



Magnetic resonance imaging following the demonstration of a normal common bile duct on ultrasound in children with suspected choledocholithiasis: what is the benefit?

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Abstract

Background The role of MRI in evaluating children with an in situ gallbladder and suspected choledocholithiasis following a negative or inconclusive US is unclear.

Objective To determine whether MRI benefits children with suspected choledocholithiasis and a normal common bile duct (CBD) without stones on US.

Materials and methods We conducted a retrospective 10-year review of paired US and MRI (within 10 days) in children 18 years or younger with suspected choledocholithiasis. With MRI as a reference standard, two reviewers independently evaluated the images for CBD diameter, choledocholithiasis, cholelithiasis and pancreatic edema. Serum lipase was recorded. We calculated exact binomial confidence limits for test positive predictive values (PPVs) and negative predictive values (NPVs) using R library epiR.

Results Of 87 patients (46 female, 41 male; mean age 14 years, standard deviation [SD] 4.6 years; mean interval between US and MRI 1.6 days, SD 1.8 days), 55% (48/87) had true-negative US, without CBD dilation/stones confirmed on MRI; 5% (4/87) had false-positive US showing CBD dilatation without stones, not confirmed on MRI; 33% (29/87) had true-positive US, with MRI confirming CBD dilatation; and 7% (6/87) had false-negative US, where MRI revealed CBD stones without dilatation (2 patients) and CBD dilatation with or without stones (4 patients). Patients with false-negative US had persistent or worsening symptoms, pancreatitis or SCD. The overall US false-negative rate was 17% (6/35). Normal-caliber CBD on US without stones had an NPV of 89% (48/54, 95% confidence interval: 0.77–0.96).

Conclusion MRI adds little information in children with a sonographically normal CBD except in the setting of pancreatitis or worsening clinical symptoms. Further evaluation is warranted in children with elevated risk of stone disease.

Keywords Children · Choledocholithiasis · Ductal dilatation · Magnetic resonance cholangiopancreatography · Magnetic resonance imaging · Ultrasound

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Introduction

While it remains uncommon, the frequency of choledocholithiasis in children older than 16 years approximates 10%, while that in younger children is not known [1]. US and MRI/magnetic resonance cholangiopancreatography (MRCP) are effective imaging modalities to evaluate children with suspected choledocholithiasis. The reported sensitivity and specificity of transabdominal US for diagnosing choledocholithiasis in children are 96.9% and 13.4%, respectively [2]. The corresponding sensitivity and specificity of MRI in children have not been reported; however, in adults they are reported as 85–100% and 90–99%, respectively [3].

MRI is particularly useful when overlying bowel gas limits adequate sonographic visualization of the biliary tree [4].

Multiple publications in the adult literature have described the benefit of performing an MRI despite the presence of a normal common bile duct (CBD) on US, particularly in people with persistently elevated liver enzymes or in those with a high clinical suspicion for choledocholithiasis [4–6]. This is supported by American College of Radiology (ACR) guidelines, which recommend US as the initial imaging modality for right upper quadrant pain and suspected choledocholithiasis, with MRI obtained as a follow-up in cases where suspicion of biliary disease persists after a negative US, the US is inconclusive, or the patient has persistent clinical or laboratory abnormalities suggesting biliary pathology [7].

While risk scores for pediatric patients with suspected choledocholithiasis have been reported, no pediatric-specific ACR guidelines exist for imaging suspected choledocholithiasis [8, 9]. The benefit of adding MRI in children who have a normal CBD on US has not been established. Currently, the decision whether to perform MRI following US in children with suspected choledocholithiasis is based on the clinician's discretion [1]. At our institution, MRI is frequently obtained based on our physicians' greater confidence in this modality compared to US, as well as patient symptomatology. While laboratory results, specifically liver function tests (LFTs), are a factor in the workup of these children, these results are not the driving force that directs imaging. MRI findings, including CBD dilatation with or without a visible stone as well as a non-dilated CBD with a visible stone, inform the decision whether to perform follow-up imaging or additional interventions such as endoscopic retrograde cholangiopancreatography (ERCP) or intraoperative cholangiography. However, MRI in children poses the challenges of affordability, availability, study time and the possible need for anesthesia to prevent motion artifact [10]. We retrospectively evaluated paired US and MR imaging findings to determine whether MRI provides a benefit in children with suspected choledocholithiasis and a normal-caliber CBD without stones on US.

Materials and methods

Our institutional review board granted approval for this retrospective review. We queried Nuance mPower Clinical Analytics (Burlington, MA) for patients younger than or equal to 18 years who underwent paired US and MRI with or without contrast agent between Jan. 1, 2012, and Feb. 8, 2022. No search terms were used.

Exclusion criteria included patients with an interval of greater than 10 days between the US and MRI, technically

suboptimal examinations with inability to identify the CBD (including motion artifact on MRI or poor sonographic penetration on US) or those unavailable for review, and clinical history including prior cholecystectomy, underlying malignancy, autoimmune condition or immunosuppression, hepatic lesion, preexisting liver disease, inflammatory bowel disease, liver transplantation, ERCP or other biliary instrumentation prior to imaging, pregnancy/postpartum, and absent laboratory results within 2 days of the US.

Data obtained from the hospital electronic medical record (Epic; Epic Systems Corp., Verona, WI) included patient age, gender and indication for the exam as provided on the imaging order. We recorded serum lipase levels (reference range < 60 U/L) closest to the date of the patient's US because of the causative association between biliary stones and pancreatitis. Given that sickle cell disease (SCD) is the leading cause of cholelithiasis in our patient population, we also recorded the presence of SCD.

Ultrasound examinations including sagittal and transverse projections of the liver, porta hepatis, pancreatic head, gallbladder and common duct were performed on a Logiq E9 or Logiq E10 (GE Healthcare, Chicago, IL) using a C1–6-MHz or C5–9-MHz curved-array transducer (depending on patient size) without cine clips. MR images were performed on a 1.5-tesla (T) Ingenia machine (Philips Healthcare, Andover, MA) using a standard abdominal MRI/MRCP protocol (Table 1).

Ultrasound and MRI studies were independently reviewed by two board-certified pediatric radiologists (R.O.F. with 30 years of experience and T.L.L. with 31 years of experience) with certificates of added qualification in pediatric radiology. Discrepancies in interpretation of CBD size as dilated or not dilated and the presence of CBD stones were reviewed by a third pediatric radiologist (E.B. with 17 years of experience, not an author). We reviewed studies for CBD diameter, CBD stones and sludge, cholelithiasis, pancreatic edema and peripancreatic fluid.

Ultrasound image review

We reviewed the US first, followed by the MRI. When reviewing the US, the radiologist was blinded to the US and MRI reports and to the MR images. On US, the CBD diameter was measured at the porta hepatis along the long axis of the main portal vein and at the level of the pancreatic head in the transverse plane. We used the larger of the two measurements and reported the duct as dilated or normal caliber based on published norms for age. On US, the upper limits of normal for CBD size are 1 mm in a neonate, 2 mm in an infant up to 1 year, 4 mm in children ages 1–10 years, and 6 mm in children older than 10 years [11]. US examinations were considered positive if the CBD was dilated or if a stone was identified in the CBD.

Table 1 Protocol for MRI with and without contrast agent, with magnetic resonance cholangiopancreatography (MRCP)

Planes	Sequences	TR (ms)	TE (ms)	ST (mm)	Spacing (mm)	Matrix
Axial	T1 in/out of phase	176	1.1, 2.3	4	4–6	124×118
Axial	T1 Dixon pre-contrast	5.5	2.1, 3.7	3	1–2	300×264
Axial	T1 Dixon dynamic post-contrast, 3 phases	6.3	2.1, 3.7	5	2.5	300×264
Coronal	T1 Dixon post-contrast	6.3	2.1, 3.7	5	2.5	300×264
Axial	T1 Dixon post-contrast, 4 min post injection	6.3	2.1, 3.7	5	2.5	300×264
Axial, coronal	T2 single shot	1,049	80	4	4	156×125
Axial	T2 fat sat	1,100	80	6	6	172×170
Axial	bTFE	3.2	1.6	5	5	132×111
Axial	DWI (b 0, 100, 800)	1,294	62	6	6	68×66
Axial, coronal	T1 Dixon post-contrast, 20 min post injection	6.3	2.1, 3.7	5	2.5	300×264
Subtractions						
Coronal, axial	3-D T2 TSE (MRCP)- respiratory triggering	1,104	662	1	0	200×132
Coronal	T2 FSE	1,100	80	5	5	172×170

Exams were performed with the patient fasted 4 h prior to exam

bTFE balanced turbo field echo, *DWI* diffusion-weighted imaging, *fat sat* fat-saturated, *FSE* fast spin echo, *h* hours, *min* minutes, *ST* slice thickness, *TE* echo time, *TR* repetition time, *TSE* turbo spin echo

Magnetic resonance imaging review

Magnetic resonance images were reviewed with the radiologist blinded to the MRI report. Because MRCP images were suboptimal in some patients due to motion, we made CBD measurements at the porta hepatis and pancreatic head on T2-weighted fat-saturated axial images and confirmed them on coronal T2-weighted images. As with the US, we used the larger of the two measurements. The reported normal limit for CBD size on MRI in children younger than 10 years is 3–4 mm [12]. For children older than 10 years, we used the adult reference standard of 6 mm for the upper limit of CBD size [13]. We also reported the presence or absence of filling defects in the duct. MRI examinations were considered positive if the CBD was dilated or if a stone or filling defect was identified in the CBD.

We calculated exact binomial confidence limits, with a confidence level of 95%, for test positive and negative predictive values using function `epi.test` in the R library `epiR` (version 2.0.50), with MRI used as a reference standard. Additionally, because pediatric MRI reference standards are only available for children younger than 10 years, we performed a subanalysis with patients stratified by age (< 10 years, 10 years and older). Inter-rater reliability on CBD diameter, CBD stones/sludge and cholelithiasis was evaluated by Cohen kappa.

Results

We identified 356 patients and excluded 269 based on the exclusion criteria, leaving 87 patients in the cohort (Fig. 1). The demographics of the study group are provided

in Table 2. Indications for obtaining both US and MRI varied and were at the discretion of the treating clinician (Table 2). The average time interval between US and MRI was 1.6 days (range 0–8 days, SD 1.8 days). Fifty-three patients had non-contrast MRI, 11 had MRI with gadoxetate disodium (Eovist; Bayer Healthcare Pharmaceuticals, Whippany, NJ) and 23 patients had MRI with gadobutrol (Gadovist; Bayer Healthcare Pharmaceuticals, Whippany, NJ). All had MRCP.

Evaluation of inter-rater reliability for determining CBD dilatation on US demonstrated that raters were in almost perfect agreement (Cohen kappa = 0.98, 95% confidence interval [CI]: 0.95–1.00). For determining CBD dilatation on MRI, the reviewers had perfect agreement (Cohen kappa = 1.00, 95% CI: 1.00–1.00). Inter-rater reliability for determining CBD stones/sludge demonstrated that raters were in substantial agreement on US (Cohen kappa = 0.71, 95% CI: 0.45–0.97) and on MR (Cohen kappa = 0.72, 95% CI: 0.59–0.85). Inter-rater reliability for determining cholelithiasis demonstrated that raters were in almost perfect agreement on US (Cohen kappa = 0.97, 95% CI: 0.92–1.00) and on MRI (Cohen kappa = 0.81, 95% CI: 0.70–0.92).

Thirty-three of 87 patients (38%) had dilatation of the CBD on US, and 7 of these patients had a CBD stone identified within the dilated duct. MRI confirmed dilatation of the duct in 29 of these patients (33% of total cohort) and identified 21 CBD stones, 14 of which were not seen on US (Table 3; Fig. 2). The remaining 4 patients with a dilated CBD on US and a normal CBD on MRI showed clinical improvement between the US and the MRI (0–2 days) and were considered to have false-positive US (5% of total cohort) (Table 3; Fig. 3).

Fig. 1 Study cohort flow-chart. ERCP endoscopic retrograde cholangiopancreatography

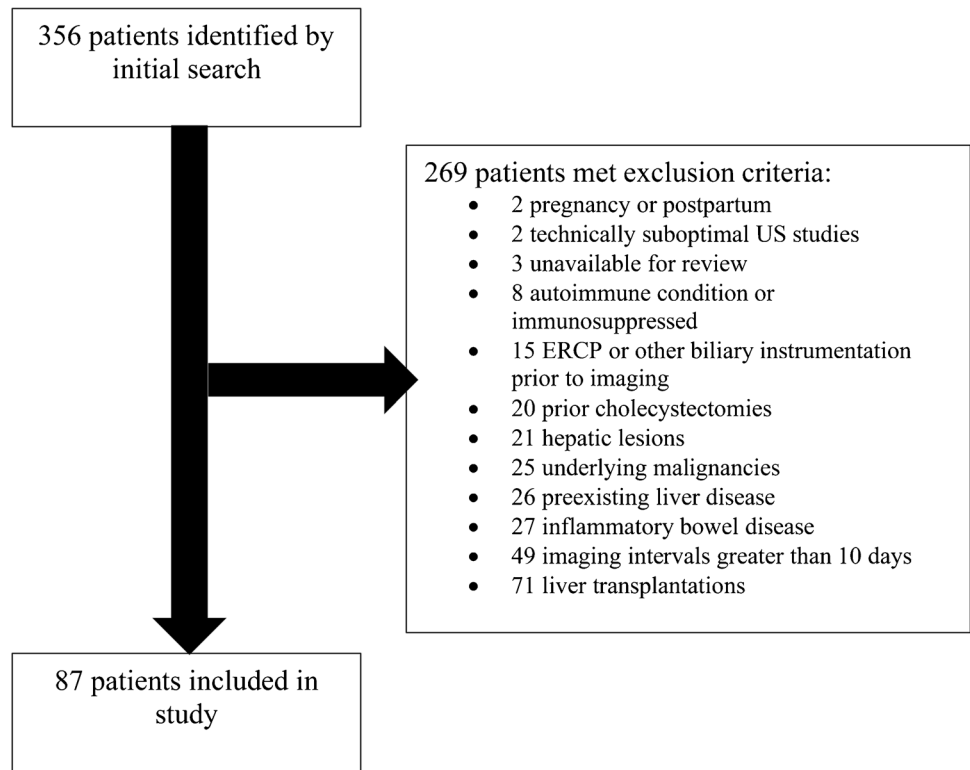


Table 2 Patient demographics (*n* = 87)

Characteristics	<i>n</i>	%
Age (years)		
Median	16	
Range	5 d–18 y	
Subjects < 10 years	12	14%
Subjects ≥ 10 years	75	86%
Gender		
Male	41	47%
Female	46	53%
Hemolytic diseases		
Sickle cell disease	14	16%
Reported indication for imaging		
Evaluation for biliary obstruction	46	53%
Gallstone pancreatitis	24	28%
Liver function test abnormalities	9	10%
Abdominal pain	7	8%
Incidentally dilated CBD on outside study	1	1%

CBD common bile duct, *d* days, *y* years

On US images, 54/87 patients (62%) had a normal CBD with no CBD stone (Table 3). MRI confirmed a normal CBD with no CBD stone in 48 patients (55% of total cohort). The remaining 6 patients with normal findings on US had discrepant findings on MRI and were considered to have

false-negative US (6/87, or 7% of total cohort); in 4 of these, MRI demonstrated CBD dilatation, and in 2 (with normal-caliber CBDs), MRI identified a distal CBD stone that was not apparent on US. All six patients had cholelithiasis identified on both US and MRI. The clinical and imaging findings of these six patients are presented in Table 4 and constitute a false-negative rate of 17% (6/35, 95% CI: 7–34%).

Using the MRI as a reference standard, in our cohort the size of the CBD or presence of CBD stones on US had a positive predictive value (PPV) of 88% (29/33, 95% CI: 72–97%) and a negative predictive value (NPV) of 89% (48/54, 95% CI: 77–96%).

Additional analysis was performed with patients stratified by age: younger than and older than or equal to 10 years. Twelve patients in the cohort (14%) were younger than 10 years (range 5 days to 9 years). Seventy-five patients (86%) were 10 years or older (range 10–18 years). All false-negative US cases in the cohort were 10 years and older. For the older age range, CBD size/stone on US had a PPV of 88% (23/26, 95% CI: 70–98%) and an NPV of 88% (43/49, 95% CI: 75–95%).

In 31 of the 87 patients (36%), the CBD was not visualized on US at the level of the pancreatic head because of overlying bowel gas. Two of these patients were found to have a stone in the distal duct on MRI despite normal ductal caliber on both US and MRI.

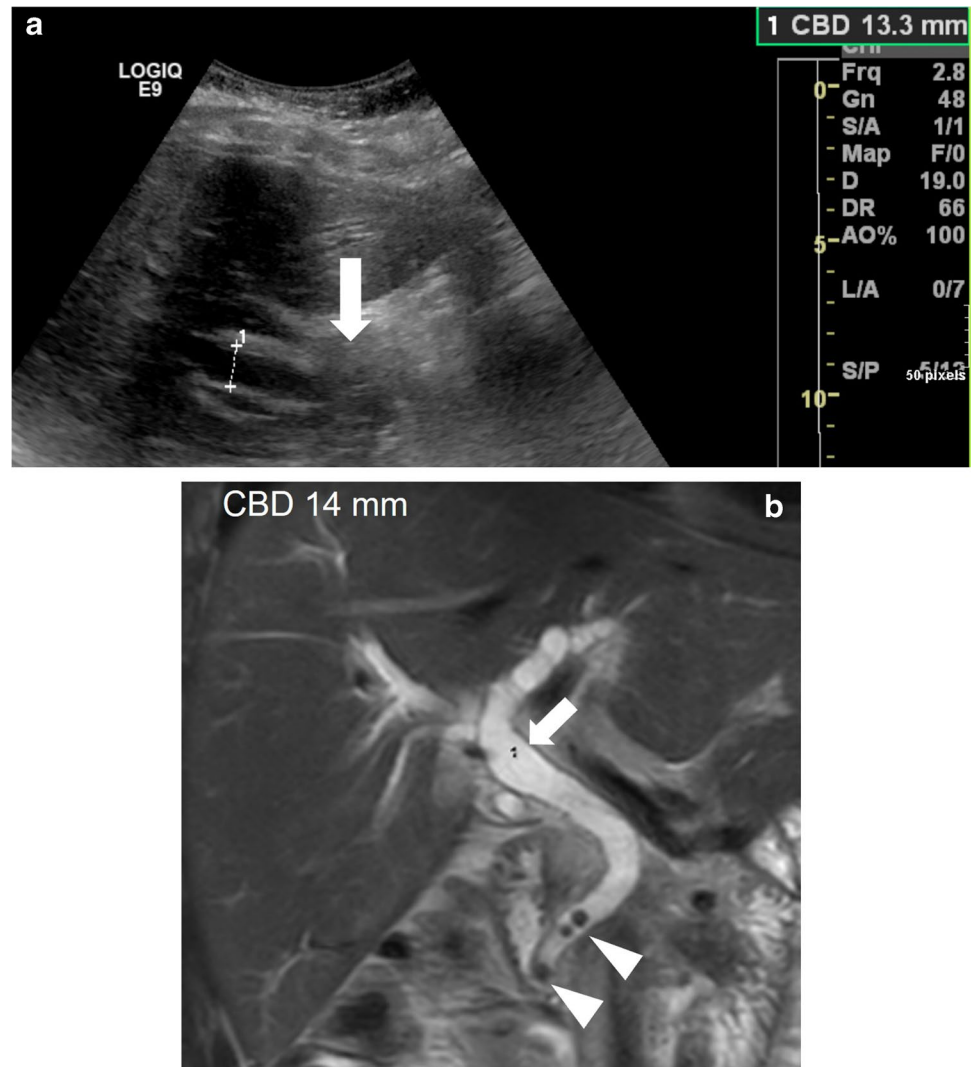
Twenty-seven of the 87 patients (31%) had clinically diagnosed pancreatitis at the time of imaging based on

Table 3 US and MR imaging findings in patient cohort. *CBD* common bile duct

Ultrasound findings	Total (n)	US (n)		MRI (n)	
		CBD dilated	CBD stones identified	CBD dilated	CBD stones identified
True-negative US	48	0	0	0	0
False-positive US	4	4	0	0	0
True-positive US	29	29	7	29	21
False-negative US	4	0	0	4	2
	2	0	0	0	2

False-negative US are separated by those with and without CBD dilatation on MR imaging

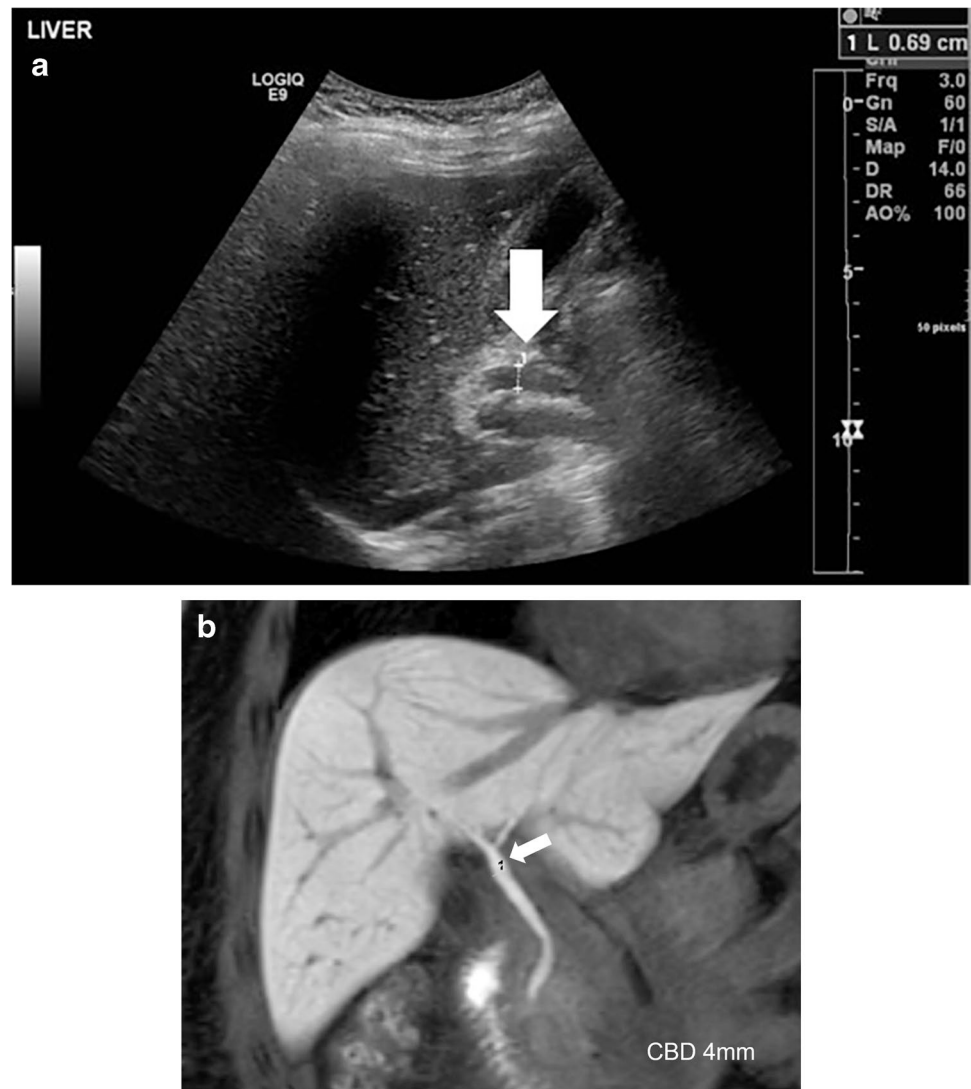
Fig. 2 True-positive US findings. **a** Oblique sonographic image of the porta hepatis in a 15-year-old boy demonstrates dilatation of the common bile duct (CBD), which measures up to 13.3 mm (*calipers*). The distal duct is obscured by bowel gas (*arrow*). **b** MRI. Corresponding coronal T2-W fat-saturated image in the same boy 1 day later confirms CBD dilatation up to 14 mm (*arrow* demarcates calipers) and shows stones in the distal CBD (*arrowheads*)



elevated serum lipase (Table 5). In the vast majority of these (23 patients), US and MRI findings were concordant; in only 2 patients was the US negative and MRI demonstrated a CBD stone or CBD dilatation (Fig. 4); and the remaining 2 patients had a false-positive US.

Fourteen patients (14/87: 16%) had SCD; five of these patients had a normal CBD on US and MRI; 2 had a normal CBD on US and a dilated CBD on MRI; 1 had a dilated CBD on US and a normal CBD on MRI; 6 had CBD dilatation on both US and MRI.

Fig. 3 False-positive US findings. **a** Oblique sonographic image of the porta hepatis in a 17-year-old boy demonstrates a dilated common bile duct (CBD) on US (7 mm) (*arrow* demarcates calipers). **b** On a coronal T2-W 20-min-delay post-contrast (gadaxetate disodium) modified Dixon image from MRI performed 1 day after the US shows the CBD measuring 4 mm and not dilated (*arrow* demarcates calipers)



Discussion

Ultrasonography is an effective imaging modality to evaluate adults and children with suspected choledocholithiasis and is the initial choice of imaging for suspected choledocholithiasis in adults based on ACR guidelines [7]. ACR guidelines advise obtaining an MRI in adults when US findings are negative or ambiguous, or if there is continued clinical suspicion for choledocholithiasis. Perhaps because of the relatively less frequent occurrence of stone disease in the pediatric population, no pediatric-specific guidelines exist to address imaging children with suspected choledocholithiasis following identification of a normal CBD on US.

In our cohort of children with suspected choledocholithiasis, when the US demonstrated neither CBD dilatation nor a CBD stone, MRI provided little additional information except in patients with clinical worsening, clinical pancreatitis and SCD. In most patients with a normal CBD

on US, MRI confirmed a normal CBD with no CBD stone (NPV = 89%). In the six patients where MRI demonstrated positive findings when the US was normal (false-negative US), four had CBD dilatation (two without CBD stones, one with a CBD stone and one where the distal CBD was not well seen) and two had a CBD stone in the absence of a dilated CBD. Clinically, three of the six had worsening or persistent symptoms, two had clinical pancreatitis confirmed on imaging, and two had SCD, suggesting that MRI is useful following a normal or inconclusive US in these clinical groups.

While a sonographically normal CBD does not exclude the presence of choledocholithiasis [5, 14], and can in fact miss choledocholithiasis, a distal CBD stone in the setting of a normal CBD in our patient population was present in only 2/54 patients with normal CBD (3.7%) and was much less frequent than that described in the adult literature. In a study of 109 adults with gallstones and choledocholithiasis,

Table 4 Imaging and clinical findings in patients with false-negative US

Patient #	Age (y)	Days between US and MRI	CBD (mm) US ^a	CBD stone(s) US	CBD (mm) MRI ^a	CBD stone(s) MRI	Gallstones on US and MRI	Elevated lipase	Pancreatic or peripancreatic inflammation	No clinical improvement following US
1	16	1	6	N	5.6	Y	Y	N	N	N
2	17	3	4	N	5.5	Y	Y	N	N	Y
3	17	1	6	N	8	N	Y	Y	Y	N
4	16	1	4	N	8	Cannot exclude ^b	Y	N	N	Y
5	12	3	4	N	8	Y	Y	Y	Y	N
6	18	0	5	N	6.5	N	Y	N	N	Y

CBD common bile duct, N no, y years, Y yes

^aFor a patient 10 years or older, 6 mm is the upper limit of normal for CBD diameter on both US and MR. Specific measurements recorded in this table were taken from Reviewer 1 and confirmed by Reviewer 2

^bWhile the CBD was dilated and measurable, the most distal portion of the duct was not well visualized and thus the presence of a distal CBD stone could not be excluded by either reviewer

Qiu et al. [4] cited a CBD diameter close to normal range on US as an important factor contributing to missed choledocholithiasis, which they reported in 45% of their study group. Similarly, Isherwood et al. [6] reported a 43% incidence of MRCP-proven choledocholithiasis in patients with a normal CBD on US, and PPV and NPV of 58% and 73%, respectively. Boys et al. [15] demonstrated no significant difference in CBD diameter on US in patients with and without confirmed choledocholithiasis on MRCP. The much lower false-negative rate (17%) and higher predictive values of ductal size on US in our study group compared to the adult literature might reflect the improved sonographic image quality in children compared to adults because of children's decreased body mass as well as their lower incidence of choledocholithiasis [16].

Diez et al. [9] proposed a diagnostic algorithm to evaluate children with suspected choledocholithiasis. Rather than obtaining an MRI following a normal US, the authors suggested that in this group of patients MRI be performed only in those with "complicated cholelithiasis" defined as biliary pancreatitis, choledocholithiasis or acute cholecystitis [9]. In this algorithm, the diagnosis of complicated cholelithiasis requires elevated white blood cell count, C-reactive protein, amylase, lipase, lactate dehydrogenase (LDH), fever and signs of inflammation or proof of choledocholithiasis on US [9]. Diez et al. also suggested that MRI be avoided except in cases where the clinical diagnosis remains uncertain. In our cohort, two of the false-negative US cases (where US failed to demonstrate an abnormality and MRI demonstrated a CBD stone or dilatation) had clinical pancreatitis (elevated serum lipase). Using Diez's algorithm, MR imaging following US was warranted in these cases.

For patients in our study group who demonstrated CBD dilatation on US, our findings concur with those in the adult literature: CBD dilatation on US was highly predictive of CBD dilatation on MRI. The finding of a dilated CBD on US had a PPV of 88%. When CBD dilatation was identified on US, the MRI confirmed the findings in all but four patients and provided additional information including the presence of biliary stones. MR imaging was far more sensitive in identifying choledocholithiasis than US, identifying three times the number of CBD stones as compared to US, and was far more sensitive in assessing the distal duct than US, particularly in cases of obscuration of the duct by overlying bowel gas [14, 17, 18]. Additionally, MRI allowed improved visualization of adjacent organs.

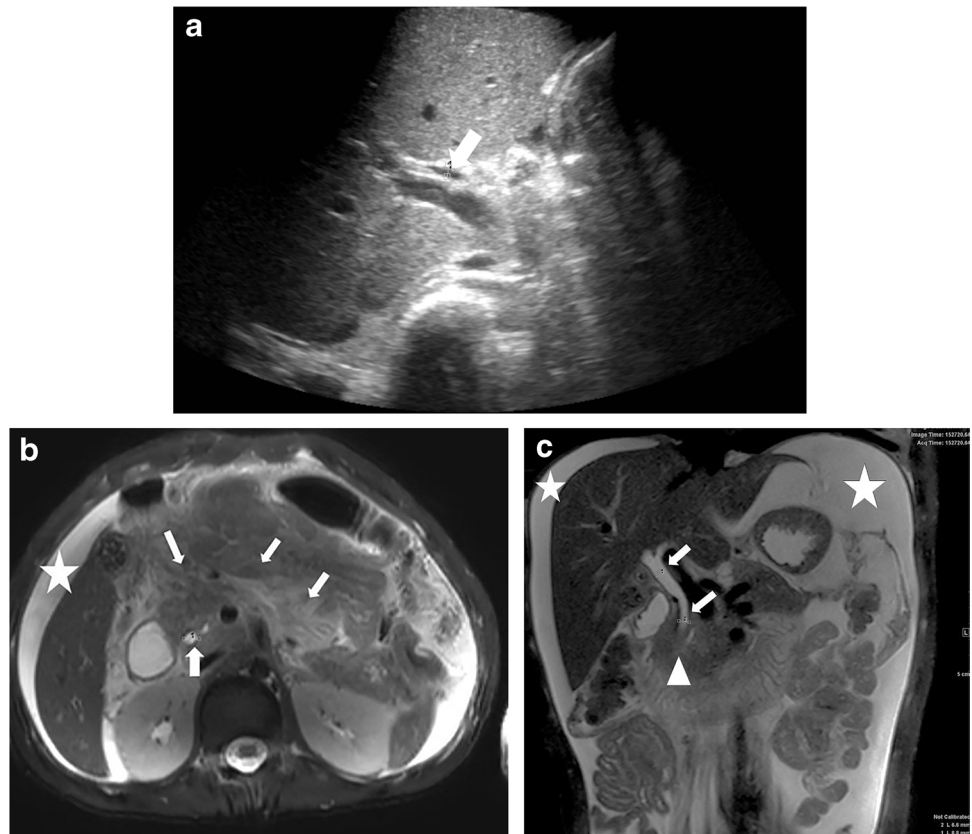
The normal age-related MRI reference standards for CBD diameter in children have been reported up to the age of 10 years. Given that no age-related norms exist for children older than 10 years, we used the adult reference CBD size on MRI for these children in our cohort. Notably, all of the patients with false-negative US were older than 10 years. When we stratified the cohort by age, the PPV and NPV

Table 5 Imaging findings in 27 patients with pancreatitis

CBD dilatation or stones	True-positive US	True-negative US	False-positive US	False-negative US
Pancreatitis	5	18	2	2
US pancreatic edema or peripancreatic fluid	3	7	0	1
MR pancreatic edema or peripancreatic fluid	5	13	0	2

CBD common bile duct

Fig. 4 False-negative US in a 12-year-old girl with pancreatitis. **a** Transverse sonographic image of the liver at the porta hepatis demonstrates a normal common bile duct (CBD) (*arrow*) measuring 4 mm in diameter. **b** Axial fat-saturated T2-W single-shot image at the level of the pancreatic head from MRI in the same girl 3 days after the US demonstrates CBD dilatation (*thick arrow* demarcating calipers), enlargement and edema of the pancreatic head with peripancreatic inflammation (*thin arrows*) and ascites (*star*). **c** Corresponding coronal fat-saturated T2-weighted MRI in the same girl confirms CBD dilatation (*arrows* demarcating calipers), enlargement and edema of the pancreatic head (*arrowhead*) and ascites (*stars*)



calculated in older children did not differ significantly from those of the overall cohort, likely because only 14% of the cohort was younger than 10 years. Nevertheless, the normal reference standards for the CBD size on MRI in this age group could differ from those in adults and could be less than the reported adult reference standard of 6 mm. Thus, as has been suggested by Lindholm et al. [1], further investigation is needed to establish normal values for CBD size on MRI in children older than 10 years.

It is unclear whether children at high risk for cholelithiasis and choledocholithiasis, such as those with hemolytic disorders, would benefit from a follow-up MRI in the setting of a normal CBD on US. Two of the patients in our study group with false-negative US and positive findings on MRI had SCD. Given the small sample size of our study group, further investigation evaluating the role of MRI following the identification of a normal CBD on US in children with a propensity for cholelithiasis might be beneficial.

Clinical presentation, history and LFTs are used to identify children with possible choledocholithiasis. Once this diagnosis is suspected, the need for imaging becomes apparent for confirmation. LFTs do not determine the choice of imaging. We therefore did not investigate the relationship between imaging findings and LFTs in this study. Further studies might be beneficial in elucidating the role of LFTs in determining the imaging workup for children with possible choledocholithiasis.

Our study is limited by its small sample size, its retrospective nature, as well as the operator-dependent nature of US. We did not account for body habitus, and while we evaluated the CBD size based on published ranges for CBD size for age, normal sizes have not been published for everyone in our patient population. As mentioned, in children older than 10 years, we used adult normal reference standards for CBD size on MRI because there are no published data for normal CBD size in these children. Although serum

lipase levels were obtained within 2 days of the US, some variability in their timing might have affected results. US cine clips were not available on all patients, which might have limited diagnosis for small stones. Our conclusions might have differed had ERCP or intraoperative cholangiogram been used as reference standards. While most patients subsequently underwent cholecystectomy, not all had ERCP or intraoperative cholangiogram. Last, our study evaluated patients who underwent US followed by MRI. Patients who did not undergo MRI were not included and this might have introduced bias into the conclusion.

Conclusion

While the diagnosis of choledocholithiasis depends on numerous factors including CBD size, in children with suspected choledocholithiasis, no history of cholecystectomy and no dilatation of the CBD on US, MRI adds little information except in cases of pancreatitis or clinical worsening. Further studies to determine the benefit of MRI following US in children with an elevated risk of stone disease, such as having SCD, are warranted.

Declarations

Conflicts of interest None

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