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Original Article

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Combined Predictors of Long-Term Outcomes of Kasai Surgery in Infants with Biliary Atresia

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ABSTRACT

Purpose: Biliary atresia (BA) is the leading cause of neonatal cholestasis (25–45%). The primary treatment is hepatic portoenterostomy (Kasai procedure), but only 20–40% provide long-term benefits. This study aimed to develop a predictive model for surgical efficacy by comparing preoperative and early postoperative indicators in infants with different outcomes.
Methods: We enrolled 166 infants with BA (93 girls, 73 boys) who underwent the Kasai procedure between September 2002 and December 2021, dividing them into favorable or adverse outcome groups. Over 40 parameters were measured, and the diagnostic significance of the prognostic model was evaluated.
Results: Kasai surgery was efficacious in 69 patients (42%) and non-efficacious in 97 (58%). Our model assesses efficacy by day 14 after surgery, improving on the <34 μmol/L direct bilirubin threshold established for 3–6 months after the procedure. Including the Desmet fibrosis score refined the model.
Conclusion: Blood cholesterol below 5.41 mmol/L, direct bilirubin below 56.3 μmol/L on postoperative days 14±3, and a low Desmet score indicate a high probability of efficacious Kasai surgery in infants with BA.

Keywords: Biliary atresia; Portoenterostomy, hepatic; Hyperbilirubinemia; Cholesterol

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Conflict of Interest
The authors have no financial conflicts of interest.

INTRODUCTION

Biliary atresia (BA) is the most common cause of neonatal cholestasis, accounting for 25–45% of all cases [1]. Manifested as inflammatory and fibrosing obliteration of the extrahepatic and intrahepatic bile ducts, BA leads to chronic cholestasis with progressive fibrosis and eventually biliary cirrhosis. Hepatic portoenterostomy (HPE), also known as the Kasai procedure, was introduced by Morio Kasai in 1959. This procedure allows for bile drainage and is widely used as a first-line treatment for BA. The long-term efficacy of HPE is undermined by profound hepatotoxic damage already present at the time of intervention. Only 20–40% of Kasai procedures independently provide long-term beneficial effects; more often, HPE serves as a palliative surgery, eventually requiring liver transplantation [2-5]. In 46% of cases, the transplantation follows within the first year after HPE [6]. The generally accepted clinical criteria to assess the Kasai surgery efficacy include the presence of stool staining, jaundice resolution, and a decrease in total bilirubin (TB) levels to <34 μmol/L within 3–6 months after the procedure [7-10].

The major known factors for adverse outcomes in HPE are patient age at surgery (>3 months) and the syndromic forms of BA [11]. The outcomes have also revealed certain associations between biochemical markers [12-14] and histopathological indicators, including fibrosis [15-17], inflammation [18], and bile duct diameter [19]. The scope of the candidate predictors is limited, and the results obtained thus far require additional reflection and refinement.

In this study, we compared the preoperative and early postoperative clinical, laboratory, and ultrasound indicators in infants with different HPE outcomes to develop a predictive model for surgical efficacy.

MATERIALS AND METHODS

This retrospective cohort study was conducted in accordance with the Code of Ethics of the World Medical Association (Declaration of Helsinki). The study protocol was reviewed and approved by the Ethics Committee of the Kulakov National Medical Research Center for Obstetrics, Gynecology, and Perinatology (Protocol No. 22 dated December 14, 2021). All the participants (children's parents) provided written informed consent for the use of any data for scientific purposes at the time of their first hospitalization.

We enrolled 166 infants with BA (93 girls and 73 boys) who underwent the Kasai procedure between September 2002 and December 2021. All patients underwent surgery by the same surgeon, and postoperative observation and management were performed in the same center following the general standards of postoperative care.

The inclusion criteria were as follows: children with a confirmed diagnosis of BA through histological analysis of bile remnants, and all children were examined to rule out other liver diseases, such as Alagille's syndrome, alpha-1 antitrypsin deficiency, and cystic fibrosis. Moreover, genetic testing using a cholestasis panel and next-generation sequencing has been performed during the preoperative examination stage since 2014. Most patients who underwent surgery between 2002 and 2014 underwent retrospective genetic testing to exclude other liver diseases. A follow-up period of at least six months was used to determine the effectiveness of the surgery.

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The exclusion criterion was insufficient data for analysis, and patients were excluded from follow-up until the effectiveness of surgery was determined.

Patients were divided into two groups depending on the outcome (favorable or adverse). Favorable outcomes were determined by the appearance of colored stools, jaundice resolution, and a decrease in TB levels to <34 μmol/L within 3–6 months after the procedure.

Comparative assessment of physical development indicators included gestational age at birth, weight at birth, age at surgery, and body weight and height at the time of surgery. A comparative histopathological evaluation of fibrosis using the Desmet score was performed on liver biopsies (n=105) collected intraoperatively. The dimensions of the liver and spleen were clinically estimated before surgery (b/s) and 14±3 days after surgery (a/s). Laboratory blood test indicators, including platelet counts, albumin, gamma glutamyl transferase, cholinesterase, total cholesterol (TC), alkaline phosphatase (ALP), TB, direct bilirubin (DB), alanine transaminase, aspartate transaminase (AST), and fibrinogen levels, as well as the prothrombin indexes (time, ratio, and international normalized ratio—prothrombin time, prothrombin ratio, and prothrombin international normalized ratio, respectively), the activated clotting time, and the aspartate aminotransferase-to-platelet ratio index were measured pre- (day 1–3 b/s) and post-operatively (day 14±3 a/s).

A comprehensive ultrasonographic examination was performed preoperatively (days 3–7, b/s). Ultrasound morphometry included common bile duct (CBD) wall thickness, CBD length and width, thickness of the fibrous portal plate, portal vein diameter, common hepatic artery diameter, hepatic artery resistance index, anteroposterior measurements of the left and right lobes of the liver, and length and width of the spleen.

Statistical analyses were performed using IBM SPSS Statistics version 26 (IBM Co.). Quantitative data are described by mean, standard deviation, median, interquartile range (Q1–Q3), and/or 95% confidence intervals (95% CI). Validation of quantitative data for the normality of distribution was carried out using the Kolmogorov-Smirnov test with the Lilliefors correction at n>50 (p>0.05). Kurtosis and asymmetry indicators were estimated, and the histogram was analyzed (visual method). For features with a normal distribution, the equality of variance of the compared samples was evaluated using Levine's test (p>0.05). The Student's t-test was used to compare quantitative variables with a normal distribution and equality of variances in each of the compared groups; in the absence of equality of variances (p<0.05), the Student's t-test was used with Welch's modification. Non-parametric statistical methods, such as the Mann-Whitney U-test, were used for non-normally distributed data. Categorical data were converted into frequencies (%) and analyzed using Fisher's exact test. Differences were considered statistically significant at p<0.05.

Logistic regression was used to identify the dependence of a binary indicator (outcome probability) on the quantitative and categorical indicators. The dependent variable was the probability of the outcome of the operation (0: operation was ineffective, 1: operation was effective), and quantitative indicators were selected as independent variables that showed statistically significant differences between the two groups during a comparative analysis (p<0.05). First, a univariate logistic regression analysis of independent variables was performed to examine their association with the outcome. Variables with p<0.05 were candidates for multivariate logistic regression analysis. Considering the high significance of the degree of liver fibrosis in the literature, despite its lack of significance in the comparative

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analysis, this indicator was included in both univariate and multivariate analyses as a predictor. Multivariate models were adjusted at each stage by removing variables with high *p*-values until a final model was reached in which all variables were statistically significant ($p<0.05$).

We used a 'complete case' analysis approach, assuming 'missing at random' conditional on all covariates included in the final model.

Using receiver operating characteristic (ROC) analysis, the diagnostic significance of the prognostic model was evaluated, and the cutoff values were determined for the most significant predictors. The quality of the model and the assessment of the prognostic significance of the studied parameters were determined using the results of the chi-square test, and the coefficient of determination R-square (Nagelkerke) was also calculated. Additionally, the ROC analysis was conducted to assess the diagnostic significance of the prognostic model, based on the area under the curve (AUC), and was determined based on the following gradation: 0.9–1.0: excellent, 0.8–0.9: very good, 0.7–0.8: good, 0.6–0.7: average, below 0.6: unsatisfactory. The optimal classification threshold value (cutoff point) was determined as the optimal ratio of sensitivity to specificity.

RESULTS

The average age at Kasai surgery was 75.8 (20.6) days. Of the 166 enrolled patients (93 girls and 73 boys), 147 (89%) were born full-term, weighing 3.290 (0.447) kg, and 19 (11%) were born preterm at 33–36 weeks, weighing 2.293 (0.343) kg.

In our study, five patients (3%) presented with the cystic form of BA, four (2.4%) presented with biliary atresia splenic malformation (BASM) syndrome, and 157 (94.5%) had type III BA. Notably, in two patients with BASM syndrome, the intervention was successful despite the reported adverse impacts of BASM syndrome; therefore, we did not exclude these cases from the study.

The procedure was efficacious in 69 patients (42%) and non-efficacious in 97 patients (58%). In the group with efficacious HPE, colored stools appeared on day 2 (0–3) a/s in all patients. In the group with non-efficacious HPE, only 57 (59%) patients developed colored stools that appeared on day 3 (2–4) a/s. In infants who underwent efficacious surgery, TB decreased to 34 μmol/L within 29 (16–64) days a/s.

In the group with efficacious HPE, preoperative total blood cholesterol levels were significantly lower, $p=0.018$ (**Table 1**), whereas other preoperative indicators were similar between the groups (**Table 1**). Ultrasound morphometry revealed no significant differences (**Table 2**), and the degree of liver fibrosis was similar between the two groups (**Table 3**). On postoperative day 14±3, the levels of TC, ALP, TB, DB, and AST in patients with efficacious Kasai surgery were significantly lower compared with the non-efficacious surgery group (**Table 4**).

Parameters such as preoperative TC level, and postoperative blood levels of TB, DB, TC, ALP, and AST are studied at 14±3 a/s. Statistically significant differences were examined in a one-way logistic regression model to determine the effect of each factor separately on the outcome.

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Pediatric Gastroenterology, Hepatology & Nutrition pghn

Table 1. Preoperative characterization of the patients grouped according to Kasai procedure outcomes

Parameter	Efficacious Kasai surgery	Non-efficacious Kasai surgery	*p*-value
No. of patients	69	97	
Weight at birth (kg)	3.235 (2.800–3.492)	3.372 (3.031–3.610)	0.158
Age at surgery (d)	80 (61–94)	77 (65–92)	0.777
Weight at surgery (kg)	4,836 (4,215–5,480)	4,800 (4,275–5,276)	0.801
Height at surgery (cm)	59.0 (57.0–60.6)	59.0 (55.0–60.5)	0.992
Platelets (10^9/L)	377 (284.5–549)	400 (307–538.5)	0.900
Albumin (g/L)	39 (36.8–41.0)	40.1 (37.0–42.2)	0.174
ChE (U/L)	6,423 (5,756–7,211)	6,642 (4,906–7,189)	0.787
GGT (U/L)	555.5 (329.3–719.9)	582.5 (409.4–967.0)	0.251
TC (mmol/L)	5.34 (4.03–6.45)	6.29 (4.93–7.51)	0.018*,†
ALP (U/L)	511.0 (375.0–621.2)	561.5 (424.5–804.3)	0.057
TB (μmol/L)	147.8 (118.7–171.9)	149.4 (132.4–189.2)	0.224
DB (μmol/L)	86.8 (70.0–105.7)	91.0 (81.6–119.7)	0.086
ALT (U/L)	159.0 (88.2–236.0)	151.0 (88.0–267.0)	0.650
AST (U/L)	228.0 (157.8–316.9)	217.0 (153.0–389.0)	0.559
Fibrinogen (g/L)	2.4 (2.0–2.7)	2.4 (1.9–2.7)	0.555
INR	1.06 (0.98–1.10)	1.04 (0.94–1.11)	0.477
PT (s)	19.0 (17.0–20.7)	18.5 (17.3–20.6)	0.723
PR (%)	97.1 (86.2–109.0)	94.4 (86.7–111.0)	0.978
APRI	1.49 (0.88–2.22)	1.40 (0.74–2.20)	0.935
Liver, anterior axillary line (cm)	4.0 (3.0–4.5)	4.0 (3.0–5.5)	0.23
Liver, midclavicular line (cm)	3.0 (2.8–4.0)	4 (3.0–4.0)	0.29
Spleen, width (cm)	2.0 (0.5–3.0)	1.0 (0.0–3.0)	0.15

Values are presented as number only or median (interquartile range).
ChE: cholinesterase, GGT: gamma glutamyl transferase, TC: total cholesterol, ALP: alkaline phosphatase, TB: total bilirubin, DB: direct bilirubin, ALT: alanine transaminase, AST: aspartate transaminase, INR: prothrombin international normalized ratio, PT: prothrombin time, PR: prothrombin ratio, APRI: aspartate aminotransferase-to-platelet ratio index.
*p-values<0.05 (significant associations); †For the candidate prognostic indicators to be tested in regression models.

Table 2. Preoperative ultrasound morphometry indicators for the patients grouped according to Kasai procedure outcomes

Parameter	Efficacious Kasai surgery	Non-efficacious Kasai surgery	*p*-value
No. of patients	69	97	
CBD length (mm)	13.0 (9.0–19.5)	9.0 (7.5–16)	0.12
CBD width (mm)	4.0 (3.0–5.0)	3.0 (2.1–4.4)	0.085
Fibrous portal plate, thickness (mm)	3.0 (0.0–4.4)	3.0 (0.0–3.7)	0.99
Liver, right lobe AP measurement (mm)	68 (62–76)	71 (67–75)	0.58
Liver, left lobe AP measurement (mm)	44 (40–52)	43.5 (40.0–48.0)	0.66
Spleen, length (mm)	62 (55–69)	58 (53–68)	0.31
Spleen, width (mm)	29 (24–32)	26 (23–30)	0.071
Hepatic artery, resistance index	0.71 (0.68–0.76)	0.74 (0.69–0.77)	0.40
Hepatic artery, blood flow (mL/min)	57.5 (39.5–66.0)	68.0 (49.0–73.0)	0.34
Hepatic artery, diameter (mm)	2.10 (1.55–2.45)	1.95 (1.55–2.45)	0.64
Hepatic portal vein, diameter (mm)	4.0 (3.7–4.5)	4.0 (3.8–4.8)	0.97
Hepatic portal vein, blood flow (mL/min)	20 (20–25)	21.5 (19.5–24.0)	0.69

Values are presented as number only or median (interquartile range).
CBD: common bile duct, AP: anteroposterior.

Table 3. Assessment of possible association between Kasai procedure outcome and the score of liver fibrosis at surgery

Fibrosis, Desmet score	Efficacy rate		*p*-value
	Efficacious/total	%	
1	5/9	55.5	0.88
2	33/61	54.1	
3	9/17	52.9	
4	8/18	44.4	

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Despite the lack of significance of the degree of liver fibrosis assessed intraoperatively, this indicator was included in both the univariate and multivariate models (**Table 5**). The multivariate model included scores with $p<0.05$ in the univariate model, and the degree of fibrosis (**Table 6**). The final model of multivariate regression analysis included 105 patients.

Table 4. Postoperative (day 14±3) characterization of patients with efficacious and non-efficacious Kasai surgery

Parameter	Efficacious Kasai surgery	Non-efficacious Kasai surgery	*p*-value
No. of patients	69	97	
Platelets (10^9/L)	361.0 (283.5–543.0)	382.5 (315.0–500.0)	0.63
Albumin (g/L)	36.40 (34.30–39.95)	38.0 (34.5–40.5)	0.372
ChE (U/L)	4,874 (4,128–5,931)	4,660 (3,817–6,020)	0.681
GGT (U/L)	796.3 (550.5–1,125.0)	893.9 (570.5–1,183.1)	0.599
TC (mmol/L)	4.70 (4.23–5.57)	5.50 (4.54–7.60)	0.004*,†
ALP (U/L)	261 (205–371)	327 (273–395)	0.019*,†
TB (μmol/L)	60.9 (36.7–88.0)	117.2 (84.0–154.3)	<0.001*,†
DB (μmol/L)	36.8 (20.9–56.3)	74.5 (49.9–95.6)	<0.001*,†
ALT (U/L)	196.5 (145.0–269.0)	222.2 (143.2–365.5)	0.07
AST (U/L)	177.9 (123.5–230.5)	211.8 (160.0–299.8)	0.038*,†
Fibrinogen (g/L)	2.41 (1.90–2.80)	2.38 (1.95–2.80)	0.685
INR	1.04 (0.97–1.12)	0.99 (0.92–1.13)	0.521
PT (s)	17.9 (16.4–19.1)	17.3 (16.3–19.3)	0.421
PR (%)	96.3 (88.5–107.0)	96.5 (80.8–109.0)	0.638
APRI	1.25 (0.79–1.66)	1.29 (0.86–2.62)	0.316
Liver, anterior axillary line (cm)	4.0 (3.0–4.0)	4.0 (4.0–5.0)	0.294
Liver, midclavicular line (cm)	4.0 (3.0–4.0)	4.0 (3.0–4.5)	0.551
Spleen, width (cm)	2.0 (0.5–3.0)	2.00 (0.75–4.25)	0.250

Values are presented as number only or median (interquartile range).
ChE: cholinesterase, GGT: gamma glutamyl transferase, TC: total cholesterol, ALP: alkaline phosphatase, TB: total bilirubin, DB: direct bilirubin, ALT: alanine transaminase, AST: aspartate transaminase, INR: prothrombin international normalized ratio, PT: prothrombin time, PR: prothrombin ratio, APRI: aspartate aminotransferase-to-platelet ratio index.
*p-values<0.05 (significant associations); †For the candidate prognostic indicators to be tested in regression models.

Table 5. Univariate analysis of laboratory variables to predict the probability of Kasai surgery efficacy

Variable	Unadjusted		
	COR	95% CI	*p*-value
TC, mmol/L (b/s)	1.00	1.00–1.00	0.056
TC, mmol/L (a/s)	0.66	0.51–0.86	0.002
ALP, U/L (a/s)	0.99	0.99–1.00	0.115
TB, μmol/L (a/s)	0.98	0.97–0.99	0.001
DB, μmol/L (a/s)	0.98	0.97–0.99	0.003
AST, U/L (a/s)	0.99	0.99–1.00	0.042
Fibrosis, Desmet score	0.91	0.56–1.47	0.698

COR: crude odds ratio, 95% CI: 95% confidence intervals, TC: total cholesterol, ALP: alkaline phosphatase, TB: total bilirubin, DB: direct bilirubin, AST: aspartate transaminase, b/s: before surgery, a/s: after surgery.

Table 6. Multivariate analysis of laboratory variables to predict the probability of Kasai surgery efficacy

Variable	Coefficient	SE	Wald	df	*p*-value	OR	95% CI	
							Lower	Upper
TC, mmol/L (a/s)	−0.625	0.023	8.215	1	0.004	0.519	0.331	0.812
DB, μmol/L (a/s)	−0.035	0.013	7.874	1	0.005	0.965	0.942	0.989
Fibrosis, Desmet score	−0.791	0.377	4.390	1	0.036	0.453	0.216	0.950
Constant	7.309	2.029	12.980	1	0.000	-	-	-

SE: standard error, df: degrees of freedom, OR: odds ratio, 95% CI: 95% confidence intervals, TC: total cholesterol, DB: direct bilirubin, a/s: after surgery.

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The association is described by the following equation:

$$P=1/(1+e^{-z})\times 100\%;$$

$$z=6.89-0.59\times X_{TC\_postop.}-0.37\times X_{DB\_postop.}-0.76\times X_{Desmet} \quad (1)$$

Where P is the probability of a favorable outcome (%), and $X_{TC\_postop.}$ stands for blood cholesterol level, mmol/L, on day 14±3 a/s; $X_{DB\_postop.}$ stands for DB level, μmol/L, on day 14±3 a/s; and X_{Desmet} stands for the Desmet score of fibrosis at surgery (1, 2, 3, or 4).

The obtained regression model was statistically significant (p<0.001). According to the coefficient of determination R-square (Nagelkerke), Model (1) explains 47.3% of the factors that determine the variance of the favorable outcome probability. The negative regression coefficients indicate that the probability of a favorable outcome for the Kasai procedure is inversely related to both cholesterol and DB blood levels 2 weeks a/s, as well as the Desmet score of liver fibrosis at the time of surgery.

The threshold value of the logistic function P was determined by ROC curve analysis; the plot is shown in **Fig. 1**. With an AUC of 0.86±0.04 (95% CI: 0.78–0.95), the cut-off falls at 54.32%. Accordingly, when P>54.32%, the probability of a positive outcome in Kasai surgery was high, whereas when P<54.32%, the probability of a positive outcome was low. The sensitivity and specificity of the model at the specified threshold point were 78.8% and 78.4%, respectively.

An increase in the severity of fibrosis by 1 point at the time of surgery reduces the chances of the effectiveness of the operation by 2.2 times (95% CI: 0.27–0.95). An increase in cholesterol by 1 mmol/L after the operation reduces the chances of the effectiveness of the operation by 1.92 times (95% CI: 0.33–0.81). An increase in DB by 1 μmol/L after Kasai surgery reduces the chances of the effectiveness of the operation by 1.04 times (95% CI: 0.94–0.98) (**Fig. 2**).

Considering the significant contributions of postoperative DB and cholesterol levels to the logistic regression model, ROC curve analysis was also applied to these indicators as such. The plot for DB measured on day 14±3 a/s (DB_postop.) is shown in **Fig. 3**. With an AUC of 0.79±0.04 (95% CI: 0.70–0.88), the cut-off falls at 56.3 μmol/L. Accordingly, when DB_postop.

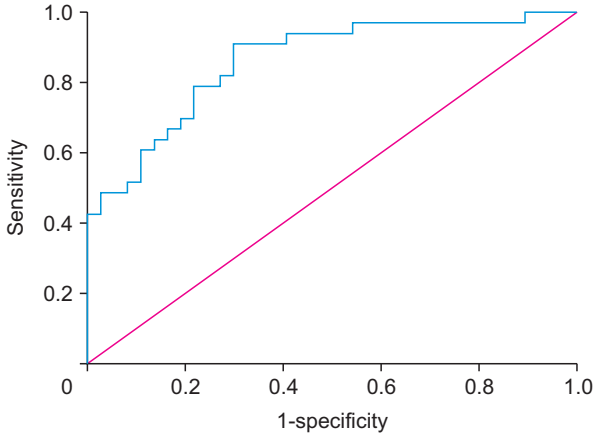

Fig. 1. Receiver operating characteristic curve for the relationship between Kasai procedure efficacy and the logistic function P (1).

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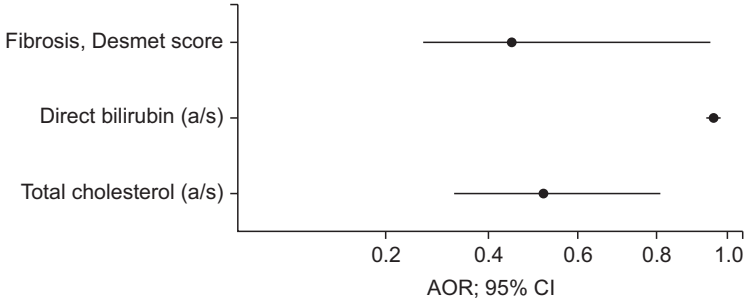

Fig. 2. Comparison of adjusted odds ratios with 95% CI for factors included in the model (1).
a/s: after surgery, AOR: adjusted odds ratio, 95% CI: 95% confidence intervals.

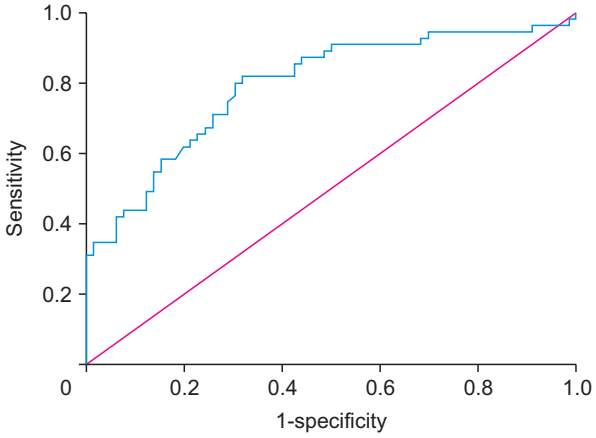

Fig. 3. Receiver operating characteristic curve for the relationship between Kasai procedure efficacy and direct bilirubin levels measured on day 14±3 after surgery.

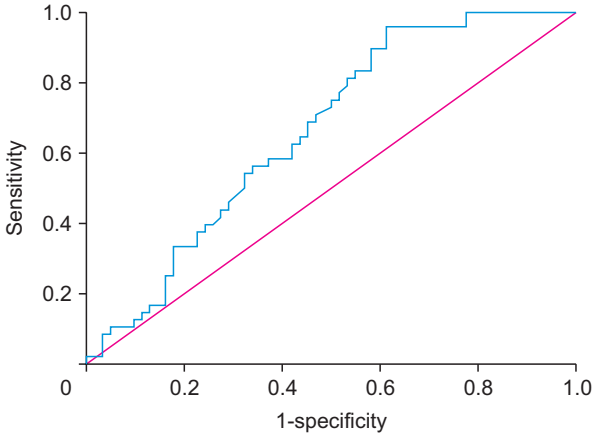

Fig. 4. Receiver operating characteristic curve for the relationship between Kasai procedure efficacy and cholesterol levels measured on day 14±3 after surgery.

is <56.3 μmol/L, the chances of a positive outcome for Kasai surgery are high, whereas when DB_postop. is >56.3 μmol/L the chances are low. The model is statistically significant (p<0.001) and exhibit 74.5% sensitivity and 71.2% specificity at the threshold point.

ROC curve for total blood cholesterol measured on day 14±3 a/s (TC_postop.) is shown in **Fig. 4**. With an AUC of 0.66±0.05 (95% CI: 0.56–0.76), the cut-off falls on 5.41 mmol/L,

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indicating that when TC_postop. is <5.41 mmol/L, the chances of a positive outcome after Kasai surgery are high, whereas when DB_postop. is >5.41 mmol/L the probability of a positive outcome is low. The model is statistically significant (p=0.004) with 70.8% sensitivity and 53.2% specificity at the threshold point.

Considering the retrospective design of the study, we examined the native liver survival rates in groups of patients who underwent efficacious and non-efficacious Kasai procedures.

The average lifespan with a native liver in the group of patients with non-efficacious Kasai procedure was 9.7±0.7 months. Seven patients with non-efficacious Kasai surgery (7.2% of this group, n=97) died before receiving transplantation, at the age of 10.4±4.4 months due to liver failure; the remaining 90 patients (92.8%) received liver transplants. In the group with efficacious Kasai surgery, the average lifespan of the native liver was 151.1±14.5 months. Despite the consistent presentation of efficacy, 11 patients (16.2% of this group, n=69) eventually developed liver failure and underwent liver transplants at 28.3 months (14.6, 58.3).

DISCUSSION

Determining early indicators for predicting the effectiveness of the Kasai operation is essential for developing comprehensive care strategies for BA. Accurate early predictions can significantly enhance patient management by informing timely decisions on critical aspects, such as the need for liver transplantation, choosing suitable donors, and refining treatment and support plans for patients and their families. Previous studies have varied in the timing of prognostic assessments, ranging from as early as 7 days to as late as 6 months postoperation [7,9,12,17,20,21]. Our study focused on a narrower early window, particularly 14 days post-HPE. The 14-day period is a critical window during which initial recovery is assessable and potential complications or successes begin to manifest clinically. Statistical analyses revealed that the data collected around this time were promising. Specifically, certain trends and indicators at the 14-day mark correlated with clinically significant outcomes, such as the stabilization of liver function tests and a reduction in bilirubin levels, which are crucial for evaluating the success of Kasai portoenterostomy.

Our previous study, which was conducted on a smaller cohort of the same patients, revealed no statistically significant differences in surgical outcomes based on the access type. Coupled with subsequent findings indicating a minimal impact of surgical access, technique, and individual surgeon experience on operative results, we inferred that these factors did not substantially influence the stability of patient outcomes in our current study [22]. Building on this understanding, we analyzed the anamnestic, clinical, laboratory, and instrumental patient data collected before the Kasai procedure and in the early postoperative period, that is, before the unequivocal clinical manifestation of its success or failure. Our goal was to identify reliable predictors among the available variables and construct more complex predictive models based on them.

In our setting, the Kasai procedure was efficacious in 42% of the cases, which is consistent with the published evidence [23-26]. The efficacious/non-efficacious distinction was of primary clinical relevance, as indicated by the high mean differences for both the lifespan with a native liver and the risk of demand for liver transplant ($p<10^{-3}$). Notably, in two patients with BASM syndrome, the intervention was successful despite the reported adverse impact of

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BASM syndrome [11]. Therefore, we did not exclude these cases from the study. The impact of patient age remains debatable, and several studies have refuted the direct correlation between age at Kasai surgery and its success [7,20]. We observed no significant influence of age at surgery on the outcome in either descriptive statistics or binary regression analyses.

Comparative statistical analysis of preoperative blood test indicators revealed significant differences in cholesterol levels (lower in the group with favorable surgical outcomes) and similar trends in ALP activity and DB levels, albeit below the established level of significance. In our cohort of children with BA, TC was assessed as a biomarker of cholestasis severity. Our literature review revealed no data on the effect of cholesterol levels on Kasai portoenterostomy outcomes. Given these promising trends, we recommend further research to elucidate this relationship and its clinical implications.

Earlier reports emphasized significantly lower preoperative blood levels of ALP activity in patients with efficacious Kasai procedure than those without (400.9±253.3 U/L vs. 586.7±274.9 U/L, p=0.004 and 410.7±177.76 U/L vs. 701.7±322.5 U/L, p<0.0001) [13,27]. In our setting, these indicators had negligible predictive utility in the binary logistic regression models, although their contributions are theoretically feasible and can be refined for larger cohorts.

The degree of fibrosis was not influenced by the Kasai procedure outcomes; this result is consistent with published evidence [19,28], including our own [22].

The same biochemical indicators analyzed as early as 2 weeks into the postoperative period (day 14±3 a/s) revealed more tangible associations with the longer-term outcomes. In particular, the blood levels of TC, ALP, TB, DB, and AST were significantly lower in patients who underwent efficacious Kasai surgery. Matching of binary classifications by ROC curve analysis revealed significant associations between blood levels of cholesterol and DB, measured on day 14±3 a/s, and the outcomes. The final binary logistic regression model included these variables in combination with the Desmet score for liver fibrosis at surgery as the most significant predictor among the variables studied.

To our knowledge, none of the studies published so far have implicated blood cholesterol levels as a predictor of Kasai procedure outcomes. The postoperative decrease in DB levels, by contrast, represents an established predictor [21,28]. However, our model allows to assess the efficacy as early as on day 14 a/s, compared with the previously established threshold of <34 μmol/L DB reached within 3–6 months after the procedure [7-10]. The inclusion of the Desmet fibrosis score refined the model, despite the lack of a corresponding correlation demonstrated by descriptive statistical comparison. Overall, the developed model, which involves blood levels of DB and cholesterol measured 2 weeks after the intervention, in combination with the Desmet score of liver fibrosis assessed at the time of intervention, represents a promising tool for BA management.

Conclusions

This study aimed to retrospectively assess the predictive utility of a range of clinical and biochemical indicators measured pre-, intra-, and/or postoperatively with regard to Kasai surgery outcomes. In patients who underwent efficacious Kasai surgery, preoperative blood cholesterol levels were significantly lower than those who underwent non-efficacious Kasai surgery. Similar trends were observed in blood ALP activity, and DB levels were below the level of significance. All the tested preoperative indicators revealed negligible predictive utility.

In the early postoperative period (day 14±3 after Kasai surgery), blood levels of cholesterol, bilirubin, ALP, and AST differed significantly between the groups. The strongest candidates, postoperative blood cholesterol, and DB levels, were included in the binary logistic regression model, and their considerable individual predictive utility was demonstrated through ROC curve analysis.

Most notably, we found that infants with BA have a high probability of efficacious Kasai surgery if their blood cholesterol levels are below 5.41 mmol/L and DB levels are below 56.3 μmol/L, as measured on postoperative day 14±3, along with a low Desmet score of fibrosis at the time of the intervention.

In addition, several limitations of our study should be noted: 1) it was retrospective; therefore, our preliminary results should be validated in future prospective longitudinal studies; 2) the proposed model has not been validated (because of the small sample size, splitting is impractical); and 3) this study did not evaluate changes in liver fibrosis from the time of the Kasai procedure to liver transplantation in patients with unsuccessful portoenterostomy, representing a gap that future research should address.

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