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# **BULLETIN OF SURGERY IN KAZAKHSTAN**

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# ACUTE PANCREATITIS IN AKMOLA REGION ACCORDING TO EMERGENCY SURGERY

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## Abstract

**Background:** Acute pancreatitis is a major issue in surgical practice, with high complications and mortality rates. It severely affects patient quality of life and places a significant economic strain on healthcare systems, making its study crucial for public health. This study aims to analyze trends in acute pancreatitis incidence in the Akmola region from 2009 to 2022.

**Materials and methods:** The study is based on a retrospective analysis of data from the Ministry of Health of the Republic of Kazakhstan according to the International Classification of Diseases-10 code: K85. Methods of health statistics and time series analysis were used to assess the dynamics of morbidity.

**Results:** There was an increase in the total number of hospitalizations from 865 cases in 2009 to 1.061 in 2022. The percentage of surgical interventions decreased from 5.7% to 4.2%, while the share of conservative treatment increased to 95.8%. The mortality rate among operated patients was 20.4% in 2019 and increased to 33.3% in 2022. The incidence of hospitalization increased from 117.1 per 100000 population in 2009 to 144.6 per 100000 population in 2022, with a decrease in the rate of late visits from 42.6 to 36.1 per 100000 population, respectively. **Conclusion:** It has been established that for patients in the second group according to the Enhanced Recovery After Surgery strategy, hemodynamic support and effective pain management can contribute to early patient mobilization after surgery. Early mobilization, in turn, can expedite recovery and reduce the length of hospital stay, ultimately leading to potential cost savings.

**Conclusion.** The study highlights the need to improve medical approaches to acute pancreatitis in the Akmola region. The results indicate the critical importance of early diagnosis and timely hospitalization to reduce complications and mortality. Additional research is needed to develop more effective clinical protocols.

## Introduction

Acute pancreatitis represents a significant challenge in contemporary sur-

gical practice, characterized by a high incidence of complications and a substantial mortality risk.<sup>1</sup> The urgency of

accurate diagnosis and the necessity for effective therapeutic strategies highlight the complexity of managing this disease and underscore the importance of a multifaceted approach.<sup>2</sup>

The study of acute pancreatitis holds considerable relevance in the realm of public health and medical practice, owing to its profound impact on patient quality of life and the economic burden on healthcare systems.<sup>3</sup> The incidence of acute pancreatitis is approximately 20 cases per 100.000 individuals annually,<sup>4</sup> with heightened risk among the elderly population. The risk factors for acute pancreatitis are varied, encompassing lifestyle factors such as alcohol consumption and smoking, as well as medical conditions like gallstone disease and metabolic disorders.<sup>5</sup>

Regional disparities in the incidence and outcomes of acute pancreatitis can be attributed to differences in the accessibility and quality of medical care, necessitating the adaptation of medical strategies to local conditions.<sup>6</sup>

In the context of the Akmola region, modifying diagnostic and treatment protocols, enhancing the training of medical personnel,<sup>7</sup> ensuring access to advanced diagnostic equipment, and establishing a rapid response system could markedly improve patient outcomes and alleviate the burden on the healthcare system.<sup>8,9</sup>

The objective of this study was to analyze the epidemiological trends of acute pancreatitis in the Akmola region.

### Materials and Methods

**Data Collection:** This study is grounded on a retrospective analysis of data provided by the Ministry of Health of the Republic of Kazakhstan concerning acute pancreatitis (ICD-10: K85) from 2009 to 2022 in the Akmola region. The data were meticulously extracted from Form 14, which encompasses comprehensive information on all reported cases of acute pancreatitis within the specified region.

### Statistical Analysis

**Descriptive Analysis:** This initial phase aimed to establish a general overview of hospital incidence through the calculation of incidence rates per 100.000 of the total population. This foundational step facilitated the subsequent in-depth analyses by providing a baseline under-

standing of the data.

**Time Series Analysis:** Advanced time series methods were employed to elucidate trends in incidence rates over the study period. This included the application of the least squares method for trend identification and calculation of the average annual growth or decline rates, thereby enabling a robust temporal assessment of disease trends.

**Parametric and Nonparametric Methods:** These statistical techniques were used to evaluate the statistical significance of the observed trends. The combination of these methods ensured a comprehensive analysis, addressing both normally and non-normally distributed data.<sup>8,9</sup>

All statistical computations were executed using Microsoft Excel for basic analyses and an advanced online statistical package for more sophisticated analyses, ensuring accuracy and reliability in the findings.

**Ethical Considerations.** This study was conducted exclusively using publicly accessible administrative data, negating the need for direct interaction with individual participants and, consequently, ethical approval. Nevertheless, all data handling procedures strictly adhered to the Law of the Republic of Kazakhstan No. 257-IV dated March 19, 2010, "On State Statistics". Additionally, the confidentiality of information was rigorously maintained following the principles outlined by the Ethical Principles for Medical Research Involving Human Subjects (World Medical Association Declaration of Helsinki, 2013), ensuring that data were utilized solely for statistical purposes.

### Results

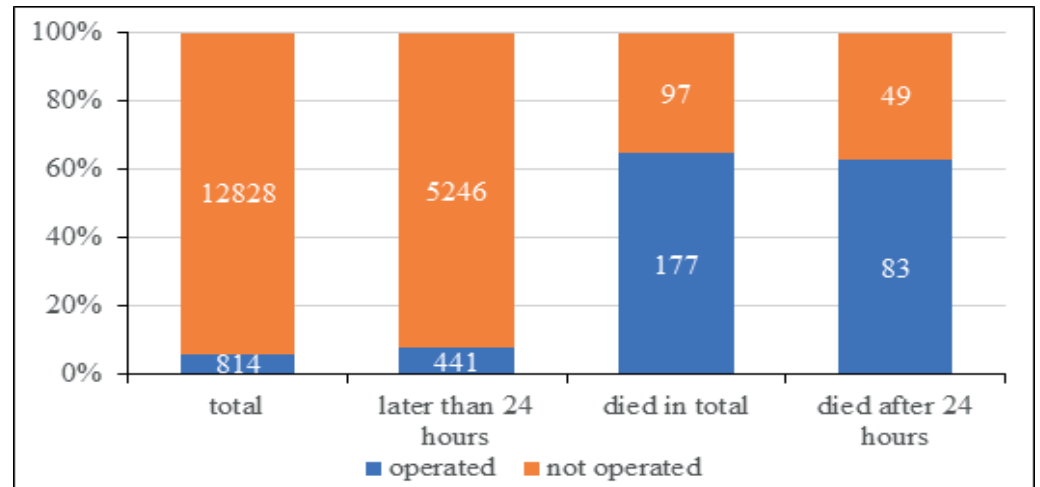
A retrospective analysis of hospitalization data for patients diagnosed with acute pancreatitis (ICD-10: K85) in hospitals within the Akmola region revealed a significant increase in the number of cases from 2009 to 2022. Specifically, in 2022, the number of hospitalized patients reached 1.061, representing a 22.7% increase compared to the 865 cases reported in 2009. Over the entire period analyzed, the total number of hospitalizations amounted to 13.642 patients.

The therapeutic approaches adopted in these cases were primarily conservative, with surgery being performed on 814

patients, accounting for 6% of the total cases. Conversely, conservative treatment was applied in 94% of cases, encompassing 12.828 patients (Figure 1).

**Figure 1.**

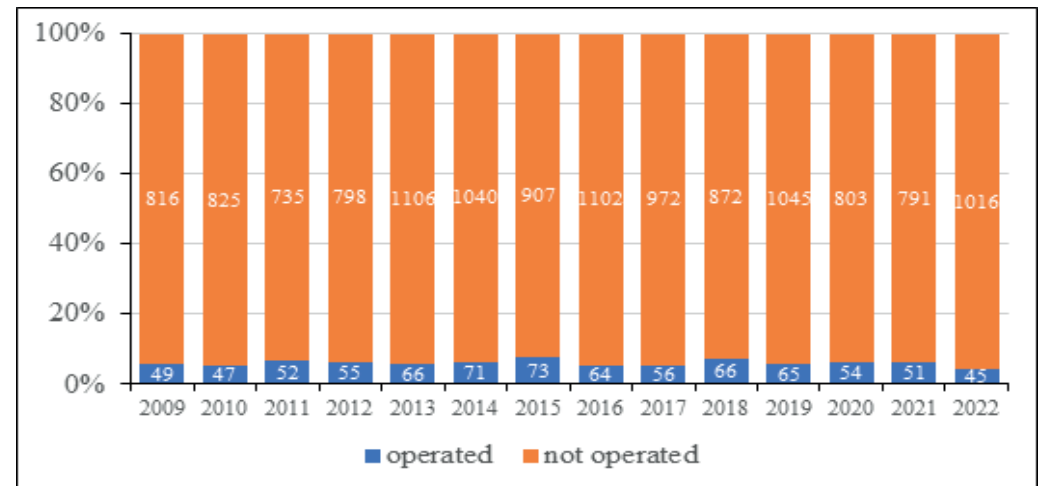
The number of patients with acute pancreatitis in hospitals in Akmola region in 2009-2022



The dynamics of the proportion of surgical interventions during the reviewed period indicated a downward trend, decreasing from 5.7% [49 cases] in 2009 to 4.2% [45 cases] in 2022. This decline may reflect advancements and improvements in conservative treatment methods, as well as potential shifts in the criteria for selecting patients for surgical intervention. Additionally, enhancements in diagnosis and the optimization of primary care have been noted, contributing to the prevention of complications and reducing the necessity for surgical interventions (Figure 2).

**Figure 2.**

Dynamics of the number of operated/non-operated patients with acute pancreatitis in hospitals of Akmola region in 2009-2022



An analysis of mortality rates among patients diagnosed with acute pancreatitis revealed that 274 individuals succumbed to the condition over the 14-year period, constituting 2% of the total number of hospitalized patients. Among those who died, 35.4% [97 individuals] had not undergone surgery, whereas 64.6% [177 individuals] had undergone surgical procedures. The mortality dynamics among operated patients warrant particular attention; in 2009, the mortality rate among operated patients was 20.4% [10 out of 49 patients], which increased to 33.3% [15 out of 45] in 2022. This upward trend suggests potential issues in clinical practice or changes in the disease's nature.

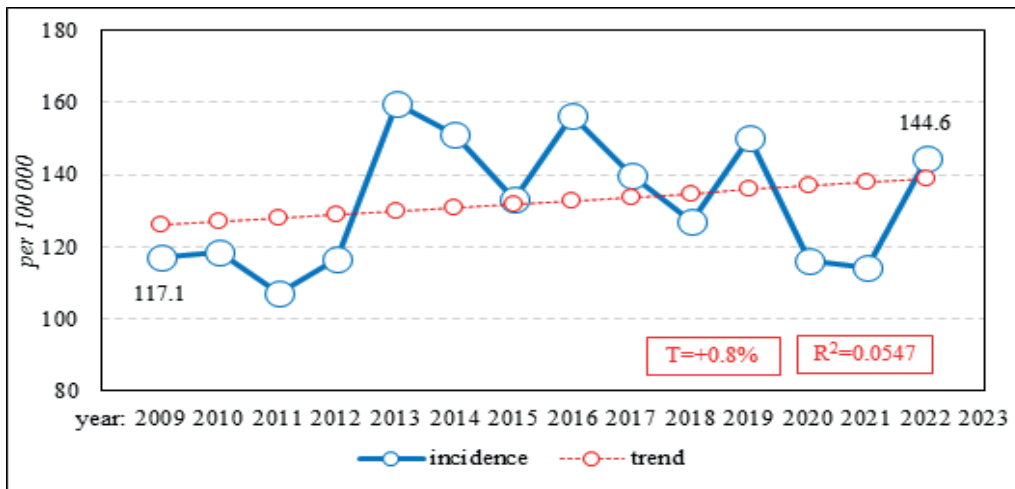
Special attention should be directed towards analyzing the timing of hospital admissions. Out of the total number of patients with acute pancreatitis, 5.687 [41.7%] were admitted to the hospital more than 24 hours after the onset of symptoms. Among these, 441 patients [7.8%] underwent surgical interven-



tion, with a mortality rate of 18.8% (83 deaths). In contrast, the mortality rate among those who did not undergo surgical treatment (5.246 patients) was significantly lower at 0.9% (49 deaths) (Figure 1). These findings underscore the critical importance of early diagnosis and timely hospitalization in reducing mortality risks associated with acute pancreatitis. Further research to investigate the underlying causes of high mortality in specific years and among particular patient categories could contribute to the develop-

ment of more effective clinical protocols and improved patient outcomes.

A study of the dynamics of hospital incidence of acute pancreatitis among the population of the Akmola region revealed a statistically significant increase in the incidence, rising from 117.1±4.0 cases per 100000 population in 2009 to 144.6±4.4 cases per 100000 population in 2022. This increase underscores the need for ongoing public health measures to address the rising burden of acute pancreatitis (Figure 3).

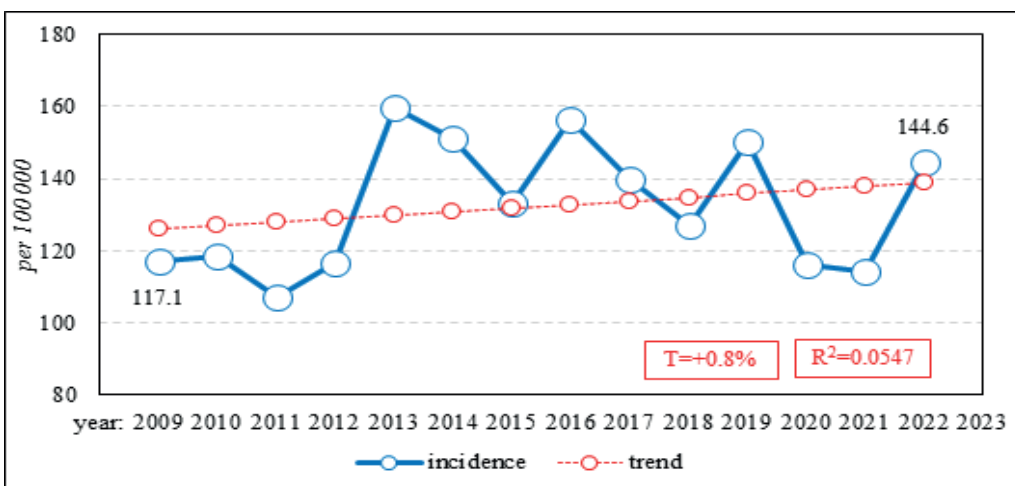


**Figure 3.** Dynamics of hospital incidence of acute pancreatitis in Akmola region in 2009-2022

The t-test value of 4.62, with  $p=0.000$ , indicates the statistical significance of the observed changes in hospital morbidity within the region's population. The average annual hospital morbidity rate for the analyzed period was  $132.4 \pm 4.8$  cases per 100000 population, with a 95% confidence interval ranging from 123.0 to 141.7. This study highlights the necessity of continuous monitoring of epidemiological indica-

tors and analyzing factors contributing to morbidity trends, which can inform the development of targeted preventive and therapeutic interventions to enhance public health outcomes.

A study of the hospital incidence dynamics of acute pancreatitis due to delayed treatment (more than 24 hours after symptom onset) in the Akmola region revealed significant changes from 2009 to 2022 (Figure 4).



**Figure 4.** Dynamics of late hospital incidence of acute pancreatitis in Akmola region in 2009-2022

In 2009, the average annual rate of hospitalizations associated with late treatment was  $42.6 \pm 2.4$  cases per 100000 population, with a 95% confidence interval from 37.9 to 47.3. By 2022, this rate had significantly decreased to  $36.1 \pm 2.2$  cases per 100000 population, with a 95% confidence interval from 31.8 to 40.5. The difference between the 2009 and 2022 data was statistically significant, as confirmed by a t-test value of 2.0 and a significance level of  $p=0.046$ . The analysis of the decline rate in late hospital morbidity indicators showed an average annual decrease of 4.5%. However, the coefficient of determination ( $R^2=0.2995$ ) indicates a low degree of model approximation, reflecting the instability of the observed decreasing trend in late applicant morbidity. This decline may be associated with improved public awareness of the symptoms and complications of acute pancreatitis, increased early diagnosis programs, better access to medical care, and enhanced quality of primary care. These results underscore the importance of sustained awareness campaigns and improving healthcare service accessibility to prevent late referrals and reduce associated morbidity and mortality.

#### Discussion

Comparing the findings from the Akmola region with global data reveals several key aspects and differences in the epidemiology, diagnosis, and treatment of acute pancreatitis.

According to the Global Burden of Disease study, morbidity and mortality from acute pancreatitis vary significantly by region. Regions such as Eastern Europe exhibit high morbidity and mortality rates, aligning with the data from the Akmola region which also shows elevated incidence and mortality. These disparities can be attributed to differences in access to healthcare, the quality of medical services, and the prevalence of major risk factors such as alcohol consumption and smoking.<sup>10,11</sup>

International studies indicate an overall improvement in the outcomes of acute pancreatitis due to early diagnosis and effective initial management, which includes adequate rehydration and early nutritional support. This trend is mirrored in the Akmola region, where a decrease in the number of surgical interventions and

an increase in conservative treatments have been observed. However, the high mortality rate among patients undergoing surgery, as noted in your study, suggests a need for further analysis of the quality of surgical care and the timeliness of medical intervention.<sup>11</sup>

The significance of timely access to qualified medical care in improving patient prognoses for acute pancreatitis is well-documented in international literature. Effective early treatment strategies, such as proper hydration and early nutrition, have been shown to reduce mortality and complication rates. These findings underscore the necessity for improving medical protocols and enhancing the training of healthcare professionals to optimize early-stage treatment of pancreatitis.<sup>11</sup>

**Limitations:** The limitations of this study include its retrospective design, which may not provide the same depth of clinical detail as prospective research. Additionally, focusing solely on the Akmola region may limit the broader applicability of the findings to other regions with varying healthcare systems and population characteristics. The study's reliance on administrative data introduces the possibility of variability in reporting accuracy and completeness.

**What's known?** Acute pancreatitis is a common and serious condition often requiring emergency surgery due to its potential for severe complications. Literature highlights the unpredictability of the disease's progression, with timely intervention being crucial to reducing mortality and minimizing the impact on healthcare resources.

**What's new?** The study provides new insights into the trends of acute pancreatitis in the Akmola region, showing an increase in hospitalizations and a shift towards conservative treatments over surgical interventions. It underscores the importance of early diagnosis and timely hospitalization in reducing complications and mortality, with the need for improved clinical protocols.

#### Conclusion

The results underscore the importance of ongoing monitoring of epidemiological indicators and the analysis of factors contributing to changes in morbidity and mortality from acute pancre-



atitis. This continuous monitoring will enable the development of targeted preventive and therapeutic measures aimed at improving public health outcomes and reducing the burden on the healthcare system. By identifying and addressing the factors contributing to high mortality rates, particularly among surgical patients, and by refining treatment protocols, healthcare providers in the Akmola region can enhance the quality of care for patients with acute pancreatitis. This approach will not only improve patient outcomes but also help in the efficient allocation of healthcare resources.

**Author's contributions:** All the authors participated equally in the study and writing of this article. TZh, NA, MR – Collection and preparation of data, primary

processing of the material and their verification. IG, JA, MR – Statistical processing and analysis of the material, writing the text of the article (material and methods, results). AS, TD, MS – Writing the text of the article (introduction, discussion). IN, BZ, RK – Concept, design and control of the research, approval of the final version of the article. All authors approved the final version of the manuscript

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# RESULTS OF GASTROINTESTINAL BLEEDING TREATMENT IN THE REPUBLIC OF KAZAKHSTAN OVER 10 YEARS

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## Abstract

Gastrointestinal bleeding (GIB) remains a significant cause of hospitalization and mortality worldwide, including in Kazakhstan. This retrospective study analyzes the incidence, treatment outcomes, and mortality of GIB in the Republic of Kazakhstan over a 10-year period (2014–2023) using data from 101,703 patients across 254 medical institutions. The study differentiates between non-variceal and variceal GIB, highlighting a 24.5% increase in non-variceal cases and a 45.1% increase in variceal cases due to higher rates of acute ulcerative lesions and liver cirrhosis, respectively. Men were disproportionately affected, accounting for 69.3% of cases, with the highest incidence in the 18–59 age group. Despite a 27.8% increase in GIB cases, overall mortality decreased from 7.8% in 2014 to 5.0% in 2023, largely due to advances in endoscopic hemostasis and critical care management. The mortality rate for non-variceal GIB decreased to 3.0%, while variceal GIB decreased from 23.8% to 13.6%. The results underscore the need for improved prevention, especially in high-risk populations using NSAIDs and anticoagulants, and in those with chronic conditions such as liver disease.

## Introduction

Gastrointestinal bleeding (GIB) remains a prevalent and dangerous complication of diseases affecting the digestive system, as well as other organs and systems. GIB is one of the leading causes of hospitalization and mortality worldwide.<sup>1–4</sup> According to the World Society of Emergency Surgery (WSES), the annual incidence of GIB ranges from 40 to 150 cases per 100,000 population, with hospital mortality rates varying from 2% to 14%.<sup>2,5,6</sup>

According to the worldwide classification, GIB can be categorized into non-variceal and variceal GIB. The primary causes of non-variceal bleeding are peptic ulcers of the stomach and duodenum, “acute” symptomatic erosions and ulcers, as well as Mallory-Weiss

syndrome. GIB of variceal etiology is a complication of liver cirrhosis and portal hypertension.<sup>1–3,5,6</sup>

In the United States, more than 300,000 individuals are hospitalized annually due to GIB.<sup>7</sup> The mortality rate for gastrointestinal bleeding reaches up to 10%.<sup>7,8</sup> In our country, GIB is a leading cause of death, accounting for 17–25% of all fatalities in surgical wards.

According to studies by *Simon et al.*, the majority of GIB cases were caused by peptic ulcers of the stomach and duodenum (31–67%).<sup>5</sup> Erosive and ulcerative lesions of the upper gastrointestinal tract accounted for 7–31%, stomach tumors for 2–8%, and Mallory-Weiss syndrome for 4–8%.<sup>5,6,8</sup>

Over the past few decades, the patterns of morbidity and mortality from

GIB have undergone significant changes. Several factors could play role in these changes. For example, advancements in pharmacology and the consequent possibility for of *Helicobacter pylori* eradication, as well as improvements in intraluminal endoscopy, and enhanced management of critically ill patients in intensive care units have all played key roles in reducing the risk of GIB.<sup>2,7</sup>

On the other hand, several factors could contribute to an increased prevalence of GIB in the population. These include a higher average life expectancy, the growing prevalence of cardiovascular diseases and other serious conditions, as well as the uncontrolled use of certain medications, such as NSAIDs, antiplatelet agents, and anticoagulants, which significantly contribute to the rise in GIB cases<sup>6</sup>.

In 2019, a study in Turkey examined the treatment outcomes of 652 patients with GIB across different periods. The patients were divided into two groups based on the treatment period: Group 1, consisting of 421 patients treated between 1993 and 1995, and Group 2, with 231 patients treated between 2015 and 2016. In the latter period, there was a significant increase in the number of elderly patients, as well as an increase in bleeding from acute ulcers in patients with comorbidities who were receiving anticoagulant therapy<sup>7</sup>.

Another study conducted in Finland examined the incidence and mortality from GIB in the general population, analyzing 39054 patients from 1987 to 2016. The incidence of upper gastrointestinal tract bleeding varied annually, ranging from 40 to 66 cases per 100000 people. Overall mortality from GIB ranged from 4.7% to 10.1%, with an average of 7.0%.<sup>9</sup>

Between 1993 and 2005, a mortality analysis of upper gastrointestinal tract bleeding was conducted in China at the Chinese University of Hong Kong. A total of 9375 patients with non-variceal bleeding were treated, with a mortality rate of 577 patients (6.2%). Notably, most patients (460 or 79.7%) died from causes unrelated to the bleeding itself. The most common causes of death were terminal-stage malignant tumors (33.7%), multiple organ failure (23.9%), and lung diseases (23.5%). Heart diseases, in-

cluding acute coronary syndrome and heart failure, accounted for 13.5% of the deaths, while cerebrovascular diseases contributed to 5.4% of the mortality.<sup>10</sup>

In Russia, a retrospective study of emergency surgical care was conducted over 17 years. From 2000 to 2017, there was a 31.4% decrease in the number of patients operated on for GIB. Postoperative mortality showed a slight reduction, from 12.8% in 2000 to 11.9% in 2017.<sup>2</sup>

The aim of the current study is to analyze the incidence and mortality of both non-variceal and variceal GIB in the Republic of Kazakhstan over the past 10 years. The findings of this study provide an assessment of the current state of GIB management and treatment in Kazakhstan.

### Materials and Methods

A retrospective study was conducted at the A.N. Syzganov National Scientific Center of Surgery to analyze the treatment outcomes of patients with gastrointestinal bleeding (GIB) who were urgently hospitalized in 254 medical organizations across the Republic of Kazakhstan over a 10-year period.

The materials were extracted from the information system of the Ministry of Health's "Electronic Registry of Hospitalized Patients" (ERHP). Data were extracted from ERIP based on the main diagnosis of patients who were treated in emergency situations for GIB on surgical wards across the country from 2014 to 2023. The selection process was comprehensive, including the entire population. Ethical standards were upheld, and no personal patient information was disclosed.

A total of 101 703 patients were treated in the Republic of Kazakhstan over 10 years, of which 69.3% were men and 30.7% were women. The age of the patients ranged from 18 to 98 years. The incidence of GIB per 100 000 population increased from 52.3 in 2014 to 82 in 2023. Over 10 years, the number of non-variceal upper gastrointestinal bleedings increased by 24.5%, largely due to a rise in acute and symptomatic ulcerative lesions of the upper GI tract. The number of cases of variceal gastrointestinal bleeding increased significantly by 45.1%, reflecting a rise in liver cirrhosis and its complications in the country.

For the analysis of non-variceal upper gastrointestinal bleeding, the following ICD-10 codes were considered for the primary diagnosis:

- K22.6 - Gastroesophageal laceration-hemorrhagic syndrome;
- K25.0 - Acute gastric ulcer with hemorrhage;
- K25.4 - Chronic or unspecified gastric ulcer with hemorrhage;
- K26.0 - Acute duodenal ulcer with hemorrhage;
- K26.4 - Chronic or unspecified duodenal ulcer with hemorrhage;
- K27.0 - Acute peptic ulcer of unspecified location with hemorrhage;
- K27.4 - Chronic or unspecified peptic ulcer with hemorrhage;
- K28.0 - Acute gastrojejunal ulcer with hemorrhage;
- K28.4 - Chronic or unspecified gastrojejunal ulcer with hemorrhage;
- K92.0 - Hematemesis;
- K92.1 - Melena;
- K92.2 - Unspecified gastrointestinal hemorrhage.

For bleeding of "variceal" etiology, the following ICD-10 codes from surgical departments were used:

- I85.0 - Esophageal varices with

bleeding;

I85.9 - Esophageal varices without bleeding;

K70.2 - Alcoholic fibrosis and sclerosis of the liver;

K70.3 - Alcoholic cirrhosis of the liver;

K74 - Fibrosis and cirrhosis of the liver;

K76.6 - Portal hypertension.

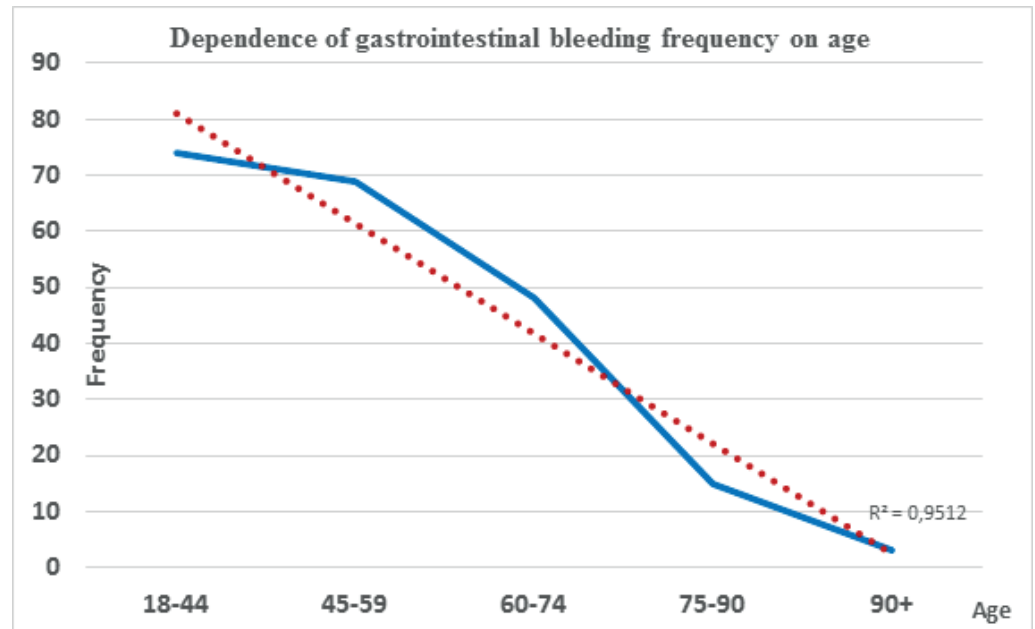
The study included individual cases of the disease, and a single patient could be included more than once if they were rehospitalized with a GIB diagnosis.

The following were excluded from the study: patients with lower gastrointestinal bleeding, rectal bleeding, patients under 18 years of age, and those admitted for planned (non-emergency) treatment.

**Statistical Analysis** The study carried out a correlation analysis using the Spearman method. Spearman's correlation coefficient ( $\rho$ ) is -1.0. The relationship between the studied characteristics is inverse, and the strength of the relationship, according to the Chaddock scale, is functional.

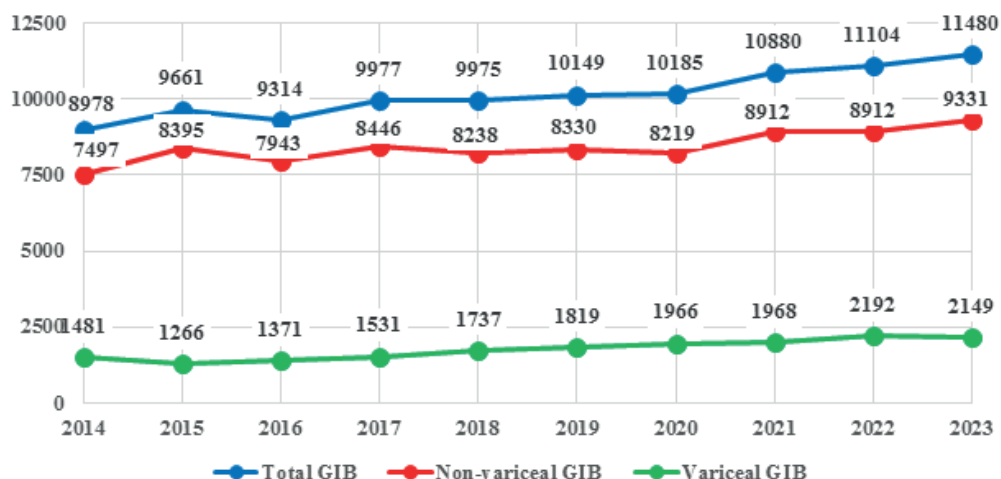
The number of cases of gastrointestinal bleeding decreases inversely with age (Figure 1).

**Figure 1.**  
Dependence of gastrointestinal bleeding frequency on age



As shown in Figure 2, the total number of treated GIB cases ranged from 8 978 in 2014 to 11 480 in 2023, an increase of 27.8%. By type of bleeding: 82.8% (84 223 cases) were non-variceal, and 17.2%

(17480 cases) were variceal in origin. There was an increase in both non-variceal bleeding cases from 7 497 in 2014 to 9 331 in 2023 and variceal bleeding cases from 1481 in 2014 to 2 149 in 2023.



**Figure 2.** Number of treated patients with GIB from 2014 to 2023. Results

Of the total number of treated patients, men accounted for 69.3% or 70 480 cases, while women accounted for 30.7% or 31 223 cases. The patients were classified according to the WHO age classification. The vast majority of the bleeding cases occurred in young and

middle-aged individuals, from 18 to 59 years, making up 70.3% or 71 518 cases. Among those affected in this age group, 74.9% were men, equating to 53 565 cases. In the elderly, senile, and long-lived age groups, the proportion of men was 56.0%, or 16 915 out of 30 185 cases.

Age Number		Total		Male		Female	
		Proportion (%)	Number	Proportion (%)	Number	Proportion (%)	Number
Young	18-44	36 482	35.9	28 333	40.2	8 149	26.1
Mid-dle-aged	45-59	35 036	34.5	25 232	35.8	9 804	31.4
Elderly	60-74	21 172	20.8	12 898	18.3	8 274	26.5
Senile	75-90	8 787	8.6	3 947	5.6	4 840	15.5
Longevity	90+	226	0.2	70	0.1	156	0.5
Total		101 703	100	70 480	69.3	31 223	30.7

\* Age according to WHO classification

**Table 1.** Distribution of Patients by Gender and Age

Table 2 presents the number of treated cases and the mortality rate from GIB during the period from 2014 to 2023. There is a noticeable annual increase in the number of hospitalized patients with GIB. A gradual decline in mortality is ob-

served, from 7.8% in 2014 to 5.0% in 2023. However, overall mortality from GIB remains high, primarily due to the high fatality rate from liver cirrhosis complications, such as bleeding from varicose veins in the esophagus and stomach.

Years	Treated, total	Mortality, Total	Overall Mortality, %
2014	8 978	699	7.8
2015	9 661	827	8.6
2016	9 314	706	7.6
2017	9 977	642	6.4
2018	9 975	696	7.0
2019	10 149	698	6.9
2020	10 185	779	7.7
2021	10 880	773	7.1

**Table 2.** Overall Mortality from Gastrointestinal Bleeding from 2014 to 2023

2022	11 104	665	6.0
2023	11 480	577	5.0
Total	101 703	7062	6.9

Figure 3 illustrates the annual dynamics of fatalities from GIB from 2014 to 2023. Over the 10-year period, a total of 7 062 patients died from GIB. Fatal outcomes from non-variceal upper gastrointestinal bleeding occurred in 3 470 patients (49.1%). Variceal bleeding was the cause of death in 3 592 patients (50.9%). Throughout the 10 years, there has been a decline in the number of fatalities from both non-variceal GIB and variceal GIB.

**Figure 3.**  
Number of Deceased Patients by Type of Gastrointestinal Bleeding from 2014 to 2023

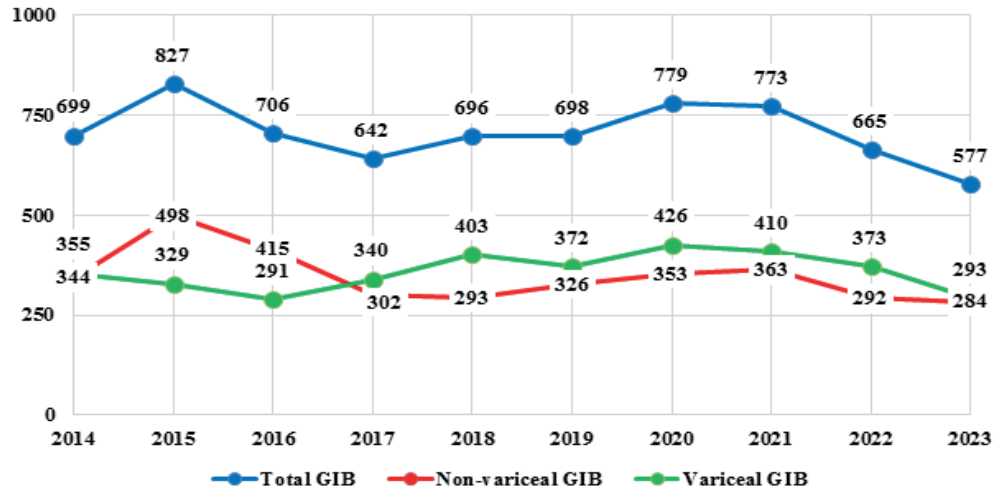
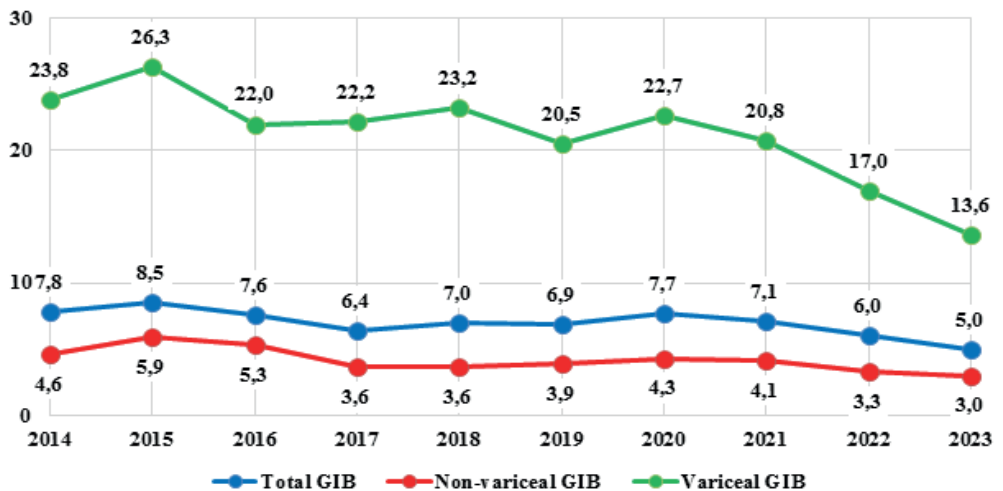


Figure 4 shows the 10-year trend in mortality for non-variceal upper gastrointestinal bleeding and variceal bleeding. Mortality from non-variceal bleeding decreased from 4.6% to 3.0%. A significant reduction was observed, from 23.8% in 2014 to 13.6% in 2023, which is attributed to improvements in treatment strategies and the widespread use of endoscopic hemostasis methods.

**Figure 4.**  
Overall Mortality Rates from Different Types of Gastrointestinal Bleeding from 2014 to 2023

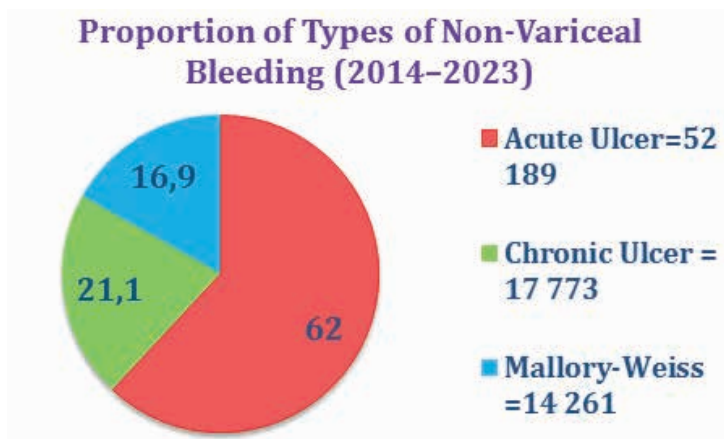


We studied the incidence and mortality associated with various types of non-variceal upper gastrointestinal bleeding. Depending on the etiological factors and pathogenesis, all non-variceal bleedings were divided into three major groups: bleeding from “acute” symptomatic ulcers, chronic ulcers, and Mallory-Weiss syndrome. Table 3 presents the number of treated patients and mortality rates for acute and chronic ulcers, as well as for Mallory-Weiss syndrome.



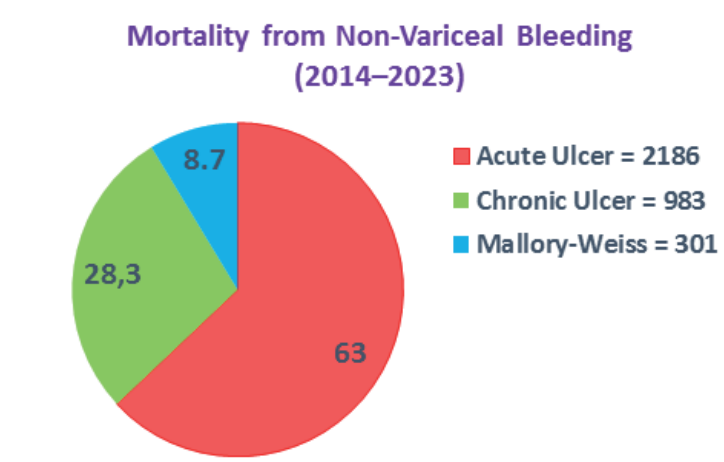
Years	Total upper Non-Variceal GIB		Acute Ulcers		Chronic Ulcers		Mallory-Weiss Syndrome	
	Treated	Mortality (%)	Treated	Mortality (%)	Treated	Mortality (%)	Treated	Mortality (%)
2014	7 497	344 (4.6)	4 462	226 (5.0)	1 705	89 (5.2)	1 330	29 (2.2)
2015	8 395	498 (5.9)	5 067	318 (6.3)	1 846	138 (7.5)	1 482	42 (2.8)
2016	7 943	415 (5.3)	4 704	268 (5.7)	1 791	112 (6.2)	1 448	35 (2.4)
2017	8 446	302 (3.6)	5 218	192 (3.7)	1 869	93 (5.0)	1 359	17 (1.3)
2018	8 238	293 (3.6)	5 130	189 (3.7)	1 765	92 (5.2)	1 343	12 (0.9)
2019	8 330	326 (3.9)	5 284	215 (4.1)	1 719	77 (4.8)	1 327	34 (2.6)
2020	8 219	353 (4.3)	5 227	231 (4.4)	1 603	85 (5.3)	1 389	37 (2.7)
2021	8 912	363 (4.1)	5 721	227 (4.0)	1 765	99 (5.6)	1 426	37 (2.6)
2022	8 912	292 (3.3)	5 801	175 (3.0)	1 684	89 (5.3)	1 427	28 (2.0)
2023	9 331	284 (3.0)	5 575	145 (2.6)	2 026	109 (5.4)	1 730	30 (1.7)
<b>Total</b>	<b>84 223 (100%)</b>	<b>3470 (4.1%)</b>	<b>52 189 (62.0%)</b>	<b>2186 (4.2%)</b>	<b>17 773 (21.1%)</b>	<b>983 (5.5%)</b>	<b>14 261 (16.9%)</b>	<b>301 (2.1%)</b>

**Table 3.** Number of treated patients and mortality rates by types of upper non-variceal bleeding (2014–2023)



**Diagram 1.** Proportion of treated cases by type of Non-Variceal Bleeding (2014–2023)

Diagram 1 shows the number and proportion of treated cases of non-variceal upper gastrointestinal bleeding from 2014 to 2023. The diagram clearly illustrates that acute symptomatic ulcers are the primary cause of non-variceal bleeding. This group includes all cases of GIB not associated with peptic ulcers of the stomach and duodenum (chronic ulcers), as well as Mallory-Weiss syndrome.



**Diagram 2.** Mortality Rate Proportion by Type of Non-Variceal Bleeding (2014–2023)

Diagram 2 presents the distribution of mortality by type of non-variceal bleeding over 10 years. It shows that 63% of fatal outcomes were caused by bleeding from acute ulcers. This indicates a shift in the structure of gastro-

duodenal ulcer bleeding, with acute symptomatic ulcers now being the predominant cause, often as a complication of severe comorbid conditions. Many authors attribute these changes in the structure of non-variceal bleeding to the increased life expectancy of the population, the rise in comorbid pathologies, the widespread use of ulcerogenic med-

ications in clinical practice, and the lack of a unified program for preventing acute erosive and ulcerative lesions of the gastrointestinal tract.<sup>11,12</sup>

The predominance of high mortality from acute symptomatic ulcers among all types of non-variceal bleeding is attributed to the severity of the underlying conditions of the patients.

**Figure 5.**  
Mortality by Types of Upper Non-Variceal Bleeding (2014–2023)

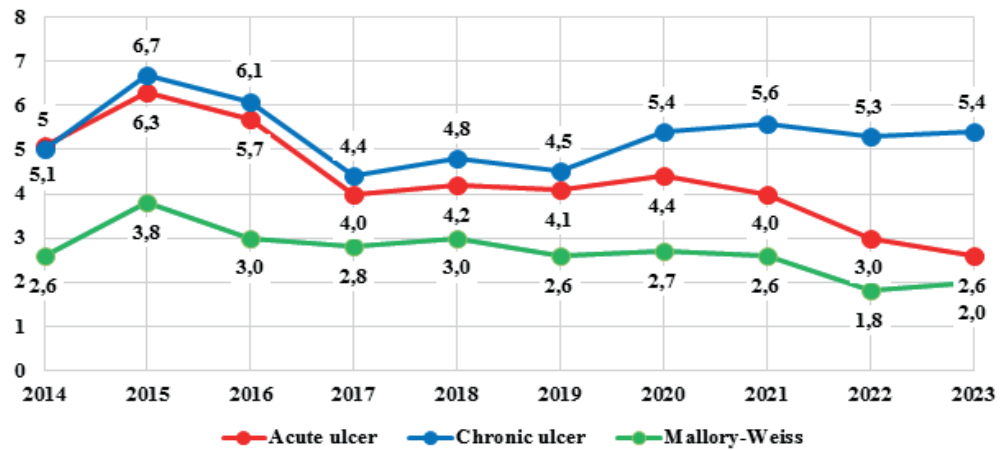


Figure 5 shows the dynamics of mortality from the main types of non-variceal bleeding from 2014 to 2023. From 2014 to 2023, there is a noticeable de-

crease in mortality by half for bleeding from acute ulcers. However, there is no downward trend in mortality for bleeding from chronic ulcers.

**Diagram 3.**  
Mortality from GIB by Gender and Age

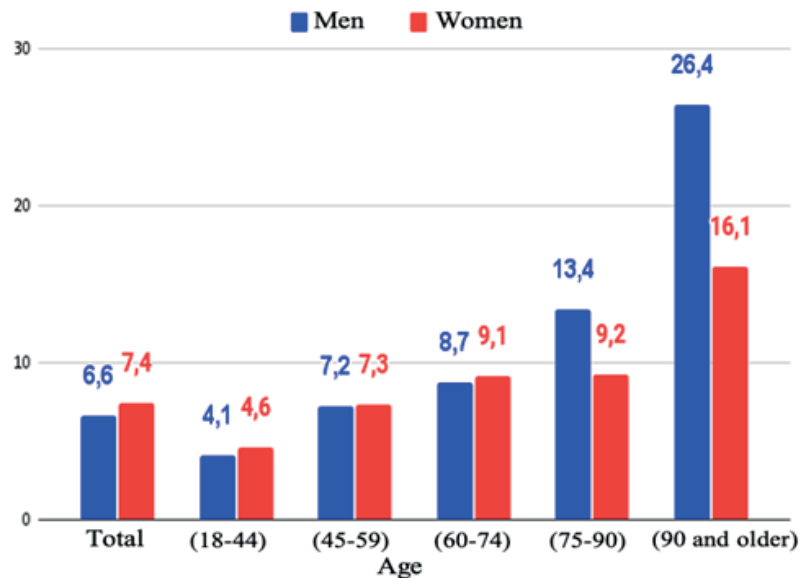


Diagram 3 provides an analysis of fatalities from GIB by gender and age. A total of 70,480 men were treated, with 5,010 fatal outcomes, resulting in a mortality rate of 7.1%. Among women, the mortality rate was 6.6%, with 2052 deaths out of 31,223 treated cases.

### Discussion

Despite advancements in the treatment of peptic ulcers in the stomach and

duodenum, the number of patients admitted to surgical hospitals with upper gastrointestinal bleeding remains quite high. Our research has shown that the incidence of gastrointestinal bleeding (GIB) in Kazakhstan increased from 52.3 per 100,000 population in 2014 to 82 per 100,000 in 2023.<sup>7</sup>

When analyzing patients by gender and age, the following was observed:

men accounted for 69.3% of the cases, while women made up 30.7%. A significant portion of GIB cases (70.3% or 71518 cases) occurred in individuals of working age (18–59 years).<sup>13</sup>

In terms of GIB types, 82.9% were non-variceal in origin, while 17.1% were variceal. The number of non-variceal bleedings increased by 24.5%, largely due to a rise in acute symptomatic ulcerations in the upper GI tract. The use of NSAIDs and antiplatelet agents, often in the context of severe comorbid conditions, is now seen as a key factor contributing to the formation of ulcers and the onset of bleeding. Severe comorbidities are also linked to increased mortality.<sup>2</sup>

Over the 10-year period, cases of variceal bleeding increased by 45.1%, rising from 1481 cases in 2014 to 2149 in 2023, indicating an increase in liver cirrhosis and its complications in Kazakhstan.

The proportion of fatal outcomes from non-variceal GIB over 10 years was 49.1% (3470 patients), while variceal GIB accounted for 50.9% of deaths (3592 patients).

Thanks to the implementation of comprehensive measures, the widespread use of endoscopic hemostasis, the development of new medications, and improved management of critically ill patients in intensive care units, overall GIB mortality decreased from 7.8% in 2014 to 5.0% in 2023. Acute symptomatic ulcers were more than twice as likely to be the source of bleeding compared to chronic ulcers.<sup>3</sup>

**Limitations:** The limitations of this study include its retrospective design, which may not provide the same depth of clinical analysis as a prospective study. The research was conducted using statistical data from the information system, which does not include data from clinical, laboratory, and instrumental examinations, nor details about the types of endoscopic hemostasis.

**What's known?** Gastrointestinal bleeding remains one of the most common problems faced by surgeons, endoscopists, and physicians from other specialties in clinical practice. Currently, despite all the advancements in modern pharmacology, endoscopy, and intensive care, gastrointestinal bleeding remains one of the most serious complications of many diseases and, in some cases, is an indication for emergency surgery. It is associated with significant morbidity, mortality, and an economic burden on healthcare.

**What's new?** This study allows us to assess the current situation regarding the prevalence of gastrointestinal bleeding in the Republic of Kazakhstan. The increase in morbidity highlights the importance of preventing gastrointestinal bleeding, particularly in patients with severe chronic conditions.

#### **Conclusion**

Based on the findings of this study, we observe a rise in the number of treated cases, which could be attributed to improved diagnostic methods, population growth, and the uncontrolled use of

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# DIAGNOSTIC ACCURACY OF MULTISPIRAL COMPUTED TOMOGRAPHY IN DETECTING AND STAGING OF ESOPHAGEAL AND GASTRIC CANCER

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## Abstract

**Background.** The sensitivity and specificity of multislice computed tomography is of great importance in the detection of gastric and esophageal cancer, and also expands the possibilities of preoperative staging using computed tomography.

**Materials and methods.** A retrospective study at the A.N. Syzganov National Scientific Center of Surgery from 2022 to 2024, included 121 patients: 48 females (39.6%), 73 males (60.3%), with an average age of 60 years. Sensitivity, specificity were calculated to assess diagnostic accuracy. Esophageal and gastric cancer staging via computed tomography was done using the TNM classification and compared with esophagogastro-duodenoscopy, pathohistological examination results.

**Results.** The sensitivity of computed tomography was 96.49%, the specificity was 85.71%. Esophagogastroduodenoscopy showed a sensitivity of 79.75%, specificity of 95.24%.

**Conclusion.** Computed tomography is highly informative, sensitive in detecting esophageal and gastric cancer, with superior diagnostic accuracy compared to esophagogastroduodenoscopy. Given the detection of esophageal and gastric cancer at T2 and T3 stages, along with the presence of distant metastases in some patients, implementing protocols for early diagnosis is advisable.

## Introduction

(EC) is the eighth most commonly diagnosed cancer and is the sixth leading cause of cancer death worldwide. There is a significant statistical difference between males and females, with 418350 cases among males and 185750 cases among females. The main risk factors of EC are gastroesophageal reflux disease (GERD), Barrett's esophagus, achalasia, tylosis, Plummer-Vinson syndrome, esophagus injuries, lifestyle and dietary habits.<sup>1</sup>

Gastric cancer (GC) is the fifth most common cancer and the third leading cause of cancer death worldwide.<sup>1-3</sup> The

incidence of GC progressively increases with age; the average age at diagnosis in Kazakhstan is lower in men ( $63.1 \pm 0.1$  years) than in women ( $65.1 \pm 0.1$  years).<sup>4</sup> On average, the incidence of GC is two to three times higher in men than in women. The incidence rate is highest in East Asian countries (35 per 100 000 people).<sup>4,5</sup> The incidence of GC in Kazakhstan is  $23.6 \pm 0.50/0000$  in men and  $13.9 \pm 0.50/0000$  in women.<sup>4</sup> The main risk factors of GC are genetic predisposition, HP-associated gastritis, peptic ulcer disease, precancerous conditions, lifestyle, and dietary habits.<sup>1</sup>

Multispiral computed tomography

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The authors declare no potential conflict of interest requiring disclosure in this article.

## Keywords:

esophageal cancer, gastric cancer, adenocarcinoma, multispiral computed tomography, biopsy, histology.

(MSCT) in combination with esophago-gastroduodenoscopy (EGD) is the standard imaging method for preoperative diagnosis and staging of EC and GC.<sup>6</sup> Recently, MSCT methods have improved the accuracy of determining the depth of invasion of the primary gastric tumor (T stage), as well as lymph node involvement (N stage) and distant metastases (M stage).<sup>7-9</sup> These studies have shown that EC and GC causes thickening of the gastric and esophageal wall with moderate or marked contrast enhancement in the early stages.<sup>10-12</sup> The sensitivity of CT in various publications ranges from 61% to 75%, the specificity - 61-75%, and for surrounding organs, it reaches 100%.<sup>13-16</sup> Nowadays, the gold standard for detecting EC and GC is upper endoscopy in combination with tissue biopsy. This method has sensitivity and specificity values of 69% and 96%, respectively.<sup>10</sup> Unlike colorectal cancer and other types of gastrointestinal cancer, GC demonstrates a variety of different pathological factors, including histological type, degree of differentiation, and infiltration pattern.

The most common histological subtype is adenocarcinoma.<sup>10,17</sup> Histological type is one of the most important factors, as it has a close relationship with tumor aggressiveness and the prognosis of GC patients.<sup>18-20</sup>

Two distinct histological subtypes predominate in EC, and should be considered biologically separate disease entities. These subtypes are esophageal adenocarcinoma (EAC) and esophageal squamous cell carcinoma (ESCC). Around 90% of worldwide cases are ESCC, which has particularly high incidence in South America and the Asian esophageal cancer belt. EAC is, by contrast, more prevalent in Europe and high income North America, where its incidence has increased fourfold over the past four decades.

The aim of the study is evaluate the sensitivity and specificity MSCT in the detection of EC and GC, also the possibilities of preoperative CT staging.

#### Materials and methods

Retrospective single-center study was performed at the Syzganov National Scientific Center of Surgery, based on the Department of Radiology, Endoscopy,

and the Laboratory of Pathomorphology, in the period from 2022 to 2024 years.

**Imaging techniques.** MSCT was performed on all patients with EC and GC using a 160-slice *Canon Aquilion* tomography scanner (*Tokyo, Japan*). Scanning parameters: slice thickness 0.5 x 80 mm, pitch 0.8, tube rotation speed 0.5 s, tube voltage 120 kV. After the native scanning phase, a water-soluble iodine-containing contrast iopromide (*Germany*) was injected intravenously using a pump injector at a rate of 1.2 ml per 1 kg of the patient's body weight, respectively, at a rate of 4-5 ml/s. After the bolus injection of the contrast substance, saline solution (40-50 ml) was administered at the same rate. Arterial, venous, and delayed scanning phases were obtained 8, 10, 15, and 120 seconds after the density in the aorta reached 100 Hounsfield units (HU).

To assess the stage of EC and GC, the international TNM classification (*AJCC, June 18, 2018*) was used.

To confirm the results of MSCT, a pathological and histological conclusion and EGD were compared. EGD was performed on 121 patients using an *Olympus video endoscope* (*Tokyo, Japan*). A pathohistological examination was conducted on 121 patients during the endoscopic examination with targeted biopsy. The biomaterial was delivered in a glass vial filled with 10% neutral buffered formalin, with appropriate labeling and a referral for research.

**Ethical approval.** This study was approved by the local ethics committee according to the protocol of meeting No.4 dated November 10, 2023.

**Statistics.** Data analysis of patients was presented as mean±standard deviation. Sensitivity and specificity were listed to assess the diagnostic accuracy of MSCT and EGD. The Kolmogorov-Smirnov test was used to determine the normal distribution of the sample, and the Mann-Whitney U test was used to determine a statistically significant difference in the prevalence of EC and GC between females and males. A p value<0.05 was considered to indicate statistical significance. Statistical analyses were conducted using SPSS software (*IBM corp., 28 version, US*).

#### Results

The research group included 121 pa-



tients: 48 women (39.6%) and 73 men (60.3%), with an average age of  $60 \pm 11.8$  years, ranging from 26 to 78 years. We did not find a statistically significant difference in the incidence of GC between females and males ( $p=0.264$ ).

EC divided by localization into: upper esophagus - 12 (24.0%), mid esophagus - 13 (26.0%), lower esophagus - 25 (50.0%).

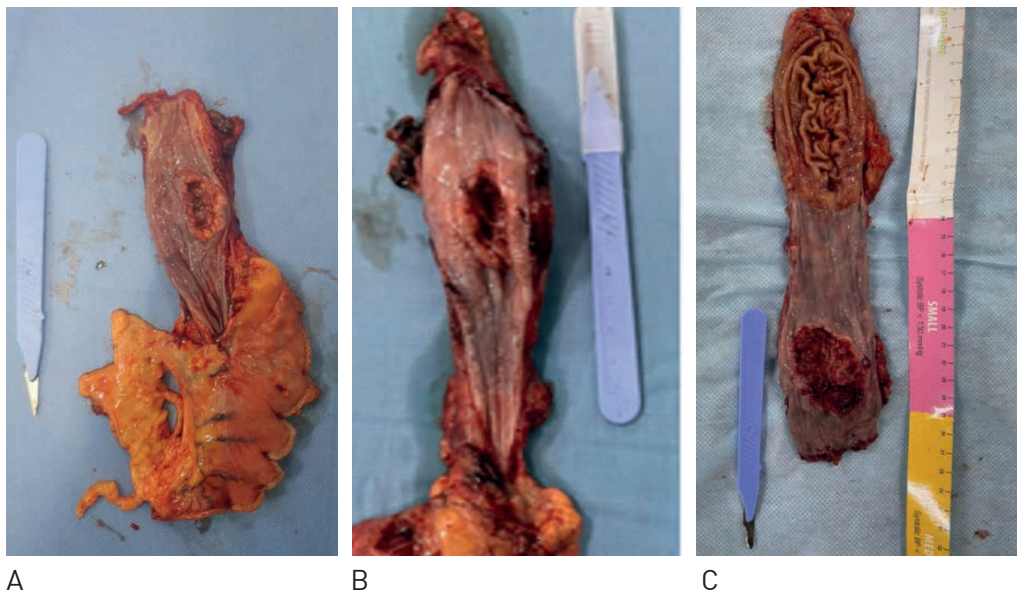
GC divided by localization into: cardioesophageal - 15 (21.1%), cardial - 13 (18.4%), fundus - 1 (0.7%), body - 22 (31.7%), antrum - 5 (7.0%), pyloric - 15 (21.1%).

MSCT compared with the pathological and histological conclusion showed

a false positive result in 1 case (0.8%), a false negative result in 4 cases (3.3%), a true positive result in 110 (90.94%) cases and false negative 6 (4.96%) cases.

EGD showed a false negative result in 16 (13.2%) cases, a false positive result in 2 (1.6%) cases, a true positive result in 63 (52.1%) cases and false negative 40 (33.1%) cases compared to biopsy.

In the pathological and histological study: 48 patients (96%) had esophageal squamous cell carcinoma (ESCC), of which G1 - 12 (24%) patients, G2 - 13 (26.0%) patients, G3 - 25 (50.0%) patients; the remaining 2 patients (4%) had esophageal adenocarcinoma (EAC). Figure 1 – A, B, C.



**Figure 1.**  
A, B, C. Macroscopic view of the esophageal tumors

**A.** Ulcerative defect of the esophageal wall in the form of a circular ulcer with raised edges of cartilaginous density and dirty gray loose deposits at the bottom, the length of the defect in its largest dimension is 4.4 cm, depth - 0.6 cm, from the level of the unchanged mucous membrane (cT2)

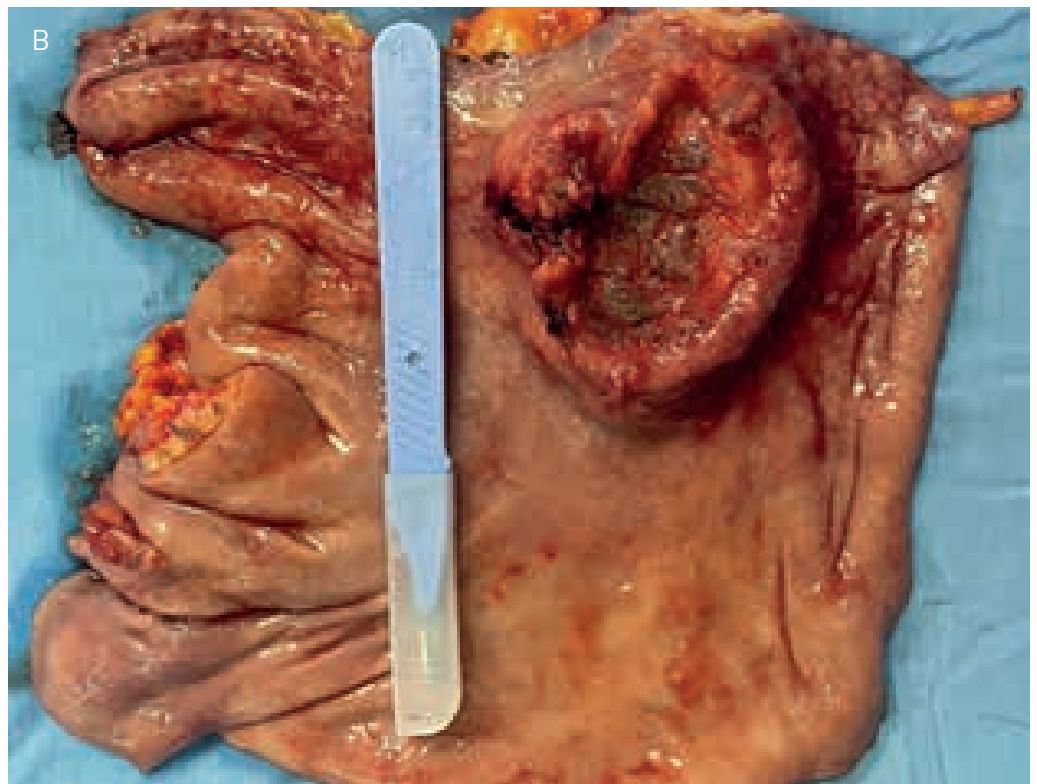
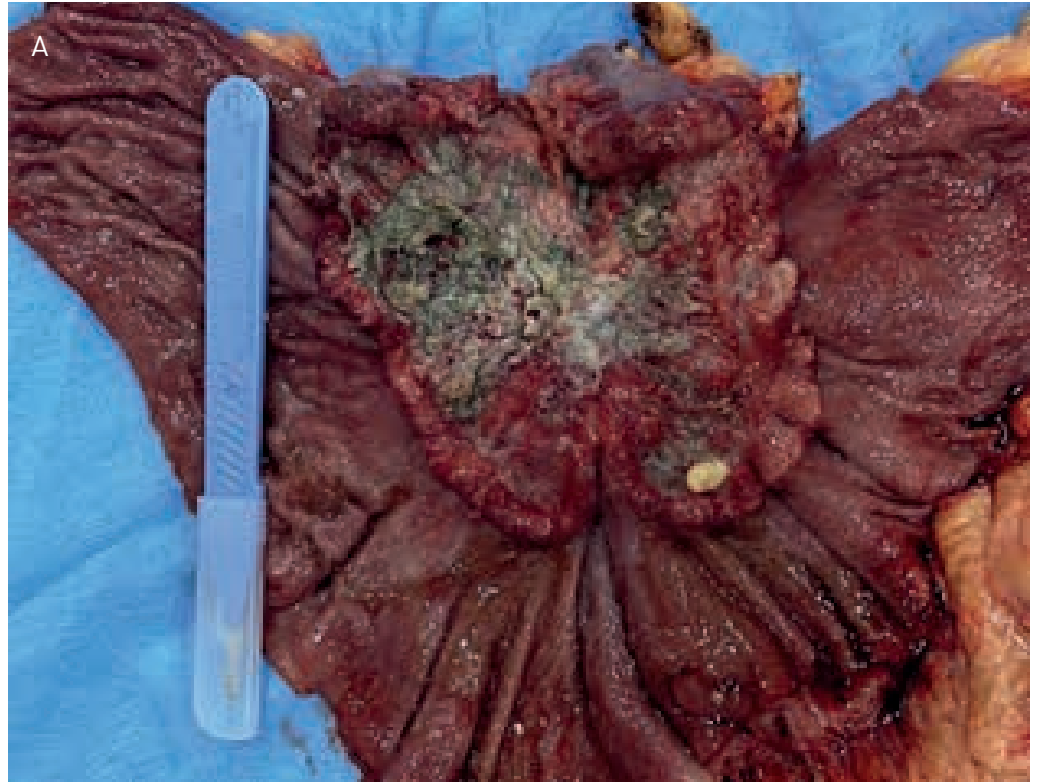
**B.** ulcerative defect of the esophageal wall in the form of a circular ulcer with raised edges of cartilaginous density and dirty gray loose deposits at the bottom, the length of the defect in its largest dimension is 3.8 cm, depth - 0.5 cm from the level of the unchanged mucous membrane (cT2).

**C.** ulcerative defect of the esophageal wall with raised edges of cartilaginous density and dirty gray loose deposits at the bottom, the length of the defect in its largest dimension is 6.0 cm, depth - 0.5 cm, from the level of the unchanged mucous membrane (cT2).

In the pathological and histological study: 68 patients (95.7%) had adenocarcinoma, of which G1 - 12 (17.6%) patients, G2 - 25 (36.8%) patients, G3 - 31 (45.6%)

patients; the remaining 3 patients (4.2%) had metaplasia, MALT lymphoma and ulcerative defect. Figure 2 – A and B.

**Figure 2.**  
A and B. Macroscopic view of  
the gastric tumors



- A.** Stomach tumor (type 3 according to Borrmann) with defect dimensions of 8.5 x 10.0 cm, depth in the central part - up to 0.5 cm from the level of unchanged mucous membrane (cT3).
- B.** Stomach tumor with ulceration in the center (type II according to Borrmann) with defect dimensions 7.0 x 5.5 cm and growth to the serous membrane (cT3).

Radical surgical interventions were performed in 84 (69.4%) patients, of which: subtotal distal resection was performed in 15 (12.3%), combined subtotal distal resection - 1 (0.8%), combined gastrectomy - 11 (9.0%), standard gastrectomy - 16 (13.2%), subtotal distal gastrectomy - 1 (0.8%) patient, Ivor Lewis esophagectomy - 32 (26.4%), McKeown esophagectomy - 8 (6.6%). The remaining 37 (30.5%) patients underwent palliative surgical treatment.

The sensitivity of MSCT is 96.49%, relative to 95%CI [91.26%; 99.04%], the specificity is - 85.71%, relative to 95%CI [42.13%; 99.64%], and the accuracy is 95.87%, relative to 95%CI [90.62%; 98.64%].

The sensitivity of EGD is 79.75%, relative to 95%CI [69.20%; 87.96%], the specificity is 95.24%, relative to 95%CI [83.84%; 99.42%], and the accuracy is 85.12%, relative to 95%CI [77.51%; 90.94%].

### Discussion

This study analyzed the gender, age of the patients, location and prevalence of EC and GC, the types of surgical interventions performed. It was determined that the number of men prevailed in the entire group of patients, the average age at the time of diagnosis was 60 years which corresponds to the indicators of literature.<sup>21,22</sup>

The most common types of surgical intervention were standard gastrectomy, Ivor Lewis esophagectomy and palliative surgical treatment. As a rule, cancer in the early stages is asymptomatic, so the key to reducing the burden of advanced cancer is its timely detection.<sup>23</sup>

MSCT is a highly informative and sensitive method for detecting EC and GC. The possibility of detecting EC and GC was 96.49% and the specificity of the method was 85.71% in the entire group of patients, which exceeds the indications of literature data and confirms the high quality of the virtual image of MSCT.

The sensitivity of EGD was 79.75%, specificity - 95.24%, which is close to the indicators of review articles. This method of early diagnosis of EC and GC is also highly informative, and it allows you to clarify preoperative histological types and morphological characteristics. However, it is an invasive method of

research, and it also cannot assess the damage to lymph nodes, the presence of metastases in other organs, the involvement of vessels and other adjacent anatomical structures in the process, nor can it assess the degree of tumor invasion, especially in early EC and GC with a small lesion, which are significant disadvantages compared to MSCT.<sup>10,17</sup>

A limitation of this research is that it was conducted in a single center with a small sample of patients, and therefore further larger-scale research on this topic is necessary. It should be noted that there are no screening programs in Kazakhstan for earlier detection of esophageal and gastric cancer in people at risk, that's why it is necessary to develop some screening protocols. Such screening methods would lead to early detection of EC and GC, ultimately increase overall survival.<sup>24,25</sup>

Modern MSCT technology facilitates not only the accurate staging of esophageal and gastric cancer, but also serves as a valuable tool for the primary diagnosis of the disease.

**Limitations:** of this research are that it was conducted in a single center with a small sample of patients, and therefore further larger-scale research on this topic is necessary; also not less important are difficulties in exchanging data with medical organizations at various levels for the analysis of instrumental research methods in the primary diagnosis of EC and GC.

**What's known?** The sensitivity of CT in various publications ranges from 61% to 75%, the specificity 61-75%. Upper endoscopy in combination with tissue biopsy has sensitivity and specificity of 69% and 96%, respectively.

**What's new?** In our single center study, high sensitivity of computed tomography was determined - 96.49% and the specificity - 85.71%, while esophagogastroduodenoscopy showed similar sensitivity of 79.75% and specificity of 95.24%.

### Conclusion

Computed tomography is highly informative, sensitive in detecting esophageal and gastric cancer, with superior diagnostic accuracy compared to esophagogastroduodenoscopy. Given the detection of esophageal and gastric cancer

at T2 and T3 stages, along with the presence of distant metastases in some patients, implementing protocols for early diagnosis is advisable.

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A.M., N.O.: Statistical processing and analysis of the material, writing the text of the article (material and methods, results); Ye.K., K.K., A.M.: Writing the text of the article (introduction, discussion). All authors approved the final version of the manuscript

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# SURGICAL MANAGEMENT OF RENAL CELL CARCINOMA WITH INFERIOR VENA CAVA THROMBOSIS: A CLINICAL CASE

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## Abstract

Kidney cancer with inferior vena cava thrombosis represents a complex condition that requires meticulous surgical treatment. The most common malignant kidney tumor in adults is renal cell carcinoma. The incidence of renal cell carcinoma has increased recently due to the enhanced resolution of imaging techniques. Most cases are discovered incidentally. Renal cell carcinoma's ability to spread to vascular systems without developing metastases is a significant feature. Venous involvement can manifest as a tumor thrombus in the renal vein on the affected side, potentially extending to the right atrium or the inferior vena cava. The risk of having a tumor thrombus in the renal vein or inferior vena cava ranges from 2-10%, with the right side being more frequently affected. The level of tumor thrombus extension can reach the hepatic veins and even the right atrium. This condition thus requires a multidisciplinary approach and a rational surgical strategy, focusing on achieving favorable outcomes in such complex cases.

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## Keywords:

renal cell carcinoma; inferior vena cava; thrombus; nephrectomy

## Introduction

Renal cell carcinoma (RCC) represents 85% of all renal malignancies and is the most prevalent kind of kidney cancer.<sup>1,2</sup> RCC frequently shows no symptoms until it progresses, at which point it may manifest as hematuria, flank discomfort, and a palpable lump. It correlates with worse prognosis, aggressive histology, and advanced illness.<sup>3-5</sup> Tumor thrombus extension into the renal vein and, in certain situations, into the inferior vena cava (IVC) is one of the more serious side effects of advanced RCC.<sup>6-10</sup> This condition's intricate anatomy and the IVC's vital function in venous return make surgical therapy extremely difficult.

About 4–10% of RCC instances result in inferior vena cava thrombosis, which is linked to an increased risk of morbidity and death.<sup>11-14</sup> When IVC thrombus is present, careful surgical technique is required, frequently requiring multidis-

ciplinary cooperation. Depending on the degree of thrombus involvement, several techniques are used, from a simple nephrectomy to more involved treatments such as thrombectomy and, in certain situations, cardiac bypass.<sup>15</sup>

RCC with IVC thrombus poses a significant surgical challenge due to the complexities of achieving complete tumor resection while minimizing complications. The presence of IVC thrombus impacts survival outcomes negatively; however, aggressive surgical intervention has shown to improve survival rates significantly. Survival rates decrease with higher levels of thrombus extension. For localized stages (like Level I), the 5-year survival rate can be around 93%. For regional involvement (Levels II and III), the survival rate drops to approximately 74%. Distant stages, which include Level IV, have a significantly lower 5-year survival rate of about 17%.<sup>16,17</sup>

This report describes a case that



demonstrates the clinical presentation, diagnostic process, and surgical treatment of a patient who has both severe IVC thrombosis and RCC. We go over the preoperative planning, intraoperative difficulties, and postoperative results, offering an understanding of the interdisciplinary approach needed in such complicated situations. We hope that this case report will add to the body of knowledge on RCC with IVC involvement and highlight the significance of specialized surgical techniques for successful treatment.

### Case presentation

Patient H, a 60-year-old male, presented to our center with a chief complaint of hematuria persisting for one week. He was referred to our urology department after a renal ultrasound revealed a mass in the right kidney. Upon admission, Patient H. underwent further evaluation, including a computed tomography (CT) scan with contrast. The imaging revealed a large mass in the right kidney, extending into the inferior vena cava (Figure 2). Laboratory investigations indicated thrombocytopenia, elevated liver enzymes (ALT and AST), while coagulation parameters remained within normal limits. A chest CT scan showed no evidence of metastasis. The renal CT scan depicted a heteroge-

neous mass measuring 12x8.5x9.6 cm, with clear, irregular contours, located in the upper and middle thirds of the right kidney. The mass deformed the renal contour and extended into the renal vein, reaching the lumen of the renal tubular vein (4.8 cm in length). Collateral vessels, up to 1.1 cm in diameter, were observed. Intense contrast agent accumulation within the mass was noted post-injection. In order to determine the complexity of the surgery required and the likelihood of complications we used The Mayo Clinic classification (Figure 1).

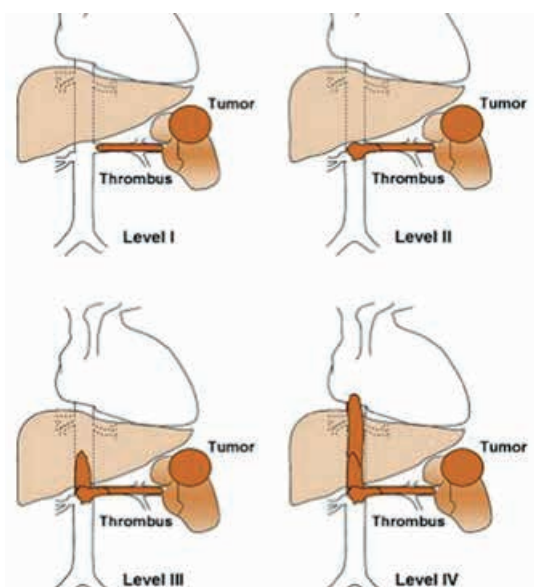
It is based on the level of the tumor thrombus extension into the inferior vena cava. This classification helps in planning the surgical approach and predicting the prognosis. The classification is divided into four levels:

**1. Level I:** The tumor thrombus extends into the renal vein but does not reach the IVC or extends slightly into the IVC but remains below the diaphragm.

**2. Level II:** The tumor thrombus extends into the IVC but remains below the liver (subhepatic).

**3. Level III:** The tumor thrombus extends into the IVC up to the liver but does not involve the heart (intrahepatic).

**4. Level IV:** The tumor thrombus extends above the diaphragm and may involve the heart or right atrium.



**Figure 1.**

The Mayo classification of macroscopic venous invasion in RCC. Level I: A tumor thrombus present at the renal vein entrance or inside the IVC less than 2 cm from the renal vein and IVC confluence. Level II: The thrombus stays below the hepatic veins but spreads more than 2 cm into the IVC above the junction of the renal and IVC veins. Level III: The intrahepatic IVC is involved in thrombosis. The thrombus can vary in size, from filling the lumen and expanding the IVC to having a small tail that reaches in to the IVC. Level IV: The thrombus grows into the right atrium or over the diaphragm. Inferior vena cava or IVC.<sup>17,18</sup>

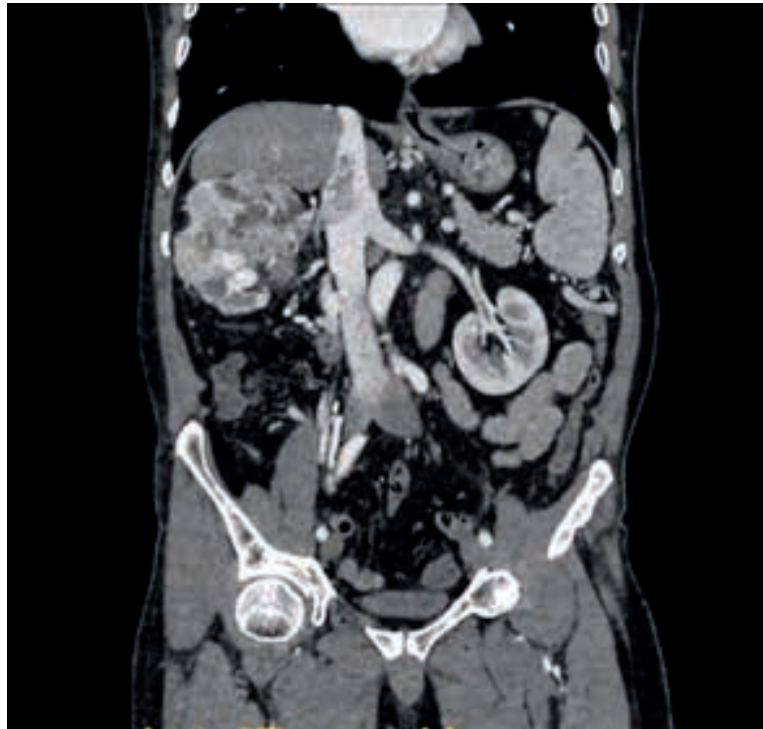
**Diagnosis:** Right kidney mass with inferior vena cava thrombosis. Staging: T3bN1M0. Level III.

**Comorbidities:** Patient H. had a his-

tory of ischemic heart disease, aneurysm of the interatrial septum, stage 1 arterial hypertension (high risk), and liver cirrhosis (Child-Turcotte-Pugh class B, MELD-9)

secondary to chronic viral hepatitis C. After thorough consultations with a cardiologist and hepatologist, Patient H. provided informed consent for surgical intervention. The proposed surgical approach included laparotomy, nephrectomy, and thrombectomy with reconstruction of the inferior vena cava.

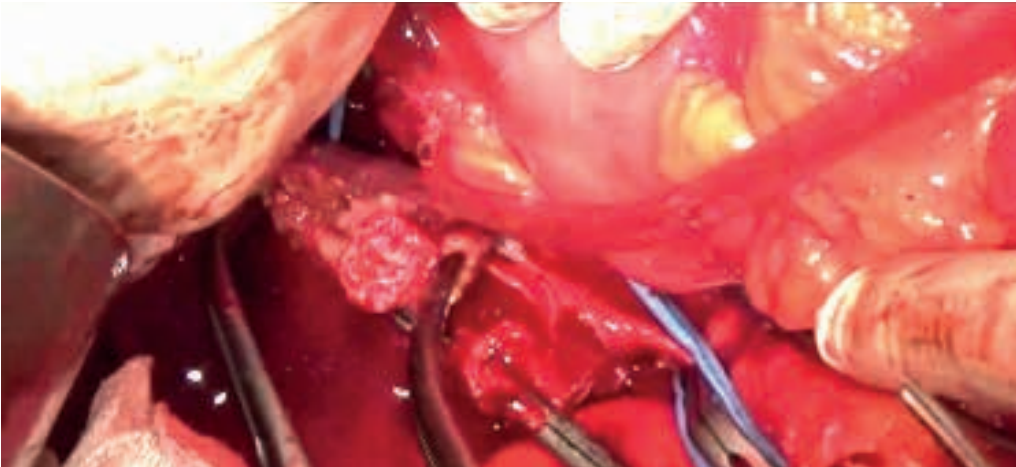
**Figure 2.**  
Contrasted computed tomography (CT) scan. Imaging showed a sizable tumor that extended into the inferior vena cava in the right kidney.



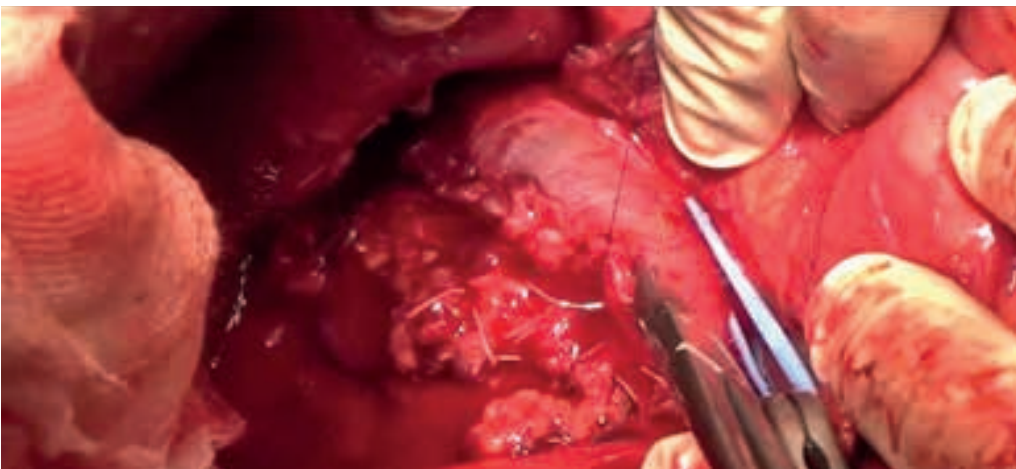
### Surgical treatment

Patient H. was positioned supine on the operating table under general anesthesia. Preoperative antibiotics were administered, and standard monitoring devices were applied. A right laparotomy was performed to access the retroperitoneal space and gain exposure to the right kidney and inferior vena cava. The incision provided adequate access to the affected structures while minimizing intraoperative complications. The right kidney was carefully dissected from the surrounding tissues, ensuring preservation of adjacent structures. Additional vessels and collaterals were isolated, ligated, and divided. The ureter in the lower third was isolated, ligated, and divided. The renal vein, along with its entry into the inferior vena cava, was isolated and secured with a vessel loop. Three renal arteries were isolated, clamped, divided, and ligated. A *Satinsky clamp* was applied to the IVC at the entry of the renal vein. The renal vein was divided, and an incision was made in the IVC. The entire kidney, including the tumor mass, was excised en bloc. Attention was then turned to the inferior vena cava, where

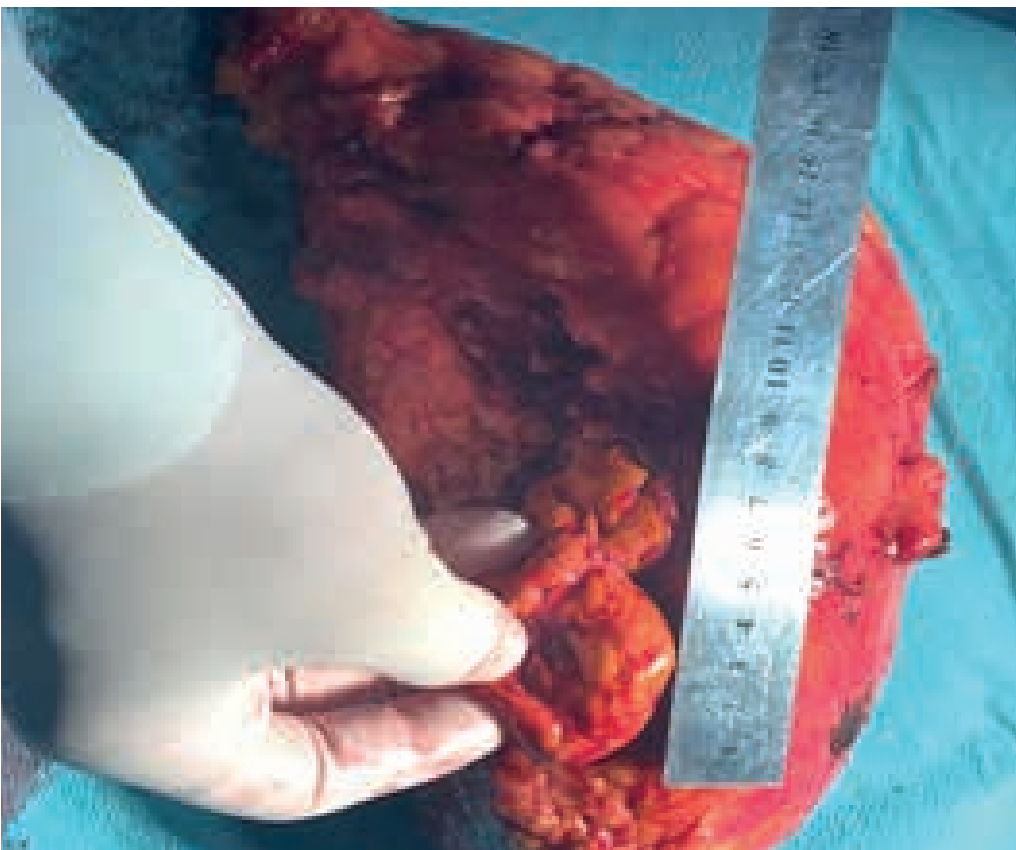
the thrombus was located. Special care was taken to avoid dislodging the thrombus during manipulation. Using meticulous dissection techniques, the 5cm thrombus was carefully removed from the lumen of the vena cava (Figure 2), ensuring complete clearance of the vessel. Following thrombus removal, the integrity of the inferior vena cava was assessed. Reconstruction of the vena cava was performed using primary closure (Figure 3). Hemostasis was ensured, and meticulous attention was paid to controlling any bleeding points. The surgical field was thoroughly irrigated with saline to remove any debris or residual thrombus. The surgical procedure was successful, with complete removal of the renal tumor and thrombus from the inferior vena cava. Patient's H. postoperative recovery was uneventful, and he was discharged home with appropriate follow-up instructions. This surgical approach highlights the importance of meticulous dissection techniques and careful vascular management in achieving favorable outcomes in Patients H. with renal cell carcinoma and inferior vena cava thrombosis.



**Figure 3.**  
Removal of a tumor thrombus  
from the IVC lumen



**Figure 4.**  
Closure of vena cava



**Figure 5.**  
Gross specimen of a kidney  
with a tumor thrombus

### Discussion

Renal cell carcinoma with inferior vena cava thrombus presents a significant surgical and clinical challenge, necessitating a multidisciplinary approach for effective management. This case highlights several critical aspects of surgical and perioperative management, contributing to the broader understanding of advanced RCC treatment.

RCC often remains asymptomatic until it reaches an advanced stage, as illustrated by our Patient's H. presentation with hematuria a common symptom of advanced renal tumors. The diagnostic journey began with a renal ultrasound, a standard initial imaging modality, which identified a mass in the right kidney. Further evaluation with contrast-enhanced computed tomography was crucial for detailed anatomical assessment. Contrast-enhanced CT scans are indispensable in RCC cases for visualizing tumor extension, vascular involvement, and potential metastases.<sup>19</sup>

The CT scan in this case revealed a large, heterogeneous mass in the right kidney with clear, irregular contours extending into the IVC. The ability of CT imaging to provide detailed visualization of the tumor thrombus was instrumental in surgical planning. This aligns with findings in the literature that underscore the importance of high-resolution imaging for accurate staging and preoperative assessment.<sup>20</sup>

The surgical management of RCC with IVC thrombus is complex and requires a highly specialized approach. The choice of a cherry right laparotomy provided optimal exposure to the kidney and IVC, facilitating meticulous dissection and thrombus removal. Nephrectomy, combined with thrombectomy and IVC reconstruction, was necessary due to the extent of the thrombus. This approach is consistent with current surgical guidelines that recommend aggressive resection to achieve complete tumor removal and minimize recurrence.<sup>17</sup>

The intricacies of performing thrombectomy from the IVC involve preventing thrombus dislodgement, which could lead to potentially fatal pulmonary embolism. In this case, careful surgical technique and intraoperative management were critical to avoiding such com-

plications. Literature reviews support that experienced surgical teams and meticulous technique are essential for successful outcomes in such high-risk surgeries.<sup>21</sup>

This case presented several intraoperative challenges, including the Patient's H. thrombocytopenia and elevated liver enzymes, indicating an increased risk of bleeding. Careful intraoperative hemostasis was paramount to manage this risk effectively. The presence of significant comorbidities—ischemic heart disease, arterial hypertension, and cirrhosis—required comprehensive preoperative optimization and interdisciplinary collaboration. Preoperative consultations with cardiology and hepatology were essential for risk stratification and management, highlighting the importance of a holistic approach to patient care.<sup>22</sup>

Postoperative care involved intensive monitoring to detect and address early complications, such as bleeding or thromboembolic events. The successful outcome in this case, marked by the uneventful recovery and confirmed patency of the IVC on postoperative imaging, underscores the effectiveness of the surgical approach and the importance of comprehensive perioperative care.<sup>23</sup>

The Patient's H. recovery was facilitated by a multidisciplinary team that included surgeons, anesthesiologists, intensivists, and nursing staff, ensuring that all aspects of the patient's care were addressed. The literature supports the role of multidisciplinary teams in improving surgical outcomes for complex cases such as RCC with IVC thrombus.<sup>24</sup>

The management of RCC with IVC thrombus has evolved significantly, with advances in imaging, surgical techniques, and perioperative care contributing to improved outcomes. Studies have shown that aggressive surgical intervention, even in advanced cases, can lead to prolonged survival and improved quality of life.<sup>25</sup> However, the inherent risks of such extensive surgeries, including morbidity and mortality, must be carefully weighed against the potential benefits.

Emerging surgical techniques, such as minimally invasive approaches and robotic-assisted surgeries, offer the po-



tential for reduced morbidity and faster recovery times. Initial studies on these techniques have shown promising results, although further research and long-term data are needed to establish their efficacy and safety in managing RCC with IVC thrombus.<sup>26</sup>

**Limitations:** The primary constraints of this research were the retrospective nature of data collection and the very small sample size, which may have resulted in underpowered statistical analyses. To validate the findings and evaluate the impact of the categorization system and related surgical techniques and methods on both short- and long-term survival, more research with a bigger sample size is required.

**What's known?** Renal cell carcinoma with inferior vena cava thrombosis is a complex and challenging condition. The involvement of the IVC raises the risk of mortality and morbidity. Surgical resection, that includes nephrectomy and thrombectomy, is the mainstay of treatment which often involves a multidisciplinary team as well as advanced surgical techniques. Survival depends on the extent of thrombus, where early stage involvement has higher survival rates

**What's new?** This particular situation emphasizes the competent surgical treatment of a patient suffering from renal cell carcinoma along with thrombosis of the inferior vena cava level three through a careful method of dissection plus reconstruction.

## Conclusion

The management of RCC with IVC thrombosis requires a tailored and multidisciplinary approach, incorporating meticulous surgical technique, comprehensive preoperative assessment, and close postoperative monitoring. This case study highlights the importance of collaboration between different specialties and the challenges encountered in the surgical management of complex renal tumors. Further research and clinical studies are warranted to refine treatment strategies and improve outcomes in this challenging patient population.

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# ULTRASOUND DIAGNOSIS OF THE RENAL ARTERY STENOSIS IN A TRANSPLANTED KIDNEY IN THE EARLY POSTOPERATIVE PERIOD

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## Abstract

In this clinical case, stenosis of a renal artery of transplant was detected in time by angiography using dynamic Doppler ultrasound control. The chosen treatment method allowed the restoration of arterial patency and thus renal graft function in the shortest possible time and with minimal trauma. However, due to the high risk of restenosis in the plastic area, continuous dynamic ultrasound monitoring and monitoring of the patient's creatinine level are required. The purpose of this presentation is to present a case of early detection of a postoperative complication by Doppler ultrasound, which made it possible to prevent vascular dysfunction, often leading to loss of the renal graft.

**Materials and Methods.** In this article, we report a case of timely detection of renal artery stenosis by ultrasound in a patient, followed by confirmation by angiography and restoration of renal artery and graft function by endovascular balloon angioplasty. All major hemodynamic changes in Doppler ultrasound parameters characteristic of renal artery stenosis are described in this article.

**Results.** Dynamic Doppler ultrasound monitoring and angiography allowed early detection of the described complication of renal transplantation. The optimal choice of treatment tactics allowed the restoration of arterial patency and renal graft function in the shortest possible time, thus preventing graft rejection.

**Conclusion.** Our clinical case demonstrates the importance of the monitor in the assessment of renal perfusion. The outcome of kidney transplantation largely depends on the successful resolution of these issues, which determines the relevance.

## Introduction

Renal graft arterial stenosis develops in 2-12%,<sup>1,2</sup> and according to some sources in up to 23% of cases,<sup>3,4</sup> and more frequently in the delayed period, from 3 months to 2 years after transplantation.<sup>4</sup> In most cases, this complication is diagnosed in the first 6 months. Stenosis of the renal artery after transplantation can lead to uncontrolled increases in blood pressure and kidney graft dysfunction.<sup>4,5</sup>

A significant amount of scientific research is devoted to analyzing the diagnostic efficacy of the resistance index. Literature data indicate that the resistance index (RI) is the most important parameter for quantitative determination of renal blood flow changes in renal pathology. Thus, for example, Patel K.N. with co-authors, when using the thresh-

old value, RI - 0.7, obtained a sensitivity equal to 78% with a low specificity of - 40%, while with the threshold value of Ri equal to 0.9, the specificity was 100%, sensitivity - 16%.<sup>5</sup>

## Case presentation

Patient Zh., born in 1980, underwent living donor kidney transplantation into the right iliac region at the Center for Hepatopancreatobiliary Surgery, Oncohepatology and Organ Transplantation of LLP NNOC on May 26, 2023. After the surgery, the kidney transplant function was satisfactory, and the creatinine level gradually decreased. However, from June 8, 2023, there was an increase in the creatinine level, which peaked at 370  $\mu\text{mol/L}$ . According to ultrasound and Doppler ultrasound: at the level of the renal artery anastomosis, the peak systolic velocity (PSV) increased to 600 cm/s

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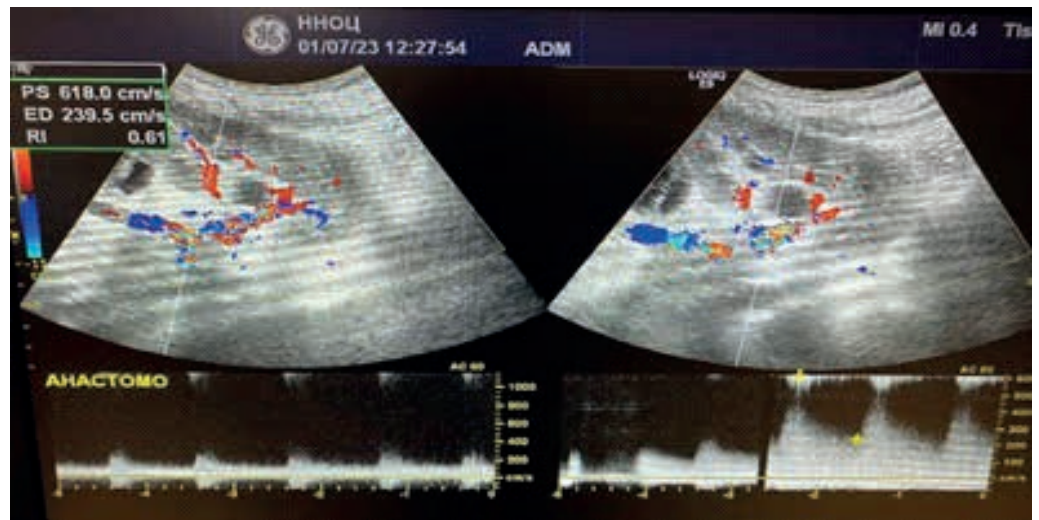
## Keywords:

kidney transplant, complication, stenosis, survival, restoration of function, angioplasty, Dopplerography of kidney vessels, anastomosis.

(Figure 1), with a stenotic blood flow pattern, resulting in decreased renal graft perfusion, the appearance of a “tardus parvus” blood flow pattern in the interlobular arteries, and a sharp decrease in resistance index (RI) to 0.29 (Figure 2).

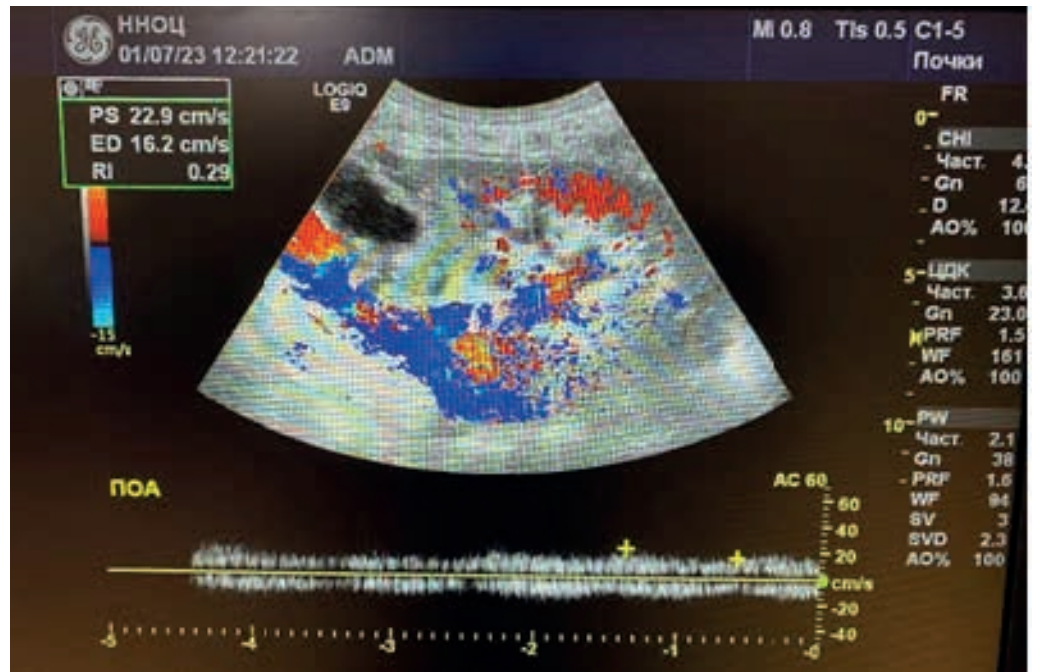
**Figure 1.**

Elevated velocity in the renal artery at the anastomosis level.



**Figure 2.**

Low velocity and RI in the renal artery in the kidney transplant parenchyma. RI - resistance index.



PSV in the external iliac artery was 219 cm/s and the iliac-renal artery ratio (RAR) was 2.7. A hemodynamically significant stenosis was noted at the renal artery anastomosis, with a progressive decrease in velocity parameters and RI at the intrarenal level.

Clinically: decreased urine output.

It was decided to perform diagnostic angiography in the Interventional Surgery Department of the NNOC. On July 11, 2023, angiography revealed: subocclusion of the renal artery at the level of the renal artery anastomosis of the kidney transplant (Figure 3).





**Figure 3.** Angiography before balloon angioplasty: stenosis at the level of the renal artery anastomosis.

Predilatation was performed with a 2.0mm\*20mm Powerline balloon in the stenotic segment followed by placement of a 4.0mm x 150mm balloon. Balloon dilatation was performed at 12-14 atm for 60 seconds. On control arteriography: patency of the renal graft artery was restored (Figure 4).



**Figure 4.** Blood flow in the interlobular and arcuate arteries of the renal artery has been restored. RI within normal limits. RI - resistance index; RA - renal artery.

On July 17, 2023, follow-up Doppler ultrasound showed: with color Doppler mapping, the vascularization of the graft was closer to satisfactory, and parenchymal blood flow was preserved.

Velocity parameters: blood flow in parenchymal arteries: PSV - 40 cm/s, RI - 0.54; in the main trunk at the hilum PSV - 127 cm/s, RI - 0.65; at the projection of the renal artery anastomosis PSV - 179 cm/s, RI - 0.74, without spectral changes.

Ultrasound and Doppler findings are within acceptable limits (Figures 3 and 4).

Laboratory and instrumental data from January 20, 2022: creatinine 101  $\mu\text{mol/L}$ .

There are several parameters to evaluate the efficacy of the procedure, i.e., changes in the arterial lumen confirmed by angiography and ultrasound, hemodynamic parameters measured by Doppler ultrasound, and clinical parameters such as decreased blood pressure, reduced edema, increased glomerular filtration, appearance of diuresis, and graft survival. All parameters should be assessed immediately after the procedure and several months later.

### Discussion

Early detection and treatment of complications helps to preserve the function of the transplanted kidney. In particular, the vascular anastomosis zones of the renal arteries require regular postoperative Doppler ultrasound monitoring due to the high risk of ischemia and graft loss. Modern methods such as ultrasound and radiography are the most minimally invasive and informative. Although only angiography provides a definitive diagnosis, Doppler ultrasound is the best screening method because it does not cause the complications associated with radiologic contrast studies. Duplex scanning requires no contrast media, no radiation exposure, is relatively inexpensive, and has high sensitivity (87-94%) and specificity (86-100%).<sup>1,2</sup>

Endovascular balloon angioplasty is currently the first-line treatment for patients with RA stenosis. This is due to the lower incidence of restenosis (10%) compared to surgical correction (16-62%).<sup>3</sup> There is also evidence that the

immediate technical success rate of this procedure is greater than 80%, with clinical success ranging from 74-87%. Long-term clinical success, defined as improvement in blood pressure or stabilization or improvement in renal function, is reported to be 53-70% within one year.<sup>4,5</sup>

Ultrasound with Doppler remains a key tool in the diagnosis and monitoring of postoperative complications with a sensitivity of 95.7%. Radiologic methods confirm the presence of complications and help to clarify their nature, thus guiding further treatment tactics.

The presented clinical case illustrates a rather dangerous but reversible complication that occurred after allotransplantation. Differentiation of complications after kidney transplantation is a complex process. The similarity of symptoms may lead to misinterpretation of the nature of the complication and incorrect treatment, possibly resulting in graft loss or death.

**Limitations:** This study is a case report and the problem requires a large-scale study of the effectiveness of monitoring for possible vascular complications after kidney transplantation.

**What's known?** Early detection of complications, followed by immediate treatment, allows preserving the functioning of the transplanted kidney. In particular, the areas of vascular anastomosis of the renal arteries require regular postoperative ultrasound Doppler monitoring due to the high risk of developing ischemia of the renal transplant and its loss.

**What's New?** In this clinical case, thanks to dynamic, regular Doppler US control, the early detection of the complication of kidney transplantation was possible. Since ultrasound and Dopplerography is an operator-dependent method, the technique of proper and accurate determination of the location of stenosis, the degree of severity and dynamic daily control of accurate speed indicators in the stenotic zone. In this clinical case, the early and accurate detection of the complication of the early post-transplant period by ultrasound made it possible to provide the patient with immediate treatment and preserve the function of the kidney transplant.



### Conclusion

In this clinical case, thanks to dynamic Doppler US, angiography was able to detect the above-mentioned complication of kidney transplantation in time. The chosen method of treatment made it possible to restore the arterial patency and thus the function of the kidney graft with minimal trauma.

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**Authors' contribution:** O.D.: Conceptualization, A.S.: methodology, A.Y.: verification, A.Y., T.A., I.G.: formal analysis, S.I., A.Y.: writing (original draft preparation), A.E.: writing (review and editing), A.S., T.A., I.G., T.G., S.I.: selection of literature and resources.

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# THE EFFECTIVENESS OF THE FUNCTIONING OF RECONSTRUCTED HEPATIC VEINS USING VARIOUS TYPES OF MATERIALS IN TRANSPLANTATION OF THE RIGHT LOBE OF THE LIVER FROM A LIVING DONOR

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## Abstract

**Background.** In adult living donor liver transplantation with the right lobe, the venous outflow of the anterior sector is typically restored during the procedure to form a neo-middle hepatic vein. Restoring the middle hepatic vein for the drainage of the anterior sector is critically important for achieving optimal graft function. Various conduits are used for this reconstruction, such as synthetic and biological grafts (e.g., the recipient's portal vein, vessels from a deceased donor, and modified great saphenous vein). However, the selection of the best option remains a topic of discussion. This study evaluates the effectiveness of using biological and synthetic grafts for MHV reconstruction.

**Materials and methods.** A retrospective analysis of outcomes was conducted in patients who underwent transplantation of a modified right liver lobe due to end-stage liver disease from 2011 to 2024.

**Results.** A transplantation of modified right liver lobes was performed on 80 patients. In 69 cases, the reconstruction of the hepatic veins was carried out using a biological graft, while in 11 cases, a synthetic graft was used. Statistically significant differences were noted in mortality and the postoperative period. No significant differences were found in the frequency of intraoperative complications.

**Conclusion.** Our study demonstrates that the use of a biological graft for the reconstruction of the hepatic veins of segments 5 and 8 is more effective than the application of a vascular prosthesis.

## Introduction

Liver transplantation from a living donor (LDLT) is a critical treatment method for end-stage liver diseases, especially in regions where there is a shortage of organs from deceased donors.<sup>1</sup> LDLT is a viable alternative, though it is technically more complex and requires a profound understanding of the anatomy of the donor's liver, careful preoperative preparation, and meticulous surgical intervention. The resection of parenchyma from the donor liver must be performed

in such a way as to ensure not only a suitable liver graft and sufficient volume of the remaining liver but also to preserve the graft with healthy vascular and biliary structures.<sup>2</sup>

The selection of the graft in LDLT is a fundamental process that takes into account not only the metabolic needs of the recipient and the preservation of the anatomical integrity of the graft but also the volume of the donor organ, which is crucial for ensuring donor safety.<sup>2</sup> In adult patients, the size of the graft is a

structural limitation since a graft from the left lobe typically constitutes less than 40% of the total liver volume, which may be inadequate to ensure an appropriate match between the donor and recipient sizes.<sup>2</sup>

In LDLT, the most common procedure is the transplantation of the right liver lobe (RL), and many centers employ a technique in which the middle hepatic vein (MHV) trunk is preserved on the donor side.<sup>3</sup> When considering the standard approach to performing right hemihepatectomy, if the MHV is not included in the graft, this provides greater safety for the donor compared to extended right hemihepatectomy, where the MHV is part of the graft.<sup>4</sup> The problem is that in LDLT using an RL graft without MHV, there can be extensive congestion in the graft, such that after reperfusion, venous outflow from the right anterior sector to the MHV may be compromise.<sup>5</sup>

The right hepatic vein drains separately into the inferior vena cava (IVC), while the middle and left hepatic veins typically have a common trunk in 65-85% of patients. The MHV drains the central part of the liver and receives tributaries from segments 4, 5, and 8.<sup>6</sup> During the transplantation of the RL of the liver, it is important to consider the potential reconstruction of significantly larger veins from segments 5 and 8 (over 5 mm in diameter) to avoid congestion in the anterior sector of the transplant.<sup>7</sup> Impairment of venous drainage from the transplant is one of the main causes of liver failure in the postoperative period.<sup>8</sup>

To ensure the integrity of the transplant function, adequate venous drainage of the transplant is as important as blood supply to the liver. Therefore, to achieve optimal outcomes for both the transplant and the recipient, it is necessary to reconstruct all hepatic veins (HV) during the transplantation of the RL of the liver.

The aim of this study is to investigate the effectiveness of using the great saphenous vein for the reconstruction of the hepatic veins in right lobe liver transplantation.

### Materials and Methods

This is cross-sectional study of the observational retrospective-prospective study involving patients with end-stage

liver disease who received treatment at the Hepatopancreatobiliary Surgery and Liver Transplantation Department of the A.N. Syzganov Scientific Center of Surgery from 2011 to 2024.

From December 2011 to August 2024, a total of 297 liver transplants (LT) were performed in adults and children. Among these, 268 (90.2%) were from living donors, including 50 (18.6%) liver transplants in children and 29 (9.8%) from deceased donors. Of the adult population, 218 liver transplants were performed, with the right lobe used in 178 cases. Reconstruction of the hepatic veins of segments 5 and 8 during right lobe liver transplantation was performed in 80 cases (44.9%). Reconstruction of the hepatic veins can indeed be justified for patients with hepatic vein diameters greater than 5 mm and a graft-to-recipient weight ratio (GRWR) of less than 1. These criteria allow for the selection of the most suitable candidates for the procedure, thereby ensuring higher chances of a successful outcome and minimizing complications.

#### *Inclusion criteria:*

Age between 18 and 60 years

Gender: male and female

Type of graft: RL with reconstruction of HV from segments 5 and 8

Voluntary consent of the patient to participate in the research study.

#### *Exclusion criteria:*

Pediatric transplantation

Transplantation from a deceased donor

Type of graft: left lobe, whole liver, RL without reconstruction of HV from segments 5 and 8.

**Ethical approval.** The clinical trial protocol, the informed consent form, and the information sheet were approved by the Local Bioethics Committee of the National Scientific Surgery Center named after A.N. Syzganov (protocol of meeting №4 dated November 10, 2023).

**Statistical analysis.** Data were analyzed using IBMSPSS Statistics software (IBMSPSS Inc.). Numerical variables were expressed as mean  $\pm$  SD and categorical variables as numbers and percentages. Nonparametric statistics were performed for dataset analysis. Between-group comparisons were assessed for numerical variables, and the

Chi-square test was used for categorical variables. P value  $\leq 0.05$  was considered statistically significant. The analysis of the main risk factors and their corresponding causal relationships was assessed by calculating the Odds Ratio (OR): OR=1 means that the odds are equal in both groups; OR>1 means that the event is directly related and has a chance of occurring in the first group; OR<1 means that the event has an inverse relationship and chance to occur in the second group.

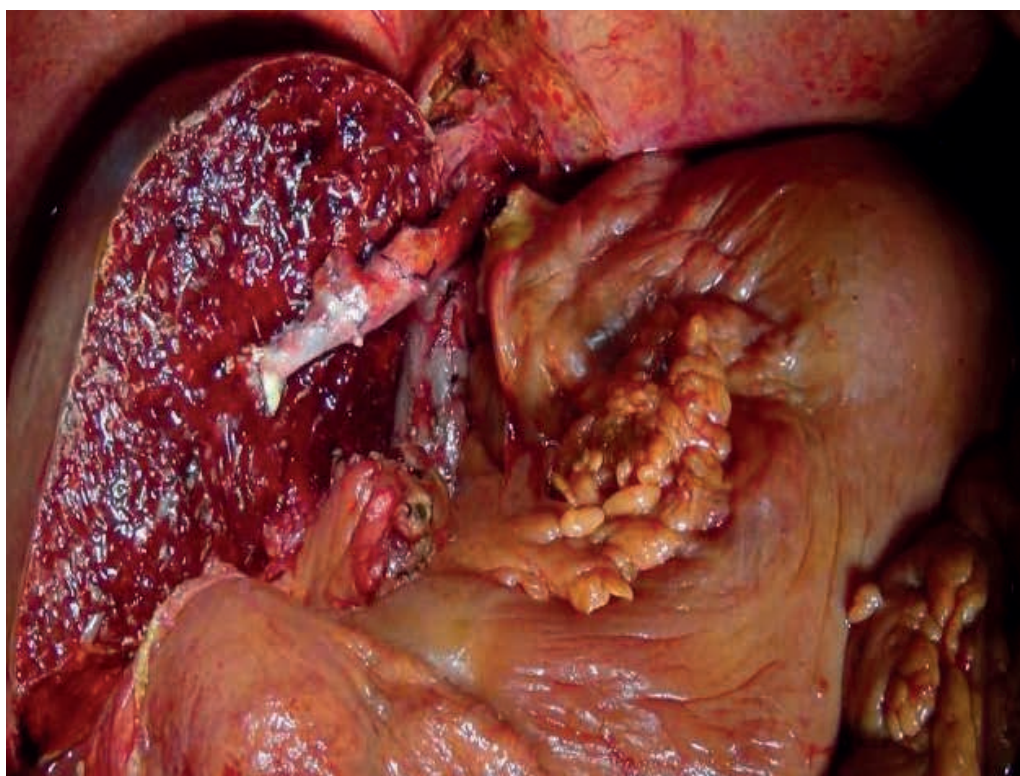
### Results

Depending on the material used for the reconstruction of the HV of segments 5 and 8, the patients (n=80) were retrospectively divided into two groups. In the first group, reconstruction of the HV of segments 5 and 8 was performed using biological grafts in 69 (86.25%) cases (recipient portal vein (PV) n=60, modified great saphenous vein (GSV) n=7, vessels from post-mortem donors n=2). The second group of patients completed the reconstruction of the HV of segments 5 and 8 using vascular prostheses in 11 (13.75%) cases. All patients underwent transplantation of the RL of the LDLT. The study was approved by the local ethics committee. Written informed consent was obtained from all patients prior to the operation.

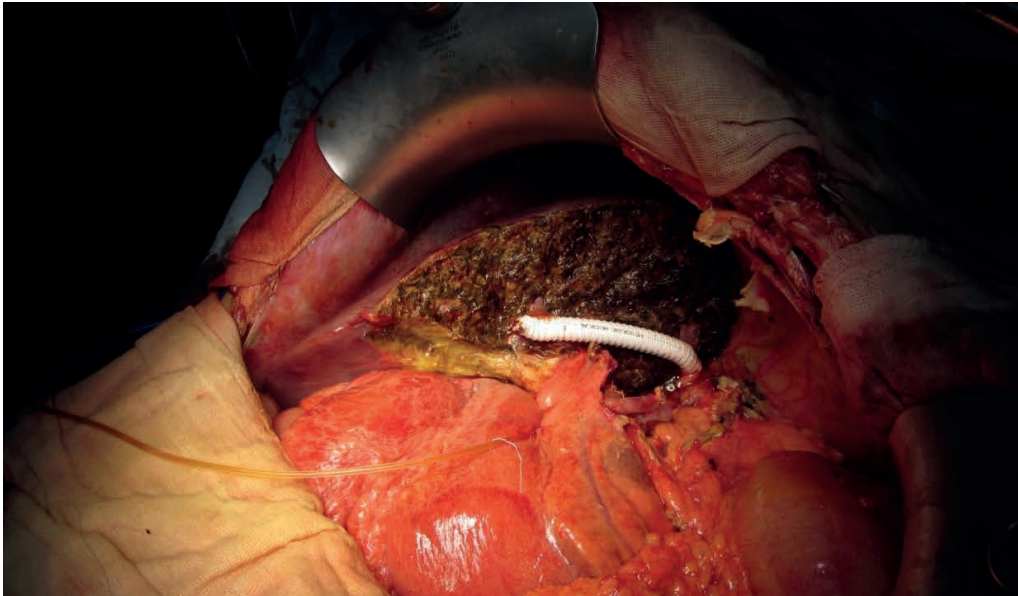
To perform differential and topical diagnosis, a comprehensive examination was conducted, including general clinical and biochemical laboratory methods, ultrasound, magnetic resonance cholangiography, and CT of the abdominal organs.

Surgical intervention in both recipients and donors was standardized for the entire group of patients. As the standard protocol for donor selection, we chose grafts with a future liver remnant (FLR) >30% and a GRWR > 0.7. The veins of segments V and VIII, which join the MHV, were separated. During the preparation of the graft on the back table, the anterior sectoral veins of the graft were reconstructed using various materials. A neo-vein was formed by performing an end-to-end anastomosis on the main vein of segment V (V5), followed by an end-to-side anastomosis on the vein of segment VIII (V8). Furthermore, all veins larger than 5 mm in diameter or with significant outflow during static perfusion were side-to-side anastomosed to create a neo-MHV. The distal end of the neo-MHV was connected to the MHV in the graft. If present, significant lower HV were anastomosed separately to the IVC. In all cases, intraoperative duplex scanning was performed, and satisfactory results were achieved before closure.

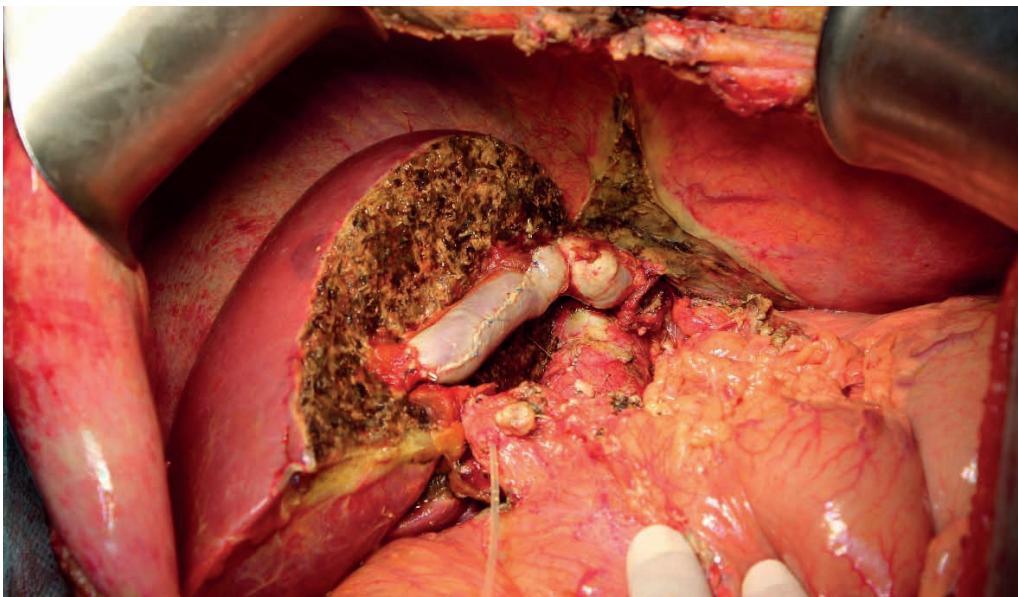
**Figure 1.**  
Reconstruction of the hepatic veins of segments 5 and 8 using the recipient's PV.







**Figure 2.** Reconstruction of the hepatic veins of segment 5 using a vascular prosthesis.



**Figure 3.** Reconstruction of the hepatic veins of segments 5 and 8 using a modified GSV.

Eighty patients who underwent LDLT operative, and intraoperative data are due to end-stage liver disease were included in our study. Their demographic, presented in Table 1.

Characteristics	Reconstruction with		t-statistic	Chi-squared	95%CI	P value
	a bio graft n=69	a vascular prosthesis n=11				
Age (years)	43.1±8.5	49.4 ±8.7	2.276 <sup>a</sup>	-	[0.7;11.8]	0.026*
Gender (%)						
Male	33 (41.3%)	5(6.3%)	-	2.230 <sup>b</sup>	[11.3;52.8]	0.135
Female	36(45.0%)	6(7.5%)	-	2.951 <sup>b</sup>	[5.2;54.8]	0.086
MELD	17.5±4.9	20.0±3.6	1.620	-	[0.5;5.6]	0.109
Ischemia (min)						
Cold	87.8±46.1	105.1±45.9	1.157	-	[12.5;47.1]	0.251
Thermal	37.8±16.7	35.0±14.6	0.524	-	[13.4;7.8]	0.602

**Table 1.** General and clinical Characteristics



GRWR	1.07 ± 0.15	1.08 ± 0.17	0.202	-	[0.09;0.1]	0.841
Duration of the operation (min)	766.7 ± 107.3	827.2 ± 128.8	1.684	-	[11.0;132.0]	0.096
Volume of blood loss (ml)	2411.5 ± 1388.02	2972.7 ± 1627.3	1.216	-	[357.3;1479.7]	0.227
Graft weight	706.6±105.6	690.2±99.4	0.482	-	[84.1;51.3]	0.631
Reconstruction HV5	19 (23.8%)	5 (6.3%)	-	0.722	[28.3;40.7]	0.396
Reconstruction HV8	16 (20.0%)	2 (2.5%)	-	0.348	[48.7;41.9]	0.556
Reconstruction HV5 and HV8	34 (42.5%)	4 (5.0%)	-	2.069 <sup>β</sup>	[13.6;54.7]	0.150
Post-op period (days)	28.7±13.7	40.7±13.7	2.698 <sup>α</sup>	-	[3.1;20,8]	0.008*

α: The value relative to the degree of freedom corresponds to a significance level <0.05;  
 β: The observed frequency distribution is significantly different from its expected frequency distribution; \*Statistically significant difference P<0.05

The risk of in-hospital mortality in the second group with a vascular prosthesis was 3 (3.8%), which is not significantly higher than in the first group with a biological graft, which was 13 (16.3%), OR = 1.62, 95% CI [0.3; 6.9], P value = 0.519. The risk of postoperative complications in the second group with a vascular prosthesis was 5 (6.3%), which was the same as in the first group with a biological graft - 28 (35.0%), OR = 1.22, 95% CI [0.3; 4.4], P value = 0.761.

The chance of impaired blood flow based on control studies using Doppler ultrasound and CT angiography within 7 days in the second group with a vascular prosthesis was 2 (2.5%), which is twice as high as in the first group with a biological graft 6 (7.5%), OR = 2.333, 95% CI [0.4; 13.4], P value = 0.342.

The assessment of the chance of absent blood flow according to the control Doppler ultrasound and CT angiography data after 7 days also showed that in the second group with a vascular prosthesis, the rate was 3 times higher - 1 (1.3%), compared to the first group with a biological graft 2 (2.5%), OR = 3.350, 95% CI [0.3; 40.4], P value = 0.341.

#### Discussion

Transplantation of the right hepatic lobe is the most commonly performed procedure for LDLT. This procedure is

believed to provide a greater likelihood of obtaining a sufficient volume of functioning graft compared to the left lobe graft, which is typically smaller in size. There are two types of RL grafts: the first is the RL graft without the main MHV.<sup>9</sup> The second is with the main MHV (known as the extended right lobe graft).<sup>10</sup> When choosing the type of graft, the main criterion is that its functional volume must be adequate to meet the metabolic needs of the recipient. A consensus has been reached regarding a standardized methodology for obtaining the RL graft, which includes preserving the MHV in the donor for safety, provided that the expected volume of the donor's remaining liver is considered sufficient (preferably more than 35%).<sup>11</sup> However, transplantation of the RL of the LDLT without the main MHV can lead to congestion of segments 5 and 8 of the graft or the right anterior sector due to impaired outflow, which raises certain concerns.<sup>12</sup> Grafts without the main MHV that are larger in size are more susceptible to damage or small graft syndrome under congestive conditions. Even with an adequate RL GRWR, ideally exceeding 0.8, a non-functioning area of the right anterior sector may require further assessment prior to surgery.<sup>13</sup>

The transplantation of the right he-

hepatic lobe without reconstruction of the HV of segments 5 and 8 may lead to early graft dysfunction, resulting in hemodynamic disturbances, increased levels of liver parameters, and insufficient liver regeneration. To prevent congestion in the anterior sectors, several technical modifications have been developed. The Toronto team described a case demonstrating the reconstruction of partial MHV using the recipient's renal vein as a bridging graft to the IVC.<sup>14,15</sup> The Asan Medical Center group in Korea has made the most significant contribution to expanding the application of RL graft while simultaneously enhancing donor safety. In their landmark study, Lee and colleagues were the first to address the problem of anterior sector overload and its impact on graft function.<sup>15</sup> They also described the clinical implications of this phenomenon for the recipient and potential solutions, including the use of intermediate vascular grafts for the anterior sector, namely the reconstruction of HV V5-V8, known as «modified RL».<sup>16</sup>

For the reconstruction of HV, various types of autologous and homologous venous grafts were used depending on availability, as recommended for this type of venous reconstruction (e.g., internal iliac vein, umbilical vein, internal jugular vein, renal vein, PV, aorta and its branches, as well as IVC, etc.).<sup>17,18</sup> Additionally, the use of vascular prostheses is well-established. Synthetic vascular grafts have their unique features, advantages, disadvantages, and patency rates: 72.4% at one week, 42.1% at three months, and 24.1% at twelve months.<sup>15</sup> Preoperative planning is critical as it ensures easy access to native or prosthetic grafts during the surgery.

Lee *et al.* in their study compared two groups, depending on the material used for reconstructing the drainage of the anterior sector, using biological grafts  $n = 252$  (recipient's veins, recipient's arterial grafts, vessels from post-mortem donors) versus synthetic grafts  $n = 177$  (vascular prostheses). The patency rate in the first group after one week was 61.9%, and after three months was 46.8%. In the second group, the patency rate after one week was 72.4% and after three months was 42.1%.<sup>15</sup> The study by Li *et al.* showed that synthetic grafts had

better early patency (at one week), but after three months, the patency turned out to be lower than that of biological grafts. Durairaj *et al.* also compared two groups, one using the recipient's PV  $n = 62$  and the other using vascular prostheses  $n = 60$ . The patency rate in the first group after two weeks was 93.5% and after three months was 85.5%; in the second group, it was 90% after two weeks and 81.7% after three months.<sup>19</sup> In our study, the patency rate using biological grafts was 91.4% after one week and 88.6% after two weeks, while the patency rate for vascular prostheses was 81.9% after one week and 72.8% after two weeks. Our study demonstrates that the use of biological grafts shows a significantly higher level of patency compared to grafts made from synthetic materials.

It is currently widely accepted that all HV of segments 5 and 8 with a diameter greater than 5 mm should be reconstructed.<sup>20</sup> If there are multiple veins V5 or V8, neighboring tributaries may be combined into a single orifice. It could also be assessed during the donor operation after the clamping of the artery and the corresponding hepatic vein, resulting in the formation of a dark zone of blood accumulation at the drainage site. When performing reconstruction using both native and prosthetic grafts, with careful surgical technique, early patency rates (within 1 month) range from 80% to 100%, which is critical for graft regeneration.<sup>2</sup> Long-term patency of intermediate grafts for hepatic veins V5 and V8 is not a major concern, as late graft occlusion typically has limited clinical consequences.<sup>21</sup>

**Limitations:** This cross-sectional analysis was conducted mainly based on the results of a retrospective analysis, however, a long-range analysis requires a wide coverage of patients before and after liver transplantation from a living donor for prospective material collection and data analysis.

**What's known?** Reconstruction of the hepatic veins of segments 5 and 8 of the right lobe liver transplant requires precise execution of the surgical technique. Venous outflow directly affects the function of the graft and the general condition of the recipient. Adequate reconstruction

of the hepatic veins determines the outcome of the right lobe liver transplant.

**What's new?** The results of the reconstruction of the use of a vascular prosthesis or with a bio graft depend on factors such as age, time of cold ischemia and MELD, which affects the risk of impaired blood flow in the transplant in the early and late postoperative periods.

#### Conclusion

Taking into account that this study recorded a higher patency rate of biological grafts compared to vascular prostheses, we believe that biological grafts should be considered the preferred option for reconstruction using neo-MHV during RL liver transplantation from a living donor. The higher patency rate of biological grafts compared to vascular prostheses may indicate better functional outcomes and a lower incidence of complications.

Larger studies are required.

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# SINGLE-CENTER EXPERIENCE OF HEART TRANSPLANTATION AT THE HEART CENTER OF ASTANA

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## Abstract

**Background.** Chronic heart failure is a major global health issue. As a complication of most cardiovascular diseases, it affects 4% of the population. Heart transplantation is the gold standard in the treatment of patients with end-stage heart failure. Objective of the study was to evaluate early and long-term outcomes of heart transplants performed at the Heart Center University Medical Center (Heart Center) over a 10-year period.

**Materials and methods.** Cross-sectional study was conducted from 2012 to 2022, 86 orthotopic heart transplants were performed at the Heart Center. The analysis of the obtained results was conducted retrospectively.

**Results.** From August 2012 to December 2022, 114 patients were on the waiting list for heart transplantation. Of these, 86 (75.4%) patients underwent transplantation; 10 (8.7%) patients were excluded. Among the 86 patients, 49 (56.9%) had previously undergone cardiac surgery. Of these, 42 (48.8%) had a left ventricular assist device implanted earlier, 3 (3.4%) had a fully artificial heart, and 2 (2.5%) were on temporary mechanical support (central veno-arterial Extracorporeal membrane oxygenation). Hospital mortality was 8 (9.3%) recipients. In 2.7% of cases, the cause of death was an acute cerebrovascular accident on the second day post-surgery. Postoperative renal dysfunction was noted in 28 (32.5%) patients. An analysis of all performed heart transplantation cases showed a 30-day survival rate of 94%, a 1-year survival rate of 84.3%, and a 5-year survival rate of 64.7%.

**Conclusion.** In the hospital period and the first 6 months after heart transplantation, infectious-septic complications were predominant, whereas in later periods, rejection reactions were more common.

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## Introduction

Chronic heart failure (CHF) is a major global health issue. As a complication of most cardiovascular diseases, it affects 4% of the population. The mortality rate within a year for this group, even with treatment in specialized hospitals, is 10.2%.<sup>1</sup> For patients with refractory CHF, the one-year mortality rate can reach 50%.<sup>2</sup> The number of patients reaching the end stage of CHF is constantly increasing. This is due to both the rise in life expectancy and the improved

effectiveness and quality of cardiovascular disease treatments. Heart transplantation (HT) is the gold standard in the treatment of patients with end-stage heart failure.

Modern pharmacotherapy includes the use of beta-blockers, angiotensin-converting enzyme inhibitors, sacubitril/valsartan, dapagliflozin and empagliflozin, and diuretics, including aldosterone receptor antagonists.<sup>3</sup> As a complement to pharmacological therapy, cardiac resynchronization therapy



(CRT) is used.<sup>4</sup> The use of CRT in patients with left ventricular dyssynchrony can prevent or delay the need for heart transplantation or serve as a bridge to transplantation.<sup>5,6</sup> For patients, with severe mitral regurgitation, the mitral clipping technique—transcatheter mitral valve repair—can be applied.<sup>7</sup> Heart transplantation is performed only when all other measures have failed to produce the desired results. Due to the increasing number of patients with end-stage heart failure and the limited availability of donor organs, not everyone in need of a heart transplant can receive one.<sup>8</sup> Survival rates after heart transplantation are significantly higher compared to the natural progression of terminal heart failure. According to the latest data provided by the International Society for Heart and Lung Transplantation, the 1-year survival rate is 84.5% and the 5-year survival rate is 72.5%.<sup>9</sup> These survival rates have significantly improved compared to the 1980s, when the 1-year survival rate was 76.9% and the 5-year survival rate was 62.7%. At the University Hospital Zurich in Switzerland, a 20-year survival rate of 55.6% was reported.<sup>10</sup> Over the past decades, there has been a significant improvement in heart transplantation outcomes, primarily related to increased survival during the first year post-operation. In the longer term, patient survival is significantly influenced by complications such as chronic transplant vasculopathy, malignancies, infectious complications, transplant rejection, and renal failure.<sup>8</sup> Until 2011, surgical treatment for heart failure was virtually unavailable in Kazakhstan. In 2011, our Center performed the first implantation of a left ventricular assist device (LVAD). We anticipated that the implementation of our mechanical circulatory support program would serve as a catalyst for developing the first heart transplantation program in our country. This vision came to fruition when the first heart transplantation was successfully performed in August 2012.

The aim of our study was to evaluate the early and long-term outcomes of heart transplantations performed at the Heart Center of University Medical Center over a period of 10 years.

## Materials and Methods

This study was an observational, analytical, cohort, retrospective analysis of 86 orthotopic heart transplantations conducted at the Heart Center of University Medical Center from 2012 to 2022. The analysis of the obtained results was conducted retrospectively.

**Ethical approval.** The study was conducted in strict accordance with the principles outlined in the Helsinki Declaration. Prior to commencement, the study received approval from the Local Bioethics Committee of the Corporate Foundation “University Medical Center,” protocol #3 dated 14/07/2023.

**Statistical Analysis.** Statistical analyses were performed applying Stata (version 3.6.3). The significance level for all statistical tests was set at 0.05. Data were presented as mean values  $\pm$  standard deviation (SD) or medians for quantitative variables and percentages for qualitative variables. The 30-day survival rate adds the 1-year survival rate was calculated by Kaplan-Meier survival analysis. The analysis of the main etiological factors in the development of terminal chronic heart failure and the corresponding causal relationship was assessed by calculating the odds ratio (OR).

## Results

**Recipients** From August 2012 to December 2022, there were 114 patients on the heart transplant waiting list. Of these: 86 patients (75.4%) underwent heart transplantation. 10 patients (8.7%) who were in the hospital setting died due to progressive heart failure with no possibility of heart transplantation or use of mechanical support as a bridge to transplantation. 4 patients (3.5%) exited the hospital setting for various reasons. One patient achieved disease remission, showing improved hemodynamic parameters and ejection fraction due to tailored therapy. The etiology of terminal heart failure among the recipients was: Dilated cardiomyopathy in 52 patients (60.4%). Ischemic cardiomyopathy in 22 patients (25.8%). Valvular pathology in 7 patients (8.1%).

Other causes (arterial hypertension, hypertrophic cardiomyopathy) in 5 patients (5.8%).

There were 68 male patients (79.5%) and 18 female patients (20.5%). The

average age of recipients was  $42 \pm 9.4$  years (ranging from 17 to 64 years). The average duration of illness at the time of transplantation was  $4.33 \pm 2.51$  years.

By the time of the operation, 60 recipients (69.7%) were classified as NYHA

functional class IV of chronic heart failure according to the New York Heart Association (NYHA) classification.

Characteristics of recipients and the etiology of terminal heart failure were detailed in Tables 1 and 2.

**Table 1.**  
Characteristics of recipients

Data	Quantity (percentage)
Men	68 (79.5%)
Women	18 (20.5%)
Age	$42 \pm 9.4$ years
Diabetes	9 (7.7%)
Cardiorenal syndrome	17 (19.7%)
Chronic obstructive pulmonary disease	19 (22.1%)
History of acute cerebrovascular accident	7 (8.1%)
Previously undergone surgery	49 (56.9%)
Left ventricular assist device	42 (48.8%)
Artificial heart for adults <i>CARMAT</i>	3 (3.4%)
Extracorporeal membrane oxygenation	2 (2.5%)

**Table 2.**  
Etiology of terminal chronic heart failure

Disease	Men (n-68)	Women (n-18)	OR	95%CI	P value
Dilated cardiomyopathy	38	14	0.316 $\gamma$	[0.10;1.21]	0.997
Cardiac ischemia	20	2	3.333 $\alpha$	[0.70;15.85]	0.130
Rheumatic disease	3	1	0.785 $\gamma$	[0.08;8.03]	0.838
Congenital heart disease	3	-	3.648 $\alpha$	[0.18;74.46]	0.400
Hypertensive cardiomyopathy	2	-	1.391 $\beta$	[0.06;30.26]	0.834
Hypertrophic cardiomyopathy	1	1	0.253 $\gamma$	[0.02;4.07]	0.341
Ivemark Syndrome	1	-	0.822 $\gamma$	[0.03;21.03]	0.906

$\alpha$  - OR>1 means that the event is directly related and has a chance of occurring in the first group;  
 $\beta$  - OR=1 means that the odds are equal in both groups;  
 $\gamma$  - OR<1 means that the event is directly related and has a chance of occurring in the second group

The echocardiographic data were characterized by significantly reduced left ventricular myocardial contractility - left ventricular ejection fraction (LVEF) of  $17.6 \pm 4.9\%$  (range 8–27%), cardiomegaly (end-systolic left ventricular dimension of  $71.3 \pm 9.8$  mm (range 35–95 mm), end-diastolic left ventricular volume of  $273.25 \pm 84.2$  ml (range 52–524 ml), and high pulmonary hypertension (mean pulmonary artery pressure of  $55.6 \pm 13.27$  mmHg (range 25 to 82 mmHg).

The evaluation included a test assessing the degree of heart failure (6-minute walk test), which averaged  $210.08 \pm 96.6$  meters. 60 recipients (69.7%) were clas-

sified as NYHA functional class IV, while the remainders were classified as NYHA functional class III.

According to the results of right heart catheterization, pulmonary vascular resistance was  $2.4 \pm 1.7$  Wood units (ranging from 1.0 to 7.4 Wood units). Peak oxygen consumption (VO<sub>2</sub>max) was determined using cardiopulmonary exercise testing. The average VO<sub>2</sub>max value was  $11.7 \pm 2.73$  ml/kg/min.

The evaluation aimed at determining eligibility for heart transplantation also included assessment of a wide range of clinically significant comorbidities. Type 2 diabetes mellitus was present in 9

(7.7%) patients, cardiorenal syndrome in 17 (19.7%), chronic obstructive pulmonary disease (COPD) in 19 (22.1%), prior cerebrovascular accident in 7 (8.1%) recipients, and a frontal lobe cavernoma in 1 (1.2%) patient.

In 49 (56.9%) cases, patients had previously undergone cardiac surgery, including 42 (48.8%) who had received a left ventricular assist device, 3 (3.4%) who had a total artificial heart *CARMAT*, and 2 (2.5%) who were on temporary mechanical support (central veno-arterial extracorporeal membrane oxygenation (ECMO)).

**Donors.** The main causes of death among donors were acute cerebrovascular events - 66.6%, traumatic brain injury - 31%, and isolated brain tumors - 2.1%. The average age of donors was  $36 \pm 0.7$  years (ranging from 20 to 67 years). There were 53 (61.2%) males and 33 (38.7%) females. The most significant limiting factor for performing heart transplantation is the insufficient number of donor organs available. Therefore, we considered donors with expanded criteria, including those older than 50 years and those with significant myocardial hypertrophy (more than 1.4 cm). When selecting donor-recipient pairs, body weight was considered, with a maximum difference of 30% between the donor and recipient.

**Surgical Features.** Considering various factors such as a significant proportion of patients previously implanted with various long-term mechanical circulatory support systems and the geographical distance between donor hospitals and the transplant center, the ex vivo donor heart conditioning system (OCS) was utilized in 56 (65.11%) cases. Bicaval and biatrial techniques were applied in 57 (66.3%) and 29 (33.7%) cases, respectively. Temporary parameters included: cross-clamp time of  $248.4 \pm 86.7$  minutes (ranging from 108 to 672), anoxia time of the donor heart when using the OCS system was  $68.9 \pm 15.4$  minutes (ranging from 45 to 129), average duration of normothermic perfusion in the Organ Care System apparatus was  $275 \pm 104$  minutes, and the mean operative time was  $386.7 \pm 129.5$  minutes (ranging from 185 to 775). In 32 (37.2%) cases, central veno-arterial ECMO was

implanted intraoperatively with an average duration of 7.7 days. Additionally, in 6 cases, superior vena cava reconstruction was performed using a xenopericardial patch. The average length of stay in the intensive care unit was  $12.2 \pm 8.67$  days.

**Immunosuppressive Therapy.** During heart transplantation, we utilized induction therapy aimed at reducing the risk of acute rejection and delaying the administration of nephrotoxic calcineurin inhibitors. In our case, induction immunosuppression included:

Oral administration of tacrolimus (Prograf) at a dose of 0.1 mg/kg over 3-6 hours before the operation,

Infusion of anti-thymocyte globulin (ATG) at a dose of 1.5 mg/kg. One-third of the ATG dose should be infused before clamping the aorta, and the remainder after unclamping, to be continuously infused for up to 6 hours,

Administration of methylprednisolone 500 mg intravenously over 30 minutes to 1 hour before surgery. In the first three days, ATG is administered every 24 hours for 6 hours under CTD monitoring. During the first day post-transplantation, methylprednisolone 125 mg was administered intravenously every 8 hours (3 times a day). On the second day, methylprednisolone 100 mg was administered intravenously every 8 hours. After extubation, patients received a three-component tablet immunosuppressive therapy based on their blood tacrolimus levels: Prograf (tacrolimus), CellCept (mycophenolic acid) 2000 mg/day, and prednisolone 1 mg/kg orally with a reduction of 5 mg every other day. The immunosuppressive therapy was tailored to minimize the toxic effects of the medications on the recipient. Histological evaluation of biopsies was conducted according to the ISHLT-2005 classification. The average length of stay in the hospital for recipients was  $46.4 \pm 11.4$  days.

#### Discussion

86 patients were included in outpatient follow-up. Hospital mortality was observed in 8 (9.3%) recipients. The most common cause of early mortality was infectious-septic complications and multi-organ failure (MOF), accounting for 54% of the fatalities. Specifically, the combi-

nation of sepsis and MOF led to death in 32%, while 30% succumbed solely due to sepsis. In 2.7% of cases, death occurred due to stroke on the 2nd day.

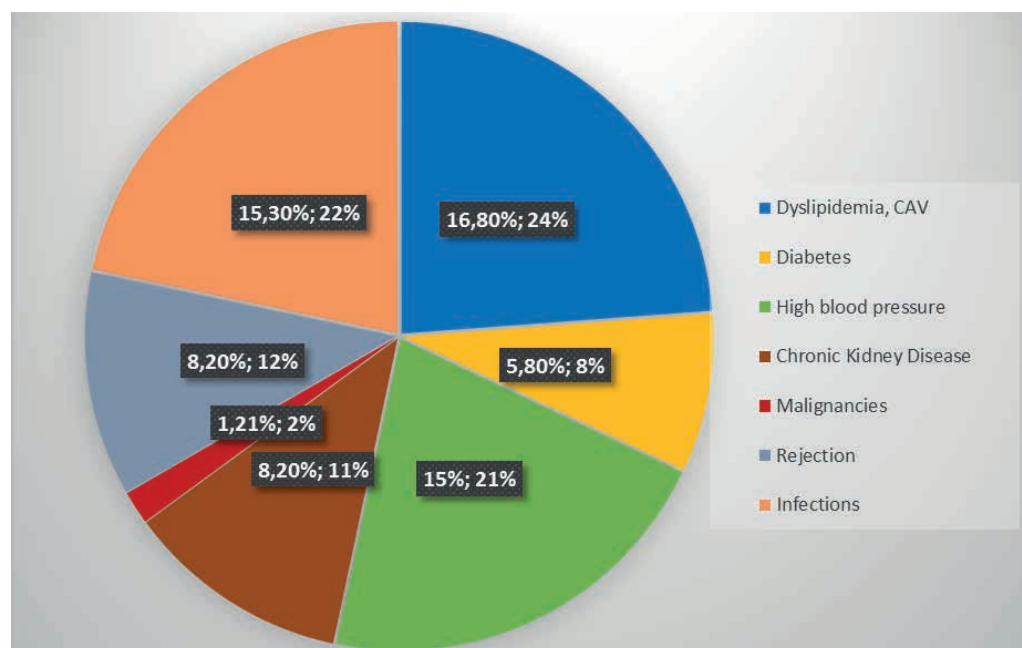
Postoperative renal dysfunction was noted in 28 (32.5%) patients. Among them, 11 recipients experienced oliguria, progressing to anuria, with significant increases in potassium, urea, and creatinine concentrations, necessitating he-

modiafiltration (HDF), with the number of sessions varying from 1 to 13 per patient. In 13 recipients, renal function fully recovered after HDF was performed.

Infectious complications during the hospital period were represented by bacterial pneumonia in 18.3% of cases among patients.

Complications after heart transplantation are presented in Figure 1.

**Figure 1.**  
Frequent complications after transplantation



Acute rejection episodes (ARE) during the hospital period were diagnosed in 4 (4.6%) recipients. To manage acute rejection crises, pulse therapy with methylprednisolone was administered (at a dose of 1000 mg over 4 hours, for 3-5 days). For cytomegalovirus infection prophylaxis, all patients received antiviral medications (valganciclovir 900 mg/day).

Two patients (2.3%) received permanent pacemakers (PPM) due to post-transplant third-degree atrioventricular block and sick sinus syndrome. In the long-term period, 19 recipients deceased. The primary cause of late fatalities was rejection reaction, occurring in 10 (52.6%) cases, with 2 cases in combination with multiorgan failure. One patient passed away after 3 years due to prostate cancer development. One patient died from pulmonary tuberculosis 4 years after HTx. Two patients died from chronic renal failure (CRF) 5 and 6 years after HTx. In 5 cases, the

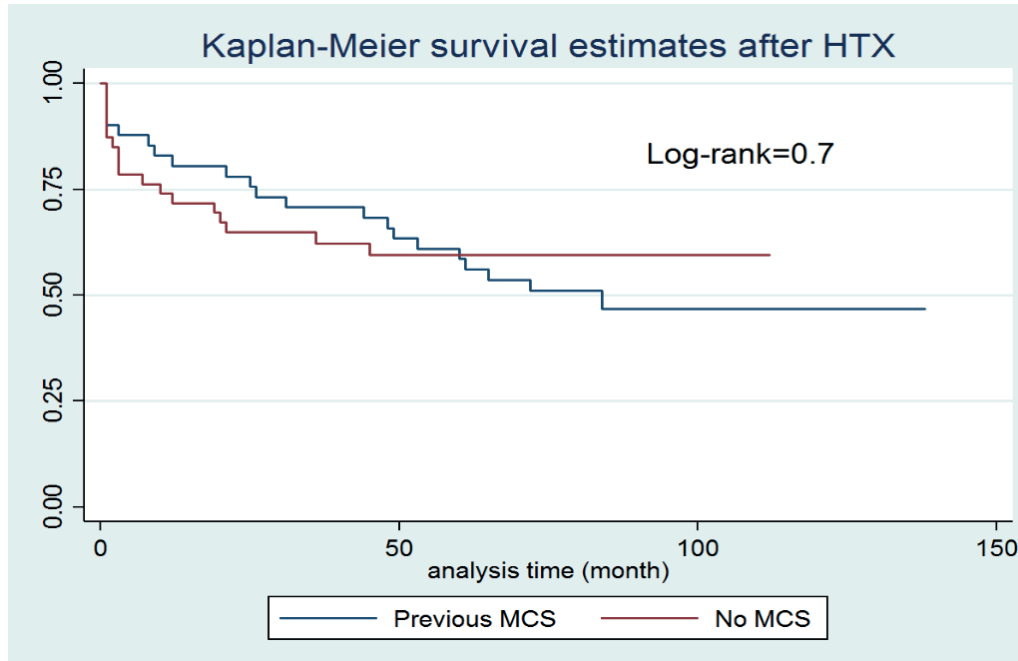
cause of death was COVID-19 after HTx. As is known, long-term survival after HTx mainly depends on coronary artery disease (the main reason), infectious complications, and acute rejection of the transplant after the first year following HTx. In the long term, rejection reactions occurred in 6 cases, accounting for 6.9%, and infectious complications in the form of pneumonia of specific origin (mainly Pneumocystis etiology) were observed in 9 (10.4%) patients. After 5 years post-HT, coronary artery disease of the transplanted heart (CADTH) was verified in 1 patient, with coronary angiography (CAG) showing two-vessel disease of the coronary artery. Mammary-coronary bypass grafting of the anterior interventricular branch and aortocoronary bypass grafting of the obtuse marginal artery were performed. Subsequently, coronary angiography + graftography confirmed adequate functioning of the grafts. Vasculopathy post-HT was noted in 6 (6.9%) cases during scheduled CAG

and intravascular ultrasound (IVUS) examination. In all cases, intensified immunosuppression and lipid control were implemented. Follow-up IVUS examinations showed improvement.

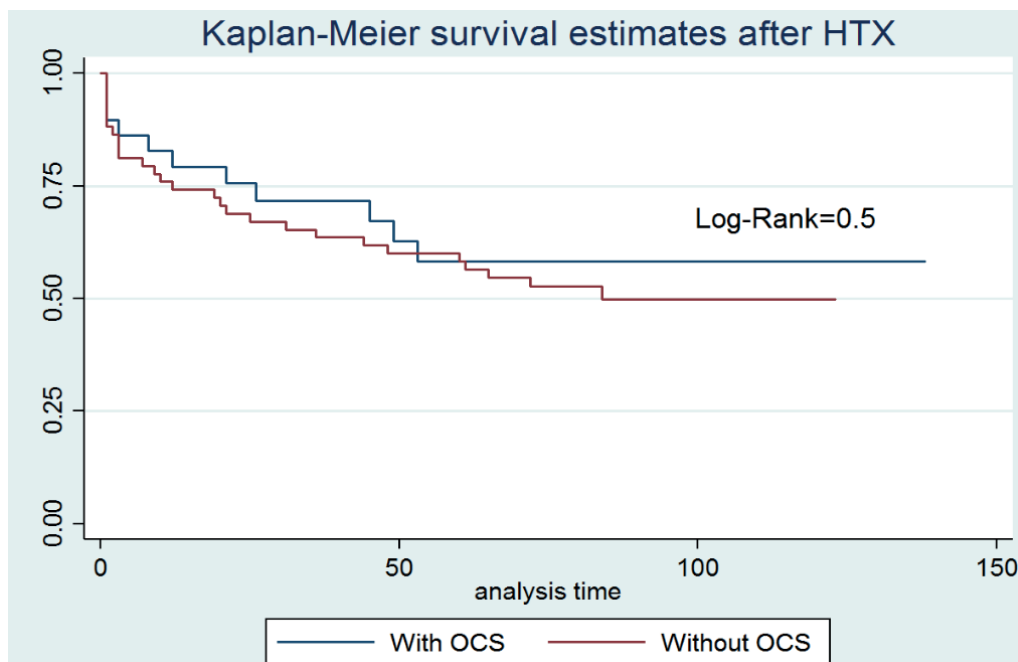
According to various sources, the most significant kidney impairment develops within the first year post-HT and directly correlates with the level of tacrolimus in the blood. In this case, the main preventive measures include fre-

quent monitoring of tacrolimus levels in the blood and maintaining fluid balance. In our case, renal dysfunction developed after HT within the first 6 months in 4 patients, and after this period, in 7 recipients.

An analysis of all performed HT cases was conducted. The 30-day survival rate was 94%, the 1-year survival rate was 84.3%, and the five-year survival rate was 64.7% (Figure 2 and 3).



**Figure 2.** Survival of patients who were previously on long-term mechanical support and without it: Previous MCS (Mechanical Circulatory Support) - patients with previously implanted long-term mechanical support devices.



**Figure 3.** Patient survival with and without OCS (Organ Care System) for donor heart conditioning.

**Limitations:** This study has potential limitations. Small sample size may restrict the generalizability of the find-

ings and increase the potential for bias. Moreover, this study describes the experience of one center and we can't gener-



alize the findings of this research. Future research with a larger number of studies and more standardized methodologies would be beneficial to confirm and extend these findings.

**What's known?** Heart transplantation is the gold standard in the treatment of patients with end-stage heart failure. Survival rates after heart transplantation are significantly higher compared to the natural progression of terminal heart failure.

**What's new?** During the hospitalization period and the first 6 months post-HT, infectious and septic complications predominated, while rejection reactions were more common in later periods. To reduce complications after HT optimization of immunosuppressive therapy is essential. Implementation of non-invasive diagnostic markers for detecting organ rejection should be integrated into practice.

#### Conclusion

Based on a 10-year experience, it can be unequivocally stated that heart transplantation is an effective treatment method for patients with severe heart failure. It increases patient survival rates, improves tolerance to physical activity, enhances quality of life, and enables most patients to return to active life. During the hospitalization period and the first 6 months post-HT, infectious and septic complications predominated, while rejection reactions were more common in later periods. To reduce complications after HT in both the

hospital and long-term settings, optimization of immunosuppressive therapy is essential. Implementation of non-invasive diagnostic markers for detecting organ rejection should be integrated into practice. The decade-long experience of HT in our center has demonstrated survival rates comparable to those reported by the International Society for Heart and Lung Transplantation.

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**Authors' Contributions:** YuP, GSh, SP – Collection and preparation of data, primary processing of the material and their verification. AG, ShA, YY – Statistical processing and analysis of the material, writing the text of the article (material and methods, results). SN, GD, AA – Writing the text of the article (introduction, discussion). SN, YuP, AA – Concept, design and control of the research, approval of the final version of the article. All authors approved the final version of the manuscript

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## MYOCARDIAL DYSFUNCTION IN POLYTRAUMA

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The authors declare no potential

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in this article.

**Keywords:**

trauma; myocardial dysfunction;

immunology.

**Abstract**

Trauma remains one of the leading causes of mortality worldwide, particularly among the young population. A significant number of people die within the first 48 hours due to acute cardiovascular pathology. Cardiac injury is a significant predictor of adverse outcomes following multiple trauma, associated with poor prognosis and prolonged hospitalization. Systemic elevation of cardiac troponin levels is linked to survival, the severity of trauma, and catecholamine consumption in patients after multiple trauma. Clinical signs of the so-called “commotio cordis” include arrhythmias, such as ventricular fibrillation and sudden cardiac arrest, as well as wall motion abnormalities. In trauma patients with inadequate hypotension and a lack of adequate response to fluid therapy, the possibility of cardiac injury should be considered. Therefore, a combination of electrocardiography, echocardiography, and the systemic determination of cardiomyocyte injury markers, such as troponin, appears to be an appropriate diagnostic method for identifying cardiac dysfunction after trauma. However, the mechanisms of post-traumatic cardiac dysfunction continue to be actively studied. The aim of this review is to discuss cardiac injury following trauma, focusing on the mechanisms of post-traumatic cardiac dysfunction related to inflammation and complement activation. The review illustrates the causal relationship between cardiac dysfunction and blunt chest trauma, multiple trauma, and hemorrhagic shock.

**Introduction**

Polytrauma, a condition in which a patient sustains multiple injuries affecting several organs or systems, is a leading cause of mortality among young people.<sup>1</sup> According to the World Health Organization (WHO) as of December 13, 2023, road traffic accidents are the primary cause of polytrauma, resulting in approximately 1.19 million deaths annually and causing disability in 20 to 50 million people.<sup>2</sup> In the early period following combined tissue damage and shock, hemostasis is disrupted, leading to the development of traumatic coagulopathy and massive bleeding. Many survivors of

massive bleeding experience organ dysfunction, including cardiac dysfunction. Even in the absence of direct cardiac injury in polytrauma, recent studies indicate the development of asymptomatic myocardial dysfunction within specific time frames—1 to 3 days, 1 to 6 months after the injury—often associated with the development of systemic inflammation or the so-called “double hit” theory.<sup>3</sup> The “double hit” theory considers early and late complications of polytrauma through the lens of primary soft tissue and organ damage; secondarily, it considers the Systemic Inflammatory Response Syndrome (SIRS), respiratory distress,

coagulopathy, acidosis, ischemia/reperfusion syndrome, and hemodynamic instability.<sup>3,4</sup> The severity of post-traumatic cardiac dysfunction is determined not only by the degree of mechanical myocardial contusion but also by damage caused by the release of damage-associated molecular patterns (DAMPs), cytokines, complementopathy, and the activation of the acquired immune response.<sup>5</sup> This reaction begins within 30 minutes after severe trauma and represents an inflammatory response to blood loss and tissue damage. SIRS arises due to the release of endogenous factors known as DAMPs ("alarmins") following tissue injury. These molecules are released from activated immune cells or necrotic cells and trigger a potent inflammatory response. DAMPs activate immune cells and complement, leading to the rapid production of inflammatory mediators such as interleukins, resulting in a systemic inflammatory response.<sup>3</sup>

This issue remains unresolved, and patients after polytrauma are often not monitored on an outpatient basis by specialists, nor do they receive preventive treatment, leading to late presentation with cardiovascular pathology (CVD), which can result in the development of heart failure (HF). Therefore, the aim of

this literature review is to study myocardial dysfunctions in polytrauma, associated with both direct cardiac injury and secondary injury due to systemic inflammation. Specifically, this review focuses on the study of all DAMPs associated with the development of heart failure.

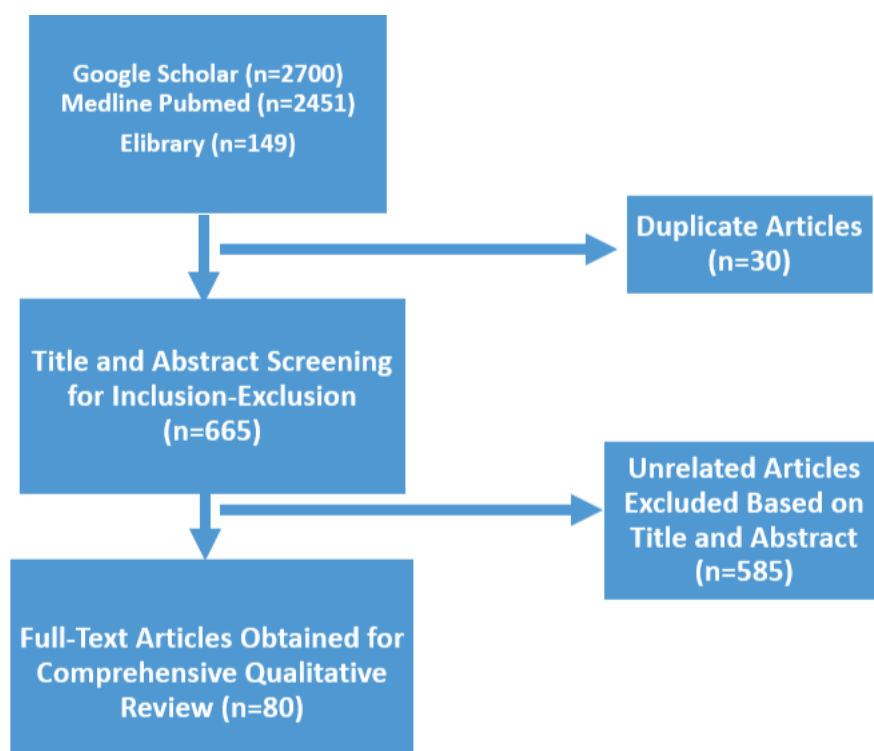
### Materials and Methods

**Literature Search.** To prepare this review article, literature search on the topic of myocardial dysfunction in polytrauma was conducted. The search included publications from PubMed and Google Scholar, Elibrary databases. The search was carried out using combinations of keywords such as "myocardial dysfunction", "heart dysfunction", "polytrauma", "immunology".

**Inclusion criteria:** articles published from 2014 to 2024, defined as original research articles, review articles, meta-analyses, clinical guidelines recommendations written in English language.

**Exclusion criteria:** non-original articles; case reports; articles without access to full texts; and duplicate articles.

As a result of the search, full text of 80 publications was reviewed. Selection of articles was made according to the inclusion and exclusion criteria. 17 articles which have met all the criteria were analyzed.



**Figure 1.** Article selection algorithm for review.

*Data Collection and Analysis.* All selected articles were analyzed and information about mechanisms of myocardial dysfunction, mechanism of the immune response, clinical consequences of myocardial dysfunction in polytrauma were added to the results and discussion part.

In addition, meta-analysis was conducted following PRISMA guidelines to evaluate the association between elevated Troponin 1 levels and myocardial dysfunction. Literature search was performed using PubMed, covering publications from 2019 to 2023. Included studies were prospective and retrospective cohort, community-based cohort and reduced trail designs involving patients aged 18 and older, with sufficient data to calculate ef-

fect sizes. Studies that were case reports, reviews, non-human, or lacked necessary data were excluded. Two independent reviewers extracted data on study characteristics, population details, and Troponin 1 measurements. Statistical analyses involved calculating pooled effect sizes using a random-effects model, assessing heterogeneity with the  $I^2$  statistic and performed by using R-studio software. The search in Pubmed returned 713 results, from which 144 full-text articles were screened covering the last 5 years. After applying the inclusion and exclusion criteria, seven studies describing the effect of Troponin 1 on heart failure were included in this meta-analysis.

**Results**

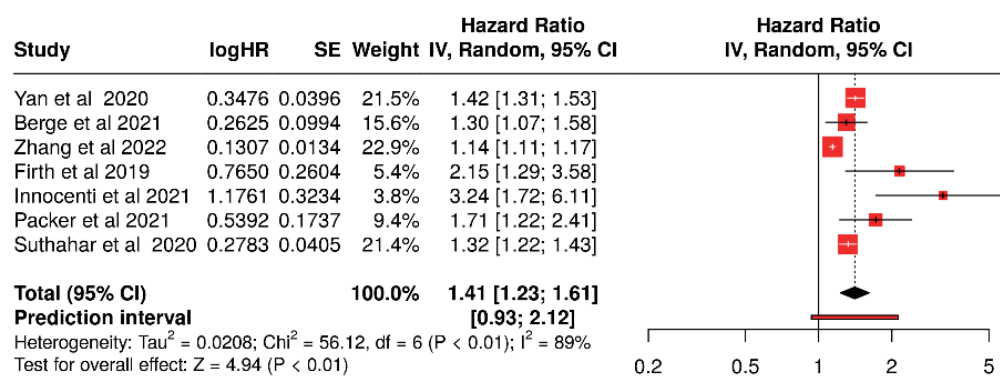
**Table 1.**  
Characteristics of studies included in meta-analysis.

Author	Publication year	Sample size	Gender (M)	Study design	Event
<i>Yan et al.</i> <sup>6</sup>	2020	48.455	23.321	Prospective population-based cohort study	Heart failure
<i>Berge et al.</i> <sup>7</sup>	2021	314	163	Prospective cohort	Heart failure
<i>Zhang et al.</i> <sup>8</sup>	2022	6487	4361	Retrospective cohort	Coronary stenosis
<i>Firth et al.</i> <sup>9</sup>	2019	561	332	Prospective	Cardiovascular events
<i>Innocenti et al.</i> <sup>10</sup>	2021	325	N/A	Prospective	Mortality
<i>Packer et al.</i> <sup>11</sup>	2021	3636	2767	EMPEROR-Reduced trial	Heart failure
<i>Suthahar et al.</i> <sup>12</sup>	2020	22.756	12.087	community-based cohorts	Heart failure

**Table 2.**  
Total troponin and hazard ratio results

	Heart failure				
	Troponin mean (ng/l)	Hazard ratio	95% CI low	95% CI high	p-value
<i>Yan et al.</i> , <sup>6</sup> 2020	2.3	1.42	1.31	1.53	<0.001
<i>Berge et al.</i> , <sup>7</sup> 2021	13	1.30	1.07	1.58	<0.009
<i>Zhang et al.</i> , <sup>8</sup> 2022	9	1.14	1.11	1.17	<0.05
<i>Firth et al.</i> , <sup>9</sup> 2019	0.068	2.15	1.29	3.58	<0.003
<i>Innocenti et al.</i> , <sup>10</sup> 2021	NA	3.24	1.72	6.11	<0.001
<i>Packer et al.</i> , <sup>11</sup> 2021	14	1.71	1.22	2.41	<0.001
<i>Suthahar et al.</i> , <sup>12</sup> 2020	NA	1.30	1.22	1.43	<0.05





**Figure 2.** Forest plot showing association between Troponin 1 and heart failure.

All hazard ratios calculated in studies were found to be greater than 1.0, which reflect the significance of the correlation. According to Figure 2 this meta-analysis suggests that elevated Troponin 1 increases the risk of heart failure by 41% on average (HR = 1.41), with a high degree of variability (heterogeneity) among the study results. The overall effect is statistically significant.

In this meta-analysis, the correlation between the increased level of troponin and the risk of heart failure highlights the potential of Troponin 1 as a biomarker for early detection and risk stratification in patients. The statistical significance of the overall effect, despite the heterogeneity among studies, suggests a robust association across diverse populations and study designs.

**Discussion**

Traumatic cardiac injury can present with a wide range of clinical manifestations, from asymptomatic conditions to near-fatal states. Studies of traumatic cardiac injury in pigs have shown reversible reductions in ejection fraction and fractional shortening.<sup>13</sup> In addition to these changes in systolic function, trauma may also affect diastolic function. To assess both systolic and diastolic functions after trauma, further research using echocardiographic measurements is required.

In addition to impairments in systolic and diastolic function, arrhythmias have been documented following trauma. Analysis of data from all trauma patients at a Level I trauma center accredited by the American College of Surgeons revealed that, over a period of two years, 258 patients were diagnosed with newly onset atrial fibrillation (AF) following trauma.<sup>14</sup> Literature on commotio cordis

cites numerous cases of sudden cardiac death caused by a ball striking the chest. Blunt chest trauma can lead to ventricular fibrillation, which in turn can cause sudden cardiac death.<sup>15</sup> Besides direct impact on the heart, there are reports of arrhythmias developing in patients following trauma not associated with chest impact. For example, one case involved a child who experienced QTc interval prolongation after a mild concussion.<sup>16</sup> In addition to systolic and diastolic dysfunction and arrhythmias, valve insufficiency has also been noted following trauma. For instance, chordae tendineae rupture caused by trauma led to acute and severe mitral regurgitation, as described in cases following motor vehicle accidents.<sup>17</sup> Several published reports on traumatic valve injury have demonstrated a wide range of symptoms: some patients could remain asymptomatic for many years, while others became hemodynamically unstable immediately after the injury.<sup>18,19</sup> Valve injuries occurred as a result of direct high-energy chest trauma, such as motor vehicle accidents and falls from heights. The most likely mechanism is a sudden deceleration or compression of the blood column in the heart during a vulnerable phase of valve operation.<sup>18</sup> In conclusion, it should be noted that the topic of traumatic valve injuries may be underappreciated in contemporary studies of cardiac contusions due to the wide range of symptoms and the complexity of diagnosing them.

*Biochemical Markers of Cardiac Injury.* During tissue damage, various molecules are released into circulation that can indicate damage to that specific tissue, serving as markers. In myocardial injury, various proteins and DNA molecules are released, which were previous-

ly markers for other acute conditions, such as myocardial infarction. For example, troponins (T, C, I) are small proteins that play a key role in calcium-regulated cardiac muscle contraction. In critically ill patients, elevated levels of cardiac troponin T are associated with increased in-hospital mortality; however, there is no correlation with long-term survival differences.<sup>20</sup> Additionally, in ICU patients following multiple trauma, elevated troponin T levels correlated with ISS and AIS scores, as well as with survival and catecholamine needs.<sup>13</sup> After trauma, systemic elevation of troponin was associated with myocardial contusion in 15–45% of cases. Systemic elevation of troponin in trauma patients has been described as a sensitive biomarker for detecting cardiac complications, especially when combined with electrocardiogram.<sup>20</sup> Recently published reports have documented elevated troponin levels in various experimental trauma models and species, including mice following multiple trauma,<sup>21</sup> asphyxia and hemorrhage in newborn piglets,<sup>22</sup> and multiple trauma with hemorrhagic shock in pigs.<sup>22</sup>

Before it was established that damaged cardiomyocyte membranes contribute to the release of troponin, cell necrosis was considered the only mechanism for its release.<sup>23</sup> Besides necrosis and apoptosis, there is growing evidence of various possible mechanisms for reversible systemic elevation of troponin.<sup>23</sup> This reversible cardiomyocyte (CM) damage has been associated with the release of microparticles, membrane vesicles, and increased cell membrane permeability.<sup>24,25</sup> Fragmented cardiac troponin is expected to result from irreversible cardiomyocyte damage, while systemic elevation of undamaged troponin is associated with reversible damage.<sup>26</sup> Structurally bound troponin undergoes degradation by calpains, which are activated by increased intracellular calcium or changes in pH levels.<sup>23</sup> Various damage-associated molecular patterns (DAMPs), such as extracellular histones, are known to induce increased intracellular calcium in cardiomyocytes, occurring due to increased membrane permeability or the formation of reactive oxygen species (ROS).<sup>13</sup> Additionally,

there is evidence that troponin I directly affects the heart; it has been shown to cause inflammatory heart disease in mice.<sup>27</sup>

Another myocardial damage biomarker is HFABP, which is detected in the bloodstream earlier after myocardial infarction compared to troponin.<sup>28</sup> Systemic elevation of HFABP was recently observed at early stages following experimental multiple trauma in pigs.<sup>13</sup> Clinical studies among polytrauma patients revealed increased levels of HFABP, as well as other proteins such as growth/differentiation factor 15 (GDF-15) and the surface receptor of the urokinase-type plasminogen activator (uPAR). Specifically, the concentrations of all three proteins in plasma were significantly higher in the subgroup of polytrauma patients with high troponin levels compared to healthy individuals. However, while the expression of HFABP decreased over time, the expression of uPAR and GDF-15 was higher at 24 hours compared to the time of admission.<sup>29</sup>

*Inflammation-Linked Heart Damage Indicators.* In response to early systemic inflammatory reactions, accompanied by the release of damage-associated molecular patterns (DAMPs) into the bloodstream,<sup>30</sup> the release of high mobility group box 1 (HMGB-1) protein has been observed in humans within 30 minutes of injury,<sup>31</sup> and it has been associated with injury severity, complement system activation, and mortality.<sup>31</sup> Additionally, in experimental models of multiple trauma, including chest trauma with hemorrhagic shock in pigs, elevated levels of HMGB-1 have been documented.<sup>32</sup> It is known that HMGB-1 can induce cardiomyocyte dysfunction, including cases of cardiac hypertrophy and heart failure,<sup>33</sup> as well as ischemia and myocardial reperfusion injury.<sup>34</sup> HMGB-1 also functions as a secondary DAMP molecule, interacting with extracellular histones through toll-like receptors (TLRs), particularly TLR-2, TLR-4, and TLR-9. Extracellular histones have been linked to traumatic lung injury and acute respiratory distress syndrome in humans,<sup>35,36</sup> as well as septic cardiomyopathy in mice.<sup>13</sup> DAMPs can contribute to increased intracellular calcium concentrations in cavernosal malformations, which are

associated with bradycardia and bigeminy.<sup>13</sup> Systemic release of circulating histones has been observed in rats with experimental blunt chest trauma, as well as in pigs and mice with multiple trauma.<sup>13,21,37</sup> Following systemic administration of extracellular histones in mice, there was an increase in inflammatory cytokines such as TNF, IL-1 $\beta$ , IL-6, and IL-10.<sup>38</sup> Additionally, HMGB-1 has been linked to the production of inflammatory cytokines,<sup>39</sup> including TNF, IL-1 $\beta$ , and IL-6.<sup>40</sup> Circulating histones accumulate in the heart and are associated with cardiomyocyte dysfunction, as well as dose-dependent production of reactive oxygen species (ROS) and increased intracellular calcium.<sup>13</sup> Histones also decrease mitochondrial membrane potential and ATP production in a dose-dependent manner, leading to reduced cardiomyocyte contractility due to energy deficiency.<sup>13,41</sup> TLR-4 has been found to play a key role in the development of cardiac dysfunction after trauma; its absence contributed to improved cardiac function in mice with traumatic hemorrhagic shock.<sup>42</sup>

Another molecule released by the heart in response to tissue damage is midkine. Midkine is an inflammatory cytokine and a heparin-binding growth and differentiation factor.<sup>43</sup> Systemic elevation of midkine levels has been observed following bone fractures, burns, and traumatic spinal cord injury.<sup>43,44</sup> After release following a fracture, midkine remains elevated in patients for up to 42 days.<sup>44</sup> Another mechanism through which midkine exerts damaging effects on human cardiomyocytes has been described. In this context, midkine caused significant changes in calcium handling by cells, manifested as increased amplitude of calcium delta peaks, reduced frequency of calcium peaks, and enhanced mRNA production of calcium-handling proteins such as sarcoplasmic/endoplasmic reticulum calcium ATPase (SERCA) and Na<sup>+</sup>/Ca<sup>2+</sup> exchanger.<sup>43</sup> Besides its effect on contractility through intracellular calcium changes, midkine also impaired mitochondrial function in cardiomyocytes and induced apoptosis.<sup>43</sup>

*Changes in Complement System Activation.* During experimental sepsis and following burn trauma, it has been found

that the complement activation product, complement factor (C5a), causes significant dysfunction in cavernous malformations both in vitro and in vivo by interacting with C5a receptors.<sup>41</sup> Another study of spinal cord injury due to contusion in the mouse model, C5a caused most damage in the acute phase, while it had some protective utility later with contribution to hypertrophy and glial scar formation.<sup>45</sup>

In trauma patients, complement system activation has been noted with increased levels of ComC.<sup>46</sup> ComC activation leads to activation of other complement elements, which also is associated with the development of acute respiratory distress syndrome and multiple organ failure.<sup>46</sup> In contrast to the threefold increase in C5a receptor (C5aR) expression in the myocardium after ischemia observed in experimental blunt chest trauma in mice,<sup>37</sup> experimental asphyxia and hemorrhage in piglets,<sup>22</sup> and experimental multiple trauma in pigs, C5a receptor factor (C5aR1) expression in the left ventricle was reduced.<sup>13</sup> This decrease in C5aR1 levels may be due to receptor internalization following binding with C5a, which significantly increases after trauma in animal models.<sup>47</sup>

Systemic consumption of both classical and alternative complement system factors was demonstrated using the CH-50 test in pigs 6 hours after multiple trauma.<sup>48</sup> Additionally, neutrophils migrate to cardiac tissue following trauma, as shown in experimental blunt chest trauma in mice.<sup>37</sup> Neutrophil serine protease cleaves C5aR1, leading to its reduction after trauma.<sup>49</sup> In case with C5aR2, its loss mouse model with spinal cord trauma caused worse outcomes.<sup>50</sup> Furthermore, in the inflammatory state of CLP sepsis, the interaction of C5a with C5aR1 leads to an excess of cytosolic ROS and Ca<sup>2+</sup> in cardiomyocytes.<sup>41,51</sup>

A biochemical marker is considered high-quality if it is detectable at early stages, measurable in peripheral materials such as blood or urine, sensitive, correlates with the severity of the patient's condition, and is analytically stable and measurable over time after the event.<sup>52</sup> A common issue with many markers is sensitivity, as these mole-

cules can be released by other organs. For example, lactate dehydrogenase (LDH) has been described as a promising indicator for screening chest trauma in patients with polytrauma. However, LDH is an enzyme found in many tissues, including the heart, lungs, liver, kidneys, skeletal muscles, and blood cells.<sup>53</sup> Therefore, elevated LDH levels in polytrauma patients require the exclusion of other sources of this enzyme.

Thus, many markers associated with cardiac injury need further investigation. For instance, GDF-15 has proven to be effective for predicting outcomes in polytrauma patients. This protein showed moderate correlation with ICU stay and hospital stay, and strong correlation with ventilation time and catecholamine requirements.<sup>29</sup> However, GDF-15 is expressed not only in the heart but also in various human tissues, including the placenta, kidneys, lungs, pancreas, skeletal muscles, liver, and brain. In this study, the authors relied on elevated GDF-15 levels in patients with high troponin levels.<sup>29</sup> Hence, clinical recommendations and protocols should consider the conditions under which specific markers were studied and their levels.

Additionally, the influence of other factors must be excluded. For instance, the correlation of complement factors C3a and C5a with the development of acute respiratory distress syndrome and multiple organ failure does not imply that these complications are solely caused by elevated levels of these factors. It is a multifactorial phenomenon influenced by the severity of the condition, the combination of injuries in polytrauma, the patient's pre-existing health status, and other factors. Therefore, when identifying certain molecules as cardiodepressive, meaning they impair cardiomyocyte function, it is essential to exclude the influence of other factors on cellular status.

Currently, the determination of molecular patterns associated with cardiac damage and other markers is not conducted at a clinical level. Existing protocols rely on troponin levels, ECG, and echocardiography when necessary, and incorporating additional markers is a lengthy process dependent on extensive research in this area.

**Limitations.** The limitations of this article include the use of a mixed method combining systematic review and meta-analysis. This could potentially cause the issue in analyzing the findings from diverse study designs. Additionally, the meta-analysis was performed only on the association between Troponin 1 and heart failure, while other relevant biomarkers were not analyzed. As a result, there can be potentially missing important markers of the condition. The relatively small number of sources included may also limit the generalizability of our findings to the broader population. Further research is needed to explore heart failure in more diverse populations and to examine additional biomarkers.

### Conclusion

Studies show that polytrauma significantly impacts the development of myocardial dysfunction, which can arise both directly from heart damage and secondarily due to systemic inflammatory response. Various biomarkers, such as troponins and HFABP, help assess the extent of cardiac injury but remain insufficiently studied. Inflammatory processes and complement system activation play a crucial role in the development of myocardial dysfunction and require further investigation to improve the diagnosis and treatment of polytrauma patients. These results highlight the need for developing preventive and therapeutic measures aimed at minimizing cardiac complications in this patient group.

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# THE EFFECT OF OVERWEIGHT AND OBESITY ON DYSLIPIDEMIA: CROSS-SECTIONAL STUDY IN HEART CENTER

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## Abstract

**Background.** Obesity has turned into a worldwide epidemic with increasing prevalence that is associated with excess mortality and morbidity. Obesity is a risk factor for many diseases including cardiovascular disease, the leading cause of death worldwide. Aim of the study was conducted to evaluate the association of obesity with dyslipidemia and hypertension among patients with low, medium and high risk of developing cardiovascular diseases

**Materials and methods.** Cross-sectional study was conducted at the tertiary hospital in Astana, Kazakhstan. In total 216 participants included in this study.

**Results.** Student's t test was performed to elicit association between body mass index and lipid panel analysis such as cholesterol, triglycerides, low-density lipoprotein and high-density lipoprotein, where all p values found to be <0.0001. Consequently, there is a statistically significant association, and increased body mass index linked with higher lipids in the body. Obesity increases risk of atherosclerosis 2.81 times in comparison those who have a normal body mass index. Obesity increases risk of coronary angioplasty with stenting 1.91 times in comparison those who did not undergo stenting procedure.

**Conclusion.** Atherogenic dyslipidemia is extremely common in obesity, both in the presence and in the absence of severe insulin resistance, and is probably the main factor in the increased risk of cardiovascular diseases in these people

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Obesity, Dyslipidemia, Cardiovascular risk factors, Cardiometabolic diseases

## Introduction

Obesity is widespread in the industrialized world. Body mass index (BMI) is a common non-invasive anthropometric measure used as a indicator of fat mass to assess obesity. The World Health Organization and the American Heart Association (AHA) define obesity as a BMI greater than or equal to 30 kg/m<sup>2</sup>.<sup>1-3</sup>

Two billion people worldwide over 18 years of age, or approximately 30% of the world's population, are overweight or obese.<sup>4</sup> Studies conducted by the Kazakh Academy of Nutrition showed that the average prevalence of overweight and obesity among the adult population of Kazakhstan (15 years and older) was 29.7% in women and 33.9% in men; obesity was 25.8% in women and 15.3% in men. This means that more than half of the adult population of Kazakhstan

(55.5% of women and 49.2% of men) is overweight or obese.<sup>5</sup>

Overweight and obesity are responsible for more than 3.4 million deaths worldwide each year.<sup>1</sup> The Association for Obesity Medicine has defined obesity as: "a serious, chronic, progressive, recurrent and treatable multifactorial, neurobehavioral disease, in which increasing obesity contributes to adipose tissue dysfunction, resulting in adverse metabolic, biomechanical and psychosocial health consequences". It has been suggested that multiple mechanisms underlie the relationship between obesity and atherosclerosis, including abnormalities in lipid metabolism, insulin resistance, and inflammation.<sup>3</sup> Adipose tissue represents the largest reservoir of free cholesterol in the body. Adipocytes and adipose tissue store the largest amount of body lipids,

including triglycerides and free cholesterol. Adipocytes and adipose tissue are endocrine and immune active. Adipocyte hypertrophy and excessive adipose tissue accumulation may contribute to the pathogenic effects of adipocytes and adipose tissue (adiposopathy), leading to abnormal levels of circulating lipids, with dyslipidemia being a major risk factor for atherosclerotic coronary heart disease.<sup>6</sup> Systemic inflammation and adipokine production by adipose tissue are important mechanisms for the adverse effects of obesity on the vascular wall.<sup>3</sup> Metabolic products, cytokines, and hormones released by adipose tissue can affect the liver by inducing changes in hepatic-derived lipoproteins, clotting factors and inflammatory factors that affect the atherogenic environment of the vessel wall. Visceral adipose tissue has access to the portal circulation and may be particularly important in this process. In addition, these same adipose tissue-derived factors have been shown to influence gene expression and cellular function of endothelial cells, arterial smooth muscle cells, and monocytes/macrophages. They represent the major cell types of the arterial wall and are key components to protect the homeostasis of the vessel wall.<sup>7</sup>

There are many mechanisms by which obesity may affect systemic lipid and lipoprotein metabolism. Increased production of fatty acids from adipose tissue in obesity with increased entry into the liver can lead to increased secretion of very low density lipoproteins, apolipoprotein B (apoB) and triglycerides.<sup>8</sup> Other factors secreted by adipose tissue may have adverse effects on circulating lipids. For example, in a study of white men with BMI values between 22 and 35 kg/m<sup>2</sup>, adiponectin was the most significant factor of plasma apoB very low density lipoprotein concentrations.<sup>4</sup> Tumor necrosis factor expression is up-regulated in adipose tissue in obese patients and may have multiple effects on lipid metabolism through both paracrine effects on adipocytes and the liver.<sup>6,9,10</sup>

Dyslipidemia is a widespread risk factor for coronary heart disease and an important feature of the metabolic syndrome. Obesity, especially visceral obesity, causes insulin resistance and is associated with dyslipidemia, im-

paired glucose metabolism, hypertension, which exacerbate atherosclerosis. Studies over the past 4 decades have consistently shown that the burden of dyslipidemia is very high in terms of morbidity, mortality, and medical costs. Dyslipidemia is an important risk factor for coronary heart disease (CHD), which is the leading cause of death worldwide. The World Health Organization estimates that dyslipidemia is associated with more than half of coronary heart disease cases worldwide and more than 4 million deaths per year.<sup>4</sup> The American Heart Association estimates that more than 100 million Americans - one-third of all Americans - have total cholesterol levels greater than 200 mg/dL and more than 34 million American adults have levels greater than 240 mg/dL, which is considered a high level requiring treatment.<sup>11</sup> Diabetes mellitus (DM) is closely associated with dyslipidemia, with people with DM having mean LDL levels greater than 140 mg/dL.<sup>12,13</sup>

Aim of the study: Obesity and dyslipidemia contribute to cardiovascular risk. This study was conducted to evaluate the association of obesity with dyslipidemia and hypertension among patients with low, medium and high risk of developing cardiovascular diseases

#### Materials and methods

Cross-sectional study was conducted at the tertiary hospital in Astana, Kazakhstan. In total 216 participants included in this study. Inclusion criteria for the study were:

- Patients with high and very high cardiovascular disease risk according to American college cardiovascular disease (ASCVD) risk estimator

- Age ranges from 18 to 65 years old
- Gave consent to be included for the cross-sectional study

Exclusion criteria included the patients who did not give consents to participate to the study or had following diseases:

- History or currently have cancer
- Alcoholic steatohepatitis
- Viral hepatitis
- Asthma and/or COPD
- Heart failure with ejection fraction lower than 40%.

Demographic characteristics including age, gender, nationality, comorbidities, blood analysis results, instrumental



analysis like ultrasound, computer tomography, liver ultrasound (fibroscan), echocardiography results were collected and analyzed to assess their potential influence on cardiovascular risk factors and outcomes.

Patients were divided into three groups obesity stages depending on BMI.

- Overweight (not obese), if BMI is 25.0 to 29.9
- Class 1 (low-risk) obesity, if BMI is 30.0 to 34.9
- Class 2 (moderate-risk) obesity, if BMI is 35.0 to 39.9
- Class 3 (high-risk) obesity, if BMI is equal to or greater than 40.0.

**Ethical approval.** Patients all signed informed consent and the study was approved by the local ethical committee (approval number № 2023/01-008 from 05.07.2024).

**Statistical Analysis.** For the categorical data set chi square test, and for the continuous data set student's t test, two tailed were used. P values less than 0.05 were considered to be statistically significant. Odds ratio were calculated to find risk of atherosclerosis development in regards of obesity.

### Results

Out of 216 patients with high and very high risk of developing cardiovascular disease, 44.5% (n=96) to be female. Average weight for patients was 80.74 ± 15.3kg, while average body mass index and body surface area (BSA) found to be 29.03 ± 5.17kg/m<sup>2</sup> and 1.86 ± 0.2m<sup>2</sup>, respectively. As mean BMI could be categorized as obese, hence we tried to break down patients on obesity stages

depending on BMI:

- Overweight (not obese), if BMI is 25.0 to 29.9
- Class 1 (low-risk) obesity, if BMI is 30.0 to 34.9
- Class 2 (moderate-risk) obesity, if BMI is 35.0 to 39.9
- Class 3 (high-risk) obesity, if BMI is equal to or greater than 40.0.

Out of 216 patients, 58 (26.8%) had normal weight, 86 (39.8%) were overweight, 54 (25%) had class 1 obesity, 12 (5.6%) had class 2 obesity and 6 (2.8%) had high risk or class 3 obesity.

190 (87.9%) had peripheral or brachiocephalic atherosclerosis. Moving to the blood analysis, mean total cholesterol level found to be 195.96 ± 43.86 mg/dL, further subdivided to low level lipoprotein (LDL) and high-density lipoprotein (HDL) which were calculated to be 132.67 ± 36.37 mg/dL and 49.18 ± 12.48. Furthermore, mean values for Non-HDL cholesterol was 146.45 ± 44.6 mg/dL and triglycerides was 143.02 ± 89.00 mg/dL. Regarding rest of the lipid panel analysis, mean Apo A was 1.29 ± 0.63 mg/dL, mean Apo B was 1.089 ± 1.26 mg/dL and LP(a) 37.47 ± 50.29 mg/dL. Among the most frequently seen comorbidities were hypertension (72.6%) and diabetes mellitus type 2 (21.2%).

Student's t test was performed to elicit association between BMI and lipid panel analysis such as cholesterol, triglycerides, LDL and HDL, where all p values found to be <0.0001. Consequently, there is a statistically significant association, and increased BMI is linked with higher lipids in the body.

	Obese n=158 (73%)	Non-obese n=58 (27%)	OR	95% CI	P value
Atherosclerosis	21	3	2.81 <sup>a</sup>	[0.81;9.80]	0.105
Stent	41	9	1.91 <sup>b</sup>	[0.86;4.22]	0.111
CABG	50	18	1,03 <sup>b</sup>	[0.54;1.97]	0.932
PCI	46	28	0,44 <sup>γ</sup>	[0.24;0.82]	0.009 *

<sup>a</sup> - OR>1 means that the event is directly related and has a chance of occurring in the first group;  
<sup>b</sup> - OR=1 means that the odds are equal in both groups;  
<sup>γ</sup> - OR<1 means that the event is directly related and has a chance of occurring in the second group  
 \* P<0.05 was considered statistically significant

**Table 1.**  
Obesity Relationship with Atherosclerosis and Interventions

Obesity increases risk of atherosclerosis 2.81 times in comparison those who have a normal BMI (Table 1).

24 (11.1%) of all patients did not have any intervention, 50 (23.2%) patients had undergone coronary angioplasty with stenting, 68 (31.5%) had coronary artery bypass grafting (CABG) surgery and lastly, 74 (34.3%) underwent both percutaneous coronary intervention (PCI) and CABG procedure.

Obese individuals are about 1.91 times more likely to have undergone stenting compared to non-obese individuals (Table 1).

### Discussion

The robust body of literature extensively elucidates the well-established correlation between obesity and the progression of atherosclerosis. According to Lee *et al.*<sup>14</sup> increased BMI is associated with the increased risk of coronary artery calcification up to 1.4 times and the tendency could be seen from the resent Gil *et al.* study<sup>15</sup>, where odds ratio for coronary artery disease development in obese patients was 1.49.<sup>14,15</sup> Our results obtained from the cross-sectional study was comparable, there was 2.97 times of increased risk for obese patients to develop atherosclerotic plaques. Moreover, interestingly, Dr. Henning described in his paper from 2021, that increase in BMI above normal weight correlating with a 10% rise in risk for atherosclerosis and coronary heart disease.<sup>16</sup>

Possible mechanism that explains atherosclerosis development in the particular subset of patients could be due to the activation of adipokines/cytokines like leptin, resistin and inflammatory factor IL-6 leads to monocyte/macrophage infiltration into adipose tissue, promoting inflammation, oxidative stress, abnormal lipid metabolism, insulin resistance, and endothelial dysfunction, contributing to atherosclerosis.

To address both obesity and the associated inflammatory responses it triggers, various therapeutic avenues such as dietary adjustments, pharmaceutical interventions, and bariatric surgical procedures are explored, especially for individuals with body mass indexes surpassing 35-40 kg/m<sup>2</sup> when conventional lifestyle interventions prove ineffective. Furthermore, in obese patients grap-

pling with conditions such as hypertension, a 10-year cardiovascular disease risk exceeding 7.5%, or prediabetes/diabetes, a comprehensive treatment approach involving antihypertensive agents, lipid-lowering medications, and glucose-lowering therapies is recommended.<sup>3,13</sup>

Further by focusing on the outcomes, there was at least twofold increased risk for obese patients to have either total occlusion or hemodynamically significant plaques in coronary artery (cover at least 70% of vessel diameter) further led to stenting of that vessel. Moreover, obesity is also associated with restenosis after coronary stenting, for instance Valera *et al.*<sup>17</sup>, there was 1.33 times higher risk in comparison with non-obese patients for the development of restenosis.

Potential limitations of this study include the absence of comparative analysis between the observed results on obesity-related atherosclerosis risk in healthy cohorts and the assessment of odds ratios within both subsets. Additionally, the sample size might not be sufficiently robust. Future investigations could explore the direct impact of waist-to-hip ratio or visceral fat on atherosclerosis development. Moreover, further research endeavors could delve into identifying potential genetic factors underlying atherosclerosis development, investigating whether these coincide with genes associated with obesity predisposition.

The strength of this study lies in its novelty as the first investigation to delineate the association between obesity and atherosclerosis development in Kazakhstan. Given the predominant Kazakh ethnicity of the study population, characterized by distinct dietary habits influenced by cultural traditions, it becomes imperative to contextualize these findings within a global perspective. Furthermore, the robust correlation observed between metabolic conditions such as obesity and subsequent cardiovascular disease underscores the potential impact on clinical decision-making, particularly regarding the initiation of preventive medication for hyperlipidemia in young obese patients, a matter subject to ongoing debate within the medical community.

Atherogenic dyslipidemia is extremely common in obesity, both in the

presence and in the absence of severe insulin resistance, and is probably the main factor in the increased risk of cardiovascular diseases in these people. A thorough understanding of the molecular mechanisms is crucial for further understanding the effects of obesity on lipoprotein metabolism and developing appropriate therapeutic approaches.

**Limitations:** This study has potential limitations. Small sample size may restrict the generalizability of the findings and increase the potential for bias. Moreover, this study describes the experience of one center and we can't generalize the findings of this research. Future research with a larger number of studies and more standardized methodologies would be beneficial to confirm and extend these findings.

**What's known?** Possible mechanism that explains atherosclerosis development in the particular subset of patients could be due to the activation of adipokines / cytokines like leptin, resistin and inflammatory factor IL-6 leads to monocyte / macrophage infiltration into adipose tissue, promoting inflammation, oxidative stress, abnormal lipid metabolism, insulin resistance, and endothelial dysfunction, contributing to atherosclerosis.

**What's new?** There was at least two-fold increased risk for obese patients to have either total occlusion or hemodynamically significant plaques in coronary artery cover at least 70% of vessel diameter further led to stenting of that vessel.

#### **Conclusion**

Atherogenic dyslipidemia is ex-

tremely common in obesity, both in the presence and in the absence of severe insulin resistance, and is probably the main factor in the increased risk of cardiovascular diseases in these people. A thorough understanding of the molecular mechanisms is crucial for further understanding the effects of obesity on lipoprotein metabolism and developing appropriate therapeutic approaches.

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# STROKE: A COMPREHENSIVE OVERVIEW OF TRENDS, PREVENTION, AND TREATMENT (LITERATURE REVIEW)

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## Abstract

A stroke is an emergency medical condition, commonly referred to as a cerebrovascular accident, occurs when the blood supply to the brain is interrupted, depriving brain tissue of oxygen and essential nutrients. This interruption can lead to rapid neurological impairment and, if not treated promptly, permanent brain damage or even death. Stroke is primarily categorized into two types: ischemic, resulting from arterial blockage, and hemorrhagic, caused by a ruptured blood vessel. Conditions such as acute cerebral circulatory disorder, atherosclerosis, and carotid artery stenosis are strongly associated with an increased stroke risk. Understanding these underlying factors is crucial for effective prevention, early detection, and management of stroke.

Globally, stroke ranks as the second lead in cause of disability and mortality, disproportion at early affecting low-and-middle - income countries. Efforts in stroke prevention emphasizes the significance of early detection, management, promoting healthy lifestyles, and implementing legislative measures. The healthcare costs associated with stroke are substantial and projected to grow significantly. Socioeconomic factors and adverse working conditions also influence stroke incidence. Advancements in surgical revascularization techniques, such as carotid endarterectomy and stenting, have demonstrated efficacy in reducing stroke risk.

Continuous research and development of optimal treatment strategies and monitoring protocols are essential for improving stroke outcomes and mitigating its global burden.

## Introduction

A stroke is an emergency medical condition, commonly referred to as a cerebrovascular accident, occurs when the blood supply to the brain is interrupted, depriving brain tissue of oxygen and essential nutrients. This disruption can precipitate the rapid onset of neurological impairments and, without timely intervention, may culminate in permanent brain damage or death.<sup>1</sup> Stroke can

be categorized into two principal types: ischemic, stemming from a blockage in an artery supplying blood to the brain, and hemorrhagic, resulting from a rupture in a cerebral blood vessel.

Several conditions are associated with stroke and increase the risk of stroke. Acute ischemic stroke is a sudden reduction in blood flow to the brain, often resulting in transient ischemic attacks or more severe strokes. Athero-

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## Keywords:

stroke, acute cerebral circulatory disorder, carotid endarterectomy, carotid artery stenting, atherosclerosis

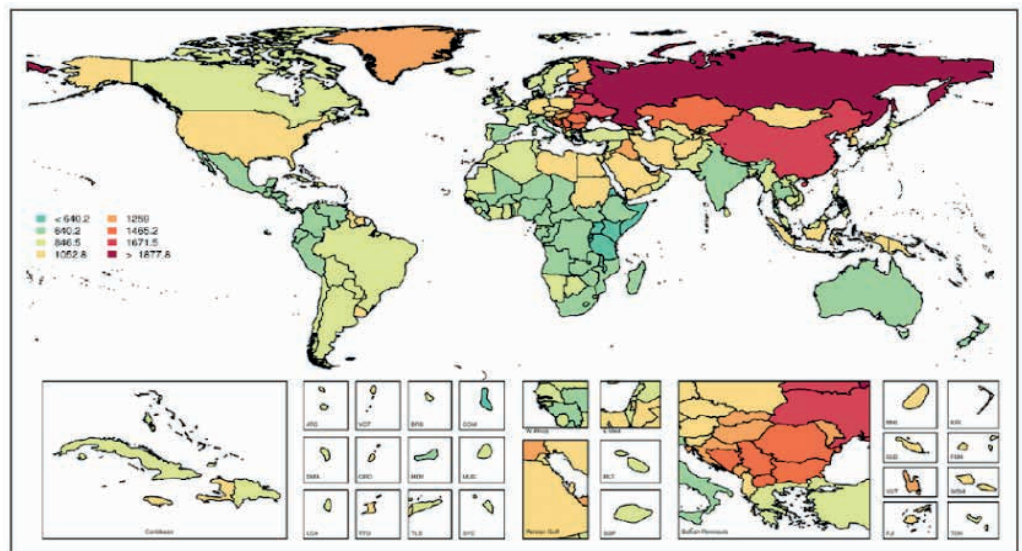


sclerosis, the buildup of fatty deposits in the arterial walls, narrows and hardens the arteries, significantly increasing the risk of ischemic stroke.<sup>2,3</sup> Carotid artery stenosis, the narrowing of the carotid arteries that supply the brain, often results from atherosclerosis and poses a critical stroke risk by potentially reducing blood flow or causing embolism.<sup>4</sup> Understanding these conditions is critical to the prevention, early detection and treatment of stroke.

Stroke is the second leading cause of disability and mortality worldwide, with the greatest burden concentrated in low- and middle-income countries.<sup>5</sup> The 2016 GBD study used statistical models

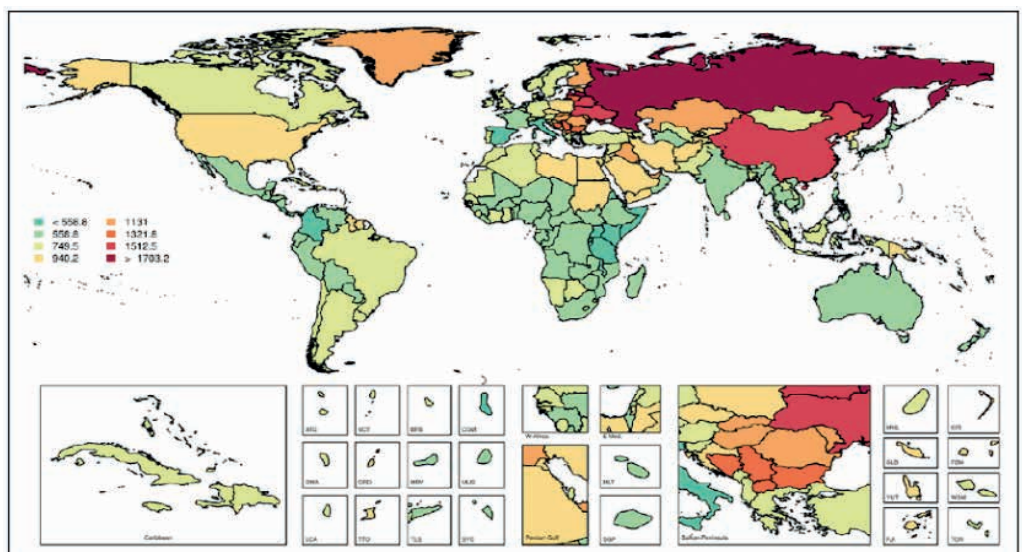
to report incidence, prevalence, mortality, and cause-specific mortality for 315 conditions in 195 countries. Globally, cerebrovascular disease affected 80.1 million people, with 67.6 million suffering ischemic stroke and 15.3 million suffering hemorrhagic stroke. From 1990 to 2016, the prevalence of ischemic stroke increased by 2.7%, while the prevalence of hemorrhagic stroke decreased by 6.8%. However, the more recent decrease from 2006 to 2016 was only 1.7%. The highest rates of cerebrovascular disease were found in Eastern Europe, Russia and East Asia, for both ischemic and hemorrhagic stroke (Figure 1, Figure 2).<sup>6</sup>

**Figure 1.**  
Age-standardized prevalence rates of cerebrovascular disease worldwide for both sexes per 100,000 people



Source: (Global Burden of Disease Study 2016. Global Burden of Disease Study 2016 (GBD 2016) results. Seattle, WA: Institute for Health Metrics and Evaluation (IHME), University of Washington; 2016.)

**Figure 2.**  
Age-standardized prevalence rates of ischemic stroke worldwide for both sexes per 100,000 people



Source: (Global Burden of Disease Study 2016. Global Burden of Disease Study 2016 (GBD 2016) results. Seattle, WA: Institute for Health Metrics and Evaluation (IHME), University of Washington; 2016.)

In 2016, there were 5.5 million deaths from cerebrovascular disease worldwide. From 1990 to 2016, the absolute number of cerebrovascular deaths worldwide increased by 28.2%, while the age-standardized mortality rate decreased by 36.2%. From 2006 to 2016, the absolute number of cerebrovascular deaths worldwide increased by 5.1%, but the age-standardized mortality rate decreased by 21.0% over the 10-year period. Globally, 2.7 million people died from ischemic stroke and 2.8 million from hemorrhagic stroke.<sup>6</sup>

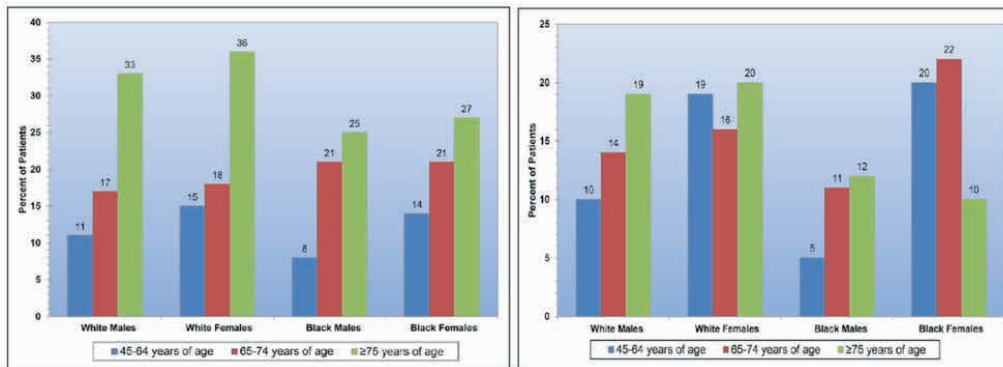
Despite the observed downward trend in cerebrovascular disease mortality in the Russian Federation, these conditions remain among the leading causes of death. In 2018-2023, between 430,000 and 470,000 strokes will be re-

ported in Russia each year, with hospital mortality rates ranging from 17.6% in 2022 to 20.7% in 2020. According to Rosstat, stroke is a leading cause of death in the country, with a mortality rate more than double that of myocardial infarction.<sup>7</sup>

Stroke remains a major medical and societal concern worldwide, including in Kazakhstan, due to its high incidence, mortality and disability rates.<sup>8</sup>

In Kazakhstan, the incidence of cerebrovascular disease increased from 208.1 cases per 100,000 population in 2013 to 433.7 cases in 2020. Despite this increase, the mortality rate from stroke decreased from 71.90 cases per 100,000 population in 2013 to 66.57 cases in 2020.<sup>9</sup> A study from Kazakhstan also shows an almost twofold increase in all-cause mortality in the stroke population.<sup>10</sup>

In the 2016 GBD study, extensive work was done to calculate 1-year and 5-year recurrent stroke mortality rates with age, sex, and race distributions (Figure 3).



**Figure 3.** Probability of stroke mortality within 1-year and 5-year

Source: Pooled data from the Framingham Heart Study, Atherosclerosis Risk in Communities Study, Cardiovascular Health Study, Multi-Ethnic Study of Atherosclerosis, Coronary Artery Risk Development in Young Adults, and Jackson Heart Study of the National Heart, Lung, and Blood Institute 2017.<sup>11</sup>

The aim of this study is to analyze recent advancements in the understanding and management of ischemic stroke, with a focus on the efficacy of various treatment modalities including carotid endarterectomy and carotid artery stenting (CAS). This study seeks to evaluate current trends in stroke prevention, identify gaps in treatment approaches, and assess the impact of emerging tech-

niques on long-term patient outcomes.

### Materials and methods

A comprehensive literature search was conducted using PubMed, Google Scholar, and the Cochrane Library databases. Keywords included stroke epidemiology, cerebrovascular disease, cardiovascular events, carotid artery stenosis, and carotid endarterectomy. Articles published between 2014 and 2024 were included. Both clinical and experimental studies were reviewed to provide a holistic understanding of stroke prevention and treatment methods. The review included a variety of article types, including clinical trials, observational studies, systematic reviews, and meta-analyses. Articles were selected

based on their relevance to stroke epidemiology, treatment methods such as carotid endarterectomy and stenting, and advances in prevention strategies. Articles were included if they contributed to the understanding of the effectiveness of different interventions, highlighted recent trends, or addressed gaps in current knowledge.

#### **Etiopathogenetic aspects of the development of ischemic stroke**

One of the key factors in the development of cerebral stroke is a disturbance in the regulation of cerebrovascular reactivity, characterized by an imbalance between vasoconstriction and vasodilation.<sup>12</sup> Accordingly, the assessment of cerebrovascular reactivity to carbon dioxide (CO<sub>2</sub>) can be used to predict the risk of stroke.<sup>13</sup> This parameter, known as cerebrovascular reactivity to CO<sub>2</sub> (CVRCO<sub>2</sub>), refers to the highly sensitive changes in cerebral blood flow velocity in response to fluctuations in arterial CO<sub>2</sub> levels.<sup>14</sup> Atherosclerosis is the predominant vascular disease, characterized by the accumulation of lipid and cholesterol deposits in the vessels, resulting in arterial occlusion and/or inadequate perfusion of organs and tissues.

Atherosclerosis is the predominant vascular disease characterized by the accumulation of lipid and cholesterol deposits within blood vessels, resulting in arterial occlusion and/or inadequate perfusion of organs and tissues.<sup>15</sup> Consequently, atherosclerosis underlies the pathogenesis of several cardiovascular diseases, including myocardial infarction, coronary heart disease, stroke, and peripheral arterial disease.<sup>16</sup> Despite the availability of therapeutic interventions aimed at reducing blood lipid and cholesterol levels, atherosclerosis remains the leading cause of disability and premature mortality worldwide.<sup>17</sup>

Recent scientific studies have shown that the pathogenesis of atherosclerosis is primarily associated with inflammatory responses involving both innate and adaptive immune cells.<sup>18,19</sup> Inflammation has been shown to play a pivotal role throughout the progression of atherosclerosis.<sup>20</sup> Early in the disease process, oxidized low-density lipoprotein (LDL) trapped in the vessel wall leads to endothelial dysfunction and increased ex-

pression of adhesion molecules, which promote leukocyte recruitment and migration into the subendothelial region. Macrophages and dendritic cells engulf lipids and transform into foam cells while producing various inflammatory cytokines.<sup>21</sup>

#### **Current trends in the approach to cerebral revascularization**

Prompt surgical revascularization of the brachiocephalic arteries has been shown to be an effective intervention for reducing the risk of cerebrovascular accidents in patients with lesions of the extracranial arteries.<sup>25</sup> The primary treatment modalities for carotid artery pathology include open surgical procedures such as carotid endarterectomy and carotid artery stenting. Timely surgical treatment of carotid artery disease has been shown to significantly reduce the incidence of acute ischemic cerebrovascular events and the severity of associated cognitive impairment.<sup>26,27</sup>

Carotid endarterectomy is a common reconstructive surgical procedure performed at the carotid bifurcation. The primary goal is to eliminate stenosis and restore patency to carotid arteries affected by atherosclerosis. During the procedure, the patient's head is positioned away from the side of the affected carotid artery. The skin and underlying tissues are dissected along the inner edge of the sternocleidomastoid muscle, exposing the common, external and internal carotid arteries. After heparinization, the arteries are clamped individually. The anterior wall of the common carotid artery is dissected and the dissection is extended to the internal carotid artery. Using specialized instruments, the surgeon removes any thrombotic debris and atherosclerotic plaque from the lumen of the common and internal carotid arteries. The lumen is then flushed with a saline solution containing heparin. Once the surgeon is satisfied that the necessary manipulations have been completed, the incision in the artery is sutured.

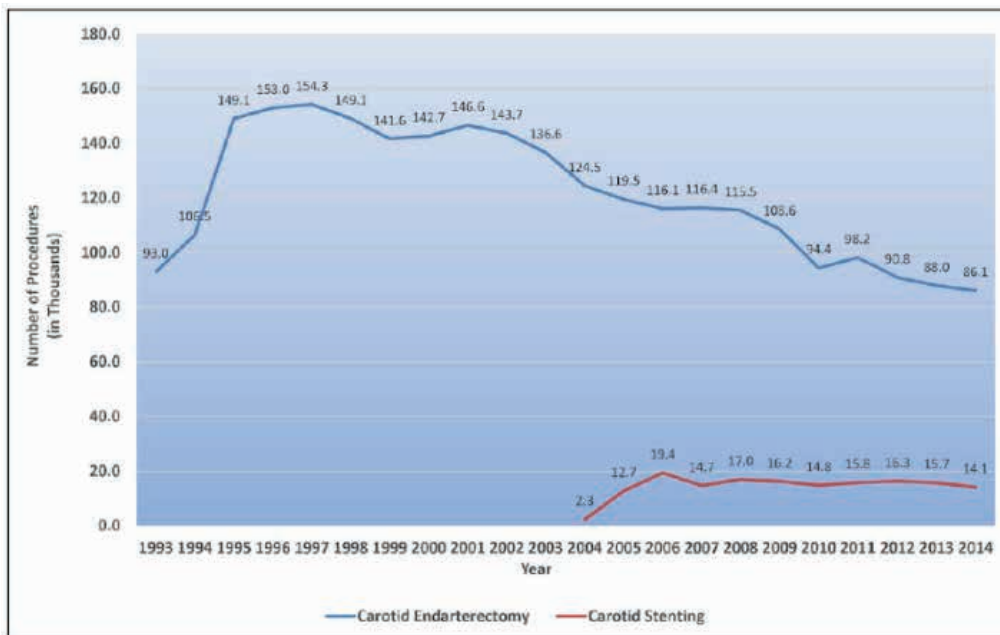
Carotid artery stenting is an emerging therapeutic approach for the treatment of carotid artery stenosis. This minimally invasive procedure involves accessing the target vessels through remote arterial routes without the need

for direct surgical intervention on the carotid artery itself. Typically, the procedure is initiated by inserting a catheter into the femoral artery and navigating it through the aorta until it reaches the narrowed segment of the carotid artery. A stent is then deployed and expanded within the affected arterial region using an inflatable balloon mechanism to restore vessel patency and improve blood flow. Finally, the catheter and balloon are withdrawn, leaving the stent in place to maintain the integrity of the carotid artery.

Compared to carotid endarterectomy (CEA), carotid artery stenting is associated with less postoperative discomfort, is often performed under local anesthesia, may shorten hospital stay, and may be more acceptable to patients. However, there is considerable uncertainty about the short-term risks and long-term du-

rability of CAS compared with CEA, even when both procedures are performed by experienced physicians. During the stenting procedure, an “unstable” atherosclerotic plaque carries the risk of a cerebral artery embolism, which can lead to a partial or complete blockage of blood flow to areas of the brain and cause a “minor” or “major” stroke. In the longer term, there is also a higher rate of in-stent restenosis with carotid artery stenting compared to endarterectomy, requiring close imaging surveillance and possible reintervention.

According to the US Agency for Healthcare Research and Quality, carotid endarterectomy was the predominant intervention for carotid artery stenosis from 1993 to 2014 (Figure 4). However, in recent years, there has been a notable increase in the use of carotid stenting as an alternative treatment approach.



**Figure 4.** Quantitative indicator of carotid endarterectomy and carotid stenting (USA, 1993-2014).

**Source:** Nationwide Inpatient Sample, Healthcare Cost and Utilization Project, Agency for Healthcare Research and Quality.<sup>28</sup>

According to estimates from the Healthcare Cost and Utilization Project (HCUP) and the National Heart, Lung, and Blood Institute (NHLBI) registry, 86,000 carotid endarterectomy procedures were performed in hospitals in the United States in 2014. CEA is the most commonly performed surgical procedure for stroke prevention. Between 2004

and 2014, the number of CEA procedures declined after the introduction of carotid stenting. A comparative analysis using Medicare data showed that the incidence of in-hospital stroke and mortality were comparable between CEA and CAS.<sup>29</sup>

Recent studies using the National Inpatient Sample (NIS) database have demonstrated significant improvements in perioperative outcomes associated with carotid artery stenting over the past decade.<sup>30</sup> In addition, in the Medicare population, 30-day readmission



rates and long-term adverse clinical outcomes were similar between carotid artery stenting and carotid endarterectomy.<sup>31</sup>

A meta-analysis of five randomized controlled trials evaluated the effectiveness of modern endovascular therapy for stroke and found compelling evidence to support thrombectomy initiated within 6 hours, regardless of patient age, NIHSS score, or prior intravenous thrombolysis.<sup>32</sup> In the study cohort of 234 eligible patients, 51% were transported by ambulance and 49% by helicopter for mechanical thrombectomy, with 27% ultimately undergoing the procedure. The average actual transfer time was 132 minutes.

Current scientific research emphasizes the importance of early detection of pathological processes in the brain by neurologists, vascular specialists and other relevant experts. This is critical because these early abnormalities can potentially progress to irreversible brain damage if left untreated.<sup>33,34</sup>

Recurrent stenosis after previous carotid endarterectomy or stenting is rare (approximately 6% at 2 years).<sup>35</sup> When restenosis occurs within the first 2 years after the procedure, it is typically due to neointimal hyperplasia. Conversely, when restenosis occurs more than 2 years after the initial procedure, the more common underlying etiology is the development of new atherosclerotic plaque. In addition, there is the concept of residual stenosis, which refers to stenosis detected within 30 days of a carotid intervention.

The optimal treatment strategy for this relatively uncommon condition is still being debated. In many countries, pharmacological treatment is recommended for asymptomatic individuals because of the reduced risk of embolic stroke associated with neointimal hyperplasia. Revascularization procedures are reserved for symptomatic patients. The specific revascularization method used is not dictated by a standardized protocol, but is at the discretion of the treating physician.

In the United States, the prevailing guideline is to perform carotid artery stenting for stenoses of  $\geq 70\%$  and  $\geq 50\%$ . Patients undergoing this procedure typi-

cally receive dual antiplatelet therapy for the first 1 to 3 months, followed by aspirin monotherapy for an indeterminate duration.<sup>36</sup>

Continuous patient monitoring, appropriate postoperative pharmacologic management, vascular specialist oversight, perioperative nursing support, and vascular health monitoring using CVDS techniques all contribute to improved long-term outcomes.<sup>37</sup>

### **Involvement of vertebral arteries in the structure of ischemic stroke and treatment approaches**

Ischemic stroke is primarily caused by atherosclerotic lesions in the arteries that supply blood to the brain, including the internal carotid and vertebral arteries. Despite the availability of treatments aimed at lowering lipid and cholesterol levels in patients, atherosclerosis remains the leading cause of disability and premature mortality worldwide.<sup>38</sup> The vertebral and basilar arteries are responsible for perfusing the brainstem, cerebellum, thalamus, and posterior temporal and occipital lobes in most people.<sup>39</sup>

Recent data suggest that 20% of all transient ischemic attacks and ischemic strokes are attributable to lesions in the vertebrobasilar region.<sup>40</sup> While the treatment of carotid artery stenosis has been well studied, some questions remain regarding vertebral artery stenosis. Treatment approaches for VA stenosis vary depending on the location of the atherosclerotic plaque, its extent, the degree of stenosis, and the volume of damage to the vertebrobasilar territory.

Current treatment modalities for symptomatic extracranial vertebral artery stenosis require further in-depth study and research.

Surgical treatment of the vertebral and basilar arteries is technically challenging and carries a high risk of stroke, transient ischemic attack, and perioperative mortality.<sup>41</sup> Endovascular treatment with percutaneous transluminal balloon angioplasty alone has not yielded satisfactory results due to elastic vessel recoil and a high rate of restenosis, while there is a lack of well-designed randomized trials to evaluate the efficacy and safety of this approach in the short and long term.<sup>42,43</sup> The use of bare-metal stents



provides favorable results and low rates of periprocedural complications in the early period, but results remain disappointing in the mid- and long-term, with a high incidence of restenosis and subsequent stent fracture associated with neointimal hyperplasia.<sup>44</sup> Trials evaluating the efficacy and safety of coronary drug-eluting stents for the prevention of in-stent restenosis are ongoing and require additional evidence.

There is also a conservative treatment approach, the so-called “best medical treatment” (BMT) approach, which includes antithrombotic drugs, statins, treatment of comorbidities and symptomatic treatment.

Several studies have demonstrated a higher risk of perioperative stroke in patients undergoing intracranial compared to extracranial interventions.<sup>45</sup> However, there is a paucity of randomized controlled trials evaluating the outcomes of treatment for vertebral artery stenosis (PsA), and the existing trials have insufficient patient numbers to meet the necessary inclusion criteria.

The CAVATAS trial randomized only 16 patients with symptomatic extracranial VA stenosis and compared the results of percutaneous transluminal balloon angioplasty with best medical therapy.<sup>46</sup> In addition, the Vertebral Artery Stenting Trial (VAST) randomized 115 patients with symptomatic hemodynamically significant VA stenosis, both intracranial and extracranial, with 57 patients receiving stenting and 58 receiving aggressive medical therapy.<sup>47</sup> Within the first 30 days, three patients in the stenting group experienced stroke, myocardial infarction, or death compared to one in the BMT group. Over a 3-year follow-up period, 12% of patients with VA stents had a stroke, compared with 7% in the BMT group.<sup>48</sup> The VAST trial was stopped early due to regulatory issues, but recent evidence suggests a high risk associated with intracranial VA stenting.

A systematic review by Feng et al. examined the outcomes of 672 patients in four randomized controlled trials and six nonrandomized trials between 2007 and 2015. The review compared the outcomes of percutaneous transluminal balloon angioplasty (PTBA) plus

best medical therapy (BMT) versus BMT alone. The results did not show a significant advantage of either approach.<sup>49</sup> It is noteworthy that this meta-analysis did not include the Vertebral Artery Stenting Trial (VIST), the results of which were presented at the European Stroke Organization Conference in 2016.<sup>50,51</sup> The VIST trial randomized 182 patients with symptomatic intra- and extracranial VA stenosis, with the primary objective of comparing BMT with PTBA with or without stenting. The trial was expected to enroll 540 patients, but was stopped early due to slow enrollment and regulatory issues. Of the 91 patients randomized to stenting, 30 were not treated, primarily because of less than 50% stenosis on duplex angiography. Patients were selected prior to randomization based on CT angiography or MR angiography. Of the 61 patients in the stent group, 48 (79%) had extracranial stenosis and 13 (21%) had intracranial stenosis. The mean follow-up for the study was 3.5 years.<sup>50,51</sup>

Duplex ultrasonography is considered the gold standard for the primary diagnosis of arterial stenosis. However, because most cases of vertebral artery stenosis are asymptomatic, there is a need to identify biomarkers that can predict the progression of atherosclerotic plaque and the subsequent development of transient ischemic attacks and ischemic stroke. According to existing research, certain cytokines may serve as potential biomarkers for this purpose.<sup>52</sup>

#### **Methods of prevention and further management of patients who have undergone cerebral revascularization**

According to several research reports, patients who undergo carotid artery revascularization have a 2.6% annual risk of stroke after carotid endarterectomy.<sup>53</sup>

There is no clear consensus on the effectiveness of surveillance strategies in reducing 30-day death and stroke rates after carotid endarterectomy.<sup>54</sup>

During the perioperative period, the primary goal of monitoring is to maintain adequate cerebral blood flow, especially when the carotid artery is clamped and during bypass grafting. This can be accomplished by several methods, including transcranial Doppler imaging, performing carotid endarterectomy un-

der local anesthesia, measuring stump pressure, subjectively assessing internal carotid artery reflux after carotid artery clamping, and using near-infrared spectroscopy. In addition, electrical brain activity is assessed using somatosensory evoked potentials and electroencephalography.

Quality control methods are aimed at modifying operational strategies to prevent technical errors. These include identification of indirect signs of embolization during carotid artery dissection, diagnosis of arterial lumen conductivity after restoration of blood flow, and diagnosis of large intimal valves to assess residual stenosis. Evidence suggests that targeted monitoring and management of cerebrovascular events may reduce perioperative mortality and stroke rates.<sup>55</sup>

Postoperative patients may undergo annual surveillance related to their carotid revascularization procedures. However, annual surveillance is not generally recommended. Clinical evaluation should include a neurological examination to detect any new stroke-like symptoms. Diagnostic testing should include noninvasive methods, such as duplex ultrasound, to detect potential recurrent stenosis or development of stenosis in the ipsilateral and/or contralateral carotid artery. In addition, patients on medical therapy should not undergo routine annual revascularization due to the possibility of disease progression and increased stenosis. The combination of neurological assessment with duplex ultrasound is considered an appropriate approach.<sup>56</sup>

Patients should be educated about the importance of active management of atherosclerotic risk factors such as hypertension, hyperlipidemia, and smoking cessation. They should also be advised to maintain lifelong aspirin therapy.<sup>57</sup>

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## Conclusion

Stroke remains a critical global health problem due to its high incidence, significant mortality and significant long-term disability. Understanding the multiple risk factors and associated conditions, such as acute cerebrovascular disease, atherosclerosis, and carotid artery stenosis, is essential for effective prevention and management strategies. Despite advances in diagnostic techniques, surgical interventions such as carotid endarterectomy and stenting, and pharmacological treatments, the burden of stroke continues to challenge healthcare systems worldwide, particularly in low- and middle-income countries.

Ongoing research and innovation are critical to developing more effective treatments and improving patient outcomes. Efforts to raise public awareness and educate individuals about stroke prevention can significantly reduce the incidence and impact of this disease. By fostering collaboration among healthcare providers, policymakers and researchers, we can improve our understanding of stroke and implement strategies that will ultimately reduce its global burden, improve patients' quality of life and reduce healthcare costs.

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# THE INFLUENCE OF PULMONARY VEIN ANATOMY ON OUTCOMES AFTER ABLATION OF PAROXYSMAL ATRIAL FIBRILLATION

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## Abstract

**Background.** Pulmonary vein isolation is the cornerstone of catheter-based treatment for atrial fibrillation. Cryoballoon ablation offers an effective and reproducible method for pulmonary vein isolation, yet recurrence of arrhythmias remains a challenge. Despite advances in catheter technologies, the role of altered pulmonary vein anatomy as a factor for atrial fibrillation recurrence is poorly studied.

**Materials and Methods.** This prospective study included 465 patients with paroxysmal atrial fibrillation who underwent cryoballoon ablation. Pulmonary vein and left atrial anatomy were evaluated using multislice computed tomography. Patients were followed for 24–48 months to assess atrial fibrillation recurrence and anatomical risk factors. Cox proportional hazard modeling and Kaplan-Meier analysis were used to evaluate predictors of arrhythmia recurrence.

**Results.** Complete Pulmonary vein isolation was achieved in all patients. During follow-up, 38% of patients experienced atrial fibrillation recurrence. Patients with altered pulmonary vein anatomy, particularly a left common pulmonary vein and additional pulmonary veins, showed a higher rate of recurrence. Cox regression analysis identified left atrial volume index >50 mL/m<sup>2</sup> and pathological pulmonary vein anatomy as independent risk factors for atrial fibrillation recurrence.

**Conclusion.** Altered pulmonary vein anatomy is a significant risk factor for atrial fibrillation recurrence following cryoballoon ablation. Comprehensive imaging of the left atrial and pulmonary vein using multislice computed tomography can improve patient selection, reducing the recurrence risk and improving long-term outcomes.

## Introduction

The cornerstone of catheter-based treatment of atrial fibrillation (AF) is pulmonary vein isolation (PVI).<sup>1</sup> Over the last few decades, all catheter technologies have targeted specifically the PVI, standard catheter RFA based on sequential 'point by point' applications and the later developed ('single shot'-technology) cryoballoon ablation (CBA).<sup>1,2</sup> Due to the

fact that arrhythmias initial foci of are often found at the ostium of the pulmonary veins (PV), primary triggers are due to stretching of the cardiac muscle at the level of the pulmonary vein junction with the left atrium (LA).<sup>3</sup>

Cryoballoon pulmonary vein isolation (CBA) is an effective treatment for atrial fibrillation (AF).<sup>4-6</sup> CBA is a competitive alternative to radiofrequency (RFA) abla-

tion with its short procedure time, rapid learning curve, and a high reproducibility of the method. Despite advancements in catheter-based therapies and operator experience, arrhythmia recurrence remains an unsolved problem.

Numerous studies still continue to investigate the prerequisites for the success of catheter-based treatment of AF, such as comorbidities, type of AF, and LA size.<sup>7-9</sup> However, PV anatomy as a potential factor is poorly studied.

Altered PV anatomy is an important factor predisposing to arrhythmia recurrence after successful PV isolation. Consideration of PV anatomy as a prognostic factor for the maintenance of sinus rhythm after ablation would help electrophysiologists determine further patient management, reduce unessential procedures, and minimize costs.

This study aimed to evaluate the significance of selected anatomical features of pulmonary veins in predicting the development of arrhythmia recurrence after cryoballoon ablation of pulmonary veins (CBA-PV) for paroxysmal AF.

#### Materials and Methods

**Study population.** In this prospective, controlled study 465 of whom 61% were male consecutive patients with paroxysmal AF (57±11 years) were included and analyzed. Patients with paroxysmal AF for whom a minimum of 2 class I-III antiarrhythmic drugs were not effective were included in the study. Exclusion criteria were as follows: left atrial (LA) dimensions >5.0 cm, left ventricular ejection fraction <40%, New York Heart Association functional class III or IV heart failure, chronic heart failure requiring intervention, stroke or transient ischemic attack within 6 months, previous LA ablation or surgery for AF, prosthetic heart valve, more than 1 cardioversion within 2 years, or implantable cardiac devices. All patients underwent CBA of PV between 2021 and 2023.

**Multislice computed tomography.** LV and LA anatomy were evaluated in all patients using multislice computed tomography (MSCT) (Aquilion, Toshiba, Japan) before the CBA of PV. The anatomy of PV and LA were assessed in all patients using multislice computed tomography (MSCT) (Aquilion, Toshiba,

Japan) before the CBA PV procedure. Initially, 3-dimensional images of the anatomical structures of the LA and PV were obtained, followed by a quantitative calculation of the LA volume index of body surface area. The normal anatomical structure of the PV is characterized by two left and two right branches, with no abrupt branching up to 2-3 cm before flowing into the LA. Any deviation from this norm was considered if a common collector of any side (more often on the left) or additional pulmonary veins were identified.<sup>10</sup> Left common collector (LCPV) was typically defined when the left ipsilateral PVs were connected by a common trunk before entering the LA. An additional PV was identified if it flowed into the PV separately from the typical superior and inferior PVs.

**Cryoablation procedure.** Cryoballoon isolation of the PV was carried out with local anesthesia and sedation using propofol and, if needed, fentanyl. First, a diagnostic catheter was guided from the femoral access into the coronary sinus. Then, a transseptal puncture was performed using a BRK-1 needle delivered inside a long Preface introducer. Heparin was administered at a rate of 100 units/kg, ensuring that the activated clotting time reached a value of at least 300 seconds. Subsequently, the entire system was replaced by a 15 Fr FlexCath controlled delivery system. Using this delivery system, a 28-mm cryoballoon catheter and a diagnostic 8-pole circular-tipped catheter were inserted into each PV, achieving electrical isolation of all four main PVs.

During the ablation of the right PV, pacing of the phrenic nerve was performed to prevent phrenic nerve palsy, using a guided diagnostic catheter. The necessary occlusion of the isolated PV was confirmed by contrast accumulation in the corresponding PV, and the cooling temperature was brought down to -50 to -60 degrees below Celsius for 180 to 240 minutes. If good occlusion of the PV and PV isolation was achieved within 30 seconds, the ablation of 180 seconds was sufficient. The endpoint was a confirmation of bidirectional block from the PV to the LA.

**Postablation management and follow-up.** After the ablation procedure, all patients were followed up for 24-48

months to assess the effect of pathological change in LV anatomy on the development of recurrences in the long-term follow-up period. Each patient had regular check-ups at 3, 6, 12, 18 and 24 months, and then twice a year. At each follow-up visit, patients were examined for the presence of any signs of AF and any reported arrhythmia recurrences. Additionally, to reveal any recurrences, whether symptomatic or asymptomatic they underwent 24-hour ambulatory Holter ECG monitoring. Any recorded episode of atrial arrhythmia lasting more than 30 seconds was considered as a recurrence. Episodes of atrial arrhythmia during the blanking period were not included as primary endpoints and were not considered chronic treatment failures.

**Treatment endpoint.** The primary goal of the study was to assess the success of the treatment. This success by the absence of: 1) any detectable arrhythmia after a blinded period, 2) use of an unspecified, antiarrhythmic drug, and 3) any off-protocol intervention for AF (such as cardioversion and ablation). Additionally, maintaining sinus rhythm after ablation with a previously ineffective antiarrhythmic drug at the same or lower dose was considered successful.

**Ethical approval.** Patients will be selected with informed consent. The study protocol was approved by the Local Ethical Commission of the Syzganov National Centre of Surgery with №4 on 10.11.2023.

**Statistical analysis.** The results for continuous variables are present-

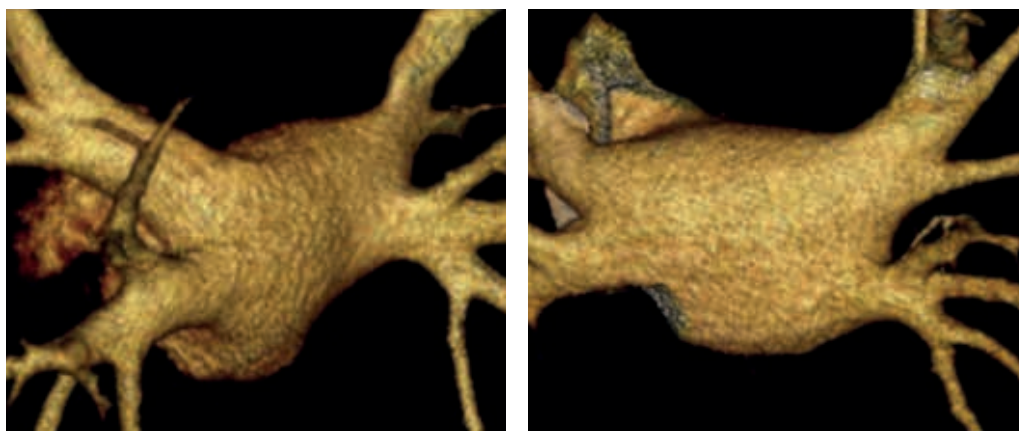
ed as the arithmetic mean  $\pm$  standard deviation. To compare mean values the Mann-Whitney U-test based on the distribution of the values was used. Cox proportional hazard model was used to estimate risk ratios (RR) and their corresponding 95% confidence intervals (CI) for independent predictors of arrhythmia recurrence. Distant outcomes were illustrated using the Kaplan-Meier curve, and the log-rank test was performed to show the significance of differences in values. To establish differences between groups proportional hazard models were used. The primary efficacy endpoint was evaluated using Fisher's two-sided exact criterion of binomial proportions. Statistical analyses were conducted using IBM SPSS Statistics-19 software.

### Results

Complete isolation of the PV ostium was successful in all patients. Of the 465 patients, 298 (64%) showed normal LA and PV anatomy, while 167 (36%) displayed pathological alterations of PV. Over the 24–48-month follow-up, 178 patients (38%) experienced a recurrence of AF. Those with recurrent AF primarily exhibited enlarged right (RSPV) and left superior (LSPV) PV ( $p < 0.001$ ) as shown in Figure 1. The presence of left common PV (LCPV) ( $n=126$ , Log-rank  $p < 0.001$ ) and additional right pulmonary veins rPV ( $n=67$ , Log-rank  $p < 0.001$ ) were associated with early development of sustained arrhythmia recurrences. Table № 1 presents the comparison between the group with recurrence and the group without recurrence.

Figure 1a. LSPV

Figure 1b. RSPV



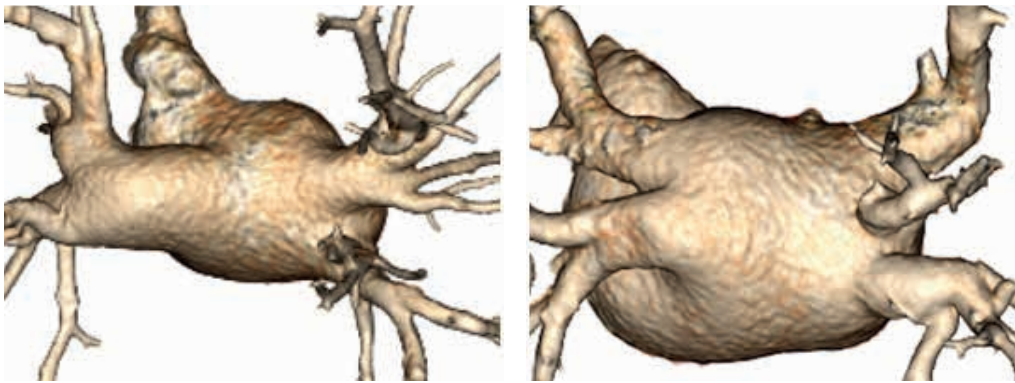


Figure 1c. LCPV

Figure 1d. rPV

Figure №1. MSCT images of the left atrium and pulmonary veins with pathologic changes. 30% of patients had enlarged LSPV – 1a, 20% of patients had enlarged RSPV – 1b, 12% of patients had left common LCPV – 1c, 6% of patients had right accessory rPV – 1d.

Table № 1 presents the comparison between the group with recurrence and the group without recurrence.

№		No recurrence (n=287)	Recurrence (n=178)	p
1	Age (yrs)	56 ± 10,2	58 ± 9,5	0,312
2	Male, n (%)	180 (63%)	104 (59%)	0,572
3	Hypertension, n (%)	138 (48%)	98 (55%)	0,784
4	Diabetes, n (%)	23 (8%)	19 (11%)	0,321
5	Structural heart disease, n (%)	75 (26%)	87 (49%)	0,225
6	Coronary heart disease, n (%)	39 (14%)	27 (15%)	0,741
7	LA diameter (mm)	39 ± 7	42 ± 6	0,02
8	LA volume index (mL/m <sup>2</sup> )	47 ± 9	53 ± 7	0,005
9	Normal PV anatomy, n (%)	238 (83%)	60 (34%)	0,1
10	Patholog PV anatomy, n (%)	49 (17%)	118 (66%)	0,05

Table 1. Clinical characteristics of patients. LA – left atrium, PV – pulmonary vein.

The LA volume index was remarkably greater in the group with recurrence than in the group without recurrence. For a more accurate assessment of the risk of AF recurrence, we calculated a cut-off value of 50 (mL/m<sup>2</sup>) for the LA volume index.

In terms of PV anatomy, the number of patients with pathologic anatomy was notably greater in the recurrence

group compared to the non-recurrence group [75 patients, 42.1% vs. 48 patients, 16.7%; p = 0.05].

As it can be seen in Kaplan-Meier analysis, the arrhythmia recurrence following the primary successful catheter ablation was remarkably higher in patients with pathologic PV anatomy (p = 0.001; see Figure 2).

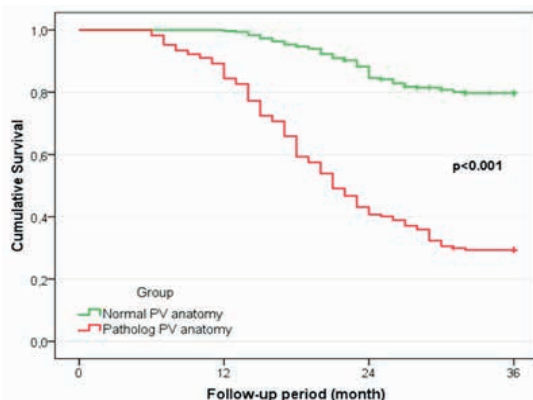


Figure 2. Kaplan-Meier analysis of freedom from AF recurrence in patients after ablation (pathologic PV vs. normal PV)



Figure №2. Kaplan–Meier analysis of freedom from AF recurrence in patients after ablation (pathologic PV vs. normal PV) during the 36-month follow-up period. Patients with pathologic PV anatomy 118 (66%) had more recurrences than those with normal PV anatomy 60 (34%). P-value <0.001.

In our study, Cox regression analysis was used to identify patterns associated with the risk of arrhythmia recurrence. In our initial analysis, we found statistically significant correlations with certain factors, such as left atrial (LA) volume index

greater than 50 (mL/m<sup>2</sup>) and pathological changes of PV anatomy. These factors were then used to create multiple models through multivariate analysis. We observed that arrhythmia recurrence ( $p < 0.001$ ) was more common in patients with an LA volume index greater than 50 (mL/m<sup>2</sup>). While all the variables were highly correlated, PV pathological anatomy and increased LA volume showed the strongest correlation (see Table 2). Importantly, we found that both of these factors are independent risk factors for arrhythmia recurrence

**Table 2.**  
Multivariate analysis for arrhythmia recurrence. The most consistent patterns included: pathological PV anatomy and high LA volume index.

Patterns	B	P	HR	95% CI for HR
<b>Pathologic PV anatomy</b>	0,75	0,04	1,8	0,97 – 3,95
<b>LA volume index (ml/m<sup>2</sup>)</b>	1,29	0,005	3,15	1,39 – 5,97

**Complications.** In our study, phrenic nerve palsy (PNP) was also the most common complication with an incidence of 2.9%. PNP is reversible to some extent, and can usually recover within the procedure or a few days afterwards, and in some cases within a few months. Additionally, the incidence of PNP decreases with experience gain.

Hemopericardium was noted in 9 (1.9%) patients, which was immediately resolved by pericardiocentesis and evacuation of blood from the pericardial cavity. There were no fatal complications such as stroke, atrio-esophageal fistula or death. The incidence of complications related to the access site during femoral puncture was 2.7. No other unforeseen complications were identified during the entire follow-up period.

#### Discussion

In recent years, catheter-based ablation (CBA) has become a well-deserved treatment option for patients with symptomatic AF. As previously reported, depending on the CBA approach, efficacy rates range from 60 to 80% for paroxysmal AF.<sup>11</sup> This study demonstrated an efficacy rate of 62% for paroxysmal AF. Persistent forms of CBA showed efficacy rates of 50–60% in the long term.<sup>5,12</sup>

Pathologically altered anatomy of the PV has a significant impact on the development of atrial fibrillation pathophysiology. Past studies have confirmed this association.<sup>13,14</sup> In our study, 64.1%

of patients had the classic anatomy with four PVs, which is consistent with recent research findings. The most common abnormalities in PV anatomy were a common left PV manifold (12.1%) and a variant involving an accessory right middle pulmonary vein (5.8%), making up 35.9% of the total cases. An article by Anselmino et al. also emphasized the common left PV manifold as the most prevalent variant in patients with atrial fibrillation.<sup>15</sup> However, another study reported that the typical four PV anatomy was only found in a minority of atrial fibrillation patients (30%). This discrepancy might be due to variations in sample sizes, as a study with 40 patients reported one outcome, while another study with 473 patients found that the typical anatomy was present in no more than 39% of cases, with most patients exhibiting altered PV anatomy.<sup>16</sup>

The pathological changes in the PV and how often they occur in patients with and without AF have been the subject of numerous studies. The findings indicate that atypical pulmonary vein anatomy is remarkably associated with the AF development.<sup>17,18</sup>

Our study revealed that patients with altered PV anatomy had a higher risk of AF recurrence compared to patients with normal LV anatomy. These findings have significant implications for the long-term outcome of cryoballoon ablation. In a recent follow-up, it was found that



patients with normal PV anatomy had a similar AF recurrence rate as those with a left common PV (67% vs. 50%). Another study, which used radiofrequency ablation, reported similar results. It demonstrated a significantly higher recurrence rate of AF in patients with abnormal PV anatomy compared to those with normal PV anatomy.<sup>19</sup>

Additionally, altered PV anatomy seemed to have prognostic significance for arrhythmia recurrence, regardless of the ablation system used. This effect was more noticeable in paroxysmal atrial fibrillation (AF). However, in the recent STOP-AF study, it was found that the variation in PV anatomy did not affect the absence of arrhythmia recurrence after cryoballoon ablation (CBA).<sup>20</sup> Furthermore, two recent studies also indicated that the presence of a common PV manifold was not prognostically significant for arrhythmia recurrence.<sup>21,22</sup>

Despite the extensive research on the outcomes of catheter ablation, identifying new predictors of arrhythmia recurrence is crucial for better patient selection and long-term outcome prediction. It is particularly important to carefully monitor patients with altered PV and LA anatomy and schedule them for repeat catheter ablation as necessary. This approach can help predict the maintenance of normal sinus rhythm without recurrence of arrhythmias for many years.

All studies show that phrenic nerve palsy is the major complication associated with CBA, occurring in the range of 2.7-12.7%.<sup>23,24</sup> In this study, using a 24-hour Holter recording for rhythm monitoring in patients may have been a major limitation. This method of monitoring might not detect symptom-free episodes of paroxysmal atrial fibrillation. We had to use this method because many patients could not be given long-term ECG recording devices.

**Limitations:** The study used 24-hour Holter ECG monitoring, which may not be sufficient to capture asymptomatic short paroxysms, but is more accessible and convenient for a large cohort of patients. Also, this study describes the experience of one center and we can't generalize the findings of this research. Future research with a larger number of

studies and more standardized methodologies would be beneficial to confirm and extend these findings.

**What's known?** Pulmonary vein isolation is a well-established treatment for atrial fibrillation, with catheter-based methods like radiofrequency ablation and cryoballoon ablation being widely used. CBA, in particular, is known for its shorter procedure time, ease of use, and reproducibility. Despite advancements in these techniques, arrhythmia recurrence remains a significant issue for many patients. Previous studies have investigated various factors, such as comorbidities, AF type, and left atrial size, which contribute to the recurrence risk after ablation. However, the impact of anatomical variations in the pulmonary veins on AF recurrence has been less thoroughly examined.

**What's new?** This study provides new insights into the role of altered pulmonary vein anatomy as a predictor of AF recurrence following cryoballoon ablation. It highlights that specific anatomical features, such as the presence of a left common pulmonary vein and additional pulmonary veins, significantly increase the likelihood of AF recurrence. By identifying these anatomical variations through multislice computed tomography, arrhythmologists can better assess the risk of recurrence and tailor post-ablation management strategies. This study emphasizes the importance of incorporating PV anatomy as a prognostic factor in the treatment of AF to improve long-term outcomes.

#### **Conclusion**

Altered PV anatomy is a risk factor for arrhythmia recurrence after CBA of PV. Mandatory imaging of the LA and PV with MSCT improves patient selection for effective catheter-based treatment of atrial fibrillation.

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U.A.: Statistical analysis, methodology. B.K., O.N.: Data curation. S.A.: Supervision. B.N.: Investigation. Y.A.: Conceptualization. M.Zh.: Visualization. All authors approved the final version of the manuscript

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## ФОТИАДИ ЮРИЙ КУЗЬМИЧ



Фотиади Юрий Кузьмич родился в 1949 году в городе Белореченске Краснодарского края, Российской Федерация, по национальности – грек. Образование высшее - в 1966 году поступил в Актюбинский государственный медицинский институт, в 1973 году успешно окончил указанное учебное заведение по специальности «Лечебное дело» и получил квалификацию «Врач».

Трудовую деятельность начал врачом скорой помощи Кызылординской городской больницы в 1973 году, в феврале 1976 года стал хирургом городской больницы №1, с марта 1980 года — хирургом Кызылординской городской больницы, с 1996 по 2017 год — заведующий хирургическим отделением, с 2017 года – врач хирург, с 2019 года – работает врачом хирургом-консультантом.

За годы работы молодым специалистом Ю. К. Фотиади был главным врачом городской больницы был Омаров Ернияз Омарулы, а Оразов Капланбек Баликбайулы – заведующим хирургическим отделением. При поддержке этих квалифицированных руководителей Юрий Кузьмич познал все тайны и направления медицинской сферы. Врач, подготовленный этими людьми, несомненно, будет лучшим в области медицины. Однако, не ограничиваясь

этим, благодаря своей любознательности, в ходе совершенствования своих знаний, он постоянно повышал их в странах дальнего и ближнего зарубежья, в частности: в Москве, России, в городах Казани, Республика Татарстан, в городе Уфе, Башкортостан, в городе Харькове, Украина, осваивая современные инновации в области хирургии своего времени и помогая больным вставать на ноги.

Юрий Кузьмич честно и достойно выполнял свои служебные обязанности и первым в больнице применил современный диагностический и лечебный метод лапароскопии, позволяющий выполнять ваготомические операции при лечении язв желудка и двенадцатиперстной кишки, выявлять заболевания органов грудной и брюшной полости, органов с помощью специального оптического инструмента, и в то же время он реализовал методы Линтона при выполнении операций при патологиях вертикальных границ и выполнении операций на синих венах ног, а также не уставал руководить и обучать молодых хирургов.

Высококласный хирург-консультант, квалифицированный врач, человек, заслуживший искреннюю благодарность среди народа. Юрий Кузьмич – один из врачей, перенесших в ходе оказания медицинской помощи множество серьезных операций, и, благодаря своему мастерству, помог многим пациентом. У него также сильно развита интуиция, благодаря чему и своему опыту, он точно ставил диагноз пациента, используя свою мастерство для выполнения сложных видов операций и в общей сложности принял участие в около 10 000 операциях.

По его показаниям, поставленные им диагнозы каждый раз подтверждались. Это конечно приходит с накопленным опытом, благодаря долгой и упорной работе.

Квалифицированный врач Юрий Кузьмич известен в народе как «Врач с золотыми руками».

За свой многолетний и честный труд он получил множество наград, в 2018 году награжден медалью «Золотой доктор». В 2023 году награжден «Знаком отличия» Министерства здравоохранения Республики Казахстан. Консультант-хирург доктор Фотиади Юрий Кузьмич – врач, который не устает обучать и направлять идущих за ним молодых специалистов, давать советы и оказывать медицинскую помощь. Человек, пользующийся уважением среди коллег и благодарностью от пациентов.





Хирургическая служба Республики Казахстан понесла невосполнимую утрату. С глубоким сожалением сообщаем об уходе из жизни выдающегося хирурга и учёного, одного из основоположников хирургии печени, желчных путей и поджелудочной железы Казахстана, основателя большой хирургической школы, председателя Казахстанского общества хирургов, Лауреата Государственной премии Республики Казахстан, доктора медицинских наук, профессора СЕЙСЕМБАЕВА МАНАСА АХМЕТЖАРОВИЧА.

Манас Ахметжарович Сейсембаев родился 2 июня 1950 года в городе Караганда. После окончания средней школы поступил на лечебный факультет Семипалатинского государственного медицинского института, который окончил в 1973 г. С 1974 г. по 1977 г. работал врачом-хирургом, затем заведующим отделением Большенарымской районной больницы Восточно-Казахстанской области. В 1977–1978 гг. М.А. Сейсембаев работал хирургом в отделении экстренной хирургии Центральной городской клинической больницы г. Алматы. В 1978 г. перешел на должность заведующего хирургическим отделением Республиканского клинического госпиталя инвалидов Отечественной войны (г. Алматы). С 1980 г.

по 1991 г. – научный сотрудник, а затем старший научный сотрудник отделения хирургии печени, желчевыводящих путей и поджелудочной железы НИИ клинической и экспериментальной хирургии им. А.Н. Сызганова (г. Алматы). В 1988 г. защитил кандидатскую диссертацию «Выбор рациональной хирургической тактики при стойкой механической желтухе». С 1991 г. по 1998 г. – заведующий отделом торакоабдоминальной хирургии того же учреждения. В 1995 г. защитил докторскую диссертацию «Диагностика и хирургическое лечение постхолецистэктомических заболеваний».

В 1988 г. Манас Ахметжарович избран членом-корреспондентом Национальной академии наук РК. В 1997 г. М.А. Сейсембаеву присвоено ученое звание профессора медицины. В 1998–2001 гг. являлся заведующим отделением хирургии печени, желчевыводящих путей и поджелудочной железы, с 2001 г. по 2003 г. – директор Научного центра хирургии им. А.Н. Сызганова. В 2003–2008 гг. – начальник Республиканского клинического госпиталя инвалидов Отечественной войны г. Алматы. С 2008 по 2010 г. вновь заведовал отделением хирургии печени, желчевыводящих путей и поджелудочной железы Национального научного центра. С 2010 г. по 2011 г. М. А. Сейсембаев назначен генеральным директором АО «ННЦХ им. А.Н. Сызганова», а в 2011 г. Манас Ахметжарович избран председателем совета директоров АО «ННЦХ им. А.Н. Сызганова».

С его именем связаны все основные достижения ННЦХ им. А.Н. Сызганова в области хирургии печени, желчных путей и поджелудочной железы. Являясь соратником и учеником М.А. Алиева, Манас Ахметжарович Сейсембаев с первых лет работы отделения руководил экспериментальными и клиническими исследованиями по проблемам лечения желчно-каменной болезни и его осложнений, ятрогенных повреждений желчных путей, постхолецистэктомическим синдромом, очаговых и диффузных заболеваний

печени и поджелудочной железы. Под руководством М.А. Сейсембаева изучались и разрабатывались способы малоинвазивных и пункционных способов лечения, реконструктивных и восстановительных операций на желчных путях.

Большая исследовательская работа была проведена по изучению способов лечения осложненного и неосложненного эхинококкоза печени. Центр проводил исследования по использованию различных способов обработки остаточных полостей с использованием лазера, электрических, плазменных и криогенных технологий, были разработаны и усовершенствованы методы их проведения.

Под руководством и непосредственном участии М.А. Сейсембаева, Центр одним из первых в Казахстане начал исследования по проблемам лечения циррозов печени у взрослых и детей.

Большой объем исследований был посвящен изучению и внедрению резекционных и реконструктивно-пластических операций при заболеваниях поджелудочной железы, начиная с использования малоинвазивных способов и до объемных реконструктивно-восстановительных вмешательств.

Под руководством М.А. Сейсембаева Центр активно внедрял лапароскопические технологии в гепатопанкреатобилиарную хирургию.

М.А. Сейсембаев активно проводил организаторскую работу, в течение многих лет руководил Обществом хирургов г. Алматы и Алматинской области. В 2015 г. избран Президентом Республиканского общественного объединения «Казахстанское общество хирургов».

Научно-практическую деятельность совмещал с педагогической деятельностью, в качестве профессора хирургических кафедр медицинских университетов, читал лекции и проводил семинары.

Автор более 350 научных работ, в том числе около 160 научных статей, опубликованных в ведущих научных журналах Казахстана и России, 9 монографий и методических руководств, 70 авторских свидетельств на изобретение (положительных патентов на изобретения РК). Под руководством профессора М.А. Сейсембаева защищено 7 докторских и 15 кандидатских диссертаций.

За вклад в развитие здравоохранения и трудовые заслуги М.А. Сейсембаев награжден Почетной грамотой Президента Республики Казахстан (1995 г.), нагрудным знаком «Отличник здравоохранения РК» (2006 г.), орденом им. Н.И. Пирогова (2011 г.), «Золотой медалью» Казахстанской ассоциации эндоскопических хирургов (2013 г.), медалью «Еңбек ардагері» (2017 г.).