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I. A. Moldovanov https://orcid.org/0000-0002-9354-6701
D. D. Zabolotna https://orcid.org/0000-0001-7807-8148

EVALUATION OF RISK FACTORS FOR INTRAOPERATIVE BLEEDING IN ENDOSCOPIC SURGERY IN PATIENTS WITH CHRONIC RHINOSINUSITIS WITH NASAL POLYPS AND ASPIRIN-EXACERBATED RESPIRATORY DISEASE

State Institution "O. S. Kolomiichenko Institute of Otolaryngology of the National Academy of Medical Sciences of Ukraine", Kyiv, Ukraine

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Background. Chronic rhinosinusitis with nasal polyps (CRSwNP) is a common inflammatory disease of the paranasal sinuses that significantly impacts the quality of life. Functional endoscopic sinus surgery is the standard surgical method; however, intraoperative bleeding is a clinically significant issue, especially in patients with aspirin-exacerbated respiratory disease (AERD).

Objective. To assess factors associated with increased intraoperative bleeding in patients with CRSwNP and AERD and compare the extent of intraoperative bleeding between AERD and non-AERD groups.

Methods. A retrospective analysis was conducted on 40 patients who underwent endoscopic endonasal pansinusotomy (EEP): 27 with AERD and 13 without AERD. Assessed parameters included intraoperative blood loss (mL), surgical field visualization (Boezaart scale), and disease severity (modified Lund–Mackay scale). Statistical analysis involved Student's t-test and Pearson's correlation coefficient ($p < 0.05$).

Results. Patients with AERD had significantly higher intraoperative blood loss (161.9 ± 39.5 mL vs. 108.5 ± 45.0 mL, $p = 0.001$) and poorer surgical field visibility (Boezaart score: 3.26 ± 0.7 vs. 2.54 ± 0.7, $p = 0.009$) compared to non-AERD patients. The modified Lund–Mackay score was also higher in AERD patients (36.07 ± 10.5 vs. 27.69 ± 9.9, $p = 0.021$), indicating an association with increased intraoperative bleeding.

Conclusion. Patients with AERD have increased intraoperative bleeding and reduced surgical field visibility. The modified Lund–Mackay score may help predict bleeding risk, highlighting the need for individualized preoperative strategies to minimize surgical complications.

Keywords: sinusitis, nasal polyps, aspirin-exacerbated respiratory disease, endoscopy, bleeding.

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І. А. Молдованов, Д. Д. Заболотна

ОЦІНКА ФАКТОРІВ РИЗИКУ ІНТРАОПЕРАЦІЙНОЇ КРОВОТЕЧІ ПРИ ЕНДОСКОПІЧНІЙ ХІРУРГІЇ У ПАЦІЄНТІВ ІЗ ХРОНІЧНИМ ПОЛІПОЗНИМ РИНОСИНУСИТОМ ТА АСПІРИНОВОЮ ТРІАДОЮ (AERD)

Державна установа «Інститут отоларингології імені проф. О. С. Коломійченка Національної академії медичних наук України», Київ, Україна

У статті представлено результати дослідження факторів, які впливають на інтраопераційну кровотечу під час ендоскопічної ендоназальної хірургії у пацієнтів із хронічним поліпозним риносинуситом (ХРСзНП), асоційованим з аспірин-екзацербованим респіраторним захворюванням (AERD). Вивчено дані 40 пацієнтів, які становили дві групи: з AERD (n = 27) та без AERD (n = 13). Встановлено, що пацієнти з AERD мали значно вищий рівень періопераційної крововтрати (161,9 ± 39,5 мл проти 108,5 ± 45,0 мл, p = 0,001), а також гіршу візуалізацію операційного поля за шкалою Боезарта (3,26 ± 0,7 проти 2,54 ± 0,7, p = 0,009). Виявлено також більшу поширеність поліпозного процесу у пацієнтів з AERD за модифікованою шкалою Lund–Mackay (36,07 ± 10,5 проти 27,69 ± 9,9, p = 0,021), що дає можливість використовувати цей показник як прогностичний маркер ризику інтраопераційної крововтрати. Результати дослідження можуть бути використані для оптимізації передопераційного ведення пацієнтів з AERD з метою профілактики ускладнень під час хірургічного втручання.

Ключові слова: синусит, назальні поліпи, аспірин-індуковане респіраторне захворювання, ендоскопія, кровотеча.

Introduction

Chronic rhinosinusitis with nasal polyps (CRSwNP) is a common inflammatory disease of the upper respiratory tract characterized by chronic inflammation of the mucous membrane of the nasal cavity and paranasal sinuses, resulting in the formation of nasal polyps. This condition significantly impairs patients' quality of life due to persistent nasal obstruction, mucous and/or purulent discharge, impaired olfaction, and chronic facial pain. According to recent data, CRSwNP occurs in approximately 2–4% of the adult population [15]. One of the most effective surgical treatments for CRSwNP is endoscopic endonasal surgery, which allows for the removal of polyps, improved sinus ventilation, and restoration of normal function of the nose and paranasal sinuses. Evidence shows that the use of modern endoscopic techniques significantly reduces

operative trauma and improves surgical outcomes [11, 12].

A distinct form of CRSwNP is the polyposis rhinosinusitis associated with intolerance to nonsteroidal anti-inflammatory drugs, known as aspirin-exacerbated respiratory disease (AERD), which is characterized by the triad of bronchial asthma, hypersensitivity to cyclooxygenase-1 (COX-1) inhibitors, and the presence of nasal and paranasal sinus polyps. Patients with AERD typically exhibit a more severe disease course and a higher risk of polyp recurrence after surgery. Laidlaw et al. indicate that AERD occurs in 7% of patients with CRSwNP and is characterized by significantly greater resistance to standard treatments [5]. In addition, this group of patients are at increased risk of intraoperative bleeding, which complicates surgical management and may increase the risk of postoperative complications [5].

Recent studies show that patients with AERD often have elevated IgE levels, associated with allergic responses and enhanced inflammation. IgE plays a key role in the pathophysiology of allergic diseases and contributes to chronic airway inflammation [7]. According to Mullol et al., elevated IgE levels in patients with AERD correlate with disease severity and increased risk of intraoperative bleeding during endoscopic procedures [4, 9]. This is due to IgE-mediated inflammation, which increases vascular permeability and bleeding risk. Studies also indicate that optimal management of anticoagulant therapy before surgery can significantly reduce the risk of intraoperative bleeding [10].

Objective. To analyze factors contributing to increased intraoperative bleeding in patients with CRSwNP and AERD during endoscopic endonasal surgery. The study will also compare intraoperative bleeding between CRSwNP patients with and without AERD, which will allow determination of management differences between these two groups and the development of recommendations to optimize surgical treatment.

Materials and Methods

To achieve the objective and accomplish the tasks, from 2023 to 2024, clinical and laboratory data of 40 patients were analyzed: including 17 females (42.5%) and 23 males (57.5%), aged 20–70 years (mean age 45.9 ± 13.2 years), who underwent surgical treatment for "Chronic rhinosinusitis with nasal polyps" (J32.0 Chronic sinusitis, J32.4 Chronic pansinusitis, J33 Nasal polyp) – "Endoscopic endonasal pansinusotomy (EEP)" at the clinic of the State Institution "O. S. Kolomiichenko Institute of Otolaryngology of the National Academy of Medical Sciences of Ukraine." The study was approved by the Committee on Bioethics and Deontology of the State Institution "O. S. Kolomiichenko Institute of Otolaryngology of the National Academy of Medical Sciences of Ukraine" (Protocol No. 22/12 dated 28.12.2021) and conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent for the processing of their personal and clinical data for scientific purposes. Among comorbid conditions, 13 (32.5%) patients had hypertrophy of the inferior nasal turbinates, 20 (50%) had nasal septal deviation (J34.2), 12 (30%) patients had bronchial asthma (J45), and 27 (67.5%) had AERD. Clinical characteristics and parameters, in addition to age and sex, included: primary diagnosis and comorbidities, medical and personal history, body mass index, and intraoperative blood pressure indicators.

General clinical blood test parameters were analyzed (platelet count, ESR, % eosinophils in the leukocyte count), as well as coagulation profile (clotting time, prothrombin index, international normalized ratio). The extent of the polipoid process was assessed by endoscopic examination of the nasal cavity (Lund–Kennedy) and CT of the paranasal sinuses (modified Lund–Mackay scale).

Objective indicators of chronic rhinosinusitis were evaluated using the endoscopic scoring system (Lund–Kennedy), which assesses pathological visual findings in the nose and paranasal sinuses, including polyps, discharge, edema, scarring, and crust formation (the modified Lund–Kennedy score includes polyps, edema, and discharge, and has high inter-rater and test–retest reliability). This scoring system is most relevant for chronic rhinosinusitis with polyposis for evaluating pre- and postoperative states in endoscopic sinus surgery [8, 16].

The duration of the endoscopic stage (minutes), surgical field visibility, assessed using the Boezaart scale – and total perioperative blood loss (mL) were evaluated and analyzed. The surgical field visualization scale proposed by Andre P. Boezaart is an instrument for assessing the quality of the operative field during surgeries, particularly endoscopic procedures on the nasal sinuses. It helps objectively determine the degree of bleeding and its impact on visibility during surgery.

Boezaart scale:

- 0 points: no bleeding.
- 1 point: minimal bleeding; isolated drops of blood that do not interfere with the surgical process.
- 2 points: light bleeding; periodic suctioning is required, visibility remains satisfactory.
- 3 points: moderate bleeding; frequent suctioning, brief loss of clarity of the surgical field.
- 4 points: significant bleeding; continuous suctioning, visibility markedly compromised.
- 5 points: massive bleeding; surgery becomes impossible due to complete lack of visualization.

This scale is widely used in studies assessing the influence of different anesthetic methods on surgical field quality [1, 13].

All cases were divided into two groups: study group (with AERD) – 27 (67.5%) patients; and control group (without AERD) – 13 (32.5%) patients.

Research materials were statistically analyzed using parametric and non-parametric methods. Data accumulation, correction, systematization, and visualization processed and visualized using Microsoft Excel. Statistical analysis was performed using Orange3-3.36.2 software. For quantitative indicators with normal distribution, data were combined into variation series in which arithmetic means (M) and standard errors (m) were calculated. Nominal data were described by absolute numbers and percentages. When comparing mean values in normally distributed quantitative datasets, Student's t-test was calculated. Obtained t-test values were compared with critical values. Differences were considered statistically significant at $p < 0.05$.

Comparison of nominal data was performed using Pearson's χ^2 test, which allows assessment of the significance of differences between the actual number of results or qualitative characteristics in each category and the theoretical number expected under the null hypothesis. The χ^2 value was compared with critical values for (r–1) × (c–1) degrees of freedom. If the obtained value exceeded the critical value, a statistical association between the studied risk factor and the outcome was concluded.

The Pearson correlation coefficient r_{xy} was used to assess the strength of association between quantitative indicators with normal distribution. The statistical significance of the correlation was evaluated using the t-test. The obtained t_r value was compared with the critical value for a given significance level and degrees of freedom n-2. Correlation coefficients r_{xy} were interpreted according to Chaddock's scale (Table 1).

Table 1

Chaddock's scale

Correlation coefficient value r_{xy}	Characteristic of the strength of the correlation
less than 0.1	no correlation
0.1–0.3	weak
0.3–0.5	moderate
0.5–0.7	noticeable
0.7–0.9	strong
0.9–0.99	very strong

To study correlation between phenomena represented by quantitative data with a non-normal distribution, the non-parametric Spearman rank correlation coefficient was used. Statistical significance of correlation was assessed by the t-test. If the calculated t value was less than the critical value for the given degrees of freedom and significance level, the correlation was considered non-significant; if greater, the correlation was considered statistically significant. Correlation coefficients ρ were also interpreted according to Chaddock's scale.

Research results and their discussion

Both groups had no statistically significant differences in the majority of the analyzed clinical and laboratory parameters, meaning that the cases included in the study adequately represent the object and subject of the research (Table 2), and thus the obtained results and conclusions can be considered well-grounded.

The parameter "total perioperative blood loss in mL" was significantly and statistically higher in patients of the study group (with AERD): mean values 161.9 ± 39.5 mL vs. 108.5 ± 45.0 mL (Student's t-test = 3.655, p = 0.001), as shown in Figure 1. At the same time, the minimum and maximum values of this parameter also differed between the groups.

Similar group differences were found in the Boezaart score (visibility of the surgical field during endoscopic surgery (bleeding level)) – a significantly and statistically higher score was observed in patients of the study group (with AERD): mean values 3.26 ± 0.7 vs. 2.54 ± 0.7 (Student's t-test = 2.858, p = 0.009), as shown in Fig. 2.

A statistically significantly higher modified Lund–Mackay score was also observed in patients of the study group (with AERD): mean values 36.07 ± 10.5 vs. 27.69 ± 9.9 (Student's t-test = 2.456, p = 0.021), as shown in Figure 3, which may serve as a prognostic criterion (factor) – an assessment of the potential expected blood loss during endoscopic endonasal pansinusotomy already at the stage of preoperative preparation.

The parameters "total perioperative blood loss in mL" and the Boezaart score had a moderate positive correlation (Pearson's r_{xy} = +0.615), and did not differ between the groups (Fig. 4), which may indicate the independence of the Boezaart score on the patient's underlying pathology.

In contrast, "total perioperative blood loss in mL" differed substantially between the groups depending on the duration of the endoscopic stage: it had a strong positive correlation (Pearson's rxy = +0.73) in the control group (patients without AERD) and did not depend on the duration of surgery in patients of the study group (with AERD), although it was statistically significantly higher in

Table 2

Analyzed clinical and laboratory indicators in groups

Characteristics and indicators	Study group (n = 27)	Control group (n = 13)	Level of significance of differences
Age	47.7 ± 13.2	42.2 ± 11.7	p = 0.2
Gender: female male	 25.0% 42.5%	 17.5% 15.0%	p = 0.5
Body Mass Index	27.0 ± 4.3	26.1 ± 4.4	p = 0.6
Systolic Blood Pressure (SBP), mmHg	68.4 ± 12.2	72.5 ± 17.8	p = 0.5
Platelet Count, ×10⁹/L	270.2 ± 56.7	262.9 ± 52.7	p = 0.7
ESR, mm/hour	7.0 ± 4.5	5.1 ± 3.2	p = 0.1
Eosinophils in the Leukocyte Formula, %	3.2 ± 2.5	3.1 ± 2.6	p = 0.9
Coagulation Time, s	236.8 ± 24.6	227.7 ± 12.5	p = 0.1
Prothrombin Index, %	95.8 ± 7.4	93.9 ± 6.3	p = 0.4
International Normalized Ratio	1.06 ± 0.09	1.07 ± 0.08	p = 0.6
Duration of the Endoscopic Stage of Surgery, min	95.9 ± 22.8	98.9 ± 38.0	p = 0.8
Lund–Kennedy scale score	10.3 ± 1.6	10.0 ± 2.0	p = 0.7

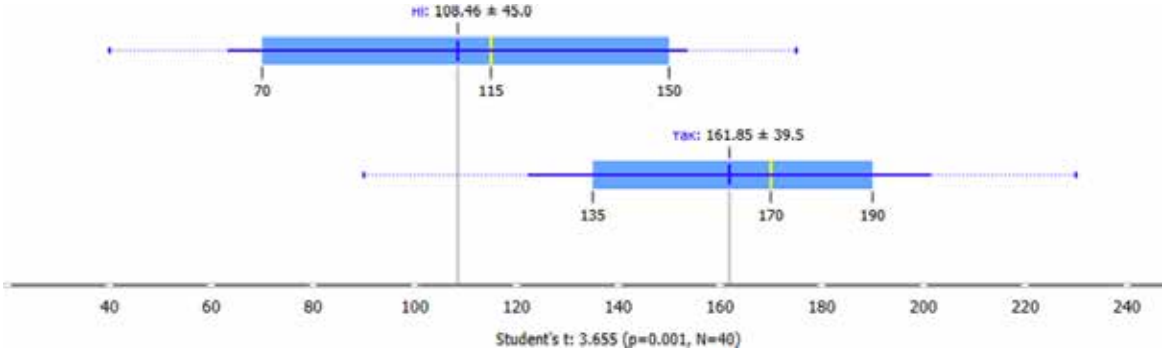

Fig. 1. Boxplot of the distribution of "total perioperative blood loss in mL" in patients of the study group ("yes") and control group ("no")

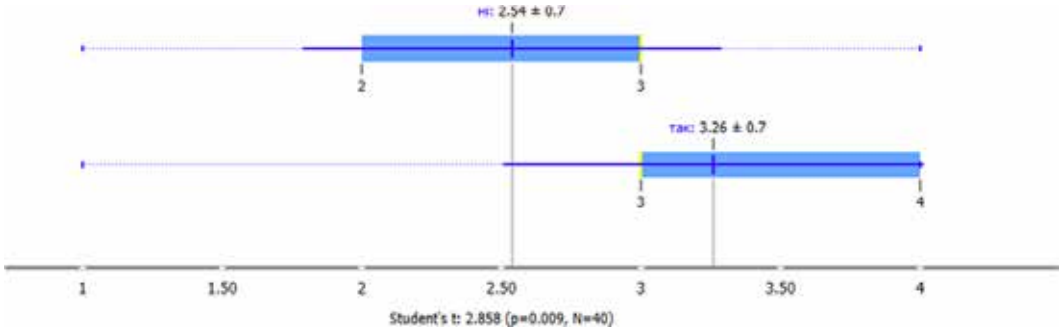

Fig. 2. Boxplot of the distribution of the Boezaart score in patients of the study group ("yes") and control group ("no")

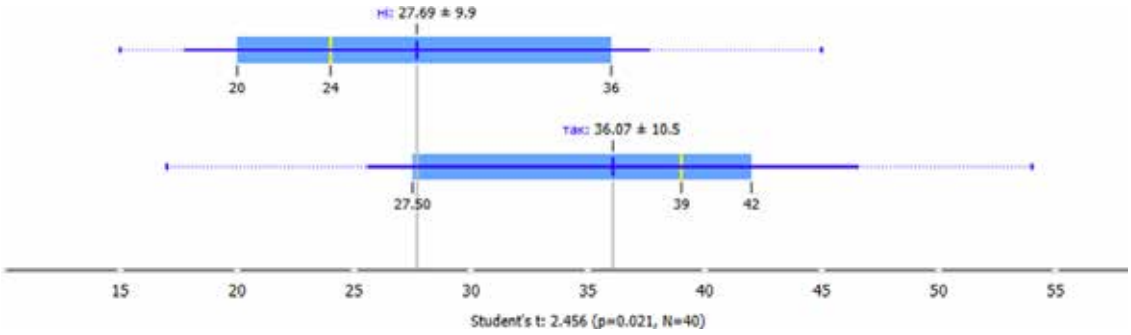

Fig. 3. Boxplot of the distribution of the modified Lund–Mackay score in patients of the study group ("yes") and control group ("no")

this group (Fig. 5). This may indicate the significant clinical relevance of AERD – whenever such pathology is present, substantial blood loss during endoscopic sinus surgery in chronic rhinosinusitis with nasal polyps should always be anticipated, predicted, and prevented.

Correlation between other characteristics and parameters was absent, weak, or of no substantial clinical significance in the context of the present study.

The results of our study confirm the data of other authors regarding the distinct clinical and pathophysiological features of AERD patients compared to patients without AERD. According to the recommendations of the European Academy of Allergy and Clinical Immunology (EAACI), NSAID-induced respiratory disease is characterized by chronic eosinophilic inflammation involving both the upper and lower airways, and manifests as a severe course of chronic rhinosinusitis with nasal polyps and bronchial asthma [4]. The pathogenesis of AERD is associated with disturbances in arachidonic acid metabolism, particularly through the blockade of cyclooxygenase-1 (COX-1), which leads to a deficiency of prostaglandin E2 (PGE2) and an excess of leukotrienes, which are potent mediators of inflammation [4].

In our study, the significantly higher blood loss and worse visibility of the surgical field in patients with AERD can be explained precisely by this enhanced eosinophilic inflammation, which is also confirmed by the results of other authors. In particular, Kowalski et al. (2018) noted

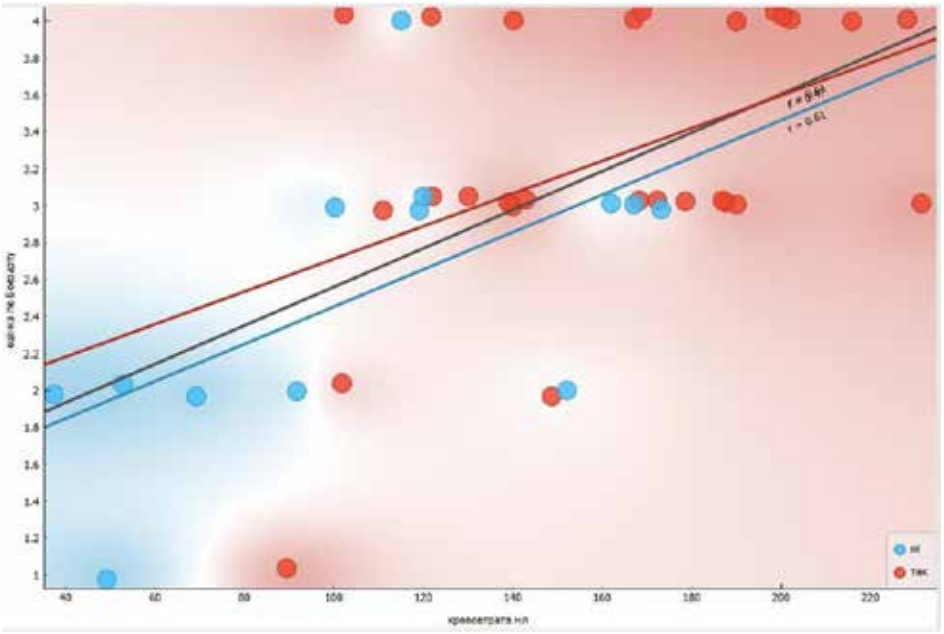

Fig. 4. Correlation between “total perioperative blood loss in mL” and the Boezaart score in patients of the study group (“yes”) and control group (“no”)

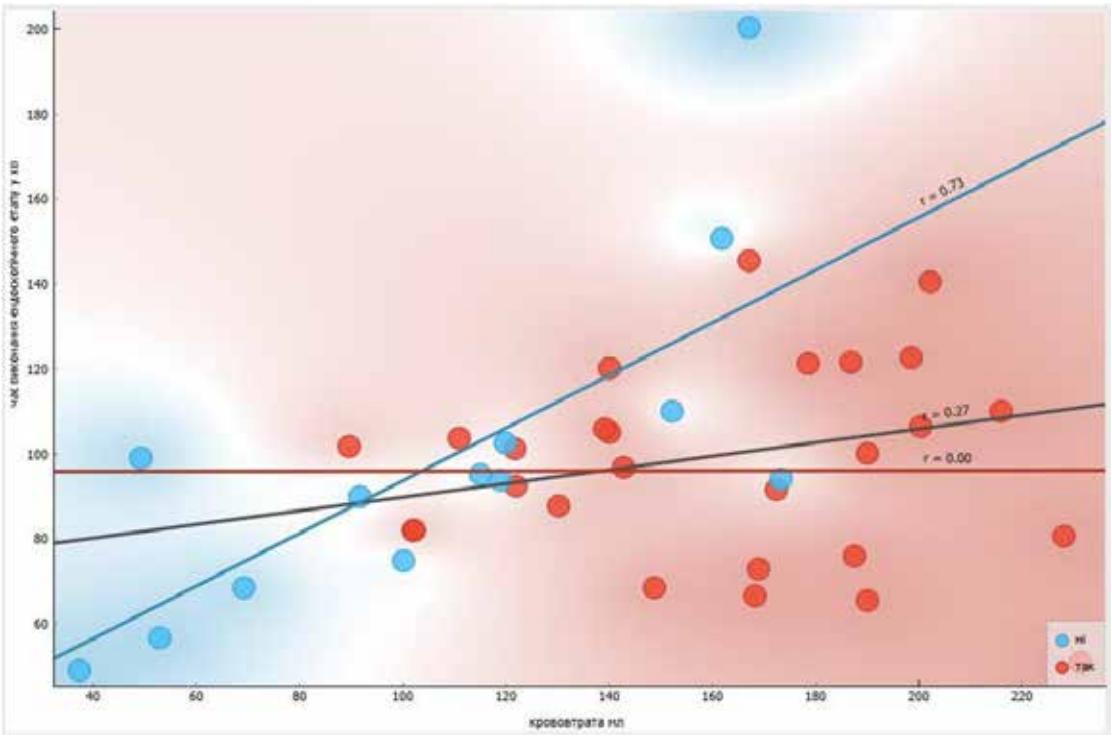

Fig. 5. Correlation between “total perioperative blood loss in mL” and “duration of the endoscopic stage in minutes” in patients of the study group (“yes”) and control group (“no”)

that patients with AERD exhibit pronounced eosinophilic infiltration of the nasal mucosa, increased levels of cysteinyl leukotrienes and PGD2, which contribute to chronic inflammation and polypoid tissue transformation [3]. This, in turn, leads to more severe disease course of chronic rhinosinusitis with nasal polyps and increases perioperative risks, including elevated intraoperative blood loss.

The obtained results are consistent with data from a domestic researcher who also reported high intraoperative bleeding in patients with AERD and emphasized the importance of preoperative preparation to provide adequate visualization of the surgical field. In his work, the use of aminocaproic acid (ACA) contributed to a gradual reduction of bleeding and

improvement of the surgical field to a level of 4–5 points. At the same time, unlike his study, in our work no changes were found in general coagulation parameters, but a significant impact of the extent of the polypoid process (according to the Lund–Mackay scale) on the level of perioperative blood loss was established. This indicates that, in addition to coagulation mechanisms, local inflammatory factors and vascular permeability play an important role in bleeding in patients with AERD, which must be considered during preoperative planning and therapy selection [2].

Thus, a comprehensive assessment of patients with AERD, taking into account the severity of the inflammatory process and the extent of polypoid changes, is necessary to optimize treatment strategies, reduce surgical risks, and improve postoperative outcomes.

Conclusions

Our study showed that intraoperative blood loss in patients with chronic rhinosinusitis with nasal polyps and AERD significantly exceeds the corresponding indicator in patients without AERD. This requires more careful planning of surgical interventions, taking into account the associated risks.

Assessment using the Boezaart scale confirmed significantly worse visualization of the surgical field in patients with AERD, which complicates the course of surgery and increases the risk of complications. The extent of the polypoid process according to the Lund–Mackay scale is an important prognostic criterion for the risk of increased bleeding.

It was also found that in patients with AERD, the level of blood loss does not depend on the duration of the surgery, which may indicate the key role of the pathogenetic features of the disease.

The obtained data support the need for enhanced preoperative preparation, including individualized hemostatic therapy and extended diagnostics to predict and prevent intraoperative bleeding.

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Електронна адреса для листування ivankriv2508199528@gmail.com