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# Russian Experience of Transport Extracorporeal Membrane Oxygenation

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**RELEVANCE** The present time can be called a period of accumulation of experience of national health systems in different countries of the world in the application of transport extracorporeal membrane oxygenation (ECMO) technology at the pre- and inter-hospital stages of evacuation of patients to specialized ECMO-therapy centers. The role of such centers is to provide timely advice and, if necessary, perform inter-hospital evacuation.

**MATERIAL AND METHODS** The study summarized and analyzed with the help of the national register "RosECMO" the own experience of 13 hospitals in the Russian Federation, who performed 68 inter-hospital evacuations under ECMO conditions by different modes of transport in patients of different age groups with symptoms of circulatory and respiratory failure. The following parameters were evaluated: characteristics of transport ECMO, clinical manifestations of potentially negative effects of transport, hospital survival, as well as the effect of experience (less and more than 10 cases of transport ECMO) of the presented clinics on the difference in the results obtained.

**RESULTS** Connecting patients to the ECMO device reduces the likelihood of death on the SOFA and APACHE IV scales by 1.2 times ($p < 0.0001$) and 1.4 times ($p < 0.0001$), respectively. Despite the absence of deaths during inter-hospital transportation of patients under ECMO conditions, 14.93% of patients died within 3 days from the moment of their execution, without a significant difference in clinics with different practical experience. The overall hospital survival rate of ECMO transport scenarios in all 13 clinics of the Russian Federation was comparable to the data of the international register 48.52% versus 48.81%, at the same time it was significantly lower (1.3 times) in the group of clinics with less clinical experience 40% versus 52.08% ($p < 0.0001$).

**CONCLUSION** The results of the first stage of the study we obtained indicate the prospects of using the method of extracorporeal membrane oxygenation at the stage of inter-hospital evacuation, due to the effective stabilization of the patient's condition and a significant reduction in the risks of the likelihood of death. Clinics with less clinical experience showed significantly worse results of hospital survival of patients who underwent inter-hospital transportation under conditions of extracorporeal membrane oxygenation compared to clinics with more clinical experience, which can be a significant argument in adopting a model for the development of specialized regional centers for extracorporeal membrane oxygenation. The experience accumulated over the past six years and the analysis of new data from the register of transport cases of extracorporeal membrane oxygenation of the national healthcare system will make it possible to formulate the correct trajectory for the development of the method of extracorporeal membrane oxygenation and its application, including at the stage of pre- and inter-hospital evacuations of patients.

**Keywords:** transport ECMO, register "RosECMO", inter-hospital evacuation

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rf - respiratory failure
rcf - respiratory and circulatory failure
MECC - minimized extracorporeal circulation contour of small filling volume with anticoagulant coating
CR - Cardiopulmonary Resuscitation
cf - circulatory failure
EXMO - extracorporeal membrane oxygenation
VA - veno-arterial perfusion
VAV - veno-arterial-venous perfusion
*VV* - veno-venous perfusion
*VA + Vent* - veno-arterial perfusion if left ventricular decompression is required.

## INTRODUCTION

At the end of the 19th century, a number of scientists (von Schröder, von Frey, Gruber) began to develop a theory of possible artificial circulation [1]. At the dawn (20s of the last century) of the development of the first successful experimental models of artificial blood circulation of a living organism using a piston-type heart-lung machine ("Автожектор" - in Russian) of his own invention (analogy with a piston engine of a car) there was an outstanding Russian scientist, clinical physiologist Sergey Bryukhonenko: perfusion body, isolated perfusion of the dog's head, resuscitation of the dead by artificial circulation. In fact, these were the first successful experimental models of extracorporeal membrane oxygenation in animals (EXMO) [2]. The successful described cases of EXMO use in humans in our current understanding of the method fall on the 70-s last century. The first experience of transport EXMO was described by a team led by Robert Bartlett in 1975 [3], however, at the beginning of the 21st century, the total number of cases of transport EXMO described in the literature did not exceed two decade [4]. The impetus for the development of this technology at the prehospital and interhospital stages of transporting patients to specialized EXMO therapy centers of the 1st level was two circumstances: the pandemic of swine flu A-H1N1 in 2009–2011. [5] and the evolution of consumables (minimized extracorporeal circulation of a small volume of filling with an anticoagulant coating), the so-called MECC type 1 (Fig. 1). The subsequent period until to date can called the period of accumulation of experience of national health systems in different countries of the world, the use of transport EXMO at the pre- and inter-hospital stages of the patients evacuation to specialized EXMO-therapy centers [6-13]. The role of such centers is to provide timely advice, and, if necessary, send a specialized team to perform cannulation, connect EXMO and then perform inter-hospital evacuation by any means of transport at different distances, including solving problems associated with cross-border evacuations.

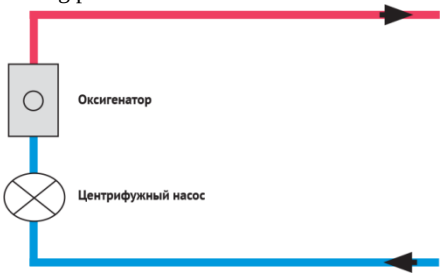


Fig. 1. MECC of the I type

Transport EXMO currently has a fairly low percentage of fatalities during evacuation, about 0.2% [6, 14]. The subsequent hospital survival of this category of patients varies, but according to various sources it is more than 50% [6–8, 13, 15]. At the same time, if the fatal outcome that occurred within the first 3 days from the moment of transportation of the patient is considered a negative event, then the feasibility of performing such a technically complex and costly measure may be questioned. That is why, while accumulating our experience of inter-hospital evacuation using transport EXMO technology, it was important for us to assess the initial severity of the patient and compare it with a number of objective parameters that ultimately would help us answer the most important question - about the appropriateness of the planned event within the framework of the general concept of transferring patients to specialized EXMO-therapy centers. Russia has 11 time zones and the largest area of the territory - 17.1 million km2, for comparison, Canada is in second place in this indicator - 9.98 million km2, which makes the concept of inter-hospital transportation of patients in conditions of extracorporeal support to large regional centers EXMO therapy even more relevant . In 2017, the RusEXMO ("РосЭКМО" in Russian) Register was created in Russia [16], which combines data from inter-hospital medical evacuations with the use of transport EXMO for isolated heart and respiratory failure or their combination for various nosological diagnoses.

**Objective of the study**: to summarize and analyze the data of EXMO transport cases for the period from 2014 to 2020, performed by thirteen clinics in different cities and regions of the Russian Federation.

## MATERIAL AND METHODS

The presented study is a retrospective multicenter study. Based on the RusEXMO register, we summarized and analyzed, within the framework of the 1st stage, the experience of the presented clinical cases for the period from 2014 to March 2020. The multicenter (13 clinics in the Russian Federation) study have included 68 inter-hospital evacuations under the conditions of transport EXMO. The study included patients of all age groups, but later children of the younger age group "up to 1 year " were excluded from the comparative analysis due to the small number of patient data (2 cases), which also had significant anatomical and physiological differences that affect the method of conducting EXMO. The criteria for connecting EXMO before the upcoming inter-hospital evacuation in all cases were the international ELSO recommendations (https://www.elso.org/). Patients' case histories were analyzed: by the frequency of DF prevalence ,CF, RCF, including the development of refractory CR; according to the perfusion scheme (VV, VA, VAV, VVV, VA + Vent); by the type of cannulation (puncture, surgery). We divided all 13 clinics that carried out patient transportation under the EXMO conditions into two subgroups according to the number of inter-hospital evacuations performed: the first subgroup (10 clinics) - “clinics with less than 10 cases”, the second (3 clinics) - “clinics with more than 10 cases ". The first and second subgroups performed 20 and 48 evacuations, respectively. In these subgroups, hospital survival and three-day mortality from the moment of inter-hospital evacuations were compared as a criterion for the negative impact of transportation. We also analyzed the total number of evacuations performed by year to understand the average annual frequency in their need. A number of parameters associated with the technology of medical transportation under EXMO conditions were obtained and analyzed: modes of transport (resuscitation ambulance, helicopter, aircraft), distance and duration of evacuation. We performed a preliminary assessment of patients in terms of the risks of forthcoming transportation and the likelihood of death according to the SOFA and APACHE IV scales before connecting EXMO in the hospital, from where patient T1 was taken before the start of evacuation, and re-evaluating patients according to the same scales after connecting EXMO at the stage evacuation T2.

## RESULTS

According to the results of the completed stage 1 of a retrospective multicenter study, cases of transport EXMO were analyzed (n = 68). From 2 to 21 procedures were performed annually, on average 10.57 ± 7.14 procedures (Fig. 2).

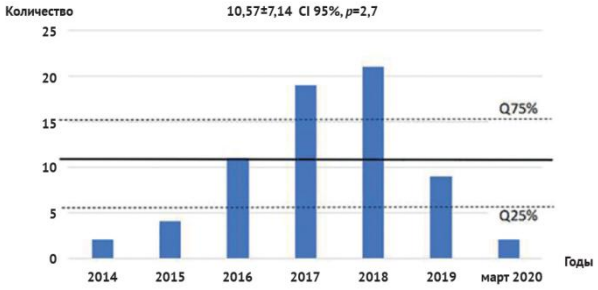


Fig. 2. The annual number of transport extracorporeal membrane oxygenations on the territory of the Russian Federation according to the RosECMO Register

Of these: with respiratory failure rfEXMO 52 patients (76.47%), with circulatory insufficiency cfEXMO 6 (8.82%) and a combination of respiratory and circulatory insufficiency rcfEKMO 10 (14.7%), including developed refractory to traditional CR, clinical death before activation of crEXMO - 5 (7.35%). All connections were performed by peripheral cannulation, mainly by puncture method (64 - 91.12%), with the exception of 4 observations (5.88%), which required open surgical cannulation of blood vessels, including 2 cases in children of the younger age group. At the same time, different schemes of perfusion were used depending on the clinical situation: veno-venous VV - 54 (79.4%), veno-arterial VA - 10 (14.7%) cases, as well as more complex schemes used at the risk of developing "Harlequin" syndrome - veno-arterial-venous VAV 2 (2.9%), if decompression of the left ventricle VA + Vent 1 (1.5%) is necessary or in cases of insufficient inflow through the intake venous line, requiring additional venous cannulation VVV 1 (1.5%) (Table 1).

*Table 1*

**Data of the analysis of transport scenarios of the EXMO register of "RusEXMO"**

| EXMO type, connection diagram and cannulation method | Number of patients, n (%) 68 (100%) |
|---|---|
| rfEXMO | 52 (76,47) |
| cfEXMO | 6 (8,82) |
| rcfEXMO | 10 (14,7) |
| crEXMO | 5 (7,35)* |
| *VV* | 54 (79,4) |
| *VA* | 10 (14,7) |
| *VAV* | 2 (2,9) |
| *VA+Vent* | 1 (1,5) |
| *VVV* | 1 (1,5) |
| puncture | 64 (91,12) |
| Surgically | 4 (5,88) |

Notes: * — crEXMO as part of rcfEXMO; rf — respiratory failure; rcf — respiratory and circulatory failure; CR — cardiopulmonary resuscitation; cf — circulatory failure; EXMO — extraoral membrane oxygenation; VA — vein-arterial perfusion; VAV — vein-arterial-venous perfusion; VV — vein-venous perfusion; VVV — vein-venous perfusion requiring additional venous cannulation; VA + Vent — vein-arterial perfusion in case of left ventricular decompression

The average age of the patients was 38 ± 12 (CI 95%) years - from 15 (0) to 64 years. At the same time, the age group over 60 years consisted of 5 patients (7.4%). The distribution between men and women in the total sample of observations was 54.5% and 45.5%, respectively.

During the evacuations, different types of transport were involved: an ambulance (n = 68) (100%) [1], a helicopter (n = 6) (8.82%), an airplane (n = 11) (16.18%). Moreover, if we talk about using a car as the only means of delivering patients (n = 51), then the share of such an evacuation scenario was 75%. The average distance of inter-hospital transportation under EXMO conditions was 423 ± 89 km (CI 95%) [1; 2800], while the median distance of all performed evacuations was Me = 30 km.

Average travel time 175 ± 14 min (CI 95%) [24; 393]. The probability of death in patients, preliminary assessed on the SOFA and APACHE IV scales before the evacuation stage, was 56.05% and 40.37%, respectively, however, against the background of connecting patients to the EXMO apparatus during the evacuation, the decrease in this probability due to the stabilization of vital functions amounted to 46.38% (p <0.0001) and 28.29% (p <0.0001) according to the same scales, which is 1.2 and 1.4 times less, respectively. It should be noted that there were no deaths during inter-hospital transportation of patients under EXMO conditions (see Table 2). When comparing in the subgroups of all thirteen clinics that have carried out the transportation of patients under EXMO conditions: 1st "clinics with experience of less than 10 cases" (10 clinics) and 2nd "clinics with experience of more than 10 cases" (3 clinics)[2] - 20 and 48 evacuations were performed, respectively, with hospital survival in the 1st subgroup having amounted 8 (40%) versus 25 (52.08%) (p <0.0001) in the 2nd subgroup. The overall hospital survival rate of all EXMO transport cases according to the registry data was 33 (48.52%), with a slightly larger number of patients disconnected from the EXMO apparatus 40 (58.82%) due to the restoration of lung and / or heart function. At the same time, 10 patients (14.93%) died within 3 days from the moment of inter-hospital evacuation during EXMO, without a significant difference in subgroups (Table 2). _____

[1] The reanimobile was used in all cases of transport ECMO, including as one of the stages (shoulder) of delivery.

[2] Two cases of transport EXMO in young children (5 days and 2 months) were excluded from the comparative analysis of age groups due to the small number of patients in this age group.

*Table 2*

**Data of the analysis of transport scenarios EXMO register "RusECMO"**

| Main characteristics | Total patients, n = 68 * | |
|---|---|---|
| Age, years | 37,56±12,62 (CI 95%) | [0; 64]* |
| Gender, % | Мужчины 54,5 | Женщины 45,5 |
| SOFA mortality before EXMO, % | 56,05±6,93 (CI 95%) | [33,3; 95,2] |
| APACHE IV mortality risk before EXMO, % | 40,37±5,27 (CI 95%) | [5; 90,3] |
| SOFA mortality on EXMO, % | 46,38±6,22 (CI 95%) | [33,3; 95,2] |
| APACHE IV mortality risk on EXMO, % | 28,29±5,07 (CI 95%) | [3,9; 82] |
| EKMO evacuation distance, km | 374±172 (CI 95%) | [1; 2800] |
| Duration of evacuation at EXMO, min | 151,2±24,6 (CI 95%) | [24; 393] |
| Reanimobile, n (%) | 68 (51)** | 100% (75%)** |
| Helicopter, n (%) | 6 | 8,82% |
| Airplane, n (%) | 11 | 16,18% |
| Mortality during transportation to EXMO, n, % | 0 | 0% |
| EXMO duration, days | 11±2,24 (CI 95%) | [1; 59] |
| Disconnected from EXMO, n, % | 40 | 58,82% |
| Discharged from hospital, all clinics, n,% | 33 | 48,52% |
| Discharged from hospital, clinic with the experience less than 10 cases, n,% | 8 | 40% |
| Discharged from hospital, clinic with the experience more than 10 cases, n,% | 25 | 52,08% |
| Died after transportation on EXMO within three days, all clinics, n,% | 10 | 14,93% |

Notes: * — two cases of transport ЭКМО in children aged 5 days and 2 months were excluded from the comparative analysis of age groups due to the small number of patients in this age group.
** — only reanimobile, one delivery shoulder. ЭКМО — extraoral membrane oxygenation

## DISCUSSION

Comparing clinics with experience of fewer and more than 10 evacuations in EXMO conditions, we see a significant difference between clinics that have isolated cases in their practice and those who operate with statistics of tens or even hundreds of EXMO cases, including transport scenarios. The so-called more complex connection schemes (VAV, VA + Vent, VVV) of the EXMO apparatus circuit are used exclusively by clinics with extensive experience, they practically do not resort to surgical setting of cannulas, they mainly choose the puncture method. As a result, we see a difference in hospital survival, which was significantly lower in the group with less clinical experience: 40% versus 52.08% ($p < 0.0001\%$). At the same time it should be noted that the overall EXMO transport scenarios hospital survival rate in all 13 Russian hospitals turned out ro be comparative to the world register data: 48,52% vs. 48,81% [17]. Thus, on one hand, we can talk about the correspondence of the hospital survival results between the EXMO transport scenarios carried out on the territory of the Russian Federation for the specified period, in comparison with the total pool of all EXMO cases of international statistics, and in this sense, the strategy of transferring patients from hospitals of a lower rank level (accessibility of technologies) to larger hospitals is quite justified. On the other hand, we undoubtedly see the potential to increase the survival rate of patients during inter-hospital evacuations under EXMO conditions due to the involvement of specialized teams with extensive experience in the transportation stage, as well as the development and implementation of methodological recommendations with effective criteria for assessing the risk / feasibility of the forthcoming transportation in conditions EXMO. These thoughts are suggested by the proportion of patients who died within 3 days from the moment of inter-hospital transportation - 14.93%. Mortality in this case, according to a number of authors, can be directly associated with the transportation episode, as an additional stress factor that can aggravate the severity of the patient's condition [18, 19]. The study showed that the patient's connection to EXMO effectively stabilizes vital functions, reduces the risks of the upcoming inter-hospital evacuation (see Table 1), however, for more accurate prediction, it is necessary to develop a scale that would take into account significant parameters and the very fact of EXMO use. Unfortunately, almost all scales that are widely used for this purpose [20–25] do not reflect, in our opinion, an objective prognosis in patients who are planned to undergo interhospital evacuation under EXMO conditions. The annual forecasted number of EXMO transport scenarios on the territory of the Russian Federation can be assumed basing on the average estimate: $10.57 \pm 7.14$ (see Fig. 2), but the accumulation of the experience and its further analysis can significantly affect these parameters. At the same time, over the past few years, according to international data, one can observe an increase in the epidemiological indicators of EXMO cases, including transport, from 7 per 1 million of the population to 35 per 1 million [26]. In the Russian Federation, the peak followed by a decline in the total number of EXMO cases peaked in 2017 (the epidemic of influenza A-H1N1) and amounted to only 0.5 per 1 million [16], according to other data, 2.4 per 1 million [27], which now, in general, indicates a rather low activity of the use of this technology. Despite the fact that the average distance, taking into account the involved ground and air vehicles, was 423 ± 89 km (CI 95%), nevertheless, the bulk of inter-hospital evacuations (75%) under EXMO conditions was performed using specialized resuscitation machines of class C and D , with a distance of calculation by the median Me = 30 km. It can be

assumed that properly equipped reanimobiles and helicopters will be mainly involved in solving regional tasks for the implementation of transport EXMO; long-distance inter-hospital transportation using aircraft (medical jets) is more likely to be in demand in much smaller quantities in regions with a low population density and a large radius of coverage of territories by large multidisciplinary centers that have the ability to conduct EXMO therapy. In addition, scenarios of cross-border evacuation of patients under EXMO conditions are not excluded (the first such transportation with the participation of specialists from Bergamo, the N.N. Meshalkin National Medical Research Center, Ministry of Emergency Situations of Russia was performed in 2011 in a child with severe heart failure under modalities of support with an implanted VAD cardiopulmonary bypass system requiring heart transplant). Undoubtedly, the data obtained require additional studies planned within the framework of the next stages, the results of which will be presented in the next publications, in particular, the assessment of transportability criteria reflecting the possibility of using EXMO. But already now we assume that having made a bet on the development strategy of specialized EXMO-therapy centers, in foreign literature they are called "Hub ECMO Centers" [28], the national healthcare system of the Russian Federation will be able to improve hospital survival rates and economic efficiency of the direction, about in question.

## INFERENCE AND CONCLUSIONS

The results of the first stage of the study, obtained by us, indicate the prospects of using the method of extracorporeal membrane oxygenation at the stage of inter-hospital evacuation, due to the effective stabilization of the patient's condition and a significant reduction in the risks of the likelihood of death. Hospitals with less clinical experience have showed authentically worse results of hospital survival of patients who were undergone inter-hospital transportation under conditions of extracorporeal membrane oxygenation in comparison to hospitals with more clinical experience. This can be a significant argument in adopting a model for the development of specialized regional centers for extracorporeal membrane oxygenation. The experience accumulated over the past 6 years and the analysis of new data from the register of transport cases of extracorporeal membrane oxygenation of the national health care system will make it possible to formulate the correct trajectory for the development of this method and its application, including at the stage of pre- and inter-hospital evacuations of patients.

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