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Mortality Risk Factors in Neonates Requiring Interhospital Transport

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Summary

Objective. To identify predictors of newborn infants mortality before medical evacuation.

Materials and methods. The observational, cohort, retrospective study included 564 newborns: 526 patients survived and 38 died after 604 visits of the resuscitation-consultation Center transport team (critical care transport — CCT team). Patient's anamnesis, objective data of a patient at the time of examination by CCT team, the volume of intensive care provided and treatment adjustments during preparation for the transfer, records of patient's monitored parameters and indicators of prognosis were analyzed.

Results. Compared to survivors, non-survivors neonates exhibited significant increases in premature newborns (gestation period <29 weeks in 55.26% vs 10.27% in survivors, $P<0.001$) and significantly increased need in a high-frequency ventilation (7.89% [1.66–21.38] vs 0.57% [0.12–1.66] in survivors, $P=0.005$), and in catecholamines support (use of adrenaline was 13.51% [4.54–28.77] in non-survivors vs 0.76% [0.21–1.94] in survivors, $P<0.001$). Both early and late neonatal infections predominated in non-survivors: ([26.32% [13.40–43.10] vs 8,75% [6,47–11,49, early infection, non-survivors vs. survivors, respectively, $P=0.002$) and (23.6% 8 [11.44–40.24] vs 10.46% [7.97–13.39], late infection, non-survivors vs. survivors, respectively, $P=0.028$). Significant differences in the fraction of inspired oxygen (30% [30–30] vs 45% [30–60], $P<0.001$), oxygenation saturation index (2.71 [2.54–3.03] vs 4.48 [2.55–7.67], $P<0.001$), and SpO_2/FiO_2 ratio (316.67 [313.33–320] vs 207.25 [151.67–313.33] $P<0.001$) were found between the groups of survived vs. non-survived neonates, respectively. Logistic regression model revealed following markers of neonatal mortality: birth weight, development of early and late neonatal infection, and the oxygenation saturation index.

Conclusion. Low birth weight, development of early or late neonatal infection and an increase in the oxygenation saturation index are the risk factors of death in newborns requiring medical evacuation.

Keywords: newborn transportation; threat-metric scale; neonatal intensive care; risk of death; oxygenation index

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Introduction

Reducing neonatal and infant mortality remains a priority task of the health care system and an integral indicator of its effectiveness [1]. The system of perinatal regionalization provides an effective way to reduce the mortality of preterm infants by referring them to medical facilities that have the required level of care and sufficient patient flow to provide optimal intensive care [2–4]. Postnatal referral aims to transfer the newborn to an institution with the required level of medical care to reduce complications [5]. At the same time, transportation of newborns with a gestational age of less than 32 weeks and a birth weight of less than 1500 grams has a significant effect on neonatal mortality after adjustment for other risk factors (OR=3.3) [6]. Determining the severity of the neonate's condition prior to transportation remains one of the most important tools for predicting future risks of morbidity and mortality based on available baseline data, which allows the best possible decision to be made for the benefit of the patient [6]. The current federal documents related to the activities of the outreach resuscitation team of the neonatal intensive care center regulate only the general organizational principles of care (Order 921n of the Russian Ministry of Health dated November 15, 2012 «On Approval of the Procedure of Medical Care in Neonatology»), and technical equipment (Order 388n of the Russian Ministry of Health dated June 20, 2013 «On Approval of the Procedure of Emergency (including Emergency Specialized) Medical Care») without precise definition

of approaches to severity and prognosis assessment, algorithms and management rationale. While there are a variety of scales for predicting outcomes in neonatal patients, no consensus exists on the choice of tool for assessing a newborn requiring medical transfer to a higher level of care [7].

The aim of the study was to identify predictors of fatal outcome in newborn patients before medical transportation.

Materials and Methods

An observational, cohort, retrospective study included data from all visits of the transport team of the Neonatal Intensive Care and Consultation Center (NICCC) of the Ekaterinburg Regional Children's Clinical Hospital (RCCH) during the period from August 1, 2017 to December 31, 2018. After excluding patients with congenital anomalies requiring emergency surgical intervention (*N*=34), the number of cases was 640. Complete data or outcomes were not available for 36 cases. The final sample consisted of 604 cases of transport team visits to 564 newborns hospitalized in medical institutions of the Sverdlovsk region and remotely monitored by the NICCC due to their severity. The decision on the possibility of transport was made jointly by the head of the neonatal department of the obstetric care organization and the responsible physician of the outreach resuscitation team on the basis of the current regional regulation (Order No. 1687p of the Ministry of Health of the Sverdlovsk Region dated October 4, 2017) after assessing the severity and possible risks.

Data on hospital outcomes were obtained from primary medical records. In the study sample, two groups were distinguished according to the outcome: survivors (*N*=526) and non-survivors (*N*=38) (Fig.). We evaluated medical history, status at the time of examination by the transport team intensivist, level of intensive care and its modification before transport, monitored parameters (heart rate and SpO_2, noninvasive blood pressure, body temperature), and neonatal assessment using three scales, including the original Clinical Assessment Scale for the Premature Newborn (CASPN) [8], the Neonatal Therapeutic Intervention Scoring System (NTISS) [9], and the Transport Risk Index of Physiologic Stability for Newborn Infants (TRIPS) [10]. The oxygen saturation index was calculated using the formula $(FiO_2 \times MAP)/SpO_2$. The umbilical venous catheter was used as the standard initial vascular access in neonates during the first day of life. If venous access was established after the first day of life, peripherally inserted central catheters or peripheral Venflon-type needle catheters were placed. Fluid therapy and parenteral nutrition were planned and administered according to the clinical guidelines for parenteral nutrition in neonates of the Russian Association of Perinatologists and Association of Neonatologists (2015). The transport equipment consisted of transport incubator ITN-1 (UOMZ, Ekaterinburg, Russia), transport ventilator Stephan F120 Mobile (Stephan, Germany), syringe dispenser B. Braun Perfusor Compact S (B. Braun, Germany), patient monitor Philips MP 40 (Philips Medizin Systeme Boblingen GmbH, Germany). During the preparation phase, the transport team equipment was used for monitoring and respiratory support.

For descriptive statistics, we used median and interquartile range, percentage, 95% CI of the per-

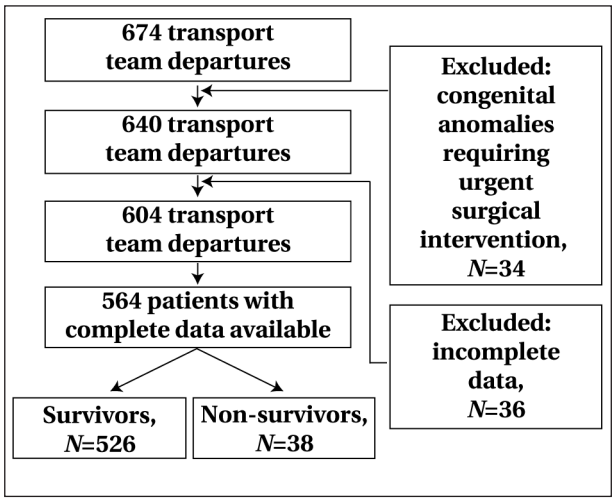

Fig. Study Design Flowchart.

Table 1. History of patients, *Me* [IQR].

Parameter	Values in groups		*P*-value
	Survivors, *n*=526	Non-survivors, *n*=38	
Age of patients on admission to the NICCC, hours	24 [4; 51]	17.5 [5; 49]	0.999
Age of patients at the time of examination by the transport team intensivist, hours	38 [24; 90]	33 [16; 110]	0.595
Age of patients at the time of transfer, hours	38 [25; 86]	30 [14.5; 83.5]	0.817
Birth weight, g	2.555 [1.730; 3.280]	1.050 [630; 2.360]	<0.001*
Gestational age, weeks	36 [33; 38]	28 [25; 37]	<0.001*
Apgar score 1, points	6 [4; 7]	4 [2; 5]	<0.001*
Apgar score 5, points	7 [6; 8]	5 [4; 6]	<0.001*

Note. For Tables 1 and 4: *Me* — median; IQR — interquartile range. For Tables 1–4: *n* — number of cases in the group; NICCC — neonatal intensive care and consultation center. * — significant differences.

centage, and standard error. Sample normality was tested using the Shapiro–Wilk method. When analyzing quantitative data with non-normal distribution of two independent samples, the Mann–Whitney test was used. Fisher's exact test was used to analyze binary data of two independent samples. Logistic regression was analyzed using BioStat Pro 7.0.1.0 and Mathlab R2017a software.

Comparison of the groups of survivors and non-survivors revealed significant differences in birth weight, gestational age, and Apgar scores at 1 and 5 minutes (Table 1).

When analyzing the level of referral, we found significant differences: referrals from level 2 facilities without an ICU occurred in 31.75% of cases [27.79–35.92] in the survivor group and in 13. 16% [4.41–28.09] in the non-survivor group, P=0.017; referrals from level 3 facilities occurred in 8.94% [6.64–11.71] in the survivor group and in 28.95% [15.42–45.90] in the non-survivor group, P<0.001.

When analyzing the underlying diseases in the study groups, we found a significant difference in the frequency of early neonatal infection (8.75% [6.47–11.49] vs. 26.32% [13.40–43.10], survivors vs. non-survivors, respectively P=0.002) and late neonatal infection (10.46% [7.97–13.39] vs. 23.68% [11.44–40.24], survivors vs. non-survivors, respectively, P=0.028) (Table 2).

The median age of fatal outcome was 6.5 [2; 17] days. Two deaths were recorded within the first 24 hours after birth. Both patients were not transferred because they were deemed non-transportable by the transport team specialists.

Results

Analysis of the distribution of patients by birth weight showed significant differences between survivors and non-survivors. More than 34% of the non-surviving neonates had a birth weight of less than 750 grams, whereas only 1.52% of the surviving patients had a birth weight of less than 750 grams. In the surviving group, there was a significant predominance of patients with a birth weight greater than 1500 grams: 81.56% [77.97 to 84.78] vs. 34.21% [19.63 to 51.35] in the non-surviving group, P<0.001. Similar patterns were observed when analyzing the distribution by gestational age: infants with a gestational age of less than 29 weeks were significantly more common in the non-surviving group (55.26% vs. 10.27%, P<0.001), while infants with a gestational age of more than 32 weeks were significantly more common in the surviving group. Patients with NEC who showed signs of perforation (3.01% [1.77–4.78] of all patients) underwent emergency laparotomy with bowel resection and stoma creation within 12 hours of admission to the tertiary hospital. The same procedure was performed in patients diagnosed with lower bowel obstruction (2.13% [1.1–3.69] of all patients). The need for emergency surgery was significantly more frequent in the non-survivors (13.16% [4.41–28.09] vs. 4.75% [3.10–6.94] in the survivors, P=0.043).

When analyzing the management strategies of the transport team, we found a significant difference in the percentage of patients deemed non-transportable, 1.71% [0.79–3.22] in the survivor group vs 28.95% [15.42–45.90] in the non-survivors (P<0.001). Successful evacuation on the first attempt was significantly more common in the survivor group (93.22% [90.56–95.32] vs 76.00 [54.87–90.64], P=0.008).

Respiratory treatment. At the time of evaluation by the transport team intensivist, there were significant differences in ventilatory support parameters

Table 2. Diseases in the groups, % [95% CI].

Diagnosis	Values in groups		*P*-value
	Survivors, *n*=526	Non-survivors, *n*=38	
Hematologic abnormalities	0.57 [0.12–1.66]	2.63 [0.07–13.81]	0.244
Coagulation abnormalities	2.28 [1.18–3.95]	0,00 [0.00–9.25]	1.000
Perinatal asphyxia	8.94 [6.64–11.71]	2.63 [0.07–13.81]	0.238
Congenital anomalies not requiring urgent surgical intervention	1.71 [0.79–3.22]	2.63 [0.07–13.81]	0.505
Chronic lung disease	1.14 [0.42–2.47]	0.00 [0.00–9.25]	1.000
Hemolytic disease of the newborn	3.04 [1.75–4.89]	0.00 [0.00–9.25]	0.616
Metabolic disorders	1.33 [0.54–2.72]	0.00 [0.00–9.25]	1.000
Nonimmune hydrops fetalis	0.19 [0.00–1.05]	2.63 [0.07–13.81]	0.130
Early neonatal infection	8.75 [6.47–11.49]	26.32 [13.40–43.10]	0.002*
Late neonatal infection	10.46 [7.97–13.39]	23.68 [11.44–40.24]	0.028*
Neonatal respiratory distress syndrome	32.51 [28.52–36.70]	34.21 [19.63–51.35]	0.859
Transient tachypnea of the newborn	11.03 [8.48–14.02]	2.63 [0,07–13.81]	0.164
Meconium aspiration syndrome	2.85 [1.60–4.66]	2.63 [0.07–13.81]	1.000
Perinatal brain injury	4.94 [3.25–7.16]	0.00 [0.00–9.25]	0.246
Prematurity	5.32 [3.57–7.60]	0.00 [0.00–9.25]	0.246
Diabetic fetal macrosomia	0.76 [0.21–1.94]	0.00 [0.00–9.25]	1.000
Rhythm and conduction disturbances	1.90 [0.92–3.47]	0.00 [0.00–9.25]	1.000
Lower intestinal obstruction	2.28 [1.18–3.95]	0.00 [0.00–9.25]	1.000

Note. For Tables 2 and 3: CI — confidence interval. * — significant differences.

Table 3. Treatment in the groups, % [95% CI].

Treatment	Values in the groups		*P*-value
	Survivors, *n*=526	Non-survivors, *n*=38	
Nasal CPAP	11.22 [8.65–14.23]	7.89 [1.66–21.38]	0.787
Lung ventilation	47.53 [43.19–51.90]	78.95 [62.68–90.45]	<0.001*
High frequency lung ventilation	0.57 [0.12–1.66]	7.89 [1.66–21.38]	0.005
Dopamine	6.65 [4.68–9.13]	29.73 [15.87–46.98]	<0.001*
Epinephrine	0.76 [0.21–1.94]	13.51 [4.54–28.77]	<0.001*
Dobutamine	0.19 [0.00–1.05]	0.00 [0.00–9.49]	1
Prostaglandins	3.04 [1.75–4.89]	5,26 [0.64–17.75]	0.345
Sedation	3.99 [2.49–6.04]	13,16 [4.41–28.09]	0.025
Myoplegia	0.19 [0.00–1.05]	2.63 [0.07–13.81]	0.13

Note. CI — confidence interval; CPAP — continuous positive airway pressure; * — significant differences.

between the study groups. Non-survivors were more likely to receive ventilatory support (78.95% [62.68 to 90.45] vs. 47.53% [43.19 to 51.90] in survivors, *P*<0.001), including high-frequency ventilation (7.89% [1.66 to 21.38] vs. 0.57% [0.12 to 1.66], *P*=0.005). Medical sedation for synchronization with a ventilator was used significantly more often in the non-surviving group (13.16% [4.41–28.09] vs 3.99% [2.49–6.04], *P*=0.025). Mechanical ventilation was performed in time-cycled pressure-limited mode. Comparison of respiratory support parameters revealed significant differences in inspiratory time (0.34 [0.33–0.35] vs. 0.28 [0.27–0.31], *P*=0.001), due to the predominance of extremely premature infants among the non-survivors, inhaled oxygen fraction (30% [30–30] vs. 45% [30–60], *P*<0.001), oxygen saturation index (2.71 [2.54–3.03] vs. 4.48 [2.55–7.67], *P*<0.001), and SpO_2/FiO_2 ratio (316.67 [313.33 to 320] vs. 207.25 [151.67 to 313.33] in the survivors and non-survivors groups, respectively (*P*<0.001, Table 4). The need to modify ventilatory parameters during the preparation for transportation was significantly more frequent in the non-survivors (31.58% [17.50–48.65] vs. 14.83% [11.90–18.16], *P*=0.012), while the difference in the percentage of patients requiring tracheal intubation or reintubation was not significant (2.85% [1.60–4.66] vs. 5.26 [0.64–17.75] in survivors and non-survivors, respectively, *P*=0.319). The difference in the frequency of tension pneumothorax drainage was also not significant between the groups (0.19% [0.00–1.05] and 0.00% [0.00–9.25] in the survivors and non-survivors, respectively, *P*=1.000).

Catecholamines were used more frequently in the non-surviving group: dopamine use was 29.73% [15.87 to 46.98] vs. 6.65% [4.68 to 9.13] in the survivors (*P*<0.001), and epinephrine use was 13.51% [4.54 to 28.77] vs. 0.76% [0.21 to 1.94] in the survivors (*P*<0.001) (Table 3). At the same time, the difference between the groups in dopamine and epinephrine dosage during continuous intravenous administration was insignificant: dopamine 5 [5–7] μg/kg/min vs 5 [5–8] μg/kg/min in survivors and non-survivors, respectively (*P*=0.8970), epinephrine 0.4 [0.2–1] μg/kg/min vs 0.25 [0.1– 0.3] μg/kg/min in survivors and non-survivors, respectively (*P*>0.05). No intergroup differences were found in inotropic index values: 5 [5–8.5] vs 7 [5–10] in survivors and non-survivors, respectively, *P*=0.379. Fluid therapy was administered at 68.97 [55.38–88.89] mL/kg/day in the survivors and 98.78 [72.73–155.84] mL/kg/day in the non-survivors (*P*=0.001), due to significant differences in weight and gestational age. Surviving patients were less likely to require vascular access (0.19% [0.00–1.05] vs. 5.26% [0.64–17.75], *P*=0.012), administration of fluid therapy or volume loading (0.57% [0. 12 to 1.66] vs 10.53% [2.94 to 24.80], *P*=0.001), catecholamine administration or dose increase (0.38% [0.05 to 1.37] vs 15.79% [6.02 to 31.25], *P*<0.001).

Significant intergroup differences were observed in the number of manipulations performed by the transport team during preparation. The survivors had an average of 0.21 [0.41] manipulations per patient, while the non-survivors had an average of 0.71 [0.46] manipulations per patient (*P*<0.001). During interhospital transportation, the frequency of intensive care modifications did not differ between groups.

When comparing the monitoring parameters, we observed significant differences in heart rate, SpO_2, systolic and diastolic blood pressure (Table–4).

The non-survivors had higher scores on all scales, including CASPN (6 [5–8] vs 4 [2–5], *P*<0.001), NTISS (19.5 [18–25] vs 15 [11–17], *P*<0.001), and TRIPS (31 [20–47] vs 14 [1–20], *P*<0.001).

Four significant predictors of fatal outcome were identified in the study sample using a logistic regression model: birth weight, early or late neonatal infection, and oxygen saturation index (Table 5).

Discussion

Analysis of putative predictors of mortality in the neonatal population points primarily to birth weight and gestational age. Preterm infants are particularly vulnerable to various complications, additional morbidity and mortality associated with respiratory disorders, feeding difficulties, susceptibility to hypothermia, and high infectious risks [11]. Complications of preterm birth are the leading

Table 4. Parameters of respiratory support and monitoring, *Me* [IQR].

Parameter	Values in groups		*P*-value
	Survivors, *n*=526	Non-survivors, *n*=38	
Respiratory rate, per minute	50 [50; 50]	50 [45; 50]	0.119
Inspiratory pressure (P_{insp}), cm H_2O	18 [18; 20]	20 [18; 21.5]	0.08
Positive end expiratory pressure (PEEP), cm H_2O	5 [5; 5]	5 [5; 5]	0.908
Inspiratory time, sec	0.34 [0.33; 0.35]	0.28 [0.27; 0.31]	0.001*
Inhaled oxygen fraction (FiO_2), %	30 [30; 30]	45 [30; 60]	<0.001*
Mean airway pressure (MAP), cm H_2O	8.75 [8.4; 9]	8,89 [7.89; 10.87]	0.357
Oxygen saturation index	2.71 [2.54; 3.03]	4.48 [2.55; 7.67]	<0.001*
SpO_2/FiO_2	316.67 [313.33; 320]	207.25 [151.67; 313.33]	<0.001*
Heart rate, per minute	142 [140; 142]	142 [130; 149]	0.282
Systolic blood pressure, mm Hg	64.5 [62; 65]	55 [40; 60]	<0.001*
Diastolic blood pressure, mm Hg	39 [38; 40]	33 [22; 39.5]	<0.001*
Body temperature, °C	36.6 [36.6; 36.6]	36.6 [36.5; 36.6]	0.157
SpO_2, %	95 [95; 95]	92.5 [91; 95]	<0.001*

Note. Me — median; IQR — interquartile range; * — significant differences.

cause of mortality in children under 5 years of age worldwide, accounting for approximately 1 million deaths in 2015 [12]. A significant prevalence of prematurity was found in the non-surviving neonates, whereas gestational age analysis showed a predominance of infants at 28 weeks' gestation or less in the non-surviving group. A lower Apgar score in the non-survivors is reasonable due to the prevalence of prematurity in this group [13]. Furthermore, a low Apgar score (5 or less at 10 minutes) is associated with an additional risk of neonatal death in both preterm and term infants [14]. However, our logistic regression analysis showed that birth weight was one of the four significant predictors of fatal outcome, while Apgar score data were not significant in the constructed model.

Another important determinant of NICU outcomes, according to the literature, is the level of medical organization providing care to the newborn. Obladen M. reported worse outcomes in NICUs with low patient volume and bed capacity [15]. Poets C. F. et al. in their review indicate a 2–3-fold increase in perinatal mortality among preterm infants in facilities with less than 500 deliveries per year and a 40–80% increase in this parameter in facilities with less than 1000 deliveries per year compared to large hospitals. For preterm infants, the risk of death was also twice as high in low volume facilities as in tertiary care facilities. In addition, the risk of death was increased by up to 56% for infants born in a birth center with fewer than 36 (or 50 very low birth weight) births per year compared with a facility with a large NICU [16]. Lasswell S. M. et al. observed an increased odds of death for very low birth weight infants (38% vs 23%, odds ratio 1.62, 95% CI, 1.44–1.83) and extremely preterm infants (15% vs 17%, odds ratio 1.55, 95% CI, 1.21–1.98) born in non-tertiary care facilities. The observed outcome did not change over time (*P*=0.87) [17]. The effect of level of care was even greater with decreasing gestational age [2].

Recently, Hentschel R. et al. confirmed the above patterns. Infants in small NICUs had an increased risk of mortality after risk adjustment using CRIB (Clinical Risk Index for Babies) (OR 1.48, 95% CI, 1.16–1.90, *P*=0.002) and PREM (Prematurity Risk Evaluation Measure) (OR 1.39, 95% CI, 1.11–1.76, *P*=0.005) scores. In a subgroup analysis, mortality was significantly higher in small NICUs in the moderate risk group (OR 1.49, 95% CI, 1.02–2.17, *P*=0.037 with CRIB) and in the high risk group (OR 1.70, 95% CI, 1.16–1.90, *P*=0.002 with CRIB and OR 1.39, 95% CI, 1.11–1.76, *P*=0.005), but not in the low and very high risk subgroups [4]. The observed differences in mortality during hospitalization in different levels of care were considered to be the result of antenatal

Table 5. Logistic regression model for death predictors.

Parameter	Estimate	SE	*P*
Intercept	–0.51	1.06	0.633
Birth in a medical institution without a NICU	0.32	0.558	0.569
Body weight at birth	–0.0016	0.000448	<0.001*
Apgar 1	–0.14	0.3	0.654
Apgar 5	0.09	0.35	0.779
Emergency surgery	–0.09	0.97	0.889
Oxygen saturation index	0.32	0.08	<0.001*
Catecholamine infusion	0.87	0.57	0.126
Intensive care modification	–0.44	0.61	0.467
Early neonatal infections	2.13	0.77	0.006*
Late neonatal infections	1.84	0.87	0.034*

Note. SE — standard error; * — significant differences.

routing. Patients in the high perinatal risk group were hospitalized in level 2 and 3 institutions with the possibility of neonatal intensive care. At the same time, level 1 and 2 institutions follow the rule of continuous observation, i. e., any patient requiring intensive care is referred to the NICCC, while level 3 institutions seek consultative care only for the most severe patients, including surgical patients. For this reason, only complicated cases from level 3 facilities came to the attention of the transport team, resulting in a high proportion of fatal outcomes. This is probably related to the lack of a significant effect of delivery in a medical facility without neonatal intensive care on the risk of death. The exclusion of patients of tertiary medical institutions from the analysis will probably allow to compensate for the sampling bias associated with selective referrals from these institutions.

Procedures to stabilize hemodynamics during pretransport preparation and transport are not uncommon in neonatal intensive care. Kumar P. P. et al. indicate that 29.8% of patients required additional volume loading and 10.6% required continuous catecholamine infusion during transport [18]. Leung K. K. Y. et al. reported that inotropes were used in 14.5% of neonatal transport cases. This is associated with a higher relative risk of complications during transport and within one hour of arrival, which reaches 2.51 (1.11 to 5.67) after adjustment for other variables [19]. The differences in blood pressure observed between the groups were consistent with normal values adjusted for gestational age. Catecholamines to stabilize hemodynamic parameters were used more frequently in non-survivors. However, logistic regression did not show an effect of the frequency of intensive care modification and catecholamine use on the risk of mortality. This may be due to the difficulty in determining the need for medical hemodynamic support in neonates. In contrast to the adult patient, maintaining a normal blood pressure early in neonates does not guarantee adequate organ perfusion [20]. The reference, albeit indirect, method of perfusion assessment in neonatology is functional echocardiography with determination of volumetric blood flow in the superior vena cava [21]. Literature data confirm that low blood flow in the superior vena cava is closely associated with subsequent intraventricular hemorrhage or neurodevelopmental disorders [22, 23]. However, even this method is not considered to be sufficiently accurate in describing hemodynamic disturbances [24]. Thus, significant difficulties remain in determining the indications for catecholamines. Level 1–2 institutions do not have routine access to perfusion assessment techniques used in neonatal intensive care, and medical management of hemodynamics is often not based on strict indications [20], which does not allow hemodynamic parameters and treatment modalities to be considered as predictors of mortality.

The higher frequency of intensive care modifications in the non-surviving group could indicate both the initial severity of the patient and the insufficient therapeutic activity of the referring medical organization. As a result, we observed a discrepancy between patient severity and the level of care available in the medical organization, which was «compensated» by the transport team. At the same time, the earliest possible provision of appropriate care is known to be associated with better clinical outcomes [25]. Inadequate pretransport preparation at the referring institution increases the need for intensive care en route [26]. Significant differences in scores on all three scales between survivors and non-survivors indicate a significantly greater severity of illness in the non-survivor group.

Adjustment of respiratory support parameters was the most common procedure performed during pre-transport preparation, especially in non-survivors. High-frequency lung ventilation is the most commonly used method of respiratory support in patients with critical respiratory illness. However, all strategies of its use lack sufficient evidence base. Furthermore, this method is only available in a small number of medical institutions, and the decision to use it is often made empirically rather than on the basis of evidence-based recommendations [27–29]. A higher incidence of HF lung ventilation was observed in the non-surviving group, but no differences in mean airway pressure were found. Therefore, the frequency of HF lung ventilation cannot be unambiguously interpreted as a marker of the severity of respiratory failure in the groups.

A greater dependence on oxygen during lung ventilation, a higher oxygen saturation index, and a lower SpO_2/FiO_2 were found in the non-survivor group. The oxygen saturation index correlates well with the Respiratory Severity Score (RSS) [30] and was, together with birth weight, a significant predictor of mortality in the logistic regression model, which is in agreement with the literature [31, 32].

The incidence of sepsis ranges from 4 to 22 cases per 1000 live births [33]. Neonatal sepsis remains an important cause of neonatal death [34]. Early neonatal sepsis, which develops in the first 72 hours after birth, is fatal in 7.0–23.1% of cases, depending on the pathogen [35]. The prevalence of late neonatal sepsis ranges from 0.61% to 14.2% of hospitalized neonates, depending on gestational age [36]. Mortality may be as high as 26.7% [37]. Logistic regression method confirmed the role of neonatal infection in the risk of mortality.

Limitations. First, because the aim of the study was to analyze the death risk predictors in patients requiring interhospital transport, we included only

data available at the time of examination by the intensivist of the transport team and relevant to medical transfer. We did not examine detailed data on obstetric history, because its influence on the probability of neonatal death has been extensively studied in the literature. Second, the observation of neonates by the intensive care and consultation center in the medical organizations of the service area was not «continuous», which created a bias in the initial sample and affected the accuracy of the logistic regression model. Third, the end point for recording outcomes in each case of medical care was completion of hospitalization. Repeated and further hospitalizations, illnesses, and fatal outcomes that occurred later were not included in the study.

Conclusion

Predictors of neonatal mortality before the medical transportation include low birth weight, early or late neonatal infection, and oxygen saturation index.

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