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NEUROLOGICAL COMPLICATIONS IN EXTRACORPOREAL MEMBRANE OXYGENATION: RISK FACTORS FOR THE DEVELOPMENT OF ACUTE CEREBROVASCULAR EVENTS

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Abstract

Introduction. Cardiovascular diseases remain the leading cause of mortality and disability worldwide, including in Kazakhstan. Extracorporeal membrane oxygenation (ECMO) is a life-saving treatment for severe cardiopulmonary failure; however, its use is associated with a high risk of complications, including acute neurological disorders such as strokes.

Objective. To determine the incidence of acute cerebrovascular events (ACE), including ischemic and hemorrhagic strokes, in patients receiving extracorporeal membrane oxygenation (ECMO), as well as to identify key risk factors for their development in the context of clinical practice in Kazakhstan.

Methods. A retrospective analysis was conducted on data from 92 patients hospitalized at the Pavlodar Regional Cardiology Center between 2015 and 2024. All patients were on ECMO during the intraoperative or postoperative periods. Study participants were stratified into two cohorts: (1) individuals with acute cerebrovascular events and (2) those without evidence of cerebrovascular compromise. The analysis included an assessment of demographic data, comorbidities, surgical characteristics, and postoperative parameters. The study data were obtained through a retrospective analysis of patients' medical records, including medical histories and electronic databases of the cardiology center. Statistical analysis was performed using IBM™ SPSS 26.0 software (IBM Corporation, Armonk, NY, 2019).

Results. Neurological complications, including strokes, were identified in 31.5% of patients on ECMO. The main risk factors were hypertension, smoking, and a history of stroke. It was also found that women and patients with a low left ventricular ejection fraction were at higher risk. The average length of hospitalization for patients with strokes was 30.2 days, which exceeded that of patients without strokes (25.6 days).

Conclusion. Strokes remain a significant complication in patients on ECMO, necessitating the development of specific preventive measures. Identified risk factors, such as hypertension, smoking, and a history of stroke, should be considered in the development of clinical guidelines. This study highlights the need for further large-scale research to improve the diagnosis and prevention of strokes in patients on ECMO.

Keywords: *extracorporeal membrane oxygenation, acute cerebrovascular event, neurological complications, risk factors for stroke.*

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Резюме

НЕВРОЛОГИЧЕСКИЕ ОСЛОЖНЕНИЯ ПРИ ЭКСТРАКОРПОРАЛЬНОЙ МЕМБРАННОЙ ОКСИГЕНАЦИИ: ФАКТОРЫ РИСКА РАЗВИТИЯ ОСТРОГО НАРУШЕНИЯ МОЗГОВОГО КРОВООБРАЩЕНИЯ

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Введение. Болезни системы кровообращения остаются ведущей причиной смертности и инвалидности в мире, включая Казахстан. Экстракорпоральная мембранная оксигенация (ЭКМО) является спасательным методом лечения при тяжелой сердечно-легочной недостаточности, однако её применение связано с высоким риском осложнений, включая острые неврологические расстройства, такие как инсульты.

Цель исследования. Определить частоту острых нарушений мозгового кровообращения (ОНМК), включая ишемические и геморрагические инсульты, у пациентов, получающих экстракорпоральную мембранную оксигенацию (ЭКМО), а также выявить ключевые факторы риска их развития в условиях клинической практики Казахстана.

Методы. Проведен ретроспективный анализ данных 92 пациентов, госпитализированных в Павлодарский областной кардиологический центр с 2015 по 2024 годы. Все пациенты находились на ЭКМО в интраоперационный или послеоперационный периоды. Пациенты были разделены на две группы: с наличием инсульта (ОНМК) и без него. Анализ включал оценку демографических данных, сопутствующих заболеваний, особенностей операций и параметров послеоперационного периода. Данные для исследования были получены на основе ретроспективного анализа медицинской документации пациентов, включая истории болезни и электронные базы данных кардиоцентра. Статистический анализ проводился на программе IBM™ SPSS 26.0 (IBM Corporation, Armonk, NY 2019).

Результаты. Неврологические осложнения, включая инсульты, были выявлены у 31,5% пациентов, подключенных к ЭКМО. Основными факторами риска стали гипертония, курение и наличие инсульта в анамнезе. Также установлено, что женщины и пациенты с низкой фракцией выброса левого желудочка были более подвержены риску. Средняя продолжительность госпитализации у пациентов с инсультами составила 30,2 дня, что превышает аналогичный показатель у пациентов без инсультов (25,6 дня).

Выводы. Инсульты остаются значительным осложнением у пациентов на ЭКМО, что требует разработки специфических профилактических мер. Выявленные факторы риска, такие как гипертония, курение и инсульт в анамнезе, должны быть учтены при разработке клинических рекомендаций. Настоящее исследование подчеркивает необходимость дальнейших масштабных исследований для улучшения диагностики и профилактики инсультов у пациентов на ЭКМО.

Ключевые слова: *экстракорпоральная мембранная оксигенация, острое нарушение мозгового кровообращения, неврологические осложнения, факторы риска инсульта.*

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Түйіндеме

ЭКСТРАКОРПОРАЛЬДЫ МЕМБРАНАЛЫҚ ОКСИГЕНАЦИЯ КЕЗІНДЕГІ НЕВРОЛОГИЯЛЫҚ АСҚЫНУЛАР: МИ ҚАН АЙНАЛЫМЫНЫҢ ЖЕДЕЛ БҰЗЫЛУЫНЫҢ ДАМУЫНА ӘКЕЛЕТІН ТӘУЕКЕЛ ФАКТОРЛАРЫ

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Кіріспе. Қан айналым жүйесінің аурулары әлем бойынша, соның ішінде Қазақстанда да, өлім мен мүгедектіктің басты себебі болып қала береді. Экстракорпоральды мембраналық оксигенация (ЭКМО) ауыр жүрек-өкпе жетіспеушілігін емдеуде құтқару әдісі ретінде қолданылады, бірақ оны қолдану осындай асқынулардың жоғары тәуекелімен байланысты, соның ішінде инсульт сияқты жедел неврологиялық бұзылулар.

Зерттеудің мақсаты. Экстракорпоральды мембраналық оксигенация (ЭКМО) алатын науқастарда ми қан айналымының жедел бұзылуларын (МҚАЖБ), соның ішінде ишемиялық және геморрагиялық инсульттердің жиілігін анықтау, сондай-ақ Қазақстан клиникалық тәжірибесінде олардың дамуына әсер ететін негізгі тәуекел факторларын анықтау.

Әдістері. 2015-2024 жылдар аралығында Павлодар облыстық кардиологиялық орталығына жатқызылған 92 науқастың деректеріне ретроспективті талдау жүргізілді. Барлық науқастарға операция кезінде немесе операциядан кейін экстракорпоралды мембраналық оксигенация (ЭКМО) қолданылды. Науқастар ми қан айналымының жедел бұзылулары (МҚАЖБ) бар және жоқ топтарға жіктелінді. Жүргізілген талдау демографиялық көрсеткіштерді, қосалқы ауруларды, операцияның ерекшеліктерін және операциядан кейінгі кезеңнің параметрлерін қамтыды. Зерттеу деректері науқастардың медициналық құжаттарының ретроспективті талдауы негізінде алынды, оған ауру тарихтары және кардиоорталықтың электрондық деректер базасы кірді. Статистикалық талдау IBM™ SPSS 26.0 (IBM Corporation, Armonk, NY 2019) бағдарламасында жүргізілді.

Нәтижесі. ЭКМО-ға қосылған науқастардың 31,5%-ында инсультті қоса алғанда, неврологиялық асқынулар анықталды. Негізгі тәуекел факторлары ретінде гипертония, темекі шегу және инсульттің анамнезде болуы анықталды. Сонымен қатар, әйелдер және сол жақ қарыншаның төмен фракциялық шығарымы бар науқастар тәуекелге бейім екені анықталды. Инсультпен ауыратын науқастардың орташа стационарда болу ұзақтығы 30,2 күн болды, бұл инсультсіз науқастарға қарағанда (25,6 күн) жоғары көрсеткіш болды.

Қорытынды. Инсульт ЭКМО-ға қосылған науқастарда маңызды асқыну болып қала береді, бұл ерекше алдын алу шараларын әзірлеуді талап етеді. Гипертония, темекі шегу және инсульттің анамнезде болуы сияқты анықталған тәуекел факторлары клиникалық ұсынымдарды әзірлеу кезінде ескерілуі керек. Бұл зерттеу ЭКМО-ға қосылған науқастарда инсультті диагностикалау мен алдын алуды жақсарту үшін әрі қарай кең ауқымды зерттеулердің қажеттілігін атап өтеді.

Түйін сөздер: *экстракорпоральды мембраналық оксигенация, ми қан айналымының жедел бұзылуы, неврологиялық асқынулар, инсульттің тәуекел факторлары.*

Дәйексөз үшін:

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Introduction

Globally, disorders of the circulatory system (CSD) persist as the foremost contributor to premature mortality and loss of functional capacity. Epidemiological data from the WHO identify cardiovascular diseases (CVD) as the causative factor in 32% of deaths classified as premature [13]. In Kazakhstan, the situation is similar: the incidence of cardiovascular diseases remains high.

As reported in the 2023 statistical yearbook of the Ministry of Health of the Republic of Kazakhstan (MOH RK), the incidence rates per 100,000 population were 657.5 for coronary artery disease, 122.1 for acute myocardial infarction, and 425.0 for cerebrovascular diseases. The overall mortality rate from CSD in 2023 was 155.47 per 100,000 population [10].

The number of patients with severe cardiac dysfunction continues to rise, necessitating the use of advanced supportive therapies, such as extracorporeal membrane oxygenation (ECMO) [7].

Extracorporeal membrane oxygenation (ECMO) is an invasive method used to oxygenate blood in cases of severe acute respiratory failure when conventional treatments prove ineffective [2]. Despite its high efficacy, ECMO is associated with a range of complications.

Studies indicate that 30% to 60% of ECMO patients experience complications, including acute neurological disorders such as ischemic and hemorrhagic strokes [13, 6]. Thrombus formation in 10–15% of patients may lead to strokes in 2–6% of cases. Stroke in the context of ECMO can arise from various factors related to both procedural specifics and patient condition. The primary mechanisms of stroke development include hypoxia, thrombosis, and bleeding [4, 15].

To date, there are no publications in Kazakhstan describing the incidence of strokes and other complications among patients undergoing ECMO therapy. This underscores the need for the present study, which aims to investigate the frequency of strokes in ECMO patients and identify risk factors for their occurrence within the Kazakhstani clinical setting. Based on the interplay of unstable hemodynamics, coagulopathies, ECMO circuit-related factors, and the epidemiological burden of CSD in

Kazakhstan, we hypothesize that the risk of stroke in this patient population may be elevated, warranting in-depth analysis and the development of tailored clinical guidelines for Kazakhstan. The primary aim of this study was to assess the frequency of strokes and identify associated risk factors in adult ECMO patients through a retrospective analysis of medical records from cardiac care facilities in the Pavlodar Region.

Materials and Methods

Study Population

The study included 92 patients hospitalized at the Pavlodar Regional Cardiology Center for cardiac indications between 2015 and 2024. Participants were aged over 18 years and underwent conservative treatment and cardiac surgery with subsequent ECMO initiation preoperatively, intraoperatively, or postoperatively.

Patients were selected from the standardized electronic medical records database "IMIS" (Integrated Medical Information System), which contains hospitalization data. Inclusion criteria were confirmed for ECMO initiation for cardiac support. Selection was based on age, ECMO use, and alignment with ICD-10 codes (International Classification of Diseases, 10th Revision) for relevant conditions (Figure 1).

The control group comprised patients with confirmed ECMO initiation but no subsequent acute cerebrovascular accident (ACVA). This design enabled comparison of outcomes between patients with stroke and those without, facilitating identification of ECMO-associated risk factors.

The definition of ACVA (acute cerebrovascular accident) followed the American Neurological Association criteria: an acute condition caused by a sudden reduction or cessation of blood supply to specific brain regions, leading to neurological deficits [1]. ACVA includes two main types: ischemic stroke (due to vascular occlusion and insufficient blood flow) and hemorrhagic stroke (resulting from vessel rupture and cerebral hemorrhage) [8].

For analysis, two groups were compared:

1.Group 1 included patients with ACVA occurring after ECMO initiation, documented in medical records under ICD-10 codes I60–I64.

2.Group 2 consisted of patients receiving ECMO without ACVA development.

Baseline demographic data included age, sex, body mass index (BMI), and comorbidities.

Intraoperative parameters assessed were surgery type and duration, cardiopulmonary bypass time, aortic cross-clamping duration, and intraoperative blood loss volume. Postoperative variables included glomerular filtration rate (GFR), biochemical parameters, ECMO duration, intensive care unit (ICU) stay length, total hospitalization duration, cardiac arrest episodes, type and volume of transfused blood components (e.g., packed red blood cells, fresh frozen plasma (FFP), and treatment outcomes.

Data were obtained through retrospective analysis of medical records, including patient histories and the cardiology center's electronic database.

Statistical analysis was performed using IBM™ SPSS 26.0 (IBM Corporation, Armonk, NY, 2019).

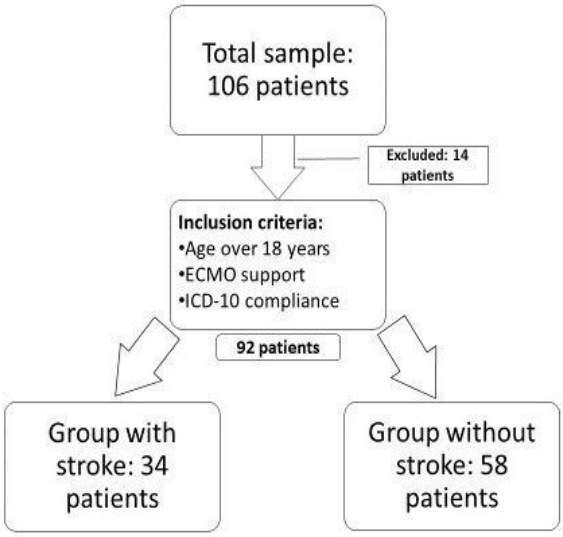

Figure 1. Study population enrollment diagram.

Results

The study included 92 patients hospitalized with cardiovascular and respiratory pathologies at the Pavlodar Regional Cardiology Center between 2015 and 2024. Of these, 31.52% (n=29) were diagnosed with neurological deficits, including coma (Figure 2).

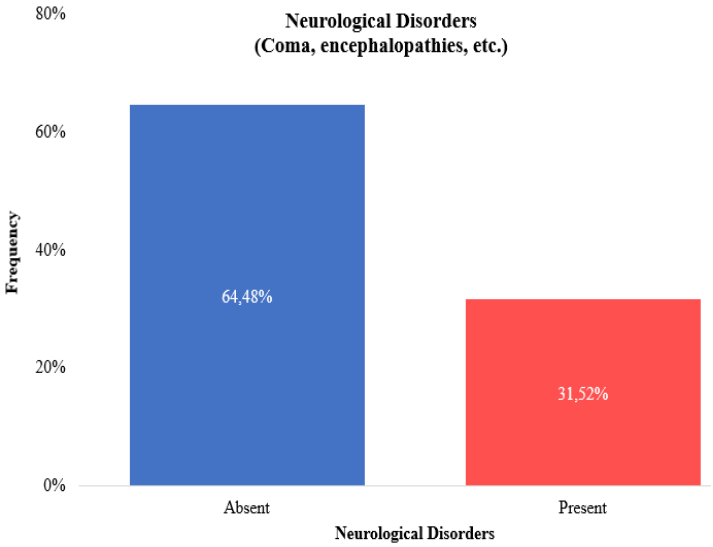

Figure 2. Distribution of Patients by Groups with Neurological Deficits.

Demographic Characteristics

Males accounted for 59.8% (n=55) of the total cohort, while females represented 40.2% (n=37). Age characteristics of patients with and without acute cerebrovascular accident (ACVA) are presented in Table 1. Statistically significant gender differences were observed in ACVA patients (p=0.038). However, age, arterial hypertension levels, coronary artery disease, and heart failure severity showed no significant intergroup differences (p>0.05 for all variables).

Table 1.

Preoperative Parameters.

Factors	with ACVA (n=29)	non-ACVA (n=63)	p-value
Female (%)	44.4	55.6	
Male (%)	23.6	76.4	0.038
Age (mean)	57.55	59.26	0.545
IHD (%)	29.7	70.3	0.572
CABG/Stent history (%)	15.8	84.2	0.063
DM (%)	20	80	0.172
HTN (%)	31.1	68.9	0.856
CVA (%)	61.8	38.2	0.001
COPD (%)	26.7	73.3	0.662
CHF (%)	29.2	70.8	0.469
LVEF (%)	50.31	49.93	0.777
MAU (%)	25	75	0.682
Smoking (smokers, %)	12	88	0.004
CKD (%)	30.4	69.6	0.866

The following standard medical abbreviations are used throughout the text: ischemic heart disease (IHD), coronary artery bypass grafting (CABG), diabetes mellitus (DM), hypertension (HTN), cerebrovascular accident (CVA), chronic obstructive pulmonary disease (COPD), chronic heart failure (CHF), left ventricular ejection fraction (LVEF), microalbuminuria (MAU), and chronic kidney disease (CKD). All abbreviations are expanded at their first occurrence in both abstract and main text.

Neurological Complications

Table 1 demonstrates that among patients with neurological deficits, 61.8% had hypertensive disease with ACVA, compared to only 38.2% in the non-ACVA group (p=0.001). Smoking emerged as a statistically significant factor (p=0.004), being more prevalent among patients with neurological deficits. Similarly, statistically significant differences (p<0.001) were observed between ACVA (61%) and non-ACVA (38.2%) groups regarding patients with a history of prior cerebrovascular events.

No statistically significant differences were found in hospitalization duration. However, non-ACVA patients had shorter hospital stays (mean 25.6 days) compared to ACVA patients (mean 30.2 days). ECMO support duration was also shorter for non-ACVA patients (13.9 days vs 17.6 days), though this difference lacked statistical significance (Figure 3).

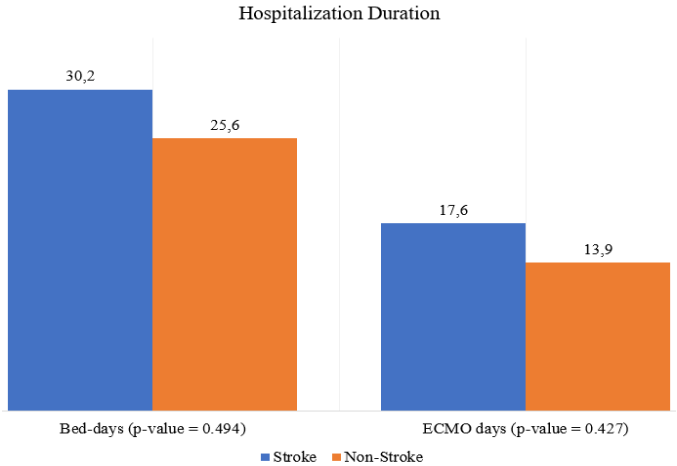

Figure 3. Duration of Hospital Stay.

Postoperative Outcomes

Statistically significant differences were observed in platelet levels, with lower values being more pronounced in the non-CVA group (p=0.034). The incidence of cardiopulmonary resuscitation (CPR) was significantly higher (p=0.040) in patients who developed CVA. No significant intergroup differences were found in: Creatinine and urea levels, ALT concentrations, complications (acute left ventricular failure, sepsis, respiratory failure), bleeding events, blood component transfusions. Mortality rates were notably high in both groups: 75.9% in CVA patients vs 65.1% in non-CVA patients (Table 2).

Table 2.

Neurological Complications.

Factors	with ACVA (n=29)	non-ACVA (n=63)	p-value
Thrombocytopenia (%)	35.5	64.5	0.034
Creatinine (mean)	245.1	188.4	0.073
Urea (mean)	19	14.7	0.084
ALT (mean)	415.2	414.8	0.999
ALVF (%)	36.4	63.6	0.460
Sepsis/Infection (%)	42.9	57.1	0.327
Respiratory failure (%)	25.7	74.3	0.345
Packed red blood cells (mean)	26.8	23.4	0.559
FFP (mean)	33	18.3	0.199
Presence of bleeding (%)	27.9	72.1	0.490
Resuscitation (CPR, %)	41.1	19	0.040
Outcome (fatal, %)	75.9	65.1	0.306
The following standard medical abbreviations are used throughout the text: alanine aminotransferase (ALT), acute left ventricular failure (ALVF), fresh frozen plasma (FFP), and cardiopulmonary resuscitation (CPR).			

We developed a decision tree model to predict the probability of cerebrovascular accident (CVA) occurrence based on risk factors using the CHAID (Chi-squared Automatic Interaction Detector) method.

The resulting model is presented in Figure 4. The decision tree contained 5 terminal nodes, whose characteristics are detailed in Table 3.

The decision tree analysis identified male sex, no history of ACVA, and left ventricular ejection fraction (LVEF) >48% as protective factors associated with below-average CVA risk (reference: 100.0%). Elevated risk profiles emerged for patients with reduced LVEF, female sex, or prior ACVA. The model achieved 79.3% sensitivity, 77.8% specificity, and 78.3% ± 4.3% overall predictive accuracy for ACVA occurrence.

Survival Outcomes

Kaplan-Meier analysis demonstrated that patients with neurological deficits had significantly longer mean survival time (44.11 ± 8.69 days, 95% CI: 27.07-61.16) compared to those without deficits (35.24 ± 4.33 days, 95% CI: 26.76-43.73). Notably, median survival times showed an inverse pattern at 24 days (deficit group) versus 28 days (non-deficit group).

Discussion

Our study revealed that 31.52% of patients on extracorporeal membrane oxygenation (ECMO) experienced acute cerebrovascular accidents (ACVA), which is consistent with international studies reporting complication rates ranging from 20% to 50% [15, 13]. Patients who underwent cardiopulmonary resuscitation (CPR) prior to ECMO initiation had a higher risk of ACVA (p=0.040), highlighting the role of hypoxia and hemodynamic instability. Statistically significant risk factors also included a history of ACVA (p<0.001) and smoking (p=0.004) [14]. These findings align with international research and emphasize the need to optimize approaches for the prevention and early diagnosis of neurological complications in ECMO patients, particularly in the context of Kazakhstani clinical practice [3, 10].

ACVA during ECMO may develop due to multiple factors related to both the procedure itself and the patient's condition [11]. The underlying mechanism involves three primary processes: hypoxia, thrombosis, and hemorrhage [14, 6].

Our analysis showed that patients with prior CPR (before ECMO initiation) had a higher incidence of ACVA (p=0.040), suggesting that hypoxia and hemodynamic instability contribute to stroke risk in ECMO patients [14]. Patients requiring ECMO are already in critical condition with severe cardiopulmonary dysfunction [9], which itself may impair cerebral perfusion.

Among comorbidities and risk factors, hypertension (p=0.001), prior ACVA (p<0.001), and smoking (p=0.004) were significantly more prevalent in the ACVA group. ECMO cannulation and maintenance may also cause blood pressure fluctuations, altered perfusion, and flow dynamics, potentially exacerbating cerebral hypoxia and increasing ischemic stroke risk. Additionally, ECMO requires systemic anticoagulation (e.g., heparin) to prevent circuit thrombosis [12]. Microthrombi may form on the oxygenator membrane or cannulae and embolize to cerebral vessels, causing ischemic stroke [14].

Statistically significant laboratory findings included lower platelet counts in non-ACVA patients post-ECMO initiation (p=0.034), which may increase bleeding risk, including intracranial hemorrhage—a particular concern during anticoagulation therapy.

Our study substantially fills knowledge gaps regarding acute neurological complications (e.g., stroke) in ECMO patients within Kazakhstani clinical practice. While international studies confirm high ECMO-associated complication rates, including stroke, such data were previously unavailable for Kazakhstan. Our results demonstrate that 31.52% of patients developed neurological deficits, underscoring the significant stroke risk in this population. These findings emphasize the need for systematic investigation of ECMO complications in local practice and may inform preventive strategies to reduce stroke incidence among ECMO-supported patients.

This study highlights the necessity of evaluating stroke and other complications in Kazakhstani ECMO patients [15]. We confirmed that this population faces high risk of acute neurological events [5]. Crucially, we identified key stroke risk factors (hypertension, smoking, and prior stroke),

corroborating international data [14]. These results advance understanding of ECMO-related pathophysiology and enable development of targeted screening and prevention tools [2]. Thus, our research enhances clinical insights and contributes to evidence-based guidelines for stroke prevention in Kazakhstani ECMO patients.

Our findings have immediate clinical implications. Male sex, no prior ACVA, and left ventricular ejection fraction (LVEF) >48% were associated with lower ACVA risk compared to the overall cohort. Conversely, reduced LVEF, female sex, and prior ACVA increased risk above the cohort average. These risk factors may guide early diagnostic and preventive protocols for ECMO patients. Clinicians can use these data to improve complication prediction and timely intervention, potentially reducing stroke incidence. Implementing such recommendations in clinical practice may enhance treatment outcomes, survival, and long-term neurological recovery. Thus, our results stress the importance of rigorous monitoring and management of these risk factors during ECMO therapy.

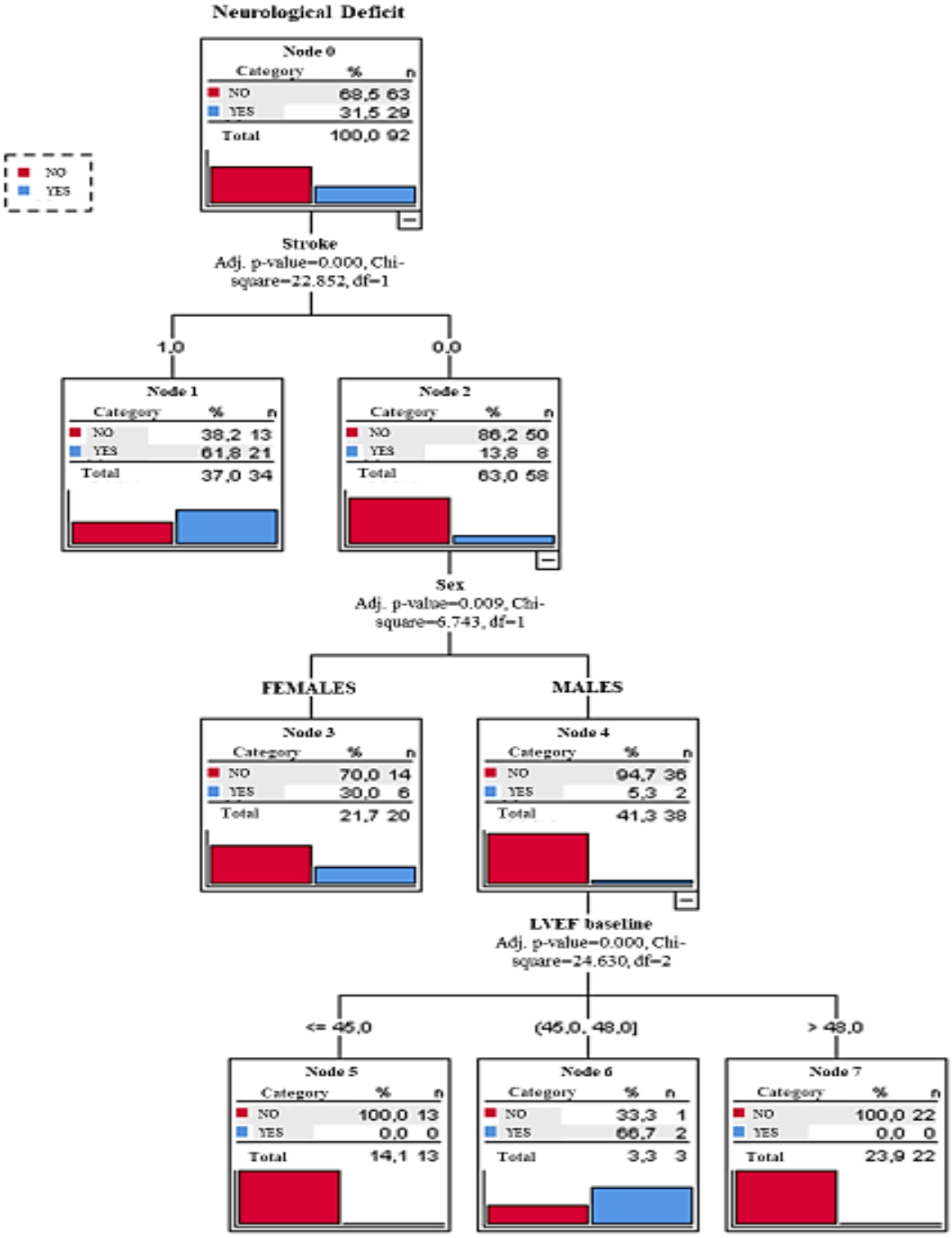

Figure 4. Decision Tree Analysis

Table 3.

Characteristics of Decision Tree Terminal Nodes.

№	Presence of Risk Factors	Number of Patients		Response Rate, %	Index, %
		Total	With ACVA		
7	No history of ACVA; Male; LVEF > 48	22	22	100.0%	146.0%
5	No history of ACVA; Male; LVEF < 45	13	13	100.0%	146.0%
3	No history of ACVA; Female	20	14	70.0%	102.2%
1	Patients with a history of ACVA	34	13	38.2%	55.8%
6	No history of ACVA; Male; LVEF 45–48	3	1	33.3%	48.7%

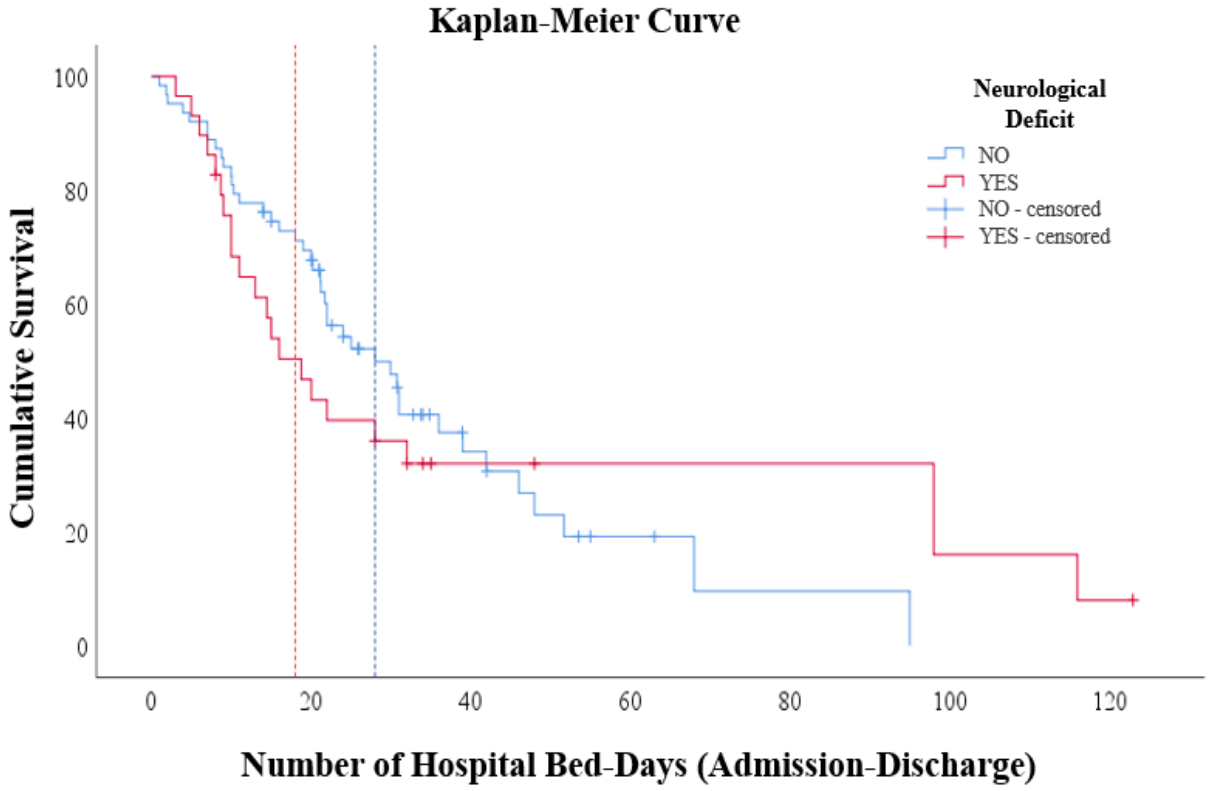

Figure 5. Kaplan-Meier Survival Curve

Study Limitations

This study has several limitations, including its retrospective design, which restricts causal inference between identified risk factors and stroke outcomes due to unaccounted confounders (e.g., medication regimens, genetic factors). The modest sample size (n=92) may further limit statistical power, necessitating cautious interpretation of the results. These constraints highlight the need for larger, prospective multicenter studies to validate and expand upon our findings.

Recommendations for Future Research

To address these limitations and advance our understanding of stroke risk factors in ECMO patients, we recommend prospective multicenter studies with larger cohorts to reduce random variability and enhance statistical reliability. Future investigations should incorporate comprehensive biomarker profiling, genetic testing, and detailed pharmacotherapeutic monitoring to better evaluate their contributions to stroke pathogenesis. Such an approach would provide more accurate insights into the underlying mechanisms of cerebrovascular complications and identify targeted preventive strategies for this high-risk population.

Consistency with Existing Literature

Our findings align with global scientific evidence highlighting elevated stroke risk in ECMO patients. Previous studies report 2-6% stroke incidence among ECMO recipients, primarily attributed to hypoxemia, thromboembolism, and bleeding complications [1, 15]. While confirming these established risk factors, our data further identify hypertension and smoking as significant contributors to stroke development. These results advance the field by enabling more personalized stroke prevention strategies for ECMO patients, both in Kazakhstan and other regions with comparable epidemiological profiles.

Conclusion

Cardiovascular diseases remain the leading cause of global mortality, including in Kazakhstan. While extracorporeal membrane oxygenation (ECMO) is an effective life-support modality, it carries significant complication risks, particularly stroke. Our study of 92 patients revealed neurological disorders in 31.5% of cases, underscoring the substantial stroke risk associated with ECMO therapy.

Key risk factors identified—hypertension, smoking, and prior stroke history—provide actionable targets for improved

screening and prevention protocols. Although limited by its retrospective design and modest sample size, these findings lay crucial groundwork for future large-scale prospective studies.

These findings provide clinically relevant data to refine stroke prediction models and optimize management strategies, which may lead to a reduction in cerebrovascular complications and better outcomes for ECMO patients in Kazakhstan.

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