

Міністерство охорони здоров'я України
Буковинський державний медичний університет

БУКОВИНСЬКИЙ МЕДИЧНИЙ ВІСНИК

Український науково-практичний журнал

Заснований у лютому 1997 року

Видається 4 рази на рік

Включений до Ulrichsweb™ Global Serials Directory, наукометричних і спеціалізованих баз даних Google Scholar (США), Index Copernicus International (Польща), Scientific Indexing Services (США), Infobase Index (Індія), Ukrainian research & Academy Network (URAN), НБУ ім. Вернадського, “Джерело”

ТОМ 27, № 2 (106)

2023

Редакційна колегія:

головний редактор Т.М. Бойчук,
О.Б. Беліков, О.С. Годованець, І.І. Заморський,
О.І. Іващук (перший заступник головного редактора),
Т.О. Ілащук, А.Г. Іфтодій, Г.Д. Коваль, О.К. Колоскова,
В.В. Кривецький (заступник головного редактора),
В.В. Максим'юк, Н.В. Пашковська,
Д.В. Проняєв (відповідальний секретар), Л.П. Сидорчук,
С.В. Сокольник, В.К. Ташук, С.С. Ткачук,
О.І. Федів, О.В. Цигикало

Чернівці: БДМУ, 2023

Редакційна рада:

К.М. Амосова (Київ), В.В. Бойко (Харків),
А.І. Гоженко (Одеса), В.М. Запорожан (Одеса),
В.М. Коваленко (Київ), З.М. Митник (Київ),
В.І. Паньків (Київ), В.П. Черних (Харків),
Герхард Дамман (Швейцарія),
Збігнев Копанські (Польща),
Дірк Брутцерт (Бельгія),
Раду Крістіан Дабіша (Румунія)
Віктор Ботнару (Респ. Молдова)

Рекомендовано до друку та до поширення через мережу Інтернет рішенням вченої ради
Буковинського державного медичного університету
(протокол № 13 від 25.05.2023 року)

Буковинський медичний вісник
(Бук. мед. вісник) – науково-
практичний журнал, що рецензується
Bukovinian Medical Herald
(Buk. Med. Herald)

Заснований у лютому 1997 р. Видається 4
рази на рік

Founded in February, 1997 Published four
times annually

Мова видання: українська, англійська

Сфера розповсюдження загальнодержавна,
зарубіжна

Свідоцтво про державну реєстрацію: серія
КВ №15684-4156 ПР від 21.09.2009

Наказом

Міністерства освіти і науки України
від 17 березня 2020 року № 409 журнал
“Буковинський медичний вісник”
включено до категорії "Б" (медичні
спеціальності – 222) переліку наукових
фахових видань України

Адреса редакції: 58002, м. Чернівці,
пл. Театральна, 2

Тел.: (0372) 55-37-54,
52-39-63

Факс: (0372) 55-37-54

e-mail: bmh@bsmu.edu.ua

Адреса електронної версії журналу в
Internet: <http://www.bsmu.edu.ua>

ANALYSIS OF PROGNOSTIC FACTORS IN PATIENTS WITH ACUTE PERITONITIS**A.I. Shurma, F.V. Grynchuk***Bukovinian State Medical University, Chernivtsi, Ukraine*

Key words: acute peritonitis; Complication; Prognostication; Prognostic Scale.

Bukovinian Medical Herald. 2023. V. 27, № 2 (106). P. 43-47.

DOI: 10.24061/2413-0737.27.2.106.2023.7

E-mail:

shurma.andrii@bsmu.edu.ua
fedir.grynchuk@bsmu.edu.ua

Resume. Prediction of postoperative complications (POC) is an important element in the choice of treatment tactics for acute peritonitis (AP). Many methods have been proposed for this. However, none of these methods have sufficient recognition. Most prognostic scales determine the risk of complications only after surgery. Therefore, the issue of developing an informative prognostic scale remains relevant.

The aim of the study was to evaluate prognostic factors in patients with acute peritonitis.

Materials and Methods. Retrospective analysis of the results of treatment of 212 patients with AP. 65 patients had POC. 22 patients died. Analysis of clinical, anthropometric data, laboratory examination results, criteria of MPI, PIPAS, WSES Sepsis Severity Score (WSSS), Charlson Comorbidity Index (CCI) was performed. Analysis of Variance (ANOVA) and Neural Network Bayesian Classifier were used to assess the influence of factors.

Results. None of the studied criteria is sufficient for prediction. MPI, PIPAS, WSSS have the greatest influence on the probability of POC occurrence in AP. But these indicators can be determined only after the operation. Therefore, we separately used a cumulative assessment of indicators that can be determined before surgery and after surgery. Multifactor ANOVA with preoperative parameters: diagnosis, clinical signs of AP, body temperature, CCI, systolic blood pressure (SBP) showed that since 5 P-values are less than 0.05, combination of these factors have a statistically significant effect on POC at the 95.0% confidence level. Multifactor ANOVA with indicators of diagnosis, body temperature, CCI, SBP, WSSS or PIPAS showed that since 5 P-values are less than 0.05, combination of these factors have a statistically significant effect on POC at the 95.0% confidence level.

Conclusions

1. Criteria MPI, PIPAS, WSSS have the greatest influence on the probability of POC occurrence in AP, but none of these criteria is sufficient alone. 2. The set of indicators of diagnosis, clinical signs of peritonitis before surgery, body temperature, CCI, SBP have a statistically significant effect on POC at the 95.0% confidence level before surgery. 3. The combination of indicators of diagnosis, body temperature, CCI, SBP, WSSS or PIPAS have a statistically significant effect on POC at the 95.0% confidence level after surgery. 4. The creation of a reliable prognostic scale is possible using a complex of the described factors.

АНАЛІЗ ПРОГНОСТИЧНИХ ФАКТОРІВ У ХВОРИХ НА ГОСТРИЙ ПЕРИТОНІТ**A.I. Шурма, Ф.В. Гринчук**

Ключові слова: гострий перитоніт, ускладнення, прогнозування, прогностична шкала.

Буковинський медичний вісник. 2023. Т. 27, № 2 (106). С. 43-47.

Резюме. Прогнозування післяопераційних ускладнень (ПОУ) є важливим елементом у виборі тактики лікування гострого перитоніту (ГП). Для цього запропоновано багато методів. Однак жоден із цих методів не має достатнього визнання. Більшість прогностичних шкал визначають ризик ускладнень тільки після операції. Тому актуальним залишається питання розробки інформативної прогностичної шкали.

Мета дослідження – оцінити прогностичні фактори у хворих на гострий перитоніт.

Матеріал і методи. Ретроспективний аналіз результатів лікування 212 хворих на ГП. 65 пацієнтів мали ПОУ. Померло 22 хворих. Проведено аналіз клінічних, антропометричних даних, результатів лабораторних досліджень, критеріїв Мангаймського перитонітного індексу (МПІ), PIPAS, WSES Sepsis Severity Score (WSSS), індекс коморбідності Чарлсона (ІКЧ). Для оцінки впливу факторів використовували дисперсійний аналіз (ДА) і Neural Network Bayesian

Оригінальні дослідження

Classifier.

Результати. Жоден із досліджуваних критеріїв не є достатнім для прогнозування. Найбільший вплив на ймовірність виникнення ПОУ при ГП мають МПІ, PIPAS, WSSS. Але ці показники можна визначити тільки після операції. Тому ми окремо використали сукупну оцінку показників, які можна визначити до і після операції. Багатофакторний ДА з передопераційними параметрами: діагноз, клінічні ознаки ГП, температура тіла, ІКЧ, систолічний артеріальний тиск (САТ) показав, що оскільки Р-критерій цих 5 факторів менше 0,05, їх комбінація має статистично значущий вплив на ПОУ на 95,0% довірчому рівні.

Висновки. 1. Критерії MPI, PIPAS, WSSS мають найбільший вплив на ймовірність виникнення ПОУ при ГП, але жоден із цих критеріїв сам по собі не є достатнім.

2. Сукупність показників діагнозу, клінічних ознак перитоніту до операції, температури тіла, ІКЧ, САТ мають статистично значущий вплив на ПОУ на 95,0% довірчому рівні до операції.

3. Комбінація показників діагностики, температури тіла, CCI, SBP, WSSS або PIPAS має статистично значущий вплив на ПОУ на 95,0% довірчому рівні після операції.

4. Створення надійної прогностичної шкали можливе за допомогою комплексу описаних факторів.

Introduction. Prediction of postoperative complications (POC) is an essential element in the choice of acute peritonitis (AP) management which makes it possible to apply preventive measures [1-4]. For this purpose, many methods have been proposed based on various indicators [1,2,3,5-7]. However, none of these methods have gained sufficient recognition. Recognized scales are PIPAS [4], WSES Sepsis Severity Score (WSSS) [8], Mannheim Peritonitis Index (MPI) [9], Peritonitis Index Altona [10], Combined Peritonitis Score [11]. These scales assess only the degree of organ dysfunction, the severity of AP and the possibility of a patient's death [12-17]. However, these scales do not assess the risk of certain complications. Most prognostic scales determine the risk of complications only after surgery [5]. It limits the possibility of justified prevention of complications already during preoperative preparation. Therefore, the problem of developing an informative prognostic scale remains relevant.

Aim of the Study. To evaluate prognostic factors in patients with acute peritonitis.

Materials and Methods. Retrospective analysis of the treatment results of 212 patients with AP. The age of the patients was from 17 to 86 years. There were 102 females, 110 males. Causes of AP: small bowel perforation – 2, large bowel perforation – 2, postoperative peritonitis – 3, acute cholecystitis – 4, acute mesenteric ischemia – 5, gynecological diseases – 5, acute large intestinal obstruction – 8, strangulated hernias – 12, acute small intestinal obstruction – 23, perforated gastroduodenal ulcer – 38, acute appendicitis – 110 (acute perforated appendicitis – 24). Local peritonitis (LP) was present in 88 patients, diffuse peritonitis (DP) was present in 59 patients, general peritonitis (GP) was present in 65 patients.

65 patients had postoperative complications (POC): inflammation of the postoperative wound – 15, suppuration of the postoperative wound – 16, eversion - 3, intra-abdominal abscess – 5, suture failure – 5, postoperative

peritonitis – 22. 22 patients died. 123 patients had concomitant diseases.

Analysis of clinical, anthropometric data, laboratory examination results, MPI, PIPAS, WSSS, Charlson Comorbidity Index (CCI) [18] was performed.

For mathematical processing, complications were evaluated as follows: 0 – no complications, 1 – wound inflammation, 2 – suppuration of the wound, 3 – eversion, 5 – intra-abdominal abscess, 7 – suture failure, 8 – postoperative peritonitis. The presence of clinical signs of peritonitis (pain on palpation, stiffness of the abdominal wall, rebound pain) before the operation was evaluated as follows: LP – 1, DP – 2, GP – 3.

Analysis of Variance (ANOVA) and Neural Network Bayesian Classifier (NNBC) were used to assess the influence of factors. The Statgraphics Centurion 18 program (Statgraphics Technologies, Inc.) was used for analysis.

Results and Discussion. According to One-Way ANOVA, there were no gender differences in the frequency of POC (F-Ratio=2.97, P-Value=0.0864).

According to One-Way ANOVA, POC distribution was statistically significantly dependent on age (F-Ratio=1.97, P-Value=0.0004). According to NNBC, the percentage of training cases correctly classified was 65.093%.

According to One-Way ANOVA, the distribution of POC indicators statistically significantly (F-Ratio=3.97, P-Value=0.0000) depended on the diagnosis. The distribution of POC was statistically significant (F-Ratio=23.48, P-Value=0.0000), dependent on clinical signs of peritonitis before surgery. According to NNBC, the percentage of training cases correctly classified was 69.3396%. The POC distribution was statistically significant (F-Ratio=4.24, P-Value=0.0000), dependent on the CCI indicator. According to NNBC, the percentage of training cases correctly classified was 67.9245%.

According to One-Way ANOVA, the distribution of

POC indicators did not depend on body temperature indicators (F-Ratio=1.52, P-Value=0.0578). But, according to NNBC, the percentage of training cases correctly classified was 71.7514%.

According to One-Way ANOVA, POC distribution was statistically significantly (F-Ratio=2.04, P-Value=0.0020) dependent on heart rate. But according to NNBC percentage of training cases correctly classified was only 11.5183%.

According to One-Way ANOVA, POC distribution was statistically significantly (F-Ratio=2.85, P-Value=0.0004) dependent on systolic blood pressure (SBP). According to NNBC, the percentage of training cases correctly classified was 69.6335%.

According to One-Way ANOVA, POC distribution did not depend on the number of leukocytes (F-Ratio=1.03, P-Value=0.4411). Instead, according to NNBC, the percentage of training cases correctly classified was 60.5911%.

According to One-Way ANOVA, POC distribution did not depend on the amount of glucose in plasma (F-Ratio=0.72, P-Value=0.9259). Instead, according to NNBC, the percentage of training cases correctly classified was 67.7419%.

According to One-Way ANOVA, POC distribution did not depend on the amount of total plasma's protein (F-Ratio=1.05, P-Value=0.4076). But according to NNBC percentage of training cases correctly classified was 62.8415%.

According to One-Way ANOVA, POC distribution did not depend on the amount of plasma's total bilirubin (F-Ratio=1.34, P-Value=0.0839). But according to NNBC, the percentage of training cases correctly classified was 63.0682%.

According to One-Way ANOVA, POC distribution was statistically significantly dependent on the amount of plasma's urea (F-Ratio=1.34, P-Value=0.0839). According to NNBC, the percentage of training cases correctly classified was 67.7966%.

According to One-Way ANOVA, POC distribution was statistically significantly dependent on the amount of plasma's creatinine (F-Ratio=2.24, P-Value=0.0269). According to NNBC, the percentage of training cases correctly classified was 58.5586%.

According to One-Way ANOVA, POC distribution was independent of prothrombin time (F-Ratio=0.98, P-Value=0.5304). But according to NNBC, the percentage of training cases correctly classified was 68.9873%. According to One-Way ANOVA, POC distribution did not depend on the amount of plasma's fibrinogen (F-Ratio=1.19, P-Value=0.2163). But according to NNBC, the percentage of training cases correctly classified was 65.4088%. According to One-Way ANOVA, POC distribution did not depend on hematocrit (F-Ratio=1.24, P-Value=0.1712). But according to NNBC, the percentage of training cases correctly classified was 60.3896%.

According to One-Way ANOVA, the distribution of POC was statistically significantly dependent on the MPI indicator (F-Ratio=4.77, P-Value=0.0000). According to NNBC, the percentage of training cases correctly classified

was 69.3396%. According to One-Way ANOVA, the distribution of POC was statistically significantly (F-Ratio=20.26, P-Value=0.0000) dependent on the PIPAS indicator. According to NNBC, the percentage of training cases correctly classified was 69.3396%. According to One-Way ANOVA, the POC distribution was statistically significantly (F-Ratio=10.08, P-Value=0.0000) dependent on the WSSS indicator. According to NNBC, the percentage of training cases correctly classified was 70.283%.

Therefore, the overall analysis shows that none of the criteria is sufficient. MPI, PIPAS, WSSS have the greatest influence on the probability of POC occurrence in AP. But these indicators can be determined only after the operation. Therefore, we separately used a cumulative assessment of indicators that can be determined before surgery and after surgery.

Multifactor ANOVA with parameters determined before surgery indicated that a specific model could not be established. When analyzing the indicators of diagnosis, clinical signs of peritonitis before surgery, body temperature, CCI, SBP, it was found that since 5 P-values are less than 0.05, a combination of these factors has a statistically significant effect on POC at 95.0 % confidence level (table 1).

Multifactor ANOVA with indicators of diagnosis, body temperature, CCI, SBP, MPI showed that MPI is a linear combination of other factors. Therefore, the analysis is impossible. Multifactor ANOVA with indicators of diagnosis, body temperature, CCI, SBP, WSSS showed that since 5 P-values are less than 0.05, combination of these factors have a statistically significant effect on POC at the 95.0% confidence level (table 2).

Multifactor ANOVA with indicators of diagnosis, body temperature, CCI, SBP, PIPAS showed that since 5 P-values are less than 0.05, combination of these factors have a statistically significant effect on POC at 95.0% confidence level (table 3).

Table 1

Results of Multifactor ANOVA analysis of the influence of factors on POC before surgery

Source	Sum of Squares	Df	Mean Square	F-Ratio	P-Value
Main effects					
Diagnosis	56,1659	11	5,10599	2,13	0,0221
Peritonitis	53,0058	2	26,5029	11,05	0,0000
Cci	69,9272	12	5,82727	2,43	0,0068
Temperature	209,261	32	6,53941	2,73	0,0000
Sbp	162,826	17	9,57802	3,99	0,0000
Residual	328,62	137	2,39869		
Total (corrected)	1481,03	211			

Table 2

Results of Multifactor ANOVA analysis of the influence of factors on POC after surgery

Source	Sum of squares	Df	Mean square	F-ratio	P-value
Main effects					

Оригінальні дослідження

Diagnosis	48,0202	10	4,80202	1,95	0,0464
Wsss	39,4228	5	7,88456	3,21	0,0099
Cci	73,9384	10	7,39384	3,01	0,0023
Temperature	103,236	24	4,30152	1,75	0,0289
Sbp	107,536	15	7,16905	2,91	0,0007
Residual	250,911	102	2,45991		
Total (corrected)	707,988	166			

Table 3

Results of Multifactor ANOVA analysis of the influence of factors on POC after surgery

Source	Sum of squares	Df	Mean square	F-ratio	P-value
Main effects					
Diagnosis	44,7859	10	4,47859	2,03	0,0376
Pipas	60,5956	3	20,1985	9,14	0,0000
Cci	63,3295	10	6,33295	2,87	0,0034
Temperature	117,049	24	4,87703	2,21	0,0032
Sbp	144,074	15	9,60492	4,35	0,0000
Residual	229,738	104	2,20902		
Total (corrected)	707,988	166			

Therefore, the analysis shows that it is advisable to use separate scales before and after surgery to predict the probability of POC development in AP. To create such scales, it is advisable to use indicators of clinical signs of peritonitis before surgery, body temperature, CCI, SBP, WSSS, PIPAS.

Conclusion

1. Criteria MPI, PIPAS, WSSS have the greatest influence on the probability of POC occurrence in AP, but none of these criteria is sufficient alone.

2. The set of indicators of diagnosis, clinical signs of peritonitis before surgery, body temperature, CCI, SBP have a statistically significant effect on POC at the 95.0% confidence level before surgery.

3. The combination of indicators of diagnosis, body temperature, CCI, SBP, WSSS or PIPAS have a statistically significant effect on POC at the 95.0% confidence level after surgery.

4. The creation of a reliable prognostic scale is possible using a complex of the described factors.

Prospects for further research. Creation of a prognostic scale for acute peritonitis taking into account the obtained data.

References

- Godinez-Vidal AR, Cinta-Egaña IA, Ornelas-Oñate LA, García-Vivanco DM, Gutiérrez-Uvalle GE, Gracida-Mancilla NI. Application of the Kiewiet-Van Ruler model to predict the need for relaparotomy in patients with secondary peritonitis. *Cir Cir.* 2019;87(2):158-63. DOI: 10.24875/CIRU.18000284.
- Tartaglia D, Marin JN, Nicoli AM, De Palma A, Picchi M, Musetti S, et al. Predictive factors of mortality in open abdomen for abdominal sepsis: a retrospective cohort study on 113 patients. *Updates Sur.* 2021;73(5):1975-82. DOI: 10.1007/s13304-021-01012-8.
- Špička P, Chudáček J, Řezáč T, Starý L, Horáček R, Klos

D. Prognostic Significance of Simple Scoring Systems in the Prediction of Diffuse Peritonitis Morbidity and Mortality. *Life (Basel).* 2022;12(4):487. DOI: 10.3390/life12040487.

4. Sartelli M, Abu-Zidan FM, Labricciosa FM, Kluger Y, Coccolini F, Ansaloni L, et al. Physiological parameters for Prognosis in Abdominal Sepsis (PIPAS) Study: a WSES observational study. *World J Emerg Surg.* 2019;14:34. DOI: 10.1186/s13017-019-0253-2.

5. Grynchuk AF, Grynchuk FV, Polianskiy Iiu. A scale for predicting postoperative septic complications at acute peritonitis. *Klinichna ta eksperymental'na patolohiia.* 2016;15(2):50-3. DOI: 10.24061/1727-4338.XV.2.56.2016.12.

6. Negi R, Bhardwaj S, Singh S, Gupta S, Kaushik R. Peritonitis-associated hyperlactatemia for evaluating mortality in secondary peritonitis. *ANZ J Surg.* 2022;90(12):2463-66. DOI: 10.1111/ans.16278.

7. Kao AM, Maloney SR, Prasad T, Reinke CE, May AK, Heniford BT, et al. The CELIOtomy Risk Score: An effort to minimize futile surgery with analysis of early postoperative mortality after emergency laparotomy. *Surgery.* 2020;168(4):676-83. DOI: 10.1016/j.surg.2020.05.037.

8. Sartelli M, Abu-Zidan FM, Catena F, Griffiths EA, Di Saverio S, Coimbra R, et al. Global validation of the WSES Sepsis Severity Score for patients with complicated intra-abdominal infections: a prospective multicentre study (WISS Study). *World J Emerg Surg.* 2015;10:61. DOI: 10.1186/s13017-015-0055-0.

9. Linder MM, Wacha H, Feldmann U, Wesch G, Streifensand RA, Gundlach E, et al. The Mannheim peritonitis index. An instrument for the intraoperative prognosis of peritonitis. *Chirurg.* 1987;58(2):84-92.

10. Luise M, Müller A. Peritonitis-Index-Altona: PIA II: Entwicklung eines prognostischen Indices an 567 Fällen. *Hamburg:* 1987. 52 p.

11. Kologlu M, Elker D, Altun H, Sayek I. Validation of MPI and PIA II in two different groups of patients with secondary peritonitis. *Hepatogastroenterology* 2001;48(37):147-51.

12. Ramteke H, Deshpande SG, Bhojar R. The Role of the Mannheim Peritonitis Index for Predicting Outcomes in Patients With Perforation Peritonitis in a Rural Hospital in India. *Cureus.* 2023;15(3):e36620. DOI: 10.7759/cureus.36620.

13. Abdel-Kader S, Sartelli M, Abu-Zidan FM. Complicated intra-abdominal infections: a prospective validation study of the WSES Sepsis Severity Score. *Singapore Med J.* 2019;60(6):317-21. DOI: 10.11622/smedj.2018120.

14. Gomes CA, Sartelli M, Podda M, Di Saverio S, Coccolini F, Segovia-Lohse HA, et al. Laparoscopic versus open approach for diffuse peritonitis from appendicitis ethiology: a subgroup analysis from the Physiological parameters for Prognosis in Abdominal Sepsis (PIPAS) study. *Updates Surg.* 2020;72(1):185-91. DOI: 10.1007/s13304-020-00711-y.

15. Iranya RN, Mbiine R, Semulimi AW, Nasige J, Makumbi T, Galukande M. Comparison of the PIPAS severity score tool and the QSOFA criteria for predicting in-hospital mortality of peritonitis in a tertiary hospital in Uganda: a prospective cohort study. *BMC Surg.* 2022;22(1):291. DOI: 10.1186/s12893-022-01743-4.

16. Gueiros LDS, Fonseca CMD, Duarte NMDM, Antunes OS. Mannheim's peritonitis index in the prediction of postoperative outcome of peritonitis. *Rev Col Bras Cir.* 2022;49:e20222991. DOI: 10.1590/0100-6991e-20222991.

17. Sánchez-Díaz JS, Escarraman-Martínez D, Guerrero-Gutiérrez MA, Meza-Comarán HD, Mancilla-Galindo J, Peniche-Moguel KG, et al. Simplified acute physiology score II and Mannheim peritonitis index are associated with in-hospital mortality in patients with abdominal sepsis admitted to ICU. *Cir*

Original research

Cir. 2022;90(S2):81-91. DOI: 10.24875/CIRU.22000219.

18. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal

studies: development and validation. J Chronic Dis.

1987;40(5):373-83. DOI: 10.1016/0021-9681(87)90171-8.

Відомості про авторів

Шурма Андрій Ігорович – аспірант кафедри хірургії № 1, Буковинський державний медичний університет, м. Чернівці, Україна.

Гринчук Федір Васильович – д-р медичних наук, професор, професор кафедри хірургії № 1, Буковинський державний медичний університет, м. Чернівці, Україна.

Information about the authors

Shurma Andriy Ihorovych – graduate student of the Department of Surgery № 1, Bukovinian State Medical University, Chernivtsi, Ukraine.

Grynychuk Fedir Vasyliovych – Doctor of Medical Sciences, Professor, Professor of the Department of Surgery № 1, Bukovinian State Medical University, Chernivtsi, Ukraine.

*Надійшла до редакції 25.05.23
Рецензент – проф. Польовий В.П.
© A.I. Shurma, F.V. Grynychuk, 2023*