatitis, most studies have focused on assessing nutritional status and CT-derived indicators of sarcopenia as predictors of disease severity and clinical outcomes [10, 12, 14]. In contrast, the present study employed serial ultrasound assessment of rectus femoris cross-sectional area during hospitalization in the perioperative period among patients with severe acute pancreatitis complicated by infected necrosis.

Unlike previous investigations, this study was designed prospectively, with measurements performed at clinically defined time points. It combined morphological evaluation of skeletal muscle mass using ultrasound with analysis of its association with CT-derived skeletal muscle parameters at the L3 vertebral level and with functional strength measures. This comprehensive approach enhances the robustness of the findings and allows a more detailed characterization of muscle deficit severity in this clinical population.

These observations also highlight the importance of opportunistic screening for reduced muscle mass using existing computed tomography examinations performed for the primary disease [10], which may facilitate early identification of patients at increased risk of developing sarcopenia.

The present findings highlight the importance of early assessment of muscle status as soon as the patient's clinical condition allows. Ultrasound examination enables effective serial bedside monitoring without additional radiation exposure or substantial resource utilization. At the same time,

although several studies have proposed cutoff values for ultrasound-derived muscle mass parameters in specific patient populations [2, 13, 24], their validity and reproducibility in surgical cohorts remain insufficiently established. This limitation complicates the diagnosis of acute secondary sarcopenia, its early detection during hospitalization, and the estimation of its prevalence among critically ill patients with acute pancreatitis.

Despite being conducted at two centers, this study has several limitations, including a relatively small sample size and a clinically homogeneous cohort. The absence of post-discharge functional status assessment precludes evaluation of the long-term clinical impact of the observed muscle deficit, particularly regarding functional recovery, rehabilitation needs, and quality of life.

A formal assessment of intra- and inter-observer reproducibility of ultrasound measurements, including calculation of concordance coefficients, was not performed. In addition, the influence of the volume and composition of nutritional support on muscle mass dynamics was not analyzed, which limits the interpretation of the potential therapeutic effect. These limitations highlight important directions for future research in this clinical population.

Future research should include larger multicenter cohorts to confirm the reproducibility of these findings and improve their external validity. An important direction for further investigation is to evaluate the association between the rate of muscle mass loss and clinically relevant outcomes, such as length of hospital stay, complication rates, need for repeat interventions, and recovery of functional capacity.

Particular attention should be given to determining whether serial ultrasound monitoring of skeletal muscles can be incorporated into risk stratification strategies, individualized nutritional support, and postoperative rehabilitation within existing clinical care pathways. In addition, long-term functional and metabolic consequences of the observed muscle deficits should be investigated, including their impact on quality of life and the risk of recurrent acute pancreatitis.

Conclusions

In this prospective cohort of patients who underwent surgical treatment for severe acute pancreatitis complicated by infected necrosis, serial ultrasound measurements demonstrated a progressive decrease in rectus femoris cross-sectional area during hospitalization. Overall, CSA declined by approximately 20 % from baseline, whereas handgrip strength decreased by nearly 37 %.

The more pronounced reduction in muscle strength may reflect the progression of skeletal muscle dysfunction alongside structural muscle loss or may precede detectable morphological changes. Adverse trends in both functional and morphological parameters were evident prior to surgical intervention and persisted during the postoperative period, suggesting sustained systemic hypercatabolism throughout the clinical course of severe acute pancreatitis.

The findings demonstrated a statistically significant correlation between ultrasound-derived measures of muscle mass and computed tomography–derived skeletal muscle area parameters, supporting the potential feasibility, accessibility, and clinical utility of ultrasound for longitudinal monitoring of muscle status in this clinical population.

Overall, the observed combination of skeletal muscle atrophy and reduced functional capacity may be consistent with the development of acute secondary sarcopenia in the context of severe systemic illness; however, the absence of validated diagnostic cut-off values for this surgical cohort necessitates cautious interpretation of the results. Further investigation of this approach may enable a more precise evaluation of the clinical relevance of serial muscle mass assessment and its potential to optimize nutritional support and rehabilitation strategies.

Declaration of interests

The authors declare that they have no conflicts of interest related to this study, its authorship, or the publication of this article.

Funding. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethics approval and written informed consent statements

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Written informed consent was obtained from all participants prior to enrollment in the study.

References

1. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013 Jan;62(1):102-11. doi: 10.1136/gutjnl-2012-302779. Epub 2012 Oct 25. PMID: 23100216.

2. Baş S, Çoban HH, Doğan A, Erölmez HN, Mutlu HH, İlhan N. Towards Rapid Bedside Detection of Sarcopenia in Cancer Patients: The Role of Rectus Femoris Muscle Ultrasonography-A Prospective Cross-Sectional Study. Medicina (Kaunas). 2026 Feb 21;62(2):413. doi: 10.3390/medicina62020413. PMID: 41752811; PMCID: PMC12941887.
3. Bender F, Marzeion L, Liese J, Hecker M, Wolff M, König T, Willis F, Thevenet IP, Tuffs C, Brose A, Pons-Kühnemann J, Padberg W, Hecker A, Strowitzki MJ. Sarcopenia is associated with an unfavorable outcome in patients with acute pancreatitis: A propensity score analysis. Dig Liver Dis. 2026 Jan;58(1):96-103. doi: 10.1016/j.dld.2025.10.013. Epub 2025 Nov 4. PMID: 41193276.
4. Boxhoorn L, Voermans RP, Bouwense SA, Bruno MJ, Verdonk RC, Boermeester MA, van Santvoort HC, Besselink MG. Acute pancreatitis. Lancet. 2020 Sep 5;396(10252):726-734. doi: 10.1016/S0140-6736(20)31310-6. Erratum in: Lancet. 2021 Nov 6;398(10312):1686. doi: 10.1016/S0140-6736(21)02377-1. PMID: 32891214.
5. Damanti S, Senini E, De Lorenzo R, Merolla A, Santoro S, Festorazzi C, Messina M, Vitali G, Sciorati C, Rovere-Querini P. Acute Sarcopenia: Mechanisms and Management. Nutrients. 2024 Oct 10;16(20):3428. doi: 10.3390/nu16203428. PMID: 39458423; PMCID: PMC11510680.
6. E Lima KM, da Matta TT, de Oliveira LF. Reliability of the rectus femoris muscle cross-sectional area measurements by ultrasonography. Clin Physiol Funct Imaging. 2012 May;32(3):221-6. doi: 10.1111/j.1475-097X.2011.01115.x. Epub 2012 Jan 24. PMID: 22487157.
7. Farquhar R, Matthews S, Baxter N, Rayers G, Ratnayake CBB, Robertson FP, Nandhra S, Lim WB, Witham M, Pandanaboyana S. Sarcopenia and Sarcopenic Obesity on Body Composition Analysis is a Significant Predictor of Mortality in Severe Acute Pancreatitis: A Longitudinal Observational Study. World J Surg. 2023 Nov;47(11):2825-2833. doi: 10.1007/s00268-023-07122-1. Epub 2023 Aug 4. PMID: 37541981; PMCID: PMC10545625.
8. Fazzini B, Märkl T, Costas C, Blobner M, Schaller SJ, Prowle J, Puthucheary Z, Wackerhage H. The rate and assessment of muscle wasting during critical illness: a systematic review and meta-analysis. Crit Care. 2023 Jan 3;27(1):2. doi: 10.1186/s13054-022-04253-0. PMID: 36597123; PMCID: PMC9808763.
9. Hermans G, Van den Berghe G. Clinical review: intensive care unit acquired weakness. Crit Care. 2015 Aug 5;19(1):274. doi: 10.1186/s13054-015-0993-7. PMID: 26242743; PMCID: PMC4526175.
10. Kolck J, Hosse C, Leimbach A, Beetz NL, Auer TA, Collettini F, Fehrenbach U, Pille C, Geisel D. Opportunistic screening for long-term muscle wasting in critically ill patients: insights from an acute pancreatitis cohort. Eur J Med Res. 2024 May 22;29(1):294. doi: 10.1186/s40001-024-01884-7. PMID: 38778361; PMCID: PMC11110383.
11. Leppäniemi A, Tolonen M, Tarasconi A, Segovia-Lohse H, Gamberini E, Kirkpatrick AW, Ball CG, Parry N, Sartelli M, Wolbrink D, van Goor H, Baiocchi G, Ansaloni L, Biffl W, Coccolini F, Di Saverio S, Kluger Y, Moore E, Catena F. 2019 WSES guidelines for the management of severe acute pancreatitis. World J Emerg Surg. 2019 Jun 13;14:27. doi: 10.1186/s13017-019-0247-0. PMID: 31210778; PMCID: PMC6567462.
12. Li P, Xing Q, Wang L, Shi J, Zhang YX, Fu H. The Individual and Joint Associations of Sarcopenic Obesity and Malnutrition on Predicting the Severity of Acute Pancreatitis. Int J Gen Med. 2025 Aug 30;18:4941-4955. doi: 10.2147/IJGM.S540037. PMID: 40909911; PMCID: PMC12407009.
13. Li S, Xu K, Wang A, Qin C, Hua N, Ling X, Xu L, He C, Zhou S, Chen J, Zhang Q, Yang Y. Determination of Ultrasound Reference Values for Diagnosing Low Muscle Mass in Older Chinese Adults. J Cachexia Sarcopenia Muscle. 2025 Dec;16(6):e70155. doi: 10.1002/jcsm.70155. Erratum in: J Cachexia Sarcopenia Muscle. 2026;17(1):e20012. doi: 10.1002/jcsm.70224. PMID: 41362106; PMCID: PMC12686591.
14. Lin C, Zhang J, Wang C, Lian W, Liu Y. The impact of skeletal muscle index at the third lumbar spine on nosocomial deterioration and short-term prognosis in acute pancreatitis: a retrospective observational study. PeerJ. 2024 Apr 30;12:e17283. doi: 10.7717/peerj.17283. PMID: 38708354; PMCID: PMC11067894.
15. Mourtzakis M, Prado CM, Lieffers JR, Reiman T, McCargar LJ, Baracos VE. A practical and precise approach to quantification of body composition in cancer patients using computed tomography images acquired during routine care. Appl Physiol Nutr Metab. 2008 Oct;33(5):997-1006. doi: 10.1139/H08-075. PMID: 18923576.
16. Mourtzakis M, Wischmeyer P. Bedside ultrasound measurement of skeletal muscle. Curr Opin Clin Nutr Metab Care. 2014 Sep;17(5):389-95. doi: 10.1097/MCO.0000000000000088. PMID: 25023190.
17. Nagae M, Umegaki H, Yoshiko A, Fujita K. Muscle ultrasound and its application to point-of-care ultrasonography: a narrative review. Ann Med. 2023 Dec;55(1):190-197. doi: 10.1080/07853890.2022.2157871. PMID: 36538042; PMCID: PMC9788691.
18. Prado CM, Lieffers JR, McCargar LJ, Reiman T, Sawyer MB, Martin L, Baracos VE. Prevalence and clinical implications of sarcopenic obesity in patients with solid tumours of the respiratory and gastrointestinal tracts: a population-based study. Lancet Oncol. 2008 Jul;9(7):629-35. doi: 10.1016/S1470-2045(08)70153-0. Epub 2008 Jun 6. PMID: 18539529.
19. Puthucheary ZA, Rawal J, McPhail M, Connolly B, Ratnayake G, Chan P, Hopkinson NS, Phadke R, Dew T, Sidhu PS, Velloso C, Seymour J, Agley CC, Selby A, Limb M, Edwards LM, Smith K, Rowlerson A, Rennie MJ, Moxham J, Harridge SD, Hart N, Montgomery HE. Acute skeletal muscle wasting in critical illness. JAMA. 2013 Oct 16;310(15):1591-600. doi: 10.1001/jama.2013.278481. Erratum in: JAMA. 2014 Feb 12;311(6):625. Padhke, Rahul [corrected to Phadke, Rahul]. PMID: 24108501.
20. Roberts HC, Denison HJ, Martin HJ, Patel HP, Syddall H, Cooper C, Sayer AA. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing. 2011 Jul;40(4):423-9. doi: 10.1093/ageing/afr051. Epub 2011 May 30. PMID: 21624928.
21. Tillquist M, Kutsogiannis DJ, Wischmeyer PE, Kummerlen C, Leung R, Stollery D, Karvellas CJ, Preiser JC, Bird N, Kozar R, Heyland DK. Bedside ultrasound is a practical and reliable measurement tool for assessing quadriceps muscle layer thickness. JPEN J Parenter Enteral Nutr. 2014 Sep;38(7):886-90. doi: 10.1177/0148607113501327. Epub 2013 Aug 26. PMID: 23980134; PMCID: PMC4502435.
22. Turton P, Hay R, Taylor J, McPhee J, Welters I. Human limb skeletal muscle wasting and architectural remodeling during five to ten days intubation and ventilation in critical care – an observational study using ultrasound. BMC Anesthesiol. 2016 Nov 29;16(1):119. doi: 10.1186/s12871-016-0269-z. PMID: 27894277; PMCID: PMC5127036.
23. Van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, van Goor H, Schaapherder AF, van Eijck CH, Bollen TL, van Ramshorst B, Nieuwenhuijs VB, Timmer R, Laméris JS, Kruyt PM, Manusama ER, van der Harst E, van der Schelling GP, Karsten T, Hesselink EJ, van Laarhoven CJ, Rosman C, Bosscha K, de Wit RJ, Houdijk AP, van Leeuwen MS, Buskens E, Gooszen HG; Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010 Apr 22;362(16):1491-502. doi: 10.1056/NEJMoa0908821. PMID: 20410514.
24. Yik V, Kok SSX, Chean E, Lam YE, Chua WT, Tan WJ, Foo FJ, Ng JL, Su SS, Chong CX, Aw DK, Khoo NAX, Wischmeyer PE, Molinger J, Wong S, Ong LW, Koh FH. Diagnosing Sarcopenia with AI-Aided Ultrasound (DINOSAUR)-A Pilot Study. Nutrients. 2024 Aug 20;16(16):2768. doi: 10.3390/nu16162768. PMID: 39203903; PMCID: PMC11357450.

Гостра втрата скелетної м'язової маси в пацієнтів, прооперованих із приводу тяжкого інфікованого некротичного панкреатиту: поздовжнє ультразвукове дослідження

В. Тетеріна

Національний медичний університет імені О. О. Богомольця, Київ

Мета — оцінити періопераційну динаміку ультразвукових показників м'язової маси на прикладі площі поперечного перерізу m. rectus femoris у пацієнтів, яким виконано хірургічне лікування з приводу тяжкого гострого панкреатиту, ускладненого інфікованим некрозом, а також дослідити супутні функціональні зміни та взаємозв'язок ультразвукових показників із параметрами м'язової маси за даними комп'ютерної томографії.

Матеріали та методи. У проспективне обсерваційне дослідження в двох клінічних центрах було залучено 28 пацієнтів віком 19—59 років, прооперованих з приводу інфікованого некротичного панкреатиту. Медіана тривалості госпіталізації становила 49 (39—59) днів. Виконано серійну оцінку площі поперечного перерізу (CSA) m. rectus femoris із використанням портативного ультразвукового пристрою з бездротовим високочастотним лінійним датчиком, а також оцінку сили стискання кисті методом динамометрії в трьох клінічно визначених часових точках (T1, T2, T3). Серійні вимірювання проводили в клінічно визначені часові точки, що відображували динаміку періопераційного перебігу тяжкого гострого панкреатиту: перше обстеження виконували на 8-й (6—10-й) день госпіталізації, друге — на 29-й (26—31-й) день. У підгрупі з 17 пацієнтів із наявними парними комп'ютерними томограмами оцінювали площу скелетних м'язів (SMA) на рівні L3 та проаналізували асоціацію змін ультразвукових параметрів і результатів комп'ютерної томографії за допомогою коефіцієнта кореляції Спірмена. Для оцінки динаміки показників скелетних м'язів використовували лінійні моделі змішаних ефектів.

Результати. Установлено статистично значуще ($p < 0{,}001$) прогресивне зменшення CSA m. rectus femoris протягом періоду спостереження. Сумарне відносне зниження CSA між T1 і T3 становило 20,5 %. Моделювання тривалості госпіталізації як безперервної змінної підтвердило незалежну асоціацію зменшення CSA з часом ($\beta = -0{,}025$ см^2/добу, $p < 0{,}001$). Зниження сили стискання кисті було виразнішим ($p < 0{,}001$), із сумарним відносним зменшенням 36,7 % між T1 і T3. У підгрупі пацієнтів із парними комп'ютерними томограмами зміни CSA за даними ультразвукового дослідження демонстрували помірну позитивну кореляцію зі змінами SMA на рівні L3 ($\rho = 0{,}65$; $p = 0{,}005$), що підтверджує узгодженість результатів обох методів.

Висновки. У пацієнтів, прооперованих з приводу інфікованого некротичного панкреатиту, спостерігалося прогресивне погіршення морфологічних і функціональних показників скелетних м'язів протягом періоду госпіталізації. Виразніше зниження показників м'язової сили порівняно зі змінами ультразвукових параметрів м'язової маси може відображувати асинхронну динаміку функціональних і морфологічних змін скелетних м'язів при тяжкому гострому панкреатиті, ускладненому інфікованим некрозом. Отримані результати обґрунтовують клінічну доцільність поєднаної морфологічної та функціональної оцінки м'язового статусу для своєчасного виявлення гострої вторинної саркопенії та оптимізації нутритивних і реабілітаційних втручань у цій популяції.

Ключові слова: виснаження скелетних м'язів, гостра саркопенія, ультразвукове дослідження м'язів, тяжкий гострий панкреатит, інфікований панкреонекроз, критичний стан, катаболізм.

FOR CITATION

Teterina V. Acute skeletal muscle loss in surgically treated patients with severe infected necrotizing pancreatitis: a longitudinal ultrasound study. General Surgery (Ukraine). 2026;(1);16-24. http://doi.org/10.30978/GS-2026-1-16.

UDC 616-008.6:577.112]: [616.379-008.64-06:617.586-002.44]-035-085
DOI http://doi.org/10.30978/GS-2026-1-25

ISSN 2786-5584 print
ISSN 2786-5592 online

Changes in ZO-1 expression as an early indicator of treatment effectiveness in patients with chronic diabetic foot wounds

D. Yakymiv, M. Prystupiuk

Bogomolets National Medical University, Kyiv

✉ Dmytro Yakymiv: dimayakimiv96@gmail.com

D. Yakymiv, http://orcid.org/0009-0008-3305-0449
M. Prystupiuk, http://orcid.org/0000-0001-7725-1498

Chronic diabetic foot wounds represent a persistent surgical challenge due to delayed healing, frequent complications, and high socioeconomic burden. Chronic hyperglycemia is known to impair epidermal barrier integrity, in part by altering the expression of tight junction proteins, including zonula occludens-1 (ZO-1).

Objective – to evaluate changes in ZO-1 expression in chronic diabetic foot wounds following combined local therapy and to assess the potential role of ZO-1 as an early molecular marker of epithelial barrier restoration.

Materials and methods. A prospective randomized study included 28 patients with chronic diabetic foot wounds. Patients were divided into an intervention group (n = 14) treated with a combined spray–and–gel regimen containing collagen, hyaluronate, amino acids, trace elements (Zn, Cu), and antiseptic components, and a control group (n = 14), receiving standard chlorhexidine dressings. Epidermal biopsy samples were obtained at baseline (Day 0) and after 10 days of treatment. ZO-1 expression was assessed using Western blot analysis, followed by densitometric quantification.

Results. Patients receiving combined local therapy demonstrated a marked increase in ZO-1 expression by Day 10 compared with baseline values, indicating restoration of intercellular junction integrity. No comparable changes were observed in the control group.

Conclusions. Combined local therapy promotes molecular recovery of the epidermal barrier in chronic diabetic foot wounds, as evidenced by increased ZO-1 expression. These findings support the clinical relevance of ZO-1 as an objective biomarker for treatment response in the surgical management of chronic diabetic wounds.

Keywords
diabetic foot, chronic wounds, tight junctions, zonula occludens-1, wound healing, local therapy.

ARTICLE • Received 2026-01-05 • Received in revised form 2026-02-13 • Published 2026-03-31

Scope and impact of chronic wounds

Chronic wounds are defined as defects of the skin and underlying tissues that fail to progress through the normal stages of healing within 3–4 weeks and may persist for months or longer [2, 9]. Unlike acute wounds, chronic wounds are characterized by prolonged inflammation, impaired tissue regeneration, and frequent recurrence. Clinically, chronic wounds represent a multifactorial surgical problem resulting from the interaction of local tissue damage and systemic disorders [1, 6].

Among chronic wounds, diabetic foot ulcers are associated with particularly high morbidity and mortality and lead to a substantial reduction in patient quality of life [10, 11]. In addition to clinical consequences, the economic impact of chronic wound care is considerable, placing a sustained burden on healthcare systems worldwide, with treatment costs reaching tens of billions of dollars annually [10]. The most prevalent categories of hard-to-heal wounds include diabetic foot ulcers, venous leg ulcers, and pressure ulcers [10, 11].

Effective management of chronic wounds requires a structured and systematic approach [4, 9]. Adequate wound bed preparation is fundamental in contemporary surgical practice. This process includes the removal of non-viable tissue, infection control, maintenance of optimal moisture balance, and stimulation of wound edge activity [2, 6, 9]. Proper wound bed preparation is widely regarded

as a prerequisite for successful surgical and conservative treatment of chronic wounds [2, 3, 9].

Principles of modern wound management

Current surgical strategies emphasize that successful healing of chronic wounds, particularly in patients with diabetes mellitus, cannot rely solely on correction of systemic metabolic or vascular abnormalities [1, 11]. Increasing attention is directed toward local therapeutic interventions aimed at modifying the wound microenvironment [1].

Clinical evidence indicates that hydrogel-based dressings improve healing outcomes by supporting epithelialization, maintaining adequate hydration, and facilitating the controlled release of bioactive substances [4]. Advanced hydrogel systems integrate biocompatibility with antimicrobial and anti-inflammatory properties, attributes that are especially important for treating diabetic wounds with impaired local defense mechanisms [4]. Adjunctive modalities, such as hyperbaric oxygen therapy, have demonstrated benefit in selected patient populations by reducing wound size and lowering the risk of major amputations [11].

Molecular pathology of diabetic wounds: the role of ZO-1

Diabetic foot ulcers develop in the setting of chronic hyperglycemia-induced metabolic disturbances affecting multiple organ systems [7, 11]. One of the key pathological mechanisms underlying delayed healing is dysfunction of the epidermal and microvascular barriers [5, 7].

Tight junctions play a critical role in maintaining epidermal integrity. Zonula occludens-1 (ZO-1) is a cytoskeleton-associated protein essential for tight junction assembly and regulation of paracellular permeability [10]. Experimental and clinical studies have shown that hyperglycemia reduces ZO-1 expression and alters subcellular localization in keratinocytes and endothelial cells [5, 7, 8]. These changes result in compromised barrier function, increased transepidermal water loss, and impaired re-epithelialization [5, 7].

During physiological wound healing, ZO-1 expression increases as epithelial continuity is restored, highlighting its role in intercellular junction repair [8]. Therefore, assessment of ZO-1 dynamics in chronic diabetic wounds may provide valuable insight into the molecular effectiveness of local therapeutic interventions [8, 11].

Rationale and objective

Restoration of epidermal barrier integrity is a fundamental goal in the surgical treatment of chronic wounds. Combining standard wound care with regenerative local agents may enhance epithelial repair by simultaneously improving the wound environment and supporting molecular mechanisms responsible for tight junction restoration [4, 8].

Objective – to evaluate changes in ZO-1 expression in chronic diabetic foot wounds following combined local therapy and to assess the potential role of ZO-1 as an early molecular marker of epithelial barrier restoration.

Materials and methods

Study population and design

This study employed a prospective, randomized design and enrolled 28 patients with chronic foot wounds secondary to diabetes mellitus. Inclusion required a wound duration of at least 3 months. Patients were assigned to two cohorts using systematic random sampling: the intervention group (n = 14) received combined local therapy, while the control group (n = 14) received standard dressings.

Intervention Protocols

Experimental group treatment

Patients in the experimental group received a two-step combined local therapeutic regimen:

- **Spray application.** The wounds were initially treated with a spray formulation containing decamethoxin (an antiseptic), low-molecular-weight hydrolyzed collagen, and the amino acids glycine, arginine, and aspartic acid, suspended in purified water.
- **Gel application.** Subsequently, a wound care gel was applied over the treated area. The gel contained low-molecular-weight hydrolyzed collagen, high-molecular-weight sodium hyaluronate, silver sulfadiazine (an antimicrobial agent), decamethoxin, colloidal anhydrous silicon dioxide (Aerosil, a structural agent), poloxamer, hypromellose (hydrogel matrix agents), and purified water.

This formulation was designed to address multiple facets of chronic wound pathology, providing structural support (collagen), maintaining hydration (hyaluronate, poloxamer), controlling infection (decamethoxin, silver sulfadiazine), and supplying cellular precursors and regulators (amino acids and trace elements, specifically Zn and Cu as discussed later).

Control group treatment

The control group received standard care, consisting solely of wound treatment with a chlorhexidine solution, followed by the application of an atraumatic sterile dressing soaked in the same solution. It is important to note that iodine-based preparations were explicitly excluded from the treatment protocols for both groups.

Sample collection and timing

To evaluate the molecular dynamics of skin intercellular contacts, ZO-1 protein expression was analyzed.1 Paired epidermis tissue samples were surgically collected from patients in both the intervention and control groups at two crucial time points:

- **Day 0.** Collected prior to the initiation of any local therapeutic intervention.
- **Day 10.** Collected immediately following the 10-day course of prescribed treatment.

Molecular expression analysis

The level of ZO-1 expression was determined using western blot analysis. The standard procedure involved separating tissue proteins by electrophoresis, transferring them onto a membrane, incubating the membrane with specific primary and secondary antibodies targeting ZO-1, and finally visualizing the resulting complexes using the chemiluminescent method. The ZO-1 protein band was successfully identified at an approximate molecular weight of 220 kDa.

Quantitative assessment of protein content was performed by densitometry, an accurate technique for determining relative protein amounts based on signal intensity on the blot. The widely available software ImageJ was used for this quantification, providing a precise means to measure the area and intensity of the signal bands. Densitometric measurements were reported as relative intensity units (i.u.), normalized to the background signal, allowing for comparative analysis between baseline (Day 0) and post-treatment (Day 10) samples within each patient.

Results

Initial qualitative findings (western blot)

Analysis of ZO-1 protein expression commenced with qualitative assessment via western blotting. At the initial baseline stage (Day 0), significant variability in ZO-1 band intensity was observed across patient samples, a finding characteristic of the diverse pathology of chronic wounds. After 10 days of combined local treatment, the analysis revealed a marked and consistent increase in ZO-1 signal intensity. Specifically, a pronounced intensification of the signal was observed in 13 of the 14 participants in the intervention group, indicating molecular activation of processes aimed at restoring tight intercellular contacts.

Following systematic organization and processing, the generalized blotograms (Fig. 1, as described below) confirmed this trend. There was a visible increase in ZO-1 expression (the protein band at 220 kDa) in the Day 10 (even) lanes compared to the corresponding baseline (odd) lanes. Notably, samples from Patient 4 showed particularly high enhancement, which correlated positively with observed clinical progress in wound healing dynamics.

Quantitative densitometric analysis

For objective quantification, the intensity of the ZO-1 bands was measured by densitometry in ImageJ. The data for the intervention group are summarized in Table 1.

The data in Table 1 reveal a substantial and consistent positive dynamic in ZO-1 expression across the majority of patients following 10 days of the combined local therapy. Several cases demonstrated exponential increases. For instance, Patient 4 exhibited an approximately 742 % increase (from 0.8683 to 6.4538 i.u.). This magnitude of molecular change suggests that the therapeutic complex initiates a powerful, targeted stimulus for cellular repair and tight junction protein synthesis, demonstrating a highly effective pro-reparative signal rapidly induced by the treatment.

Treatment response dynamics

The quantitative data were visually represented using bar charts to clearly illustrate the treatment effects in both cohorts (Fig. 2, 3).

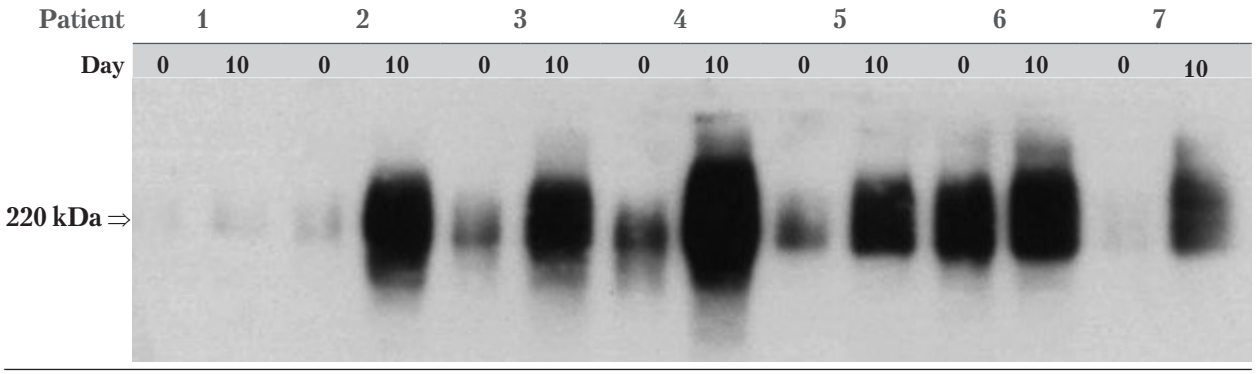

Figure 1. **Western blot expression of ZO-1 in patients with chronic foot wounds on days 0 and 10 of treatment. The arrow indicates the ZO-1 protein band at 220 kDa**

Table 1. **Densitometric values of ZO-1 band intensity in intervention group patients on days 0 and 10 of treatment, i.u.**

Patient	Day 0	Day 10
1	0.0622	0.0669
2	0.1285	2.5019
3	0.4640	2.1926
4	0.8683	6.4538
5	0.3272	1.7172
6	2.0024	3.5765
7	0.1757	1.2642
8	0.7149	3.8429
9	1.3824	4.7561
10	0.2593	0.4678
11	0.9475	1.3982
12	0.0368	5.2279
13	1.7249	3.1425
14	0.5031	2.9041

Fig. 2 shows the densitometry results for the intervention group, demonstrating a marked increase in ZO-1 band intensity after treatment. This visible upregulation confirms the therapeutic complex's ability to enhance ZO-1 expression. The sole exception was Patient 1, whose baseline expression was minimal (0.0622 i.u.) and whose subsequent post-treatment growth was marginal. This low response may indicate a subgroup of wounds with an exceptionally profound or non-responsive underlying barrier dysfunction.

In contrast, Fig. 3, representing the control group that received standard chlorhexidine dressings, showed no substantial increase in ZO-1 band intensity over the 10-day period. This clear differentiation underscores that the observed molecular restoration of the epithelial barrier is a specific therapeutic effect of the combined spray-and-gel regimen, rather than a non-specific response to basic antiseptic care.

Discussion

The role of combined therapy in tight junction restoration

Chronic diabetic wounds are characterized by decreased ZO-1 protein levels, a condition directly associated with impaired epithelial barrier function and delayed wound healing. The primary finding of this study–a significant increase in ZO-1 expression in the intervention group by Day 10–confirms that the combined local therapeutic approach successfully counters and reverses this fundamental molecular deficit.

The increased intensity observed on the western blot indicates successful molecular restoration of tight intercellular junctions, resulting in a demonstrable improvement in epithelial structural integrity. The specificity of this therapeutic response, entirely absent in the control group treated with chlorhexidine, highlights the unique biological activity of the bioactive components within the spray and gel. These components include collagen and hyaluronate, which provide a scaffold and maintain moisture, as well as crucial trace elements such as Zn and Cu. Zinc is indispensable for critical processes such as keratinocyte proliferation and immune system modulation, while copper is vital for promoting angiogenesis and stabilizing the extracellular matrix constituents,

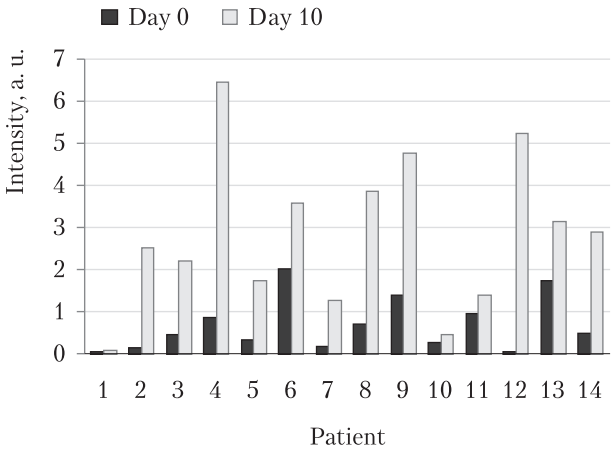

Figure 2. **Column chart of ZO-1 protein densitometry in 14 patients of the intervention group on day 0 and day 10 of treatment**

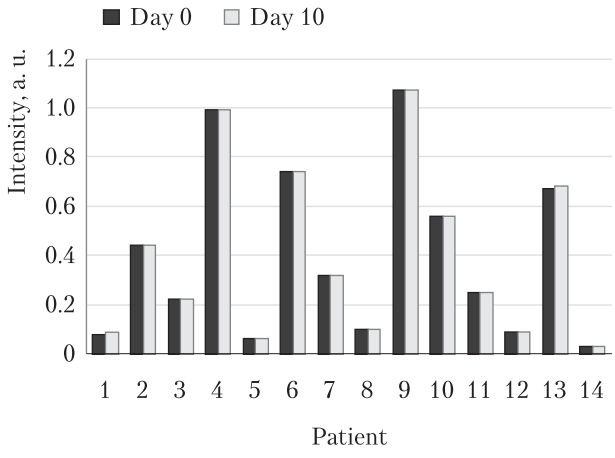

Figure 3. **Column chart of ZO-1 protein densitometry in 14 patients of the control group on day 0 and day 10 of treatment**

including collagen and elastin. The collective action of these components likely initiates and accelerates the cellular signaling cascades required for the rapid synthesis and accurate localization of ZO-1, thereby rapidly pushing the chronic wound environment toward an acute, pro-reparative state.

Correlation with clinical improvements

Molecular evidence of barrier recovery, as manifested by ZO-1 upregulation, aligns with favorable clinical observations in the experimental group. Patients receiving combined local therapy demonstrated faster wound cleansing, a marked reduction in local inflammation, and more robust granulation tissue formation compared to the control group. The rapid biochemical shift, captured by the Day 10 biopsies, signifies that the molecular foundation for successful healing – the restoration of the epithelial barrier – is established early in the treatment phase. This rapid commencement of molecular repair mechanisms precedes and predicts subsequent macroscopic clinical improvement, indicating that the complex formulation is designed to drive biological regeneration beyond simple wound coverage or antisepsis.

ZO-1 as a validated early biomarker

The findings provide strong evidence that ZO-1 expression dynamics represent a reliable, objective, and early tool for assessing therapeutic success in chronic wounds. The exclusive increase in ZO-1 observed in the cohort treated with the specialized spray and gel indicates that this protein is a sensitive indicator of molecular response to regenerative local therapy.

This objective molecular assessment provides significant advantages over traditional subjective clinical evaluations. By quantifying the protein level via densitometry within a short 10-day period, clinicians can obtain definitive evidence of whether the wound's underlying cellular machinery is responding to the regenerative agents. This objective validation capability allows for a faster assessment of treatment efficacy, enabling prompt clinical decisions regarding the continuation of a successful treatment path or the necessary modification of care for patients who show minimal molecular response, such as Patient 1. This advancement contributes to a more personalized and evidence-based approach to chronic wound management.

Perspectives

While the current study successfully confirms the molecular efficacy of the combined therapy in restoring ZO-1 expression, future research should focus on establishing a direct, long-term correlation between the magnitude of the Day 10 ZO-1 increase and definitive clinical endpoints, such as rates of complete healing and risk of wound recurrence. Further investigations are also required to fully elucidate the specific synergistic contributions of individual complex components (e.g., zinc versus collagen or hyaluronate) to optimize future wound care product development. Additionally, the case of the patient who exhibited minimal response highlights the need for dedicated research into the mechanisms of treatment resistance, potentially involving genetic factors or localized pathologies that may override the pro-reparative effects of the topical agents.

Clinical significance

The findings of this research establish several points of clinical importance derived from the molecular evidence:

- **Restoration of barrier integrity.** The significant increase in ZO-1 expression following treatment confirms the therapeutic regimen's ability to actively restore intercellular contacts and reinforce epithelial barrier function, a crucial step often stalled in diabetic pathology.
- **Regenerative efficacy.** The wound care spray and gel formulated with trace elements (Zn, Cu) should be considered effective therapeutic agents for actively stimulating molecular regeneration in chronic diabetic wounds.
- **Novel monitoring strategy.** ZO-1 expression analysis offers a quantifiable and valuable early laboratory marker for evaluating patient response to modern regenerative local therapies, providing objective data for guiding clinical management decisions.

Conclusions

The study conclusively demonstrated that the implementation of a comprehensive local therapy, incorporating standard antiseptic treatment with a mineral wound spray and gel containing trace elements (Zn, Cu), significantly restores impaired epithelial barrier properties in chronic diabetic foot wounds.

Densitometric quantification of ZO-1 protein showed a substantial increase in expression by the 10th day of treatment compared with baseline. This positive molecular dynamic was recorded across the majority of the treated patient cohort, clearly indicating improved intercellular contacts and accelerated tissue repair.

The totality of the data supports the conclusion that the application of trace element-based wound agents plays an important role in restoring the structural integrity of the epithelial barrier and normalizing tight junction function, specifically by increasing the level of ZO-1. This targeted molecular approach is recommended as an effective supplement to standard treatment protocols for chronic diabetic wounds.

Declaration of interests

The authors declare no conflict of interest.

Funding. This research received no external funding. The study was conducted at the authors' own expense.

Authors contributions

D.Yakymiv: data processing, statistical analysis, and interpretation of results, and prepared the manuscript text; M. Prystupiuk: conceptualization, research design development, data collection.

References

1. Atkin L, Bućko Z, Conde Montero E, et al. Implementing TIMERS: the race against hard-to-heal wounds. J Wound Care. 2019 Mar 1;23(Sup3a):S1-S50. doi: 10.12968/jowc.2019.28.Sup3a.S1.
2. Gallagher KE, Alberto EC, Getchell J, Powell J, Cardenas L. Expediting acute wound healing by integrating multiple therapeutic strategies: a case series. Wound Manag Prev. 2024 Dec;70(4). doi: 10.25270/wmp.23119. PMID: 39788879.
3. Ghazi K, Deng-Pichon U, Warnet JM, Rat P. Hyaluronan fragments improve wound healing on in vitro cutaneous model through P2X7 purinoreceptor basal activation: role of molecular weight. PLoS One. 2012;7(11):e48351. doi: 10.1371/journal.pone.0048351. Epub 2012 Nov 16. PMID: 23173033;
4. Hosseini SA, Noruzi S, Kesharwani P, Sahebkar A. Hydrogel-based dressing for wound healing: A systematic review of clinical trials. Int J Biol Macromol. 2025 May;308(Pt 1):142322. doi: 10.1016/j.ijbiomac.2025.142322. Epub 2025 Mar 19. PMID: 40118421.
5. Kim DY, Kang MK, Kang YH. Umbelliferone preserves skin epidermal barrier integrity in diabetes-induced keratinocytes by regulating actin dynamics and suppressing ROS-mediated apoptosis. Nutr. Diabetes. 2025;15:51(2025). https://doi.org/10.1038/s41387-025-00407-5.
6. Mokhtar AMF, Moreljab MH, Idress EA, et al. Nurses Application of the «TIME» Framework in the Wounds Assessment and its Impact on the Wound Care Competences. Nurs Health. 2023;8(1):11-17. doi: 10.13189/nh.2023.080102.
7. Okano J, Kojima H, Katagi M, et al. Hyperglycemia Induces Skin Barrier Dysfunctions with Impairment of Epidermal Integrity in Non-Wounded Skin of Type 1 Diabetic Mice. PLoS One. 2016 Nov 15;11(11):e0166215. doi: 10.1371/journal.pone.0166215. PMID: 27846299; PMCID: PMC5113047.
8. Petrenko O, Badziukh S, Korsa V, Kolosovych I, Tykhomyrov A. Topical Application of Autologous Plasma-Derived Plasminogen Accelerates Healing of Chronic Foot Ulcers in Type 2 Diabetes Patients. Int J Low Extrem Wounds. 2024 May 17:15347346241256025. doi: 10.1177/15347346241256025.
9. Prystupiuk M, Trembovetska Y, Chemodanov P, Yakymiv D. Modern aspects of the comprehensive treatment of patients with the neuroischemic form of diabetic foot. The International Journal of Endocrinology (Ukraine). 2025;21(5):471-476. doi: 10.22141/2224-0721.21.5.2025.1594.
10. Shu H, Xia Z, Qin X, Wang X, Lu W, Luo Q, Zhang Z, Xiong X. The clinical efficacy of collagen dressing on chronic wounds: A meta-analysis of 11 randomized controlled trials. Front Surg. 2022 Aug 31;9:978407. doi: 10.3389/fsurg.2022.978407. PMID: 36117827; PMCID: PMC9473315.
11. Yakymiv D, Prystupyuk M. Treatment of acute and chronic foot wounds in patients with diabetes mellitus. The Odesa Medical Journal. 2025;2:74-81. https://doi.org/10.32782/2226-2008-2025-2-12

Зміни експресії ZO-1 як ранній показник ефективності лікування у пацієнтів з хронічними ранами стопи при цукровому діабеті

Д. Якимів, М. Приступюк

Національний медичний університет імені О. О. Богомольця, Київ

Хронічні рани стопи при цукровому діабеті становлять значну проблему для хірургії через повільне загоєння, часті ускладнення та велике соціально-економічне навантаження. Відомо, що хронічна гіперглікемія порушує цілісність епідермального бар'єра, зокрема через зміну експресії білків щільних міжклітинних контактів, серед яких важливе місце посідає zonula occludens-1 (ZO-1).

Мета — оцінити зміни експресії ZO-1 у хронічних ранах діабетичної стопи після застосування комбінованої місцевої терапії та визначити потенційну роль ZO-1 як раннього молекулярного маркера відновлення епітеліального бар'єра.

Матеріали та методи. У проспективне рандомізоване дослідження було залучено 28 пацієнтів із хронічними ранами діабетичної стопи. Пацієнтів розподілили на групу дослідження (n=14), якій призначали комбіновану місцеву терапію у вигляді спрею та гелю, що містили колаген, гіалуронат, амінокислоти, мікроелементи (Zn, Cu) й антисептичні компоненти, та контрольну групу (n=14), в якій застосовували стандартні пов'язки з хлоргексидином. Біоптати епідермісу отримували на початку дослідження (0-й день) та через 10 днів лікування. Експресію ZO-1 визначали методом Western blot із подальшим денситометричним аналізом.

Результати. У пацієнтів, які отримували комбіновану місцеву терапію, на 10-й день спостерігали вірогідне підвищення експресії ZO-1 порівняно з вихідними показниками, що свідчило про відновлення цілісності міжклітинних контактів. У контрольній групі такі зміни не виявлено.

Висновки. Застосування комбінованої місцевої терапії сприяє молекулярному відновленню епідермального бар'єра при хронічних ранах діабетичної стопи, що підтверджується підвищенням експресії ZO-1. Отримані результати свідчать про клінічну значущість ZO-1 як об'єктивного біомаркера відповіді на терапію при хірургічному лікуванні хронічних діабетичних ран.

Ключові слова: хронічні рани, діабетична стопа, ранова репарація, щільні міжклітинні контакти, ZO-1 (zonula occludens-1), денситометрія, місцева терапія.

FOR CITATION

Yakymiv D, Prystupiuk M. Changes in ZO-1 expression as an early indicator of treatment effectiveness in patients with chronic diabetic foot wounds. General Surgery (Ukraine). 2026:(1);25-30. http://doi.org/10.30978/GS-2026-1-25.

UDC 616-007.43-089.844-06
DOI http://doi.org/10.30978/GS-2026-1-31

ISSN 2786-5584 print
ISSN 2786-5592 online

Implant rejection in alloplasty of abdominal hernias: analysis of causes and surgical correction methods

A. I. Moiseienko, K. O. Korolova

Bogomolets National Medical University, Kyiv

✉ Anatolii Moiseienko: a.moyseenko1977@gmail.com

A. I. Moiseienko, http://orcid.org/0000-0002-2606-8383
K. O. Korolova, http://orcid.org/0000-0002-6088-7884

Hernias of the anterior abdominal wall, particularly postoperative ones, remain an ever-present problem in modern abdominal surgery. The introduction of alloplasty using mesh implants has significantly improved the results of surgical treatment of abdominal hernias, reducing the recurrence rate to 8–20 % and with hybrid-laparoscopic techniques to 2.7 %. However, the use of mesh implants is accompanied by specific complications. Unsatisfactory results of the mesh integration process after alloplasty are explained by the distorted course of the local inflammatory reaction, namely, the transformation of aseptic inflammation into bacterial inflammation.

Objective – to systematize and generalize modern ideas and own experience in the surgical treatment of infectious complications of abdominal hernia alloplasty, analyze the causes of their occurrence, and identify promising areas for improving treatment outcomes.

Materials and methods. We studied 28 patients who had previously undergone abdominal hernia repair and subsequently developed inflammatory complications at the site of implantation. The diagnosis of mesh implant rejection was based on a comprehensive assessment of clinical, laboratory, instrumental, and morphological data. The presence of persistent clinical symptoms for a prolonged period after alloplasty was considered an indication for an in-depth examination to exclude or confirm implant rejection and to determine the optimal treatment strategy for a particular patient. Laboratory tests, ultrasound, CT, or MRI were used for this purpose.

Results. The leading cause of implant rejection in the general group was chronic infection of the implantation site, detected in 46.4 % of cases, which was combined with fistula formation in 28.6 % of patients. In all 7 patients with inflammatory complications after alloplasty of inguinal hernias, complete explantation of the mesh implant, careful restoration of the normal anatomy of the inguinal canal, tissue sanitation, and excision of fistula passages with autoplasty in the presence of concomitant hernia recurrence were performed. Among patients with ventral hernias, complete explantation of the mesh was performed in 15 of 21 cases (71.4 %), while partial explantation was performed in 6 cases (28.6 %), prioritizing preservation of integrated areas.

Conclusions. Complications after alloplasty of ventral hernias, especially when the onlay method and heavy polypropylene meshes are used, account for 75.0 % of cases of mesh implant rejection. The leading cause of implant rejection is chronic infection of the alloplasty area, whereas the formation of branched multiple fistulas is one of the most common clinical manifestations. Complete explantation of the infected implant, combined with autoplasty and vacuum drainage, is the method of choice for the surgical treatment of such complications. Partial explantation with staged reconstruction is possible in carefully selected patients with ventral hernias, but it is accompanied by longer treatment and increases the risk of recurrence.

Keywords
implant rejection reaction, alloplasty, ventral hernias, inguinal hernias, implant explantation.

ARTICLE • Received 2026-01-15 • Received in revised form 2026-02-13 • Published 2026-03-31

Hernias of the anterior abdominal wall, particularly postoperative ones, remain an ever-present problem in modern abdominal surgery. The frequency of their occurrence after laparotomies, according to various data, reaches 10–20 %, and the proportion of surgical interventions for abdominal hernias remains consistently high in both planned and urgent surgery [8]. The introduction of alloplastic

reconstruction with mesh implants has significantly improved the results of surgical treatment of abdominal hernias, particularly by reducing the recurrence rate to 8–20 % compared with autoplastic reconstruction and, when using hybrid laparoscopic techniques, to 2.7 % [5, 10]. Autoplasty of ventral hernias is associated with a high recurrence rate. According to various authors, it ranges from 15 % to 45 % [9]. However, the use of surgical mesh implants is accompanied by specific complications that were not typical for autoplastic techniques. Among them, a special place is occupied by inflammatory tissue reactions, which are often assessed by surgeons as a process of disruption of the integration of the implant into the body – that is, «mesh rejection» [7, 11]. The lack of a clear definition of this concept and the confusion between immunological rejection, foreign body reaction, and infection complicate the interpretation of treatment results. The process of integration of a mesh implant into the recipient's body has been studied in detail at the pathophysiological level. In response to mesh implantation, cellular and humoral factors are activated, leading to the absorption of blood plasma proteins and macrophage accumulation on its surface, the activation of pro-inflammatory cytokines, and the formation of acute aseptic inflammation in the implant area [3]. Subsequently, it enters a chronic phase characterized by changes in the cellular composition around the implant: the appearance of foreign body granuloma cells, a decrease in macrophages, and an increase in fibroblasts, which form a fibrous capsule around the mesh [4, 6]. Since polypropylene and other synthetic materials used in the construction of hernioplasty meshes lack antigenic properties, rejection reactions to these implants are rare [8]. According to most authors, the unsatisfactory results of the mesh integration process after alloplasty of abdominal hernias are explained by the distorted course of the local inflammatory reaction, namely, the transformation of aseptic inflammation into bacterial inflammation [1, 7, 10, 11]. Among the causes and risk factors for infectious complications after alloplasty, the patient's comorbid conditions, the surgical procedure, and the type of implant are the most prominent [8]. Among the comorbid conditions that significantly increase the risk of local infection in the area of alloplasty are type 2 diabetes mellitus, obesity (BMI ≥30–35 kg/m^2), smoking, systemic administration of steroid hormones for immunosuppressive therapy [2,8].

However, many controversial and underexplored issues remain in understanding the infectious complications of abdominal hernia repair. Increased intra-abdominal pressure syndrome after alloplasty of abdominal hernias requires further study as a possible predisposing factor for the development of implant infection [1]. In particular, there is much debate about whether the mesh should be retained if complications arise. There are no meta-analyses in the available literature comparing surgical outcomes in patients with mesh retention versus those after early mesh removal. An interesting and not yet fully understood question remains the role of bacterial films on the surface of an infected implant in maintaining the chronicity of the infectious process. The potential for solving this problem with modern antibiotic therapy has also not been studied.

Objective – to systematize and generalize modern ideas and own experience in the surgical treatment of infectious complications of abdominal hernia alloplasty, analyze the causes of their occurrence, and identify promising areas for improving treatment outcomes.

Materials and methods

During 2014–2025, on the basis of Surgery Department No 2 of Bogomolets National Medical University, we operated on 28 patients, 11 men and 17 women, who had previously undergone abdominal hernia repair, which was subsequently complicated by inflammatory processes in the area of implant localization. The study group ranged in age from 28 to 79 years, with an average age of 52.7 ± 5.8 years. Inguinal hernias accounted for 25.0 % (n = 7), while the majority of cases were ventral hernias – 75.0 % (n = 21), with 53.6 % (n = 21) of them being postoperative recurrent hernia defects. Most patients with clinical signs of impaired implant engraftment had certain risk factors, among which obesity of 3–4 degrees and type 2 diabetes mellitus prevailed (Table 1).

Table 1. **Distribution of patients with clinical signs of implant failure after abdominal hernia alloplasty according to the presence of risk factors**

Risk factor	Inguinal hernias (n = 7)	Ventral hernias (n = 21)	Total (n = 28)
Type 2 diabetes mellitus	3	10	13 (46.4 %)
Body mass index > 30 kg/m^2	2	15	17 (60.7 %)
Smoking	2	10	12 (42.9 %)
Recurrent hernia	4	3	7 (25.0 %)
History of hormone therapy/chemotherapy	–	7	7 (25.0 %)

Table 2. **Clinical manifestations of implant rejection after abdominal hernia repair**

Clinical manifestation	Number of patients
Chronic pain at the implant site	21 (75.0 %)
Fistula formation	18 (64.3 %)
Purulent exudate from the wound	15 (53.6 %)
Hyperemia and infiltration	8 (28.6 %)
Abdominal wall deformity	10 (35.7 %)
Recurrence of local inflammation after improvement following antibiotic therapy	6 (21.4 %)

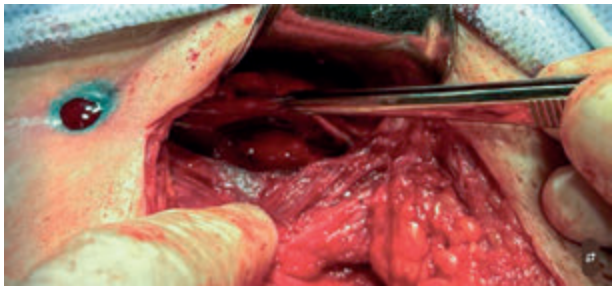

Figure 1. **A foreign body granuloma was found in the projection of the right inguinal canal, a fistula was found lateral to the performed access, the spermatic cord and the edge of a heavy polypropylene implant were isolated**

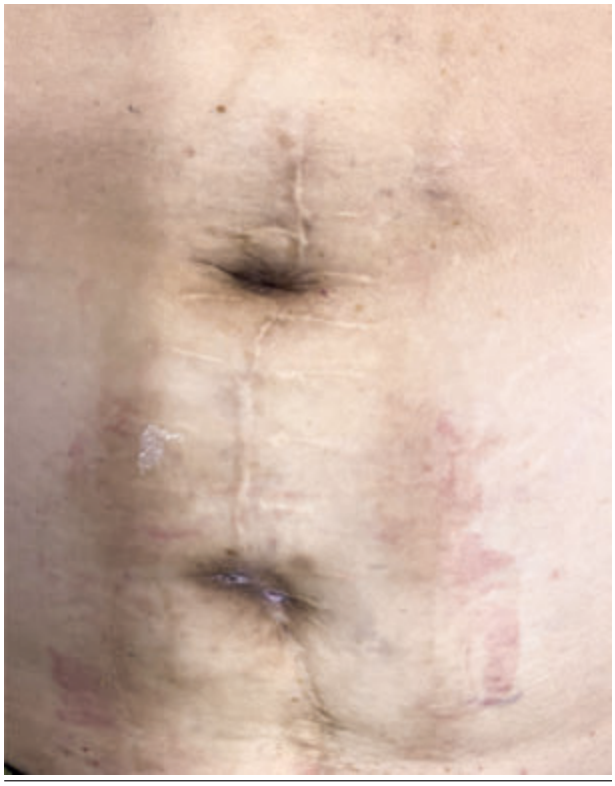

Figure 2. **Anterior abdominal wall with external openings of fistulas on the postoperative scar after ventral hernia alloplasty**

The main clinical manifestations characterizing the local inflammatory reaction in cases of impaired implant engraftment (Table 2) included varying degrees of pain in the projection of the implanted mesh, reported by 21 (75 %) patients. In 18 (64.3 %) patients, the formation of fistulas on the skin with constant mucous or mucopurulent exudation was observed. We noted the presence of fistulas in the mesh projection in 4 patients with inguinal hernias (Fig. 1) and in 14 with ventral hernias (Fig. 2). Moreover, inflammatory processes in inguinal hernias were manifested by the formation of a single fistula, while the complicated course of alloplasty of ventral hernias was manifested by the formation of multiple fistulas. The duration of existence of such fistulas in our observations varied from 3 months to 5 years, while the total daily output was from 50 to 500 ml of inflammatory exudate. In 6 (21.4 %) patients, fistula recurrence in the implant projection was noted after conservative treatment at other medical institutions.

The diagnosis of mesh implant rejection was based on a comprehensive assessment of clinical, laboratory, instrumental, and morphological data. The final diagnosis was established based on the combination of the above criteria, taking into account the duration of the postoperative period and the dynamics of the clinical course of the complications identified in the patient. The presence of persistent clinical symptoms (see Table 2) for a prolonged period after alloplasty was considered an indication for an in-depth examination to exclude or confirm implant rejection and to determine the optimal treatment tactics for a particular patient. The assessment of laboratory indicators focused on the dynamics of acute inflammatory changes in the blood formula. Specifically, it revealed leukocytosis with a left shift and an elevated erythrocyte sedimentation rate. An increase in blood C-reactive protein concentration was observed, which persisted or recurred shortly after the end of antibiotic therapy. Based on these instrumental methods, indications were given, and the course of surgical interventions was planned. For the diagnosis of inflammatory complications after inguinal hernia alloplasty, most patients needed only ultrasound, which allowed visualization of the implant itself, the presence of hydrophilic accumulations – seromas, abscesses, and perifocal soft-tissue induration. CT or MRI of the abdominal organs was considered the method of choice for diagnosing inflammatory complications of ventral hernia alloplasty. This allowed us to assess the localization of the implant, the presence of fistulas, follow their course in the soft tissues, identify the connection with hydrophilic accumulations in the projection of

the implant, assess the depth and prevalence of the inflammatory process, and, in some cases, identify the involvement of the abdominal organs, in particular, intestinal loops.

Statistical analysis was performed using Statistica 10 (Serial Number: STA999K347150-W) and MedStat.

Results and discussion

Surgical treatment of patients with mesh implant rejection was determined by the clinical course of the complication, hernia location, extent of the inflammatory response, presence of concomitant risk factors, and findings from instrumental examinations. The main goal of surgery was to eliminate the source of chronic inflammation, remove affected tissues, and restore the anatomical integrity of the abdominal wall while minimizing the risk of recurrence and infectious complications. Comparisons between additional preoperative imaging methods and intraoperative data were used to categorize patients into groups based on the type of prior alloplasty and the synthetic implants used.

All inguinal hernia alloplasties complicated by implant rejection were performed by open methods, as evidenced by the presence of a typical postoperative scar in the projection of the inguinal canal. During the operation, the implant, its dimensions, and the fixation method, which is typical for the Lichtenstein operation, were identified in only 4 (57.1 %) patients. In another 3 (42.9 %) patients, technical deviations from the Lichtenstein alloplasty standard were detected during surgery: fixation of the implant on the surface of the aponeurosis of the external oblique muscle of the abdomen; a small implant was found in the projection of the medial inguinal fossa and the exit of the spermatic cord into the layer of subcutaneous fat with fixation of the implant underneath it on the aponeurosis of the external oblique muscle of the abdomen (these patients are shown in Table 3 in the column other alloplasty). In all these patients, recurrences of inguinal hernia and fistula were detected against the background of an inflammatory process in the implant projection (see Fig. 1).

Among patients with a history of ventral hernias complicated by implant rejection, patients after onlay plastic surgery predominated, their number was 42.9 %. The leading cause of implant rejection in the general group was chronic infection of the implantation site, detected in 46.4 % of cases, which was combined with fistula formation in 28.6 % of patients.

During surgical treatment, the same surgical tactics were used in all 7 patients with inflammatory complications after alloplasty of inguinal hernias: complete explantation of the mesh implant and careful, high-quality restoration of the normal anatomy of the inguinal canal. After removal of the implant, thorough tissue sanitation and excision of the fistula passages were performed. It should be noted that in the presence of a chronic, long-standing inflammatory process within the inguinal canal, which is maintained by an infected implant, we observed the formation of significant cicatricial-infiltrative changes in the soft tissues of the walls of the inguinal canal. This feature allows simultaneous autoplasty in the presence of concomitant hernia recurrence. In all cases, the surgical intervention is completed by suturing the superficial tissues after vacuum drainage of the inguinal canal. Postoperative antibiotic therapy was prescribed empirically in accordance with established clinical protocols. Notably, after mesh explantation in patients who underwent inguinal hernia alloplasty, long-term antibiotic therapy was not required in any postoperative case.

Surgical tactics for ventral hernias were more differentiated and depended on the prevalence of the process and the degree of implant damage. In 15 of 21 patients (71.4 %), complete explantation of the mesh implant was performed, which was due to the total involvement of the mesh in the inflammatory process and the presence of multiple branched fistula tracts (Fig. 3). In some cases, signs of fragmentary complete degradation of the implant structure were encountered with the formation of defects, which were the basis for the formation of hernia recurrence. During the expansion process, the edges of the implant should be carefully excised, since the implant perimeter is mostly involved in the perifocal scarring process (Fig. 4). It is in these areas that, when

Table 3. **Distribution of patients who underwent surgery for infectious complications after alloplastic surgery by type of surgical intervention and location of implants**

Type of alloplasty	Inguinal hernias (n = 7)	Ventral hernias (n = 21)	Total (n = 28)
Lichtenstein	4 (57.1 %)	–	4 (57.1 %)
Other alloplasty	3 (42.9 %)	–	3 (42.9 %)
Onlay	–	9 (42.9 %)	9 (42.9 %)
Inlay	–	4 (19.0 %)	4 (19.0 %)
Sublay	–	6 (28.6 %)	6 (28.6 %)
Intraperitoneal alloplasty	–	2 (9.5 %)	2 (9.5 %)

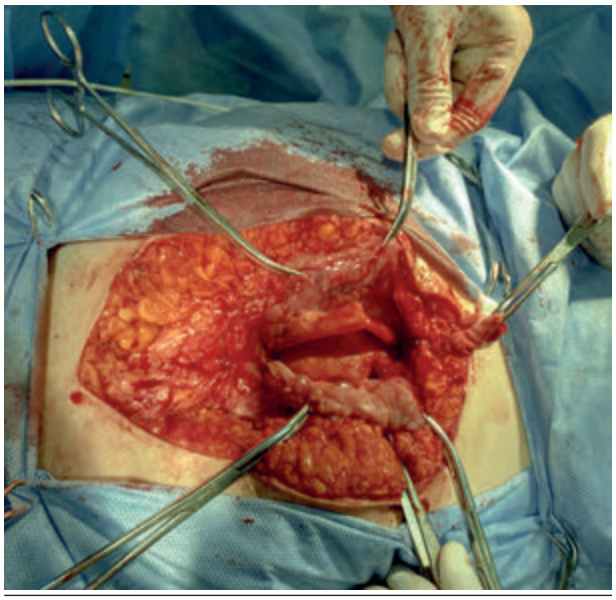

Figure 3. **The beginning of the surgical intervention. The foreign body granuloma is opened, and the internal openings of the fistulous passages shown in Figure 2 are visualized, which communicate with the cavity around the deformed, corrugated mesh implant in 2 topographic and anatomical planes**

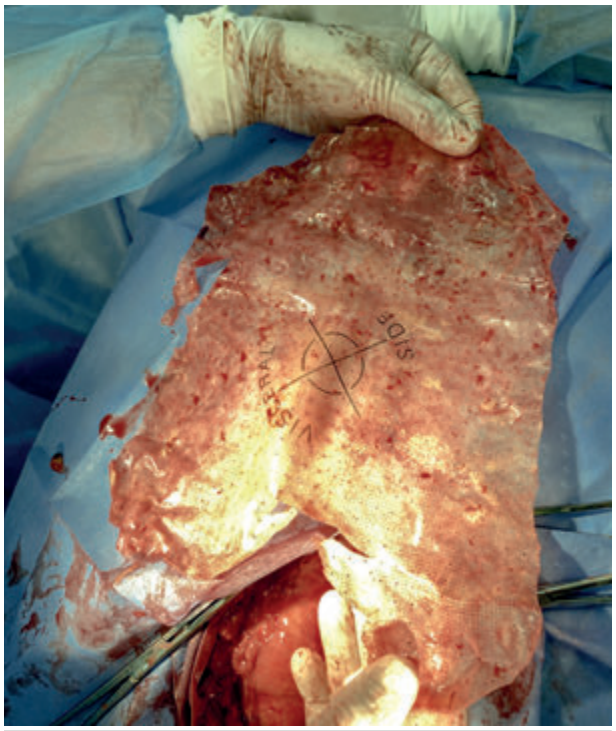

Figure 5. **Infected implant after explantation**

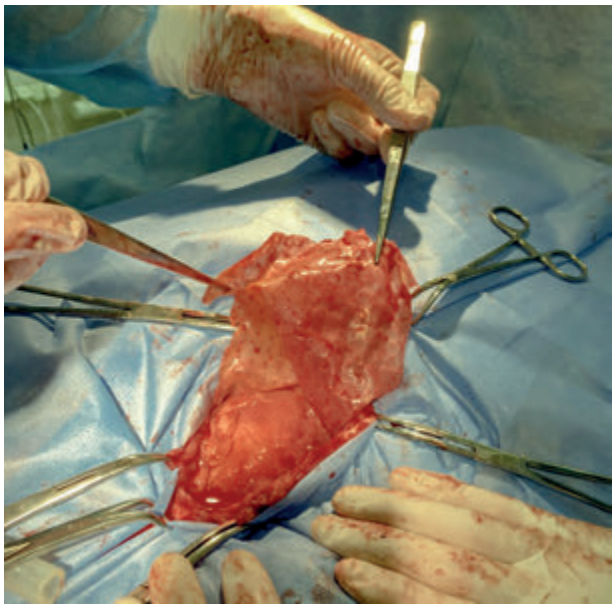

Figure 4. **Intermediate stage of surgery. One third of the implant perimeter has been mobilized**

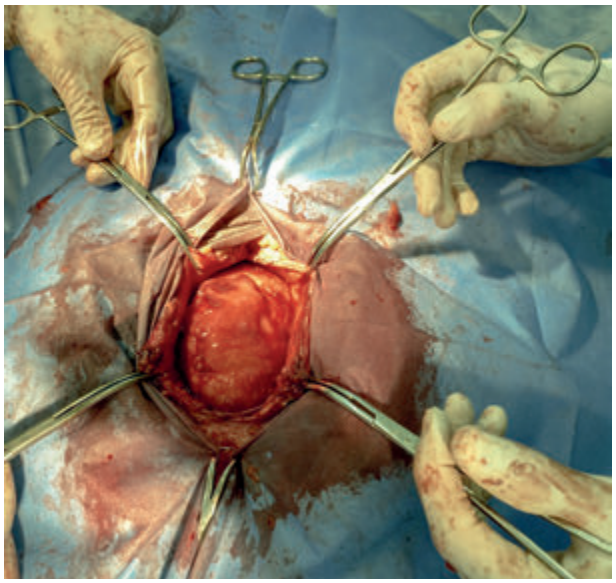

Figure 6. **The surgical field after completion of implant explantation before performing autoplasty**

removing an infected implant, there is a high risk of damage to internal organs that are involved in the inflammatory process. Partial implant explantation was performed in 6 patients (28.6 %), involving removal of only the affected mesh fragments while preserving integrated areas. This tactic was adequate in the case of a localized process and a satisfactory condition of the surrounding tissues. After implant explantation (Fig. 5), the abdominal wall defect was most often temporarily closed by autoplasty and drainage of the implant site with several vacuum drains (Fig. 6). Analysis of implant types showed that in more than half of the cases (53.6 %), heavy polypropylene meshes were used, which were most often associated with the development of chronic infection and the formation of branched, multiple fistulous tracts. Lightweight polypropylene and composite implants were used less frequently (28.6 %

Table 4. **Early results of surgical treatment**

Indicator	Inguinal hernias (n = 7)	Ventral hernias (n = 21)
Duration of hospitalization, days	7.1 ± 1.3	14.8 ± 3.2
Postoperative complications	1 (14.3 %)	6 (28.6 %)
Early relapses	–	2 (9.5 %)
Lethality	–	–

and 14.3 %, respectively). Implants with antibacterial coating were used in only one case.

Early results of surgical treatment are shown in Table 4. The average length of hospital stay for patients with ventral hernias was almost twice that for patients with inguinal hernias (14.8 ± 3.2 versus 7.1 ± 1.3 days). In the early postoperative period, 14.3 % of patients after explantations for inguinal hernias and 28.6 % of patients who underwent mainly partial explantations after alloplasty of ventral hernias exhibited inflammatory and infiltrative changes of varying severity in the soft tissues of the postoperative wound area. Treatment of these complications in the early postoperative period included antibiotic therapy based on sensitivity and local treatment combined with vacuum drainage. Drains were removed after the inflammatory exudation had stopped, usually on the 5th–7th day of the postoperative period. In 60 % of cases, the microbial landscape is dominated by pyogenic staphylococcal and streptococcal flora. Preliminary results from microbiological and histological studies of mesh explants suggest a potential etiological role of fungal flora in the chronicity of the infectious process. Further research in this area may contribute to improved management strategies for the postoperative period in patients with chronic implant infection, particularly by assessing the feasibility of conservative treatment without explantation.

The course of the wound-healing process was monitored visually and by serial ultrasound assessments of soft tissues. Concomitant pathologies, particularly diabetes mellitus, were also managed. All patients underwent follow-up examinations 24 to 36 months after surgery, with repeated alloplasty required in only 17.9 % of cases.

Conclusions

The implant rejection reaction associated with its primary infection after alloplasty of abdominal hernias is a pressing problem in modern herniology. The main proportion of cases of mesh implant rejection (75.0 %) are complications after alloplasty of ventral hernias when performing the operation using the onlay method and when using heavy polypropylene meshes. The leading cause of implant rejection is chronic infection of the alloplasty area, and the formation of branched multiple fistulas is one of the most frequent clinical manifestations. Complete explantation of the infected implant, combined with autoplasty and vacuum drainage, is the method of choice for the surgical treatment of such complications. Partial explantation with staged reconstruction is possible in carefully selected patients with ventral hernias, but it is accompanied by longer treatment and increases the risk of recurrence.

Declaration of interests

The authors declare no conflict of interest.

Ethics approval and written informed consent statements

All procedures performed in this study were in accordance with the ethical standards of the current Ukrainian regulations and with the 1964 Helsinki Declaration and its later amendments.

Authors contributions

A. I. Moiseienko: work concept and design, data collection and analysis, statistical analysis, critical review, final approval of the manuscript; K.O. Korolova: work concept and design, writing the manuscript.

References

1. Безродний БГ, Теплий ВВ, Колосович АІ. Діагностика, профілактика та лікування внутрішньочеревної гіпертензії у хворих на хірургічну патологію органів черевної порожнини. Київ: Валрус Дизайн; 2017. 138 с. ISBN 978-966-1562-09-6.
2. Ahmed MW, Elshoura Y, Mohamedahmed A, Ramasamy S, Kakaniaris G, Muras Z, Marzook H. Risk Factors for Wound Complications and Hernia Recurrence in Abdominal Wall Reconstruction: A Single-Institution Retrospective Study. Cureus. 2025 Jul 23;17(7):e88565. doi: 10.7759/cureus.88565. PMID: 40861686; PMCID: PMC12374597.
3. Ahmed U, Rosenberg J, Baker JJ. Chronic pain and foreign body sensation based on mesh placement in primary ventral hernia repair: a systematic review highlighting the evidence gap and a call to action. Langenbecks Arch Surg. 2025 Apr 21;410(1):132. doi: 10.1007/s00423-025-03671-2. PMID: 40257596;.
4. Fadaee N, Huynh D, Khanmohammed Z, Mazer L, Capati I, Towfigh S. Patients With Systemic Reaction to Their Hernia Mesh: An Introduction to Mesh Implant Illness. J Abdom Wall Surg. 2023 Jan 30;2:10983. doi: 10.3389/jaws.2023.10983. PMID: 38312397; PMCID: PMC10831643.
5. Maskal SM, Miller BT, Ellis RC, Beffa LRA, Prabhu AS, Rosen MJ, Krpata DM, Huang LC, Petro CC. A modern comparison of suture repair versus mesh repair for incisional hernia: a study protocol for a randomized controlled trial. Trials. 2025 Oct 29;26(1):450. doi: 10.1186/s13063-025-08924-5. PMID: 41163187; PMCID: PMC12574033.
6. Pogson-Morowitz K, Porras Fimbres D, Barrow BE, Oleck NC, Patel A. Contemporary Abdominal Wall Reconstruction: Emerging Techniques and Trends. J Clin Med. 2024 May 13;13(10):2876. doi: 10.3390/jcm13102876. PMID: 38792418; PMCID: PMC11122627.
7. Proctor VK, Tolstrup MB, Rosenberg J, Kehlet H. Surgical site infections after emergency hernia repair: A BJS Open substudy. BJS Open. 2023;7(1):zrac155. doi: 10.1093/bjsopen/zrac155.

8. Quiroga-Centeno AC, García-Ureña MA, López-Monclús J, Blázquez Hernando LA, López-Andújar R. Systematic review and meta-analysis of risk factors for mesh infection following abdominal wall hernia repair surgery. Am J Surg. 2022;224(1):239-246. doi: 10.1016/j.amjsurg.2021.12.024.
9. Smith SM, Khoja AA, Jacobsen JHW, Kovoor JG, Tivey DR, Babidge WJ, Chandraratna HS, Fletcher DR, Hensman C, Karatassas A, Loi KW, McKertich KMF, Yin JMA, Maddern GJ. Mesh versus non-mesh repair of groin hernias: a rapid review. ANZ J Surg. 2022 Oct;92(10):2492-2499. doi: 10.1111/ans.17721. Epub 2022 Apr 21. PMID: 35451174; PMCID: PMC9790697. doi: 10.1111/ans.17721.
10. Wilson RB, Farooque Y. Risks and prevention of surgical site infection after hernia mesh repair and the predictive utility of ACS-NSQIP. J Gastrointest Surg. 2022;26(4):950-964. doi: 10.1007/s11605-021-05185-0.
11. Zainy HMA. Postoperative Infection in Mesh Repair Hernias, Risk Factors and Management. South Asian Journal of Social Sciences and Humanities [Internet]. 2025 Feb 6;6(1):1-11. Available from: http://dx.doi.org/10.48165/sajssh.2024.6101.

Реакція відторгнення імплантату при алопластиці черевних гриж: аналіз причин і способів їх хірургічної корекції

А. І. Мойсеєнко, Х. О. Корольова

Національний медичний університет імені О. О. Богомольця, Київ

Грижі передньої черевної стінки, зокрема післяопераційні, є актуальною проблемою сучасної абдомінальної хірургії. Впровадження алопластики із застосуванням сітчастих імплантатів дало змогу значно поліпшити результати хірургічного лікування черевних гриж, знизивши частоту рецидивів до 8–20 %, а при застосуванні гібридно-лапароскопічних методик – до 2,7 %. Однак використання імплантатів супроводжується специфічними ускладненнями. Незадовільні результати перебігу процесів інтеграції сітки після алопластики черевних гриж пояснюються спотвореним перебігом місцевої запальної реакції, а саме трансформацією асептичного запалення в бактеріальне.

Мета — систематизувати й узагальнити сучасні уявлення та власний досвід хірургічного лікування інфекційних ускладнень алопластики черевних гриж, провести аналіз причин їхнього виникнення та визначити перспективні напрями поліпшення результатів лікування.

Матеріали та методи. Проаналізовано дані 28 хворих, яким раніше були виконані алопластики черевних гриж, що в подальшому ускладнились запальними процесами в зоні локалізації імплантату. Діагностика реакції відторгнення сітчастого імплантату ґрунтувалася на комплексній оцінці клінічних, лабораторних, інструментальних і морфологічних даних. Наявність стійких клінічних симптомів протягом тривалого періоду після алопластики розцінювали як показання для поглибленого обстеження для заперечення або підтвердження відторгнення імплантату та визначення оптимальної для хворого тактики лікування. Для цього використовували лабораторні дослідження, ультразвукове дослідження, комп'ютерну чи магнітно-резонансну томографію.

Результати. Основною причиною відторгнення імплантатів у загальній групі була хронічна інфекція зони імплантації, виявлена в 46,4 % випадків, яка поєднувалася з формуванням нориць у 28,6 % пацієнтів. У всіх 7 хворих із запальними ускладненнями після алопластики пахових гриж виконано повну експлантацію сітчастого імплантату, ретельне відновлення нормальної анатомії пахового каналу, санацію тканин і висічення норицевих ходів з автопластикою за наявності супутнього рецидиву грижі. При вентральних грижах у 15 із 21 пацієнта (71,4 %) проведено повну експлантацію сітчастого імплантату, у 6 (28,6 %) – часткову експлантацію з максимально можливим збереженням інтегрованих ділянок.

Висновки. Більшість випадків відторгнення сітчастих імплантатів (75,0 %) зареєстрували після алопластики вентральних гриж, особливо при виконанні пластики за методикою onlay та при застосуванні важких поліпропіленових сіток. Основною причиною відторгнення імплантатів є хронічна інфекція зони алопластики, а формування розгалужених множинних нориць – один із найчастіших клінічних виявів. Повна експлантація інфікованого імплантату в поєднанні з автопластикою та вакуумним дренуванням є методом вибору при хірургічному лікуванні таких ускладнень. Часткова експлантація з поетапною реконструкцією можлива в ретельно відібраних пацієнтів із вентральними грижами, але потребує тривалішого лікування та підвищує ризик рецидиву.

Ключові слова: реакція відторгнення імплантату, алопластика, вентральні грижі, пахові грижі, експлантація імплантату.

FOR CITATION

Moiseienko AI, Korolova KO. Implant rejection in alloplasty of abdominal hernias: analysis of causes and surgical correction methods. General Surgery (Ukraine). 2026;(1):31-37. http://doi.org/10.30978/GS-2026-1-31.

UDC 616.12-007.2-053.1/.3-089-036
DOI http://doi.org/10.30978/GS-2026-1-38

ISSN 2786-5584 print
ISSN 2786-5592 online

Prognostic model of integral renal risk in infants after correction of congenital heart defects

M. H. Melnychenko[1], V. P. Buzovskyi[2], L. B. Elii[1]

[1] Odesa National Medical University
[2] Odesa Regional Children's Clinical Hospital

✉ Maryna Melnychenko: marina64gm@gmail.com

M. H. Melnychenko, http://orcid.org/0000-0001-9066-4801
V. P. Buzovskyi, http://orcid.org/0000-0002-4505-2731
L. B. Elii, http://orcid.org/0009-0005-8219-4770

Renal complications and subclinical renal stress are frequent components of the early postoperative period in infants after cardiac surgical correction of congenital heart defects and require early risk stratification.

Objective – to develop a prognostic scoring index for assessing the integral renal risk index in infants after correction of congenital heart defects in the early postoperative period.

Materials and methods. A retrospective single-center descriptive-analytical study was conducted (n = 101; age 1–12 months). The dependent variable was the integral renal risk index (a continuous scale of integral renal risk or stress) formed within the analysis of the early postoperative period. The following predictors were considered: disease severity, physical development as a proxy for nutritional status, class or complexity of the surgical intervention, syndromic or genetic features, creatinine level, and left ventricular ejection fraction. Multiple linear regression was constructed with diagnostics of assumptions (normality of residuals, linearity, homoscedasticity, multicollinearity assessed by the variance inflation factor, and influential observations).

Results. The model was statistically significant ($F(6, 94) = 9.82$; $p < 0.001$) and explained 38.5 % of the variance in risk (adjusted $R^2 = 0.346$). The largest independent contribution was made by the operation class (surgical complexity) ($b = 0.578$; $p < 0.001$), whereas ejection fraction demonstrated an inverse association with risk ($b = -0.0167$; $p = 0.016$).

Conclusions. A scoring index, X, defined by a formula and within-cohort thresholds ($X > 1$ – high risk; $X > 1.5$ – very high risk), is proposed. This index integrates perioperative burden and perfusion reserve and may be used for early nephroprotective management.

Keywords
congenital heart defects, infants, postoperative period, acute kidney injury, renal stress, scoring, regression model.

ARTICLE • Received 2026-01-05 • Received in revised form 2026-02-13 • Published 2026-03-31

The early postoperative period in infants after cardiac surgical correction of congenital heart defects (CHD) is accompanied by hemodynamic lability and a systemic inflammatory-stress response, which increases the risk of organ dysfunction [5, 7]. The kidneys are among the most sensitive target organs to hypoperfusion/reperfusion, fluctuations in cardiac output, hemodilution or anemia, vasoactive therapy, and nephrotoxic drugs [5, 7]. The combination of perfusion disorders, cytokine-mediated changes, microcirculatory disturbances, and fluid imbalance can lead to both clinically overt acute kidney injury (AKI) and early manifestations of renal dysfunction, which may occur before an increase in creatinine levels [5, 6].

According to contemporary summaries, AKI in pediatric cardiac surgery is associated with worse clinical outcomes (longer stay in the intensive care unit and hospital, higher complication rates, the need for renal replacement therapy, and increased mortality) [5, 8]. Prognostic significance is attributed not only to the presence of AKI but also to its severity, duration of impairment, and fluid overload; the timing of initiation of renal replacement therapy in critically ill children is also important [1].

Key predictors include age and body weight, complexity of the intervention, perioperative burden, the need for vasopressor support, and markers of reduced perfusion capacity; meta-analytic data emphasize the central role of the «operative burden + perfusion reserve» complex [8], and instrumental indicators (in particular, Doppler-derived variables of renal blood flow) may have additional prognostic value [2].

Thus, there is a practical need for a simple calculated index that combines available clinical, laboratory, and instrumental parameters and allows assessment of integral renal risk at the bedside in the first postoperative days. Such a tool should not aim to replace AKI diagnosis but rather to support early decisions: intensification of hemodynamic and diuresis monitoring, correction of infusion strategy, limitation of nephrotoxic combinations, and optimization of the perfusion regimen with regard to cardiac perfusion reserve [2, 4, 6, 8].

Objective – to develop a prognostic scoring index for assessing the integral renal risk index in infants after correction of congenital heart defects in the early postoperative period.

Materials and methods

Design: A retrospective single-center study was conducted using de-identified data of 101 infants (1–12 months) who underwent cardiac surgical CHD correction, with assessment of the early postoperative period course during the first hospitalization at the Department of Cardiovascular Surgery of the Odesa Regional Children's Clinical Hospital. The analysis covered clinical characteristics of the early postoperative period, basic laboratory parameters, and echocardiographic variables.

The endpoint was the integral renal risk index, reflecting the gradient of renal risk or stress in the early postoperative period. The use of linear regression was justified by the continuous scale of risk and the need to obtain a numerical index for bedside stratification.

Predictor selection was performed according to three interrelated criteria: data availability, pathophysiological association with mechanisms of renal hypoperfusion and stress in the early postoperative period, and minimal reliance on protocol-based descriptive variability. The most suitable instrumental parameter for inclusion in the model was left ventricular ejection fraction (EF; n = 101), as it is a standardized integral marker of pump function and perfusion reserve. From a pathogenetic perspective, EF is associated with the risk of systemic hypoperfusion and secondary target-organ injury, in particular renal injury. Among clinical and systemic predictors, preference was given to parameters (severity), physical development as a proxy for nutritional status and metabolic reserves (Physical), type or surgical intervention complexity (Operation class), presence of syndromic and genetic features (Stigmata), as well as creatinine (Creatinine) as a laboratory marker of renal stress. Such a set of variables allows combining three levels of risk in a single equation: baseline vulnerability, the intensity of surgical and perioperative impact, and early laboratory «response» of the kidneys.

Statistical analysis [3]: multiple linear regression was constructed with assessment of model quality (multiple correlation coefficient (R), coefficient of determination (R^2), adjusted R^2, F-statistic, p), analysis of coefficients (unstandardized coefficients (b), standard error (SE), t-statistic, p), and diagnostics of model assumptions. Homoscedasticity (homogeneity of residual variance) was assessed graphically (scatter of residuals relative to predicted values). Multicollinearity was assessed using variance inflation factors (VIFs). Influential observations were analyzed using Cook's distance. The level of statistical significance was set at $p < 0.05$. Calculations were performed using IBM SPSS Statistics and Microsoft Excel.

The study was conducted using de-identified data in compliance with ethical principles of biomedical research and the provisions of the Declaration of Helsinki. As the study was retrospective and used de-identified data, informed consent was obtained in accordance with local procedures.

Results

In infants after CHD correction, even with formally preserved systolic function, perfusion fluctuations may occur in some patients, triggering transient renal stress. Therefore, a multifactor prognostic index was constructed to assess individual risk from the combined effect of hemodynamic, clinical, and systemic factors (Fig. 1).

Fig. 1 presents the conceptual scheme for score formation: integration of predictors reflecting baseline vulnerability (severity, physical, stigmata), perioperative complexity (operation class), a laboratory signal of renal stress (Creatinine), and instrumental perfusion reserve (EF).

The constructed model included 101 observations (children under 1 year of age after CHD correction) and six predictors, which ensured an observation-to-parameter ratio sufficient for multiple regression estimation without excessive parametrization. Table 1 presents the integral indicators

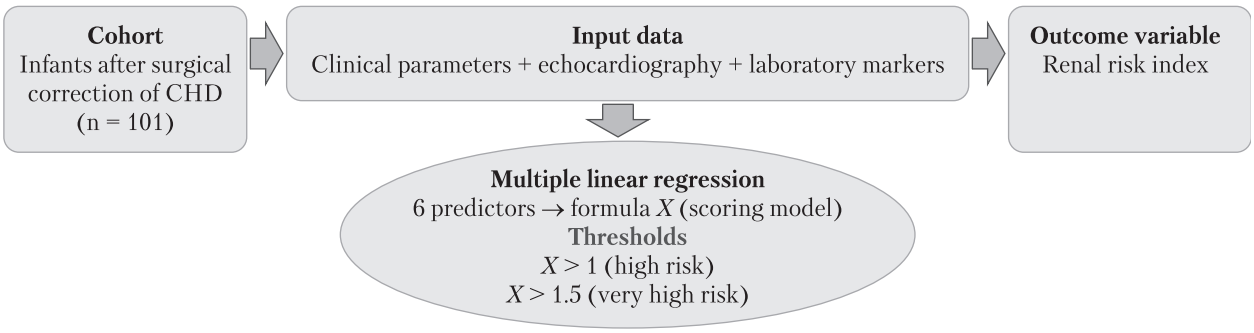

Figure 1. **Scheme of construction of the prognostic integral renal risk index**

of the quality of the linear regression model and its statistical significance for predicting the integral renal risk index (risk of renal complications) in infants after CHD correction.

As shown in Table 1, R = 0.621 indicates moderate agreement between the observed risk values and the model predictions. The coefficient of determination, $R^2 = 0.385$, indicates that the set of predictors explains 38.5 % of the variance in risk in the sample. After adjustment for the number of variables, the explanatory power is 34.6 % (adjusted $R^2 = 0.346$), which is expected for clinical data with a multifactorial endpoint. The F statistic ($F(6, 94) = 9.82$; $p < 0.001$) confirms that the model significantly improves predictive performance compared with the null model (without predictors). The obtained values indicate that the constructed regression model has practical prognostic value and establishes a basis for calculated scoring to facilitate early stratification of postoperative renal risk.

The logic of inclusion of the selected predictors corresponds to the three-component concept of renal risk: (1) patient vulnerability (severity, physical, stigmata); (2) intensity of perioperative impact (operation class); (3) early laboratory signal of renal stress (Creatinine) in combination with the instrumental marker of perfusion reserve (EF).

Before constructing the equation, data quality control was performed: verification of ranges, detection of outliers, and assessment of predictor correlations to prevent multicollinearity. For linear regression, it is important to ensure the adequacy of basic assumptions; therefore, normality of residuals, homoscedasticity, and influential observations were also evaluated (Table 2).

The largest independent contribution to the predicted risk is made by operation class ($b = 0.577951$; $p < 0.001$). This means that with increasing class and complexity of the intervention, the risk index increases, reflecting a higher probability of renal stress under conditions of greater perioperative burden. The second statistically significant predictor is EF: the inverse association ($b = –0.016666$; $p = 0.016$) indicates that lower EF is associated with a higher risk, which is pathophysiologically consistent with mechanisms of reduced perfusion reserve and increased renal sensitivity to hemodynamic fluctuations. The variables severity, physical, stigmata, and Creatinine did not demonstrate independent statistical significance in this model; they should be considered risk modifiers and indicators of background vulnerability, with effects that may

Table 1. **Quality of the regression model (basis for scoring)**

Indicator	Value
N	101
R	0.621
R^2	0.385
Adjusted R^2	0.346
F (6, 94)	9.82
p (overall model)	< 0.001
Dependent variable	risk

Table 2. **Regression coefficients for the construction of index X**

Predictor	b	SE(b)	t	p
Intercept	0.817678	0.710820	1.15033	0.253
Severity	0.141593	0.142791	0.99161	0.324
Physical	0.097574	0.412245	0.23669	0.813
Operation class	0.577951	0.082910	6.97086	< 0.001
Stigmata	0.020198	0.019659	1.02743	0.307
Creatinine	0.000398	0.003856	0.10328	0.918
EF	–0.016666	0.006805	–2.44899	0.016

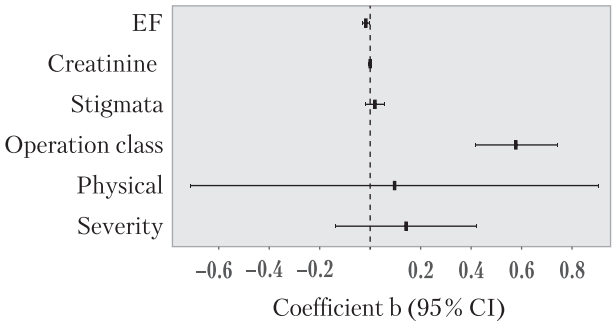

Figure 2. **Model coefficients with 95 % confidence intervals (linear regression)**

become apparent with a larger sample, a different endpoint definition, or in nonlinear models.

Fig. 2 graphically illustrates the magnitude and direction of the associations between each predictor and risk: the most pronounced positive contribution is observed for operation class, whereas EF has a negative coefficient.

The multiple linear regression equation (unstandardized coefficients) was transformed into a practical, calculated index, *X*, for individual assessment of integral renal risk in the first postoperative days. This presentation allows the model to be used as a bedside tool for risk stratification and planning the intensity of monitoring and nephroprotective interventions. The formula for index *X* is given below:

$$X = 0.817678 + 0.141593 \cdot \text{Severity} + 0.097574 \cdot \text{Physical} + 0.577951 \cdot \text{Operation class} + 0.020198 \cdot \text{Stigmata} + 0.000398 \cdot \text{Creatinine} - 0.016666 \cdot \text{EF}.$$

For practical interpretation of the index within the studied cohort, intra-empirical thresholds were used: $X > 1$ – high risk; $X > 1.5$ – very high risk. These thresholds should be regarded as indicative until external validation is obtained.

The *X* score is intended for rapid stratification of infants by renal risk level immediately after surgery and during the first postoperative days. The most unfavorable profile in the model is the combination of a higher intervention-complexity class and lower EF. For such patients, the following are advisable:

- intensified perfusion monitoring (arterial pressure trends, urine output, laboratory parameters);
- nephroprotective strategy (optimization of hemodynamics, avoidance of nephrotoxic combinations, early correction of hypovolemia/overload);
- more frequent monitoring of creatinine/urea during the first 24–48 hours;
- closer control of fluid balance and adjustment of infusion strategy.

The advantage of the index lies in its simplicity: it is based on parameters that are usually available in routine practice (surgical characteristics, EF, and basic clinical and laboratory variables) and can be used as an auxiliary decision-support tool for determining the intensity of monitoring.

Discussion

The proposed model represents an attempt to transform the descriptive postoperative profile of infants after CHD correction into an applied tool for predicting renal risk. The key methodological idea was to combine within a single index two «core» mechanisms: (1) the intensity of operative and perioperative burden and (2) the perfusion reserve of the cardiovascular system. In our sample, these components – the operation class and EF – were statistically significant independent predictors of risk, supporting the pathophysiological concept of renal stress as a derivative of perfusion stability in the context of intervention complexity.

The scientific novelty of the approach consists in (1) formalization of renal risk as a continuous gradient (risk) rather than a binary «presence/absence of AKI», which allows more sensitive identification of the «grey zone» of subclinical renal stress; (2) development of a within-cohort scoring index *X* with a simple formula based on routinely available parameters; and (3) demonstration of the priority role of the combination «operative burden + perfusion reserve» in shaping the predicted risk compared with a number of traditionally plausible but, in this sample, statistically non-dominant modifiers (baseline severity, physical development, stigmata, and baseline creatinine).

In practical terms, index *X* may be applied within the first 24–48 hours after surgery to intensify nephroprotective management in the higher-risk group: intensified perfusion monitoring, adjustment of infusion strategy to maintain fluid balance, limitation of nephrotoxic drug combinations, and more frequent laboratory monitoring (creatinine/urea).

Conclusions

The constructed multiple linear regression model for predicting the integral renal risk index in infants after CHD correction is statistically significant and has practical prognostic value ($R = 0.621$; $R^2 = 0.385$; adjusted $R^2 = 0.346$; $F(6, 94) = 9.82$; $p < 0.001$), which allows its use as the basis for a calculated clinical index.

The largest independent contribution to the increase in the predicted risk in the sample is made by

the class or complexity of the surgical intervention (operation class) ($b = 0.578$; $p < 0.001$), reflecting the priority role of perioperative burden in the development of renal stress in the early postoperative period.

Left ventricular ejection fraction demonstrates an inverse association with risk ($b = -0.0167$; $p = 0.016$): lower EF is associated with higher predicted renal risk, which is pathophysiologically consistent with reduced perfusion reserve and greater renal sensitivity to hemodynamic fluctuations.

A calculated scoring index X (based on unstandardized regression coefficients) is proposed along with within-cohort stratification thresholds ($X > 1$ – high risk; $X > 1.5$ – very high risk). These tools help facilitate early identification of a higher renal risk group and selection of monitoring intensity during the first 24–48 hours after surgery.

Clinical application of index X is appropriate as a decision-support tool for nephroprotection (intensification of perfusion and diuresis monitoring, optimization of infusion strategy, minimization of nephrotoxic combinations, and more frequent laboratory monitoring). At the same time, the thresholds and coefficients require external validation in an independent sample (prospectively/multicenter) to refine calibration and generalizability.

Declaration of interests

The authors declare no conflicts of interest.

Funding. This study did not receive any specific grants from public, commercial, or non-profit funding agencies.

Ethics approval and written informed consent statements

The study was conducted in accordance with the ethical principles of biomedical research and the provisions of the Declaration of Helsinki and was approved by the Ethics Committee of Odesa National Medical University (Protocol No. 1a dated January 14, 2026). Written informed consent was obtained from the parents or legal guardians of all patients.

Authors contributions

M. H. Melnychenko: study concept and design, critical revision of the manuscript, scientific supervision; V. P. Buzovskyi: clinical procedures, patient follow-up, data analysis, manuscript preparation, and editing; L. B. Elii: data collection, literature review, manuscript preparation.

References

1. Cortina G, McRae R, Hoq M, Donath S, Chiletti R, Arvandi M, Gothe RM, Joannidis M, Butt W. Mortality of Critically Ill Children Requiring Continuous Renal Replacement Therapy: Effect of Fluid Overload, Underlying Disease, and Timing of Initiation. Pediatr Crit Care Med. 2019 Apr;20(4):314-322. doi: 10.1097/PCC.0000000000001806. PMID: 30431556.
2. De Souza FM, De Carvalho AV, Ferraz IS, Damiano AP, Brandão MB, Nogueira RJN, De Souza TH. Acute kidney injury in children undergoing cardiac surgery: predictive value of kidney arterial Doppler-based variables. Pediatr Nephrol. 2024 Jul;39(7):2235-2243. doi: 10.1007/s00467-024-06319-3. Epub 2024 Feb 28. PMID: 38416215.
3. Hickey GL, Kontopantelis E, Takkenberg JJM, Beyersdorf F. Statistical primer: checking model assumptions with regression diagnostics. Interact Cardiovasc Thorac Surg. 2019 Jan 1;28(1):1-8. doi: 10.1093/icvts/ivy207. PMID: 30010875.
4. Melink KF, Stanski NL, Gorrell E, Alten JA, Pettit KA, Goldstein SL, Zang H, Ollberding NJ, Basu RK, Menon S, SooHoo M, Gist KM. Modification of the Cardiac Renal Angina Index for Predicting Adverse Kidney Events After Pediatric Cardiac Surgery. J Am Heart Assoc. 2025 Aug 19;14(16):e042941. doi: 10.1161/JAHA.125.042941. Epub 2025 Aug 12. PMID: 40792581; PMCID: PMC12533677.
5. Sharma A, Chakraborty R, Sharma K, Sethi SK, Raina R. Development of acute kidney injury following pediatric cardiac surgery. Kidney Res Clin Pract. 2020 Sep 30;39(3):259-268. doi: 10.23876/j.krcp.20.053. PMID: 32773391; PMCID: PMC7530361.
6. Shi S, Fan J, Shu Q. Early prediction of acute kidney injury in neonates with cardiac surgery. World J Pediatr Surg. 2020 Jun 25;3(2):e000107. doi: 10.1136/wjps-2019-000107. PMID: 36474915; PMCID: PMC9716980.
7. Tariq A, Bora V. Perioperative Management of Patients With Congenital Heart Disease. 2023 Sep 4. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan. PMID: 36256750.
8. Van den Eynde J, Delpire B, Jacquemyn X, Pardi I, Rotbi H, Gewillig M, Kutty S, Mekahli D. Risk factors for acute kidney injury after pediatric cardiac surgery: a meta-analysis. Pediatr Nephrol. 2022 Mar;37(3):509-519. doi: 10.1007/s00467-021-05297-0. Epub 2021 Sep 30. PMID: 34595570.

Прогностична модель інтегрального ренального ризику в немовлят після корекції вроджених вад серця

М. Г. Мельниченко [1], В. П. Бузовський [2], Л. Б. Елій [1]

[1] Одеський національний медичний університет

[2] КНП «Одеська обласна дитяча клінічна лікарня»

Ренальні ускладнення та субклінічний ренальний стрес є частими компонентами раннього післяопераційного періоду в немовлят після кардіохірургічної корекції вроджених вад серця та потребують ранньої стратифікації ризику.

Мета — розробити прогностичний скоринговий індекс для оцінки інтегрального показника ренального ризику (risk) у немовлят після корекції вроджених вад серця в ранній післяопераційний період.

Матеріали та методи. Проведено ретроспективне одноцентрове описово-аналітичне дослідження (n = 101; 1—12 міс). Залежною змінною був інтегральний показник risk (безперервна шкала інтегрального ренального ризику або стресу), сформований у межах аналізу раннього післяопераційного періоду. Як предиктори розглядали: тяжкість стану, фізичний розвиток як проксі нутритивного статусу, клас або складність оперативного втручання, синдромальні або генетичні стигми, креатинін і фракцію викиду лівого шлуночка. Побудовано множинну лінійну регресію з діагностикою припущень (нормальність залишків, лінійність, гомоскедастичність, мультиколінеарність за VIF (the variance inflation factor), впливові спостереження).

Результати. Модель була статистично значущою ($F(6, 94) = 9{,}82$; $p < 0{,}001$) і пояснювала 38,5 % варіації risk (Adjusted $R2 = 0{,}346$). Найбільший незалежний внесок мав operation_class ($b = 0{,}578$; $p < 0{,}001$), тоді як фракція викиду демонструвала негативний зв'язок із risk ($b = -0{,}0167$; $p = 0{,}016$).

Висновки. Запропоновано скоринговий індекс X із формулою та внутрішньокогортними порогами ($X > 1$ — високий, $X > 1{,}5$ — дуже високий ризик), який інтегрує періопераційне навантаження та перфузійний резерв і може застосовуватися для раннього нефропротективного ведення.

Ключові слова: вроджені вади серця, немовлята, післяопераційний період, гостре ураження нирок, ренальний стрес, скоринг, регресійна модель.

FOR CITATION

Melnychenko MH, Buzovskyi VP, Elii LB. Prognostic model of integral renal risk in infants after correction of congenital heart defects. General Surgery (Ukraine). 2026;(1);38-43. http://doi.org/10.30978/GS-2026-1-38.

UDC 616.37-002.1-002.4-089:616-072.1
DOI http://doi.org/10.30978/GS-2026-1-44

ISSN 2786-5584 PRINT
ISSN 2786-5592 ONLINE

Endoscopic transluminal interventions in the management of acute infected necrotizing pancreatitis. Literature review

N. V. Puzyr [1,2], A. Y. Tkachenko [3]

[1] Bogomolets National Medical University, Kyiv
[2] Kyiv City Clinical Emergency Hospital
[3] Ukrainian Military Medical Academy, Kyiv

✉ Nazar Puzyr: dr.puzyr@ukr.net

N. V. Puzyr, http://orcid.org/0009-0008-3878-0715
A. Y. Tkachenko, http://orcid.org/0000-0002-3371-497X

Acute necrotizing pancreatitis remains one of the most challenging diseases in general surgery. Infection of necrotic tissue, sepsis, and organ failure are the main determinants of mortality in this pathology. Other life-threatening complications include intestinal obstruction, biliary obstruction, abdominal compartment syndrome, external fistulas, bleeding, and thrombosis of the splenic and portal veins. The formation of walled-off necrosis after the fourth week of disease creates anatomical conditions for a transluminal endoscopic access to the pathological focus when appropriate indications are present. Current management of acute necrotizing pancreatitis is based on a step-up minimally invasive strategy in which endoscopic interventions occupy a leading role. International clinical guidelines, particularly those of ESGE, AGA, and ASGE, support the endoscopic step-up approach as first-line therapy for infected walled-off necrosis. This strategy focuses on controlling septic manifestations rather than performing immediate necrosectomy. Key factors for success include appropriate timing of intervention, a multidisciplinary approach, and individualization of the treatment strategy. The optimal indications for escalation to more invasive procedures remain unresolved and are subject to ongoing debate, often depending on the experience of a particular specialized center. The complexity of clinical decision-making may also be related to differences in treatment approaches between general surgeons and endoscopists, which necessitates a balanced interdisciplinary collaboration.

This literature review highlights the main aspects of managing acute necrotizing pancreatitis with endoscopic transluminal interventions. A comprehensive understanding of the advantages and limitations of this technique promotes its further technical and tactical refinement to improve treatment outcomes.

Keywords
acute necrotizing pancreatitis, acute infected pancreatic necrosis, walled-off necrosis, endoscopic transluminal necrosectomy, direct endoscopic necrosectomy.

ARTICLE • Received 2026-01-26 • Received in revised form 2026-09-03 • Published 2026-03-31

Acute pancreatitis (AP) is the most common disease of the digestive system requiring urgent hospitalization [13]. In most cases (about 80 %), AP follows a mild interstitial edematous course and resolves rapidly [69]. Approximately 20 % of patients develop acute necrotizing pancreatitis (ANP), which is associated with multiple organ failure (38 %), the need for invasive intervention (38 %), and a mortality rate of 15–30 %, depending on the presence of infected necrosis [9, 50, 78, 86]. In the setting of open surgical procedures, mortality reaches 11–39 % [17].

Key aspects in the management of patients with acute pancreatitis include early diagnosis, early pharmacological therapy, and dynamic assessment of the clinical course; in severe forms of AP, early enteral nutrition, antibiotic therapy in the presence of signs of (or proven) infection, and the availability of an appropriate spectrum of minimally invasive interventions, with strict adherence to indications and timing, are essential.

Open surgical necrosectomy historically was the mainstay of treatment for symptomatic necrotic collections; however, management strategies have

evolved. Currently, preference is given to minimally invasive approaches, primarily endoscopic necrosectomy and/or percutaneous catheter drainage (PCD) as the initial step of treatment [62]. Among invasive interventions for complicated AP, endoscopic transluminal interventions are increasingly being applied [3].

Indications for invasive interventions in acute necrotizing pancreatitis

Surgical interest in ANP primarily concerns walled-off necrosis (WON) according to the 2012 Revised Atlanta Classification of acute pancreatitis [8]. WON develops after the fourth week of acute pancreatitis as a result of persistent acute (peri-)pancreatic necrosis and is characterized by a mature, encapsulated collection of both fluid and necrotic material enclosed by a well-defined wall [8, 75].

According to international guidelines for the management of acute pancreatitis, indications for invasive intervention (radiological, endoscopic, or surgical) in acute necrotizing pancreatitis include [3, 13]:

- Documented infected necrotizing pancreatitis (INP).
- Clinical suspicion of INP: in the absence of documented INP, but in the presence of persistent organ dysfunction or ongoing clinical deterioration for several weeks after the onset of acute pancreatitis despite optimal conservative therapy, preferably after the formation of WON; in other words, in the setting of persistent systemic inflammatory response syndrome. A retrospective study by Rodriguez involving 167 patients found that 42 % of such patients had INP [57].
- Compression of adjacent organs without signs of INP, including gastric outlet obstruction, intestinal or biliary obstruction, as well as pain caused by the mass effect of a large WON. Interventions should preferably be performed more than 4–8 weeks after the onset of acute pancreatitis [35, 43]. Secondary infection represents a key risk in this group of indications [3].
- Abdominal compartment syndrome: this condition is less common but may require early decompression (radiological or surgical) during the course of acute pancreatitis. At the same time, revision of the lesser sac or performance of necrosectomy during such a procedure is not recommended due to the risk of bleeding and infection of sterile necrosis [77, 82].
- Fistulas that fail to regress with conservative treatment [3, 12].

Conservative management in acute necrotizing pancreatitis

Recent studies and international guidelines generally support a watchful waiting strategy for uncomplicated asymptomatic WON and pancreatic pseudocysts, as most of these collections regress spontaneously without the need for intervention [19, 22]. There is substantial evidence that asymptomatic WON should be managed conservatively, regardless of its extent or size [13, 21, 27, 32, 71, 92].

In a study by Jagielski et al., asymptomatic WON was identified in 44 of 168 patients (26 %). The mean follow-up period for patients with asymptomatic WON was 417.02 days (range: 47–1149 days). Complete regression of WON occurred in 30 of the 44 asymptomatic patients. Symptoms related to WON developed in 13 of 44 patients (30 %) during follow-up. The most common indication for interventional treatment of WON was infected pancreatic necrosis, which was diagnosed in 6 of 13 patients (46 %). Overall, 137 of 168 patients (82 %) with WON required interventional treatment [33].

The 2024 Chinese multicenter consensus allows observation of pancreatic pseudocysts and WON smaller than 6 cm in the absence of evident symptoms or complications [98].

With regard to INP, data from small cohort studies and a recent meta-analysis (including studies with considerable heterogeneity) suggest that a subset of patients with INP (6/42; 14 % [10]) may be treated with antibiotics alone [10, 25, 53, 60]. However, the exact subgroup of such clinically stable patients has not been clearly defined. Moreover, in some studies, conservative treatment also included PCD, which complicates the identification of patients who received antibiotics as the sole therapy [25, 41].

Diagnosis of infected necrosis

In patients with acute pancreatitis, the absolute impact of infected pancreatic necrosis and organ failure on mortality is comparable; therefore, the presence of either factor indicates severe disease [50]. The relative risk of death doubles when infected pancreatic necrosis and organ failure coexist, indicating a very severe or critical form of acute pancreatitis [50]. Infected necrosis develops in approximately one-third of patients with ANP, on average after the 10th day of disease, and is associated with a mortality rate of about 30 % [9].

INP may be suspected in the presence of clinical signs of sepsis (e.g., temperature > 38 °C, features of persistent systemic inflammatory response syndrome, and clinical deterioration or lack of improvement), or when extraluminal gas is detected within the pancreatic or peripancreatic tissues on computed tomography (CT) [25]. The diagnosis of INP is established when samples of (peri-)pancreatic tissue obtained via percutaneous, endoscopic, or surgical drainage yield positive results for bacteria

and/or fungi on Gram staining or microbiological culture [3].

The additional diagnostic value of fine-needle aspiration (FNA) is limited when clinical and/or imaging findings are already suggestive of infection [79]. Furthermore, a substantial proportion of false-negative (20–29 %) and false-positive (4–10 %) results has been reported [57, 79].

In a Dutch retrospective analysis involving 208 patients, clinical deterioration (persistent sepsis, new-onset or prolonged organ dysfunction, increasing need for cardiovascular, respiratory, or renal support, leukocytosis, elevated or rising C-reactive protein levels, and fever), despite adequate therapy and in the absence of an alternative source of infection, was attributed to INP in 74 of 92 patients (80.4 %); the false-positive rate was 19.6 % [3, 79].

A systematic review demonstrated that procalcitonin is the most accurate biomarker for INP. At a cutoff value of 3.5 ng/mL, sensitivity and specificity were 0.90 and 0.89, respectively [94]. Nonetheless, procalcitonin is a nonspecific marker of infectious complications in critically ill patients; therefore, other potential sources of infection must be excluded [39].

The presence of gas within (extra-)parenchymal necrosis on CT showed limited diagnostic value for assessing INP in the aforementioned study (sensitivity 45.9 %, specificity 81.5 %, accuracy 50.5 %) [79]. Magnetic resonance imaging (MRI) is a potential tool for detecting INP; however, large-scale studies evaluating its diagnostic performance remain limited [3].

Fungal colonization of pancreatic necrosis remains poorly studied. It is associated with the development of severe acute pancreatitis, formation of WON, and high mortality, although the benefit of prophylactic antifungal therapy in severe pancreatitis has not been demonstrated. Fungal infection of the pancreas occurs in approximately 40 % of patients with severe acute pancreatitis who develop WON [91, 56]. Importantly, patients with positive cultures for pancreatic *Candida* infection exhibited significantly higher mortality compared with those without *Candida* (35.2 % vs 13.4 %) [56]. A recent meta-analysis of 22 publications evaluating the incidence of *Candida* infection and its impact on mortality in INP further confirmed that local or systemic *Candida* infection is associated with increased mortality in INP [70].

Owing to the diagnostic complexity and the lack of a single sensitive and specific marker for INP, the diagnosis should be based on a comprehensive assessment of the patient's general condition, laboratory parameters, and imaging findings, rather than solely on microbiological findings.

Timing of minimally invasive intervention

European and American guidelines recommend postponing invasive interventions until at least 4 weeks after the onset of pancreatitis to allow maturation of the necrotic collection and liquefaction of necrotic debris [3, 62].

In the randomized controlled trial (RCT) POINTER (104 patients) [15], management of infected necrosis was compared between immediate drainage (percutaneous or endoscopic) within 24 hours after establishing the diagnosis of infected necrosis and postponed drainage after a 4-week waiting period to allow maturation of WON. More than 33 % of patients in the postponed-drainage group improved with antibiotic therapy alone and did not require any intervention. Moreover, necrosectomy was performed more frequently in the early-drainage group (51 % vs 22 %; RR 2.27; 95 % CI 1.27–4.06), as were combined endoscopic and radiological drainage procedures (4.4 vs 2.6). Mortality was 13 % in the immediate-drainage group and 10 % in the postponed-drainage group (relative risk 1.25; 95 % CI 0.42–3.68) [15].

The «step-up approach» strategy

In the context of invasive interventions for patients with ANP, the step-up approach should be highlighted. This strategy was first introduced in the publication describing the design and rationale of the PANTER trial in 2006 [14]. In 2010, van Santvoort et al., in a study involving 88 selected patients with INP, demonstrated the effectiveness of this strategy, whereby the least invasive intervention (e.g., percutaneous or endoscopic drainage) is applied first in INP, followed – only in case of failure – by a stepwise escalation to more invasive procedures (e.g., video-assisted retroperitoneal debridement (VARD) or open surgery) [87].

The step-up approach aims to minimize surgical trauma. In contrast to open necrosectomy, its primary goals are control of the infectious focus and mitigation of sepsis, rather than immediate complete removal of infected necrotic tissue [87]. According to the study, the use of minimally invasive techniques within the step-up approach (percutaneous or endoscopic drainage followed by VARD if required), compared with primary open necrosectomy, allows postponement or avoidance of open surgical necrosectomy, reduces the incidence of recurrent multiple organ failure (12 % vs 40 %) and late complications (including new-onset pancreatic insufficiency); however, no advantage in terms of mortality was demonstrated (19 % vs 16 %) [87]. The authors noted that detecting a clinically meaningful difference in mortality would require a trial including several

thousand patients, making such a study unlikely to be conducted [87].

The TENSION trial demonstrated advantages of the endoscopic step-up approach over the surgical step-up approach, including a lower incidence of enteric or pancreatocutaneous fistulas, shorter hospital stay, and reduced treatment costs, without an increase in major complications or mortality [7, 26, 83]. In addition, one meta-analysis [81] and a large international risk-adjusted study including 1980 patients showed reduced mortality when endoscopic or percutaneous drainage was used as the initial step compared with primary minimally invasive surgery [40].

A Cochrane meta-analysis (8 RCTs, 306 patients) demonstrated that: (i) compared with open necrosectomy, the step-up approach was associated with lower rates of both overall and serious complications, as well as lower mean costs; and (ii) compared with the video-assisted minimally invasive step-up approach (VARD), the endoscopically assisted step-up approach resulted in better outcomes in terms of complications, although it required a higher number of procedures (median difference: 2) [27]. The analysis also concluded that differences in short-term mortality among the compared approaches were imprecise.

Effectiveness and limitations of endoscopic transluminal interventions

Outcomes of endoscopic transgastric necrosectomy are encouraging. A systematic review of 10 studies on endoscopic necrosectomy reported complete resolution of WON in 76 % of cases, with an overall long-term complication rate of 27 % and a mortality rate of 5 %, although patient characteristics varied across the included studies [28]. Another systematic review of endoscopic necrosectomy (455 patients) reported a success rate of 81 % with endoscopic therapy alone and a complication rate of 36 % [80].

The randomized controlled trial by Bakker et al. (22 patients) demonstrated advantages of endoscopic transgastric necrosectomy over VARD and/or open necrosectomy, including a lower risk of recurrent organ failure (0 % vs 50 %, $p = 0.03$), a reduced incidence of pancreatic fistulas (10 % vs 70 %, $p = 0.02$), and lower post-procedural interleukin-6 levels ($p = 0.004$) [6].

A retrospective study by Tan et al. confirmed that endoscopic transgastric necrosectomy was associated with fewer complications and a shorter hospital stay compared with surgical necrosectomy [74]. However, a subsequent larger randomized trial (98 patients) [83] comparing the endoscopic step-up approach (drainage followed by necrosectomy if required) with the surgical step-up approach (PCD followed by VARD if required) did not demonstrate superiority of endoscopic necrosectomy in terms of major complications or mortality. Nevertheless, the endoscopic group showed lower fistula rates and shorter hospitalization [83].

Compared with PCD, a matched cohort study ($n = 24$) found that endoscopic necrosectomy was associated with a higher clinical success rate (92 % vs 25 %), a shorter hospital stay, and reduced healthcare resource utilization [36].

Limitations of the endoscopic approach include the need for multiple interventions, limited ability to endoscopically assess the full extent of necrotic debris, technical difficulties in removing large volumes of necrotic material, restricted applicability of transgastric endoscopic necrosectomy in cases with extensive retroperitoneal spread, and challenges or inability to adequately treat distally located left-sided necrotic collections [21]. Owing to these limitations, adjunctive PCD is required in approximately 40 % of patients, particularly when WON extends into the paracolic gutters or pelvis, and surgical intervention due to failure of endoscopic therapy is necessary in about 20 % of patients [47].

Endoscopic ultrasound or conventional endoscopy?

The first description of irrigation of a WON cavity via a transnasal catheter placed endoscopically through a transmural route in combination with endoscopic drainage using two double-pigtail plastic stents (DPPS) 10 Fr, 3 cm was reported by Baron in 1996 in a series of 11 patients [11]. The first direct transluminal endoscopic necrosectomy for WON was described by Seifert in 2000 [66]. Over more than two decades, this technique has undergone substantial evolution. Endoscopic transluminal access to WON can currently be achieved using either a therapeutic gastroscope or an echoendoscope [3, 12].

Selection of the access site to the WON cavity during endoscopic transluminal interventions often represents a challenge for the endoscopist. In approximately 50–60 % of cases of acute necrotizing pancreatitis, 4–6 weeks after disease onset, the WON cavity compresses the gastric wall (typically the posterior wall) and/or the duodenal wall [21]. During diagnostic esophagogastroduodenoscopy, a visible bulge into the gastric or duodenal lumen, often accompanied by inflammatory mucosal infiltration, may be observed, indicating close apposition of the WON cavity to the adjacent hollow organ. In such cases, endoscopic transluminal intervention may be performed without endoscopic ultrasound (EUS) at the site of bulging, provided there is no evidence of significant portal hypertension [34, 96].

Two randomized controlled trials confirmed the superiority of EUS-guided access in terms of technical success (100 % vs 33 % and 94 % vs 72 %, respectively) [48, 90]. In cases of «non-bulging» (peri-)pancreatic fluid collections where conventional transmural drainage was not feasible, EUS guidance enabled successful transmural access. Although both studies included only pancreatic pseudocysts, the results can reasonably be extrapolated to patients with WON.

However, a prospective comparative study found no difference between conventional (n = 53) and EUS-guided drainage (n = 46) in patients with pancreatic pseudocysts with regard to short-term (94 % vs 93 %) and long-term success rates (91 % vs 84 %), or complication rates (18 % vs 19 %) [34]. Notably, the conventional approach was applied exclusively in patients with bulging (peri-)pancreatic collections and in the absence of portal hypertension [34]. It is likely that the principal advantage of EUS-guided transluminal access lies in the ability to access the WON cavity even in the absence of a typical luminal bulge, provided that the collection is within the EUS field of view [89].

In our study involving 28 patients, a 100 % technical success rate for transgastric access to the WON using a duodenoscope was achieved under two combined conditions: supine patient positioning during the procedure and external compression of the stomach by the adjacent WON [52]. These findings suggest that the supine position during endoscopic transluminal interventions allows more accurate endoscopic localization of the WON relative to the stomach, as the intra-abdominal organ configuration more closely matches CT/MRI findings [52]. In contrast, the left lateral position may lead to displacement of intra-abdominal organs, thereby reducing the likelihood of successful access to the WON cavity.

To date, large randomized trials directly comparing transluminal access using a gastroscope versus a therapeutic EUS are lacking. Nevertheless, expert consensus suggests that EUS-guided transluminal intervention is safer with respect to bleeding risk and offers a higher likelihood of access to the WON cavity [3]. Accordingly, the European Society of Gastrointestinal Endoscopy (ESGE) recommends the use of EUS for creating transluminal access to the WON [3].

Technique of endoscopic interventions

Endoscopic transluminal interventions are performed under general anesthesia with endotracheal intubation [7, 52, 51, 62, 65], which protects the airway from aspiration of infected WON contents and provides better cardiopulmonary control during prolonged procedures.

Current endoscopic options in ANP include [3]:

- Endoscopic transluminal drainage: placement of transmural DPPS or fully covered self-expanding metal stents into the WON cavity;
- Endoscopic drainage using the multiple transluminal gateway technique (MTGT), which involves up to three access points [3, 88];
- Direct endoscopic necrosectomy (DEN): insertion of the endoscope into the WON cavity to remove necrotic debris [64]. In the English-language literature, synonymous terms include peroral endoscopic necrosectomy and endoscopic transluminal necrosectomy;
- Combined interventions (dual-modality drainage, DMD), in which endoscopic transluminal drainage is combined with percutaneous drainage of WON [58]; this approach should be strongly considered when necrosis extends into the paracolic gutters or the pelvis [3, 47, 62].

The endoscopic approach is best suited for the treatment of central necrosis [11], which is predominantly located within the lesser sac, as this region is most readily accessible endoscopically via the stomach or duodenum [47]. Successful endoscopic treatment of WON requires creation of a wide transmural tract and additional irrigation and/or debridement [47]. Depending on the anatomical relationship between the necrotic collection and the gastric or duodenal wall, and considering technical feasibility, access to the WON cavity is achieved via a transgastric or transduodenal route. The transgastric approach is preferred for its technical convenience in endoscopic necrosectomy and for providing the most direct access to the WON cavity [12].

Two main strategies are used during endoscopic transluminal treatment of WON: performing DEN, if required, several days after initial endoscopic drainage (DEN as a secondary procedure) [42, 95], or performing DEN during the primary access session (DEN as a primary procedure) [24, 36, 76]. Several studies have demonstrated the advantages of a step-up endoscopic strategy aimed at avoiding DEN, showing that 20–90 % of patients with WON can be successfully treated with endoscopic drainage alone using plastic stents or large-diameter fully covered metal stents, including dedicated lumen-apposing metal stents (LAMS) [37, 45, 55]. At present, however, studies directly comparing early DEN (during the index procedure) with delayed DEN are lacking [3].

The number of sessions varies and depends on WON size, the amount of solid necrotic debris, use

of cavity lavage, type of stents, endoscopic strategy (primary drainage alone vs immediate necrosectomy), availability of dedicated devices, and the use of combined interventions (DMD) or MTGT. On average, 1–7 DEN sessions per patient may be required to achieve adequate cavity clearance: Ang et al. (8 patients) – 1 (1–3) [2]; Gardner et al. (104 patients) – 3 [24]; Papachristou et al. (53 patients) – 3 (1–12) [47]; Smoczyński et al. (64 patients) – 4.75 (3–9) [72]; Seifert et al. (93 patients) – 6.2 (1–35) [65]; Seewald et al. (13 patients) – 7 (2–23) [64]. Attempts at aggressive cavity debridement may be associated with an increased risk of bleeding. Over time, necrotic sequestra become more clearly demarcated from viable tissue as granulation tissue forms, allowing safer, more controlled removal with a lower risk of injury to viable structures.

With conventional access to the WON cavity, the endoscope is advanced orally, and transmural puncture is performed at the site of luminal compression caused by the adjacent necrotic collection. Gastric wall puncture (fistulotomy) is carried out using a cystotome or a needle-knife papillotome. In EUS-guided access [62]: (1) an optimal puncture site is selected based on (a) absence of large vessels, (b) close apposition to the gastric or duodenal wall (< 1 cm), and (c) favorable orientation for DEN; (2) the WON is punctured using a 19-G FNA needle; (3) cavity contents are aspirated for microbiological analysis; (4) a 0.025–0.035-inch guidewire is advanced into the WON cavity.

The created fistulous tract is then dilated to 4–20 mm, depending on the planned intervention (drainage or DEN), using an endoscopic balloon, dilation catheter, or a guidewire-mounted cystotome [62, 31]. Placement of cautery-enhanced LAMS does not require prior balloon dilation of the tract and allows single-step creation of access to the WON cavity. When multiple DPPS are planned, the fistulous tract is typically dilated to 10–20 mm [62].

During the index session (access session), regardless of whether DEN is performed, a 7–8 Fr transnasal catheter may be placed into the WON cavity for continuous lavage (Fig. 1), provided the patient tolerates nasal tubes [3, 12, 47, 62, 63].

Duration of direct endoscopic necrosectomy session

The duration of a single DEN session should be limited. Prolonged necrosectomy in patients weakened by a long-standing infectious-toxic process, under general anesthesia and mechanical ventilation, may impose significant pathophysiological stress, increase the risk of complications, and predispose to bleeding. Based on original studies, the optimal duration of a single DEN session is 60–90 minutes [47, 52, 65].

Irrigation of walled-off necrosis

In the interval between sessions, the necrotic cavity may be irrigated via an endoscopically placed transnasal drain into the WON cavity (see Fig. 1) or via PCD. The type of irrigating solution, volume, duration, and frequency are not standardized and vary between centers. Most commonly, 500–1000 mL of normal saline is used daily, administered either in divided doses 3–6 times per day or as a continuous instillation.

Some authors recommend administering antibiotics through the drain during intersession intervals for WON irrigation, guided by microbiological culture results [38, 63, 76], or using antiseptic solutions. In addition, during necrosectomy, some specialists advocate lavage of the WON cavity with large volumes of warm bacitracin solution (1–2 L at 25,000 IU/L) or with 100–300 mL of 0.1 %–0.3 % hydrogen peroxide (H_2O_2) delivered through the endoscope channel [1, 36, 76].

In the ASGE Technology Review (2023), data are presented on the safety and effectiveness of using 3 % hydrogen peroxide (H_2O_2), diluted with normal saline at ratios ranging from 1 : 2 to 1 : 10, for irrigation of the WON cavity, both during DEN

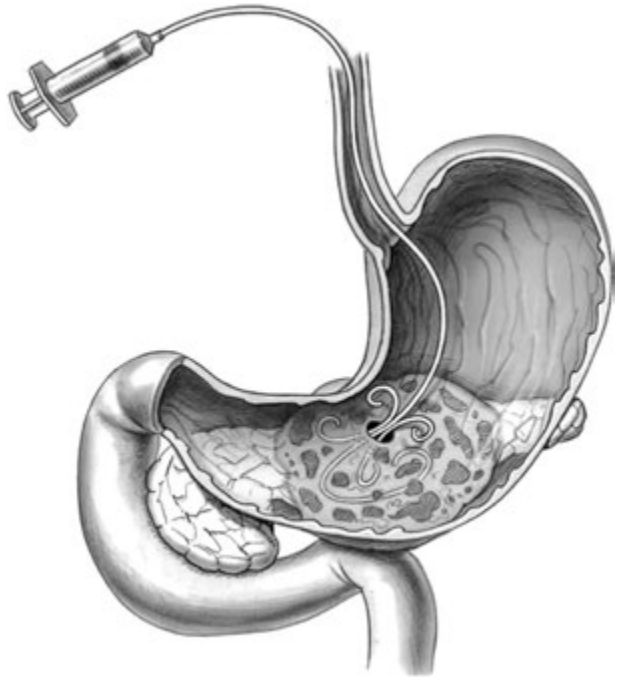

Figure 1. **A 7-Fr pigtail-type nasobiliary drain placed adjacent to transmural internal pigtail stents within the WON cavity for the purpose of intensive irrigation and/or debridement [47]**

Figure 2. **Solus® double-pigtail plastic stent, Cook Medical™, USA**

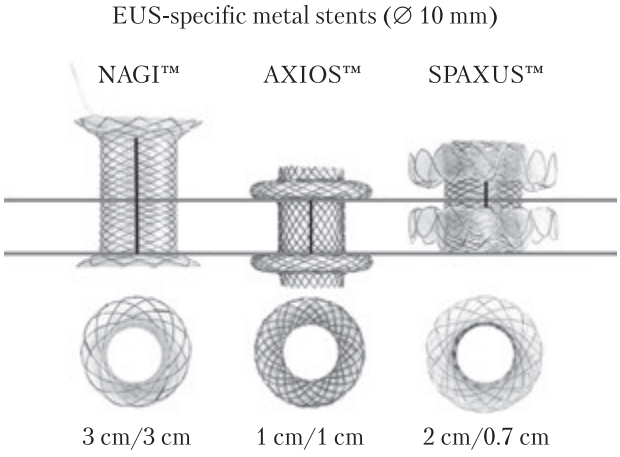

Figure 3. **Examples of specialized covered lumen-apposing metal stents (LAMS) [73]**

sessions and via a transnasal drain. However, there is insufficient prospective evidence to support routine use of H_2O_2 for this indication [12, 62].

The choice between irrigation of the necrotic cavity and DEN remains controversial. The need for DEN should be justified by the amount of solid necrotic debris present within the WON cavity [12]. Routine DEN at the time of LAMS placement is also controversial, and it remains unclear whether it should be performed on a scheduled or on-demand basis [12]. Some data suggest that DEN improves outcomes of endoscopic therapy compared with irrigation alone when plastic stents are used [12, 23]. Experienced endoscopists who perform a high volume of endoscopic necrosectomies recommend avoiding antisecretory therapy after transluminal drainage, as gastric acid secretion may facilitate spontaneous cleansing of the WON cavity [12].

Endoscopic stents

For endoscopic drainage of the WON cavity, 10 Fr double-pigtail plastic stents (Fig. 2) or fully covered self-expandable metal stents (SEMS) are most commonly used. Specialized LAMS (Fig. 3) are being used with increasing frequency.

LAMS reduce procedure time by facilitating faster access to the WON cavity and making necrosectomy through the stent lumen more convenient [67].

In a large retrospective multicenter study involving 124 patients with WON who underwent EUS-guided transmural drainage using LAMS, the authors reported a technical success rate of 100 %, a clinical success rate of 86 %, and the need for DEN in 30.6 % of patients, with a median number of procedures of 2 [67].

Available data suggest that placement of one or two plastic stents coaxially within the lumen of a LAMS (Fig. 4) improves WON drainage and LAMS patency, prevents early occlusion by necrotic debris, and reduces the risk of bleeding and stent migration [30].

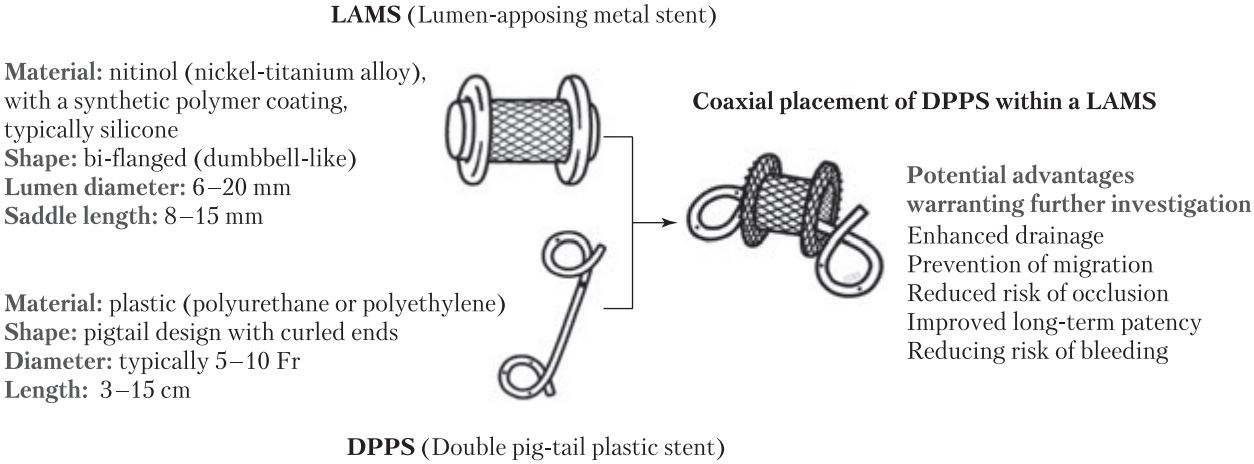

Figure 4. **Schematic illustration of coaxial placement of a double-pigtail plastic stent (DPPS) within a LAMS [30]**

Endoscopic instruments for direct endoscopic necrosectomy

Mechanical endoscopic removal of necrotic sequestra is performed using lavage and devices such as tripod grasper, grasping forceps, polypectomy snares, baskets, and retrieval nets. Recently, promising results of DEN have been reported with the use of innovative endoscopic devices:

- the motorized EndoRotor device (Micro-Tech™, Germany) (Fig. 5), which consists of a rotating blade for resection of necrotic tissue with simultaneous suction; the device is available in two diameters, 3.0 mm and 5.0 mm, for use with endoscopes with different working channel sizes [46, 85];
- an over-the-scope grasper (Xcavator™ – Ovesco Endoscopy AG, Germany) (Fig. 6) [16];
- the multifunctional Necrolit® device, which combines a snare and a basket, allowing sequential resection and retrieval of necrotic debris without the need to change instruments (Fig. 7);
- a waterjet necrosectomy device, a prototype single-use instrument that uses a high-pressure water jet to fragment necrotic tissue and can be employed for irrigation, fragmentation, and aspiration (Fig. 8) [93].

Factors predicting the need for necrosectomy

In a retrospective analysis of 53 patients, larger WON size (median diameter 18 cm [12–21 cm] vs 14 cm [3–46 cm]; p = 0.01), extension of WON into the paracolic gutters (p = 0.003; OR 8.5; 95 % CI 1.4–52.2), and a history of diabetes mellitus (p = 0.035; OR 4.1; 95 % CI 1.0–19.9) were significantly associated with the need for open surgical intervention following primary endoscopic treatment [47]. At the same time, the authors emphasized that patients with extension of WON into the paracolic gutters should not be categorically excluded from endoscopic therapy; on the contrary, aggressive percutaneous treatment (PCD with intensive irrigation) should be considered as an adjunctive modality that complements endoscopic therapy and may be applied concurrently [47].

In a post hoc analysis of a prospective multicenter database including 639 patients with ANP, the need for surgical intervention was lower in patients with isolated extrapancreatic necrosis compared with those with parenchymal or mixed necrosis (18 % vs 57 %; p < 0.001) [5].

In a retrospective study of 43 patients with WON, the extent of necrosis (r = 0.703; p < 0.001),

Figure 5. **EndoRotor®, powered endoscopic debridement catheter (Micro-Tech™, Germany)**

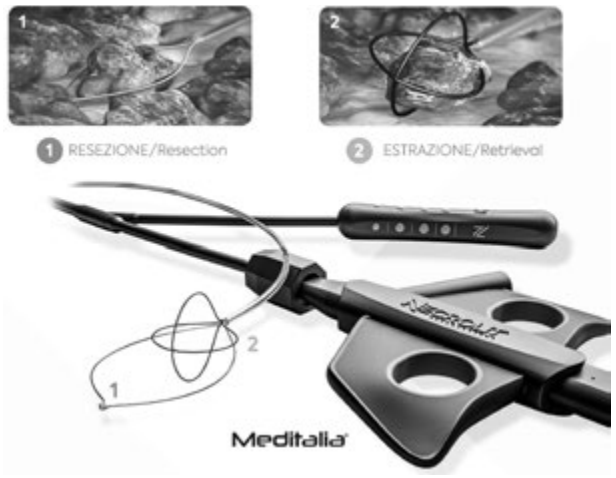

Figure 7. **Necrolit®, multiaction catheter for necrosectomy, Meditalia S.r.l., Italy)**

Figure 6. **Xcavator™, over-the-scope grasper (Ovesco Endoscopy AG, Germany)**

Figure 8. **Waterjet necrosectomy device, prototype [93]**

increasing WON size (r = 0.320; p = 0.047), and the amount of solid necrotic debris assessed by EUS (r = 0.800; p < 0.001) correlated with the need for more aggressive therapeutic interventions [54].

In a prospective cohort of 109 patients with acute pancreatitis (80 with ANP and 39 with WON) who underwent contrast-enhanced CT within the first 5–7 days after symptom onset, a blood urea nitrogen level ≥ 20 mg/dL at admission and an initial necrotic collection > 6 cm were associated with subsequent development of WON, with odds ratios of 10.96 (95 % CI 2.57–46.73; p = 0.001) and 14.57 (95 % CI 1.60–132.35; p = 0.017), respectively [61].

In a post hoc analysis of 130 patients who underwent catheter drainage (113 percutaneous, 17 endoscopic) for suspected INP, the extent of pancreatic necrosis (< 30 %, 30–50 %, > 50 %; OR 0.44; 95 % CI 0.23–0.83; p = 0.01) and heterogeneous morphology of the collection (OR 0.19; 95 % CI 0.06–0.61; p = 0.005) were two imaging-related factors associated with a lower likelihood of success (defined as survival without necrosectomy) [29].

Two additional studies identified predictors of failure of catheter drainage and the need for subsequent surgery, including persistent single- or multiple organ failure, higher C-reactive protein levels, and extensive necrosis involving more than 50 % of the pancreas [4, 68].

Based on our experience, documenting the contents of the WON cavity at the end of each endoscopic session in the procedure report and video recording is essential for assessing the completeness of necrosectomy and planning further management during clinical case discussions.

Complications of endoscopic transluminal interventions

Based on a systematic review including 13 retrospective cohort series (n = 455) [80] and one randomized controlled trial (n = 98) [84], the overall rate of endoscopy-related complications was 36 % [3]. The most common complication was bleeding, occurring in 18 % of cases. Perforation (excluding gastric or duodenal perforation) occurred in 4 % of patients, and pancreatic fistula developed in 5 %.

Clinical recommendations

According to international clinical guidelines for the management of patients with acute necrotizing pancreatitis – including those of the European Society of Gastrointestinal Endoscopy (ESGE, 2018) [3], the American Society for Gastrointestinal Endoscopy (ASGE, 2023) [62], the American Gastroenterological Association (AGA, 2020) [12], and other authoritative sources – we summarize the key recommendations grounded in a multidisciplinary approach. These recommendations are of particular relevance to routine clinical practice for surgeons, interventional endoscopists, and physicians specializing in interventional ultrasonography.

1. For assessment of disease severity, morphological subtype, and the presence or absence of infected necrosis, use of the Revised Atlanta Classification of acute pancreatitis (2012) is recommended [8].

2. Contrast-enhanced CT is recommended, when indicated, as the primary diagnostic modality at hospital admission and within the first 4 weeks of disease, provided no contraindications exist. MRI may be performed instead of CT in patients with contraindications to contrast-enhanced CT and after 4 weeks of disease when invasive intervention is planned, as MRI better characterizes the content of pancreatic collections with respect to fluid and solid components. In addition, secretin-enhanced MRI is recommended to assess the integrity of the main pancreatic duct and to evaluate for disconnected pancreatic duct syndrome, particularly prior to removal of transluminal stents [3]. However, MRI is more susceptible to motion artifacts, and many patients with necrotizing pancreatitis are unable to adequately hold their breath [17].

The following indications for imaging are proposed [3]:

- at hospital admission, if diagnostic uncertainty exists;
- within the first week after disease onset (or after 72 hours from symptom onset) if no clinical improvement occurs despite conservative therapy;
- between weeks 2 and 4 after disease onset to assess the evolution of complications;
- after 4 weeks from disease onset for planning further management, when invasive intervention is required, and for monitoring treatment response.

3. Routine percutaneous FNA of (peri-)pancreatic collections is not recommended and should be reserved for cases with suspected infection, an equivocal clinical course, and inconclusive imaging findings [3].

4. Routine antibiotic or probiotic prophylaxis to prevent infectious complications is not recommended in acute necrotizing pancreatitis [3, 12].

5. In patients with suspected or confirmed infected necrosis, antibiotic therapy targeting enteric bacteria is recommended, guided by microbiological cultures and antibiograms when available [3]. Empirical use of broad-spectrum antibiotics that penetrate necrotic tissue – such as quinolones, carbapenems, metronidazole, and high-dose cephalosporins – is appropriate; routine antifungal therapy is not recommended [12]. Once blood culture or

FNA results become available, antibiotic therapy should be adjusted accordingly [3].

6. Enteral tube feeding with polymeric formulas is recommended in all patients with predicted severe acute pancreatitis who cannot tolerate oral intake after 72 hours. Initial enteral feeding should be started via a nasogastric tube, except in hemodynamically unstable patients, with transition to nasojejunal feeding in cases of intolerance to nasogastric feeding [3]. Multiple randomized controlled trials have shown no advantage of nasojejunal over nasogastric feeding with respect to tolerance or mortality [18, 44, 49, 97]. A 2020 Cochrane meta-analysis also demonstrated no superiority of one feeding route over the other in severe pancreatitis [20].

7. Parenteral nutrition should be initiated in cases of persistent intolerance to enteral feeding or when adequate caloric intake cannot be achieved enterally [3].

8. Selection of the treatment strategy in necrotizing pancreatitis should follow the widely accepted step-up approach, taking into account the time from disease onset and the dynamics of the clinical course [3, 12].

9. Endoscopic or percutaneous drainage is recommended as the first invasive intervention in patients with (suspected) infected WON, based on collection location and local expertise [3]. An advantage of endoscopic over percutaneous drainage in (suspected) infected WON is the absence of risk for pancreatocutaneous fistula formation [12].

10. When the patient's condition allows, the first intervention for infected necrosis should preferably be delayed for 4 weeks [3, 12].

11. PCD should be strongly considered as an adjunct to endoscopic drainage in cases of WON with deep extension into the paracolic gutters or pelvis [3, 12, 62], or following endoscopic or surgical debridement for additional treatment of residual necrosis [12]. In a prospective study by Ross et al. (107 patients) using DMD for WON, no cases of pancreatocutaneous fistula occurred after successful removal of percutaneous drains during long-term follow-up [59].

12. LAMS are preferred over plastic stents for endoscopic transluminal drainage of necrotic collections according to some guidelines [12]. However, European guidelines consider both plastic stents and LAMS acceptable options for WON management, noting that data on long-term indwelling LAMS are limited [3].

13. As a subsequent step in the absence of clinical improvement after endoscopic transluminal drainage of WON using LAMS or plastic stents combined with irrigation, endoscopic necrosectomy (DEN) or minimally invasive surgical intervention (if PCD has already been performed) should be prioritized over open surgery, taking into account collection location and institutional expertise [3, 12]. In contemporary management of ANP, open surgical necrosectomy is reserved for patients who are not technically suitable candidates for minimally invasive surgical or endoscopic procedures [12].

14. Long-term placement of transluminal plastic stents is recommended in patients with disconnected pancreatic duct syndrome [3], or distal pancreatectomy may be considered when appropriate in selected candidates [12]. LAMS should be removed within 3–4 weeks to prevent stent-related complications [3, 62].

15. Urgent (≤ 24 hours) endoscopic retrograde cholangiopancreatography (ERCP) with biliary decompression is recommended in patients with acute biliary pancreatitis complicated by cholangitis. ERCP should be performed within 72 hours in patients with persistent biliary obstruction. ERCP is not recommended in patients with acute biliary pancreatitis without evidence of cholangitis or ongoing biliary obstruction [3].

16. Patient management should be individualized, incorporating all available clinical, radiological, and laboratory data, as well as local expertise [3].

17. Optimal management of patients with ANP requires a multidisciplinary approach involving gastroenterologists, surgeons, interventional radiologists, intensivists, infectious disease specialists, and clinical nutrition experts [12]. When local resources are limited, transfer of patients with severe necrotizing pancreatitis to specialized centers with advanced endoscopic capabilities, interventional radiology, and surgical options should be considered [12].

Declaration of interests

The authors declare no conflict of interest. The authors received no financial support for this study.

Authors contributions

N.V. Puzyr performed the literature search and selection of relevant sources, conducted data analysis, and prepared the initial draft of the manuscript. A.Y. Tkachenko contributed to the finalization of the review, critical analysis of the selected sources, structuring of the material, and editing of the manuscript.

References

1. Abdelhafez M, Elnegouly M, Hasab Allah MS, Elshazli M, Mikhail HM, Yosry A. Transluminal retroperitoneal endoscopic necrosectomy with the use of hydrogen peroxide and without external irrigation: a novel approach for the treatment of walled-off pancreatic necrosis. Surg Endosc. 2013 Oct;27(10):3911-20. doi: 10.1007/s00464-013-2948-x. Epub 2013 Apr 13. PMID: 23584819.
2. Ang TL, Kwek AB, Tan SS, Ibrahim S, Fock KM, Teo EK. Direct endoscopic necrosectomy: a minimally invasive endoscopic technique for the treatment of infected walled-off pancreatic necrosis and infected pseudocysts with solid debris. Singapore Med J. 2013 Apr;54(4):206-11. doi: 10.11622/smedj.2013074. PMID: 23624447.
3. Arvanitakis M, et al. Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. Endoscopy. 2018 May;50(5):524-546. doi: 10.1055/a-0588-5365. Epub 2018 Apr 9. PMID: 29631305.
4. Babu RY, Gupta R, Kang M, Bhasin DK, Rana SS, Singh R. Predictors of surgery in patients with severe acute pancreatitis managed by the step-up approach. Ann Surg. 2013 Apr;257(4):737-50. doi: 10.1097/SLA.0b013e318269d25d. PMID: 22968079.
5. Bakker OJ, van Santvoort H, Besselink MG, Boermeester MA, van Eijck C, Dejong K, van Goor H, Hofker S, Ahmed Ali U, Gooszen HG, Bollen TL; Dutch Pancreatitis Study Group. Extrapancreatic necrosis without pancreatic parenchymal necrosis: a separate entity in necrotising pancreatitis? Gut. 2013 Oct;62(10):1475-80. doi: 10.1136/gutjnl-2012-302870. Epub 2012 Jul 7. PMID: 22773550.
6. Bakker OJ, van Santvoort HC, van Brunschot S, Geskus RB, Besselink MG, Bollen TL, van Eijck CH, Fockens P, Hazebroek EJ, Nijmeijer RM, Poley JW, van Ramshorst B, Vleggaar FP, Boermeester MA, Gooszen HG, Weusten BL, Timmer R; Dutch Pancreatitis Study Group. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. JAMA. 2012 Mar 14;307(10):1053-61. doi: 10.1001/jama.2012.276. PMID: 22416101.
7. Bang JY, Arnoletti JP, Holt BA, Sutton B, Hasan MK, Navaneethan U, Feranec N, Wilcox CM, Tharian B, Hawes RH, Varadarajulu S. An Endoscopic Transluminal Approach, Compared With Minimally Invasive Surgery, Reduces Complications and Costs for Patients With Necrotizing Pancreatitis. Gastroenterology. 2019 Mar;156(4):1027-1040.e3. doi: 10.1053/j.gastro.2018.11.031. Epub 2018 Nov 16. PMID: 30452918.
8. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013 Jan;62(1):102-11. doi: 10.1136/gutjnl-2012-302779. Epub 2012 Oct 25. PMID: 23100216.
9. Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. Am J Gastroenterol. 2006 Oct;101(10):2379-400. doi: 10.1111/j.1572-0241.2006.00856.x. PMID: 17032204.
10. Baril NB, Ralls PW, Wren SM, Selby RR, Radin R, Parekh D, Jabbour N, Stain SC. Does an infected peripancreatic fluid collection or abscess mandate operation? Ann Surg. 2000 Mar;231(3):361-7. doi: 10.1097/00000658-200003000-00009. PMID: 10714629; PMCID: PMC1421007.
11. Baron TH, Thaggard WG, Morgan DE, Stanley RJ. Endoscopic therapy for organized pancreatic necrosis. Gastroenterology. 1996 Sep;111(3):755-64. doi: 10.1053/gast.1996.v111.pm8780582. PMID: 8780582.
12. Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association Clinical Practice Update: Management of Pancreatic Necrosis. Gastroenterology. 2020 Jan;158(1):67-75.e1. doi: 10.1053/j.gastro.2019.07.064. Epub 2019 Aug 31. PMID: 31479658.
13. Besselink MG, van Santvoort, Freeman ML, et al. Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013 Jul-Aug;13(4 Suppl 2):e1-15. doi: 10.1016/j.pan.2013.07.063. PMID: 24054878.
14. Besselink MG, et al. Dutch Acute Pancreatitis Study Group. Minimally invasive 'step-up approach' versus maximal necrosectomy in patients with acute necrotising pancreatitis (PANTER trial): design and rationale of a randomised controlled multicenter trial [ISRCTN13975868]. BMC Surg. 2006 Apr 11;6:6. doi: 10.1186/1471-2482-6-6. PMID: 16606471; PMCID: PMC1508161.
15. Boxhoorn L, et al. Dutch Pancreatitis Study Group. Immediate versus Postponed Intervention for Infected Necrotizing Pancreatitis. N Engl J Med. 2021 Oct 7;385(15):1372-1381. doi: 10.1056/NEJMoa2100826. PMID: 34614330.
16. Brand M, Bachmann J, Schlag C, Huegle U, Rahman I, Wedi E, Walter B, Möschler O, Sturm L, Meining A. Over-the-scope-grasper: A new tool for pancreatic necrosectomy and beyond — first multicenter experience. World J Gastrointest Surg. 2022 Aug 27;14(8):799-808. doi: 10.4240/wjgs.v14.i8.799. PMID: 36157364; PMCID: PMC9453329.
17. Bugiantella W, Rondelli F, Boni M, Stella P, Polistena A, Sanguinetti A, Avenia N. Necrotizing pancreatitis: A review of the interventions. Int J Surg. 2016 Apr;28 Suppl 1:S163-71. doi: 10.1016/j.ijsu.2015.12.038. Epub 2015 Dec 18. PMID: 26708848.
18. Chang YS, Fu HQ, Xiao YM, Liu JC. Nasogastric or nasojejunal feeding in predicted severe acute pancreatitis: a meta-analysis. Crit Care. 2013 Jun 20;17(3):R118. doi: 10.1186/cc12790. PMID: 23786708; PMCID: PMC4057382.
19. Dell'Anna G, et al. Clinical, Radiological, and Endoscopic Features of Pancreatic Pseudocyst and Walled-Off Necrosis: How to Diagnose and How to Drain Them. J Clin Med. 2025 Nov 3;14(21):7818. doi: 10.3390/jcm14217818. PMID: 41227213; PMCID: PMC12608859.
20. Dutta AK, Goel A, Kirubakaran R, Chacko A, Tharyan P. Nasogastric versus nasojejunal tube feeding for severe acute pancreatitis. Cochrane Database Syst Rev. 2020 Mar 26;3(3):CD010582. doi: 10.1002/14651858.CD010582.pub2. PMID: 32216139; PMCID: PMC7098540.
21. Freeman ML, Werner J, van Santvoort HC, Baron TH, Besselink MG, Windsor JA, Horvath KD, vanSonnenberg E, Bollen TL, Vege SS; International Multidisciplinary Panel of Speakers and Moderators. Interventions for necrotizing pancreatitis: summary of a multidisciplinary consensus conference. Pancreas. 2012 Nov;41(8):1176-94. doi: 10.1097/MPA.0b013e318269c660. PMID: 23086243.
22. García García de Paredes A, López-Durán S, Foruny Olcina JR, Albillos A, Vázquez-Sequeiros E. Management of pancreatic collections: an update. Rev Esp Enferm Dig. 2020 Jun;112(6):483-490. doi: 10.17235/reed.2020.6814/2019. PMID: 32450706.
23. Gardner TB, Chahal P, Papachristou GI, Vege SS, Petersen BT, Gostout CJ, Topazian MD, Takahashi N, Sarr MG, Baron TH. A comparison of direct endoscopic necrosectomy with transmural endoscopic drainage for the treatment of walled-off pancreatic necrosis. Gastrointest Endosc. 2009 May;69(6):1085-94. doi: 10.1016/j.gie.2008.06.061. Epub 2009 Feb 24. PMID: 19243764.
24. Gardner TB, Coelho-Prabhu N, Gordon SR, Gelrud A, Maple JT, Papachristou GI, Freeman ML, Topazian MD, Attam R, Mackenzie TA, Baron TH. Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: results from a multicenter U.S. series. Gastrointest Endosc. 2011 Apr;73(4):718-26. doi: 10.1016/j.gie.2010.10.053. Epub 2011 Jan 14. PMID: 21237454.
25. Garg PK, Sharma M, Madan K, Sahni P, Banerjee D, Goyal R. Primary conservative treatment results in mortality comparable to surgery in patients with infected pancreatic necrosis. Clin Gastroenterol Hepatol. 2010 Dec;8(12):1089-1094.e2. doi: 10.1016/j.cgh.2010.04.011. Epub 2010 Apr 24. PMID: 20417724.
26. Gluck M, Ross A, Irani S, Lin O, Gan SI, Fotoohi M, Hauptmann E, Crane R, Siegal J, Robinson DH, Traverso LW, Kozarek RA. Dual modality drainage for symptomatic walled-off pancreatic necrosis reduces length of hospitalization, radiological procedures, and number of endoscopies compared to standard percutaneous drainage. J Gastrointest Surg. 2012 Feb;16(2):248-56; discussion 256-7. doi: 10.1007/s11605-011-1759-4. Epub 2011 Nov 29. PMID: 22125167.
27. Gurusamy KS, Belgaumkar AP, Haswell A, Pereira SP, Davidson BR. Interventions for necrotising pancreatitis. Cochrane Database Syst Rev. 2016 Apr 16;4(4):CD011383. doi: 10.1002/14651858.CD011383.pub2. PMID: 27083933; PMCID: PMC10422681.
28. Haghshenasskashani A, Laurence JM, Kwan V, Johnston E, Hollands MJ, Richardson AJ, Pleass HC, Lam VW. Endoscopic necrosectomy of pancreatic necrosis: a systematic review. Surg Endosc. 2011 Dec;25(12):3724-30. doi: 10.1007/s00464-011-1795-x. Epub 2011 Jun 9. PMID: 21656324.
29. Hollemans RA, Bollen TL, van Brunschot S, Bakker OJ, Ahmed Ali U, van Goor H, Boermeester MA, Gooszen HG, Besselink MG, van Santvoort HC; Dutch Pancreatitis Study Group. Predicting Success of Catheter Drainage in Infected Necrotizing Pancreatitis. Ann Surg. 2016 Apr;263(4):787-92. doi: 10.1097/SLA.0000000000001203. PMID: 25775071.

30. Infantino G, Rancatore G, Quintini D, Carrozza L, Ligresti D, Giacchetto M, Belluardo N, Rizzo G, D'Amore E, Rizzo GEM, Tarantino I. A Critical Narrative Review of Coaxial Double-Pigtail Stenting Within the LAMS in the Management of Pancreatic Fluid Collections. Medicina (Kaunas). 2025 Aug 21;61(8):1500. doi: 10.3390/medicina61081500. PMID: 40870545; PMCID: PMC12388403.
31. Jagielski M, Smoczyński M, Adrych K. Single transluminal gateway transcystic multiple drainage for extensive walled-off pancreatic necrosis — a single-centre experience. Prz Gastroenterol. 2018;13(3):242-248. doi: 10.5114/pg.2018.78290. Epub 2018 Sep 17. PMID: 30302171; PMCID: PMC6173077.
32. Jagielski M, Smoczyński M, Jabłońska A, Marek I, Dubowik M, Adrych K. The role of endoscopic ultrasonography in endoscopic debridement of walled-off pancreatic necrosis-A single center experience. Pancreatology. 2015 Sep-Oct;15(5):503-507. doi: 10.1016/j.pan.2015.06.001. Epub 2015 Jun 17. PMID: 26122305.
33. Jagielski M, Smoczyński M, Studniarek M, Adrych K. Spontaneous regression of asymptomatic walled-off pancreatic necrosis. Arch Med Sci. 2019 Sep;15(5):1278-1287. doi: 10.5114/aoms.2018.75606. Epub 2018 May 4. PMID: 31572474; PMCID: PMC6764315.
34. Kahaleh M, Shami VM, Conaway MR, Tokar J, Rockoff T, De La Rue SA, de Lange E, Bassignani M, Gay S, Adams RB, Yeaton P. Endoscopic ultrasound drainage of pancreatic pseudocyst: a prospective comparison with conventional endoscopic drainage. Endoscopy. 2006 Apr;38(4):355-9. doi: 10.1055/s-2006-925249. PMID: 16680634.
35. Khreiss M, Zenati M, Clifford A, Lee KK, Hogg ME, Slivka A, Chennat J, Gelrud A, Zeh HJ, Papachristou GI, Zureikat AH. Cyst Gastrostomy and Necrosectomy for the Management of Sterile Walled-Off Pancreatic Necrosis: a Comparison of Minimally Invasive Surgical and Endoscopic Outcomes at a High-Volume Pancreatic Center. J Gastrointest Surg. 2015 Aug;19(8):1441-8. doi: 10.1007/s11605-015-2864-6. Epub 2015 Jun 2. PMID: 26033038.
36. Kumar N, Conwell DL, Thompson CC. Direct endoscopic necrosectomy versus step-up approach for walled-off pancreatic necrosis: comparison of clinical outcome and health care utilization. Pancreas. 2014 Nov;43(8):1334-9. doi: 10.1097/MPA.0000000000000213. PMID: 25083997; PMCID: PMC5019103.
37. Lakhtakia S, Basha J, Talukdar R, Gupta R, Nabi Z, Ramchandani M, Kumar BVN, Pal P, Kalpala R, Reddy PM, Pradeep R, Singh JR, Rao GV, Reddy DN. Endoscopic «step-up approach» using a dedicated biflanged metal stent reduces the need for direct necrosectomy in walled-off necrosis (with videos). Gastrointest Endosc. 2017 Jun;85(6):1243-1252. doi: 10.1016/j.gie.2016.10.037. Epub 2016 Nov 11. PMID: 27845053.
38. Mathers B, Moyer M, Mathew A, Dye C, Levenick J, Gusani N, Dougherty-Hamod B, McGarrity T. Percutaneous debridement and washout of walled-off abdominal abscess and necrosis using flexible endoscopy: a large single-center experience. Endosc Int Open. 2016 Jan;4(1):E102-6. doi: 10.1055/s-0041-107802. Epub 2015 Nov 27. PMID: 26793778; PMCID: PMC4713176.
39. Mofidi R, Suttie SA, Patil PV, Ogston S, Parks RW. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: systematic review. Surgery. 2009 Jul;146(1):72-81. doi: 10.1016/j.surg.2009.02.013. Epub 2009 May 8. PMID: 19541012.
40. Mohamadnejad M, Anushiravani A, Kasaeian A, Sorouri M, Djalalinia S, Kazemzadeh Houjaghan A, Gaidhane M, Kahaleh M. Endoscopic or surgical treatment for necrotizing pancreatitis: Comprehensive systematic review and meta-analysis. Endosc Int Open. 2022 Apr 14;10(4):E420-E428. doi: 10.1055/a-1783-9229. PMID: 35433210; PMCID: PMC9010078.
41. Mouli VP, Sreenivas V, Garg PK. Efficacy of conservative treatment, without necrosectomy, for infected pancreatic necrosis: a systematic review and meta-analysis. Gastroenterology. 2013 Feb;144(2):333-340.e2. doi: 10.1053/j.gastro.2012.10.004. Epub 2012 Oct 12. PMID: 23063972.
42. Mukai S, Itoi T, Moriyasu F. Interventional endoscopy for the treatment of pancreatic pseudocyst and walled-off necrosis (with videos). J Hepatobiliary Pancreat Sci. 2014 Oct;21(10):E75-85. doi: 10.1002/jhbp.146. Epub 2014 Aug 20. PMID: 25139501.
43. Munene G, Dixon E, Sutherland F. Open transgastric debridement and internal drainage of symptomatic non-infected walled-off pancreatic necrosis. HPB (Oxford). 2011 Apr;13(4):234-9. doi: 10.1111/j.1477-2574.2010.00276.x. Epub 2011 Mar 2. PMID: 21418128; PMCID: PMC3081623.
44. Nally DM, Kelly EG, Clarke M, Ridgway P. Nasogastric nutrition is efficacious in severe acute pancreatitis: a systematic review and meta-analysis. Br J Nutr. 2014 Dec 14;112(11):1769-78. doi: 10.1017/S0007114514002566. Epub 2014 Oct 21. PMID: 25333639.
45. Nemoto Y, Attam R, Arain MA, Trikudanathan G, Mallery S, Beilman GJ, Freeman ML. Interventions for walled off necrosis using an algorithm based endoscopic step-up approach: Outcomes in a large cohort of patients. Pancreatology. 2017 Sep-Oct;17(5):663-668. doi: 10.1016/j.pan.2017.07.195. Epub 2017 Jul 31. PMID: 28803859.
46. Olsen GA, Schmidt PN, Novovic S, Hansen EF, Karstensen JG. Novel powered 5.0-mm endoscopic debridement catheter for endoscopic transmural necrosectomy of pancreatic walled-off necrosis: a case series of consecutive patients from a tertiary referral center (with video). Gastrointest Endosc. 2024 Feb;99(2):267-270. doi: 10.1016/j.gie.2023.10.044. Epub 2023 Oct 20. PMID: 37865281.
47. Papachristou GI, Takahashi N, Chahal P, Sarr MG, Baron TH. Peroral endoscopic drainage/debridement of walled-off pancreatic necrosis. Ann Surg. 2007 Jun;245(6):943-51. doi: 10.1097/01.sla.0000254366.19366.69. PMID: 17522520; PMCID: PMC1876949.
48. Park DH, Lee SS, Moon SH, Choi SY, Jung SW, Seo DW, Lee SK, Kim MH. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: a prospective randomized trial. Endoscopy. 2009 Oct;41(10):842-8. doi: 10.1055/s-0029-1215133. Epub 2009 Oct 1. PMID: 19798610.
49. Petrov MS, Correia MI, Windsor JA. Nasogastric tube feeding in predicted severe acute pancreatitis. A systematic review of the literature to determine safety and tolerance. JOP. 2008 Jul 10;9(4):440-8. PMID: 18648135.
50. Petrov MS, Shanbhag S, Chakraborty M, Phillips AR, Windsor JA. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology. 2010 Sep;139(3):813-20. doi: 10.1053/j.gastro.2010.06.010. Epub 2010 Jun 9. PMID: 20540942.
51. Pinto S, Bellizzi S, Badas R, Canfora ML, Loddo E, Spada S, Khalaf K, Fugazza A, Bergamini S. Direct Endoscopic Necrosectomy: Timing and Technique. Medicina (Kaunas). 2021 Nov 28;57(12):1305. doi: 10.3390/medicina57121305. PMID: 34946249; PMCID: PMC8707414.
52. Puzyr NV, Susak YM. Endoscopic transluminal necrosectomy in patients with acute infected necrotizing pancreatitis. Experience of a specialized center. General Surgery (Ukraine). 2025;(1):50-59. http://doi.org/10.30978/GS-2025-1-50.
53. Ramesh H, Prakash K, Lekha V, Jacob G, Venugopal A. Are some cases of infected pancreatic necrosis treatable without intervention? Dig Surg. 2003;20(4):296-9; discussion 300. doi: 10.1159/000071694. Epub 2003 Jun 5. PMID: 12789025.
54. Rana SS, Bhasin DK, Sharma RK, Kathiresan J, Gupta R. Do the morphological features of walled off pancreatic necrosis on endoscopic ultrasound determine the outcome of endoscopic transmural drainage? Endosc Ultrasound. 2014 Apr;3(2):118-22. doi: 10.4103/2303-9027.131039. PMID: 24955341; PMCID: PMC4064159.
55. Rana SS, Sharma V, Sharma R, Gupta R, Bhasin DK. Endoscopic ultrasound guided transmural drainage of walled off pancreatic necrosis using a «step — up» approach: A single centre experience. Pancreatology. 2017 Mar-Apr;17(2):203-208. doi: 10.1016/j.pan.2017.02.007. Epub 2017 Feb 8. PMID: 28202234.
56. Rasch S, Mayr U, Phillip V, Schmid RM, Huber W, Algül H, Lahmer T. Increased risk of candidemia in patients with necrotising pancreatitis infected with candida species. Pancreatology. 2018 Sep;18(6):630-634. doi: 10.1016/j.pan.2018.07.005. Epub 2018 Jul 14. PMID: 30017450.
57. Rodriguez JR, Razo AO, Targarona J, Thayer SP, Rattner DW, Warshaw AL, Fernández-del Castillo C. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. Ann Surg. 2008 Feb;247(2):294-9. doi: 10.1097/SLA.0b013e31815b6976. PMID: 18216536; PMCID: PMC3806106.
58. Ross A, Gluck M, Irani S, Hauptmann E, Fotoohi M, Siegal J, Robinson D, Crane R, Kozarek R. Combined endoscopic and percutaneous drainage of organized pancreatic necrosis. Gastrointest Endosc. 2010 Jan;71(1):79-84. doi: 10.1016/j.gie.2009.06.037. Epub 2009 Oct 27. PMID: 19863956.

59. Ross AS, Irani S, Gan SI, Rocha F, Siegal J, Fotoohi M, Hauptmann E, Robinson D, Crane R, Kozarek R, Gluck M. Dual-modality drainage of infected and symptomatic walled-off pancreatic necrosis: long-term clinical outcomes. Gastrointest Endosc. 2014 Jun;79(6):929-35. doi: 10.1016/j.gie.2013.10.014. Epub 2013 Nov 15. PMID: 24246792.
60. Runzi M, Niebel W, Goebell H, Gerken G, Layer P. Severe acute pancreatitis: nonsurgical treatment of infected necroses. Pancreas. 2005 Apr;30(3):195-9. doi: 10.1097/01.mpa.0000153613.17643.b3. PMID: 15782093.
61. Sarathi Patra P, Das K, Bhattacharyya A, Ray S, Hembram J, Sanyal S, Dhali GK. Natural resolution or intervention for fluid collections in acute severe pancreatitis. Br J Surg. 2014 Dec;101(13):1721-8. doi: 10.1002/bjs.9666. Epub 2014 Oct 20. PMID: 25329330.
62. Saumoy M, Trindade AJ, Bhatt A, et al. American Society for Gastrointestinal Endoscopy Technology Committee. Summary: endoscopic therapies for walled-off necrosis. Gastrointest Endosc. 2023 Jun;97(6):1001-1002. doi: 10.1016/j.gie.2023.02.008. Epub 2023 Apr 26. PMID: 37115165.
63. Schmidt PN, Novovic S, Roug S, Feldager E. Endoscopic, transmural drainage and necrosectomy for walled-off pancreatic and peripancreatic necrosis is associated with low mortality-a single-center experience. Scand J Gastroenterol. 2015 May;50(5):611-8. doi: 10.3109/00365521.2014.946078. Epub 2015 Feb 3. Erratum in: Scand J Gastroenterol. 2015 May;50(5):625. doi: 10.3109/00365521.2015.1017265. PMID: 25648776.
64. Seewald S, Groth S, Omar S, Imazu H, Seitz U, de Weerth A, Soetikno R, Zhong Y, Sriram PV, Ponnudurai R, Sikka S, Thonke F, Soehendra N. Aggressive endoscopic therapy for pancreatic necrosis and pancreatic abscess: a new safe and effective treatment algorithm (videos). Gastrointest Endosc. 2005 Jul;62(1):92-100. doi: 10.1016/s0016-5107(05)00541-9. PMID: 15990825.
65. Seifert H, Biermer M, Schmitt W, Jürgensen C, Will U, Gerlach R, Kreitmair C, Meining A, Wehrmann T, Rösch T. Transluminal endoscopic necrosectomy after acute pancreatitis: a multicentre study with long-term follow-up (the GEPARD Study). Gut. 2009 Sep;58(9):1260-6. doi: 10.1136/gut.2008.163733. Epub 2009 Mar 11. PMID: 19282306.
66. Seifert H, Wehrmann T, Schmitt T, Zeuzem S, Caspary WF. Retroperitoneal endoscopic debridement for infected peripancreatic necrosis. Lancet. 2000 Aug 19;356(9230):653-5. doi: 10.1016/S0140-6736(00)02611-8. PMID: 10968442.
67. Sharaiha RZ, et al. Endoscopic Therapy With Lumen-apposing Metal Stents Is Safe and Effective for Patients With Pancreatic Walled-off Necrosis. Clin Gastroenterol Hepatol. 2016 Dec;14(12):1797-1803. doi: 10.1016/j.cgh.2016.05.011. Epub 2016 May 14. PMID: 27189914.
68. Shenvi S, Gupta R, Kang M, Khullar M, Rana SS, Singh R, Bhasin DK. Timing of surgical intervention in patients of infected necrotizing pancreatitis not responding to percutaneous catheter drainage. Pancreatology. 2016 Sep-Oct;16(5):778-87. doi: 10.1016/j.pan.2016.08.006. Epub 2016 Aug 13. PMID: 27592206.
69. Singh VK, Bollen TL, Wu BU, Repas K, Maurer R, Yu S, Mortele KJ, Conwell DL, Banks PA. An assessment of the severity of interstitial pancreatitis. Clin Gastroenterol Hepatol. 2011 Dec;9(12):1098-103. doi: 10.1016/j.cgh.2011.08.026. Epub 2011 Sep 3. PMID: 21893128.
70. Singh RR, Mitchell W, David Y, Cheesman A, Dixon RE, Nagula S, DiMaio CJ, Greenwald DA, Kumta NA. Pancreatic Fungal Infection in Patients With Necrotizing Pancreatitis: A Systematic Review and Meta-analysis. J Clin Gastroenterol. 2021 Mar 1;55(3):218-226. doi: 10.1097/MCG.0000000000001467. PMID: 33252558.
71. Smoczyński M, Marek I, Dubowik M, Rompa G, Kobiela J, Studniarek M, Pieńkowska J, Adrych K. Endoscopic drainage/debridement of walled-off pancreatic necrosis-single center experience of 112 cases. Pancreatology. 2014 Mar-Apr;14(2):137-42. doi: 10.1016/j.pan.2013.11.005. Epub 2013 Nov 23. PMID: 24650969.
72. Smoczyński M, Jagielski M, Jabłońska A, Adrych K. Endoscopic necrosectomy under fluoroscopic guidance — a single center experience. Wideochir Inne Tech Maloinwazyjne. 2015 Jul;10(2):237-43. doi: 10.5114/wiitm.2015.52058. Epub 2015 Jun 9. PMID: 26240624; PMCID: PMC4520837.
73. Song TJ, Moon JH, Lee YN, Lee SS. Design considerations of the novel lumen-apposing metal stents (Niti-S SPAXUS). Techniques and Innovations in Gastrointestinal Endoscopy. 2020;22(1):9-13. https://www.tigejournal.org/article/S1096-2883(19)30076-2/abstract.
74. Tan V, Charachon A, Lescot T, Chafaï N, Le Baleur Y, Delchier JC, Paye F. Endoscopic transgastric versus surgical necrosectomy in infected pancreatic necrosis. Clin Res Hepatol Gastroenterol. 2014 Dec;38(6):770-6. doi: 10.1016/j.clinre.2014.06.016. Epub 2014 Aug 19. PMID: 25153999.
75. Thoeni RF. The revised Atlanta classification of acute pancreatitis: its importance for the radiologist and its effect on treatment. Radiology. 2012 Mar;262(3):751-64. doi: 10.1148/radiol.11110947. PMID: 22357880.
76. Thompson CC, Kumar N, Slattery J, Clancy TE, Ryan MB, Ryou M, Swanson RS, Banks PA, Conwell DL. A standardized method for endoscopic necrosectomy improves complication and mortality rates. Pancreatology. 2016 Jan-Feb;16(1):66-72. doi: 10.1016/j.pan.2015.12.001. Epub 2015 Dec 22. PMID: 26748428; PMCID: PMC4762002.
77. Trikudanathan G, Vege SS. Current concepts of the role of abdominal compartment syndrome in acute pancreatitis — an opportunity or merely an epiphenomenon. Pancreatology. 2014 Jul-Aug;14(4):238-43. doi: 10.1016/j.pan.2014.06.002. Epub 2014 Jun 17. PMID: 25062870.
78. Trikudanathan G, Wolbrink DRJ, van Santvoort HC, Mallery S, Freeman M, Besselink MG. Current Concepts in Severe Acute and Necrotizing Pancreatitis: An Evidence-Based Approach. Gastroenterology. 2019 May;156(7):1994-2007.e3. doi: 10.1053/j.gastro.2019.01.269. Epub 2019 Feb 15. PMID: 30776347.
79. van Baal MC, Bollen TL, Bakker OJ, van Goor H, Boermeester MA, Dejong CH, Gooszen HG, van der Harst E, van Eijck CH, van Santvoort HC, Besselink MG; Dutch Pancreatitis Study Group. The role of routine fine-needle aspiration in the diagnosis of infected necrotizing pancreatitis. Surgery. 2014 Mar;155(3):442-8. doi: 10.1016/j.surg.2013.10.001. Epub 2013 Oct 12. PMID: 24287142.
80. van Brunschot S, Fockens P, Bakker OJ, Besselink MG, Voermans RP, Poley JW, Gooszen HG, Bruno M, van Santvoort HC. Endoscopic transluminal necrosectomy in necrotising pancreatitis: a systematic review. Surg Endosc. 2014 May;28(5):1425-38. doi: 10.1007/s00464-013-3382-9. Epub 2014 Jan 8. Erratum in: Surg Endosc. 2014 Jun;28(6):2003. PMID: 24399524.
81. van Brunschot S, et al. Minimally invasive and endoscopic versus open necrosectomy for necrotising pancreatitis: a pooled analysis of individual data for 1980 patients. Gut. 2018 Apr;67(4):697-706. doi: 10.1136/gutjnl-2016-313341. Epub 2017 Aug 3. PMID: 28774886.
82. van Brunschot S, Schut AJ, Bouwense SA, Besselink MG, Bakker OJ, van Goor H, Hofker S, Gooszen HG, Boermeester MA, van Santvoort HC; Dutch Pancreatitis Study Group. Abdominal compartment syndrome in acute pancreatitis: a systematic review. Pancreas. 2014 Jul;43(5):665-74. doi: 10.1097/MPA.0000000000000108. PMID: 24921201.
83. van Brunschot S, et al. Dutch Pancreatitis Study Group. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial. Lancet. 2018 Jan 6;391(10115):51-58. doi: 10.1016/S0140-6736(17)32404-2. Epub 2017 Nov 3. PMID: 29108721.
84. van Brunschot S. Endoscopic or surgical step-up approach for necrotizing pancreatitis, a multi-center randomized controlled trial. United European Gastroenterol J 2016; 4: A2. doi: 10.1177/2050640616663688.
85. van der Wiel SE, Poley JW, Grubben MJAL, Bruno MJ, Koch AD. The EndoRotor, a novel tool for the endoscopic management of pancreatic necrosis. Endoscopy. 2018 Sep;50(9):E240-E241. doi: 10.1055/a-0628-6136. Epub 2018 Jun 19. PMID: 29920619.
86. van Santvoort HC, et al. Dutch Pancreatitis Study Group. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology. 2011 Oct;141(4):1254-63. doi: 10.1053/j.gastro.2011.06.073. Epub 2011 Jul 8. PMID: 21741922.
87. van Santvoort HC, et al. Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010 Apr 22;362(16):1491-502. doi: 10.1056/NEJMoa0908821. PMID: 20410514.
88. Varadarajulu S, Phadnis MA, Christein JD, Wilcox CM. Multiple transluminal gateway technique for EUS-guided drainage of symptomatic walled-off pancreatic necrosis. Gastrointest Endosc. 2011 Jul;74(1):74-80. doi: 10.1016/j.gie.2011.03.1122. Epub 2011 May 25. PMID: 21612778.
89. Varadarajulu S, Wilcox CM, Tamhane A, Eloubeidi MA, Blakely J, Canon CL. Role of EUS in drainage of peripancreatic fluid collections not amenable for endoscopic transmural drainage. Gastrointest Endosc. 2007 Dec;66(6):1107-19. doi: 10.1016/j.gie.2007.03.1027. Epub 2007 Sep 24. PMID: 17892874.

90. Varadarajulu S, Christein JD, Tamhane A, Drelichman ER, Wilcox CM. Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos). Gastrointest Endosc. 2008 Dec;68(6):1102-11. doi: 10.1016/j.gie.2008.04.028. Epub 2008 Jul 21. PMID: 18640677.
91. Werge M, Roug S, Novovic S, Schmidt PN, Hansen EF, Knudsen JD. Fungal Infections in Patients With Walled-off Pancreatic Necrosis. Pancreas. 2016 Nov;45(10):1447-1451. doi: 10.1097/MPA.0000000000000675. PMID: 27518465.
92. Wroński M, Cebulski W, Pawłowski W, Krasnodębski IW, Słodkowski M. Walled-off necrosis: safety of watchful waiting. Dig Dis Sci. 2015 Apr;60(4):1081-6. doi: 10.1007/s10620-014-3395-9. Epub 2014 Oct 18. PMID: 25326117; PMCID: PMC4408372.
93. Yachimski P, Landewee CA, Campisano F, Valdastri P, Obstein KL. The waterjet necrosectomy device for endoscopic management of pancreatic necrosis: design, development, and preclinical testing (with videos). Gastrointest Endosc. 2020 Sep;92(3):770-775. doi: 10.1016/j.gie.2020.04.024. Epub 2020 Apr 22. PMID: 32334018; PMCID: PMC7483624.
94. Yang CJ, Chen J, Phillips AR, Windsor JA, Petrov MS. Predictors of severe and critical acute pancreatitis: a systematic review. Dig Liver Dis. 2014 May;46(5):446-51. doi: 10.1016/j.dld.2014.01.158. Epub 2014 Mar 16. PMID: 24646880.
95. Yasuda I, Nakashima M, Iwai T, Isayama H, Itoi T, Hisai H, Inoue H, Kato H, Kanno A, Kubota K, Irisawa A, Igarashi H, Okabe Y, Kitano M, Kawakami H, Hayashi T, Mukai T, Sata N, Kida M, Shimosegawa T. Japanese multicenter experience of endoscopic necrosectomy for infected walled-off pancreatic necrosis: The JENIPaN study. Endoscopy. 2013 Aug;45(8):627-34. doi: 10.1055/s-0033-1344027. Epub 2013 Jun 27. PMID: 23807806.
96. Zeng Y, Yang J, Zhang JW. Endoscopic transluminal drainage and necrosectomy for infected necrotizing pancreatitis: Progress and challenges. World J Clin Cases. 2023 Mar 26;11(9):1888-1902. doi: 10.12998/wjcc.v11.i9.1888. PMID: 36998953; PMCID: PMC10044952.
97. Zhu Y, Yin H, Zhang R, Ye X, Wei J. Nasogastric Nutrition versus Nasojejunal Nutrition in Patients with Severe Acute Pancreatitis: A Meta-Analysis of Randomized Controlled Trials. Gastroenterol Res Pract. 2016;2016:6430632. doi: 10.1155/2016/6430632. Epub 2016 Jun 2. PMID: 27340401; PMCID: PMC4909901.
98. Zhu H, Du Y, Wang K, Li Z, Jin Z. Consensus guidelines on the diagnosis and treatment of pancreatic pseudocyst and walled-off necrosis from a Chinese multiple disciplinary team expert panel. Endosc Ultrasound. 2024 Jul-Aug;13(4):205-217. doi: 10.1097/eus.0000000000000080. Epub 2024 Aug 21. PMID: 39318749; PMCID: PMC11419518

Ендоскопічні транслюмінальні втручання в менеджменті гострого інфікованого некротичного панкреатиту. Огляд літератури

Н. В. Пузир [1, 2], А. Є. Ткаченко [3]

[1] Національний медичний університет імені О. О. Богомольця, Київ

[2] КНП «Київська міська клінічна лікарня швидкої медичної допомоги»

[3] Українська військово-медична академія, Київ

Гострий некротичний панкреатит залишається одним із найскладніших захворювань у загальній хірургії. Інфікування некрозу, сепсис й органна недостатність — визначальні чинники летальності при цій патології. Серед інших загрозливих ускладнень — обструкція кишечника, біліарна обструкція, абдомінальний компартмент-синдром, зовнішні нориці, кровотечі, тромбоз селезінкової та портальної вен. Формування відмежованого некротичного скупчення після 4 тиж від початку захворювання створює анатомічні передумови для транслюмінального ендоскопічного доступу до патологічного вогнища за наявності відповідних показань. Сучасне лікування гострого некротичного панкреатиту ґрунтується на поетапній малоінвазивній стратегії, в якій ендоскопічні втручання посідають провідне місце. Міжнародні клінічні настанови, зокрема Європейського товариства гастроінтестінальної ендоскопії (ESGE), Американського товариства гастроінтестінальної ендоскопії (ASGE), Американської гастроентерологічної асоціації (AGA) підтримують ендоскопічний «step-up» підхід як терапію першої лінії при інфікованому відмежованому некротичному скупченні. В основі цього підходу лежить контроль виявів сепсису, а не негайне виконання некрозектомії. Важливими чинниками успіху є правильний вибір часу втручання, мультидисциплінарний підхід й індивідуалізація стратегії лікування. Досі не визначено оптимальних показань до переходу на більш інвазивні оперативні втручання. Це питання залишається дискусійним і зазвичай вирішується з огляду на досвід спеціалізованого центру. Складність прийняття клінічних рішень також може бути пов'язана з відмінностями в підходах до лікування між загальними хірургами й ендоскопістами, що потребує виваженої міждисциплінарної співпраці.

В огляді літератури висвітлено основні аспекти менеджменту гострого некротичного панкреатиту в контексті ендоскопічних транслюмінальних втручань. Розуміння переваг й обмежень цієї методики сприяє її технічному та тактичному вдосконаленню для поліпшення результатів лікування.

Ключові слова: гострий некротичний панкреатит, гострий інфікований панкреонекроз, обмежене некротичне скупчення, ендоскопічна транслюмінальна некрозектомія, пряма ендоскопічна некрозектомія.

FOR CITATION

Puzyr VN, Tkachenko AY. Endoscopic transluminal interventions in the management of acute infected necrotizing pancreatitis. Literature review. General Surgery (Ukraine). 2026;(1);44-57. http://doi.org/10.30978/GS-2026-1-44.

UDC 616.36+616.61]-008.6-092-07-08(091)
DOI http://doi.org/10.30978/GS-2026-1-58

ISSN 2786-5584 PRINT
ISSN 2786-5592 ONLINE

Hepatorenal syndrome: historical perspectives on the recognition of the problem. Review

M. I. Tutchenko, D. M. Patrakh

Bogomolets National Medical University, Kyiv

✉ Denys Patrakh: dr.patrakh.denys@gmail.com

M. I. Tutchenko, http://orcid.org/0000-0002-5050-6494
D. M. Patrakh, http://orcid.org/0000-0001-9724-0470

Hepatorenal syndrome (HRS) is a severe functional complication of portal hypertension and liver cirrhosis, characterized by profound renal hemodynamic dysfunction in the absence of significant structural kidney damage and associated with high mortality. Recent studies report a 90-day mortality of 40–60 %, depending on disease severity and therapeutic interventions. The pathophysiology of HRS is primarily driven by marked splanchnic vasodilation, resulting in reduced effective arterial blood volume, renal vasoconstriction, and a decline in glomerular filtration rate. The association between advanced liver disease and renal dysfunction was first recognized in the 19th century, whereas a clear clinical definition of HRS emerged in the mid-20th century. Subsequent advances led to the classification of HRS into two major types: type I, an acute, rapidly progressive form with a very poor prognosis, and type II, a more indolent form commonly associated with refractory ascites. Therapeutic strategies focus on restoring effective arterial circulation. The most evidence-based pharmacological treatment is the combination of vasoconstrictors, particularly terlipressin, combined with albumin. Invasive approaches, including transjugular intrahepatic portosystemic shunt (TIPS), peritoneovenous shunting, albumin-based extracorporeal liver support systems, and renal replacement therapy, are considered as supportive or bridging options in selected patients, especially those awaiting liver transplantation. Prevention of HRS is based on early infection control, avoidance of nephrotoxic agents, adequate correction of hypovolemia, and routine administration of albumin after large-volume paracentesis. Overall, HRS represents a hallmark of advanced hepatic decompensation and requires early recognition and a multidisciplinary therapeutic approach.

Keywords
hepatorenal syndrome, liver cirrhosis, portal hypertension, terlipressin, albumin, variceal bleeding, ascites.

ARTICLE • Received 2026-01-05 • Received in revised form 2026-02-13 • Published 2026-03-31

Hepatorenal syndrome (HRS) is a severe complication of portal hypertension (PH) [43] and is associated with high morbidity and mortality. Recent case series and meta-analyses report 90-day mortality rates of 40–60 % in patients with HRS, which vary by disease severity and available treatments [30]. The syndrome involves disruptions of renal circulation that outweigh physiological compensatory mechanisms, leading to reduced glomerular filtration rate. Restoration of adequate renal perfusion improves kidney function and can be achieved through liver transplantation [30] or the administration of vasoconstrictor agents. Over the past decade, the terminology, diagnostic criteria, and classification of HRS have undergone substantial revisions, driven by updated approaches to diagnosing and stratifying acute kidney injury (AKI). This review highlights key contemporary advances that have shaped current understanding, diagnostic criteria, and therapeutic strategies for HRS [42].

Historical development of the concept of hepatorenal syndrome

The association between renal dysfunction and progressive liver disease was recognized as early as the late 19th century. This relationship was first described independently by the German clinician and pathologist Friedrich Theodor von Frerichs in 1861 and the American physician Austin Flint in 1863, both of whom reported oliguria in patients with liver cirrhosis and ascites [14].

As the kidney began to be regarded as an independent organ capable of primary pathological involvement, researchers increasingly considered the potential link between renal impairment and liver disease. This pathological process was later

designated as hepatorenal syndrome. Early medical literature already contained isolated reports of concurrent liver and kidney involvement, particularly in studies focused on ascites. Richard Bright laid the foundations of nephrology as a distinct medical discipline. In his seminal «Reports of Medical Cases» published in 1827, Bright described seven cases of ascites etiologically associated with liver disease. In his introductory remarks, he noted that in cases of ascites caused by renal pathology, the liver was «rarely absolutely healthy», although deviations from normal structure were often subtle and manifested as a tendency toward morphological alteration. In patients with liver disease complicated by ascites, he observed a tendency toward oliguria preceding death. Macroscopically, urine was described as «brightly colored» or containing a «pink sediment» that did not coagulate upon heating. Morphologically, in 26 cases in which ascites was attributed to liver disease, the kidneys were described as «rather pale, with uneven vascularity but normal structure», whereas in 29 cases they were characterized as «large and unhealthy» [52].

Frerichs proposed that oliguria resulted from inadequate filling of the systemic circulation due to blood pooling within the splanchnic vascular bed. However, a detailed clinical characterization of the syndrome was not provided until the late 1950s, when Hecker and Sherlock, as well as Papper [32], published comprehensive analyses of two cohorts of patients with cirrhosis complicated by renal failure. The key findings of these studies, which formed the basis of the modern understanding of acute HRS, can be summarized as follows: (1) renal failure typically demonstrates rapid progression and, in some cases, develops after identifiable precipitating factors such as minor gastrointestinal bleeding, paracentesis without adequate plasma volume expansion, or surgical intervention; (2) arterial hypotension is observed in the majority of patients, indicating that the reduction in glomerular filtration rate is driven by systemic hemodynamic disturbances; (3) despite the severity of renal failure, morphological changes in the kidneys are absent or minimal; and (4) prognosis remains extremely poor, with most patients dying within the first month after diagnosis [8].

Even as recently as two decades ago, the pathogenesis of HRS had not been fully elucidated, although it was already hypothesized to represent an extreme manifestation of arterial underfilling caused by predominant arterial vasodilation within the splanchnic circulation [5]. Nevertheless, the mechanisms underlying renal vasoconstriction remained poorly understood [42].

Classification of hepatorenal syndrome

As HRS research progressed, it became evident that two fundamentally distinct clinical types exist. The introduction of HRS classification into type I and type II enabled significant improvements in the principles of diagnosis, treatment, and prevention of this syndrome [11]. A hallmark of HRS is the presence of peripheral vasodilation accompanied by marked renal vasoconstriction [19, 21].

HRS is traditionally classified into type I and type II. Type I HRS is characterized by rapidly progressive renal failure, defined by a doubling of serum creatinine to > 2.5 mg/dL (221 μmol/L) or a creatinine clearance < 20 mL/min within two weeks. The prognosis of type I HRS is extremely poor: approximately 80 % of patients die within two weeks, and only about 10 % survive longer than three months. In contrast, type II HRS is defined by a serum creatinine level > 1.5 mg/dL (132.6 μmol/L) and/or a creatinine clearance < 40 mL/min; however, renal function deteriorates more slowly, and the prognosis is comparatively better [1, 7, 47].

Additional diagnostic criteria for HRS include urine output < 500 mL/day, urinary sodium concentration < 10 mmol/L, urine osmolality exceeding plasma osmolality, fewer than 50 erythrocytes per high-power field in the urine sediment, and a serum sodium concentration < 130 mmol/L. There should be no evidence of shock, ongoing bacterial infection, or current or recent exposure to nephrotoxic drugs. Gastrointestinal fluid losses must be excluded, defined as weight loss > 500 g/day over several days in patients with ascites without peripheral edema or ≥ 1000 g/day in patients with peripheral edema. Furthermore, there should be no sustained improvement in renal function, defined as a decrease in serum creatinine to ≤ 1.5 mg/dL (132.6 μmol/L) or an increase in creatinine clearance to ≥ 40 mL/min [1, 42].

Therapeutic management of hepatorenal syndrome

In 2000, terlipressin therapy was first introduced for the treatment of patients with HRS [46]. Terlipressin is a synthetic analogue of vasopressin, a naturally occurring hormone secreted by the posterior pituitary gland. Its most prominent pharmacological effects include potent vasoconstrictor and antihemorrhagic actions. Of particular importance is the reduction in blood flow within the splanchnic circulation, leading to decreased hepatic blood flow and lower portal venous pressure [4].

In 2000, Mark G. Hamilton (Calgary, Canada) reported regression of HRS in seven of nine treated patients [16]. Treatment was associated with

a significant improvement in mean arterial pressure (from 68 ± 2 to 80 ± 4 mm Hg) and suppression of vasoconstrictor activity, evidenced by reductions in plasma renin activity and plasma norepinephrine levels. No signs of ischemia were observed in any patient. Therapy was discontinued in one patient on the fifth day due to the development of acute pancreatitis [4]. At that time, terlipressin was already being used in the symptomatic management of portal hypertension complicated by bleeding from esophageal and gastric varices [34].

It has been demonstrated that the combination of terlipressin and albumin is effective in the treatment of HRS [20, 29]. The majority of studies have shown a favorable therapeutic response to combined terlipressin and albumin therapy, characterized by an increase in mean arterial pressure and a reduction in serum creatinine to levels below 1.5 mg/dL (132.6 μmol/L) [31, 35, 51].

Currently, three classes of vasoconstrictors are available for the treatment of HRS: vasopressin receptor agonists (vasopressin, terlipressin, and ornipressin), α-adrenergic receptor agonists (norepinephrine and midodrine), and somatostatin receptor agonists (octreotide) [19]. Among these agents, terlipressin is the most extensively studied, followed by norepinephrine, midodrine, and octreotide. A 2019 study demonstrated that the combination of terlipressin and albumin is the most effective therapeutic strategy for the management of HRS [12].

Invasive management of hepatorenal syndrome

In parallel with pharmacological therapy, several invasive and device-based treatment strategies have been used to manage HRS. These include: (1) transjugular intrahepatic portosystemic shunt (TIPS) [39]; (2) peritoneovenous shunt (PVS) [41]; (3) the Molecular Adsorbent Recirculating System (MARS) [36]; and (4) renal replacement therapy (RRT) [5, 40].

Studies indicate that early creation of an intrahepatic portosystemic shunt using the transjugular approach (TIPS) can effectively reduce portal pressure [17] and control variceal bleeding in severely ill patients with liver cirrhosis who are not candidates for surgical intervention [39, 53]. Although initial results suggest temporary shunt patency and clinical improvement, the long-term efficacy and durability of this method remain uncertain and require further evaluation in larger patient cohorts [13].

Peritoneovenous shunting as a therapeutic option for refractory ascites was first proposed by Harry H. LeVeen in 1974 [22, 24]. This technique diverts ascitic fluid from the peritoneal cavity into the venous system (most commonly the internal jugular vein) via a subcutaneously tunneled catheter equipped with a one-way valve [3]. The shunt connects the peritoneal cavity to the internal jugular vein or the superior vena cava, enabling continuous fluid drainage driven by a pressure gradient of approximately 30–50 mm H_2O (2.2–3.6 mm Hg). When the pressure falls below 30 mm H_2O (2.2 mm Hg), the valve closes, preventing retrograde blood flow [27].

Both TIPS and PVS are used in the management of medically refractory ascites [49]. Complete resolution of ascites following either procedure is uncommon. PVS provides more rapid control of ascites, whereas TIPS offers superior long-term efficacy [38]. After either shunting procedure, repeated interventions are often required to maintain shunt patency [50]. Treatment of diuretic-resistant ascites with TIPS carries a risk of early shunt-related mortality but may offer the potential for prolonged survival with sustained ascites control. TIPS implantation should therefore be considered a bridging rather than definitive therapy for persistent ascites in patients with moderate hepatic decompensation. Persistent ascites following TIPS has been identified as a strong predictor of liver transplantation and mortality [49].

The Molecular Adsorbent Recirculating System (MARS), an albumin-based dialysis device that utilizes a hybrid membrane impregnated with albumin to remove albumin-bound toxins that accumulate in liver failure, has been used clinically for more than two decades [33]. Its application in both acute and acute-on-chronic liver failure has consistently demonstrated improvements in biochemical profiles, resolution of hepatic encephalopathy, correction of hemodynamic disturbances, reduction of intracranial pressure, and partial improvement of hepatic synthetic function [26]. In several studies, albeit with small sample sizes, a survival benefit has also been observed. However, key issues such as optimal timing of initiation, duration of therapy, session frequency, and the role of adjunctive supportive treatments remain unresolved [15, 26].

The first experimental demonstration of the dialysis principle (often referred to as the concept of the «artificial kidney» or extracorporeal dialysis) dates back to 1913 and is frequently cited as the origin of RRT. Georg Haas performed the earliest documented attempts at hemodialysis in humans in Giessen between 1924 and 1928 [18]. In 1972, O. S. Better and colleagues reported a clinical case describing the successful use of concurrent hemodialysis (RRT) and massive blood transfusion in a 35-year-old patient who developed HRS following a blast-related liver injury [9]. RRT improves

short-term survival in severe acute kidney injury (AKI) and may serve as an effective bridge to transplantation or as supportive therapy in patients with acute but potentially reversible decompensation [48]. The use of RRT may be particularly beneficial in patients with HRS and AKI who are hemodynamically unstable, as well as in those at risk of elevated intracranial pressure, such as patients with acute fulminant liver failure or acute-on-chronic liver failure [25].

Prevention of hepatorenal syndrome

Preventive strategies aimed at reducing the risk of HRS include abstinence from alcohol [28], regular monitoring of serum creatinine and electrolyte levels in patients receiving diuretic therapy [2], albumin infusion during therapeutic paracentesis [10], administration of antibiotics during episodes of gastrointestinal bleeding [44], antibiotic prophylaxis against spontaneous bacterial peritonitis [45], and the use of non-selective beta-blockers [37]. The use of pharmacological agents such as angiotensin-converting enzyme inhibitors, angiotensin II receptor blockers, and non-steroidal anti-inflammatory drugs should be avoided [1, 10]. Nephrotoxic agents, including aminoglycosides and iodinated contrast media, should be used with particular caution [36].

It has been established that plasma volume expansion, especially with albumin, significantly reduces the incidence of HRS following large-volume paracentesis – from nearly 10 % in patients who did not receive specific preventive treatment to approximately 2 % in those treated with plasma-expanding agents [6, 23].

Conclusions

Hepatorenal syndrome was first described nearly 70 years ago as a functional form of renal failure occurring in patients with cirrhosis in the absence of overt morphological kidney damage [52]. Its development is driven by profound splanchnic vasodilation, leading to renal vasoconstriction and reduced glomerular filtration. Two major clinical forms have been traditionally distinguished: an acute, rapidly progressive type (type I) and a more slowly progressive form (type II). Therapeutic strategies are primarily aimed at restoring effective circulatory volume and renal perfusion and include terlipressin in combination with albumin, TIPS, peritoneovenous shunting, and, ultimately, liver transplantation. Preventive measures focus on infection control, avoidance of nephrotoxic agents, correction of hypovolemia, and albumin administration following paracentesis.

Declaration of interests

The authors declare no conflicts of interest and no financial relationships that could be construed as a potential conflict in the preparation of this article.

Authors contributions

M. I. Tutchenko: conceptualization, study design, data analysis, methodology, and manuscript editing;
D. M. Patrakh: conceptualization, study design, data collection and processing, data analysis, methodology, and drafting of the original manuscript.

References

1. Angeli P, Ginès P, Wong F, Bernardi M, Boyer TD, Gerbes A, Moreau R, Jalan R, Sarin SK, Piano S, Moore K, Lee SS, Durand F, Salerno F, Caraceni P, Kim WR, Arroyo V, Garcia-Tsao G. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. J Hepatol. 2015 Apr;62(4):968-74. doi: 10.1016/j.jhep.2014.12.029. Epub 2015 Jan 28. Erratum in: J Hepatol. 2015 Jul;63(1):290. PMID: 25638527.
2. Attieh RM, Wadei HM. Acute Kidney Injury in Liver Cirrhosis. Diagnostics (Basel). 2023 Jul 13;13(14):2361. doi: 10.3390/diagnostics13142361. PMID: 37510105; PMCID: PMC10377915.
3. Ayllón MD, Ciria R, Gómez-Luque I, Rodriguez-Perálvarez M, Padial A, Luque A, López-Cillero P, de la Mata M, Briceño J. Use of Peritoneovenous Shunt for the Management of Refractory Ascites. Transplant Proc. 2019 Jan-Feb;51(1):41-43. doi: 10.1016/j.transproceed.2018.04.089. Epub 2018 Jun 30. PMID: 30655143.
4. Ayyad A, Al-Horani RA. Terlipressin for the Prevention and Treatment of Renal Decline in Hepatorenal Syndrome: A Drug Profile. Gastroenterol Insights. 2023 Dec;14(4):420-430. doi: 10.3390/gastroent14040031. Epub 2023 Sep 28. PMID: 37873544; PMCID: PMC10587779.
5. Badura K, Frąk W, Hajdys J, Majchrowicz G, Młynarska E, Rysz J, Franczyk B. Hepatorenal Syndrome-Novel Insights into Diagnostics and Treatment. Int J Mol Sci. 2023 Dec 14;24(24):17469. doi: 10.3390/ijms242417469. PMID: 38139297; PMCID: PMC10744165.
6. Bai Z, Méndez-Sánchez N, Romeiro FG, Mancuso A, Philips CA, Tacke F, Basaranoglu M, Primignani M, Ibrahim M, Wong YJ, Nery FG, Teschke R, Ferreira CN, Muñoz AE, Pinyopornpanish K, Thevenot T, Singh SP, Mohanty A, Satapathy SK, Ridola L, Maruyama H, Cholongitas E, Levi Sandri GB, Yang L, Shalimar, Yang Y, Villa E, Krag A, Wong F, Jalan R, O'Brien A, Bernardi M, Qi X; Liver Cirrhosis-related Complications (LCC)-International Special Interest Group. Use of albumin infusion for cirrhosis-related complications: An international position statement. JHEP Rep. 2023 May 5;5(8):100785. doi: 10.1016/j.jhepr.2023.100785. PMID: 37456673; PMCID: PMC10339261.
7. Baraldi O, Valentini C, Donati G, Comai G, Cuna V, Capelli I, Angelini ML, Moretti MI, Angeletti A, Piscaglia F, La Manna G. Hepatorenal syndrome: Update on diagnosis and treatment. World J Nephrol. 2015 Nov 6;4(5):511-20. doi: 10.5527/wjn.v4.i5.511. PMID: 26558188; PMCID: PMC4635371.
8. Bataller R, Ginès P, Guevara M, Arroyo V. Hepatorenal syndrome. Semin Liver Dis. 1997;17(3):233-47. doi: 10.1055/s-2007-1007201. PMID: 9308128.
9. Better OS, Garty J, Barzilai A, Erlik D. Traumatic hepatorenal failure. Supportive treatment with simultaneous hemodialysis and exchange transfusion. Arch Surg. 1972 Mar;104(3):347-8. doi: 10.1001/archsurg.1972.04180030093023. PMID: 5010849.
10. Biggins SW, Angeli P, Garcia-Tsao G, Ginès P, Ling SC, Nadim MK, Wong F, Kim WR. Diagnosis, evaluation, and management of ascites, spontaneous bacterial peritonitis and hepatorenal syndrome: 2021 practice guidance by the American Association for the Study of Liver Diseases. Hepatology. 2021 Aug;74(2):1014-1048. doi: 10.1002/hep.31884. Erratum in: Hepatology. 2024;80(5):E89. doi: 10.1097/HEP.0000000000000983. PMID:33942342.
11. Bodh V, Sharma B, Sharma R. Hepatorenal syndrome: a review into changing definition, diagnostic criteria, pathophysiology, and management. CHRISMED J Health Res. 2020 Apr–Jun;7(2):83-89. doi: 10.4103/cjhr.cjhr_117_19.
12. Braga QM, Schacher FC, Mattos AA, Mattos ÂZ. Terlipressin for the treatment of hepatorenal syndrome: a meta-analysis of randomized controlled trials. Eur J Gastroenterol Hepatol. 2025 Jun 1;37(6):753-760. doi: 10.1097/MEG.0000000000002954. Epub 2025 Feb 27. PMID: 40207491.

13. Chen JW, Chen PF, Li J, Duan XH, Ren JZ, Zhang WG. Transjugular Intrahepatic Portosystemic Shunt for Preventing Rebleeding of Esophageal Varices in Patients with Portal Cavernous Transformation. Dig Dis Sci. 2025 May;70(5):1897-1905. doi: 10.1007/s10620-025-08955-7. Epub 2025 Mar 3. PMID: 40032713; PMCID: PMC12125086.
14. Eknoyan G, Epstein M. Hepatorenal syndrome: a historical appraisal of its origins and conceptual evolution. Kidney Int. 2021 Jun;99(6):1321-1330. doi: 10.1016/j.kint.2021.02.037. Epub 2021 Mar 27. PMID: 33781792.
15. Gadour E, Kaballo MA, Shrwani K, Hassan Z, Kotb A, Aljuraysan A, Miuțescu B, Sherwani N, Mahallawi W. Safety and efficacy of Single-Pass Albumin Dialysis (SPAD), Prometheus, and Molecular Adsorbent Recycling System (MARS) liver haemodialysis vs. Standard Medical Therapy (SMT): meta-analysis and systematic review. Prz Gastroenterol. 2024;19(2):101-111. doi: 10.5114/pg.2024.139297. Epub 2024 Apr 29. PMID: 38939063; PMCID: PMC11200067.
16. Hamilton M. Hepatorenal syndrome treatment with terlipressin and albumin. Crit Care. 2000;2:6039. doi: 10.1186/ccf-2000-6039.
17. Huerta A, García-Guix M, Villanueva C. Role of TIPS in acute variceal bleeding. Curr Hepatol Rep. 2025;24(1):27. doi: 10.1007/s11901-025-00694-7.
18. Husain-Syed F, Enke U, Lübbecke F, Fassbinder W, Grimminger F, Birk HW. 100 Years of Dialysis at University Hospital Giessen. Blood Purif. 2025;54(4-5):211-217. doi: 10.1159/000543874. Epub 2025 Feb 5. PMID: 39908004.
19. Hasan I, Rashid T, Chirila RM, Ghali P, Wadei HM. Hepatorenal syndrome: pathophysiology and evidence-based management update. Rom J Intern Med. 2021 Aug 26;59(3):227-261. doi: 10.2478/rjim-2021-0006. PMID: 33544554.
20. Israelsen M, Dahl EK, Madsen BS, Wiese S, Bendtsen F, Møller S, Fialla AD, Jensen BL, Krag A. Dobutamine reverses the cardio-suppressive effects of terlipressin without improving renal function in cirrhosis and ascites: a randomized controlled trial. Am J Physiol Gastrointest Liver Physiol. 2020 Feb 1;318(2):G313-G321. doi: 10.1152/ajpgi.00328.2019. Epub 2019 Dec 16. PMID: 31841026.
21. Kolesnyk M. Guideline updates for definition, diagnosis and management of hepatorenal syndrome. Ukr J Nephr Dial. 2020;2(66):62-70. doi: 10.31450/ukrjnd.2(66).2020.09.
22. Koyama S, Nogami A, Yoneda M, Cheng S, Koike Y, Takeuchi Y, Iwaki M, Kobayashi T, Saito S, Utsunomiya D, Nakajima A. Chronological Course and Clinical Features after Denver Peritoneovenous Shunt Placement in Decompensated Liver Cirrhosis. Tomography. 2024 Mar 25;10(4):471-479. doi: 10.3390/tomography10040036. PMID: 38668394; PMCID: PMC11055000.
23. Lan T, Chen M, Tang C, Deltenre P. Recent developments in the management of ascites in cirrhosis. United European Gastroenterol J. 2024 Mar;12(2):261-272. doi: 10.1002/ueg2.12539. Epub 2024 Feb 10. PMID: 38340308; PMCID: PMC10954428.
24. Leveen HH, Christoudias G, Ip M, Luft R, Falk G, Grosberg S. Peritoneo-venous shunting for ascites. Ann Surg. 1974 Oct;180(4):580-91. doi: 10.1097/00000658-197410000-00023. PMID: 4415019; PMCID: PMC1344147.
25. Loeffler J, Hassan M, Qaqish F, Dimachkie R, Dehghani S, Sasso R, Abou Yassine A, Deeb L. Predictors of Renal Replacement Therapy Requirement in Cirrhotic Patients with Acute Kidney Injury. Dig Dis Sci. 2025 Apr;70(4):1540-1546. doi: 10.1007/s10620-025-08881-8. Epub 2025 Feb 15. PMID: 39954191.
26. MacDonald AJ, Subramanian RM, Olson JC, Speiser JL, Durkalski-Mauldin VL, Abraldes JG, Bigam DL, Flynn MM, Rapaka B, Shropshire BM, Vora RS, Karvellas CJ; U.S. Acute Liver Failure Study Group. Use of the Molecular Adsorbent Recirculating System in Acute Liver Failure: Results of a Multicenter Propensity Score-Matched Study. Crit Care Med. 2022 Feb 1;50(2):286-295. doi: 10.1097/CCM.0000000000005194. PMID: 34259656.
27. Malik TF, Anjum F. Peritoneovenous Shunt. 2023 Jul 31. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. PMID: 32965831.
28. Marot A, Henrion J, Knebel JF, Trépo E, Moreno C, Deltenre P. A model for individualized prediction of liver-related death in outpatients with alcohol-associated cirrhosis. Hepatol Commun. 2023 Aug 31;7(9):e0229. doi: 10.1097/HC9.0000000000000229. PMID: 37655969; PMCID: PMC10476762.
29. Mohamed MMG, Rauf A, Adam A, Kheiri B, Lacasse A, El-Halawany H. Terlipressin effect on hepatorenal syndrome: Updated meta-analysis of randomized controlled trials. JGH Open. 2021 Jul 1;5(8):896-901. doi: 10.1002/jgh3.12600. PMID: 34386597; PMCID: PMC8341180.
30. Nadim MK, Kellum JA, Forni L, Francoz C, Asrani SK, Ostermann M, Allegretti AS, Neyra JA, Olson JC, Piano S, VanWagner LB, Verna EC, Akcan-Arikan A, Angeli P, Belcher JM, Biggins SW, Deep A, Garcia-Tsao G, Genyk YS, Gines P, Kamath PS, Kane-Gill SL, Kaushik M, Lumlertgul N, Macedo E, Maiwall R, Marciano S, Pichler RH, Ronco C, Tandon P, Velez JQ, Mehta RL, Durand F. Acute kidney injury in patients with cirrhosis: Acute Disease Quality Initiative (ADQI) and International Club of Ascites (ICA) joint multidisciplinary consensus meeting. J Hepatol. 2024 Jul;81(1):163-183. doi: 10.1016/j.jhep.2024.03.031. Epub 2024 Mar 26. PMID: 38527522; PMCID: PMC11193657.
31. Narayanan V, Devadas K, Sreesh S, Varghese J, Solanki R, Mohapatra SD, Pal R, Madhu D, Chakravorty A. Novel predictors of response to therapy with terlipressin and albumin in hepatorenal syndrome-acute kidney injury. Ann Gastroenterol. 2024 Jan-Feb;37(1):81-88. doi: 10.20524/aog.2023.0853. Epub 2023 Dec 23. PMID: 38223250; PMCID: PMC10785019.
32. Patel A, Zhang C, Minacapelli CD, Gupta K, Catalano C, Li Y, Rustgi VK. Outcomes, Mortality, and Cost Burden of Acute Kidney Injury and Hepatorenal Syndrome in Patients with Cirrhosis. J Gastrointestin Liver Dis. 2023 Mar 31;32(1):39-50. doi: 10.15403/jgld-4618. PMID: 37004233.
33. Pinceaux K, Bélicard F, Coirier V, Le Pabic E, Guillot P, Delamaire F, Painvin B, Quelven Q, Lesouhaitier M, Maamar A, Gacouin A, Houssel-Debry P, Boudjema K, Bardou-Jacquet E, Tadié JM, Reizine F, Camus C. Transplant-free survival in acute liver failure patients receiving MARS®, plasma exchange or no liver support. A real-life 21-year retrospective cohort study in a referral center. Ann Intensive Care. 2025 Aug 26;15(1):124. doi: 10.1186/s13613-025-01506-3. PMCID: PMC12381347.
34. Roberts D, Best LM, Freeman SC, Sutton AJ, Cooper NJ, Arunan S, Begum T, Williams NR, Walshaw D, Milne EJ, Tapp M, Csenar M, Pavlov CS, Davidson BR, Tsochatzis E, Gurusamy KS. Treatment for bleeding oesophageal varices in people with decompensated liver cirrhosis: a network meta-analysis. Cochrane Database Syst Rev. 2021 Apr 10;4(4):CD013155. doi: 10.1002/14651858.CD013155.pub2. PMID: 33837526; PMCID: PMC8094233.
35. Rockey DC, Gordon F, Thuluvath PJ, Victor D, Kemmer N, Cardoza S, Jamil K, Frederick RT. Terlipressin for Hepatorenal Syndrome in Patients With Early-Stage Acute-on-Chronic Liver Failure. Liver Int. 2025 Dec;45(12):e70399. doi: 10.1111/liv.70399. PMID: 41200852; PMCID: PMC12593294.
36. Roy P, Minhaz N, Shah-Riar P, Simona SY, Tasha T, Binte Hasan T, Abbasi FK, Alam F, Nila SA, Akter J, Akter S, Biswas S, Sultana N. A Comprehensive Systematic Review of the Latest Management Strategies for Hepatorenal Syndrome: A Complicated Syndrome to Tackle. Cureus. 2023 Aug 7;15(8):e43073. doi: 10.7759/cureus.43073. PMID: 37680416; PMCID: PMC10481992.
37. Rudyk DV, Tutchenko MI, Chub SL, Besedinsky MS. Portal hypertension and emergency care. Wiad Lek. 2024;77(7):1485-1489. doi: 10.36740/WLek202407125. PMID: 39241149.
38. Schütte SL, Tiede A, Mauz JB, Rieland H, Kabelitz M, Iker R, Richter N, Meyer B, Heidrich B, Wedemeyer H, Maasoumy B, Tergast TL. Comparison of clinical outcomes in patients with refractory ascites treated with either TIPS, tunneled peritoneal catheter, or ascites pump. Hepatol Commun. 2025 Jan 16;9(2):e0620. doi: 10.1097/HC9.0000000000000620. PMID: 39813591; PMCID: PMC11737501.
39. Shalaby S, Nicoară-Farcău O, Perez-Campuzano V, Olivas P, Torres S, García-Pagán JC, Hernández-Gea V. Transjugular Intrahepatic Portosystemic Shunt (TIPS) for Treatment of Bleeding from Cardiofundal and Ectopic Varices in Cirrhosis. J Clin Med. 2024 Sep 24;13(19):5681. doi: 10.3390/jcm13195681. PMID: 39407741; PMCID: PMC11476950.
40. Sherman M, DiSilvio B, Cheema T. Overview and management of hepatorenal syndrome. Curr Opin Anaesthesiol. 2025 Aug 1;38(4):492-497. doi: 10.1097/ACO.0000000000001526. Epub 2025 Jun 17. PMID: 40523009.
41. Shimura Y, Komatsu S, Hashimoto Y, Nishio M, Hashimoto Y, Yoshida M, Yoshida T, Fukushima K, Fujita I, Fukumoto T. Biomarker-guided strategy for Denver peritoneovenous shunts in refractory ascites: a retrospective single-center study. Langenbecks Arch Surg. 2025 Apr 23;410(1):140. doi: 10.1007/s00423-025-03710-y. PMID: 40266319; PMCID: PMC12018634.
42. Simonetto DA, Gines P, Kamath PS. Hepatorenal syndrome: pathophysiology, diagnosis, and management. BMJ. 2020 Sep 14;370:m2687. doi: 10.1136/bmj.m2687. PMID: 32928750.
43. Tutchenko MI, Besedinskyi MS, Aslanian SA, Kluzko IV, Rudyk DV, Chub SL. Hepatorenal syndrome in decompensated portal hypertension. Medicni Perspekt. 2024 Dec;29(4):94-101. doi: 10.26641/2307-0404.2024.4.319225.

44. Tutchenko MI, Rudyk DV, Klyuzko IV, Besedinskyi MS, Chub SL, Sirenko OA. Treatment of portal hypertension complicated by variceal bleeding. Emerg Med. 2024;20(3):180-185. doi: 10.22141/2224-0586.20.3.2024.1690.
45. Tutchenko MI, Rudyk DV, Besedinskyi MS, Chub SL. Spontaneous bacterial peritonitis. East Ukr Med J. 2024;12(2):221-228. doi: 10.21272/eumj.2024;12(2):221-228.
46. Uriz J, Ginès P, Cárdenas A, Sort P, Jiménez W, Salmerón JM, Bataller R, Mas A, Navasa M, Arroyo V, Rodés J. Terlipressin plus albumin infusion: an effective and safe therapy of hepatorenal syndrome. J Hepatol. 2000 Jul;33(1):43-8. doi: 10.1016/s0168-8278(00)80158-0. PMID: 10905585.
47. Velez JCQ, Therapondos G, Juncos LA. Reappraising the spectrum of AKI and hepatorenal syndrome in patients with cirrhosis. Nat Rev Nephrol. 2020 Mar;16(3):137-155. doi: 10.1038/s41581-019-0218-4.
48. Wang Q, Liu F, Tao W, Qian K. Timing of renal replacement therapy in patients with sepsis-associated acute kidney injury: A systematic review and meta-analysis. Aust Crit Care. 2024 Mar;37(2):369-379. doi: 10.1016/j.aucc.2023.06.011. Epub 2023 Sep 19. PMID: 37734999.
49. Will V, Rodrigues SG, Berzigotti A. Current treatment options of refractory ascites in liver cirrhosis – A systematic review and meta-analysis. Dig Liver Dis. 2022 Aug;54(8):1007-1014. doi: 10.1016/j.dld.2021.12.007. Epub 2022 Jan 10. PMID: 35016859.
50. Wong F. Management of refractory ascites. Clin Mol Hepatol. 2023 Jan;29(1):16-32. doi: 10.3350/cmh.2022.0104. Epub 2022 Jun 9. PMID: 35676862; PMCID: PMC9845666.
51. Wong F. Terlipressin for hepatorenal syndrome. Curr Opin Gastroenterol. 2024 May 1;40(3):156-163. doi: 10.1097/MOG.0000000000001016. Epub 2024 Mar 7. PMID: 38353275.
52. Wong F, Blendis L. Historical Aspects of Ascites and the Hepatorenal Syndrome. Clin Liver Dis (Hoboken). 2021 Oct 29;18(Suppl 1):14-27. doi: 10.1002/cld.1090. PMID: 34745581; PMCID: PMC8555459.
53. Zhou GP, Jiang YZ, Sun LY, Zhu ZJ. Early transjugular intrahepatic portosystemic shunt for acute variceal bleeding: a systematic review and meta-analysis. Eur Radiol. 2021 Jul;31(7):5390-5399. doi: 10.1007/s00330-020-07525-x. Epub 2021 Jan 6. PMID: 33409783.

Гепаторенальний синдром: історичні аспекти усвідомлення проблеми. Огляд

М. І. Тутченко, Д. М. Патрах

Національний медичний університет імені О. О. Богомольця, Київ

Гепаторенальний синдром (ГРС) є тяжким функціональним ускладненням декомпенсованої портальної гіпертензії та цирозу печінки, що характеризується різким порушенням ниркової гемодинаміки без виражених морфологічних змін у нирках і супроводжується високою летальністю. Сучасні дослідження свідчать про 90-денну смертність на рівні 40—60 %, залежно від тяжкості стану та проведеної терапії. Патогенетично ГРС зумовлений спланхнічною вазодилатацією з подальшою ниркową вазоконстрикцією та зниженням швидкості клубочкової фільтрації. Історично взаємозв'язок між ураженням печінки та ниркową дисфункцією був описаний ще у XIX столітті, однак чітке клінічне окреслення синдрому сформувалося лише в середині XX століття. Подальший розвиток уявлень дозволив виокремити два типи ГРС: тип I — гострий, швидко прогресивний з вкрай несприятливим прогнозом, та тип II — хронічний, повільніший перебіг, частіше асоційований з рефрактерним асцитом. Терапевтичні підходи спрямовані на відновлення ефективного артеріального кровообігу. Найбільш обґрунтованою медикаментозною стратегією є застосування вазоконстрикторів, насамперед терліпресину в комбінації з альбуміном. Інвазивні методи, такі як трансяремне інтрапечінкове портосистемне стентування, перитонеовенозне шунтування, системи альбумінового діалізу (MARS) та замісна ниркова терапія, розглядаються як етап підготовки до трансплантації печінки або тимчасова підтримка у відібраних пацієнтів. Профілактика ГРС ґрунтується на контролі інфекцій, уникненні нефротоксичних препаратів, адекватній корекції гіповолемії та рутинному застосуванні альбуміну після великооб'ємного парацентезу. ГРС залишається маркером глибокої декомпенсації цирозу і потребує раннього розпізнавання та агресивної міждисциплінарної тактики лікування.

Ключові слова: гепаторенальний синдром, цироз печінки, портальна гіпертензія, терліпресин, альбумін, варикозна кровотеча, асцит.

FOR CITATION

Tutchenko MI, Patrakh DM. Hepatorenal syndrome: historical perspectives on the recognition of the problem. Review. General Surgery (Ukraine). 2026;(1);58-63. http://doi.org/10.30978/GS-2026-1-58.

UDC 616.147.17-007.64-089:616-08
DOI http://doi.org/10.30978/GS-2026-1-64

ISSN 2786-5584 PRINT
ISSN 2786-5592 ONLINE

Mechanism-oriented three-level classification of treatment methods for chronic hemorrhoidal disease. Review

L. Y. Markulan, L. S. Bilianskyi, I. V. Voloshyn

Bogomolets National Medical University, Kyiv

✉ Leonid Markulan: markulan@ukr.net

L. Y. Markulan, http://orcid.org/0000-0003-2879-5012.
L. S. Bilianskyi, http://orcid.org/0000-0003-1025-9019,
I. V. Voloshyn, http://orcid.org/0009-0000-9913-9800,

Objective – to synthesize current approaches to the treatment of chronic hemorrhoids and to develop a mechanism-oriented classification of treatment methods that integrates the pathophysiological mechanism of action of interventions, the anatomical target of treatment, the degree of surgical invasiveness, and the organ-preserving potential of the procedures.

A comprehensive analysis of current literature on the pathogenesis of hemorrhoidal disease and its treatment modalities was conducted. The principal pathophysiological mechanisms underlying the disease, major therapeutic strategies for their correction, and corresponding clinical intervention technologies were systematized. Based on a conceptual analysis, a model of the interrelationships between pathogenic mechanisms, therapeutic strategies, and clinical treatment methods was constructed, forming the foundation for the proposed classification system. A mechanism-oriented classification of treatment methods for hemorrhoidal disease was developed, integrating pathophysiological mechanisms, therapeutic strategies for their correction, and clinical intervention technologies within a unified conceptual framework. The main therapeutic strategies identified include symptom control, induction of fibrosis of hemorrhoidal cushions, reduction of arterial inflow, intratissue remodeling, reconstruction of anal canal anatomy, and radical excision of pathologically altered tissues. Within each strategy, corresponding clinical treatment methods were systematized, allowing diverse modern technologies to be interpreted as specific implementations of a limited number of fundamental therapeutic mechanisms.

Conclusions. The proposed classification enables systematic organization of contemporary treatment methods for hemorrhoidal disease according to their underlying pathophysiological mechanisms and integrates them within a unified conceptual model. This approach provides a methodological basis for a more consistent interpretation of modern treatment technologies and may be applied in future comparative clinical studies.

Keywords
hemorrhoidal disease, hemorrhoids, mechanism-based classification, treatment strategies, minimally invasive procedures, hemorrhoidectomy.

ARTICLE • Received 2026-01-26 • Received in revised form 2026-03-03 • Published 2026-03-31

Hemorrhoidal disease (HD) is one of the most common disorders of the anorectal region and remains a significant medical and social challenge in modern coloproctology. According to epidemiological studies, clinically significant manifestations of hemorrhoids occur in 25–40 % of the adult population over a lifetime, while the annual number of medical consultations related to HD in developed countries reaches millions of cases [12, 19, 44]. The high prevalence of the disease, its chronic relapsing course, and its negative impact on patients' quality of life account for the sustained clinical interest in optimizing treatment strategies [46, 47].

Despite the long history of HD research, current clinical practice is characterized by substantial heterogeneity in treatment approaches, particularly for grades I–III chronic HD. Contemporary clinical guidelines describe a wide spectrum of conservative, minimally invasive, and surgical interventions; however, a unified classification system for these methods is still lacking [5, 8, 15, 58, 61]. In most recommendations, treatment modalities are

grouped primarily by degree of invasiveness, setting of performance, or clinical indications based on the Goligher classification, which does not always reflect the underlying pathophysiological targets of the interventions [10, 18, 21, 23, 60].

Historically, the development of surgical treatment for HD has progressed from radical excisional procedures to organ-preserving and minimally invasive techniques. Classical hemorrhoidectomies, particularly the Milligan–Morgan and Ferguson procedures, have long been considered the «gold standard» for the treatment of advanced forms of the disease, providing the lowest recurrence rates but being associated with significant postoperative pain, prolonged recovery, and a risk of complications [38, 52].

Further advances in understanding HD pathogenesis have led to the emergence of organ-preserving techniques aimed at correcting specific components of the pathological process without complete removal of the cavernous vascular tissue. These methods include Doppler-guided dearterialization, stapled hemorrhoidopexy, and intratissue energy-based ablation technologies [6, 11, 20, 29, 32, 33, 40, 53, 62]. In parallel, outpatient minimally invasive procedures have been actively developed, enabling the treatment of a substantial proportion of patients in a day-care setting [2, 50].

As a result, a broad spectrum of treatment options for HD has emerged, ranging from conservative therapy to high-tech energy-based interventions. However, this diversity itself creates a methodological challenge—namely, the absence of a unified classification system that would allow for accurate comparison of different treatment technologies and determination of their role within an overall therapeutic strategy.

Current concepts of HD pathogenesis are based on a combination of hemodynamic and mechanical mechanisms, including impaired venous outflow in the cavernous tissue, arteriovenular shunting, and weakening of the supporting ligamentous apparatus of the anal cushions [1, 31]. From a pathophysiological perspective, most contemporary interventions can be considered as targeting one of several principal therapeutic mechanisms: induction of fibrosis of the hemorrhoidal cushions, reduction of arterial inflow, intratissue remodeling of the cavernous vascular tissue, reconstructive restoration of anal canal anatomy, or radical excision of pathologically altered tissue.

The diversity of modern treatment methods for HD, along with differences in their underlying pathophysiological mechanisms of action, necessitates their systematization within a unified classification framework.

Objective – to synthesize current approaches to the treatment of chronic hemorrhoids and to develop a mechanism-oriented classification of treatment methods that integrates the pathophysiological mechanism of action of interventions, the anatomical target of treatment, the degree of surgical invasiveness, and the organ-preserving potential of the procedures.

This study was conducted as a narrative literature review with elements of conceptual synthesis. The aim of the analysis was to systematize contemporary treatment methods for chronic HD and to develop a mechanism-oriented classification of interventions.

A literature search was performed in the PubMed/MEDLINE, Scopus, and Web of Science databases. In addition, current clinical guidelines of professional societies, including ASCRS, ESCP, and SICCR, were analyzed [8, 15, 58, 61]. Combinations of the following keywords were used: hemorrhoids, hemorrhoidal disease, surgical treatment, minimally invasive procedures, hemorrhoidectomy, dearterialization, laser hemorrhoidoplasty, radiofrequency ablation, stapled hemorrhoidopexy, classification, pathophysiology.

The analysis included original studies, systematic reviews, meta-analyses, and clinical guidelines addressing treatment methods for HD. Particular attention was paid to studies describing the mechanisms of therapeutic action of various interventions, their anatomical targets, clinical indications, and their role within contemporary stepwise treatment strategies [5, 8].

The classification was developed based on three interrelated principles:

1. The dominant mechanism of therapeutic action.
2. The anatomical target of the intervention.
3. The level of technological implementation of the method.

The integration of these criteria formed the basis of a three-level classification model.

Results

The findings allowed for the synthesis of relationships between the main pathophysiological mechanisms of HD, therapeutic strategies for their correction, and clinical treatment methods. A conceptual model of these relationships is presented in Figure.

The presented figure illustrates that most contemporary treatment methods for HD can be interpreted as implementations of a limited number of fundamental therapeutic strategies aimed at correcting key components of the disease pathogenesis. Specifically, different interventions may target the induction of fibrosis of the hemorrhoidal cushions, reduction of arterial inflow, intratissue remodeling of the cavernous vascular tissue, reconstruction of

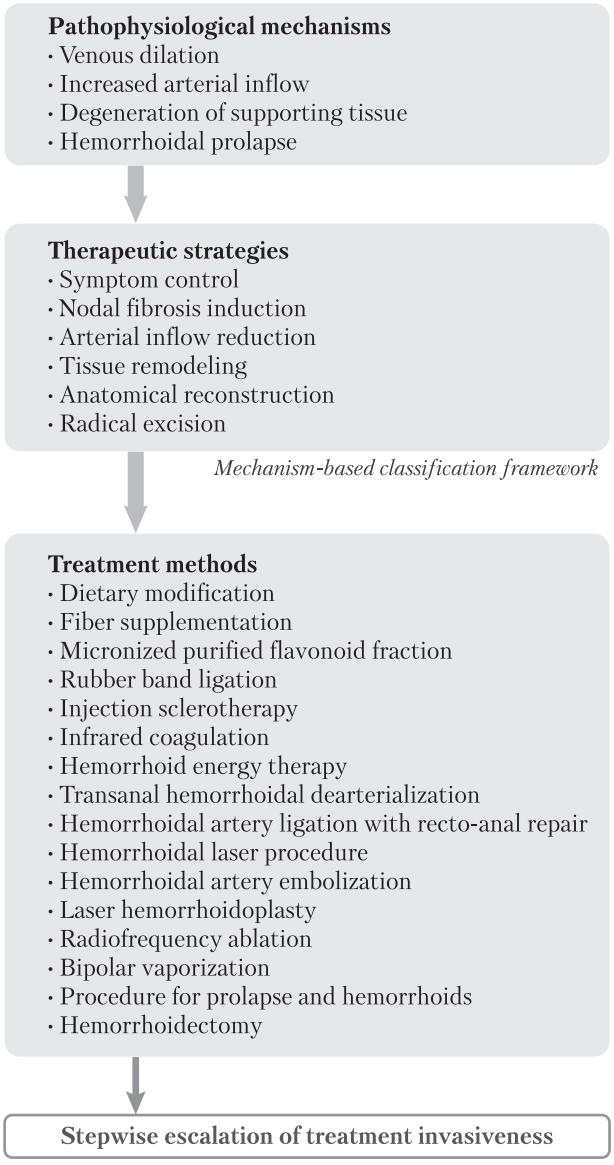

Figure. **Conceptual relationship between the pathophysiology of hemorrhoidal disease, therapeutic strategies, and treatment methods with stepwise escalation of treatment invasiveness**

anal canal anatomy, or radical excision of pathologically altered tissue.

Such a mechanism-oriented approach allows different technological solutions to be viewed not as isolated procedures, but as variants of implementing shared therapeutic strategies. This provides a basis for the systematization of modern treatment methods for HD within a unified pathophysiological framework.

The proposed classification is based on a three-level structure. At the first level (Level 1), treatment methods are systematized according to the primary therapeutic strategy. At the second level (Level 2), technological groups of interventions that implement the respective strategy are identified. At the third level (Level 3), specific clinical methods are presented. This approach allows for the integration of different technologies within a unified pathophysiological treatment model while preserving the flexibility for further expansion of the classification as new methods emerge (Table).

Clinical positioning of surgical methods within the proposed classification

The proposed mechanism-oriented classification enables systematic positioning of contemporary surgical methods for HD treatment according to their point of impact on the disease pathogenesis. In this context, different interventions can be viewed as implementations of several principal therapeutic strategies: induction of fibrosis of the hemorrhoidal cushions, modulation of arterial inflow, intratissue remodeling of the cavernous vascular tissue, reconstruction of anal canal anatomy, or radical removal of pathological tissue. This approach not only allows for the systematization of various technological solutions but also facilitates a clearer understanding of their role within the modern treatment algorithm for hemorrhoids.

Methods for inducing fibrosis of the hemorrhoidal cushions

This group includes outpatient minimally invasive procedures aimed at localized injury of the hemorrhoidal cushion, followed by fibrosis formation and fixation to the underlying tissues. The most common representatives of this category are rubber band ligation [3, 8, 24, 30, 61, 65], sclerotherapy [15, 18, 41], and infrared coagulation [28, 42]. These methods are primarily used in hemorrhoids of grades I–II and, in selected cases, grade III without significant prolapse. Their main advantages lie in their minimal invasiveness and the feasibility of outpatient application; however, their effectiveness in addressing prolapse remains limited.

Sclerotherapy occupies a distinct position within this category, as its primary mechanism differs somewhat from that of rubber band ligation (RBL) or coagulation-based methods. In sclerotherapy, the agent is injected into the submucosal layer adjacent to the hemorrhoidal cushion, causing chemical endothelial damage, aseptic inflammation, vascular obliteration, and subsequent fibrosis formation. Therefore, from a pathophysiological perspective, it is more appropriately classified not as a method of intratissue remodeling, but as an intervention inducing fibrosis of the mucosal–submucosal layer with a fixation effect. In most contemporary guidelines, RBL, sclerotherapy, and infrared coagulation (IRC) are effectively grouped under the category

Table. **Proposed three-level mechanism-oriented classification of treatment methods for chronic hemorrhoidal disease**

Level 1: Therapeutic strategy	Level 2: Technology group	Anatomical target	Mechanism of therapeutic action	Level 3: Methods
Conservative treatment	Pharmacological and non-pharmacological therapy	Functional factors (defecation disorders, venous tone, inflammation)	Symptom control	Dietary therapy, normalization of bowel habits, MPFF, topical agents
Induction of fibrosis	Office-based minimally invasive procedures	Mucosal–submucosal layer of hemorrhoidal cushions	Formation of fibrosis or vascular obliteration	RBL, IS, IRC, HET
Hemodynamic modification	Dearterialization technologies	Arterial branches of the superior rectal artery	Reduction of arterial inflow	THD, HAL-RAR, HeLP, HAE
Tissue remodeling	Energy-based intratissue ablation methods	Cavernous vascular tissue of hemorrhoidal cushions	Controlled intratissue coagulation and fibrosis	LHP, RFA, BPV
Anatomical reconstruction	Reconstructive procedures	Rectal mucosa and hemorrhoidal cushions	Restoration of anatomical position	PPH/SH
Radical tissue removal	Excisional procedures	Hemorrhoidal tissue and adjacent mucosa	Radical excision	Hemorrhoidectomy (Milligan–Morgan, Ferguson), LigaSure hemorrhoidectomy, Harmonic hemorrhoidectomy

Note. MPFF – micronized purified flavonoid fraction; RBL – rubber band ligation; IS – injection sclerotherapy; IRC – infrared coagulation; HET – hemorrhoid energy therapy; THD – transanal hemorrhoidal dearterialization; HAL-RAR – hemorrhoidal artery ligation with recto-anal repair; HeLP – hemorrhoidal laser procedure; HAE – hemorrhoidal artery embolization; LHP – laser hemorrhoidoplasty; RFA – radiofrequency ablation; BPV – bipolar vaporization; PPH/SH – procedure for prolapse and hemorrhoids/stapled hemorrhoidopexy.

of office procedures, supporting the validity of this classification approach [8, 21, 61].

Methods of arterial inflow modulation

The second group includes interventions aimed at reducing the arterial blood supply to the hemorrhoidal cushions. These include transanal hemorrhoidal dearterialization, Doppler-guided hemorrhoidal artery ligation with mucopexy [22, 33, 52, 59], and the hemorrhoidal laser procedure [9, 17, 57], as well as endovascular embolization of hemorrhoidal arteries [34, 63]. Despite differences in technical modifications and instrumentation, all these methods share a common pathophysiological principle–reduction of arterial inflow to the cavernous vascular tissue, resulting in a gradual decrease in the volume of hemorrhoidal cushions and regression of symptoms.

In clinical practice, these methods are most commonly applied in grades II–III hemorrhoids and are characterized by relatively low postoperative pain and rapid recovery. It is particularly important to emphasize that transanal hemorrhoidal dearterialization (THD) and hemorrhoidal artery ligation with recto-anal repair (HAL-RAR) do not represent distinct pathophysiological categories but rather variants of a shared therapeutic strategy. THD/HAL provides dearterialization as the primary hemodynamic component, while HAL-RAR complements it with mucopexy to address mucosal prolapse.

Although reduction of arterial inflow ultimately also leads to a decrease in hemorrhoidal cushion volume and fibrosis formation, these methods are classified as a separate group in the proposed system because their primary point of application differs. Office-based procedures directly target the mucosal–submucosal layer of the hemorrhoidal cushion, whereas dearterialization techniques modify its arterial blood supply. This difference in anatomical target justifies their distinct positioning within the classification.

Methods of intratissue remodeling of cavernous vascular tissue

A distinct category comprises energy-based intratissue ablation technologies, including laser hemorrhoidoplasty [25, 26, 54], radiofrequency ablation [20, 56], and bipolar vaporization [4]. Unlike office-based procedures or dearterialization techniques, these interventions directly target the internal structure of the hemorrhoidal cushion. The formation of a controlled zone of coagulative injury within the thickness of the cavernous vascular tissue leads to its gradual fibrosis and volume reduction without tissue excision. This characteristic defines the role of energy-based technologies as an organ-preserving approach that combines adequate clinical effectiveness with relatively low invasiveness.

Reconstructive interventions

Reconstructive treatment methods are primarily aimed at correcting mucosal prolapse and restoring the normal anatomical position of the hemorrhoidal cushions. The most well-known representative of this group is the procedure for prolapse and hemorrhoids/stapled hemorrhoidopexy, introduced by Longo [32]. The mechanism of action of this procedure involves circumferential resection of the rectal mucosa and submucosa, followed by cranial fixation of the hemorrhoidal cushions. Despite favorable short-term outcomes in terms of prolapse control and pain reduction [55], the use of this method is limited by the potential for specific complications and a risk of recurrence in the long term [43, 45].

Excisional surgical interventions

Excisional hemorrhoidectomy remains the most radical method for HD treatment. Classical procedures, such as the Milligan–Morgan and Ferguson techniques, achieve the lowest recurrence rates, as they involve complete removal of the pathologically altered cavernous vascular tissue [52, 64]. The use of modern energy-based instruments, including LigaSure and the Harmonic scalpel, has reduced intraoperative blood loss and somewhat decreased postoperative pain; however, it does not fundamentally alter the radical nature of the procedure [26, 36, 37]. In current guidelines, excisional operations are generally considered the treatment of choice for grade III–IV hemorrhoids or in cases of failure of organ-preserving approaches [8, 15, 61].

Thus, the proposed mechanism-oriented classification allows different surgical methods for HD treatment to be interpreted as implementations of several fundamental therapeutic strategies that differ in their point of application within the disease pathogenesis. This approach provides a logical framework for the comparative evaluation of various treatment technologies and supports a more evidence-based selection of surgical strategy depending on the clinical scenario.

The proposed classification reflects not only the mechanisms of therapeutic action of different interventions but also, to some extent, the evolution of surgical treatment for HD. Historically, hemorrhoid therapy has progressed from symptomatic control and local fibrosis induction to methods aimed at modulating the hemodynamics of hemorrhoidal cushions and intratissue remodeling of cavernous vascular tissue. The emergence of energy-based technologies reflects the modern trend toward organ-preserving treatment, whereas excisional hemorrhoidectomy remains a radical option reserved for more advanced forms of the disease.

Discussion

In this study, a mechanism-oriented classification of treatment methods for chronic HD was proposed, integrating the pathophysiological mechanisms of the disease, therapeutic strategies for their correction, and contemporary clinical interventions within a unified conceptual framework. This approach allows diverse technological solutions to be interpreted not as isolated procedures, but as implementations of fundamental therapeutic strategies.

Despite significant progress in HD treatment over recent decades, the need to systematize existing treatment methods remains relevant. Analysis of current clinical guidelines and scientific literature indicates that most authors primarily focus on comparing individual techniques, whereas the issue of their positioning within a unified classification system is addressed only fragmentarily or remains largely overlooked [15, 35].

The most commonly used classification of treatment methods into conservative, minimally invasive, and surgical categories has limited analytical value, as it does not reflect the underlying mechanisms of therapeutic action. Within such frameworks, methods with fundamentally different points of application to the pathological process may be grouped together, thereby complicating the comparative analysis of treatment outcomes.

In a large network meta-analysis by Simillis et al., which included 98 randomized controlled trials and over 7,800 patients, substantial heterogeneity in clinical outcomes across different hemorrhoid treatment methods was demonstrated, partly attributable to the lack of a unified pathogenetic classification system [50]. Similar conclusions have been reported in other studies, highlighting the difficulty of directly comparing the effectiveness of different interventions due to significant methodological and clinical heterogeneity [14, 40, 48, 51].

The findings indicate that, despite the diversity of technical approaches, most contemporary HD treatment methods implement only a limited number of fundamental therapeutic mechanisms. This observation formed the basis for the proposed mechanism-oriented classification, in which interventions are systematized according to their dominant pathophysiological effect and anatomical target.

From a pathogenetic perspective, most interventions can be regarded as implementations of several principal therapeutic strategies: induction of fibrosis of the hemorrhoidal cushions, modulation of arterial inflow, intratissue remodeling of the cavernous vascular tissue, reconstruction of anal canal anatomy, or radical removal of pathological tissue. This approach allows different technological solutions to be integrated

within a unified pathophysiological treatment model.

An important feature of the proposed system is that it accounts not only for the mechanism of therapeutic action but also for the anatomical target of the intervention. In particular, office-based procedures primarily target the mucosal–submucosal layer of the hemorrhoidal cushions, dearterialization techniques act on the arterial branches supplying the cushions, whereas energy-based technologies directly affect the cavernous vascular tissue of the hemorrhoidal nodes. It is this combination of mechanism and anatomical target that makes the classification more robust to the emergence of new technical modifications.

A separate explanation is required regarding the position of sclerotherapy within the classification. Formally, it differs from RBL or coagulation-based methods, as its primary effect is achieved through chemical endothelial injury followed by vascular obliteration. However, the ultimate clinical outcome of this intervention is the formation of fibrosis in the mucosal–submucosal layer and fixation of the hemorrhoidal cushion. For this reason, in the proposed system, sclerotherapy is grouped together with RBL, IRC, and hemorrhoid energy therapy within the category of fibrosis-inducing methods, rather than being classified as an energy-based technology or placed in a separate category.

Particular attention should also be given to the group of methods aimed at reducing arterial inflow to the hemorrhoidal cushions. This category includes THD, HAL-RAR, hemorrhoidal laser procedure, and hemorrhoidal artery embolization. Despite differences in technical execution, all these interventions share a common pathophysiological principle – reduction of arterial blood supply to the cavernous vascular tissue, resulting in a gradual decrease in the volume of hemorrhoidal cushions and regression of symptoms. This approach allows different technological modifications to be interpreted as variants of a single therapeutic mechanism, facilitating their comparison in clinical studies and supporting a more rational development of treatment algorithms.

Particular attention should be given to the identification of intratissue energy-based ablation methods as a distinct category within the classification. Unlike office-based procedures, which are aimed at direct induction of fibrosis of the hemorrhoidal cushions, or dearterialization techniques that modify arterial blood supply, energy-based technologies – such as laser hemorrhoidoplasty, radiofrequency ablation, and bipolar vaporization – operate through a mechanism of intratissue remodeling of the cavernous vascular tissue. This distinctive feature justifies their consideration as an independent pathophysiological group of interventions, occupying an intermediate position between dearterialization techniques and excisional surgery, and reflecting the modern trend toward organ-preserving HD treatment.

The proposed classification also allows for clearer positioning of different treatment methods within the framework of a contemporary stepwise treatment strategy, in which therapy begins with the least invasive methods and progressively advances to more radical interventions in cases of insufficient effectiveness.

In this context, conservative treatment and office-based procedures occupy the initial stages of therapy, dearterialization techniques and energy-based technologies constitute the group of organ-preserving surgical interventions, while excisional hemorrhoidectomy remains the radical treatment option for advanced forms of the disease or in cases of failure of less invasive approaches.

An important factor influencing the choice of treatment method is also the economic accessibility of technologies. A substantial proportion of modern minimally invasive procedures require specialized equipment and disposable materials, limiting their applicability in healthcare systems with constrained resources [7, 27].

In this regard, the proposed classification distinguishes the principle of therapeutic action from the specific technical implementation of each method. This provides a basis for using alternative technological solutions that achieve the same therapeutic mechanism but may differ in cost and availability.

The proposed mechanism-oriented classification allows for a formalized description of individual treatment methods by combining three key characteristics: therapeutic strategy (S – therapeutic strategy), anatomical target of intervention (T – target of intervention), and mechanism of action (M – mechanism of action). Each of these parameters may be assigned a specific index reflecting a particular variant of the strategy, target, or mechanism. In a simplified form, this approach can be represented as a conceptual formula:

$$\text{Method} = S_i + T_j + M_k,$$

where S_i denotes a specific therapeutic strategy, T_j the anatomical target of the intervention, and M_k the mechanism of therapeutic action. The combination of these parameters reflects the pathophysiological essence of a given intervention.

For example, rubber band ligation can be described as a method that implements the fibrosis-induction strategy (S), targets the mucosal–submucosal tissue of the hemorrhoidal cushion (T), and operates through mechanical induction of ischemic necrosis followed by fibrosis (M). In contrast, dearterialization techniques (THD or HAL-RAR) differ in their parameter combinations. These methods

primarily target the arterial branches of the superior rectal artery, aiming to reduce arterial inflow to the hemorrhoidal cushions.

Such a formalized approach does not constitute an independent clinical classification; however, it may be considered a conceptual tool for the standardized description of treatment methods within the proposed system and may potentially facilitate the integration of new technologies in the future.

The proposed mechanism-oriented classification has certain limitations. First, it is conceptual in nature and is based on the synthesis of literature data regarding the mechanisms of action of various interventions. It is not intended as a clinical decision-making algorithm and does not define specific indications for individual procedures. In addition, some contemporary technologies may simultaneously engage multiple therapeutic mechanisms, complicating their unambiguous assignment to a single category. Further clinical studies are required to evaluate the practical value of the proposed classification system for the comparative analysis of the effectiveness of different treatment methods for HD.

The proposed mechanism-oriented classification not only systematizes contemporary approaches to HD treatment but also, to some extent, reflects the evolution of surgical methods – from the induction of fibrosis of hemorrhoidal cushions to technologies aimed at modulating hemodynamics and achieving intratissue remodeling of the cavernous vascular tissue. Future research should focus on standardizing the technical parameters of organ-preserving methods and on comparative evaluation of their clinical effectiveness, with long-term treatment outcomes taken into account.

Declaration of interests

The authors declare that they have no conflict of interest.

Funding. This research received no external funding.

Ethics approval and written informed consent statements

This study is based on the analysis and conceptual synthesis of previously published data. No human participants, animals, or patient data were involved; therefore, ethical approval and informed consent were not required.

Authors contributions

L. Y. Markulan conceived the study, developed the conceptual framework and classification, performed literature analysis, prepared the figures and tables, and wrote the first draft of the manuscript; L. S. Bilianskyi contributed to the methodological design and interpretation of the classification system and critically revised the manuscript; V. I. Voloshyn contributed to the literature review, discussion development, and final manuscript editing.

References

1. Aigner F, Conrad F, Eder J, et al. The vascular nature of hemorrhoids. Gastrointest Surg. 2006;10(7):1044-50 https://doi.org/10.1016/j.gassur.2005.12.004.
2. Ashburn JH. Hemorrhoidal Disease: A Review. JAMA. 2025 Aug 18. doi: 10.1001/jama.2025.13083.
3. Barron JL. Office ligation treatment of hemorrhoids. Am J Surg. 1963;105(4):563-570. doi: 10.1007/BF02633461.
4. Bilianskyi LS, Voloshyn I. V Bipolar vaporization of hemorrhoidal nodes in stage III chronic hemorrhoids: a single-centre comparative study involving laser hemorrhoidoplasty, transanal dearterialization, and Longo surgery General Surgery. 2025;(3):20-28. doi: https://doi.org/10.30978/GS-2025-3-20.
5. Brown SR. Haemorrhoids: an update on management. Ther Adv Chronic Dis. 2017 Oct;8(10):141-147. doi: 10.1177/2040622317713957. Epub 2017 Jun 21. PMID: 28989595; PMCID: PMC5624348..
6. Brown S, Tiernan J, Biggs K, et al.: The HubBLe Trial : haemorrhoidal artery ligation (HAL) versus rubber band ligation (RBL) for symptomatic second- and third-degree haemorrhoids : a multicentre randomised controlled trial and health-economic evaluation. Health Technol. Assess., 2016 Nov;20(88):1-150. doi: 10.3310/hta20880.
7. Burch J, Epstein D, Baba-Akbari A, Weatherly H, Fox D, Golder S, Jayne D, Drummond M, Woolacott N. Stapled haemorrhoidectomy (haemorrhoidopexy) for the treatment of haemorrhoids: a systematic review and economic evaluation. Health Technol Assess. 2008 Apr;12(8):iii-iv, ix-x, 1-193. doi: 10.3310/hta12080.
8. Davis BR, Lee-Kong SA, Migaly J, Feingold DL, Steele SR. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Hemorrhoids. Dis Colon Rectum. 2018 Mar;61(3):284-292. doi: 10.1097/DCR.0000000000001030.
9. De Nardi P, Maggi G, Pagnanelli M, Vlasakov I, Corbetta D. Hemorrhoid laser dearterialization: systematic review and meta-analysis. Lasers Med Sci. 2023 Jan 25;38(1):54. doi: 10.1007/s10103-022-03703-z.
10. De Schepper H, Coremans G, Denis MA, et al. Belgian consensus guideline on the management of hemorrhoidal disease. Acta Gastroenterol Belg. 2021 Jan-Mar;84(1):101-120. doi: 10.51821/84.1.497.
11. Emile SH, Elfeki H, Sakr A, Shalaby M. Transanal hemorrhoidal dearterialization (THD) versus stapled hemorrhoidopexy (SH) in treatment of internal hemorrhoids: a systematic review and meta-analysis of randomized clinical trials. Int J Colorectal Dis. 2019 Jan;34(1):1-11. doi: 10.1007/s00384-018-3187-3.
12. Esmaeilnia Shirvani A, Pakdaman K, et al. Worldwide prevalence of haemorrhoids: a systematic review and meta-analysis. Ann Med. 2026 Dec;58(1):2606433. doi: 10.1080/07853890.2025.2606433.
13. Fernandes V, Fonseca J. Polidocanol foam injected at high doses: a perfect treatment. GE Port J Gastroenterol. 2019;26:169-175. doi: 10.1159/000492202.
14. Gaj F, Trecca A, Carboni M. Verso una nuova classificazione della malattia emorroidaria [Towards a new classification of hemorrhoidal disease]. Chir Ital. 1999 May-Jun;51(3):227-34. Italian. PMID: 10793769.
15. Gallo G, Martellucci J, Sturiale A, et al. Consensus statement of the Italian society of colorectal surgery (SICCR): management and treatment of hemorrhoidal disease. Tech Coloproctol 2020;24:145-64. 10.1007/s10151-020-02149-1.
16. Gallo G, Picciariello A, Armellin C, et al. Sclerotherapy for hemorrhoidal disease: systematic review and meta-analysis. Tech Coloproctol. 2024 Jan 23;28(1):28. doi: 10.1007/s10151-023-02908-w.
17. Giamundo P, Braini A, Calabrò G, et al. Doppler-guided hemorrhoidal dearterialization with laser (HeLP): indications and clinical outcome in the long-term. Results of a multicenter trial. Surg Endosc. 2022 Jan;36(1):143-148. doi: 10.1007/s00464-020-08248-2.
18. Goligher JC. London: Ballierè Tindal; 1980. Surgery of the Anus, Rectum and Colon. 4th Edition.
19. Guo C, Che X, Lin Z, Cai S, Liu G, Pan L, Lv J, Li L, Man S, Wang B, Yu C. Beijing Da Xue Xue Bao Yi Xue Ban. Epidemiological characteristics of hemorrhoids in a healthy physical examination population in China. 2024 Oct 18;56(5):815-819. doi: 10.19723/j.issn.1671-167X.2024.05.010.
20. Hassan S, McGrath D, Barnes R, Middleton S. Radiofrequency ablation (Rafaelo Procedure) for the treatment of hemorrhoids: a case series in the United Kingdom. Ann Coloproctol. 2023 Apr;39(2):164-167. doi: 10.3393/ac.2021.00276.0039.

21. Hawkins AT, Davis BR, Bhama AR, Fang SH, Dawes AJ, Feingold DL, Lightner AL, Paquette IM; Clinical Practice Guidelines Committee of the American Society of Colon and Rectal Surgeons. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Hemorrhoids. Dis Colon Rectum. 2024 May 1;67(5):614-623. doi: 10.1097/DCR.0000000000003276.
22. Hoyuela C, Carvajal F, Juvany M, Troyano D, Trias M, Martrat A, Ardid J, Obiols J. HAL-RAR (Doppler guided haemorrhoid artery ligation with recto-anal repair) is a safe and effective procedure for haemorrhoids. Results of a prospective study after two-years follow-up. Int J Surg. 2016 Apr;28:39-44. doi: 10.1016/j.ijsu.2016.02.030.
23. Hu B, Zou Q, Lu L, Ren D. Chinese clinical practice guidelines of hemorrhoids (2020) and comparison with European and American guidelines. Chinese Journal of Colorectal Diseases (Electronic Edition), 2021, Vol. 10, Issue (06): 561-571. doi: 10.3877/cma.j.issn.2095-3224.2021.06.001.
24. Iyer VS, Shrier I, Gordon PH. Long-term outcome of rubber band ligation for symptomatic primary and recurrent internal hemorrhoids. Dis. Colon Rectum, 2004, 47(8) : 1364-1370. doi: 10.1007/s10350-004-0591-2.
25. Kavraal Ş, Avcıoğlu BÜ, Hoşafcı MC, Akkuyu FZ, İnci G, Ortaç B, Seymen AA. Hemorrhoidal laser ablation procedure: a minimally invasive treatment for grades II, III, and IV using a 1470 nm diode laser. Pol Przegl Chir. 2024 Jan 2;96(3):1-6. doi: 10.5604/01.3001.0054.4819.
26. Khadr MA, El Shazly WG, Zakria MM, Moaz AM Laser hemorrhoidoplasty versus LigaSure™ hemorrhoidectomy versus diathermy hemorrhoidectomy in treatment of grade III and IV hemorrhoids: a non-randomized prospective trial. Surg Open Digestive Adv 2024. 13:100129. https://www.researchgate.net/publication/378461514_Laser_hemorrhoidoplasty_versus_LigaSure_TM_hemorrhoidectomy_versus_diathermy_hemorrhoidectomy_in_treatment_of_grade_III_and_IV_Hemorrhoids_A_non-randomized_prospective_trial-NC-_ND_license_httpcreativ.
27. Lehur PA, Didnée AS, Faucheron JL, et al.; LigaLongo Study Group. Cost-effectiveness of New Surgical Treatments for Hemorrhoidal Disease: A Multicentre Randomized Controlled Trial Comparing Transanal Doppler-guided Hemorrhoidal Artery Ligation With Mucopexy and Circular Stapled Hemorrhoidopexy. Ann Surg. 2016 Nov;264(5):710-716. doi: 10.1097/SLA.0000000000001770.
28. Leicester RJ, Nicholls RJ, Mann CV. Infrared coagulation: a new treatment for hemorrhoids. Dis Colon Rectum. 1981;24(8):602-605. doi: 10.1007/BF02605755.
29. Lie H, Caesarini EF, Purnama AA, Irawan A, Sudirman T, Jeo WS, Budiono BP, Prabowo E, Rivai MI, Sitepu RK. Laser hemorrhoidoplasty for hemorrhoidal disease: a systematic review and meta-analysis. Lasers Med Sci. 2022 Dec;37(9):3621-3630. doi: 10.1007/s10103-022-03643-8.
30. Liew AN, Wang J, Chen MZ, Tay YK, Kong JCH. Haemorrhoid artery ligation – recto anal repair (HAL-RAR) blind versus Doppler: a systematic review and meta-analysis. ANZ J Surg. 2024 Nov;94(11):2053-2061. doi: 10.1111/ans.19258.
31. Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. World J Gastroenterol. 2012 May 7;18(17):2009-17. doi: 10.3748/wjg.v18.i17.2009.
32. Longo A. Treatment of haemorrhoidal disease by reduction of mucosa and haemorrhoidal prolapse with a circular suturing device: a new procedure. In: Proceedings of the 6th World Congress of Endoscopic Surgery. Bologna: Monduzzi Editore; 1998. p. 777-784.
33. Morinaga K, Hasuda K, Ikeda T. A novel therapy for internal hemorrhoids: ligation of the hemorrhoidal artery with a newly devised instrument in conjunction with a Doppler flowmeter. Am J Gastroenterol. 1995;90(4):610-613. PMID: 7717320.
34. Moussa N, Sielezneff I, Sapoval M, Tradi F, Del Giudice C, Fathallah N, Pellerin O, Amouyal G, Pereira H, de Parades V, Vidal V. Embolization of the superior rectal arteries for chronic bleeding due to haemorrhoidal disease. Colorectal Dis. 2017 Feb;19(2):194-199. doi: 10.1111/codi.13430. PMID: 27338153.
35. Muldoon R. Review of American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Hemorrhoids. JAMA Surg. 2020 Aug 1;155(8):773-774. doi: 10.1001/jamasurg.2020.0788.
36 Mushaya CD, Caleo PJ, Bartlett L, Buettner PG, Ho YH. Harmonic Scalpel compared with conventional excisional haemorrhoidectomy: a meta-analysis of randomized controlled trials. Tecn Coloproctol. 2014 Nov;18(11):1009-1016. doi: 10.1007/s10151-014-1169-1.
37. Mustapha B, Alatise OI, Olasehinde O, et al. LigaSure versus conventional Milligan MORGAN hemorrhoidectomy in Nigerian patients with symptomatic hemorrhoids.World J Surg. 2025 Feb;49(2):334-342. doi: 10.1002/wjs.12416. Epub 2024 Nov 22.
38. Naderan M, Shoar S, Nazari M, Elsayed A, Mahmoodzadeh H, Khorgami Z. A Randomized Controlled Trial Comparing Laser Intra-Hemorrhoidal Coagulation and Milligan-Morgan Hemorrhoidectomy. J Invest Surg. 2017 Oct;30(5):325-331. doi: 10.1080/08941939.2016.1248304.
39. Naldini G, Sturiale A. Stapled hemorrhoidopexy and THD/HAL-RAR: false myths of the third millennium. Tech Coloproctol. 2020 Sep;24(9):985-986. doi: 10.1007/s10151-020-02267-w. Epub 2020 Jun 29. PMID: 32601751.
40. Ng KS, Holzgang M, Young C. Still a Case of «No Pain, No Gain»? An Updated and Critical Review of the Pathogenesis, Diagnosis, and Management Options for Hemorrhoids in 2020. Ann Coloproctol. 2020 Jun;36(3):133-147. doi: 10.3393/ac.2020.05.04.
41. Patel J, McKechnie T, Wu K, Sharma S, Lee Y, Doumouras A, Hong D, Eskicioglu C. HEmoRhoidal disease management with Band ligation versus polidocanol Sclerotherapy: a systematic review and meta-analysis (the HerBS Review). Int J Colorectal Dis. 2023 May 3;38(1):112. doi: 10.1007/s00384-023-04394-w.
42. Poen AC, Felt-Bersma RJ, Cuesta MA, Devillé W, Meuwissen SG. A randomized controlled trial of rubber band ligation versus infrared coagulation in the treatment of internal hemorrhoids. Eur J Gastroenterol Hepatol. 2000;12(5):535-539. doi: 10.1097/00042737-200012050-00010.
43. Porrett LJ, Porrett JK, Ho YH. Documented complications of staple hemorrhoidopexy: a systematic review. Int Surg. 2015 Jan;100(1):44-57. doi: 10.9738/INTSURG-D-13-00173.1.
44. Ratto C, Parello A, Litta F, Donisi L, Doglietto GB. Epidemiology, Anorectal Anatomy, Physiology and Pathophysiology of Hemorrhoids. In: Ratto C, Parello A (eds). Hemorrhoids: Modern Diagnosis and Treatment. Springer, Cham; 2022. p. 9-24. doi: 10.1007/978-3-031-08392-1_2.
45. Ravo B, Amato A, Bianco V, Boccasanta P, Bottini C, Carriero A, et al. Complications after stapled hemorrhoidectomy: can they be overcome? Tech Coloproctol. 2002;6(2):67-72. doi: 10.1007/s101510200018.
46. Riss S, Weiser FA, Riss T, Schwameis K, Mittlböck M, Stift A. Haemorrhoids and quality of life. Colorectal Dis. 2011 Apr;13(4):e48-52. doi: 10.1111/j.1463-1318.2010.02480.x.
47. Rørvik HD, Styr K, Ilum L, McKinstry GL, Dragesund T, Campos AH, Brandstrup B, Olaison G. Hemorrhoidal Disease Symptom Score and Short Health ScaleHD: New Tools to Evaluate Symptoms and Health-Related Quality of Life in Hemorrhoidal Disease. Dis Colon Rectum. 2019 Mar;62(3):333-342. doi: 10.1097/DCR.0000000000001234.
48. Rubbini M, Ascanelli S. Classification and guidelines of hemorrhoidal disease: Present and future. World J Gastrointest Surg. 2019 Mar 27;11(3):117-121. doi: 10.4240/wjgs.v11.i3.117.
49. Salgueiro P, Ramos MI, Castro-Poças F, Libânio D. Office Based Procedures in the Management of Hemorrhoidal Disease: Rubber Band Ligation versus Sclerotherapy – Systematic Review and Meta-Analysis. GE Port J Gastroenterol. 2022 Mar 8;29(6):409-419. doi: 10.1159/000522171.
50. Simillis C, Thoukididou SN, Slesser AA, Rasheed S, Tan E, Tekkis PP. Systematic review and network meta-analysis comparing clinical outcomes and effectiveness of surgical treatments for haemorrhoids. Br J Surg. 2015 Dec;102(13):1603-18. doi: 10.1002/bjs.9913. Epub 2015 Sep 30. PMID: 26420725.
51. Sobrado CW, Obregon CA, Eltweri AM, Sobrado LF, Nahas SC, Cecconello I. A New Classification for Hemorrhoidal Disease: The Creation of the «BPRST» Staging and Its Application in Clinical Practice. Ann Coloproctol. 2020 Jun;36(3):164-173. doi: 10.3393/ac.2020.02.06.
52. Symeonidis D, Spyridakis M, Zacharoulis D, Tzovaras G, Samara AA, Valaroutsos A, Diamantis A, Tepetes K. Milligan-Morgan hemorrhoidectomy vs. hemorrhoid artery ligation and recto-anal repair: a comparative study. BMC Surg. 2022 Dec 6;22(1):416. doi: 10.1186/s12893-022-01861-z. PMID: 36474223; PMCID: PMC9724411.
53. Tantinam T, Sutharat P, Sanmee S, Supatrakul E, Bhatanaprabhabhan K, Ngamsirimas B, Santrakul N, Thiengthiantham R, Chandrachamnong P. Propensity score-matched comparative study of radiofrequency ablation (with the Rafaelo device) versus hemorrhoidectomy for the treatment of grades II-III internal hemorrhoids. Ann Coloproctol. 2025 Oct;41(5):409-416. doi: 10.3393/ac.2025.00458.0065.

54. The LHP Recommendation Development Group. Best clinical practice recommendations for the management of symptomatic hemorrhoids via laser hemorrhoidoplasty (The LHP Recommendations 2024). Tech Coloproctol. 2025;29(2):1-14. doi: 10.1007/s10151-024-03022-1.
55. Tjandra JJ, Chan MKY. Systematic review on the procedure for prolapse and hemorrhoids (stapled hemorrhoidopexy). Dis Colon Rectum 2007;50:878-92. 10.1007/s10350-006-0852-3.
56. Tolksdorf S, Tübergen D, Vivaldi C, et al. Early and midterm results of radiofrequency ablation (Rafaelo® procedure) for third-degree haemorrhoids: a prospective, two-centre study. Tech Coloproctol. 2022;26(6):479-487. doi: 10.1007/s10151-022-02608-x.
57. Trigui A, Rejab H, Akrout A, Trabelsi J, Zouari A, Majdoub Y, Amar MB, Mzali R. Laser utility in the treatment of hemorrhoidal pathology: a review of literature. Lasers Med Sci. 2022 Mar;37(2):693-699. doi: 10.1007/s10103-021-03333-x.
58. Trompetto M, Clerico G, Cocorullo GF, Giordano P, Marino F, Martellucci J, Milito G, Mistrangelo M, Ratto C. Evaluation and management of hemorrhoids: Italian society of colorectal surgery (SICCR) consensus statement. Tech Coloproctol. 2015 Oct;19(10):567-75. doi: 10.1007/s10151-015-1371-9. Epub 2015 Sep 24. Erratum in: Tech Coloproctol. 2016 Mar;20(3):201. doi: 10.1007/s10151-015-1416-0. PMID: 26403234.
59. Tutino R, Picciariello A, Santarelli M, De Simone V, Lobascio P, Cocorullo G, Massani M, Graziano G, Santoro GA, Gallo G. Haemorrhoidal artery ligation: Is Doppler guidance useful? A systematic review and meta-analysis of randomized controlled trials. Colorectal Dis. 2025 Jul;27(7):e70163. doi: 10.1111/codi.70163.
60. van Oostendorp JY, Grossi U, Hoxhaj I, Kimman ML, Kuiper SZ, Breukink SO, Han-Geurts IJM, Gallo G. Limitations of the Goligher classification in randomized trials for hemorrhoidal disease: a qualitative systematic review of selection criteria. Tech Coloproctol. 2025 Jun 10;29(1):133. doi: 10.1007/s10151-025-03170-y.
61. Van Tol RR, Kimman ML, Melenhorst J, Stassen LPS, Dirksen CD, Breukink SO; Members of the Steering Group. European Society of Coloproctology Core Outcome Set for haemorrhoidal disease: an international Delphi study among healthcare professionals. Colorectal Dis. 2019 May;21(5):570-580. doi: 10.1111/codi.14553. Epub 2019 Feb 8. PMID: 30628177.
62. Verre L, Gallo G, Grassi G, Bussolin E, Carbone L, Poto GE, Carpineto Samorani O, Marano L, Marrelli D, Roviello F. Transanal hemorrhoidal dearterialization (THD) for hemorrhoidal disease: An Italian single-institution 5-year experience analysis and updated literature review. Front Surg. 2022 Dec 21;9:1088546. doi: 10.3389/fsurg.2022.1088546.
63. Vidal V, Sapoval M, Sielezneff Y, De Parades V, Tradi F, Louis G, Bartoli JM, Pellerin O. Emborrhoid: a new concept for the treatment of hemorrhoids with arterial embolization: the first 14 cases. Cardiovasc Intervent Radiol. 2015 Feb;38(1):72-8. doi: 10.1007/s00270-014-1017-8. Epub 2014 Nov 4. PMID: 25366092.
64. Wee IJY, Koo CH, Seow-En I, Ng YYR, Lin W, Tan EJK. Laser hemorrhoidoplasty versus conventional hemorrhoidectomy for grade II/III hemorrhoids: a systematic review and meta-analysis. Ann Coloproctol. 2023 Feb;39(1):3-10. doi: 10.3393/ac.2022.00598.0085.
65. Yamana T. Japanese Practice Guidelines for Anal Disorders I. Hemorrhoids. J Anus Rectum Colon. 2018 May 25;1(3):89-99. doi: 10.23922/jarc.2017-018.

Механізм-орієнтована трирівнева класифікація методів лікування хронічної гемороїдальної хвороби. Огляд

Л. Ю. Маркулан, Л. С. Білянський, І. В. Волошин

Національний медичний університет імені О.О. Богомольця, Київ

Мета — розробити механізм-орієнтовану класифікацію сучасних методів лікування гемороїдальної хвороби на підставі їхнього впливу на ключові патофізіологічні механізми захворювання.

Проведено аналіз сучасних літературних джерел, присвячених патогенезу гемороїдальної хвороби й методам її лікування. Узагальнено патофізіологічні механізми розвитку захворювання, основні терапевтичні стратегії їхньої корекції та клінічні технології втручань. На основі концептуального аналізу сформовано модель взаємозв'язку між патогенетичними механізмами, терапевтичними стратегіями та клінічними методами лікування, що стала підґрунтям для розробки класифікаційної системи. Запропоновано механізм-орієнтовану класифікацію методів лікування гемороїдальної хвороби, яка інтегрує патофізіологічні механізми захворювання, терапевтичні стратегії їхньої корекції та клінічні технології втручань у межах єдиної концептуальної моделі. Виділено основні терапевтичні стратегії лікування: контроль симптомів, індукція фіброзу гемороїдальних подушок, редукція артеріального притоку, внутрішньотканинне ремоделювання, реконструкція анатомії анального каналу та радикальне видалення патологічно змінених тканин. У межах кожної з цих стратегій систематизовано відповідні клінічні методи лікування, що дає змогу розглядати сучасні технології як варіанти реалізації обмеженої кількості базових терапевтичних механізмів.

Висновки. Запропонована класифікація дає змогу систематизувати сучасні методи лікування гемороїдальної хвороби відповідно до їхнього патофізіологічного механізму дії та інтегрувати їх у межах єдиної концептуальної моделі. Такий підхід створює методологічну основу для послідовнішої інтерпретації сучасних технологій лікування й може бути використаний для порівняльних клінічних досліджень.

Ключові слова: гемороїдальна хвороба, геморой, механізм-орієнтована класифікація, лікувальні стратегії, малоінвазивні процедури, гемороїдектомія.

FOR CITATION

Markulan LY, Bilianskyi LS, Voloshyn VI. Mechanism-oriented three-level classification of treatment methods for chronic hemorrhoidal disease. Review. General Surgery (Ukraine). 2026;(1):64-72. http://doi.org/10.30978/GS-2026-1-64.

General Surgery has specific **instructions and guidelines for submitting manuscripts.** The instructions and guidelines comply with the requirements of the Ministry of Education and Science of Ukraine for publications presenting the results of dissertations for obtaining Doctor of Sciences, Candidate of Sciences or Doctor of Philosophy degree and published in the scientific professional editions of Ukraine (orders of the Ministry of Education and Science of Ukraine No32 of January 15, 2018, No1437 of November 18, 2020), as well as with the requirements of the International Committee of Medical Journal Editors for manuscripts submitted to the biomedical editions. The Editorial Board will not consider submissions that do not adhere to the Author Guidelines.

General Surgery accepts manuscript submissions through the journal website or via email **office.generalsurgery@gmail.com.**

MANUSCRIPT COMPONENTS

To submit a manuscript, authors must check off their submission's compliance with all of the following items.

Title page

- Index of the Universal Decimal Classification (UDC).
- Full name of each author followed by each author's highest academic degree(s). Name of institution(s) with which each author is affiliated (if the work should be attributed to different institutions, it is necessary to personify each author with numbers 1, 2, 3), address and ORCID ID.
- Full name, academic degree and academic title, phone number, and e-mail of the author responsible for correspondence concerning the manuscript.

Note. The Ukrainian authors must provide the above-mentioned data both in Ukrainian and English. Please note that names and last names are not corrected by the editorial staff and, therefore, are published exactly as they appear in the manuscript.

- For the collective paper, the signatures of all authors are required.
- The paper must be submitted with the official assignment from the institution where the research was carried out.
- A copy of the form of article licensing terms must be completed and submitted with the manuscript.
- All submitted manuscripts must be written in English.

Formatting

The length of the manuscript, including references, tables, illustrations and figures is up to 15 pages for an empirical paper and up to 20 pages for a review paper.

Tables, illustrations, figures, diagrams and formulas should be included in the text and cited consecutively in the manuscript.

Tables should be designed using the Microsoft Word format. Each table must have a title and a number. Number them in the order in which they are discussed.

Other illustrations (photographs, figures, graphs, diagrams etc.) must be marked as «Fig.». Number them in the order in which they are discussed.

Photographs, echograms must be submitted in the original or digital format. The digital artwork must be saved at a resolution of 300 dpi as JPG or TIFF files and additionally submitted as a separate file. Each figure should have a concise caption describing accurately what it depicts. If photographs of patients are used, they must be accompanied by written permission to use the photograph, or the subjects must not be identifiable.

Abstract. The abstract should not be less than 1800 characters, including spaces. The structure of the abstract must follow the structure of the article. The abstract for original research manuscript should contain the same sections as the article. *The Ukrainian authors must provide the abstract both in Ukrainian and English. Two abstracts should be identical.*

Keywords. 3—7 keywords or phrases that capture the most important aspects of the paper. The keywords must be relevant to a subject of research and included into the Medical Subject Headings 2021 (MeSH) thesaurus, which is available online at https://meshb.nlm.nih.gov/search; https://www.ncbi.nlm.nih.gov/mesh.

Article structure for original research section. The article should contain the next sections: Introduction (summarize the relevance of the study or rationale for it, providing the scientific context for the research. Do not review the subject exhaustively); Objective; Materials and methods; Results and discussion; Conclusions. Other types of manuscripts (clinical observations, lectures, reviews, etc.) could be drafted in another way.

The requirements for other types of manuscripts (review papers, case reports, meta-analysis, lectures, history of surgical science, and etc.) can be found at: https://www.care-statement.org/ for clinical case reports; http://www.consort-statement.org/ for CONSORT's randomized research and execution standards; https://www.equator-network.org/ for all types of medical research in all fields of medicine.

Acknowledgements (not obligatory). Acknowledge those who contributed to the manuscript providing technical help or writing assistance, or who provided general support.

Author contributions. Participation of each author in the manuscript writing (concept and design of the study; material collection, material processing, statistical data processing, writing text, and etc.)

Declaration of interests. Declare the presence or absence of a financial/personal interest or belief, consultant, institutional and other relationships that might affect the objectivity of the research.

Funding. All sources of funding must be acknowledged in the manuscript.

References. References must be numbered in alphabetical order with the literature sources in the Ukrainian language (Cyrillic letters) followed by the literature sources in the English language (Latin letters). Use the AMA style: https://www.enago.com/academy/unique-characteristics-of-the-ama-style-guide/. Specify a unique numeric identifier for the DOI article. Check the availability of the DOI identifier at http://search.crossref.org or http://www.citethisforme.com. For information on DOI, you need to enter the English title in the search box.

Ethical policies

In studies, involving human subjects, the authors must indicate if the experiments were conducted in accordance with the ethical standards of the Helsinki Declaration of 1964 that were revised by the 59th General Assembly of the Military Medical Academy, Seoul, October, 2008. Confirmation should be provided that the patient's informed consent has been obtained. The authors should note that the procedures were duly approved by the local ethics committee. The protocol details, issued by the local ethics committee, must be provided.

The experiments with animal subjects must comply with the principles of the European Convention for the Protection of Vertebrate Animals Used for Research and Other Scientific Purposes (Strasbourg, 1986) and the Law of Ukraine «On the Protection of Animals from Cruelty». It is necessary to indicate the type and number of experimental animals, methods of anaesthesia and euthanasia.

Editorial Policies

The Editorial Board will consider the papers meeting the high standards of the journal and significantly contributing to the advancement of surgical science.

All forms of plagiarism and data fabrication are unethical and unacceptable.

The Editorial Board will not consider manuscripts that were previously published in other journals.

For all articles, the scientific originality of a paper is measured by means of software developed for determining the level of originality.

The editors reserve the right to change the style of the article formatting. The article may be returned to the authors with the request to revise or to answer queries.

The proof-sheet will not be sent to the authors. Pre-publishing preparation of the author's manuscript is completed by the editors.

In compliance with the Laws of Ukraine «On Media» and «On Advertising», advertising materials are designated and distinguished from other content by the term «advertisement». The content of advertising materials is the responsibility of the advertiser.

The journal's editorial board comprehensively supports the principle of transparency in integrating **artificial intelligence (AI)** in scientific research and the compliance of manuscripts accepted for publication with modern legal and ethical standards.

Authors of manuscripts created by AI systems are required to:

- identify (mark/label) artificially generated content. For example, use the caption «The material (article, manuscript) was generated using artificial intelligence»;
- verify the authenticity of AI-generated content;
- comply with the requirements for protecting intellectual property rights and non-property rights of third parties;
- comply with the current legislation of Ukraine on the protection of personal data and human rights;
- refrain from using AI systems created by the aggressor state.

The researchers submitting their manuscripts bear responsibility for the consequences of using AI in the scientific, legal, and ethical domains.

For additional information on the journal's editorial policy, publication and article retraction terms, please see the «About the Journal» section at http://generalsurgery.com.ua/.

Subscriptions to the periodical *General Surgery* can be made at the editorial office.

The amount of advertising is about 5% of the total volume of the periodical.

Contact phone: +38096-70-21-152
E-mail: vitapol3@gmail.com

License Terms

Manuscript Title _____

_____

Authors' Full Names _____

_____

_____

_____

_____

We, the authors, hereby confirm that the manuscript has been read and approved by all named authors. By signing this agreement, we certify that our manuscript is original, has never been published before, and is not currently being considered for publication elsewhere. The corresponding author _____ is the sole contact for the editorial process and is responsible for communicating with the other authors about progress, submissions of revisions, and final approval of proofs.

We confirm that all named authors satisfy the criteria for authorship and declare that the results are verifiable, reliable, and accurately interpreted. By signing this agreement, the authors agree to submit the manuscript for publication in the General Surgery journal.

We further confirm that the spelling of the names and the order of the authors listed in the manuscript have been approved by all of us.

All authors agree to the Editor-in-Chief's decision to accept or reject the submitted manuscript and understand that if any ethical standards established by the General Surgery journal are violated, the retraction of the manuscript is undisputable and final.

We, the authors of the manuscript (the «Licensors»), certify that we have exclusive rights to the manuscript and grant «VIT-A-POL» LLC (the «Licensee»), the publisher of the General Surgery journal, a free non-exclusive license for its publication and use, including:

- initial publication of the submitted manuscript in General Surgery under the terms of the CC BY-ND 4.0 license;
- revision of the manuscript in accordance with the editorial requirements;
- checking the submitted manuscript for plagiarism;
- the use of metadata of the article through processing and systematization, making it public;
- distribution of electronic copies of the article by placing it on the journal's website and on specialized medical information websites;
- participation in scientometric databases and search engines;
- translation of the article into other languages;
- distribution of the article in an unlimited number of copies in any format for commercial and non-commercial purposes via various electronic and digital means;
- transfer, storage, and processing of personal data without a time limit in accordance with the Law of Ukraine «On the Protection of Personal Data».

These License Terms are valid for an unlimited period and have the legal force of a public offer agreement.

In all matters not provided for by these License Terms, the Licensee and the Licensors shall be governed by the provisions of the applicable legislation of Ukraine.

Authors (Licensors):

_____ _____

_____ _____

_____ _____

(surnames and signatures)

Publisher (Licensee):

_____ Date _____