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Research

Imaging based flowchart for gallbladder polyp evaluation

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ABSTRACT

Background: Preoperative differentiation between neoplastic and nonneoplastic gallbladder polyps, and the subsequent indication for cholecystectomy remains a clinical dilemma. The current 1 cm size threshold for neoplasia is unspecific. The aim of this study was to improve diagnostic work-up for gallbladder polyps using sonographic and MRI characteristics of neoplastic and nonneoplastic polyps.

Methods: A prospective, exploratory study including patients undergoing cholecystectomy for gallbladder polyp(s) was conducted. Patients underwent targeted transabdominal ultrasound (TAUS) and MRI. Outcomes were sensitivity and specificity for polyp diagnosis, and the radiological characteristics of neoplastic and nonneoplastic polyp types. Histopathology after cholecystectomy was used as reference standard.

Results: Histopathology demonstrated gallbladder polyps in 20/27 patients (74%): 14 cholesterol polyps, three adenomyomatosis, two adenomas and one gastric heterotopia. Sensitivity of polyp identification were 72% (routine TAUS) and 86% (targeted TAUS and MRI). Both adenomas were identified as neoplastic on targeted TAUS and MRI. Sonographic presentation as multiple, pedunculated polyps, either heterogeneous or with hyperechoic foci, or as single polyps containing cysts were limited to nonneoplastic polyps. On MRI hyperintense polyps on T1-weighted image were cholesterol polyps. An adenoma with high-grade dysplasia showed foci of decreased ADC values. We propose a checklist for polyp evaluation by targeted TAUS and a flowchart for radiological work-up of gallbladder polyps.

Conclusions: The presented checklist and flowchart could aid diagnostic work-up for gallbladder polyps compared to current routine ultrasound, by elimination of nonneoplastic polyps and ultimately improve treatment decision for patients with gallbladder polyps.

RÉSUMÉ

Contexte : La différenciation préopératoire entre les polypes de vésicule biliaire néoplasiques et non néoplasiques, et l'indication ultérieure de cholécystectomie reste un dilemme clinique. Le seuil actuel de 1 cm de taille pour une néoplasie n'est pas spécifique. L'objectif de cette étude était d'améliorer le diagnostic des polypes de la vésicule biliaire en utilisant les caractéristiques échographiques et IRM des polypes néoplasiques et non-néoplasiques.

Méthodologie : Une étude prospective et exploratoire a été menée auprès de patients subissant une cholécystectomie pour un ou plusieurs polypes de la vésicule biliaire. Les patients ont subi une échographie transabdominale ciblée (TAUS) et une IRM. Les résultats ont porté sur la sensibilité et la spécificité du diagnostic des polypes, ainsi que sur les caractéristiques radiologiques des types de polypes néoplasiques et non-néoplasiques. L'histopathologie après cholécystectomie a été utilisée comme norme de référence.

Résultats : L'histopathologie a mis en évidence des polypes de la vésicule biliaire chez 20 patients sur 77 (74%): 14 polypes de cholestérol, trois adénomatoses, deux adénomes et une hétérotopie gastrique. La sensibilité de l'identification des polypes était de 72%

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Ethical approval: This study was reviewed and approved by the Medical Ethical Committee of the academic hospital (2015–2042, NL55090.091.15).

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(TAUS de routine) et de 86% (TAUS ciblée et IRM). Les deux adénomes ont été identifiés comme néoplasiques sur la TAUS ciblée et l'IRM. La présentation échographique sous forme de polypes multiples pédiculés, soit hétérogènes, soit avec des foyers hyperéchogènes, ou sous forme de polypes uniques contenant des kystes, a été limitée aux polypes non néoplasiques. En IRM, les polypes hyperintenses sur l'image pondérée T1 étaient des polypes de cholestérol. Un adénome avec une dysplasie de haut grade a montré des foyers de valeurs ADC diminuées. Nous proposons une liste de contrôle pour l'évaluation des polypes par TAUS ciblé et un organigramme pour le bilan radiologique des polypes de la vésicule biliaire.

Conclusions : La liste de contrôle et l'organigramme présentés pourraient faciliter le diagnostic des polypes de la vésicule biliaire par rapport à l'échographie de routine actuelle, en éliminant les polypes non néoplasiques et en améliorant au final la décision de traitement pour les patients présentant des polypes de la vésicule biliaire.

Keywords: Ultrasonography; Magnetic resonance imaging; Gallbladder; Polyps

Introduction

Gallbladder (GB) polyps are classified as neoplastic (5–10%; including adenomas, carcinomas and other malignancies) or nonneoplastic (mainly cholesterol polyps or adenomyomatosis).[1] Since nonneoplastic GB polyps are considered harmless, cholecystectomy is only required for neoplastic polyps in order to prevent the development of GB cancer, a highly lethal tumour.[2,3]

The European guideline on management of GB polyps[4] recommends identification of GB polyps on transabdominal ultrasound (TAUS) as elevated immobile lesions of the GB wall, without acoustic shadowing, that project into the GB lumen. Cholecystectomy is recommended for polyps $\geq$1 cm, in view of elevated risk of neoplasia in these polyps.[5–8]

A recent Cochrane review reported good overall sensitivity (84%) of TAUS to detect GB polyps,[9] but showed large inter-study variations of 45–100%.[10–13] Additionally, the recommended cut-off $\geq$ 1 cm is incorrect regarding neoplastic nature of the polyp in approximately one third of patients, attributing to many unnecessary cholecystectomies.[14] Previous studies have suggested that to improve preoperative polyp type differentiation, TAUS can be used to help identify detailed sonographic features of gallbladder polyps.[15–22] Interestingly, the European guidelines do not advise on which sonographic features should be evaluated to properly identify and differentiate GB polyps, except for exclusion of definite nonneoplastic polyp based on "comet tail" artefacts, indicating some adenomyomatosis or cholesterol polyp cases.[4] Targeted TAUS with structured, detailed evaluation of GB polyp characteristics, could potentially increase preoperative differentiation of neoplastic and nonneoplastic polyps and improve patient selection for surgery.

Other imaging modalities, such as computed tomography (CT) and endoscopic ultrasonography (EUS) have been suggested as an added value in the diagnostic work-up. However, these modalities do not provide the desired diagnostic accuracy and have not been incorporated in routine clinical practice.[17–19,23–26] High b-value diffusion-weighted magnetic resonance imaging (DWI-MRI) has been able to differentiate GB cancer from benign GB polyps based on differences in signal intensity on DWI and apparent diffusion coefficient (ADC), and morphological characteristics.[27–30] No previous studies have analysed the value of MRI in the differentiation of polyp types.

The aim of this prospective, exploratory study was to improve diagnostic work-up for gallbladder polyps using sonographic and MRI characteristics of neoplastic and non-neoplastic polyps.

Methods

Study design and patient inclusion

This prospective, exploratory study was performed at a single academic hospital in the Netherlands. All patients in a two year period (May 2016 to March 2018) of $\geq$18 years of age at the surgical outpatient clinic with gallbladder polyps on routine TAUS were eligible for participation, if they were considered to undergo cholecystectomy. The latter being essential as histopathology was used as reference standard. Exclusion criteria were; known pregnancy, renal dysfunction (defined as Chronic Kidney Disease stage 4 or higher (MDRD-GFR < 30 ml/min/1.73m2), haemo- or peritoneal dialysis, or a phase of acute renal dysfunction, and inability to undergo MRI (due to known allergy to gadolinium-based contrast agent, claustrophobia or non MRI-compatible implants). Written informed consent was obtained. The reports of the routine TAUS were retrieved from patients' medical file for all included patients.

Upon inclusion, patients underwent a standardized targeted TAUS examination followed by a MRI on the same day in the study institute. Subsequent cholecystectomy could either be performed at the academic hospital or a referring non-academic hospital. If results from the targeted TAUS or MRI altered the indication for cholecystectomy, a shared decision with the patient was made whether to proceed with the planned cholecystectomy (e.g. because of gallstones or abdominal symptoms). Patients who did not undergo cholecystectomy, were excluded. This study was reviewed and approved by the Medical Ethical Committee of the academic hospital (2015–2042, NL55090.091.15).

Targeted transabdominal ultrasound examination and image analysis

All targeted TAUS examinations were performed after 4 h of fasting. The examination was started using a low fre-

quency transducer (1.9–6 Mhz) and additionally a higher frequency transducer (7–12 Mhz) if possible (e.g. because of patient habitus). The examinations were done with the patient in supine position and in left lateral decubitus position. Additional scans in other positions were made if necessary to assess lesion mobility. Identified lesions were evaluated according pre-set criteria (Supplementary Table 1). Polyps were defined as immobile pedunculated or sessile lesions of the GB wall without acoustic shadowing, projecting into the lumen of the GB. Based on available literature at time of study conception,[17–19] a table with sonographic characteristics of main neoplastic and nonneoplastic polyp types was composed (Supplementary Table 2). Diagnosis of polyp type on targeted TAUS was based on the combination of sonographic characteristics from this table. Targeted TAUS was performed and evaluated by one radiologist with 17 years of experience in ultrasonography of the upper abdomen, without knowledge of the MRI results or histopathological diagnosis.

MRI protocol and image analysis

Patients underwent MRI examination using a 3.0 T system (Magnetom Skyra, Siemens Healthcare, Erlangen, Germany) after a minimum of 4 h of fasting. An anterior body matrix coil/torso phased array coil (16/9 channel) and a posterior phased array coil/spine coil (16/9 channel) were used in all MR sequences. Patients were imaged in the supine position. A routine liver MRI-scan with DWI was performed (Field of view 430 mm), containing the following sequences: axial and coronal T2 weighted, axial T1 weighted pre- and post-contrast injection, axial diffusion weighted imaging (b-value 50, 400, 800 s/mm2). Fifteen ml of contrast agent (gadoterate meglumine 0.5 mmol/mL (Gd-DOTA, Dotarem) was injected in an antecubital vein at 2.5 ml/s with a saline flush (NaCl 0.9%) of 20 ml at 2.5 ml/s using a pump injector (Mallinckrodt Optistar Elite). Patients were also administered butylscopolamine (20 mg intravenously), to minimize bowel movements during scanning.

All MRI images were reviewed by the same radiologist who evaluated the TAUS images. Identified lesions were evaluated according pre-set criteria (Supplementary Table 3). ADC maps were calculated based on the available b-values on a voxel-by-voxel basis using the software supplied with the MR unit (Syngo VD; Siemens). The Region of Interest (ROI) was selected manually because of the small nature of the lesions and was placed to cover the largest possible area of the polyp in ADC maps. In case the smallest ROI was larger than the polyp, no ADC values were calculated. Images that were not interpretable due to motion or other artefacts were excluded from analysis. Differential diagnosis of the GB polyps was based on size, number, shape, surface and signal intensities of the polyps with reference to Supplementary Table 2, and expert opinion. Image evaluation was performed without knowledge of the histopathological diagnosis.

Reference standard

Histopathological diagnosis of GB polyp was used as reference standard. Routine histopathological analysis of the GB specimens was performed, and macroscopic photos of the gallbladder mucosa were taken. Two gastrointestinal pathologists of the academic hospital (with over ten years of experience) microscopically revised the GB polyps and determined polyp type. All histopathological analyses and (re)-evaluations were done without knowledge of the imaging results.

Outcomes and statistical analysis

The study outcomes were the sensitivity and specificity of targeted TAUS and MRI for diagnosis of gallbladder polyps and the imaging characteristics of the different types of GB polyps on targeted TAUS and MRI. Characteristics were reported at patient level per polyp type. If multiple presentations of the same polyp type were present within one patient, the most prominent presentation was used for analysis. Echogenicity on targeted TAUS was expressed compared to GB wall. Specific patterns of signal intensities (at b = 800 s/mm2 for DWI) or ADC-values within GB polyps were described. Signal intensities on MRI were expressed as hyper-, iso- or hypointense compared to signal intensity of the liver. Consistencies and inconsistencies of sonographic characteristics on targeted TAUS compared to literature, as shown in Supplementary Table 2, were described.

Sonographic characteristics on targeted TAUS that were present in only one histopathological polyp type (e.g. cholesterol polyp or adenoma), and consistent with previous literature were identified. MRI characteristics seen in only one histopathological polyp type were also identified. Based on these characteristics a flowchart for radiological work-up and diagnosis of GB polyps was composed.

Results

Patient inclusion and polyp diagnosis

A total of 50 patients were approached for participation in the study. Eleven patients declined to participate, nine were excluded, and three could not participate due to logistic reasons. A total of 27 patients (mean age 55 years (SD 13.3), 48% female) could be included for analysis. Full patient inclusion details are depicted in Fig. 1.

On histopathological analysis 20 patients (74%) had a gallbladder polyp. Routine TAUS had a sensitivity for polyp diagnosis of 72%, and showed seven false positive diagnoses. In the two false negative diagnoses routine TAUS mistook gallstones for gallbladder polyps, and missed a concomitant polypoid lesion in the gallbladder. Sensitivity and specificity of targeted TAUS and MRI for polyp diagnosis were identical, respectively 86% and 67%. The three false positive diagnoses were seen in patients with histopathologically mucosal folding, a single gallstone stuck to GB wall, and cholesterol agglomerates. The two false negative diagnoses

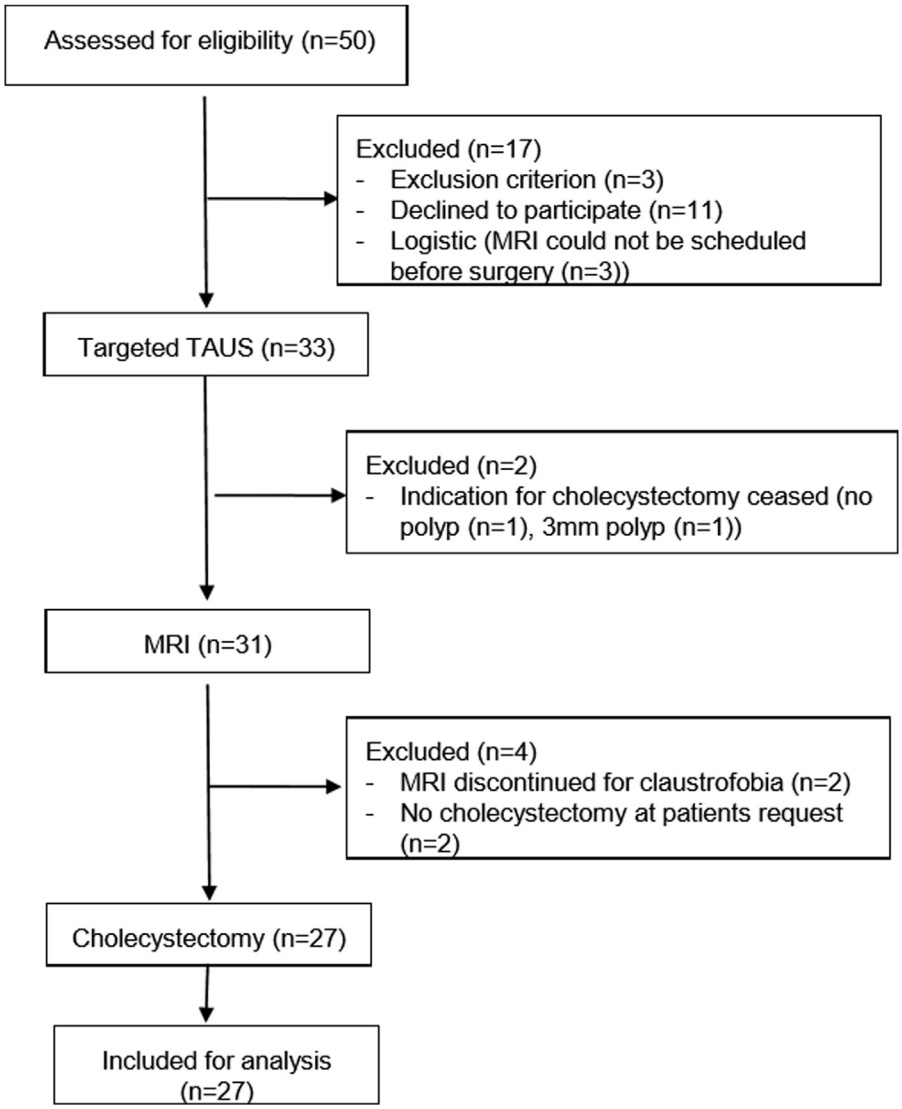

Fig. 1. Patient inclusion flow-diagram.

included a 2 mm polyp and one polyp overshadowed by concomitant agglomerates of microlithiasis.

The 20 patients with gallbladder polyps were included for further analysis; 14 patients with cholesterol polyps (52%), three with adenomyomatosis (11%), two with an adenoma (7%, one high- and one low-grade dysplasia) and one with gastric heterotopia (4%).

Targeted TAUS

All identified sonographic characteristics of different polyp types and correspondence of these characteristics with characteristics from literature are depicted in Table 1. Adenomas presented as a single pedunculated polyp >10 mm with a homogeneous aspect, with either a smooth or nodular surface. Adenomyomatosis was depicted as a focal hypoechogenic, smooth, sessile lesion >10 mm, and could contain cysts or hyperechoic foci. One focal adenomyomatosis was not visualised on targeted TAUS since this GB also contained multiple agglomerations of microlithiasis overshadowing the adenomyomatosis, and therefore not incorporated in Table 1 or the results.

The majority of cholesterol polyps presented as multiple pedunculated lesions <10 mm, but larger, single and sessile cholesterol polyps were seen as well. The surface of larger polyps was predominantly irregular whereas smaller polyps appeared smoother. Internal pattern of cholesterol polyps on targeted TAUS was in 38% homogeneous (hypo- or isoechogenic (60%) (Fig. 2A) or hyperechogenic (40%)), in 8% heterogeneous (Fig. 2B) and in 23% with hyperechoic foci (Fig. 2A). A combination of different internal patterns in one gallbladder (Fig. 2A) was seen in 31% of cholesterol polyps. One cholesterol polyp (2 mm) was not seen on targeted TAUS and therefore not incorporated in Table 1 or the results; only two concurrent gallstones were illustrated in this patient.

Gastric heterotopia presented as a single, pedunculated, smooth polyp >10 mm with a heterogeneous iso/

Table 1
Sonographic polyp characteristics literature vs present study.

Characteristic	Cholesterol polyp (n = 13)		Adenomyomatosis (n = 2)		Adenoma (n = 2)	
	Literature	Present study	Literature	Present study	Literature	Present study
Number						
Single		3	+	2	+	2
Multiple	+	10				
Size						
<10 mm	+	10	+			
≥10 mm		3	+	2	+	2
Echogenicity						
Hypo echogenic		6		2		1
Iso echogenic	+	5			+	1
Hyper echogenic	+	2				
Internal structure						
Homogeneous		7		1	+	2
Heterogeneous	+	1		1		
Hyperechoic foci	+	5		1		
Microcysts		1	+	1		
Shape						
Pedunculated	+	10			+	2
Sessile		2	+	2		
Surface						
Smooth		5	+	2	+	1
Irregular	+	6	+		+	
Nodular		1				1
GB wall						
Disrupted		1				1

Left column per polyp type: + indicated main sonographic polyp characteristics from literature. Right column per polyp type: numbers of patients with sonographic characteristic in present study.
One cholesterol polyp and one adenomyomatosis were not visualised on targeted TAUS and therefore not included in this table.

hyperechogenic internal pattern containing microcysts (not incorporated in Table 1). Because targeted TAUS described cysts the gastric heterotopia was estimated to be adenomyomatosis. Histopathological microscopic analysis showed strongly dilated glands within the polyp, mimicking cysts (Fig. 3).

Both neoplastic lesions were specified as such by targeted TAUS: the high-grade adenoma was correctly diagnosed as adenoma. The low-grade adenoma was diagnosed as carcinoma, due to suspected GB wall intrusion. Four nonneoplastic cholesterol polyps (all close to or >10 mm) were mistaken for adenomas. Three were pedunculated hypoechogenic polyps (one with cysts and one with hyperechoic foci), and one was a sessile homogeneous hyperechogenic polyp.

Additionally, one irregular 11 mm heterogeneous hypoechogenic cholesterol polyp and one adenomyomatosis were mistaken for an inflammatory polyp. The adenomyomatosis was part of a phrygian cap (i.e. congenital deformity of the gallbladder caused by folding of the fundus on the body) and therefore more difficult to characterise (Fig. 4).

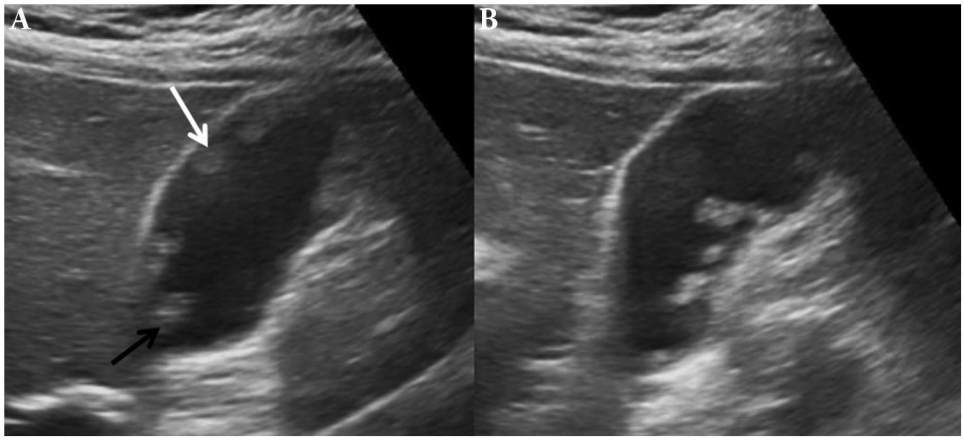

Fig. 2. Different sonographic presentations of cholesterol polyps (A). Hypoechogenic homogeneous polyps (white arrow) and polyps with hyperechoic foci (black arrow) within one patient (B). Heterogenous polyps.

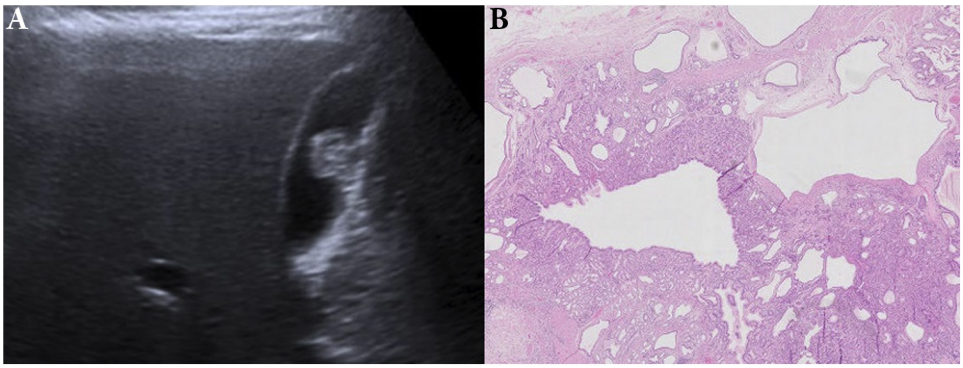

Fig. 3. Polyp based on gastric heterotopia with dilated glands mimicking cysts (A). Sonographic image, broad-based polyp with small cysts (B). Histopathological image, showing dilated glands mimicking cysts.

MRI

All MRI characteristics of the different polyp types are shown in Table 2. For none of the polyps reliable ADC values could be calculated. Adenomas presented as a single pedunculated nodular polyp >10 mm. High-grade dysplasia was consistent with a heterogeneous internal structure while low-grade dysplasia was homogeneous. One adenoma was not seen on T1W until after administration of intravenous contrast agent, the MRI study on the other adenoma lacked T1W series. The GB wall in the high-grade dysplasia polyp looked disrupted at the level of the vascular stem. Both adenomas showed a ringlike pattern on DWI (Figs. 5A and C). The low-grade adenoma showed a similar ringlike pattern on ADC (Fig. 5B) and the high-grade adenoma had foci with decreased ADC values (Fig. 5D).

Adenomyomatosis presented as a smooth sessile lesions >10 mm, either with cysts or an overall heterogeneous aspect. In one adenomyomatosis a ringlike pattern was seen on DWI (Fig. 5E) with an overall decreased ADC value (Fig. 5F). Artefacts caused by air in the colon and patient motion prohibited proper analysis of one adenomyomatosis case on pre-contrast T1W and DWI. The third case of adenomyomatosis was seen as a single cyst in the fundus of the GB, and no further characteristics of this lesion were depicted.

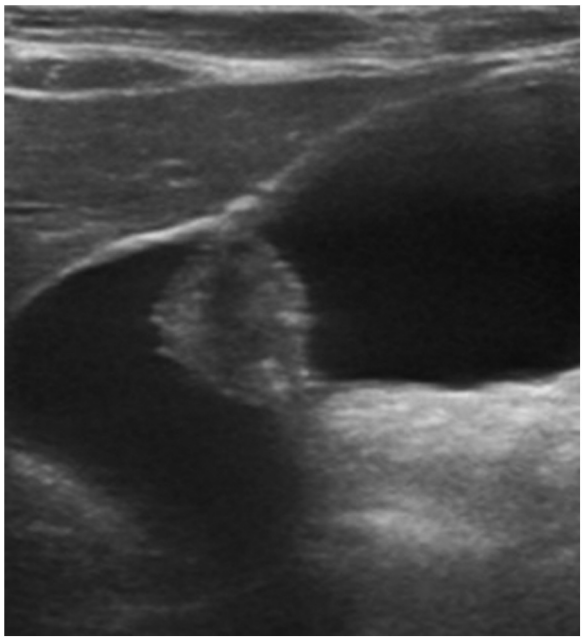

Fig. 4. Adenomyomatosis as part of Phrygian cap.

In small cholesterol polyps (<5 mm) internal pattern, shape and surface of the polyps on DWI could not be established. For evaluable cholesterol polyps, the majority consisted of multiple pedunculated polyps <10 mm with a smooth surface and homogeneous internal pattern. Other characteristics showed considerable inter- and intra-patient variety. Interestingly, only seven (out of 13) polyps were visualised on T1W of which four (57%) were hyperintense in signal intensity. No other polyp type showed hyperintensity on T1W.

Gastric heterotopia was seen as a single, sessile, smooth polyp >10 mm, containing cystlike structures on T2W. The polyp had a ringlike pattern on DWI and ADC: a hyperintense centre with hypointense ring on DWI, and decreased central ADC value with increased value in the outer ring.

On MRI both adenomas were indicated as neoplastic: the high-grade as adenoma and the low-grade adenoma as carcinoma due to a "rugged" nodular aspect. Two large cholesterol polyps were mistaken for adenomas and in five patients polyp type could not be specified due to small size (<5 mm) or artefacts. As on TAUS the gastric heterotopia was estimated to be adenomyomatosis because of the cysts and in one patient a tiny cholesterol polyp (2 mm) was not seen.

Flowchart

On targeted TAUS and in literature (Table 1), multiple, pedunculated polyps, either heterogeneous or with hyperechoic foci were only seen in cholesterol polyps. Single polyps containing cysts were only seen in nonneoplastic polyps (mostly adenomyomatosis). Especially single homogeneous polyps represented both neoplastic and nonneoplastic polyp types. On MRI, polyps showing high signal intensity on T1W were cholesterol polyps, and cysts on T2W were only seen in nonneoplastic polyp types. Foci of decreased ADC were only present in the adenoma with high-grade dysplasia.

Table 2
MRI characteristics per polyp type.

	Cholesterol polyp (n = 13)	Adenomyomatosis (n = 3)	Adenoma (n = 2)
Number of polyps			
Single	3	3	2
Multiple	10		
Size (mm)			
<5	6		
5–10	6	1	
≥10	1	2	2
Internal pattern			
Homogeneous	9	1	1
Heterogeneous	1	1	1
Specific internal features			
Hyperintense foci			
Microcysts		2	
Shape			
Pedunculated	10		2
Sessile	1	2	
Surface			
Smooth	8	2	
Irregular	2		
Nodular	1		2
GB wall			
Disrupted			1
T1W with FS			
Hyperintense	4		
Isointense	1		
Hypointense	2	1	
T1W contrast enhancement	11	2	1
Early arterial contrast, decrease venous phase	1		
Wash-in with plateau	6	2	1
Slowly increasing enhancement	4		
T2W			
Hyperintense	2		
Isointense	9	2	2
Hypointense	2		
DWI			
Hyperintense			
Isointense	6		
Hypointense	2		
Ringlike pattern	3[a]	1[b]	2[b]
ADC			
Value	Decreased (n = 2)	Decreased (n = 1)	Decreased foci (n = 1)
Ringlike pattern	2[c]		1[c]

[a] Hyperintense centre, iso/hypointense ring.
[b] Hyperintense centre, hypointense ring.
[c] ADC value: low centre and high ring.

Based on these polyp characteristics from targeted TAUS and MRI, the flowchart in Fig. 6 was composed.

Discussion

This study indicates that targeted TAUS can improve diagnosis and characterisation of GB polyps compared to routine TAUS by assessing specific sonographic characteristics of GB polyps. Our study suggests that MRI can be of added value for polyp evaluation in large polyps (>10 mm) without non-neoplastic characteristics on targeted TAUS. Ultimately, we provide a checklist for polyp evaluation by targeted TAUS, and a flowchart that may be used for radiological work-up and analysis gallbladder polyps.

In this prospective, exploratory cohort the sensitivity of targeted TAUS was comparable with results of a recent Cochrane review[9] (86% vs 84%) and substantially improved compared to routine TAUS (from 72% to 86%). Specificity of targeted TAUS was lower compared to the Cochrane review (67% vs 96%) due to a few false positive diagnoses in our small cohort. Besides less false positive diagnoses by targeted TAUS compared to routine TAUS in our study cohort (three vs seven), it also prevented an unnecessary cholecystectomy (and thereby participation in this study) in two patients; one patient did not possess a GB polyp and the other patient had a 3 mm sized polyp. Still, targeted TAUS had a few flaws in polyp diagnosis, mainly in patients with concomitant gallstones.

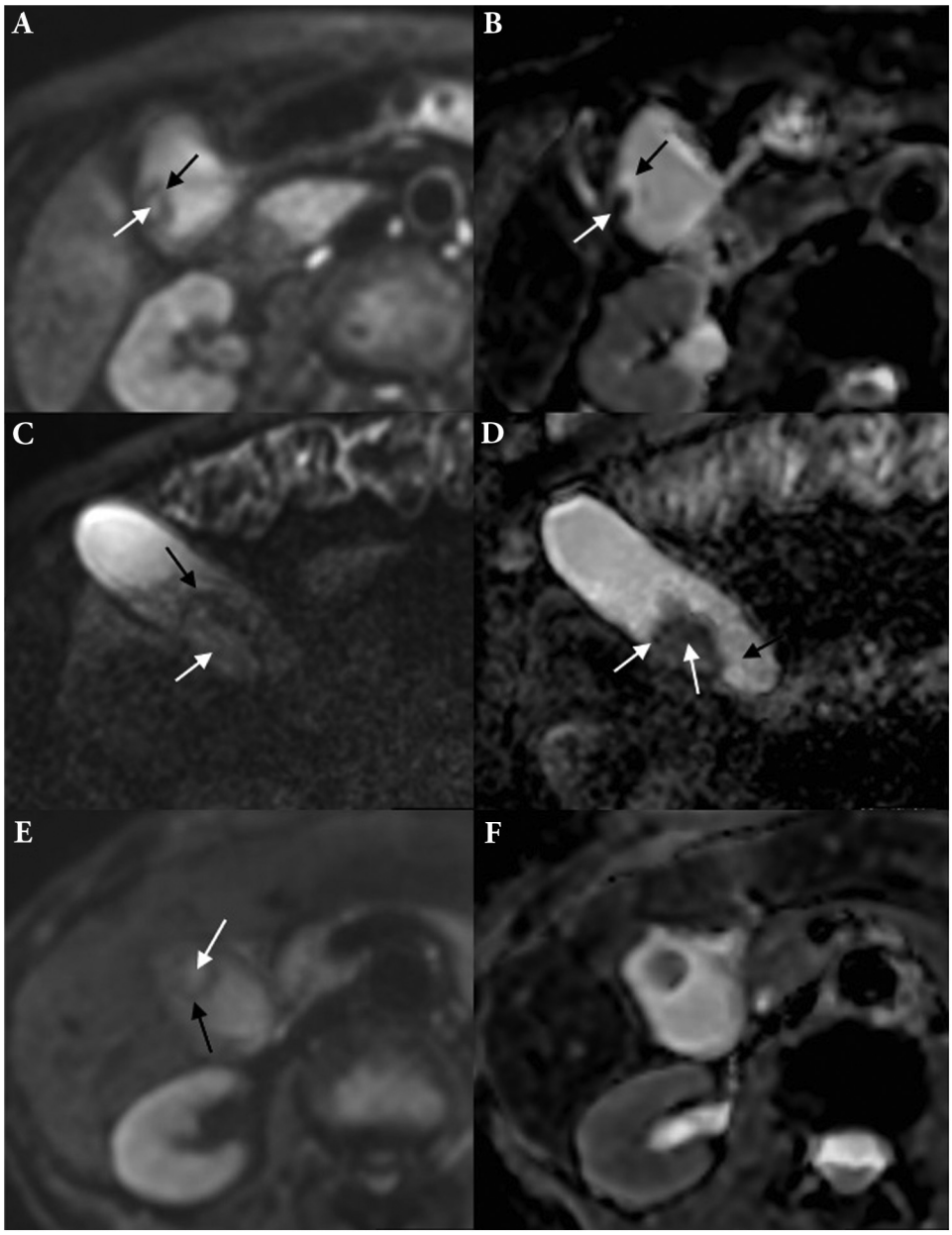

Fig. 5. DWI and ADC pattern Three cases, left column DWI and right column ADC image (A). Adenoma showing hyperintense centre (white arrow) with hypointense ring (black arrow) on DWI (B). Adenoma showing decreased value in centre (white arrow), and a ring with increased value (black arrow) on ADC (C). Adenoma with high grade dysplasia showing hyperintense centre (white arrow) with hypointense ring (black arrow) on DWI (D). Adenoma with high grade dysplasia showing foci with decreased value (white arrow) and outer ring with increased value making the polyp seem smaller (black arrow) on ADC (E). Adenomyomatosis showing hyperintense centre (white arrow) with hypointense ring (black arrow) on DWI (F). Adenomyomatosis showing decreased value on ADC.

On routine TAUS polyp type was determined in only five patients (data not shown). The lack of specifying polyp type on TAUS is common in routine practice,[31] possibly due to the lack of detailed description of polyp characteristics. The current European guidelines, only advise evaluation of ''comet tail'' artefacts to exclude definite nonneoplastic polyps.[4] Literature describes ''comet tail'' artefacts or cysts on ultrasound as the most characteristic feature of adenomyomatosis.[17–19,32,33] Our results indicate that these features may be missing from adenomyomatosis, and that microcysts may be detected in other types of nonneoplastic polyps. Gastric heterotopia, a rare type of polyp which has only been reported in 34 patients in literature,[34] mimicked cysts on both TAUS and MRI which were dilated glands on microscopy, and one cholesterol polyp demonstrated cysts on targeted TAUS.

Literature has also shown other sonographic characteristics that can improve polyp differentiation, which are not incorporated into current guidelines.[15–22] With detailed polyp evaluation by targeted TAUS incorporating such characteristics (see checklist in Fig. 6) polyp type could be specified in all polyps, and correctly identified both neoplastic polyps. The sonographic characteristics of adenomas on targeted TAUS were

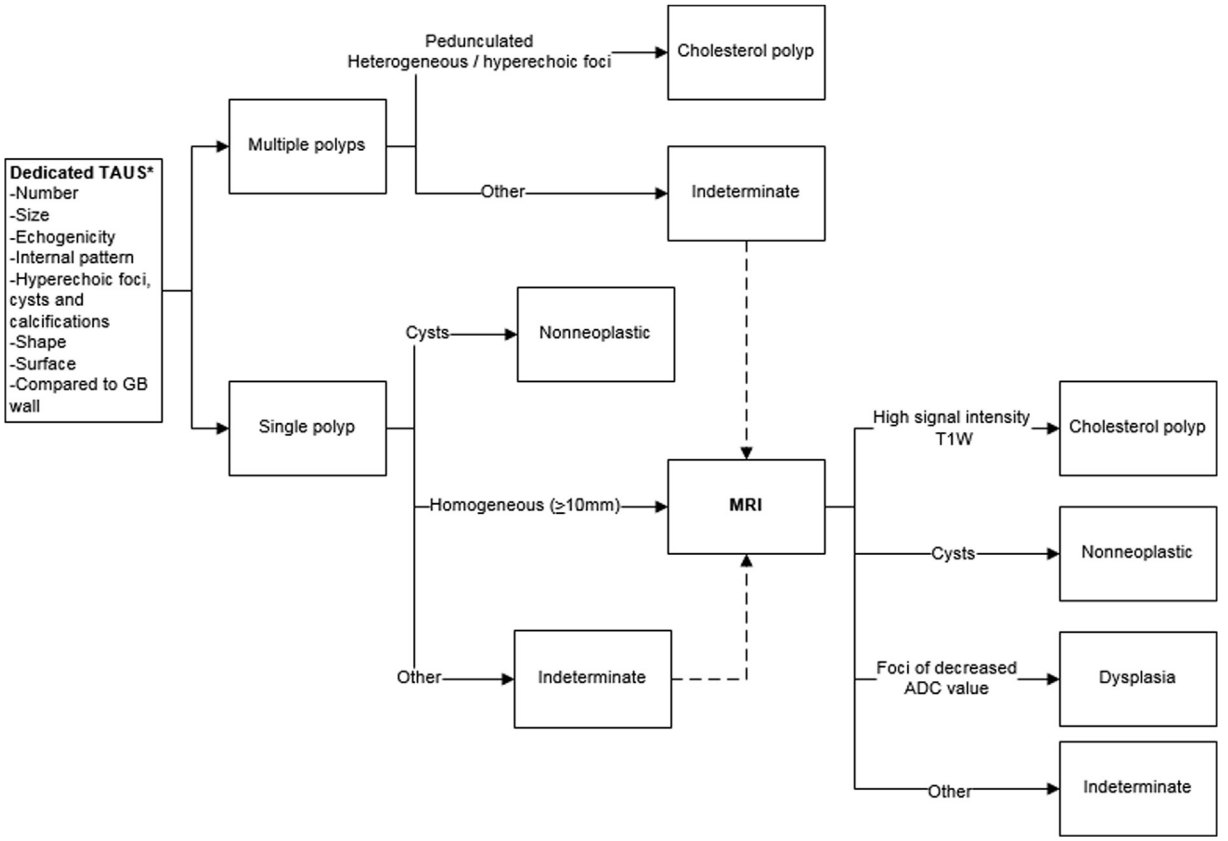

Fig. 6. Checklist for targeted TAUS and flowchart for polyp analysis *Performed by an experienced ultrasonographer (e.g. HPB radiologist). This checklist for targeted ultrasound contains a summary of the pre-set criteria for polyp evaluation, as presented in Supplementary Table 2. MRI is mainly useful in single homogeneous polyps, as they were seen in neoplastic and nonneoplastic types, and especially for polyps ≥10 mm, as small polyps were difficult to visualize on MRI due to the size of the voxels and (motion) artefacts. MRI in other and smaller polyps could be contemplated. Dotted line: to be contemplated.

concordant with the literature.[17–19] As in literature, cholesterol polyps were small irregular pedunculated polyps, with a heterogeneous pattern or hyperechoic foci. However we found that cholesterol polyps may also be homogeneous (iso-, hypo-, or hyperechogenic) polyps, smooth or sessile, and that multiple presentations of cholesterol polyps could be seen within one patient. In polyps not displaying distinct sonographic features, specifying polyp type remained difficult, illustrating the shortcomings in differentiation of gallbladder polyps.

Previous studies on MRI of gallbladder polyps have focused on differentiating malignant from benign lesions, irrespective of polyp subtype. These studies illustrated higher signal intensities on DWI and decreased ADC-value in malignant polyps compared to benign lesions.[27–30] A pearl necklace sign[1] on MRI suggests adenomyomatosis.[32,33] In line with the literature, we found foci of decreased ADC-value in one adenoma with foci of high-grade dysplasia. Cysts were illustrated in adenomyomatosis. We further found that high signal intensity on T1W was unique to cholesterol polyps, probably due to the accumulation of cholesterol. The variation in the amount of cholesterol or degree of crystallization within polyps, could explain the T1W variation. Alternatively, richness of cholesterol in the bile, which has the same signal intensity as the polyps, could mask the presence of cholesterol polyps.

Interestingly, on MRI several polyps of different polyp types demonstrated two concentric rings of high and low signal intensity on DWI and ADC. No histopathological substrate could be found for these patterns. We hypothesize that since these outer rings were iso/hypointense on DWI with an increased value on ADC, this reflects the deposit of bile or cholesterol covering the polyp.

Based on the present exploratory study we suggest a checklist for targeted TAUS (Fig. 6) to improve GB polyp evaluation in clinical practice. Considering the low prevalence of GB polyps, ideally such TAUS should be performed by an experienced ultrasonographer (e.g. HPB radiologist). Additionally, we propose a flowchart to improve diagnostic

[1] Small, round, high-intensity foci caused by contrast-filled Rokitansky Archoff sinuses (i.e. intramural diverticula).

work-up for gallbladder polyps, better define polyp type and aid treatment decision. Polyps with typical characteristics of cholesterol polyps or cysts on targeted TAUS or MRI do not require cholecystectomy or follow-up. Foci of decreased ADC value on MRI could indicate high-grade dysplasia, wherefore cholecystectomy is advised. All other polyps cannot be characterised yet, and should be treated according current guidelines. Due to the exploratory nature of this study, the proposed checklist and flowchart will be evaluated in a larger long-term prospective cohort study, to exclude variations due to technical settings and inter-observer variability. Interruption of the GB wall, which seemed variably present in different polyp types on targeted TAUS, and vascularity in the polyps are to be evaluated in that study as well. The latter was not yet systematically scored in the current exploratory study, and therefore not incorporated in the results, but vascularity was seen in the high grade dysplasia case on both targeted TAUS (by colour doppler) and MRI, in line with literature suggesting vascular flow as major indication for neoplasia of GB polyps.[15,35]

A large cohort of GB polyps evaluated by targeted TAUS could also further enable identification of new sonographic patterns of neoplastic and nonneoplastic polyp types, also including more sophisticated ultrasound techniques such as elastography and shear wave imaging, or superb microvascular imaging, which are currently used to differentiate benign and malignant lesions in the liver, breast and thyroid.[36–40] Regarding MRI, a more targeted MRI protocol should be considered to reduce artefacts and improve polyp visualization, to enable identification of more detailed MRI characteristics of GB polyps. For instance by adding additional b-values for DWI, incorporating breathing correction or improving bowel preparation. All future studies should include targeted histopathological evaluation of polyps, to ensure an optimal reference standard for the imaging modalities.

Strengths of our study include image evaluation according pre-set criteria, without knowledge of the histopathological diagnosis. Potential study limitations include image interpretation by a single radiologist. Image interpretation by a single radiologist could have introduced observer bias when evaluating accuracy of two separate modalities. Selection bias may have also been introduced by including only patients who underwent cholecystectomy, although this was inevitable because of the need for histopathology as reference standard. Other limitations include the small cohort size and lack of malignant polyps. These limitations are inherent to the exploratory nature of this study where we included all eligible patients in two years and the low prevalence of GB polyps.[41–44] We therefore only included polyp characteristics in our flowchart that were concurrent with literature. Finally, routine macroscopic histopathological analysis might have resulted in less detailed histopathological information for some radiological-pathological correlations.

In conclusion, this study illustrated improvement of radiological polyp evaluation by targeted TAUS compared to current routine TAUS, using a checklist of sonographic characteristics. In specific cases MRI can be of added value to differentiate neoplastic from nonneoplastic polyps. The presented checklist and flowchart could aid radiological polyp evaluation, diagnosis of nonneoplastic polyps and, ultimately, treatment decision for patients with GB polyps.

Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jmir.2020.12.003.

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