Supplementary Material for the 2024 Clinical Practice Guideline Update by the

Infectious Diseases Society of America on Complicated Intra-abdominal Infections:

Diagnostic Imaging of Suspected Acute Cholecystitis and Acute Cholangitis in Adults,

Children, and Pregnant People

Table of Contents

METHODS

<u>Literature Search</u>

Eligibility Criteria

TABLES AND FIGURES

<u>Supplementary Table 1: Characteristics of included studies</u>

Supplementary Table 2: Risk of bias assessment

<u>Supplementary Table 3: GRADE Evidence Profile: Should US vs. CT be used to diagnose acute</u> cholecystitis in patients with suspected cholecystitis?

<u>Supplementary Table 4: GRADE Evidence Profile: Should MRI/MRCP vs. HIDA be used to diagnose</u> acute cholecystitis in patients with suspected acute cholecystitis and inconclusive US and CT?

<u>Supplementary Table 5: GRADE Evidence Profile: Should US vs. CT be used to diagnose acute</u> cholangitis in patients with suspected acute cholangitis?

Supplementary Table 6: US, then HIDA for adults with suspected acute cholecystitis

Supplementary Table 7: Imaging in pts with diagnosed acute cholecystitis

<u>Supplementary Figure 1: Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology</u>

Supplementary Figure 2: Initial US for adults with suspected acute cholecystitis

<u>Supplementary Figure 3: Initial CT for adults with suspected acute cholecystitis</u>

Supplementary Figure 4: Initial HIDA for adults with suspected acute cholecystitis

REFERENCES

METHODS

Panel formation and conflicts of interest

The chair of the guideline panel was selected by the leadership of IDSA. Fifteen additional panelists comprised the full panel. The panel included clinicians with expertise in infectious diseases, pediatric infectious diseases, surgery, emergency medicine, microbiology, and pharmacology. Panelists were diverse in gender, geographic distribution, and years of clinical experience. Guideline methodologists oversaw all methodological aspects of the guideline development and identified and summarized the

scientific evidence for each clinical question. IDSA staff oversaw all administrative and logistic issues related to the guideline panel.

All members of the expert panel complied with the IDSA policy on conflict of interest (COI), which requires disclosure of any financial, intellectual, or other interest that might be construed as constituting an actual, potential, or apparent conflict. Evaluation of such relationships as potential conflicts of interest was determined by a review process which included assessment by the Standards and Practice Guideline Committee (SPGC) Chair, the SPGC liaison to the Guideline panel and the Board of Directors liaison to the SPGC, and if necessary, the Conflicts of Interests Task Force of the Board. This assessment of disclosed relationships for possible COI was based on the relative weight of the financial relationship (i.e., monetary amount) and the relevance of the relationship (i.e., the degree to which an independent observer might reasonably interpret an association as related to the topic or recommendation of consideration). The reader of these guidelines should be mindful of this when the list of disclosures is reviewed. See the Notes section at the end of this guideline for the disclosures reported to IDSA.

Practice recommendations

Clinical Practice Guidelines are statements that include recommendations intended to optimize patient care by assisting practitioners and patients in making shared decisions about appropriate health care for specific clinical circumstances. These are informed by a systematic review of evidence and an assessment of the benefits and harms of alternative care options [IOM 2011]. The "IDSA Handbook on Clinical Practice Guideline Development" provides more detailed information on the processes followed throughout the development of this guideline [IDSA CPG Handbook].

Review and approval process

Feedback was obtained from five external individual peer expert reviewers as well as the endorsing organizations. The IDSA Standards and Practice Guidelines Subcommittee (SPGS) and Board of Directors reviewed and approved the guideline prior to publication.

Process for updating

IDSA guidelines are regularly reviewed for currency. The need for updates to the guideline is determined by a scan of current literature and the likelihood that any new data would impact the recommendations. Any changes to the guideline will be submitted for review and approval to the appropriate Committees and Board of IDSA.

Clinical questions

Each clinical question was formatted according to the PICO style: Patient/Population (P), Intervention/Indicator (I), Comparator/Control (C), Outcome (O). For each PICO question, outcomes of interest were identified a priori and rated for their relative importance for decision-making.

Literature search

A medical librarian designed the literature searches for Ovid Medline, Embase, and Cochrane Library, including appropriate MeSH terms, where applicable. Searches were limited to studies published in English. The initial formal literature searches were performed in July to November 2018, and updated literature searches were conducted in March 2021 and October 2022. To supplement the electronic searches, reference lists of related articles and guidelines were reviewed for relevance.

OVID MEDLINE

#1 exp Tomography, X-Ray Computed/

```
#2 exp Ultrasonography/
        #3 (ultraso* or ultra-so* or echograph* or echo-graph* or echotomograph* or echoto-
        mograph* or sonograph* or sono-graph* or echocardiograph* or echo-cardiograph* or
        echoencephalograph* or echo-encephalograph* or endosonograph* or endo-sonograph*).tw,kf.
        #4 ((tomodensitometr* or (ct or comput* or cat or electron)) adj3 (cine or scan* or xray* or x-
        ray* or tomograph*)).tw,kf.
       #5 (HIDA or ((hepatobiliar* or hepato-biliar*) adj2 (scan* or imag*))).tw,kf.
       #6 exp Magnetic Resonance Imaging/
       #7 (MRI or MRIs or MRCP or MRCPs or (magn* adj3 resonanc*) or ((magn* or MR or MRs) adj2
        (imaging* or tomograph* or tomo-graph*))).tw,kf,jw.
       #8 or/1-7
        #9 exp Cholecystitis/
       #10 exp Cholangitis/
       #11 (cholangit* or (cholecystit* or ((gallbladder* or gall-bladder*) adj1 (infection* or
        empyema*)))).tw,kf.
       #12 or/9-11
       #13 8 and 12
       #14 Animals/ not (Animals/ and Humans/)
       #15 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or
        monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or
        rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).ti,kf.
        #16 13 not (14 or 15)
       #17 limit 16 to english
       #18 limit 17 to yr="2021 -Current"
       #19 remove duplicates from 18
EMBASE
       #1 exp x-ray computed tomography/
       #2 exp echography/
       #3 (ultraso* or ultra-so* or echograph* or echo-graph* or echotomograph* or echoto-
        mograph* or sonograph* or sono-graph* or echocardiograph* or echo-cardiograph* or
        echoencephalograph* or echo-encephalograph* or endosonograph* or endo-
       sonograph*).tw,kw,kf.
        #4 ((tomodensitometr* or (ct or comput* or cat or electron)) adj3 (cine or scan* or xray* or x-
        ray* or tomograph*)).tw,kw,kf.
       #5 (HIDA or ((hepatobiliar* or hepato-biliar*) adj2 (scan* or imag*))).tw,kw,kf.
       #6 exp nuclear magnetic resonance imaging/
```

```
#7 (MRI or MRIs or MRCP or MRCPs or (magn* adj3 resonanc*) or ((magn* or MR or MRs) adj2
        (imaging* or tomograph* or tomo-graph*))).tw,kw,jx,kf.
       #8 or/1-7
       #9 exp cholecystitis/
       #10 exp cholangitis/
       #11 (cholangit* or (cholecystit* or ((gallbladder* or gall-bladder*) adj1 (infection* or
       empyema*)))).tw,kw,kf.
       #12 or/9-11
       #13 8 and 12
       #14 (exp animal/ or exp juvenile animal/ or adult animal/ or animal cell/ or animal experiment/
        or animal model/ or animal tissue/ or nonhuman/) not human/
       #15 ((animal or animals or canine* or cat or cats or dog or dogs or feline or hamster* or mice or
        monkey or monkeys or mouse or murine or pig or pigs or piglet* or porcine or primate* or
        rabbit* or rats or rat or rodent* or sheep*) not (human* or patient*)).ti,kw,kf.
       #16 13 not (14 or 15)
       #17 limit 16 to english
       #18 limit 17 to yr="2021 -Current"
       #19 remove duplicates from 18
       #20 limit 19 to (conference abstract or conference paper or "conference review")
       #25 23 not 24
COCHRANE (WILEY)
       #1 (ultraso* or ultra-so* or echograph* or echo-graph* or echotomograph* or echoto-
        mograph* or sonograph* or sono-graph* or echocardiograph* or echo-cardiograph* or
        echoencephalograph* or echo-encephalograph* or endosonograph* or endo-
       sonograph*):ti,ab,kw
       #2 ((tomodensitometr* or (ct or comput* or cat or electron)) NEAR/3 (cine or scan* or xray* or
       x-ray* or tomograph*)):ti,ab,kw
       #3 (HIDA or ((hepatobiliar* or hepato-biliar*) NEAR/2 (scan* or imag*))):ti,ab,kw
       #4 (MRI or MRIs or MRCP or MRCPs or (magn* NEAR/3 resonanc*) or ((magn* or MR or MRs)
        NEAR/2
       #5 (imaging* or tomograph* or tomo-graph*))):ti,ab,kw,so
       #6 #1 OR #2 OR #3 OR #4
       #7 (cholangit* or (cholecystit* or ((gallbladder* or gall-bladder*) NEAR/1 (infection* or
```

empyema*)))):ti,ab,kw

#8 #5 AND #6

Study selection

Titles and abstracts were screened in duplicate for all identified citations using Rayyan [Ouzzani 2016]. All potentially relevant citations were subjected to a full-text review, using predefined inclusion and exclusion criteria tailored to meet the specific population, intervention, and comparator of each clinical question. The steps of the literature selection process were supervised and reviewed by a guideline methodologist for the final selection of the relevant articles.

The following eligibility criteria were used:

Inclusion criteria:

- Patient population- Adults with suspected acute cholecystitis or cholangitis, gangrenous cholecystitis, emphysematous cholecystitis, or calculous or acalculous cholecystitis
- Intervention (diagnostic imaging modalities)- Ultrasound, CT, MDCT, MRI or MRCP (MR CholangioPancreatography), HIDSA scan for cholecystitis only (not cholangitis)
- Comparator- Clinical or surgical findings (e.g., histopathology)
- Outcomes- Diagnostic accuracy (e.g., sensitivity, specificity)
- *Study design* Randomized controlled trials (RCTs) with no date limit, observational studies published 2010-present.

Exclusion criteria:

- Patient population- Children, patients with suspected primary sclerosing cholangitis, choledocholithiasis, xanthogranulomatous cholecystitis, immunoglobulin IgG4-associated cholangitis, stiffness/fibrosis only, differential diagnosis studies (e.g. acute vs. chronic cholangitis)
- Intervention- Magnetic resonance elastography (MRE), ERCP, POCUS, Endoscopic ultrasound-guided (EUS) biliary drainage
- *Comparator* No comparator
- *Study design* Observational studies published prior to 2010, abstracts and conference proceedings, letters to the editor, editorials, and review articles

Data extraction and analysis

A guideline methodologist in conjunction with panelists extracted the data for each pre-determined patient-important outcome. If a relevant publication was missing raw data for an outcome prioritized by the panel, an attempt was made to contact the author(s) for the missing data. Where applicable, data were pooled using random-effects model (fixed effects model for pooling of rates) using RevMan [RevMan].

Evidence to decision

Guideline methodologists prepared the evidence summaries for each question and assessed the risk of bias and the certainty of evidence. Risk of bias was assessed by using the QUIPS tool for studies addressing risk/prognostic factors [Hayden 2013] and the QUADAS-2 tool for diagnostic test accuracy studies [Whiting 2011]. The certainty of evidence was determined first for each critical and important outcome and then for each recommendation using the GRADE approach for rating the confidence in the evidence [Guyatt 2008, GRADE Handbook]. Evidence profiles were developed using the GRADEpro Guideline Development Tool [Guyatt 2008] and reviewed by panel members responsible for each PICO.

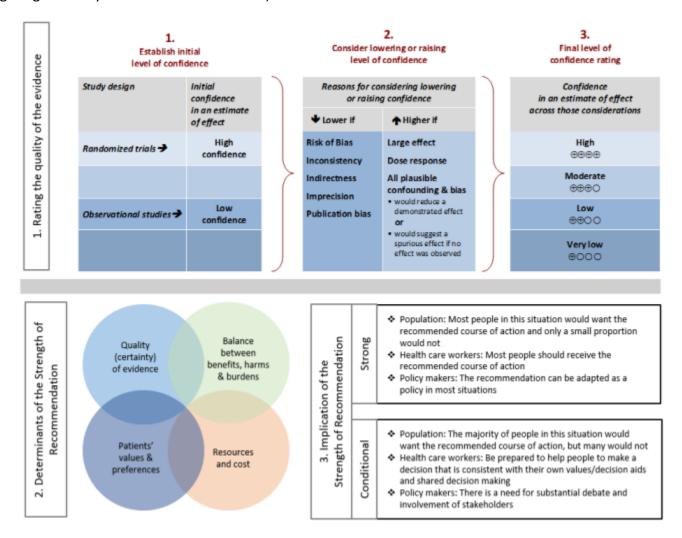
The Evidence to Decision framework [GRADEpro] was used to translate the evidence summaries into practice recommendations. All recommendations were labeled as either "strong" or "conditional" according to the GRADE approach [IDSA CPG Handbook]. The words "we recommend" indicate strong recommendations and "we suggest" indicate conditional recommendations. Supplementary Figure 1

provides the suggested interpretation of strong and conditional recommendations for patients, clinicians, and healthcare policymakers. For recommendations where the comparator treatment or tests are not formally stated, the comparison of interest is implicitly referred to as "not using the intervention" (either not using a specific treatment or a diagnostic test).

All members of the panel participated in the preparation of the draft guideline and approved the recommendations.

TABLES AND FIGURES

Supplementary Figure 1. Approach and implications to rating the quality of evidence and strength of recommendations using GRADE methodology (unrestricted use of figure granted by the U.S. GRADE Network)



Supplementary Table 1. Characteristics of included studies for acute cholecystitis (and acute cholangitis, indirectly)

Author, year of publication	Location, years of data collection	Study design	Number of patients, diagnosis, and age / Pre- test probability	Population included	Index test	Reference standard	Flow and timing
Changphaisarnkul 2015	Thailand Retrospective cohort study		412 patients whose pathology results indicated acute cholecystitis Mean age 62.07 years (range 15-98) 412 diagnosed with acute cholecystitis; pre-test probability: 100%	results indicated acute cholecystitis Mean age 62.07 years (range 15-98) 412 diagnosed with acute cholecystitis; pre-test Patients who underwent cholecystectomy surgeries and had pathology results indicating acute cholecystitis		Pathology	All patients underwent ≥1 of the following: US, HIDA, or CT (some patients received >1 imaging modality).
Kaoutzanis 2014	USA 2010-2012	Retrospective cohort study	406 patients undergoing cholecystectomy Mean ± SD age 49.4 ± 18.5 years 214 diagnosed with acute cholecystitis; pre-test probability: 53%	ED patients with acute upper abdominal pain who underwent cholecystectomy Some overlap with Kaoutzanis 2015	US, HIDA	Histology	Patients underwent US or HIDA or both. Results for each are presented, whether performed standalone or before/after another imaging modality.
Kaoutzanis 2015	USA 2009-2011	Retrospective cohort study	1,217 patients with suspected acute cholecystitis Mean ± SD age 48.9 ± 19.3 years 115 diagnosed with acute cholecystitis (9%)	ED patients with acute abdominal pain suspicious for acute cholecystitis Some overlap with Kaoutzanis 2014	US, HIDA	Histology	Patients underwent US or HIDA or both. Results for each are presented, whether performed standalone or before/after another imaging modality.
Naidu 2016	Australia 2008-2012	Retrospective cohort study	169 adults who underwent cholecystectomy Median age 43 years (range 14.9-87.6) 89 diagnosed with acute cholecystitis; pre-test probability: 52.7%	Patients presenting to the ED who had an emergency cholecystectomy with a working diagnosis of acute cholecystitis or persistent biliary colic and who had a preoperative abdominal US maximum 5 days prior to surgery	US	Histology	US was part of the study inclusion criteria; US was not necessarily performed as first- line imaging.
Rodriguez 2018	USA/Puerto Rico Prospective 2017-2018 Retrospective 2013-2014	Prospective and retrospective cohort study	169 patients with highly suspected acute cholecystitis Mean age 50 years in the RIP/prospective cohort, 44 years in the delayed/historical cohort 79 diagnosed with acute cholecystitis (46.7%)	Prospective: patients presenting with suspected acute cholecystitis Retrospective: patients admitted through the ER with a preliminary diagnosis of acute cholecystits	US, CT, HIDA	Pathology	For the prospective cohort, HIDA or CT was performed first OR US before HIDA or CT. For the retrospective cohort, most patients had US then HIDA.

Stogryn 2016	Canada 2011	Retrospective cohort study	245 patients who underwent US and subsequent cholecystectomy Mean 47.9 years (range 18- 92) 183 diagnosed with acute cholecystitis; pre-test probability: 75%	Patients admitted to the acute care surgical service with suspected biliary pathology who underwent US and subsequent cholecystectomy	US	Intraoperative diagnosis	US was part of the study inclusion criteria. Patients with diagnostic CT, MRI, or other imaging modality were excluded.
Summers 2010	USA 2006-2008	Prospective cohort study	164 patients with suspected acute cholecystitis Mean age 36 years (range 18-87) 23 diagnosed with acute cholecystitis; pre-test probability: 12%	ED patients presenting with suspected cholecystitis	US	Surgical pathology results	Bedside US, then radiology US as needed (technically 2 nd line US)
Wertz 2018	USA 2013-2015	Retrospective cohort study	182 patients with/without acute cholecystitis who underwent imaging Mean age 66 years (range 31-94) 60 patients (62 encounters) diagnosed with acute cholecystitis; pre-test probability 100%	Patients at a VA medical center with acute cholecystitis who underwent imaging	US, CT	Pathology or clinical/radiologic	US or CT performed.

Supplementary Table 2. Risk of bias for included studies

			Risk	of bias dom	ains	
		D1	D2	D3	D4	Overall
	Changphaisarnkul 2015	+	+	+	+	+
	Kaoutzanis 2014	+	+	+	+	+
	Kaoutzanis 2015	+	+	+	+	+
Study	Naidu 2016	+	+	+	+	+
Str	Rodriguez 2018	+	+	+	+	+
	Stogryn 2016	+	+	X	+	X
	Summers 2010	X	+	+	+	X
	Wertz 2018	+	X	+	+	X

Domains:

D1: Patient selection.
D2: Index test.
D3: Reference standard.
D4: Flow & timing.

Judgement

N High

Supplementary Table 3. GRADE Evidence Profile: Should US vs. CT be used to diagnose acute cholecystitis in patients with suspected cholecystitis?

US vs. reference standa 2016, Rodriguez 2018, Stogryn	ord (Kaoutzanis 2014, Kaoutzanis 2015, Naidu 2016, Summers 2010)	CT vs. reference s (Rodriguez 2018)	tandard
Sensitivity	0.32 to 0.83 (range)	Sensitivity	0.73
Specificity	Specificity	0.94	

Prevalences	10% (some included studies clustered around 10%)	50% (some included studies clustered around 50%)	42% (average from included studies)
-------------	--	--	---

							Effect _l	per 1,000) patients	stested				
Outcome	№ of studies (№ of patients)	Study design	Fe	Factors that may decrease certainty of evidence					pre-test probability of 10%		test oility of 1%	pre-test probability of 42%		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	US	СТ	US	СТ	US	СТ	
True positives (patients with acute cholecystitis)	6 studies (Kaoutzanis 2014, Kaoutzanis 2015, Naidu 2016, Rodriguez	cross- sectional (cohort type	serious ^a	serious ^b	serious ^c	not serious	none	32 to 83	73 to 73	160 to 415	365 to 365	134 to 349	307 to 307	⊕⊖⊖⊖ VERY LOW
	2018, Stogryn 2016, Summers 2010) 2370 patients	accuracy study)						41 fewer to 10 more TP in US		205 fewer to 50 more TP in US		173 fewer to 42 more TP in US		
False negatives (patients incorrectly classified as not having acute cholecystitis)								17 to 68	27 to 27	85 to 340	135 to 135	71 to 286	113 to 113	
								41 mor fewer F US		205 mo 50 fewer in US		173 mo 42 fewe in US		
True negatives (patients without acute cholecystitis)	6 studies ^{(Kaoutzanis} 2014, Kaoutzanis 2015,	cross- sectional (cohort type	serious ^a	serious ^b	serious ^c	not serious	none	414 to 792	846 to 846	230 to 440	470 to 470	267 to 510	545 to 545	⊕○○○ VERY LOW
Choledysuus)	Naidu 2016, Rodriguez 2018, Stogryn 2016,	accuracy study)							54 fewer TN		240 fewer to 30 fewer TN in US		ver to er TN	VEIXI LOW

								Effect per 1,000 patients tested						
Outcome	№ of studies (№ of patients)	ients) design probability of probabi								-test bility of 2%	Test accuracy CoE			
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	US	СТ	US	СТ	US	СТ	
False positives (patients incorrectly classified as having acute cholecystitis)	Summers 2010) 2370 patients							108 to 486	54 to 54	60 to 270	30 to 30	70 to 313	35 to 35	
20210 3.13.30 yours)				432 more to 54 more FP in US 240 more FP in US US 278 more US US					ore to e FP in					

Explanations

- a. Per QUADAS-2 assessment
- b. Indirect comparisons
- c. Populations varied: Patients with suspected cholecystitis in some, patients who underwent cholecystectomy in others

Supplementary Table 4. GRADE Evidence Profile: Should MRI/MRCP vs. HIDA be used to diagnose acute cholecystitis in patients with suspected acute cholecystitis and inconclusive US and CT?

No studies found for MRI/MRCP.

MRI/MRCP (No studies four	nd)	HIDA ^{(Kaoutzanis} 2014, Kaoutzanis 2015, Rodriguez 2018)					
Sensitivity	N/A	Sensitivity	0.85 to 0.92				
Specificity	N/A	Specificity	0.34 to 0.86				

Outcome	№ of studies (№ of patients)	Study design		Test accuracy CoE				
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	
True positives (patients with acute cholecystitis) False negatives (patients incorrectly classified	3 studies ^{(Kaoutzanis 2014,} Kaoutzanis 2015, Rodriguez 2018) 1792 patients	cross-sectional (cohort type accuracy study)	not serious	serious ^a	serious ^b	not serious	none	⊕⊕⊖⊖ Low
as not having acute cholecystitis)								
True negatives (patients without acute cholecystitis)	3 studies (Kaoutzanis 2014, Kaoutzanis 2015, Rodriguez 2018) 1792 patients	cross-sectional (cohort type accuracy study)	not serious	serious ^a	serious ^b	not serious	none	ФФОО
False positives (patients incorrectly classified as having acute cholecystitis)								

Explanations

- a. Indirect comparisons
- b. Populations varied: Patients with suspected cholecystitis in some, patients who underwent cholecystectomy in others

Supplementary Table 5. GRADE Evidence Profile: Should US vs. CT be used to diagnose acute cholangitis in patients with suspected acute cholangitis?

US vs. reference stand Kaoutzanis 2015, Naidu 2016, 2016, Summers 2010)		CT vs. reference standard (Rodriguez 2018)				
Sensitivity	0.32 to 0.83	Sensitivity	0.73 to 0.73			
Specificity	Specificity	0.94 to 0.94				

Prevalences	10% (some included studies clustered around 10%)	50% (some included studies clustered around 50%)	42% (average from included studies)
-------------	--	--	---

			_						Effect	per 1,000) patients	stested		
Outcome	№ of studies (№ of patients)	Study design	F	Factors that may decrease certainty of evidence					pre-test probability of 10%		pre-test probability of 50%		test cility of 2%	Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	US	СТ	US	СТ	US	СТ	
True positives (patients with acute cholangitis)	6 studies (Kaoutzanis 2014, Kaoutzanis 2015, Naidu 2016, Rodriguez 2018, Stogryn 2016,	cross-sectional (cohort type accuracy study)	serious ^a	serious ^b	serious ^c	not serious	none	32 to 83	73 to 73	160 to 415	365 to 365	134 to 349	307 to 307	⊕○○○ VERY LOW
	Summers 2010) 2370 patients							41 few 10 moi in US		205 fev 50 moi in US		173 fev 42 mor in US		
False negatives (patients incorrectly classified as not having acute cholangitis)								17 to 68	27 to 27	85 to 340	135 to 135	71 to 286	113 to 113	
								41 moi 10 few in US		205 mc 50 few in US		173 mc 42 few in US		

									Effect p	per 1,000	er 1,000 patients tested			
Outcome	№ of studies (№ of patients)	Study design	F	Factors that may decrease certainty of evidence				pre-test probability of 10%		pre-test probability of 50%		pre-test probability of 42%		Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	US	СТ	US	СТ	US	СТ	
True negatives (patients without acute cholangitis)	6 studies (Kaoutzanis 2014, Kaoutzanis 2015, Naidu 2016, Rodriguez 2018, Stogryn 2016, Summers 2010) 2370 patients	cross-sectional (cohort type accuracy study)	serious ^a	serious ^b	serious ^c	not serious	none	414 to 792	846 to 846	230 to 440	470 to 470	267 to 510	545 to 545	⊕⊖⊖ VERY LOW
								432 fev 54 few in US		240 fev 30 few in US		278 few 35 few in US		
False positives (patients incorrectly classified as having								108 to 486	54 to 54	60 to 270	30 to 30	70 to 313	35 to 35	
acute cholangitis)								432 mo 54 mor in US		240 mo 30 moi in US		278 mo 35 mor in US		

Explanations

- a. Per QUADAS-2 assessment
- b. Indirect populations; pulled from suspected acute cholecystitis since no studies were found for suspected acute cholangitis
- c. Populations varied: Patients with suspected cholecystitis in some, patients who underwent cholecystectomy in others

Supplementary Figure 2. Initial US for adults with suspected acute cholecystitis*

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kaoutzanis 2014	137	94	50	79	0.73 [0.66, 0.79]	0.46 [0.38, 0.53]	-	-
Kaoutzanis 2015	69	128	28	951	0.71 [0.61, 0.80]	0.88 [0.86, 0.90]	-	•
Naidu 2016	70	35	19	45	0.79 [0.69, 0.87]	0.56 [0.45, 0.67]	-	-
Rodriguez 2018	19	15	40	60	0.32 [0.21, 0.46]	0.80 [0.69, 0.88]	-	-
Stogryn 2016	134	9	49	53	0.73 [0.66, 0.79]	0.85 [0.74, 0.93]	-	-
Summers 2010	19	13	4	77	0.83 [0.61, 0.95]	0.86 [0.77, 0.92]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

*Some overlap in populations of Kaoutzanis 2014 and Kaoutzanis 2015

Total n: 6 studies, 2,197 patients Median sensitivity: 0.73 (0.32-0.83) Median specificity: 0.83 (0.46-0.88)

Supplementary Figure 3. Initial CT for adults with suspected acute cholecystitis



Total n: 39 patients

Supplementary Figure 4. Initial HIDA for adults with suspected acute cholecystitis*

Study	TP	FP	FN	TN	Sensitivity (95% CI)	Specificity (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)
Kaoutzanis 2014	143	78	13	40	0.92 [0.86, 0.95]	0.34 [0.25, 0.43]	-	-
Kaoutzanis 2015	83	69	10	139	0.89 [0.81, 0.95]	0.67 [0.60, 0.73]	-	-
Rodriguez 2018	23	4	4	24	0.85 [0.66, 0.96]	0.86 [0.67, 0.96]	0 0.2 0.4 0.6 0.8 1	0 0.2 0.4 0.6 0.8 1

*Some overlap in populations of Kaoutzanis 2014 and Kaoutzanis 2015

Total n: 3 studies, 630 patients Median sensitivity: 0.89 (0.85-0.92) Median specificity: 0.67 (0.34-0.86)

Supplementary Table 6. US, then HIDA[^] for adults with suspected acute cholecystitis [^]Sensitivity provided is for either study positive; 94% had US, then HIDA, 6% had HIDA, then US

Imaging modality	Sensitivity (95% CI)	Specificity (95% CI)			
US and HIDA (Kaoutzanis	96% (for either study +; 94% had US, then	16 F0/			
2015*)	HIDA)	46.5%			

^{*}Some overlap in populations for Kaoutzanis 2014 and Kaoutzanis 2015.

Supplementary Table 7. Imaging in pts with *diagnosed* acute cholecystitis (100% pre-test probability; a selected cohort)

Imaging modality	Sensitivity (95% CI)	Specificity (95% CI)		
US (Changphaisarnkul 2015, Wertz	60% (55-65)	N/A		
2018)	68% (54-80)	IN/A		
CT (Changphaisarnkul 2015, Wertz	67% (57-76)	N/A		
2018)	85% (72-94)	IN/A		
HIDA (Changphaisarnkul 2015)	84% (60-97)	N/A		
MRI	No studies found	No studies found		
US and CT (Wertz 2018)	88% (for either study +; 21% had US, then CT; 79% had CT, then US)	N/A		

CIs calculated in RevMan.

REFERENCES

- Changphaisarnkul P, Saengruang-Orn S, Boonya-Asadorn T. The diagnosis of acute cholecystitis: sensitivity of sonography, cholescintigraphy and computed tomography. J Med Assoc Thai, **2015**; 98(8): 812-819.
- Guyatt GH, Oxman AD, Vist GE, et al.; GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. BMJ, **2008**; 336: 924-926.
- Hayden JA, van der Windt DA, Cartwright JL, Cote P, Bombardier C. Assessing bias in studies of prognostic factors. Ann Intern Med, **2013**; 158(4): 280-286.
- Infectious Diseases Society of America. IDSA Handbook on Clinical Practice Guideline Development. Available at: https://www.idsociety.org/practice-guideline/clinical-practice-guidelines-development-training-and-resources/. Accessed May 1, 2021.
- IOM (Institute of Medicine). Clinical Practice Guidelines We Can Trust. Washington, DC: The National Academies Press, **2011**.
- Kaoutzanis C, Davies E, Leichtle SW, et al. Abdominal ultrasound versus hepato-imino diacetic acid scan in diagnosing acute cholecystitis--what is the real benefit? J Surg Res **2014**; 188(1): 44-52.
- Kaoutzanis C, Davies E, Leichtle SW, et al. Is hepato-imino diacetic acid scan a better imaging modality than abdominal ultrasound for diagnosing acute cholecystitis? Am J Surg **2015**; 210(3): 473-482.
- McMaster University and Evidence Prime Inc. GRADEpro GDT. Available at: https://gradepro.org/. Accessed 24 May 2020.
- Naidu K, Beenen E, Gananadha S, Mosse C. The yield of fever, inflammatory markers and ultrasound in the diagnosis of acute cholecystitis: a validation of the 2013 Tokyo Guidelines. World J Surg **2016**; 40(12): 2892-2897.
- Ouzzani M, Hammady H, Fedorowicz Z, Elmagarmid A. Rayyan-a web and mobile app for systematic reviews. Syst Rev, **2016**; 5(1): 210.
- Review Manager 5 (RevMan 5). 5.4 ed. Copenhagen: The Cochrane Collaboration, 2020.
- Rodriguez LE, Sanchez-Vivaldi JA, Velez-Quinones MP, et al. The impact of a rapid imaging protocol in acute cholecystitis-prospective cohort study. Int J Surg Case Rep **2018**; 51: 388-394.
- Schünemann H, Brożek J, Guyatt GH, Oxman A. Introduction to GRADE Handbook. Available at: https://gdt.gradepro.org/app/handbook/handbook.html. Accessed 25 May 2020.
- Stogryn S, Metcalfe J, Vergis A, Hardy K. Does ultrasonography predict intraoperative findings at cholecystectomy? An institutional review. Can J Surg **2016**; 59(1): 12-18.
- Summers SM, Scruggs W, Menchine MD, et al. A prospective evaluation of emergency department bedside ultrasonography for the detection of acute cholecystitis. Ann Emerg Med **2010**; 56(2): 114-122.

- Wertz JR, Lopez JM, Olson D, Thompson WM. Comparing the diagnostic accuracy of ultrasound and CT in evaluating acute cholecystitis. AJR Am J Roentgenol **2018**; 211(2): W92-W97.
- Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med **2011**; 155(8): 529-536.