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ESPR

Practical approach for the diagnosis of biliary atresia on imaging, part 2: magnetic resonance cholecystopancreatography, hepatobiliary scintigraphy, percutaneous cholecysto-cholangiography, endoscopic retrograde cholangiopancreatography, percutaneous liver biopsy, risk scores and decisional flowchart

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Abstract

We aim to present a practical approach to imaging in suspected biliary atresia, an inflammatory cholangiopathy of infancy resulting in progressive fibrosis and obliteration of extrahepatic and intrahepatic bile ducts. Left untreated or with failure of the Kasai procedure, biliary atresia progresses to biliary cirrhosis, end-stage liver failure and death within the first years of life. Differentiating biliary atresia from other nonsurgical causes of neonatal cholestasis is difficult as there is no single method for diagnosing biliary atresia and clinical, laboratory and imaging features of this disease overlap with those of other causes of neonatal cholestasis. In this second part, we discuss the roles of magnetic resonance (MR) cholecystopancreatography, hepatobiliary scintigraphy, percutaneous biopsy and percutaneous cholecysto-cholangiography. Among imaging techniques, ultrasound (US) signs have a high specificity, although a normal US examination does not rule out biliary atresia. Other imaging techniques with direct opacification of the biliary tree combined with percutaneous liver biopsy have roles in equivocal cases. MR cholecystopancreatography and hepatobiliary scintigraphy are not useful for the diagnosis of biliary atresia. We propose a decisional flowchart for biliary atresia diagnosis based on US signs, including elastography, percutaneous cholecysto-cholangiography or endoscopic retrograde cholangiopancreatography and liver biopsy.

Keywords Bile duct · Biliary atresia · Endoscopic retrograde cholangiopancreatography · Hepatobiliary scintigraphy · Infants · Liver · Magnetic resonance imaging · Percutaneous cholecysto-cholangiography · Percutaneous liver biopsy

Introduction

Biliary atresia is an important cause of obstructive jaundice in infants causing progressive fibrosis and obliteration of extrahepatic and intrahepatic bile ducts and resulting in biliary cirrhosis in the absence of early surgery. Jaundice with pale stools and dark urine is present within the first days or weeks of life. The prevalence of biliary atresia ranges from 1 in 5,000 to 1 in 20,000 worldwide depending on the geographic area, with the highest prevalence in Taiwan [1–3]. The aetiology of biliary atresia is unknown and different causes have been proposed including viral infections, genetic factors or toxins [4].

There are two forms of biliary atresia: the non-syndromic form, which accounts for about 80% of cases, and the syndromic form, also called biliary atresia splenic malformation syndrome, which accounts for about 20% of cases [3]. The syndromic form is associated with polysplenia (asplenia), intestinal malrotation, preduodenal portal vein, interrupted

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inferior vena cava, aberrant hepatic artery, abdominal heterotaxia and congenital heart disease [5]. There are also different subtypes of biliary atresia according to the extent of fibrosis in extrahepatic bile ducts and the presence of a cyst of the extrahepatic bile duct. In all cases, intrahepatic bile ducts are fibrotic, which explains the absence of bile duct dilatation despite a biliary obstacle [6] (Fig. 1). The histology is characterized by bile duct proliferation, bile plugs, portal or perilobular fibrosis, oedema and the preservation of the basic hepatic lobular architecture [7, 8]. Histology is not specific

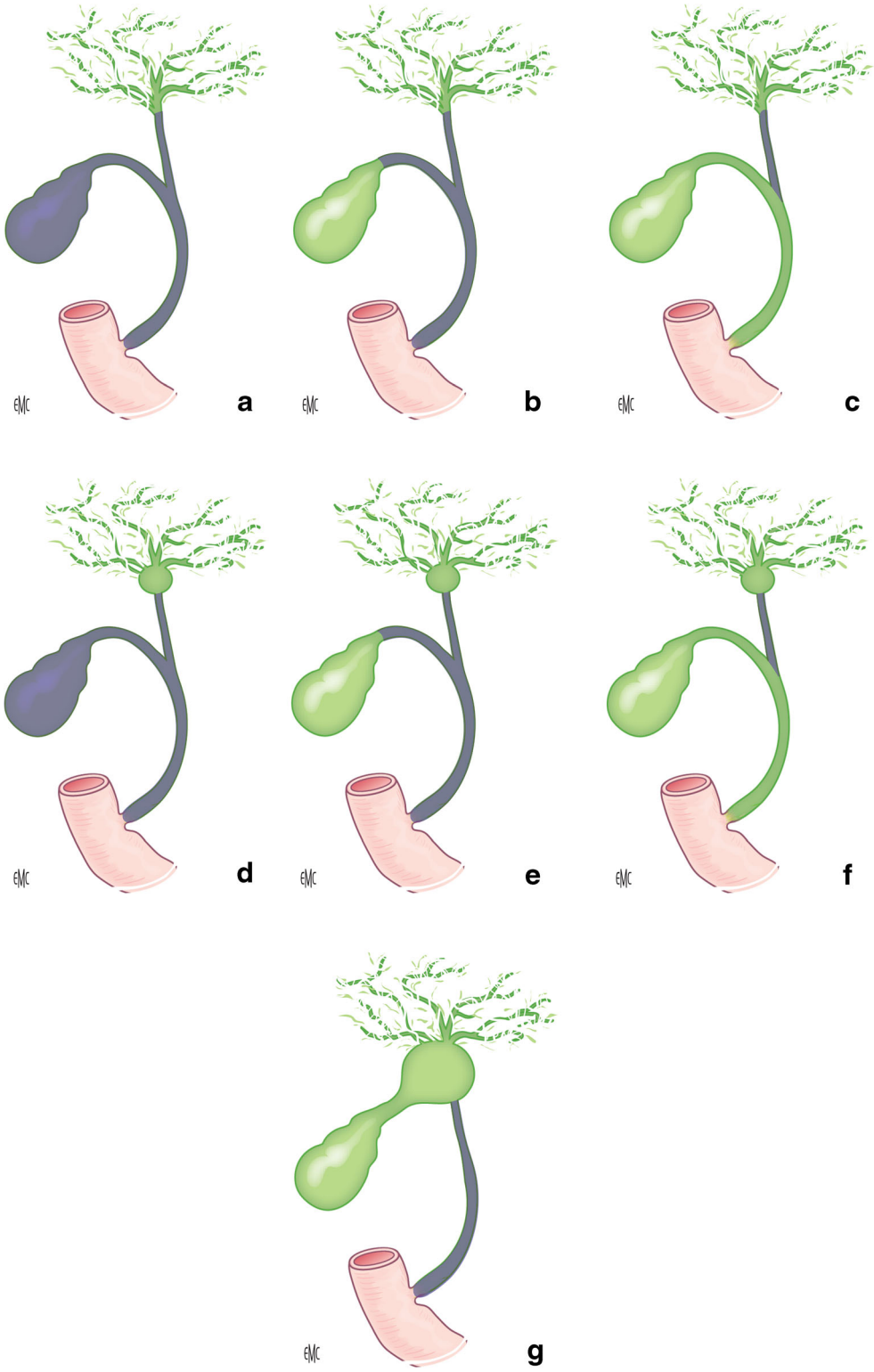

Fig. 1 Different types of biliary atresia, with the obstructed bile ducts and/or gallbladder in grey and the patent parts in green. **a** Complete atresia of the extrahepatic bile duct and the gallbladder. This is the most frequent type accounting for about 2/3 of patients. **b** Patent gallbladder with atretic cystic duct and extrahepatic bile duct. **c** Patent gallbladder, cystic duct and choledochus with atretic main common bile duct. **d–g** Cystic forms with a macrocyst at the liver hilum and variable atresia of the gallbladder and the extrahepatic bile ducts. Note that intrahepatic bile ducts are always pathological, hence they do not display dilation. Reproduced with permission from [6]

and disorders such as parenteral nutrition-associated cholestasis, cystic fibrosis and α-1-antitrypsin deficiency may mimic biliary atresia. Liver biopsy specimens obtained before 6 weeks of age could be indistinguishable from neonatal hepatitis [8–10]. If left untreated, patients with biliary atresia will die within the first years of life from complications of biliary cirrhosis and end-stage liver disease.

The primary treatment for biliary atresia is the Kasai hepatoportoenterostomy, which consists of resecting the choledocal remnants, gallbladder and portal plate and constructing a jejunal Roux-en-Y anastomosis (Kasai procedure) or cholecystostomy to restore biliary drainage. If biliary atresia patients have surgery within the first 60 days of life, bile flow can be established in 70% of cases; patients who have surgery after 90 days of life achieve sufficient bile flow only in 20% of cases [11]. Liver transplantation is performed if primary Kasai hepatoportoenteostomy fails or in case of delayed diagnosis with advanced cirrhosis that contraindicates Kasai surgery. Rapid diagnosis at the onset of symptoms is the main goal of imaging considering the paramount importance of early surgical treatment.

Differentiating biliary atresia from other nonsurgical causes of neonatal cholestasis is challenging. Gamma-glutamyl transpeptidase is an important biomarker in the differential diagnosis of neonatal cholestasis showing higher levels in children with biliary atresia than in those without biliary atresia [12]. Ultrasound (US), magnetic resonance (MR) cholangiopancreatography, hepatobiliary scintigraphy, liver percutaneous biopsy, percutaneous cholecysto-cholangiography and endoscopic retrograde cholangiopancreatography (ERCP) are used in the work-up for biliary atresia, but surgery with intraoperative cholangiography and biopsy is the only reference standard for diagnosis.

We divided our results in two linked papers. In part 1 [13], we discussed the prenatal US and magnetic resonance imaging (MRI) diagnosis and the early postnatal US findings. In this second part, we discuss the role of MR cholecystopancreatography, nuclear medicine, percutaneous biopsy, percutaneous cholecysto-cholangiography and risk scores. Based on this literature review and discussions within the European Society of Paediatric Radiology (ESPR) Abdominal Taskforce, both via e-mails and during plenary sessions, a suggested diagnostic pathway for patients with suspected biliary atresia is proposed as a consensus statement from the ESPR.

Systematic review

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement was applied to this review. In December 2019, two of the authors (M.N. and B.M.D., both with 16 years of experience) independently and systematically searched on PubMed all articles published from Jan. 1999 to Dec. 1, 2019. Keywords included (MRI) AND (biliary atresia), (percutaneous cholecystocholangiography) AND (biliary atresia), (ERCP) AND (biliary atresia), (percutanous liver biopsy) AND (biliary atresia), (nuclear medicine) AND (biliary atresia), (biliary atresia) AND (risk scores). The two readers in consensus selected eligible papers based on title and abstract. Only articles in English were considered for analysis. We matched author names and affiliations to avoid data duplication and we included only the most recent or complete study of the same authors including the same patients. No papers were dismissed due to the children's ages or the type of study.

Imaging techniques

Magnetic resonance cholecystopancreatography

One hundred fifty-two studies were identified for initial review. On the basis of title or abstract, 141 papers were excluded and 11 [14–24] papers were identified as relevant.

A fast spin echo three-dimensional (3-D) MR cholangiopancreatography is recommended with echo time (TE) 600–700 ms, repetition time (TR) 1,500–2,500 ms (theoretical, dependent on respiratory gating), flip angle 140° and fat suppression using a 1.5-tesla (T) unit (Fig. 2). Acquisitions are strictly coronal and almost isotropic to allow for non-distorted detection and assessment of the smaller structures. Real-time navigator gating is necessary to synchronize breathing. Field of view 18–24 cm and acquisition matrix 256×256 are adequate. We suggest using a flexible surface coil according to the child's weight (minimum 12 channels).

Gentle swaddling and natural sleep or sedation are both possible options. We recommend the patient fast for at least 4 h before the MRI and no digestive contrast.

The MR cholecystopancreatography diagnosis of biliary atresia was made on the basis of the non-visualization of the extrahepatic biliary tree [15, 17, 19, 22, 24] or the non-visualization of the extrahepatic bile duct and gallbladder, also considering periportal thickening and high signal intensity in the porta hepatis on T2-weighted images [14, 21] (Fig. 2). Other authors considered the non-visualization of the extrahepatic bile duct and gallbladder abnormalities [20, 23] (Fig. 3).

The meta-analysis performed by He et al. [25] included 7 MR cholecystopancreatography studies (age range: 1–15 days) for biliary atresia diagnosis reporting a sensitivity of 89.7% (range: 84.8–93.4%), a specificity of 64.7% (range: 58.0–71.0%), a positive likelihood ratio of 3.10 (range: 1.59–6.06), a negative likelihood ratio of 0.16 (range: 0.06–0.44) and a diagnostic odds ratio of 32.48 (range: 8.22–128.29).

Kim et al. [16] used a conditional inference tree analysis to select discriminators for the diagnosis of biliary atresia. Visibility of the common bile duct, abnormality of the

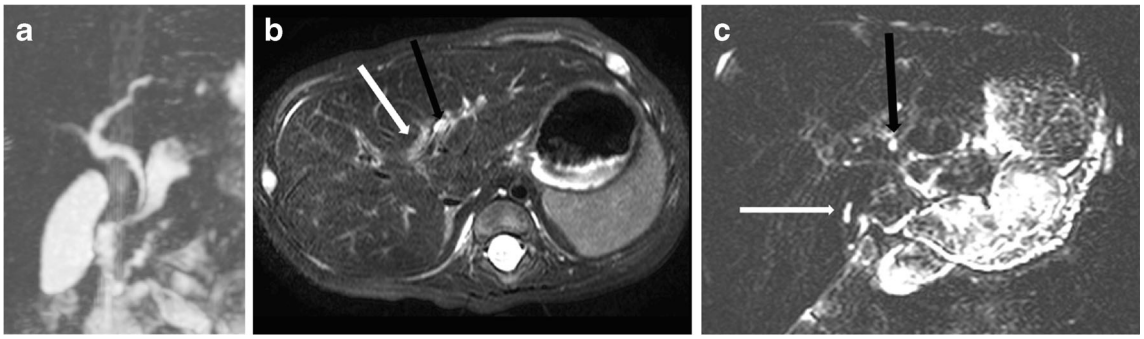

Fig. 2 Non-obstructing and obstructing cholestasis. **a** A 1-month-old girl with cholestasis due to hepatitis. Three-dimensional MR cholecystopancreatography (repetition time [TR]/echo time [TE] 1,600/650 ms) with coronal maximum intensity projection reconstruction shows normal biliary tree. **b, c** A 2-month-old girl with biliary atresia. An axial T2-weighted fat-saturated image (**b**) (TR/TE 2,500/100 ms) shows a 3-mm porta hepatis microcyst (*black arrow*) inside periportal thickening with high signal intensity (*white arrow*). A coronal T2-weighted thick-slab single-shot turbo spin echo MR cholecystopancreatography (**c**) (TR/TE 4,000/900 ms) shows a porta hepatis microcyst (*black arrow*), a small gallbladder (*white arrow*) and the non-visualization of extrahepatic biliary tree

gallbladder and MRI triangular cord thickness were good discriminators for the diagnosis of biliary atresia. The MRI-based decision tree using these findings with MRI triangular cord thickness cutoff of 5.1 mm showed 97.3% sensitivity, 94.8% specificity and 96.2% accuracy, comparable to US. MRI scans in this study were performed using sedation. This was a retrospective study with the possibility of bias. The authors did not assess the reproducibility of MRI triangular sign thickness and the baseline characteristics (gender and laboratory results) were different between the biliary atresia and non-biliary atresia groups. The proportion of patients with visible or dilated common bile duct on MRI in the non-biliary atresia group (94/96, 97.9%) was much higher than in other studies because the authors included 42 patients with choledochal cyst and partially visualized common bile duct in the visible common bile duct group, compared with previous studies that excluded these cases (mean age±standard deviation in the biliary atresia group 59.3 ±30.2 days and in the non-biliary atresia group 57.9±43.1 days).

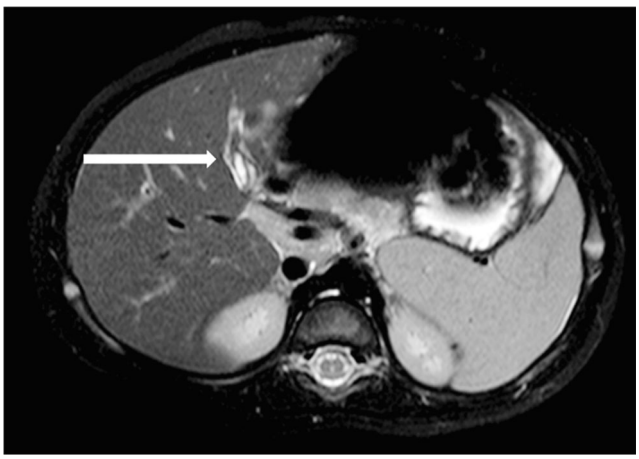

Fig. 3 A 3-month-old girl with biliary atresia. An axial T2-weighted fat-saturated image (repetition time/echo time 2,500/100 ms) shows a small and dysmorphic gallbladder (*arrow*)

According to Siles et al. [18], non-enhanced MR cholecystopancreatography visualization of the entire extrahepatic bile duct system, including confluence of intrahepatic bile ducts, is possible but was only observed in 62.5% of neonates and infants younger that 3 months in a normal physiological state. For infants younger than 30 days, this result dropped to 50%. This compromises the ability of MR cholecystopancreatography to exclude the diagnosis of biliary atresia at the optimal time for surgery.

Hepatobiliary scintigraphy

Hepatobiliary scintigraphy uses Tc-99 m-labelled iminodiacetic acid derivatives as a radiotracer. Patient preparation for imaging should include phenobarbital to activate liver excretory enzymes and increase bile flow for a minimum of 3–5 days before the hepatobiliary imaging study. Scintigraphy can exclude biliary atresia by demonstrating transit of radiotracer into the bowel (Fig. 4). Cholescintigraphic images should be acquired at multiple times up to 24 h.

A meta-analysis by Kianifar et al. [26] included 81 studies (age range: 4–180 days) reporting a sensitivity of 99.3% (range: 98.3–99.8%), a specificity of 75.1% (range: 72.2–77.9%), a positive likelihood ratio of 3.19 (range: 2.47–4.11), a negative likelihood ratio of 0.07 (range: 0.04–0.11) and a diagnostic odds ratio of 60.1 (range: 31.6–114.3). The negative predictive value was high, about 100%, but the positive predictive value was lower and false-positive results occured in some patients with severe medical cholestasis. In hepatobiliary scintigraphy studies, renal or urinary excretion of the tracer could be confused with transit of radiotracer into the bowel and lead to a false-negative result.

Percutaneous cholecysto-cholangiography

Seven percutaneous cholecysto-cholangiography studies were identified for initial review. Four [27–30] were identified as

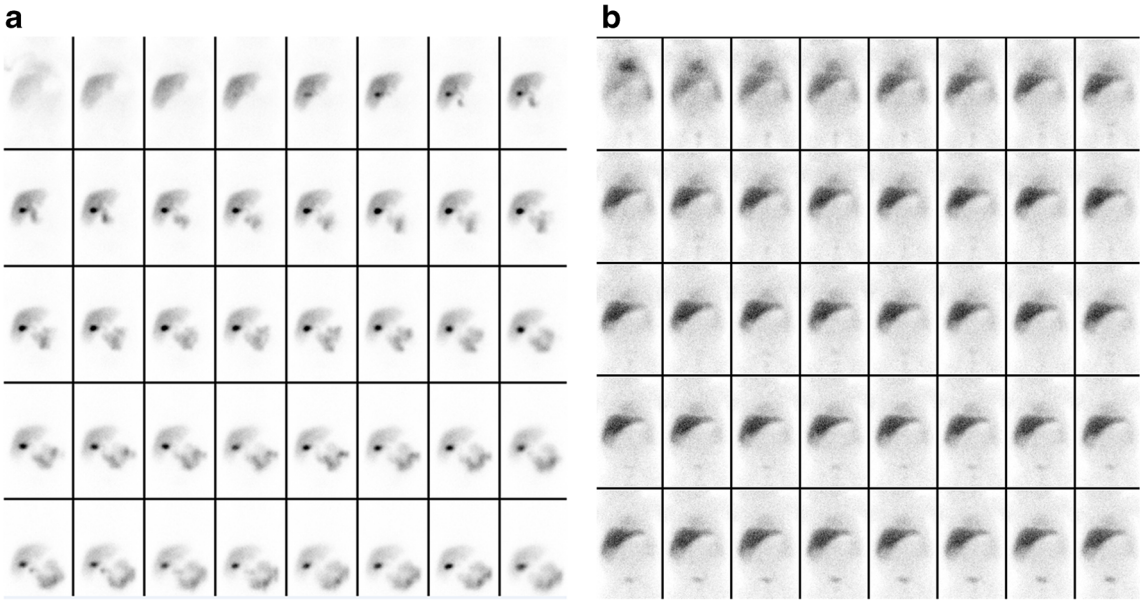

Fig. 4 Hepatobiliary scintigraphy. **a** A 45-day-old girl with Down syndrome and a nonspecific liver disease. Hepatobiliary scintigraphy with an 8×5 matrix, 2 min per image with the first 80 min after injection of 99-Tc-mebrofenin, shows excretion of tracer into the intestine (clearly visible after 12–14 min). A normal gallbladder is filled with tracer (visible after 8–10 min). There is some retention and slightly delayed excretion of tracer in the liver parenchyma. However, excretion of tracer to the intestine excludes biliary atresia. **b** A 77-day-old boy with biliary atresia. Hepatobiliary scintigraphy with an 8×5 matrix, 2 min per image with the first 80 min after injection of 99-Tc-mebrofenin, shows retention of tracer within the liver parenchyma and no visible gallbladder or excretion of tracer into the intestine. Image courtesy of Dr. Jan G. Fjeld, Oslo University Hospital

relevant. Percutaneous cholecysto-cholangiography is a US-guided technique performed under general anaesthesia or sedation with local anaesthesia. A 22- to 25-gauge needle is used to puncture the gallbladder through the liver parenchyma and inject a nonionic contrast medium to obtain a cholangiogram. Antibiotic prophylaxis is usually given. Bile aspiration, when the gallbladder is distended enough, allows for sampling of bile for biochemical studies in suspected genetic cholestasis. The decision to perform a percutaneous cholecysto-cholangiography is informed by case-by-case discussion. If the gallbladder is visible, one may try to puncture it, while acknowledging the risk involved. Lee et al. [28] reported no complications related to percutaneous cholecysto-cholangiography and obtained a technical success in 18 of 22 procedures (age range: 1–138 days, mean age: 49.7 days). Percutaneous cholecysto-cholangiography has a spatial resolution higher than MR cholecystopancreatography and allows observation of the direct progression of the iodine in the biliary tract. It is useful to confirm or rule out biliary atresia in difficult cases. The absence of retrograde filling of contrast in the intrahepatic bile ducts is highly suggestive of biliary atresia. In some cases of biliary atresia, there is a very thin and irregular opacification of the intrahepatic bile ducts and no opacification of the duodenum. In non-biliary atresia cholestasis, opacification of intrahepatic and extrahepatic bile ducts and duodenum is always seen. Some typical patterns may allow differential diagnosis, such as in neonatal sclerosing cholangitis (Fig. 5). Percutaneous cholecysto-cholangiography can determine the type of biliary atresia and gallbladder patency. Zhou et al. [27] proposed percutaneous cholecysto-cholangiography by using contrast-enhanced US in infants suspected of having biliary atresia with equivocal US findings and a gallbladder longer than 1.5 cm. This is an interesting pilot study in which biliary atresia was diagnosed in four patients and excluded in five patients without procedural-related complications. However, further studies are necessary to evaluate the diagnostic performance and limits of this technique. It is noteworthy that the technique can be performed only when a gallbladder lumen is accessible.

Endoscopic retrograde cholangiopancreatography

Endoscopic retrograde cholangiopancreatography was performed to evaluate the patency of the biliary tree in the diagnosis of biliary atresia in some tertiary referral centres. Full delineation of the biliary system excludes biliary atresia. Another sign includes the absence or presence of bile at the site of the papilla. Endoscopic retrograde cholangiopancreatography requires specific infant endoscopy equipment not available at many centres; it is usually performed under general anaesthesia. The endoscopic retrograde cholangiopancreatography sensitivity ranges between 86% and 100%, with the specificity 79–94%, positive predictive value 88–96% and negative predictive value 100% (age range: 19–175 days) [31–34].

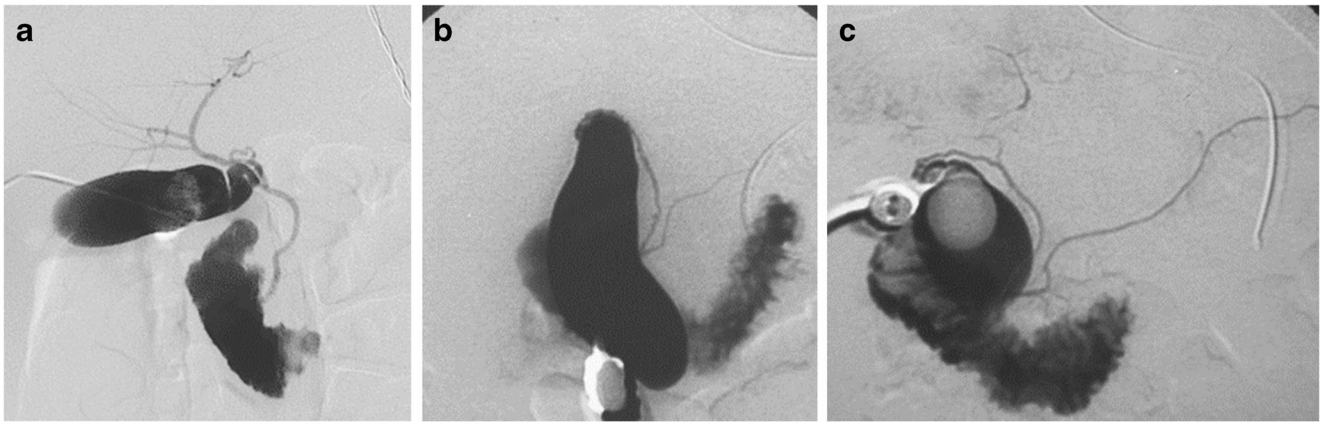

Fig. 5 Percutaneous cholecysto-cholangiography. **a** A 2-month-old girl with normal biliary tree shown in percutaneous cholecysto-cholangiography in a posteroanterior (PA) projection. **b** A 5-week-old boy with biliary atresia type C (see Fig. 1). Percutaneous cholecysto-cholangiography in a PA projection shows opacification of the gallbladder and cystic and common bile ducts with no reflux in intrahepatic bile ducts. **c** A 6-week-old girl with neonatal sclerosing cholangitis. Percutaneous cholecysto-cholangiography in a PA projection shows a normal gallbladder, and a cystic duct, choledochus and reflux in very irregular and thin intrahepatic bile ducts

Percutaneous liver biopsy

Percutaneous liver biopsy is performed in most paediatric centres during the diagnostic work-up of infants with cholestatic jaundice. The diagnosis is challenging because the histological features of many disorders causing infantile cholestasis overlap, evolve and vary with age. The diagnostic accuracy of liver biopsy for biliary atresia diagnosis is between 60% and 95% [10, 35–39]. We have analyzed studies with liver biopsy as the only method for diagnosis. The earliest histological changes of biliary atresia might be relatively nonspecific, and biopsies performed too early in the course of the disease might result in a false-negative result [8, 9]. In a meta-analysis performed by Wang et al. [40] including 38 papers, the sensitivities and specificities of individual studies varied from 90% to 100% and from 84% to 100%, respectively (age range: 12–120 days). The percutaneous liver biopsy showed pooled sensitivity of 98% (95% confidence interval [CI] 96–99%), specificity of 93% (95% CI 89–95%), positive likelihood ratio of 12.09 (95% CI 8.28–17.63) and negative likelihood ratio of 0.03 (95% CI 0.02–0.06). The positive predictive value was 93.0% and the negative predictive value was 97.7%.

In a meta-analysis performed by Lee et al. [41], 22 articles were included (mean or median age at diagnosis or age at presentation range: 6.7–11.5 weeks); the pooled accuracy of preoperative liver biopsy was 91.7%, with a sensitivity of 91.2% (95% CI 75.0–100%), specificity of 93.0% (95% CI 66.7–100%), positive predictive value of 91.2% (95% CI 75.0–100%), negative predictive value of 92.5% (95% CI 47.6–100%) and accuracy of 91.6% (95% CI 65.6–100%).

A large multicentre study performed by Russo et al. [42] addressed histopathological features of liver biopsies that distinguish biliary atresia from other causes of infantile cholestasis. They found a diagnostic accuracy of the needle biopsy of 90.1% (95% CI: 85.2–94.9%), whereas sensitivity and specificity for biliary atresia were 88.4% (95% CI: 81.4–93.5%) and 92.7% (95% CI: 84.8–97.3%), respectively (median age at the time of the needle biopsy: 58 days). This study revealed large variability in the severity of histological changes in biliary atresia; for example, bile duct proliferation was absent in as many as 22.8% of biliary atresia cases and bile duct/ductular plugs were absent in 25% of biliary atresia cases. Histological features of biliary atresia also overlapped with non-biliary atresia cases; more than 40% of the latter had some degree of bile ductular reaction and bile plugs were present in 15%. According to these data, percutaneous liver biopsy cannot exclude biliary atresia. The general reported complication rate of US-guided percutaneous liver biopsy ranges from 1.7% [43] and 4.6% [44] but has not been reported in this specific population.

Risk scores

Differentiation of biliary atresia from other nonsurgical causes of neonatal cholestasis is challenging so a diagnostic risk score is desirable. We searched for biliary atresia risk score papers in the literature including all imaging techniques.

Kim et al. [45] used both clinical (gestational age at birth) and imaging criteria (triangular cord thickness at US, gallbladder structure at US, hepatobiliary scan findings) to develop a risk score for biliary atresia that stratifies patients in a low-risk group in which liver biopsy may be postponed, an intermediate-risk group in which liver biopsy can be considered and a high-risk group in which prompt liver biopsy with or without intraoperative cholangiography should be considered. There are concerns about Kim et al.'s [45] risk score. First, hepatobiliary scintigraphy causes a diagnostic delay of 1 week (5 days for preparation with phenobarbital and 2 days for the examination — we need 24-h delayed imaging) and it

is not recommended because of its limited specificity. According to Kim et al.'s [45] risk score, a full-term birth infant with triangular cord sign and gallbladder abnormalities has only a 15.88% probability of biliary atresia. This is not in agreement with the very high sensitivity and specificity of the combination of triangular cord sign and gallbladder abnormalities reported in the first part of our meta-analysis (87%, 90% and 99%, respectively) [13]. According to those results, this infant has a very high probability of having biliary atresia. Kim et al.'s [45] risk score underweights the role of an optimised US scan. In that paper, US was performed after a 2-h fast, which in our opinion is too short. The US criteria did not include signs such as micro- or macrocyst or syndromic presentation. In Kim et al.'s [45] strategy, biopsy is indicated in the high-risk group, but we consider it more important to do a cholangiography than a biopsy, according to the results of our review. We agree that the high-risk group should get a cholangiography and a biopsy and that the low-risk group can be monitored by close follow-up according to the age. However, our major concern with these results is that they give no answer to how to handle the patients with intermediate (15.88–59.99%) risk of biliary atresia.

El-Guindi et al. [46] used stool colour (clay), US signs (triangular cord sign, contractile gallbladder, gallbladder length ≥20.5 mm, hepatic artery diameter ≥2.05 mm, hepatic artery diameter/portal vein diameter ≥0.445 mm, hepatic subcapsular flow), laboratory tests and histopathology to develop a 12-parameter diagnostic score to discriminate biliary atresia from other causes of neonatal cholestasis, reporting a sensitivity and specificity of 100% each. The main concern is the reproducibility of these measurements and of this diagnostic score; Macaluso et al. [47], applying the same diagnostic score to their population, obtained less encouraging results: global sensitivity was 31% (5/16) with a specificity of 90.9% (10/11).

Chen et al. [48] developed a noninvasive algorithm to identify biliary atresia in cholestasis using five predictors (shear wave speed >1.35 m/s, triangular cord sign, gamma-glutamyl transpeptidase, abnormal gallbladder and clay stool). They divided patients into three risk groups and achieved high diagnostic performance (sensitivity of 98.7% and specificity of 91.4%) in the high and intermediate risk groups.

Discussion

According to this analysis, MR cholecystopancreatography has no role in the diagnosis of biliary atresia mainly because of the absence of visibility of the normal extrahepatic bile duct, considered a diagnostic criterion by most authors, is observed in almost 40% of non-cholestatic neonates leading to low specificity [18]. Moreover, MR cholecystopancreatography is more complex to perform than US and has lower diagnostic performance. This conclusion is in agreement with ESPGHAN (European Society for Paediatric Gastroenterology, Hepatology and Nutrition) and NASPGHAN (North American Society for Pediatric Gastroenterology, Hepatology and Nutrition) guidelines [49].

Concerning hepatobiliary scintigraphy, this analysis shows its very limited role in the diagnosis of biliary atresia because its specificity is very limited with false-positive results in patients presenting with severe medical cholestasis with very limited or even absent choleresis. This again is in agreement with ESPGHAN and NASPGHAN guidelines [49].

More invasive imaging techniques with direct opacification of the biliary tract using percutaneous cholecysto-cholangiography or endoscopic retrograde cholangiopancreatography have been evaluated and show good diagnostic performance. However, the use of endoscopic retrograde cholangiopancreatography is very limited by the need of specific endoscopic equipment with trained operators. Percutaneous cholecysto-cholangiography has very good diagnostic performance to confirm or rule out biliary atresia in difficult cases.

Percutaneous liver biopsy remains an important but imperfect tool for the diagnosis of biliary atresia since histological biliary atresia features vary with time related to the evolution of the disease and may overlap with non-biliary atresia cholestatic diseases.

According to the results of our systematic review, parts 1 [13] and 2, and consensus of the ESPR Abdominal Taskforce, we proposed at the 2019 ESPR annual meeting in Helsinki a biliary atresia decisional flowchart (Fig. 6). In a neonate with conjugated hyperbilirubinemia with or without acholic stools, US should be the first imaging examination. The sufficient duration of fasting for US (>4 h) is of paramount importance, and we suggest repeating US on the same day after adequate fasting in doubtful cases. Gallbladder abnormalities, triangular cord sign, micro- or macrocyst, polysplenia, intestinal malrotation, preduodenal portal vein, interrupted inferior vena cava and abdominal heterotaxia have to be searched for and, if possible, elastography should be applied to assess liver stiffness. Dilated intrahepatic bile ducts can rule out biliary atresia. In an infant (<30 days old) with low clinical suspicion and normal US findings, we could consider repeating clinical examination, US and biological tests every week; if US findings are normal and cholestasis resolves, no further imaging is needed, but if cholestasis with acholic stools persists or occurs, percutaneous cholecysto-cholangiography or endoscopic retrograde cholangiopancreatography should be performed at the same time as liver biopsy. In cases of equivocal findings on US and very young patients with partially acholic stools, atypical patterns suggestive of medical causes or normal US findings and children between 30 and 60 days of age, we propose percutaneous cholecysto-cholangiography or endoscopic retrograde cholangiopancreatography, according to local facilities, and liver biopsy. In cases of suggestive US liver findings and syndromic presentation or suggestive US liver findings and high clinical and biological suspicion, biliary opacification should be done under general anesthesia in the operating room and

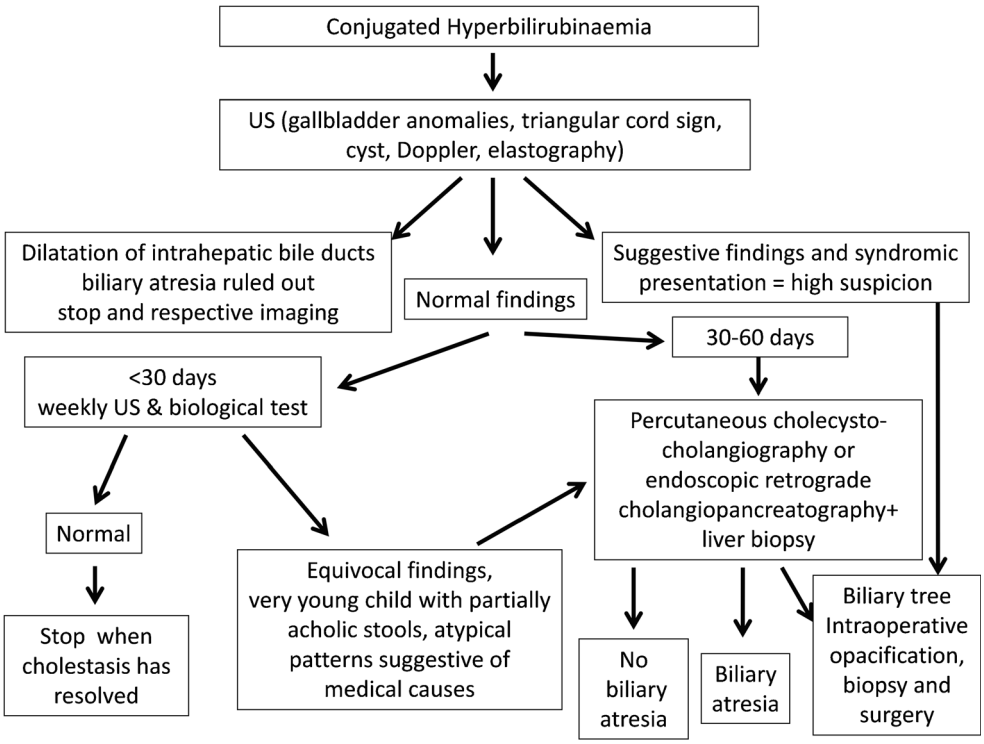

Fig. 6 Decisional flowchart for biliary atresia proposed by the European Society of Paediatric Radiology (ESPR) Abdominal Taskforce at the 2019 ESPR annual meeting in Helsinki. Syndromic presentation: polysplenia (asplenia), intestinal malrotation, preduodenal portal vein, interrupted inferior vena cava, abdominal heterotaxia. US liver suggestive findings: gallbladder anomalies + triangular cord sign or gallbladder anomalies + hilar cyst, or triangular cord sign + hilar cyst

followed by surgical biopsy and a Kasai procedure if normal bile ducts are absent.

Our study has several limitations. The papers included a patient age range of 3–360 days, which is very large for an evolutive pathology that we must diagnose as early as possible, and it creates a real bias especially because some US signs (triangular cord sign and hilar cysts) are age dependent as are the results of liver biopsy. Patient characteristics among studies were different; for example, cystic forms of biliary atresia were excluded in some studies. There is a heterogeneity of study design and we included only English language papers.

Conclusion

Early diagnosis of biliary atresia is of paramount prognostic importance and is the main goal of imaging. No single diagnostic test has an accuracy of 100% and, because biliary atresia is a progressive disease, the diagnostic signs could have a late onset; hence, sensitivity and specificity will vary with age. Among imaging techniques, US has a high specificity, although a normal US examination does not rule out biliary atresia diagnosis. Other imaging techniques with direct opacification of the biliary tree associated with percutaneous liver biopsy have roles in doubtful cases. MR cholecystopancreatography and hepatobiliary scintigraphy have no role in diagnosing biliary atresia. According to the results of our systematic review parts 1 [13] and 2 and consensus of the ESPR Abdominal Taskforce, we propose a decisional flowchart for biliary atresia diagnosis based on US signs, including elastography, percutaneous cholecysto-cholangiography or endoscopic retrograde cholangiopancreatography and liver biopsy.

Declarations

Conflicts of Interest None

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