Arch Biol Sci. 2021;73(2):175-183 https://doi.org/10.2298/ABS210121012V

Correlation between echocardiographic findings and biochemical markers in term newborns with moderate to severe perinatal asphyxia

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Received: January 21, 2021; **Revised**: February 25, 2021; **Accepted**: March 6, 2021; **Published online**: March 17, 2021

Abstract: Perinatal asphyxia (PA) is a condition characterized by a gas exchange disorder due to a lack of blood flow or gas exchange, with potential multiorgan dysfunction**.** Our study aimed to determine the correlation between biochemical markers and echocardiography findings in a group of asphyxiated newborns. The prospective cohort study included 120 neonates (52/120 with PA) treated at a tertial referral pediatric center, from 2012 to 2014. A moderate-strong positive correlation was recorded between the transtricuspid pressure gradient (TRPG) and serum lactate, and between TRPG and NT-proBNP in the PA group (P<0.001) on the 1st day of life. A moderate positive correlation was found between NT-proBNP, lactate and troponins on one side, and TRPG on the other in the PA group after the 2nd measurement. Multinomial regression analysis showed that the lactate level was an independent factor for survival on the 1st (odds ratio (OR) 41.3, 95% confidence interval (CI) 2.14-797.1) and 3rd (OR 136.4, 95% CI 2.27-8206.7) days. Our research confirmed a significant correlation between echocardiographic and biochemical parameters of the myocardial lesion and cardiac function. Due to their complementarity, the use of the biochemical and echocardiographic parameters may be conditioned by their availability.

Keywords: neonate; perinatal asphyxia; lactate; NT-proBNP; troponin; echocardiography

INTRODUCTION

Perinatal asphyxia is a lack of blood flow or gas exchange to or from the fetus in the period immediately before, during or after the birth process. This results in progressive hypoxemia and hypercapnia, and if the hypoxemia is severe enough, tissues and vital organs (muscle, liver, heart and ultimately the brain) develop an oxygen debt with consequent anaerobic glycolysis and lactic acidosis [1]. Despite significant progress in perinatal care during previous decades, asphyxia remains among the leading factors of morbidity and mortality in newborns. The incidence of PA in term neonates is from 1 to 6 per 1000 live births, making PA the third cause of infant deaths (23%), following prematurity and severe infections [2,3].

PA can cause significant disorders of organ systems, the most prominent being hypoxic-ischemic encephalopathy and intracranial hemorrhages, respiratory distress and ischemic damage of the myocardium, kidney, liver and gastrointestinal tract. The myocardium is the most frequently affected in 28-73% of all cases [4]. Hypoxia and ischemia and subsequent reperfusion can lead to structural and functional disorders of cardiomyocytes, with a consequent increase

How to cite this article: Vasiljević M, Nešić D, Krasić S, Ninić S, Prijić S, Ašanin M, Stanković S, Cerovic I, Milićević S, Knežević-Rangelov S, Vukomanović V. Correlation between echocardiographic findings and biochemical markers in term newborns with moderate to severe perinatal asphyxia. Arch Biol Sci. 2021;73(2):175-83.

of cardiac-specific enzymes in serum. Injury at the cellular level can lead to cardiac function disorders and circulatory insufficiency, depending on the severity of the initial insult. Early echocardiography examination allows for a more accurate cardiac function evaluation, enabling the early initiation of inotropic support [5]. Thus, our aim was to determine the correlation of biochemical markers of cardiac injury and circulatory insufficiency with echocardiography findings in the group of newborns with PA.

MATERIALS AND METHODS

Ethics statement

The prospective cohort study included 120 neonates treated at the Mother and Child Health Institute of Serbia "Dr. Vukan Čupić" from January 2012 to December 2014. The study group consisted of 52 infants transferred to the Institute because of moderate or severe PA. The control group was comprised of 68 neonates. The study was approved by the institutional ethics committee (reference number 11386/3; December 21, 2011).

Inclusion and exclusion criteria

The diagnosis of perinatal asphyxia was based on metabolic acidosis (umbilical artery pH<7.0 or base deficit ≥12 mmol/L measured in the delivery room) at birth and signs of multiorgan dysfunction. Apgar scores (AS) were determined in the delivery room. The infants were transferred to our center in neonatal intensive care 1-12 h after birth. A subgroup of patients with severe PA included oligoanuric neonates with signs of hypotension and hypoperfusion of vital organs, heart decompensation, respiratory distress and impaired consciousness [6-9]. These patients required inotropic support, vasoactive drugs and mechanical respiratory support. In the group of asphyxiated newborns, 43/52 had severe PA.

Infants with moderate PA had: (i) transitory oliguria without an increased level of serum creatinine which was recovered after decongestive therapy; (ii) did not demand inotropic support; (iii) required noninvasive respiratory support (oxygen therapy, nasal CPAP, noninvasive mechanical ventilation, high-flow nasal cannula) [6-9]. Infants in the control group were predominantly hospitalized due to convulsions, suspected infection and hyperbilirubinemia, which required only phototherapy. Patients with congenital heart diseases, heart rhythm disorders were excluded from the study; likewise, patients with congenital or acquired lung disease were omitted. Patients with other organ anomalies or chromosomal disorders and those with early septicemia were not considered in this study.

Measurement of laboratory parameters

The arterial blood samples were taken at admission (between the 6th and 12th h of life) and the 3rd day of life from each neonate, and analyses included the N-terminal prohormone of natriuretic peptide (NT-proBNP), cardiac troponin I (cTnI), cardiac troponin T (cTnT) and lactate. The umbilical artery pH at the time of birth is not stated herein as this parameter was measured in the delivery room in other hospitals.

Measurement of echocardiographic parameters

Point-of-care echocardiographic examinations were performed on the 1st and 3rd days of life in all neonates. The following echocardiographic parameters were taken into consideration: the peak systolic transtricuspid pressure gradient (TRPG), fractional shortening (FS), left ventricular eccentricity index (LVEI). LVEI was defined as the ratio of the anteroinferior (D2) and septal-posterolateral diameters of the left ventricular cavity (D1), measured at its midpoint at the end of the diastole (EI = D2 / D1).

Statistical analysis

Basic (descriptive) statistics included mean values, standard deviations, medians and interquartile ranges (IQR) of monitored parameters. The difference in the distribution of certain features among the tested groups was determined using the χ^2 or Fisher's test. The normality of the distribution of numerical variables was tested using the Shapiro Wilk and Kolmogorov Smirnov tests. Comparison between the groups was made using the Student t-test, Mann-Whitney and Kruskal Wallis tests. Univariate and multivariate analysis of parameters with possible influence

Table 1. Perinatal parameters of the patients.

	AS first minute	AS fifth minute	CS	meconium-stained liquor	birth weight (kg)	birth length (cm)
PA group (52)	5 IQR 3-5	6 IQR 5-8	26	36	3.26±0.49	51.21±2.26
Control group (68)	9 IQR 8-9	9 IQR 9-10	28	16	3.32±0.48	51.33±2.24
P value	**< 0.001**	**< 0.001**	0.34	**< 0.001**	0.46	0.77
Severe PA (43)	5 IQR 3-6	6 IQR 5-7	22	30	3.33±0.51	51.33±2.25
Moderate PA (9)	6 IQR 6-7	7 IQR 7-8	4	6	3.29±0.29	51.33±2.3
P-value	**0.012**	**0.015**	1.0	1.0	0.81	0.99

PA – perinatal asphyxia, AS – Apgar score, IQR – interquartile range, CS – caesarean section

on survival were conducted in different subgroups of patients with PA. The receiver operating characteristic (ROC) curve was determined by plotting the cut-off value to expand the outcome of the PA. All statistical methods were significant if P<0.05. Data processing was performed using statistical software SPSS 25.0 for Windows 10.

RESULTS

Our study included 120 newborns, 69 males and 51 females. Delivery was on average in the 39th week of gestation; 66 children had a natural birth, 54 were born by cesarean section. Meconium-stained liquor was noted in 58.3% of cases. The average weight at birth was 3.29±0.49 kg, while the average length was 51.26±2.48 cm. The median Apgar score (AS) in the 1st min was 8 (IQR 6-9), and in the 5th min was 9 (IQR 6-9.75). There was no statistically significant difference after comparing the two groups of neonates considering sex distribution, gestational age at birth, birth weight and length. A significant difference was found between groups after comparing the liquor's characteristics, the median AS in the 1st and the 5th min of life (Table 1).

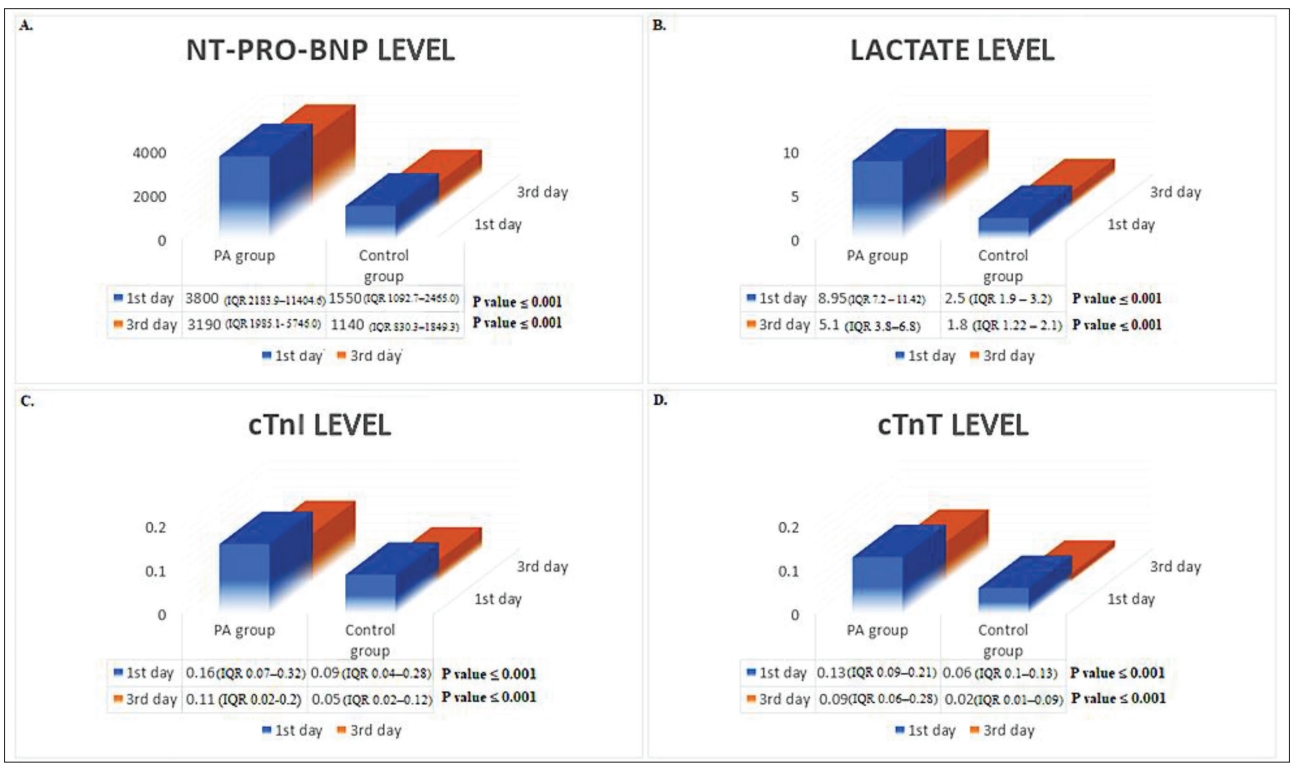

Fig. 1. Average values of biochemical parameters on the 1st and 3rd days of life. PA-perinatal asphyxia; NT-proBNP – N terminal pro-hormone of the natriuretic peptide; cTnI-cardiac troponin I; cTnT – cardiac troponin T.

Table 2. Correlation between biochemical and echocardiographic parameters on the 1st and 3rd days of life.

			1st day of life			3rd day of life		
			TRPG (mmHg)	**LV EI**	**FS (%)**	**TRPG (mmHg)**	**LV EI**	**FS (%)**
All patients	NT-proBNP	Correlation	**0.62**	**0.23**	**-0.38**	**0.54**	**0.24**	**-0.27**
		P-value	0.00	0.01	0.00	0.00	0.00	0.04
	cTnI	Correlation	**0.29**	0.09	-0.05	**0.42**	**0.22**	**-0.23**
		P-value	0.00	0.29	0.60	0.03	0.01	0.00
	cTnT	Correlation	**0.23**	0.12	-0.11	**0.56**	**0.34**	**-0.27**
		P-value	0.01	0.19	0.22	0.00	0.00	0.00
	Lactate	Correlation	**0.86**	0.04	**-0.44**	**0.83**	**0.45**	**-0.38**
		P-value	0.00	0.63	0.00	0.00	0.00	0.00
PA group	NT-proBNP	Correlation	**0.60**	**0.38**	-0.25	**0.52**	0.09	**-0.28**
		P-value	0.00	0.01	0.08	0.00	0.53	0.04
	cTnI	Correlation	0.20	0.19	0.05	**0.41**	0.10	-0.18
		P-value	0.15	0.16	0.72	0.00	0.47	0.21
	cTnT	Correlation	0.14	0.16	-0.02	**0.54**	0.17	-0.26
		P-value	0.32	0.27	0.89	0.00	0.23	0.07
	Lactate	Correlation	**0.65**	**0.27**	-0.26	**0.64**	0.11	**-0.44**
		P-value	0.00	0.05	0.06	0.00	0.43	0.001
Control group	NT-proBNP	Correlation	0.11	0.12	**-0.32**	-0.01	-0.04	-0.04
		P-value	0.37	0.32	0.01	0.96	0.73	0.77
	cTnI	Correlation	-0.02	0.01	0.10	0.14	0.06	-0.19
		P-value	0.87	0.96	0.41	0.28	0.63	0.13
	cTnT	Correlation	-0.05	0.09	-0.02	0.09	0.15	-0.10
		P-value	0.69	0.47	0.88	0.48	0.21	0.41
	Lactate	Correlation	**0.68**	**-0.37**	-0.03	**0.61**	-0.03	0.05
		P-value	0.00	0.00	0.79	0.00	0.83	0.67

PA – perinatal asphyxia; NT-proBNP – N terminal pro-hormone of the natriuretic peptide; cTnI – cardiac troponin I; cTnT – cardiac troponin T; TRPG – transtricuspid pressure gradient; LVEI – left ventricular eccentricity index; FS –fraction of shortening

Table 3. Differences between biochemical and echocardiography parameters between asphyxiated newborns with different outcomes on the 1st and 3rd days of life.

		First day of life			Third day of life		
		survived	**died**	**P-value**	**survived**	**died**	**P-value**
Laboratory parameters	NT-proBNP (pg/ml)	2100.24, IQR 1230.2–3680.0	35000.0, IQR 15552.9 – 35000.0	**0.001**	1720.0, IQR 980.0 – 3310.0	35000.0, IQR 4163 – 35000.0	**< 0.001**
	cTnI (ng/ml)	0.15, IQR 0.06-0.3	0.22, IQR 0.11-0.53	NS	0.1, IQR 0.03-0.22	0.4, IQR 0.25-0.73	**0.001**
	cTnT (ng/ml)	0.13, IQR 0.09-0.2	0.2, IQR 0.11-0.5	NS	0.09, IQR 0.02-0.2	0.48, IQR 0.35-0.6	**<0.001**
	Lactates (mmol/l)	8.8, IQR 7.0-10.2	14.0, IQR 13.4-17.0	**< 0.001**	4.8, IQR 3.8-6.5	11.8, IQR 9.35-14.0	**< 0.001**
Echocardiography parameters	TRPG (mmHg)	28.02 ± 8.25	52.8 ± 5.93	**< 0.001**	22.08 ± 7.16	44.2 ± 7.46	**< 0.001**
	LV EI	1.1 ± 0.1	1.1 ± 0.08	NS	1.25 ± 0.09	1.34 ± 0.5	**0.04**
	FS (%)	36.79 ± 4.36	31.8 ± 5.8	**0.02**	39.23 ± 4.12	31.8 ± 4.12	**0.001**

PA – perinatal asphyxia; NT-proBNP – N terminal pro-hormone of the natriuretic peptide; cTnI – cardiac troponin I; cTnT – cardiac troponin T; TRPG – transtricuspid pressure gradient; LVEI – left ventricular eccentricity index; FS – fraction of shortening; NS – no significance

Biochemical and echocardiographic cardiac evaluation

At the admission, asphyxiated neonates had a lower pH of arterial blood (7.23±0.17) than controls (7.33±0.06) (P<0.001). The average serum biomarker concentrations on the 1st day are presented in Fig. 1. A mild-to-moderate negative correlation was detected between AS on the 1st and 5th min of life and NT-proBNP values (cc=-0.43 and -0.41, P<0.001) and cTnT (cc=-0.27 and -0.26, P=0.003 and 0.005, respectively). A strong negative correlation was established between AS in the 1st and 5th min of life and lactate (cc=-0.73 and -0.67, P<0.001). Patients with PA on the 1st day of life had statistically higher TRPG (P<0.001) and lower FS (P<0.001) compared to the control group. NT-proBNP values on the 1st day of life correlated positively with TRPG and negatively with FS (Table 2). Lactate correlated strongly positively with TRPG. A strong positive correlation was shown between TRPG and NT-proBNP and lactate in the PA group. On the 3rd day of life, laboratory parameters were also significantly higher in the PA group than in the control group (Fig. 1), TRPG (P<0.001) and LVEI (P<0.001) were higher in the PA group than in the control group, while FS was significantly lower (P=0.008). The correlation between echocardiographic and laboratory parameters on the 3rd day of life is shown in Table 2.

Analysis of the risk factors for death in patients with PA

Only neonates from the PA group died (5/52; P=0.01). Sepsis was the cause of death in 2/5 patients, and pulmonary hypertension in 3/5. Neonates with fatal outcome had lower AS on the 1st (3, IQR 3-5) and 5th (5, IQR 3-5.5) min of life than newborns with PA who survived (5, IQR 4-7; 6, IQR 5-8, respectively) (P=0.001, P=0.003, respectively). All patients who died (5/5) were treated with mechanical ventilation, dopamine, dobutamine and inhaled nitric oxide (NO). Patients who died had significantly higher NT-proBNP (P=0.001) and lactate (P<0.001) on the 1st as well as 3rd day of life (P<0.001) compared to the survivors. Cardiac TnT and cTnI were higher in patients with a fatal outcome only on the 3rd day of life (P=0.001). Those patients had significantly higher TRPG and lower FS on the 1st and 3rd days of life than other patients with PA (Table 3).

Table 4. The impact of biochemical parameters (divided into subgroups) on the survival in patients with perinatal asphyxia.

	Univar. P-value	Multivar. P-value	OR	95% CI
NT-proBNP - 1st	**0.02**	0.79	1.28	0.19-8.35
cTnI-1st	0.43	0.91	1.1	0.17-6.97
cTnT-1st	0.78	0.92	0.88	0.06-12.12
Lactate - 1st	**0.00**	**0.01**	**41.29**	**2.14-797.1**
NT-proBNP - 3rd	**0.02**	0.67	2.17	0.06-75.2
cTnI-3rd	**0.01**	0.79	1.89	0.01-249.77
cTnT-3rd	**0.02**	0.13	12.43	0.45-340.21
Lactate-3rd	**0.00**	**0.02**	**136.41**	**2.27-8206.7**

According to the specificity of 75 and 90% on the ROC curve, patients with PA were divided into three subgroups based on the level of biochemical parameters: lactate on the 1st day of life: 0-5, 5-13 and >13 mmol/L; 3rd day of life: 0-4, 4-9 and >9 mmol/L; NT-proBNP on the 1st day: from 0-3000, 3000-13000 and >13000 pg/mL; NT-proBNP on the 3rd day: 0-2000, 2000-5000 and >5000 pg/mL; cTnI and cTnT on the 1st and 3rd days of life: from 0-0.1, 0.1-0.5 and >0.5 ng/mL.

OR-odds ratio; CI-confidence interval; cTnI-cardiac troponin I; cTnT-cardiac troponin T; NT-proBNP – N terminal pro-hormone of the natriuretic peptide.

Multinomial logistic regression analysis showed that the lactate level was an independent factor for survival on the 1st and 2nd measurements, with the probability of death outcome being 41-fold higher when moving to the next subgroup (higher value range) on the 1st day and even 136-fold higher on the 3rd day of life (Table 4).

Cut-off values of NT-proBNP and lactate on the 1st and 3rd days of life for survival prediction of neonates with asphyxia are presented in Fig. 1. Troponin cut-off values on the 3rd day of life were 0.29 ng/mL for cTnI (specificity 91.3%, sensitivity 80%) and 0.26 ng/mL for cTnT (specificity 88.7%, sensitivity 80%). The cut-off values of echocardiographic parameters for the survival of neonates with asphyxia are presented in Fig. 2.

Analysis of risk factors for death in patients with severe PA

In our study group, 43/52 infants had severe PA. After comparing two groups of asphyxiated neonates (moderate and severe) with regard to sex distribution (P=1.0), characteristics of the amniotic fluid and

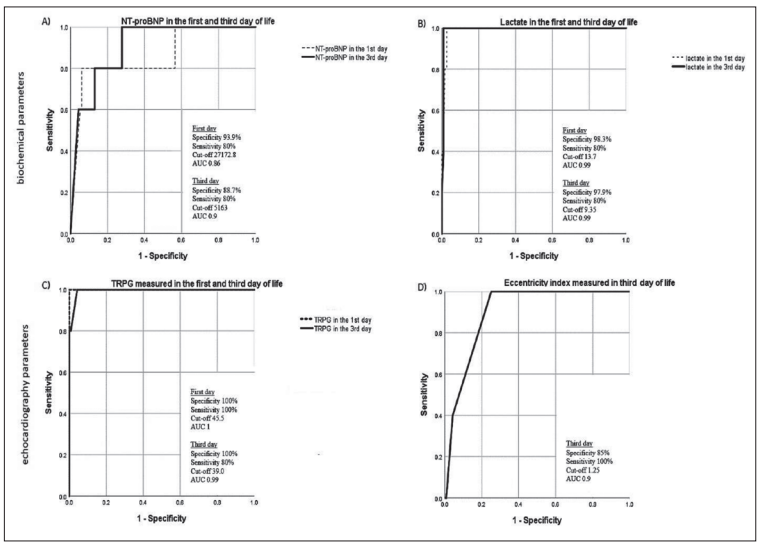

Fig. 2. Analysis of risk factors for death in patients with PA. **A**-27172.83 pg/mL for NT-proBNP on the 1st day of life with a specificity of 93.9% and a sensitivity of 80% (dotted line) and 5163 pg/mL for NT-proBNP on the 3rd day of life with a specificity of 88.7% and a sensitivity of 80% (solid line); **B**-13.7 mmol/L for lactate on the 1st day of life with a specificity of 98.3% and a sensitivity of 80% (dotted line) and 9.35 mmol/L for NT-proBNP on the 3rd day of life with a specificity of 97.9% and a sensitivity of 80% (solid line); **C**-45.5 mmHg for TRPG on the 1st day of life with a specificity of 100% and a sensitivity of 100% (dotted line) and 39 mmHg for TRPG on the 3rd day of life with a specificity of 100% and a sensitivity of 80% (solid line); **D**-1.25 for LVEI on the 3rd day of life with a specificity of 85% and a sensitivity of 100% (solid line).

mode of delivery, there was no statistically significant difference. However, newborns with severe PA were resuscitated, exhibiting a moderate PA (22/43 vs. 0/9; P=0.007) (Table 1). On admission, severely asphyxiated newborns had a lower pH of arterial blood sample (7.2±0.18) than moderately asphyxiated neonates (7.34±0.04) (P=0.04).

Neonates with severe PA had significantly higher NT-proBNP (3800, IQR 2860-25040.2 vs. 1634.8, IQR 1100.0-2665.1 pg/mL P=0.01) than moderately asphyxiated newborns on the 1st day of life, along with higher cTnT and cTnI on the 3rd day of life (cTnT 0.17, IQR 0.07-0.31 vs 0.01, IQR 0.005-0.09 ng/mL, P=0.002; cTnI 0.17, IQR 0.06-0.30 vs 0.02, IQR 0.01-0.1 ng/mL, P=0.008). These newborns had higher TRPG and LVEI on the 1st and 3rd days of life.

The cut-off values of laboratory parameters for survival prediction of neonates with inotropic support were as follows: 27171.83 pg/mL for NT-proBNP on the 1st day of life with specificity 84.2% and sensitivity 80%; 0.27 ng/mL for cTnI on the 3rd day of life, with specificity 75% and sensitivity 80%; 0.41 ng/mL for cTnT on the 3rd day of life, with specificity 98% and sensitivity 80%. The cut-off values of echocardiographic parameters for survival prediction of neonates with inotropic support were as follows: 45.5 mmHg TRPG on the 1st day, with specificity 100% and sensitivity 100%; 39 mmHg TRPG on the 3rd day, with specificity 100% and sensitivity 80%.

DISCUSSION

Neonatal asphyxia has been shown to result in significant myocardial abnormalities, including clinical, biochemical, electrocardiographic and echocardiographic changes consistent with ischemic damage. In our study, patients with PA had higher values of cardiospecific enzymes on the 1st and 3rd days of life, with values depending on the severity of the PA. On the 3rd day of life, this difference was even more apparent than in the first measurement. The NT-proBNP level is very high on the 3rd day of life and then rapidly declines [10-12]. Normal B-type natriuretic peptide (BNP) concentrations do not exclude heart disease, structural heart defects, or chamber hypertrophy, but are more often correlated with the degree of damage to chamber function [13].

Previous studies have reported that echocardiographic examination is inefficient in detecting myocardial injury in asphyxiated neonates, and postulated that echocardiographic findings such as left ventricular dysfunction might be obscured by compensatory mechanisms occurring in the early days of life [11]. However, we showed that neonates with PA have compromised LV systolic function and higher TRPG. Further, positive correlations were proven between biochemical and echocardiographic parameters. In the first measurement, NT-proBNP correlated well with echocardiographic parameters, especially in the PA group. This result could be explained as the result of a myocardial injury that often co-occurs with elevated ventricular tension and a compensatory cardiac output increase. Notably, in the event of heart failure, the

ventricle is stretched by atrial and ventricular dilatation. Simultaneously, pulmonary vasodilation stimulates pulmonary and cardiac nerve receptors, regulating BNP release [11]. Immediately after birth, BNP is released from existing depots in atrial cardiomyocytes, regardless of the synthesis process. However, in cases of a subacute and chronic injury-induced increase of heart volume, the rise in BNP in the circulation is due to its synthesis in ventricle cardiomyocytes [14]. Consequently, on the 3rd day of life, NT-proBNP positively correlated with TRPG and negatively with FS, but only in the PA group. The BNP level correlated well with the gradient pressure on the tricuspid valve [15]. Therefore, elevated serum NT-proBNP in the acute phase of myocardial injury in children was associated with acute phase-localized myocardial ischemic injury, which was concluded in prior studies [11,12]. Tricuspid valve regurgitation was a prominent finding after birth asphyxia, which could be a consequence of papillary muscle ischemia in asphyxiated neonates or persistent pulmonary hypertension [5].

Although some authors claimed that the correlations between cTnI and echocardiographic measurements in perinatal asphyxia did not exist [16], we showed that the troponin level correlates positively with TRPG in the PA group only on the 3rd day of life. An explanation could be because levels of cTnT and cTnI start increasing 4 to 9 h after acute myocardial injury [4], and the cTnI value correlated positively with the traditional markers of asphyxia after 12 h of life [17]. In our study, the values of cTnT and cTnI on the 1st day of life were statistically higher in patients with PA. Also, the difference among asphyxiated patients with and without myocardial injury was described only in cases with high troponin levels [4]. The cTnT level was significantly higher in neonates with echocardiographic signs of myocardial damage, while no differences were detected concerning functional items [18]. We found that a mild negative correlation existed between troponins and FS in all patients, while a significant negative correlation between serum cTnI and FS among asphyxiated neonates was previously described [19]. Some studies showed that cTnT levels correlated with echocardiographic findings of myocardial dysfunction, meaning it correlated positively with the left and right ventricle Tei index, stroke volume and left ventricular output, and negatively with mitral and tricuspid systolic velocity [19,20].

Infants with PA have lower cardiac output than healthy neonates, but the disappearance rate of lactate was not statistically significantly related to this [21]. The slow rate of lactate disappearance could be explained by microcirculatory dysfunction with regional tissue hypoxia, anaerobic glycolysis in response to stress, or delayed lactate clearance from the liver [22]. In our study, lactates strongly positively correlated with TRPG, but negatively with FS in both measurements.

We defined the cut-off values of biochemical and echocardiographic parameters on the 1st and 3rd days of life for survival prediction in neonates with PA. Namely, lactate exhibited the highest sensitivity and specificity, with cut-off values of 13.7 mmol/L on the 1st day and 9.35 mmol/L on the 3rd day of life. Values of lactates higher than 10 mmol/L in the 1st h of life had weak prognostic significance. A considerable risk of severe systemic damage and death occurs if the lactate concentration is higher than 15 and 20 mmol/L, respectively, in the 1st h of life [23]. Lactates were apparently an independent factor for survival in the 1st and 2nd measurements, with a probability of a fatal outcome being 41-fold higher when moving to the next subgroup on the 1st day, and even 136-fold higher on the 3rd day of life.

An important biochemical parameter was NT-proBNP, with cut-off values of 27172.83 pg/mL for the 1st and 5163 pg/mL for the 3rd days of life. Previously, a cut-off value for NT-proBNP was 3612.5pg/L, with a sensitivity of 83.3% and a specificity of 80.5%, for myocardial damage reported in neonates with PA [14]. However, investigators have suggested that BNP cannot be used as an independent prognostic indicator of myocardial injury [4].

The troponin values were also important for PA outcome, but only on the 3rd day of life. Namely, the cut-off value for cTnI was 0.29 ng/mL and 0.26 ng/mL on the 1st and 3rd days of life, respectively. Nevertheless, in patients with severe PA, the cut-off value was 0.41 ng/mL for cTnT in the 3rd day, with a specificity of 98% and sensitivity of 80%. It was found that the cut-off value for cTnT was 0.19 μg/L with a specificity of 100% and a sensitivity of 57% [19]. Slightly higher values of cardiac cTnI in the prediction of mortality after perinatal asphyxia with a cut-off at 0.135 μg/L (sensitivity 84.6%, specificity 85.9%) were described [24]. Because cTnI is considered the most specific cardiac biomarker, several studies have concluded that

it is superior to BNP in predicting mortality or other outcomes in neonates [4], which is in disagreement with our study since we found better sensitivity and specificity for NT-proBNP than for troponins.

We showed that newborns with the worst echo findings had a fatal outcome, as was previously demonstrated [25]. We showed that TRPG had a significant impact on the survival rate, with values of 45.5 mmHg on the 1st day (sensitivity 100%, specificity 100%) and 39 mmHg on the 3rd day (sensitivity 80%, specificity 100%).

All patients who died required inotropic drug support and received NO therapy. Although many studies support a protective effect of inhaled NO on both regional and global myocardial ischemia, some studies have shown that NO is deleterious due to its putative prooxidant actions and a negative inotropic effect [26].

CONCLUSIONS

The presented results confirm that patients with PA had higher values of cardiospecific enzymes on the 1st and 3rd days of life, and that the values were dependent on the severity of the PA. The average values od NT-proBNP and lactate correlated well with the echocardiographic parameters on the 1st day of life. A correlation was proven between cTn and lactate values on the one side and echocardiographic parameters on the other on the 3rd day of life. The cut-off values were defined for biochemical and echocardiography parameters. The lactate values in the serum of neonates with PA had the highest specificity and sensitivity, followed by NT-proBNP and troponins. Of all followed parameters, only the value of lactate on the 1st and 3rd days of life was an independent predictor for the survival of neonates with perinatal asphyxia. Our research confirmed the correlation between echocardiographic and biochemical parameters of the myocardial lesion and cardiac function. Their complementarity in monitoring the course of the disease and prognosis of neonates with PA was also shown. However, due to their complementarity, the use of biochemical and echocardiographic parameters may be conditioned by their availability.

Funding statement: This work received no funding.

Acknowledgements: Project of the Ministry of Health: "National program for palliative care of children in Serbia".

Author contributions: MV, DN, SS, SM, MA and VV contributed to data acquisition, data analysis and data interpretation. SK, SN, SP, IC and SKR designed the study and wrote the paper. All authors approved the final version of the manuscript.

Conflict of interest disclosure: The authors declare no conflict of interest.

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