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[Original Articles]

Prediction of Survival in Extrahepatic Biliary Atresia by Hepatic Duplex Sonography

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ABSTRACT

Background: The clinical course of biliary atresia patients is extremely variable. To optimize conservative treatment and correctly schedule liver transplantation, noninvasive investigations that are predictive of individual survival and that can be performed regularly are needed. In this study, the prognostic value of Doppler sonography was investigated in these patients.

Methods: Thirty biliary atresia patients (age range, 1 month to 15.2 years; mean, 4.0 years) and 38 control subjects underwent standardized Doppler sonography of liver and spleen. Biochemical tests of liver function and of fibrogenesis were performed in parallel. Individual clinical outcome was registered 1 and 2 years later.

Results: In control subjects, maximum portal flow velocity (V_{max}) was more than 16 cm/sec, and the hepatic vein flow pattern was triphasic. Among children with biliary atresia, those with diminished portal V_{max}, a flattened hepatic vein flow curve, or a hepatic artery resistance index of 0.8 or more had significantly lower indices of hepatic protein synthesis (albumin, cholinesterase), higher bilirubin levels, and higher concentrations of markers of connective tissue turnover (procollagen peptides, laminin P1) than did those with normal Doppler sonography measurements. The rate of survival without transplantation during the following 2 years was significantly lower in children with abnormal Doppler findings. From portal and hepatic vein flow measurements, patient survival 2 years later could be predicted with an accuracy of 93%.

Conclusions: In children with extrahepatic biliary atresia, Doppler sonography of the hepatic blood flow is a noninvasive indicator of disease severity. Moreover, it allows a highly accurate prediction of patient survival for the following 2 years.

In chronic and progressive liver disorders, noninvasive or only minimally invasive methods to assess disease severity and predict individual prognosis are demanded for regular counseling of patients, control of therapeutic efforts, and timing of liver transplantation. This is especially true in children, in whom liver biopsies (as an invasive approach to demonstrate hepatic injury directly) are more difficult and distressing than in adults. To this end, various combinations of clinical and biochemical parameters have been used in prognostic models (1).

Because Doppler sonography has become widely available, correlations were sought between sonographic measurements of blood flow in hepatic vessels and disease severity (2-11). Decreased portal flow velocity (4) and flattening of the hepatic venous flow curve (8) have been shown to be predictive of reduced survival in adults with cirrhosis, whereas publications on Doppler sonography investigations in pediatric liver diseases are scarce. Reports on children with biliary atresia have shown shorter survival in patients with low portal flow velocity (in small series of 8 and 10 patients, respectively) (12,13) or with hepatic artery resistance index (RI) more than 1.0 (14). The significance of the hepatic vein flow pattern in chronic liver diseases of childhood has not yet been investigated.

We report on a series of Doppler investigations of hepatic blood vessels in 30 children with the most frequent progressive liver disorder of early childhood, extrahepatic biliary atresia (EHBA), in whom associations were sought between flow measurements of portal and hepatic veins as well as the hepatic artery, disease severity, and survival during the 2 years after the sonographic examination.

PATIENTS AND METHODS

Thirty patients with EHBA in the age of 1 month to 15.2 years (mean, 4.0 years), all of whom had had Kasai hepatoportoenterostomy, were enrolled in the study. At our institution, patients with biliary atresia undergo outpatient clinical review every 3 months or more frequently. Study patients were recruited prospectively over a 5-month period when attending for this routine follow-up. There were no selective inclusion criteria other than diagnosis. Patients with hemodynamically relevant cardiac defects or arrhythmias were excluded, as were those with acute illnesses or acute complications.

Children were subjected to a detailed ultrasound investigation during morning hours, after a light meal. An ultrasound scanner (128 XP; Acuson, Mountain View, CA, U.S.A.) with color and duplex sonography equipment was used with 3.5 and 5 MHz probes. The following data were recorded with the patient supine: echogenicity; echostructure; shape and size of liver and spleen; gallbladder and biliary tract abnormalities; and presence of ascites, presence of patent portofugal collaterals. To identify these, the hilum and lower margins of the liver and spleen and the lesser omentum were carefully screened with color-coded Doppler sonography, with input settings highly sensitive to detect low-velocity blood flow. The diameter of the portal vein was measured in an oblique view along the axis of the vessel in the porta hepatis.

Organometric data were transformed into height-adjusted standard deviation scores (SDS) using published reference data (15,16). Direction, maximum velocity (V_{max}), and time-average velocity (TAV) of portal blood flow were measured at the porta hepatis, as was systolic and diastolic flow velocity in the hepatic artery from which the resistance index (RI; Pourcelot) was calculated. The flow curve in the middle hepatic vein was registered, with the sample volume located about 2 cm from the junction with the inferior vena cava. The flow pattern was classified similarly to the method of Ohta et al. (7,8) (Fig. 1): type I, triphasic flow including a phase of reversed flow direction; type II, triphasic curve similar to type I, but without reversed flow phase; type III, biphasic curve with decreased undulation amplitude; type IV, flat waveform, no undulation. For all Doppler recordings, the Doppler angle was kept below 30°, and an exact angle adjustment was performed before each measurement.

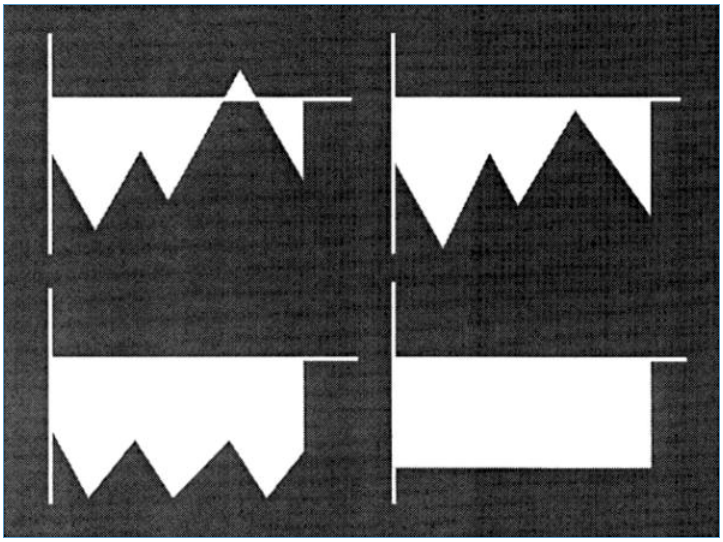

FIG. 1. Schematic patterns of hepatic vein flow undulation, *y*-Axis: flow velocity; *x*-axis: time. *Upper left:* Type I, triphasic with reversed phase; *upper right:* Type II, triphasic without reversed phase. *Lower left:* Type III, biphasic; *lower right:* Type IV, flat.

On the same day, or with an interval of less than 8 weeks, serum analysis was performed during routine follow-up of patients. Serum bilirubin, [gamma]-glutamyl transferase, albumin, and cholinesterase (CHE), measured by standard procedures, served as classic indicators of disease severity. When serum was available for further analysis, the following serum markers of connective tissue turnover (MCTT) were also measured in radioimmunoassays: aminoterminal procollagen III peptide (PIIIP), using test tubes coated with monoclonal mouse anti-PIIP antibodies MAK 238/3/1 (Hoechst AG, Frankfurt, Germany) and monoclonal mouse ^{125}J-anti-PIIIP antibodies; carboxyterminal procollagen IV-peptide (NC 1), using lyophilized ^{125}J-NC 1 collagen, lyophilized rabbit anti-NC 1 collagen antiserum (Hoechst), and anti-rabbit [gamma]globulin serum as the precipitation agent; and laminin P1 (LamP1), using a commercially available radioimmunoassay kit (RIA-gnost Laminin P1, Behringwerke AG, Marburg, Germany).

One and 2 years after the individual ultrasound investigations, the patients' outcomes were recorded (survivor, alive without liver transplantation; nonsurvivor, liver transplantation, or death before transplantation could be performed). Patients were placed on a waiting list for transplantation in case of persistent severe hyperbilirubinemia (<200 µmol/l) in combination with severely reduced liver function (clotting factor V <50%, CHE <2.0 kU/l, albumin <32 g/l) and/or severe growth failure, ascites, or portal hypertension refractory to conventional therapy and nutritional support. Portal vein and hepatic vein flow dynamic data were not considered when the decision for listing an individual patient for transplantation was made.

Thirty-eight children (age range, 9 months to 17 years; mean, 7.5 years) without evidence of hepatologic, gastrointestinal, reticuloendothelial, or cardiopulmonary disorder served as a control group and underwent the same standardized ultrasound procedure. In control subjects, no blood sampling was performed, and the time-consuming search for an exact measurement of arterial flow was omitted. An upper limit of normal RI in children (0.8) was taken from the literature (17).

Commercial statistical software (SPSS for Windows, ver. 6.12, SPSS, Chicago, IL, U.S.A.) was used for data analysis. The Kolmogorov-Smirnov test was used to test for normal distribution of data. Differences in parameters between groups were tested for significance using the Mann-Whitney test, chi-square test, and Kruskal-Wallis test, when appropriate. Univariate analysis of prediction of survival was performed by chi-square test. The Spearman rank

coefficient was calculated to test for correlation between parameters without a Gaussian distribution. Differences with a probability of error $p <= 0.05$ were considered statistically significant.

ETHICAL CONSIDERATIONS

None of the children with biliary atresia underwent any procedure for the purpose of this study, because serum analysis and sonography were performed as routine follow-up examinations. No patient had venipuncture performed solely for study purposes. In control subjects, no blood sampling was performed, and sonography took place only with informed oral consent of parents and, in cases of an older child, consent was obtained from the child. When children felt uneasy because of the long duration of the Doppler investigation, the examination was terminated. Thus, the study did not put any of the children at health risk or subject them to pain or to an invasive procedure.

RESULTS

Completeness of Data

The portal vein was adequately visualized and the flow measured in all patients and control subjects. The hepatic veins were seen and the flow pattern established in all control subjects and in all but one patients in whom the veins were too narrow for a flow signal to be identified. Because of uncooperative patients, respiration artifacts, or small vessel size, the hepatic artery RI could be established in only 22 patients. Serum concentrations of MCTTs were measured in 22 (PIIIP, NC1) and 16 (LamP1) patients.

Control Subjects

In control subjects, portal vein diameter was found to be strongly correlated ($r = 0.84$; $p < 0.001$) to body length (Fig. 2). Portal vein blood flow velocities (V_{max} and TAV) were independent of body length or age ($r < 0.3$) and normally distributed within the control group (V_{max}, 27 ± 5 cm/sec; TAV, 13 ± 3 cm/sec). Thus, the lower limit of normal (mean - 2 standard deviations [SD]) was calculated to be 17 cm/sec for V_{max} and 7 cm/sec for TAV, regardless of age. Hepatic vein flow pattern was triphasic in all control subjects (type I, $n = 36$; type II, $n = 2$). Thus, both triphasic types were considered normal. Types III and IV were not seen in any of the control subjects.

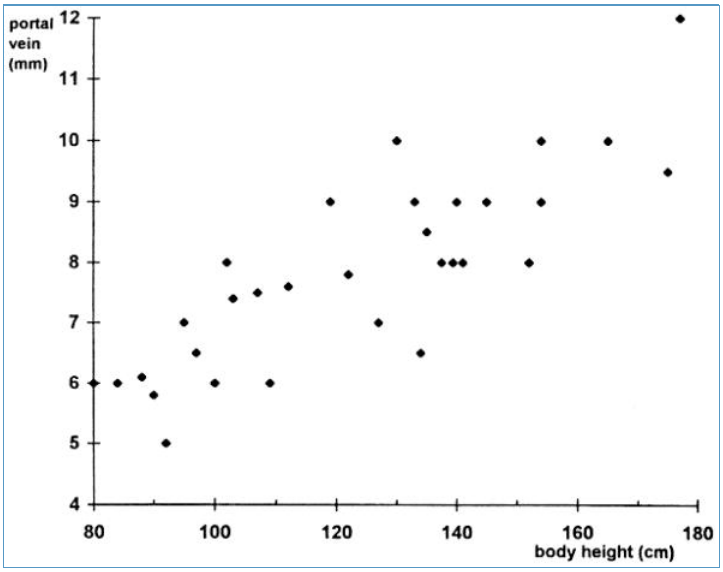

FIG. 2. Portal vein diameter (in millimeters) at porta hepatis by body height (in centimeters) in 30 healthy control children.

Children With Extrahepatic Biliary Atresia

Portal Vein

Mean height-adjusted SDS of the diameter of the portal vein was -0.2 in patients and 0.2 in control subjects (not significant). Patients with portal vein dilatation (SDS > 2) did not significantly differ from others in any biochemical or other sonographic parameter. In patients with V_{max} of 16 cm/sec or less ($n = 9$; 30%), levels of albumin and CHE were significantly lower, and bilirubin and MCTT concentrations were significantly higher than in children with normal portal flow. Moreover, the hepatic artery RI was significantly higher in this group (Table 1)

Parameter	V_{max} > 16 cm/sec (n = 21)	V_{max} ≤ 16 cm/sec (n = 9)	p
Albumin (g/l)	45.4 (36.5–51.1)	33.3 (29.7–38.0)	<0.001
CHE (kU/l)	5.8 (2.2–9.2)	2.0 (1.3–4.7)	<0.001
γ-GT (U/l)	51 (10–534)	118 (32–333)	NS
Bilirubin (μmol/l)	10 (3–99)	204 (60–475)	<0.001
Laminin (U/ml)	1.84 (1.42–2.50)	4.18 (2.17–6.66)	<0.01
PIIIP (U/ml)	0.77 (0.36–2.42)	4.80 (0.84–7.24)	<0.01
NC-1 (ng/ml)	15.0 (8.5–41.0)	38.9 (16.7–182.0)	<0.01
Hepatic artery RI	0.76 (0.53–0.86)	0.88 (0.78–1.16)	<0.01

V_{max}, portal flow velocity; CHE, cholinesterase; γ-GT, γ-glutamyl transferase; PIIIP, procollagen III peptide; NC-1 carboxyterminal procollagen IV peptide; RI, resistance index; NS, not significant.
p according to Mann–Whitney test.

TABLE 1. *Median values and ranges of biochemical and sonographic parameters in patients with normal* (>16 cm/sec) *and diminished* (<=16 cm/sec) *maximum portal flow velocity*

Hepatic Artery

The resistance index RI of the hepatic artery did not correlate with age or body length. In patients with RI of 0.80 or more (n = 11; 50%), albumin, CHE, and bilirubin, but not MCTT serum levels, were significantly more abnormal than among those with RI less than 0.80 (Table 2).

Parameter	Artery RI < 0.80 (n = 11)	Artery RI ≥ 0.80 (n = 11)	p
Albumin (g/l)	45.4 (38.0–51.1)	34.2 (29.7–46.9)	<0.01
CHE (kU/l)	5.6 (4.2–8.9)	2.3 (1.3–9.2)	<0.01
γ-GT (U/l)	76 (10–534)	118 (32–333)	NS
Bilirubin (μmol/l)	8 (3–99)	200 (6–475)	<0.01
Laminin (U/ml)	1.82 (1.47–2.16)	3.68 (1.84–6.66)	0.05
PIIIP (U/ml)	0.79 (0.46–7.24)	0.96 (0.43–6.18)	NS
NC-1 (ng/ml)	15.6 (10.6–51.5)	23.8 (12.3–182.0)	NS

RI, resistance index; CHE, cholinesterase; γ-GT, γ-glutamyl transferase; PIIIP, procollagen III peptide; NC-1 carboxyterminal procollagen IV peptide; NS, not significant.
p according to Mann–Whitney test.

TABLE 2. Median values and ranges of biochemical parameters by categories of hepatic artery resistance index

Hepatic Veins

Of 29 patients with technically satisfactory venous flow recordings, 10 had a triphasic pattern (type I, n = 8; type II, n = 2), 14 a biphasic pattern (type III), and 5 a flat pattern (type IV). Types III and IV were associated with lower albumin and CHE, and with higher bilirubin and spleen size (Table 3). Hepatic vein TAV differed significantly between normal (type I and II) and pathologic (type III and IV) flow patterns (median, -8 vs. -18 cm/sec, respectively; p = 0.01).

	Type I or II (n = 10)	Type III (n = 14)	Type IV (n = 5)	p
Albumin (g/l)	46.4 (38.0–51.1)	41.6 (29.8–47.5)	32.0 (29.7–38.3)	<0.01
CHE (kU/l)	5.8 (4.1–7.9)	4.7 (1.6–9.2)	2.0 (1.3–2.3)	<0.01
γ-GT (U/l)	50 (13–319)	76 (10–534)	162 (45–333)	NS
Bilirubin (μmol/l)	8 (3–60)	18 (3–380)	200 (10–475)	<0.05
Laminin (U/ml)	1.52 (1.42–2.42)	2.04 (1.77–4.67)	4.42 (2.17–6.66)	NS
PIIIP (U/ml)	0.76 (0.36–7.24)	0.97 (0.43–6.18)	2.82 (0.84–4.80)	NS
NC-1 (ng/ml)	13.1 (9.3–51.5)	17.1 (11.2–182)	27.8 (16.7–38.9)	NS
Spleen SDS	6.9 (3.8–10.4)	8.3 (5.0–10.3)	11.4 (6.3–13.3)	<0.05

CHE, cholinesterase; γ-GT, γ-glutamyl transferase; PIIIP, procollagen III peptide; NC-1 carboxyterminal procollagen IV peptide; SDS, standard deviation score; NS, not significant.
p according to Kruskal–Wallis test.

TABLE 3. Median values and range of biochemical and sonographic parameters in patients with different hepatic vein flow patterns

Portosystemic Collaterals and Ascites

Pathologic shunts with portofugal flow were visualized in nine patients, in whom portal V_{max} was lower than normal (median, 13 vs. 20 cm/sec, respectively; p = 0.05). Arterial RI was higher (0.86 vs. 0.75; p < 0.05) than in patients in whom no shunt vessels were detected, despite a deliberate search. Ascites was present in three patients. These had significantly lower portal V_{max} than the others (median, -12 cm/sec vs. 21 cm/sec; p < 0.01).

Survival

One and 2 years after the ultrasound examination, the course of the disease was unfavorable in 7 and 10 of the 30 EHBA patients, respectively: One died before liver transplantation could be performed, and the others underwent liver transplantation. The prevalence of such unfavorable outcome (referred to as nonsurvivors) was significantly higher among those who had reduced portal V_{max} increased hepatic artery RI, or abnormal venous flow pattern (Table 4). As a rule, patients who did not survive for the following 2 years had either a flat hepatic vein flow pattern or a reduced portal V_{max}. Survivors had normal portal V_{max} and triphasic or biphasic venous pattern. Only 2 of the 30 patients did not fulfill this rule (Fig. 3). Thus, the specificity and sensitivity of the combination low portal V_{max} or flat flow pattern in identifying 2-year nonsurvivors was 95% and 90%, respectively; the overall accuracy was 93%. Including the arterial RI as another prognostic parameter in this algorithm did not improve the accuracy of the prediction.

			% Nonsurvivors			
		n	after one year	after two years	Chi-square	*p*
Portal V_{max}	>16 cm/sec	21	0	5		
	≤16 cm/sec	9	78	100	25.7	<0.001
Venous flow pattern	Type I or II	10	0	10		
	Type III	14	21	36		
	Type IV	5	80	80	12.0	<0.01
Arterial RI	<80%	11	0	2		
	≥80%	11	55	64	8.3	<0.01
Portal diameter	SDS ≤ 2	23	17	26		
	SDS > 2	3	0	0	0.6	NS

V_{max}, portal flow velocity; RI, resistance index; SDS, standard deviation score; NS, not significant.
Univariate analysis of prediction of 2-year outcome by chi-square test.

TABLE 4. *Proportion of nonsurvivors* (death or liver transplantation) *1 and 2 years after ultrasound investigation among patients with normal versus pathologic Doppler findings*

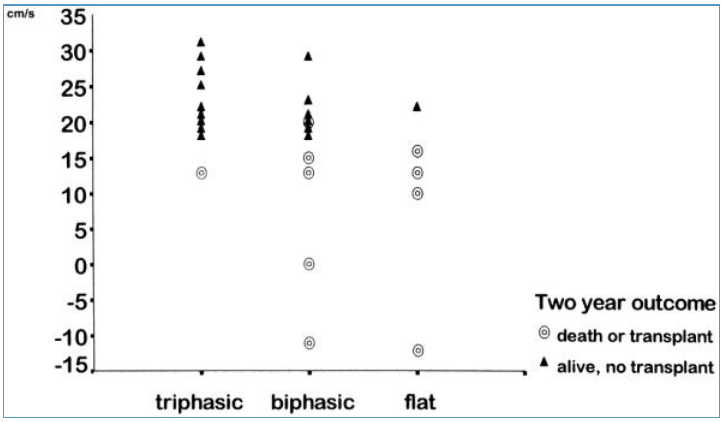

FIG. 3. Representation of portal maximum flow velocity (*y*-axis; in centimeters per second) and hepatic vein flow pattern (*x*-axis) in children with EHBA who survived for 2 years without liver transplantation (*triangles*) and those who did not (*circles*).

DISCUSSION

This prospective study was designed to investigate whether results of Doppler sonography in children with EHBA correlate with the present severity of their liver disease and to evaluate whether Doppler sonography can contribute to the prediction of prognosis of these patients. In adults, a flat hepatic vein flow curve has been found to be predictive of cirrhosis (2,5-8,10), with a correlation between flow pattern and Child-Pugh scores in most studies, but a preserved undulation of hepatic vein flow does not exclude cirrhosis (2,5,9). Portal flow velocity in patients with cirrhosis may be decreased or even reversed (3,9,11,18,19). In chronic liver disorders before cirrhosis becomes established, findings usually are intermediate between those in patients with cirrhosis and those in healthy control subjects (9,18).

The pathophysiologic mechanism leading to loss of hepatic vein flow undulation has not been clearly established. It has been related to increased stiffness of the distorted liver parenchyma (5). Others have argued that narrowing of the hepatic veins causing an increase of hepatic vein flow velocity is more important (8). This theory is supported by our observation that in hepatic veins with pathologic flow patterns TAV was significantly higher. To maintain an accelerated flow, the pressure gradient along a vessel must be increased. In relation to this increased forward gradient, the rhythmic changes of central venous pressure are probably too small to modify the venous flow curve significantly.

Available data on Doppler sonography in children with chronic liver disorders show lower portal flow velocities and higher hepatic artery RI compared with those in healthy control subjects (13,17,18,20,21). No studies have been published on hepatic vein flow patterns in children, although in our experience, this parameter can be recorded more easily and satisfactorily in a restless infant than can flow velocities of the hepatic artery. Moreover, an optimal Doppler angle is not needed to establish the flow pattern.

In our patients, hepatic Doppler sonography results frequently deviated from the findings encountered in the control group. Sixty-six percent of the patients with EHBA had abnormal hepatic vein flow patterns (type III or IV), with 50% having an increase of the arterial RI to 0.80 or more and 30% having a reduced portal V_{max} of 16 cm/sec or less. Hepatic protein synthesis was lower, hyperbilirubinemia was more pronounced, and levels of MCTT were higher in patients who had any of these abnormalities shown on Doppler sonography.

High bilirubin and impaired protein synthesis are well-established features of advanced chronic liver disease (1). Procollagen peptides and laminin P1 are molecules that appear in serum because of cleavage processes during collagen formation or because of liberation during degradation of collagen or basement membranes. They thus reflect the turnover of connective tissue constituents (22). Although several MCTTs have been shown to reflect the degree and progression of liver fibrosis in adults (22,23), their diagnostic value in individual children is limited, because levels are significantly influenced by skeletal growth especially during the first years of life (24). However, in a homogeneous group of children with defined chronic hepatopathy, such as the patients in this study, high MCTT levels can be expected to be related to more severe liver fibrosis. From the close correlations between Doppler results and bilirubin, albumin, and MCTT levels, we therefore conclude that Doppler parameters are significantly related to the severity of hepatic disease in EHBA.

Dilatation of the portal trunk to more than height-adjusted normal ranges, however, was not found to be related to disease severity. Portal vein dilatation probably is a multifactorial process in which hepatic vascular resistance plays a role, but the presence or absence of a splanchnic hyperdynamic state and the size and location of portosystemic collaterals may also be causative. Although usually recorded because it is obviously simple to measure, the portal vein diameter does not seem to be helpful in the staging of EHBA children.

Few investigators have directly examined the correlation of hepatic Doppler sonography with survival: Zoli et al. (4) observed shorter survival in adults with cirrhosis who had portal V_{max} below 10 cm/sec, Lopez Gutierrez et al. (12) reported that portal V_{max} below 14 cm/sec was related to poor prognosis in a group of 10 children with EHBA, and Broide et al. (14) found that a hepatic artery resistance index of 1.0 or more indicated a high risk of death or transplantation in 32 patients with EHBA, compared with the risk in matched control subjects (14). Ohta, et al. (7) presented a multivariate analysis demonstrating that the hepatic vein flow pattern was the only independent predictor of survival besides the established parameters, bilirubin and prothrombin index.

Our data demonstrate that not only portal but also hepatic vein flow measurements are significantly correlated with survival in children with EHBA. Combining both parameters, 2-year survival could be predicted with an accuracy of 93%, because only one child survived despite a flat venous flow pattern, and only one other did not, although the child had normal portal V_{max} and an only moderately abnormal (type III) venous flow pattern. None of the patients with portal V_{max} below 17 cm/sec survived for 2 years without liver transplantation. The prediction of survival was not improved further by using the hepatic artery RI as a third prognostic parameter. In contrast to the results of Broide et al. (14), we therefore suggest that the effort to measure the RI exactly is unnecessary when a patient with EHBA is evaluated by Doppler sonography.

A direct comparison of the prognostic value of Doppler parameters with that of classic indicators such as bilirubin, albumin, or clotting factors (1) is not possible from the present data set, because the decision to proceed to transplantation in clinical practice was based on the latter. Moreover, it should be kept in mind that, of course, the outcome "transplantation" is not identical with the strict outcome definition of "death," although the decision to proceed to transplantation reflects the responsible clinicians' anticipation that fatal deterioration is imminent. Transplantation usually prevents death, which would probably have been the natural outcome. In the era of liver transplantation, transplantation versus survival without transplantation thus replaced the classic dichotomy of death versus survival (25), although conclusions drawn on this basis are weakened by the influence of subjective criteria for listing for transplantation.

In summary, this study shows that loss of hepatic vein flow undulation, decrease of portal blood flow V_{max}, and increase of hepatic artery resistance index are all significantly related to the severity of hepatic derangement in children with extrahepatic biliary atresia. Based on maximum flow velocity in the portal vein and flow pattern in the middle hepatic vein, children surviving for more than the following 2 years without transplantation could be separated from those who died or required transplantation with an accuracy above 90%.

We suggest that portal and hepatic vein Doppler flowmetry should be an integral part of clinical follow-up studies and therapeutic trials in patients with EHBA, and possibly in children with other progressive liver disorders as well. If future studies confirm our main findings, the use of hepatic Doppler sonography as a surrogate indicator of probability of survival may be justified in therapeutic intervention trials.

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Clinical Quiz Section

Short cases with accompanying photographs of diagnostic biopsies, endoscopic findings, or physical characteristics are welcomed for the Clinical Quiz section. Please send a short history, glossy photograph, and answers to quiz questions to:

ESPGHAN Clinical Quiz Editor; Dr. Riccardo Troncone; Department of Pediatrics; University Federico II; Via S. Pansini, 5; 80131 - Naples; ITALY; Tel: 39-81-7463394; Fax: 39-81-5469811

NASPGN Clinical Quiz Editor; Dr. Joseph F. Fitzgerald; Department of Pediatrics; James Whitcomb Riley Hospital for Children; 702 Barnhill Drive; Indianapolis, IN 46202-5225; Tel: 317-274-3774; Fax: 317-274-8521

Key Words: Biliary atresia; Doppler; Hepatic veins; Portal vein; Prognosis; Ultrasonography

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BILDGALERIE

Alles markieren **Auswahl nach PowerPoint exportieren**

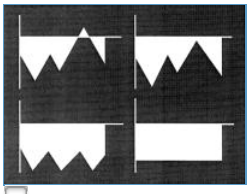

Fig. 1

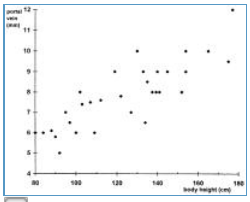

Fig. 2

Parameter	V_{max} > 16 cm/sec (n = 21)	V_{max} ≤ 16 cm/sec (n = 9)	p
Albumin (g/l)	45.4 (36.5–51.1)	33.3 (29.3–38.0)	<0.001
CHE (kU/l)	5.8 (2.2–9.2)	2.0 (1.3–4.7)	<0.001
γ-GT (U/l)	51 (10–534)	118 (32–333)	NS
Bilirubin (μmol/l)	10 (3–99)	204 (60–475)	<0.001
Laminin (U/ml)	1.84 (1.42–2.50)	4.18 (2.17–6.66)	<0.01
PIIIP (U/ml)	0.77 (0.36–2.42)	4.80 (0.84–7.24)	<0.01
NC-1 (ng/ml)	15.0 (8.5–41.0)	38.9 (16.7–182.0)	<0.01
Hepatic artery RI	0.76 (0.53–0.86)	0.88 (0.78–1.36)	<0.01

V_{max}, portal flow velocity; CHE, cholinesterase; γ-GT, γ-glutamyl transferase; PIIIP, procollagen III peptide; NC-1 carboxyterminal procollagen IV peptide; RI, resistance index; NS, not significant.
p according to Mann–Whitney test.

Table 1

Parameter	Artery RI < 0.80 (n = 11)	Artery RI ≥ 0.80 (n = 11)	p
Albumin (g/l)	45.4 (38.0–51.1)	34.2 (29.7–46.9)	<0.01
CHE (kU/l)	5.6 (4.2–8.9)	2.3 (1.3–9.2)	<0.01
γ-GT (U/l)	76 (10–534)	118 (32–333)	NS
Bilirubin (μmol/l)	8 (3–99)	200 (6–475)	<0.01
Laminin (U/ml)	1.82 (1.47–2.16)	3.68 (1.84–6.66)	0.05
PIIIP (U/ml)	0.79 (0.46–7.24)	0.96 (0.43–6.18)	NS
NC-1 (ng/ml)	15.6 (10.6–51.5)	23.8 (12.3–182.0)	NS

RI, resistance index; CHE, cholinesterase; γ-GT, γ-glutamyl transferase; PIIIP, procollagen III peptide; NC-1 carboxyterminal procollagen IV peptide; NS, not significant.
p according to Mann–Whitney test.

Table 2

	Type I or II (n = 10)	Type III (n = 14)	Type IV (n = 5)	p
Albumin (g/l)	46.4 (38.0–51.1)	41.6 (29.8–47.5)	32.0 (29.7–36.3)	<0.01
CHE (kU/l)	5.8 (4.1–7.9)	4.7 (1.6–9.2)	2.0 (1.3–2.2)	<0.01
γ-GT (U/l)	70 (13–319)	76 (18–534)	192 (45–333)	NS
Bilirubin (μmol/l)	8 (3–60)	10 (3–380)	200 (10–475)	<0.05
Laminin (U/ml)	1.52 (1.42–2.42)	2.84 (1.37–4.67)	4.42 (2.17–6.99)	NS
PIIIP (U/ml)	0.78 (0.36–7.24)	0.97 (0.43–6.18)	2.82 (0.84–4.80)	NS
NC-1 (ng/ml)	11.5 (9.3–51.5)	17.1 (11.2–182)	27.8 (16.7–36.9)	NS
Spleen SDS	6.9 (3.8–10.4)	8.3 (5.0–10.3)	11.4 (8.3–13.3)	<0.05

CHE, cholinesterase; γ-GT, γ-glutamyl transferase; PIIIP, procollagen III peptide; NC-1 carboxyterminal procollagen IV peptide; SDS, standard deviation score; NS, not significant.
p according to Kruskal–Wallis test.

Table 3

		n	% Nonsurvivors after one year	% Nonsurvivors after two years	Chi-square	p
Portal V_{max}	≥16 cm/sec	21	0	5		
	<16 cm/sec	9	56	100	25.7	<0.001
Venous flow pattern	Type I or II	10	0	10		
	Type III	14	21	36		
	Type IV	5	80	80	12.0	<0.01
Arterial RI	<80%	11	0	2		
	>80%	13	23	84	8.5	<0.01
Portal diameter	SDS < 2	23	17	26		
	SDS > 2	3	0	0	0.6	NS

V_{max}, portal flow velocity; RI, resistance index; SDS, standard deviation score; NS, not significant.
Univariate analysis of prediction of 2-year outcome by chi-square test.

Table 4

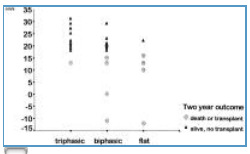

Fig. 3

Zum Seitenanfang