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FACTORS AFFECTING THE RESULTS OF TREATMENT FOR CHRONIC ANAL FISSURES

L. Hrytsak, M. Aksan, L. Bilyansky

Bogomolets National Medical University
(Kyiv, Ukraine)

Summary.

Chronic anal fissure is a common proctological condition characterized by severe pain and a substantial reduction in quality of life. Despite the availability of various treatment modalities, rates of incomplete healing and recurrence remain high, underscoring the multifactorial nature of the disease and the necessity to identify determinants of treatment effectiveness.

Objective. *To identify factors associated with complete healing of chronic anal fissures at week 4 of treatment. The study was conducted in accordance with ethical standards and principles governing medical research involving human subjects. The work was performed under the departmental research project «Development and improvement of methods for diagnosis, surgical treatment, and rehabilitation of patients with pathologies of the digestive tract and perineum,» implementation period 2024-2026, state registration number 0123U1051738.*

Materials and methods. *This prospective single-center study analyzed 155 patients with chronic anal fissures treated between 2022 and 2024. Univariate and multivariate analyses, including odds ratio regression, were performed to identify factors influencing complete defect healing at week 4. Patients were stratified into two subgroups according to treatment strategy: personalized management algorithm (n = 83) and standardized therapy (n = 72). The study was conducted in accordance with the principles of the Helsinki Declaration. All patients provided informed consent to participate in the study. The study protocol was approved by the Bioethics Committee of the Bogomolets National Medical University (protocol No. 2 dated October 17, 2022). Statistical processing was performed using IBM SPSS Statistics Base v.22, R-Statistics v.3.2.0, and Medstat software. Standard methods of variational statistics were applied. The work was performed as part of the departmental research project entitled «Development and improvement of methods for diagnosis, surgical treatment, and rehabilitation of patients with pathologies of the digestive tract and perineum», implementation period 2024-2026, state registration number 0123U1051738.*

Results. *Complete healing was achieved in 128 (82.6%) patients. The personalized target-to-treat algorithm significantly increased the likelihood of healing compared with standardized therapy (92.1% vs 71.8%; $p < 0.001$). In multivariate analysis, independent predictors of complete healing were treatment type (OR = 4.31; 95% CI 1.63-11.41; $p = 0.003$) and disease duration (OR = 0.73; 95% CI 0.61-0.87; $p = 0.001$). Age, gender, fissure location, pain intensity, and presence of concomitant pathology had no independent effect on treatment outcome. The predictive performance of the model was excellent (AUC = 0.97).*

Conclusions. *The principal factors influencing complete healing of chronic anal fissures at week 4 of treatment are the treatment strategy and disease duration. Implementation of a personalized target-to-treat algorithm reliably improves treatment efficacy and can be recommended for clinical practice.*

Keywords: *Minimally Invasive Surgery; Combined Pathology; Anal Fissure; Healing; Prognostic Factors; Personalized Treatment.*

Introduction

Chronic anal fissure remains one of the most prevalent proctological conditions, characterized by severe pain, defecation disorders, and a substantial decline in quality of life. According to Lohsiriwat and Schlichtemeier, this condition accounts for approximately 10-15% of consultations with proctologists [1,2]. Despite the availability of multiple treatment modalities, including conservative, injection-based, and surgical approaches, rates of incomplete healing and recurrence remain considerable [3-5]. The pathogenesis of chronic anal fissures is primarily attributed to persistent hypertonicity of the internal anal sphincter, fibrotic changes at the anoderm defect, ischemic alterations, and impaired local blood supply [1-4]. Consequently, treatment strategies are directed toward addressing these factors and facilitating epithelialization of the defect [2,6,7]. Nevertheless, complete healing within the expected timeframe is not achieved in a proportion of patients. This observation underscores the multifactorial etiology of the condition and highlights the importance of identifying determinants that may influence treatment efficacy.

Although the majority of published studies focus on comparative evaluation of treatment methods for chronic anal fissures, the impact of various anamnestic, clinical, and functional factors on therapeutic outcomes remains inadequately addressed [8-11]. The role of disease duration, clinical course, and pain intensity in predicting complete healing continues to be debated [2,11-13].

Identification of factors associated with successful treatment of chronic anal fissures therefore holds substantial practical value. Such knowledge may contribute to the optimization of treatment algorithms, implementation of individualized approaches, and improvement of long-term results.

Objective. To identify factors influencing complete healing of chronic anal fissures at week 4 of treatment.

Materials and methods. This prospective analytical study was conducted at the Department of Surgery with a course in hepatobiliary and vascular surgery during 2022-2024 and included 155 patients diagnosed with chronic anal fissure. The primary aim was to determine factors affecting treatment outcomes. Patients were stratified into two subgroups according to the treatment strategy applied: the main subgroup (treated according to

the proposed algorithm; n = 83) and the control subgroup (treated with standard therapy; n = 72). Stratification by treatment approach was performed to evaluate the type of treatment as one of the potential factors influencing efficacy, rather than to directly compare the effectiveness of the two regimens.

Inclusion criteria were as follows: confirmed chronic anal fissure, defined by symptoms persisting for more than 6 weeks and the presence of characteristic clinical signs; patient age over 18 years; and a minimum follow-up period of 6 months after treatment completion.

Exclusion criteria included malignant neoplasms of the rectum or anal canal; inflammatory bowel diseases involving the colon or rectum; anal canal pectenosis; severe concomitant systemic diseases in subcompensated or decompensated stages; systemic connective tissue diseases; known allergy to calcium channel blockers, nitrates, or botulinum toxin type A; alcohol abuse, medication misuse, or drug addiction; positive HIV/AIDS status; pregnancy or lactation; age under 18 years or over 70 years; follow-up period less than 6 months; or non-adherence to the recommended diagnostic and treatment protocol.

The clinical characteristics of the patients enrolled in the study are presented in Table 1. The mean age of patients with chronic anal fissures was 41.76 ± 13.5 years. The study population comprised 66 men (42.6%) and 89 women (57.4%).

Table 1

Clinical characteristics of patients

Indicator		Format	Total (n=155)	Main group (n=83)	Control group (n=72)	p
Age, years		M ± SD	41.76 ± 13.5	40.6 ± 13.7	43.11 ± 13.24	0.25
Gender	Men	n (%)	66 (42.6%)	35 (42.2%)	31 (43.1%)	1.00
	Women	n (%)	89 (57.4%)	48 (57.8%)	41 (56.9%)	
Duration of illness, months		M ± SD	3.69 ± 1.32	3.76 ± 1.36	3.61 ± 1.28	0.49
VAS pain, points		M ± SD	7.21 ± 2.17	7.11 ± 2.27	7.32 ± 2.06	0.55
Localization	Anterior	n (%)	73 (47.1%)	38 (45.8%)	35 (48.6%)	0.85
	Posterior	n (%)	82 (52.9%)	45 (54.2%)	37 (51.4%)	
Concomitant perineal pathology		n (%)	85 (54.8%)	38 (45.8%)	45 (62.5%)	0.48
History of diarrhea/constipation		n (%)	82 (52.9%)	43 (51.8%)	39 (54.2%)	0.89

Patients in the main group were treated according to the proposed target-to-treat algorithm. Initial clinical assessment of anal canal functional characteristics was performed, followed by stratification of patients based on the predominant pathogenetic mechanism into one of the following categories: patients without evidence of sphincter dysfunction; patients with prior perineal surgical interventions or women with obstetric anal sphincter injury; patients with marked hypertonicity of the internal anal sphincter; and patients with pronounced fibrotic changes in the anal canal.

Subsequently, the initial treatment line was determined, which could consist of conservative therapy or surgical intervention. In the absence of clinical response, treatment was escalated to include botulinum toxin injections, surgery, or combined approaches. When conservative therapy was applied, patients adhered to a diet aimed at normalizing bowel movements and received topical calcium channel blockers. Surgical interventions included lateral internal sphincterotomy (LIS), fissurectomy, sphincterotomy when indicated, and flap plasty. In contrast, patients in the control group received standard treatment without pathogenetic stratification. This consisted of either surgical intervention or conservative management (dietary modification, topical analgesics, and venotonics). Detailed descriptions of the treatment protocols are not provided in this publication.

The primary outcome was complete healing of the chronic anal fissure at week 4 of treatment, defined as full epithelialization of the defect confirmed by proctological examination and recorded as a binary variable (yes/no). To identify factors associated with healing, clinical and anamnestic variables were analyzed, including treatment type (proposed target-to-treat algorithm versus standard therapy), baseline pain intensity on the visual analog scale (VAS), disease duration, history of bowel habit disturbances, and other relevant indicators. Variables for multivariate analysis were selected based on univariate analysis results ($p < 0.10$) and clinical relevance.

The study was conducted in accordance with the ethical principles outlined in the Declaration of Helsinki. Informed consent was obtained from all participants. The study protocol was approved by the Bioethics Committee of Bogomolets National Medical University (protocol No. 2, dated 17 October 2022).

Statistical processing was performed using IBM SPSS Statistics Base v.22, R-Statistics v.3.2.0, and Medstat software. Standard variational statistics were applied. Quantitative data with normal distribution were expressed as mean ± standard deviation (M ± SD), while categorical variables were reported as absolute numbers and percentages. Comparisons between two independent groups for quantitative variables were conducted using Student's t-test or Welch's t-test, depending on variance equality. Categorical variables were compared using the χ^2 test or Fisher's exact test. To assess the factors associated with achieving complete healing of chronic anal fissures, univariate analysis was followed by multivariate logistic regression, incorporating variables with $p < 0.10$ and clinically significant indicators. Results are presented as odds ratios (OR) with 95% confidence intervals (CI). Statistical significance was set at $p < 0.05$.

The work was performed as part of the research project of the department entitled «Development and improvement of methods for diagnosis, surgical treatment, and rehabilitation of patients with pathologies of the

digestive tract and perineum,» implementation period 2024-2026, state registration number 0123U1051738.

Results and discussion

Complete healing of chronic anal fissures was achieved in 128 (82.6%) patients by week 4 of treatment. Analysis demonstrated that treatment type was one of the most influential factors associated with therapeutic outcomes. As shown in Table 2, application of the proposed algorithm was associated with a significantly increased likelihood of complete healing (OR = 4.18; 95% CI 1.6-10.9).

The relative risk of complete healing in the main group was 27% higher than in the control group (RR = 1.27; 95% CI 1.11-1.46). Thus, treatment strategy represents the primary modifiable factor determining successful management of patients with chronic anal fissures.

Table 2

Frequency of complete healing of chronic anal fissures according on the treatment group.

Group	n	Complete healing, n (%)	Non-healing, n (%)	p	RR (95% CI)	OR (95% CI)
Main	83	76 (92.1%)	7 (7.9%)	<0,001	4,18 (1.6-10.9)	1,27 (1.11-1.46)
Control	72	52 (71.8%)	20 (28.2%)			
Total	155	128 (82.6%)	27 (17.4%)	-	-	-

To identify additional factors potentially influencing complete healing, univariate analysis of clinical and anamnestic variables was performed.

The results of univariate analysis (Table 3) confirm that treatment efficacy depends on several anamnestic and clinical factors. As anticipated, complete healing by week 4 was most strongly associated with the treatment strategy employed, underscoring the importance of a personalized approach in managing patients with chronic anal fissures.

In addition to treatment type, disease duration significantly influenced outcomes. Patients with shorter symptom duration exhibited higher healing rates (median 3.4 months in the healed group versus 5.3 months in the non-healed group; $p < 0.001$). Prolonged disease duration is associated with the development of chronic morphological changes that adversely affect treatment response. Baseline pain intensity at treatment initiation was another important predictor. Lower VAS scores were linked to better outcomes (median 7.0 points in the healed group versus 9.0 points in the non-healed group; $p = 0.002$). Reduced internal anal sphincter spasm and consequent lower pain likely create more favorable conditions for healing.

Among anamnestic factors, a history of diarrhea or constipation was significantly associated with poorer treatment results ($p < 0.001$), likely due to repeated mechanical trauma to the anal canal and impaired epithelialization.

Table 3

Univariate analysis of factors associated with complete healing

Factor	Categories	Complete healing n = 128	Non-healing n=27	p
Type of treatment	proposed/standard	76 / 52	7 / 20	<0.001*
Age	years, median	43.0	46.5	0.50
Gender	male/female	55/74	11/15	1.00
Duration of illness	months, median	3.4	5.3	<0.001*
VAS pain	points, median	7.0	9.0	0.002*
Localization	anterior/ posterior	61/67	12/14	1.00
Concomitant perineal pathology	yes/no	62/67	12/14	0.75
History of diarrhea/constipation	yes/no	77/52	5/21	<0.001*

*Note: *- statistically significant result*

Factors such as age, gender, fissure location, and presence of concomitant perineal pathology showed no statistically significant association with healing rates ($p > 0.05$) and were therefore excluded from subsequent multivariate logistic regression analysis. Variables demonstrating significant univariate associations and clinical relevance – treatment type, disease duration, baseline VAS pain score, and history of diarrhea/ constipation – were included in the multivariate model.

The results of the multivariate analysis are presented in Table 4 Independent predictors of complete healing of chronic anal fissures at week 4 of treatment were treatment strategy (personalized target-to-treat algorithm versus standard therapy) and disease duration. The personalized algorithm was associated with a statistically significant increase in the odds of achieving complete epithelialization compared with standard therapy (OR = 4.31; 95% CI 1.63-11.41; $p = 0.003$). Conversely, longer disease duration was associated with a decreased probability of successful treatment (OR = 0.73; 95% CI 0.61-0.87; $p = 0.001$). Factors that were significant in univariate analysis, such as baseline pain intensity on the VAS scale and history of bowel movement disorders, showed no independent effect in the multivariate model ($p > 0.05$).

Table 4

Multifactorial logistic regression analysis of factors associated with complete healing

Factor	Categories	OR	95%CI	p
Type of treatment	proposed/standard	4.31	1.63-11.41	0.003*
Duration of illness	months, median	0.73	0.61-0.87	0.001*
VAS pain	points, median	0.94	0.79-1.11	0.45
History of diarrhea/constipation	yes/no	0.88	0.36-2.12	0.77

*Note: *- statistically significant result*

The prognostic performance of the model was evaluated by ROC analysis. The area under the ROC curve (AUC) was 0.97 (Figure 1), indicating excellent discriminatory ability for predicting complete healing of chronic anal fissures.

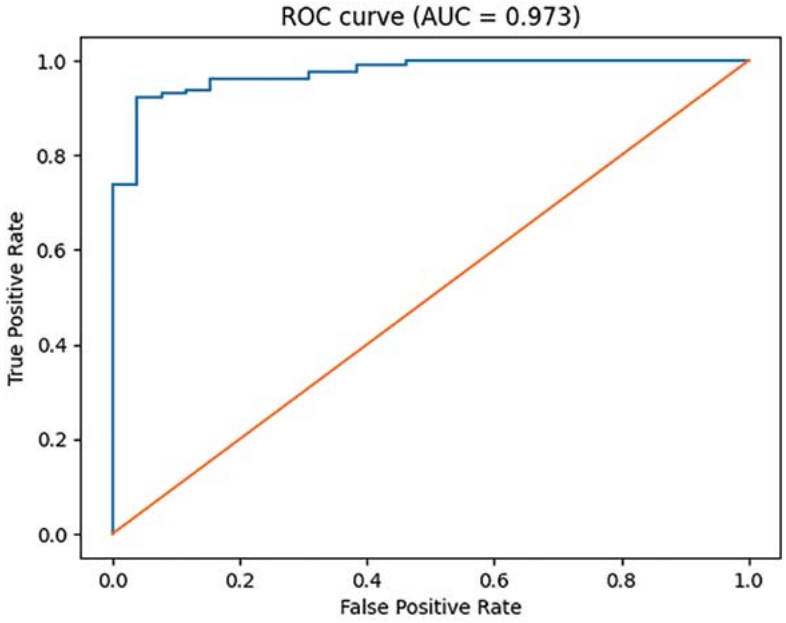

Figure 1. ROC curve of a multivariate logistic regression model for predicting complete healing of chronic anal fissures (AUC = 0.97)

Chronic anal fissure remains one of the most prevalent proctological conditions, characterized by persistent pain, defecation disorders, and a substantial reduction in patients' quality of life. Numerous treatment modalities are currently available, including conservative approaches, botulinum toxin injections, and various surgical interventions [3, 14-18]. Nevertheless, literature reports persistently high rates of recurrence and incomplete healing, influenced by multiple anamnestic and clinical factors [1, 6-9].

The present study identified treatment strategy as a key independent predictor of complete healing (p = 0.003). Application of the personalized target-to-treat algorithm increased the odds of complete healing more than fourfold compared with standard therapy. These findings indicate that a uniform approach to patient management is suboptimal, consistent with existing evidence [5-8, 15, 19]. Personalization based on pathogenetic mechanisms significantly improves outcomes.

The results align with published data demonstrating that pharmacological interventions aimed at reducing internal anal sphincter tone are most effective in cases of functional hypertonicity [2-5, 14, 20], whereas surgical intervention is preferred in the presence of severe fibrotic changes [5, 7, 12, 17]. Current guidelines often lack explicit criteria for selecting between these options, resulting in sequential rather than rationally targeted use of therapies. The proposed algorithm addresses this limitation by providing a structured, pathogenetically oriented clinical decision-making framework.

Disease duration emerged as another independent predictor of healing (p = 0.001 Longer symptom duration was associated with reduced odds of successful treatment (OR = 0.73; 95% CI 0.61-0.87). This reflects the progressive nature of morphological alterations in chronic anal fissures, including increasing fibrosis, ischemia, and anal canal deformation, which diminish the potential for epithelialization [4, 9, 11, 19]. These observations reinforce the importance of early intervention and timely escalation of therapy.

Baseline pain intensity and history of bowel movement disorders warrant separate consideration. Although these factors are not commonly emphasized in the literature as direct causes of early recurrence or impaired healing, univariate analysis suggested their potential relevance. However, they lost independent prognostic significance in the multivariate model. This indicates that elevated VAS scores and bowel habit disturbances likely serve as markers of disease severity and clinical course rather than primary

causes of treatment failure. High pain levels may reflect pronounced internal anal sphincter spasm or deeper tissue involvement, while diarrhea and constipation contribute to ongoing mechanical trauma of the anal canal. Correction of these secondary factors alone, without addressing the underlying pathogenetic mechanism, appears insufficient for optimal outcomes.

The present findings align with published data showing no significant influence of gender, age, or fissure location on treatment results ($p > 0.05$) [15, 20, 21]. This reinforces the notion that the core pathogenetic processes in chronic anal fissures are largely universal across demographic subgroups. The multivariate model demonstrated excellent discriminatory performance (AUC = 0.97), supporting its potential utility as a clinical prediction tool. Such a tool could facilitate selection of the most appropriate individualized treatment strategy at initial consultation and enable timely escalation in patients at high risk of non-healing. These observations highlight the substantial clinical relevance of the study.

Implementation of the target-to-treat strategy not only increases healing rates but may also shorten treatment duration, reduce the need for escalation interventions, and lower recurrence rates.

Limitations of the study include its retrospective design, absence of randomization, and single-center setting. Nevertheless, the adequate sample size and consistency between univariate and multivariate results enhance the reliability of the conclusions. Prospective multicenter studies are required to validate the proposed algorithm and support its incorporation into clinical guidelines.

Conclusions

The present study confirms that chronic anal fissure is a multifactorial condition in which treatment outcomes are determined by a combination of clinical and anamnestic factors. Application of a personalized algorithm represents the primary determinant of successful healing. Longer disease duration was independently associated with reduced odds of complete healing, underscoring the importance of early intervention before irreversible fibrotic and ischemic changes develop.

These results support the adoption of a pathogenetically oriented, individualized treatment algorithm for patients with chronic anal fissures to improve healing rates, clinical outcomes, and quality of life.

Perspectives for Future Research. The identified influence of anamnestic and clinical factors on healing efficacy provides a foundation for further investigation. Inclusion of objective functional parameters of the anal canal (e. g., manometry, endoanal ultrasound) in future analyses would enable more precise evaluation of pathogenetic contributions. Development and validation of prognostic scoring systems based on the independent predictors identified in this study are warranted.

Contribution of co-authors to the preparation of materials for the scientific article: L. Hrytsak– concept and design, collection and analysis of material, writing of text; M. Aksan – writing of text, editing, concept and design; L. Bilyansky – concept and design, analysis of material, editing.

Conflict of interest. The authors declare no conflict of interest.

Use of Artificial Intelligence. Artificial intelligence was used only as an auxiliary tool for stylistic editing.

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ФАКТОРИ, ЩО ВПЛИВАЮТЬ НА РЕЗУЛЬТАТИ ЛІКУВАННЯ ХРОНІЧНОЇ АНАЛЬНОЇ ТРІЩИНИ

Л. І. Грицак, М. В. Аксан, Л. С. Білянський

Національний медичний університет імені О. О. Богомольця
(м. Київ, Україна)

Резюме.

Хронічна анальна тріщина є значно поширеним проктологічним захворюванням, що супроводжується вираженим больовим синдромом і значним зниженням якості життя. Незважаючи на наявність різних методів лікування, частота неповного загоєння та рецидивів залишається високою, що свідчить про мультифакторний характер захворювання та необхідність визначення чинників, які впливають на ефективність терапії.

Мета дослідження. Визначити фактори, які впливають на повне загоєння хронічної анальної тріщини на 4-му тижні лікування.

Матеріали і методи. Дане проспективне одноцентрове дослідження включало аналіз 155 пацієнтів із хронічною анальною тріщиною, які отримали лікування у 2022-2024 роках. Було проведено однофакторний та багатофакторний аналіз чинників, які впливали на повне загоєння дефекту на 4-тий тиждень лікування з оцінкою відношення шансів регресійний аналіз з оцінкою відношення шансів. Додатково пацієнтів було поділено на дві підгрупи щодо вибору тактики лікування (персоналізований алгоритм ведення – 83 пацієнта; стандартизована терапія – 72 пацієнта). Наукові дослідження виконані відповідно до етичних норм та принципів, що регулюють медичні дослідження людини. Протокол дослідження був схвалений комісією з біоетики Національного медичного університету імені О. О. Богомольця (протокол № 2 від 17.10.2022 р.). Статистичну обробку проведено програмним забезпеченням IBM SPSS Statistics Base v.22, R-Statistics v.3.2.0, Medstat. Для її проведення використовували стандартні методи варіаційної статистики. Робота виконана в рамках НДР кафедри «Розробка і удосконалення методів діагностики, хірургічного лікування та реабілітації пацієнтів з патологією травного каналу та промежини»», термін виконання 2024-2026 р., державний реєстраційний номер: 0123U1051738.

Результати. Повного загоєння досягнуто у 128 (82,6%) пацієнтів. Застосування алгоритму target-to-treat достовірно підвищувало ймовірність загоєння порівняно зі стандартною терапією (92,1% проти 71,8%; p<0,001). У багатофакторному аналізі незалежними предикторами повного загоєння були тип лікування (OR=4,31; 95% CI 1,63-11,41; p=0,003) та тривалість захворювання (OR=0,73; 95% CI 0,61-0,87; p=0,001). Вік, стать, локалізація тріщини, інтенсивність болю та наявність супутньої патології не мали незалежного впливу на результат лікування. Прогностична здатність моделі була високою (AUC=0,97).

Висновки. Ключовими фаткорами, які впливають на повне загоєння хронічної анальної тріщини на 4-му тижні лікування, є тип тактики лікування та тривалість захворювання. При цьому персоналізований алгоритм target-to-treat вірогідно покращує ефективність лікування і може бути впровадженим у клінічну практику.

Ключові слова: малоінвазивна хірургія; поєднана патологія; анальна тріщина; загоєння; фактори прогнозу; персоналізоване лікування.

Contact information:
Liliia Hrytsak – Assistant, Department of Surgery with a course in hepatobiliary and vascular surgery, Bogomolets National Medical University (Kyiv, Ukraine).
e-mail: lylychka5@gmail.com
ORCID ID: https://orcid.org/0000-0003-1779-8912
ResearcherID: https://www.webofscience.com/wos/author/record/ISV-6340-2023

Mykhailo Aksan – PhD, Assistant, Department of Surgery with a course in hepatobiliary and vascular surgery, Bogomolets National Medical University (Kyiv, Ukraine).
e-mail: aksanmv@gmail.com
ORCID ID: https://orcid.org/0000-0001-6420-3382
ResearcherID: https://www.webofscience.com/wos/author/record/AIB-8810-2022

Leonid Bilansky – Doctor of Medical Sciences, Professor of the Department of Surgery with a course in hepatobiliary and vascular surgery at Bogomolets National Medical University (Kyiv, Ukraine).
e-mail: bls@gmail.com
ORCID ID: https://orcid.org/0000-0003-1025-9019
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=6602761174

Контактна інформація:
Грицак Лілія Ігорівна – асистент кафедри хірургії з курсом гепатобіліарної та судинної хірургії Національного медичного університету імені О. О. Богомольця (м. Київ, Україна).
e-mail: lylychka5@gmail.com
ORCID ID: https://orcid.org/0000-0003-1779-8912
Researcher ID: https://www.webofscience.com/wos/author/record/ISV-6340-2023

Аксан Михайло Валерійович – PhD, асистент кафедри хірургії з курсом гепатобіліарної та судинної хірургії Національного медичного університету імені О. О. Богомольця (м. Київ, Україна).
e-mail: aksanmv@gmail.com
ORCID ID: https://orcid.org/0000-0001-6420-3382
Researcher ID: https://www.webofscience.com/wos/author/record/AIB-8810-2022

Білянський Леонід Семенович – доктор медичних наук, професор кафедри хірургії з курсом гепатобіліарної та судинної хірургії Національного медичного університету імені О. О. Богомольця (м. Київ, Україна).
e-mail: bls@gmail.com
ORCID ID: https://orcid.org/0000-0003-1025-9019
Scopus Author ID: https://www.scopus.com/authid/detail.uri?authorId=6602761174

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