Agreement of emergency physician-performed ultrasound versus RADiology-performed UltraSound for cholelithiasis or cholecystitis: a systematic review

Florence Dupriez[a], Paul Geukens[b], Andrea Penaloza[a], Dominique Vanpee[c], Geertruida Bekkering[d,e,f] and Xavier Bobbia[g]

Cholecystitis secondary to gallstone migration is the most common suspected diagnosis for right upper quadrant pain in emergency departments, with radiology-performed ultrasound (RADUS) being the main diagnostic tool. The primary aim of this review was to assess the ability of emergency physicians to perform emergency ultrasound (EUS) compared to RADUS to diagnose cholelithiasis and cholecystitis. A systematic search was performed using Embase, Central (Cochrane library), Web of Science, MEDLINE, Google Scholar, prospective trial registries, and OpenSIGLE databases as well as hand-search of articles. Two physicians independently selected the articles. Assessment of methodological quality was performed using the Quality Assessment of Diagnostic Accuracy Studies 2 tool. Clinical and methodological heterogeneity were qualitatively reported and discussed. Seven prospective studies were selected involving a total of 1061 subjects undergoing EUS. The included studies all used RADUS as the reference standard and emergency physician-performed EUS as the index test. Included studies mostly reported diagnostic accuracy for cholelithiasis diagnosis whereas only one study mentioned diagnostic accuracy for cholecystitis. Clinical and methodological heterogeneity between included studies prevented a meta-analysis. This review shows there is good agreement between EUS and RADUS to assess the gallbladder for cholelithiasis and therefore supports its use by emergency physicians for that matter. Nevertheless, this work identified clinical and methodological heterogeneity along with a poor description EUS operators' experience. In the future, larger studies should include a larger population of EUS operators, specify their background, and compare EUS to the final diagnosis to evaluate performances for gallbladder diagnostic accuracy. ***European Journal of Emergency Medicine*** **XXX: 000–000**

European Journal of Emergency Medicine 2021, **XXX**:000–000

Keywords: emergency medicine, cholecystitis, cholelithiasis, point-of-care systems, ultrasonography

[a]Emergency Department (ED), Cliniques Universitaires Saint-Luc (CUSL), Brussels, [b]Intensive Care Unit, Hôpital de Jolimont, rue Ferrer 159, La Louvière, [c]Institute of Health and Society and CHU UCL Namur, Université Catholique de Louvain, Brussels, [d]Center for Evidence-Based Medicine, Kapucijnenvoer, [e]Cochrane Belgium, [f]Department of Public Health and Primary Care, Academic Centre for General Practice, KU Leuven, Belgium and [g]Department of Anesthesiology, Emergency and Critical Care Medicine, Intensive Care Unit, Montpellier University, EA 2992 CAFEDIVAS, Nîmes University Hospital, place du Pr Debré, 30029 Nîmes, France

Correspondence to Florence Dupriez, MD, Cliniques Universitaires Saint-Luc (CUSL), Emergency Department, 1200 Brussels, Belgium
Tel: +3227641613; e-mail: Florence.dupriez@uclouvain.be

Received 24 November 2020 **Accepted** 17 February 2021

Introduction

Right upper quadrant (RUQ) pain is a common complaint in emergency departments (EDs) [1]. Cholecystitis is the most common suspected diagnosis associated with such pain in the ED [2]. About 95% of cholecystitis cases are reported to be secondary to gallstone migration [3,4]. Among patients presenting to ED with acute abdominal pain, 3–10% are diagnosed with calculous cholecystitis [5]. This percentage increases to 60% among patients suffering from RUQ pain [6]. Ultrasound is considered an essential tool for evaluating these conditions [2,7,8].

Emergency UltraSound (EUS) is a focused ultrasound exam performed at the bedside by the treating physician and used to respond to a specific question during the clinical examination [9]. Currently, the diagnosis of gallbladder pathologies relies mostly on RADiology-performed UltraSound (RADUS). RADUS is often a time-consuming part of patient care [10] and its use is limited by its variable availability in hospitals, especially out of hours [11]. Instead of ultrasound, a CT scan may be used to assess RUQ pain. However, this is not in accordance with current recommendations [8] and leads to a non-negligible radiation risk for the patient.

Few literature reviews and meta-analyses have examined the performance of EUS in gallbladder assessments compared to RADUS [11]. In 2011, in a systematic review evaluating the use of EUS for cholelithiasis diagnosis, Ross *et al.* [11] suggested that bedside ultrasound

Supplemental Digital Content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.euro-emergencymed.com).

DOI: 10.1097/MEJ.0000000000000815

was a useful tool to confirm or exclude the presence of cholelithiasis. Furthermore, prospective studies such as that of Summers *et al*. [12] in 2010 underlined that the presence of gallstones combined with additional findings is highly sensitive and specific to diagnose acute cholecystitis. Summers *et al*. [12] reported sensitivity and specificity of 0.89 [95% confidence intervals (CIs), 0.79–0.95] and 0.86 (95% CI, 0.73–0.95), respectively, for the diagnosis of gallstones using EUS. A single-center study led by Villar *et al*. [13] in 2015 concluded that the absence of cholelithiasis rules out the presence of acute cholecystitis in an emergency setting. This is consistent with the strong correlation between gallstones and cholecystitis.

Despite these valuable findings, in the aforementioned articles, the variable experience of the EUS operators is not taken into account, while the comparison group is not consistently RADUS. Both elements can lead to a significant comparison bias when assessing the performance of ultrasound use by emergency physicians. This systematic review was performed to provide insight into the characteristics of the different diagnostic accuracy studies and to report the experience of EUS operators using a step-by-step approach and considering cholecystitis and gallstones as a gallbladder pathology that can accurately be assessed by EUS. RADUS was used for comparative purposes to accurately assess ultrasound performance. Indeed, the primary outcome of this systematic review was assessing the ability of emergency physicians to use ultrasound compared to radiologists or sonographers.

Methods

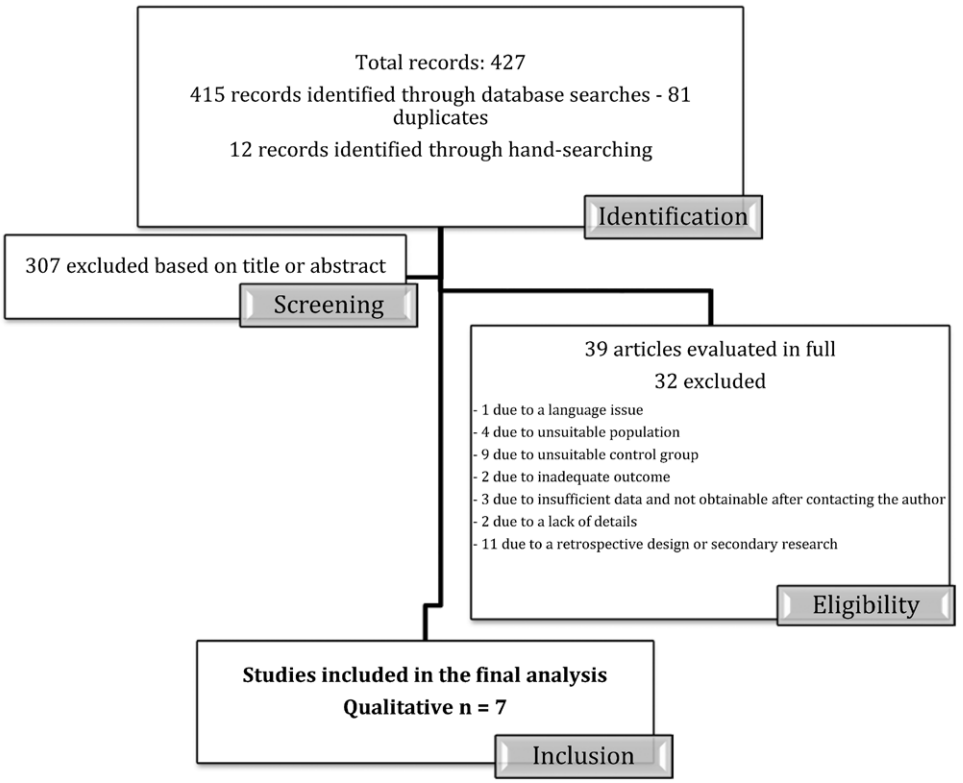
The following research question was considered in this review: is EUS (I) performed by emergency physicians (P) accurate, compared to RADUS (C), for the diagnosis of acute cholecystitis or cholelithiasis (O)? After a scoping literature review, a protocol was written a priori and registered on PROSPERO (CRD42020161871) before performing an extended literature search. An amendment was made towards the initially chosen title. This systematic review was conducted according to Cochrane's methodology [14], and reported following the Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies statement [15].

Table 1 Quality Assessment for Diagnostic Accuracy Study tool[a]

	Katirci *et al*. [18]	Kendall *et al*. [19]	Kozaci *et al*. [20]	Miller *et al*. [21]	Rosen *et al*. [22]	Shekarchi *et al*. [23]	Torres-Macho *et al*. [24]
Domain 1: Patient selection							
A. Risk of bias							
Consecutive or random sample of patients? (yes/no/unclear)	Unclear	No	No	No	No	No	Unclear
Case-control design avoided? (yes/no/unclear)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Inappropriate exclusions? (yes/no/unclear)	No	Yes	Yes	No	Unclear	Yes	Yes
Biased selection of patients? (low/high/unclear)	Low	Low	Low	Low	Unclear	Low	Low
B. Concerns regarding applicability?							
Concerns that the included patients do not match the review question? (low/high/unclear)	Low	Low	Low	Low	Low	Low	Low
Domain 2: Index test							
A. Risk of bias							
Index test results interpreted without knowledge of the reference standard results? (yes/no/unclear)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Prespecified threshold? (yes/no/unclear)	NA	NA	NA	NA	NA	NA	NA
Conduct or interpretation of the index test introduced bias? (low/high/unclear)	Low	Low	Low	Low	Low	Low	Low
B. Concerns regarding applicability?							
Concerns that the index test, its conduct, or interpretation differ from the review question? (low/high/unclear)	Low	Low	Low	Low	Low	Low	Low
Domain 3: Reference standard							
A. Risk of bias							
Reference test likely to correctly classify the target condition? (yes/no/unclear)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Reference test results interpreted without knowledge of the index test results? (yes/no/unclear)	Yes	Yes	Unclear	Yes	Yes	Unclear	Yes
Risk of reference test, conduct, or interpretation introducing bias? (low/high/unclear)	Low	Low	Low	Low	Low	Low	Low
B. Concerns regarding applicability?							
Concerns that the target condition as defined by the reference standard does not match the review question? (low/high/unclear)	Low	Low	Low	Low	Low	Low	Low
Domain 4: Flow and timing							
A. Risk of bias							
Patients not receiving index test and/or reference standard or being excluded from 2 × 2 table	None	None	None	None	None	None	None
Apprsopriate interval between index test and reference standard? (yes/no/unclear)	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	Yes
Did all patients receive reference standard? (yes/no/unclear)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Did all patients receive the same reference standard? (yes/no/unclear)	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Were all patients included in the analysis? (yes/no/unclear)	Yes	Yes	Yes	Yes	No	Yes	Yes
Risk of patient flow introducing bias? (low/high/unclear)	Low	Low	Low	Low	Unclear	Low	Low

[a]QUADAS-2 tool.

Fig. 1



Results of the search strategy using a Preferred Reporting Items for a Systematic Review and Meta-analysis flowchart.

Search strategy, information sources, and eligibility criteria

Regarding the narrow scope of the review, a large number of databases were used: Embase, Central (Cochrane library), Web of Science, MEDLINE, Google Scholar, and prospective trial registries. The openSIGLE database was searched for grey literature. Although the user guide of each database was taken into account, the search string was based on a combination of medical subject headings and free text words (Supplemental Material 1, Supplemental digital content 1, *http://links.lww.com/EJEM/A305*). The search was performed using English and French terms. In addition, a snowballing method was used, whereby reference lists and citations of relevant articles were screened for articles of interest. The conference archives of following national emergency medicine societies were also screened: American College of Emergency Physicians (ACEP), Royal College of Emergency Medicine, Society of Academic Emergency Medicine, American Academy of Emergency Medicine, American Institute of Ultrasound in Medicine, Société Française de Médecine d'Urgence (SFMU), Belgian Society of Emergency Medicine and Disaster Medicine, Canadian Association of Emergency Physicians, and Association des spécialistes en Médecine d'Urgence du Québec. The EUS recommendations of ACEP and SFMU were also explored. ZOTERO software was used for bibliographic management. The search period was chosen from 01 January 1991 to 02 March 2020. The studied outcome was EUS performance for the detection of cholelithiasis or cholecystitis when conducted by emergency physicians compared to RADUS. Only prospective diagnostic accuracy studies were considered for inclusion.

Article selection

Using the different databases listed in the previous section, articles were identified according to the built search string. During the identification process, the number of articles found was reported at each phase along with the sources of the identified records. After removing duplicates, the selection process began by evaluating the title, then the abstract, and finally the article in full. Articles excluded at the full-text screening stage were recorded, along with the reason for exclusion. Two reviewers screened articles independently. A third reviewer assessed any discrepancies if no consensus was reached. Inclusion and exclusion criteria were strictly applied to all the selected articles. Any articles comparing the diagnostic accuracy of both EUS and RADUS to the final diagnosis were excluded if the

Table 2 Characteristics of the included studies[a]

Study	Center	Comparison	Included patients	Total abdomen vs. focused EUS	Outcome
Katirci *et al.* [18]	Tertiary hospital, Turkey 250 000 annual admissions	RADUS	RUQ pain	Focused RUQ	Primary: EUS accuracy for cholecystitis diagnosis
Kendall *et al.* [19]	University-affiliated hospital, USA 55 000 annual ED consultations	RADUS	RUQ or epigastric pain or jaundice	Focused RUQ	Primary: EUS accuracy for hepatobiliary assessment Secondary: How sonographic experience affects accuracy in gallbladder evaluations and the time required for a focused RUQ assessment
Kozaci *et al.* [20]	Tertiary hospital, Turkey Admissions not specified	RADUS	Acute abdominal pain	EUS in 10 steps: gallbladder in step 2	Primary: EUS accuracy for differential diagnosis of acute abdominal pain
Miller *et al.* [21]	University-affiliated center, USA 140 000 annual ED consultations	RADUS	RUQ or epigastric pain	Focused RUQ	Primary: EUS accuracy for hepatobiliary assessment Secondary: How history, physical examination, and laboratory findings combined with gallbladder EUS predicts normal gallbladder, symptomatic cholelithiasis, and complicated symptomatic cholelithiasis
Rosen *et al.* [22]	University-affiliated hospital, USA 66 000 annual ED consultations	RADUS	Abdominal pain of suspected biliary origin	Focused RUQ	Primary: EUS accuracy for diagnosis of gallstones and cholecystitis Secondary: Characteristics of EUS and RADUS to diagnose cholecystitis
Shekarchi *et al.* [23]	2 tertiary centers, Iran Admissions not specified	RADUS	RUQ or epigastric pain with suspected acute cholecystitis	Focused RUQ	Primary: EUS accuracy for cholecystitis diagnosis
Torres-Macho *et al.* [24]	Urban university hospital, Spain Admissions not specified	RADUS	Suspected cholecystitis	Unclear	Primary: EUS accuracy for multiple indications (cholecystitis, hydronephrosis, deep vein thrombosis, cardiovascular problems)

[a]RUQ, right upper quadrant pain.
EUS, Emergency UltraSound; RADUS: RADiology-performed UltraSound.

authors did not share the original data used for RADUS as the reference standard.

Data management and extraction

Any article meeting the eligibility criteria was reviewed in full in order to extract data. During the data collection, reviewers verified the inclusion criteria, reported them appropriately in a standardized form (Supplemental Material 2, Supplemental digital content 1, *http://links.lww.com/EJEM/A305*) developed a priori, and justified any exclusion.

Quality and risk of bias assessment

The Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2), the current standard used to assess the risk of bias of diagnostic accuracy studies [16], was used in this review (Table 1). Each domain was evaluated in terms of risk of bias and applicability.

Data analysis

Following the Standards for Reporting Diagnostic Accuracy Studies [17], 2×2 tables were used to calculate sensitivity and specificity of EUS compared to RADUS. Clinical and methodological heterogeneity were qualitatively reported and discussed with respect to the population of EUS operators, reference standard, index test, and outcome. Given the observed clinical and methodological heterogeneity, meta-analysis was deemed inappropriate. Distribution of the individual sensitivity and specificity estimates with 95% CIs reported in the included studies was illustrated in a coupled forest plot and in the receiver operating characteristic plane.

Results

Figure 1 illustrates the results of the search strategy. Substantial agreement was found after article screening and eligibility assessment before consensus using Cohen's Kappa statistics ($k = 0.8$). Out of 39 articles evaluated in full, 7 studies [18–24] were included, with a total of 1061 patients undergoing EUS, with RADUS as the reference standard.

Characteristics of the included studies

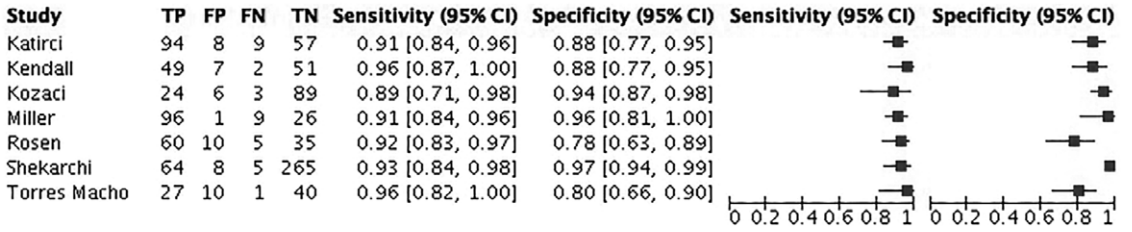
Characteristics of the seven included studies are reported in Table 2. The included studies all used RADUS as the reference standard and EUS performed by emergency physicians, consultants or residents, as the index test. All studies used appropriate ultrasound devices and a curvilinear low-frequency probe as recommended for gallbladder evaluation [25]. All studies described gallstone findings. However, except for Torres-Macho *et al.* [24] who reported sensitivity and specificity for cholecystitis diagnoses, other studies described cholecystitis signs independently and were therefore not included for cholecystitis analysis. Torres-Macho *et al.* [24] did not specify whether they performed an ultrasound of the biliary tree, while Shekarchi *et al.* [23], Katirci *et al.* [18], and Rosen *et al.* [22] did not include the biliary tree in the gallbladder examination. Although the number of EUS examinations and reference standards was clearly reported in each study, the number of EUS operators as well as their experience varied substantially (Table 3). Prior to inclusion, the physicians using EUS all underwent specific training in bedside ultrasound, although the length and the content varied in the included studies.

Table 3 Characteristics of emergency ultrasound operators[a]

Study	EUS operators	Number of EUS operators	EUS experience and training prior to inclusion	EUS devices
Katirci *et al.* [18]	Emergency physician consultants	Not specified	EUS operators attended a certification program with theoretical and practical training before inclusion No other course specified before inclusion	Mindray DC-3; Mindray, Shenzhen, P. R. China
Kendall *et al.* [19]	Emergency physician consultants and residents	8 full-time emergency physicians 39 residents	Partly inexperienced operators with <25 examinations performed and 1 operator with >100 EUS examinations 3h training in abdominal EUS and 10h hands-on experience for different EUS, including RUQ	Toshiba Capasee, Toshiba SSH-140A, New-York, USA
Kozaci *et al.* [20]	Emergency physician consultants with at least 6 months' experience	6 emergency physicians	Trained in E-FAST Theoretical and practical training for 8 h per week for three consecutive weeks given by a radiologist; practical comparison with RADUS for 1 month with minimum 10 patients before inclusion	Mindray DC-T6; Mindray
Miller [21]	1 experienced EUS user and residents	1 experienced operator, unknown number of residents	Unexperienced EUS users and one experienced EUS operator who performed 43% of EUS 2-h didactic course on hepatobiliary EUS and 15 min individual hands-on session	Treason 2000, Teratech Inc, Houston, Texas, USA
Rosen *et al.* [22]	15 full-time emergency physician consultants	15 full-time emergency physicians	Heterogeneous experience between operators, some with <30 EUS 2-h theoretical sessions and 2-h hands-on training	Aloka Echo Camera SSD-500, Tokyo, Japan, Siemens Sonoline Prima, Erlangen, Germany
Shekarchi [23]	Attending emergency physicians expert in POCUS or trained emergency residents supervised by POCUS expert	Not specified	Experienced EUS user or residents under their supervision 2-h theoretical courses and 2-h hands-on training, following by 12 supervised cases before individual inclusion	HM-70 Samsung, New Jersey, USA and M-turbo Sonosite, Frankfurt, Germany
Torres-Macho [24]	5 full-time attending emergency physicians	5 full-time emergency physicians	No EUS experience 10-h training program given over 2 days	Siemens Sonoline G-20, Erlangen, Germany

[a]EUS, Emergency UltraSound.
POCUS, Point Of Care UltraSound; RADUS: RADiology performed UltraSound; RUQ, Right Upper Quadrant Pain.

Fig. 2



Coupled forest plot. CI, confidence interval.

Risk of bias assessment

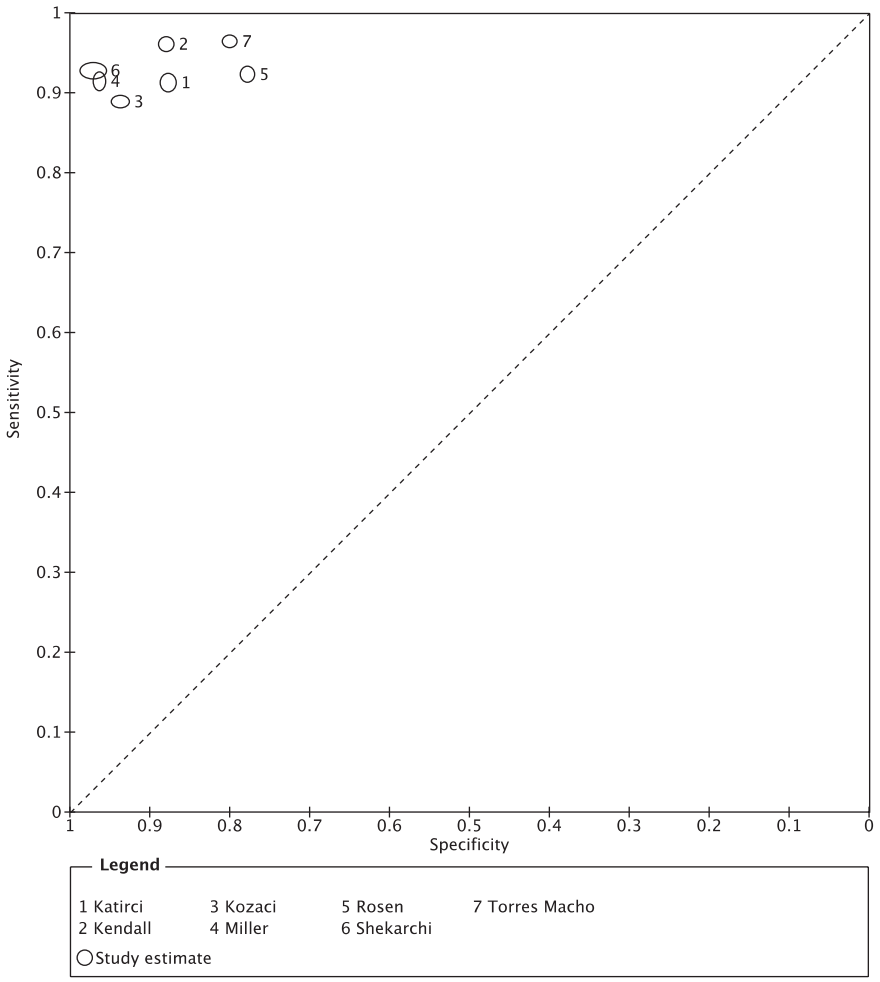
Before consensus, a major kappa agreement ($k = 0.9$) was found between reviewers for all four domains of the QUADAS-2 tool. Concerns about bias induced by the included patients, index test conduct or interpretation, reference standard used, or patient flow were mostly low, although they were viewed as unclear for the study of Rosen *et al.* [22]. Indeed, Rosen *et al.* [22] included patients according to the opinion of EUS operator. In the other studies [18–21], the selection of patients undergoing EUS was; however, not consecutive, which gave rise to a convenience sample. Katirci *et al.* [20] and Miller *et al.* [21] did not avoid inappropriate exclusions, as they, respectively, excluded patients who recently ate a meal and those with a normal laboratory test. All EUS operators performed gallbladder assessments before the control. RADUS operators were mostly blinded to the EUS results, although this is not clearly specified in Kozaci *et al.* [20] and Sherkachi *et al.* [23].

Accuracy and heterogeneity

Reported sensitivity and specificity for gallbladder assessment ranged from 0.89 to 0.96 and from 0.78 to 0.97, respectively, in included studies. The total number of EUS performed was 1061, with a range from 78 to 342.

The primary outcome of most studies [18,19,21–23] focused on determining the diagnostic accuracy of hepatobiliary EUS compared to RADUS. Kozaci *et al.* [20] and Torres-Macho *et al.* [24]; however, considered gallbladder

Fig. 3



Receiver operating characteristic plane.

EUS as a subgroup. Clinical heterogeneity was reported for the population of EUS operators as well as EUS use. Indeed, EUS operator's background was either not specified or poorly described in the included studies. Kendall *et al.* [19] based EUS experience on the number of previous EUS examinations, whereas Katirci *et al.* [18], Kozaci *et al.* [20], Miller *et al.* [21], Rosen *et al.* [22], and Sherckachi *et al.* [23] gave a rather poor definition for previous EUS experience. Moreover, the description of EUS was quite variable in the different studies. In all studies; however, physicians were required to search for cholelithiasis. Previously to patient inclusion, EUS operators received dedicated training to EUS use for gallbladder assessment. Estimates of the included studies were shown in a coupled forest plot (Fig. 2) and the ROC plane (Fig. 3) depicting more heterogeneity for specificity between studies.

Discussion

This rigorously performed systematic review confirms the value of EUS performance when investigating gallbladders in an emergency setting, as good sensitivity (0.89–0.96) and specificity (0.78–0.97) were found in the included studies. Moreover, the risk of bias for included studies was mostly low, which increases confidence in these results. The sensitivity and specificity estimates found in the literature for RADUS when compared to the final diagnosis are, respectively, 0.84 and 0.99 for the detection of cholelithiasis [11,26] and range from 0.84 to 0.98 and from 0.90 to 0.99 for cholecystitis [27]. Although further studies are needed to compare EUS to the final diagnosis, the emergency physicians' ability to use EUS compared to RADUS as described in this review may further reflect its good diagnostic accuracy for gallbladder assessments.

In an emergency setting, gallbladder EUS specifically searches for cholelithiasis and/or cholecystitis. The coupled forest plot (Fig. 2) and ROC plane (Fig. 3) illustrate the estimates for each study, which concern gallstone diagnosis using EUS in retrieved articles. Except for Torres-Macho *et al.* [24], estimates

for cholecystitis were not presented in the reviewed articles.

Due to the observed clinical and methodological heterogeneity, it was decided that pooling the individual sensitivity and specificity estimates in a meta-analysis was not appropriate [28]. Although the review population was strictly limited to emergency physicians, ultrasound is known to be operator-dependent, and variations in ultrasound experience may give this factor even more importance. Therefore, this review reported this particular issue as accurately as possible (Table 3). To diminish the clinical heterogeneity and homogenize the interventions in the included studies, EUS operators were required to undergo ultrasound training for hepatobiliary assessments. However, this training differed across studies, and its impact was poorly evaluated. Unlike radiologists and sonographers, emergency physicians are unequally familiar with EUS. The studied population was therefore perhaps not representative of emergency physicians in general and demonstrated a selection bias. In the different studies presented here, two did not report the size of the operator sample [18,23], whereas one [21] did not specify the number of residents using EUS. This number could provide precious information to estimate the studied population. The ratio of EUS operators to the total number of emergency physicians on site as well as the ratio of consultants to residents is also important in evaluating the representative characteristics of the population. The small number of EUS operators also explained the use of convenience patient samples, which was another source of bias in the included studies. These were supplementary sources of clinical and methodological heterogeneity preventing a meta-analysis.

Attention should also be given to the reference standard, when assessing sources of heterogeneity. Among the seven included articles, the signs described on RADUS were accurately documented by most studies [19,21–23]. Furthermore, as ultrasound has been part of the official curriculum of radiologists for decades and is the specialty of sonographers, the control group was considered to be homogenous for all the included studies. This; however, does not avoid the known operator-dependent nature of ultrasound use.

Concerning the outcome, although patients assessed for cholelithiasis were a subgroup in two studies [18,24], the aim of all studies was to analyze EUS accuracy compared to RADUS. This was considered a factor of homogeneity.

The inability to perform a meta-analysis confirms the need for larger studies assessing the ability of EUS operators in gallbladder evaluation. Ideally, these studies should use larger sample sizes of emergency physicians and include operators with a uniform ultrasound background.

Limitations

Searching multiple databases and screening grey literature reduces publication bias. Therefore, we are confident that we identified all relevant studies. However, the development of an a priori protocol may have generated some difficulties in finding previously selected information among the included studies. For instance, except for the study by Torres-Macho *et al*. [24], none of the studies compare EUS use for cholecystitis diagnosis. This review, which initially aimed to assess gallbladder ultrasound for both, cholelithiasis and cholecystitis, subsequently had to depict mostly the sensitivity and specificity for cholelithiasis.

Our main interest in this review was the emergency physicians performing EUS. In most articles, the number of EUS operators and their EUS experience was poorly documented and thus impossible to accurately compare. EUS operators were simply described as expert or not without specifying the level of expertise. This was a clear limitation for accurately assessing the population.

The clinical setting of the EUS could be considered a strength. Nonetheless, some EUS operators were supervised by more experienced emergency physicians. This supervision possibly influenced the way in which the EUS was performed. Likewise, due to the lack of emergency physicians trained and experienced in EUS, most studies had to include naive operators. Besides Muller *et al*. [21], the other authors did not characterize the influence of ultrasound background on EUS ability or compare supervised and unsupervised EUS.

While the consistent use of RADUS as the reference standard in the different studies could be taken as a strength in this review, the diagnostic accuracy of EUS was not assessed in terms of the final diagnosis. Although RADUS is mostly used in ED to diagnose gallbladder pathologies, it could be argued that the only way to confirm the ultrasound findings is by surgery or discharge reports. However, the primary outcome of this study was to assess EUS performance rather than diagnostic accuracy itself, which reduced the influence of this potential limitation.

The 7 studies included in this work compared the diagnosis made using EUS without assessing the complementary information given by the radiological structural analysis such as liver assessments or other RADUS findings. Moreover, some studies did not include biliary tree in their analysis while it is important for patient management.

Conclusion

The good sensitivity and specificity reported in all seven selected articles for EUS compared to RADUS support the use of EUS to assess gallbladder in an emergency setting. This could represent a great opportunity to improve

bedside patient care, target treatments, and ease patient flow in the ED for patients presenting with potential gallbladder pathology.

This systematic review; however, sheds light on the clinical and methodological heterogeneity of the included studies, which prevented a meta-analysis. As a result, any EUS gallbladder examination should be interpreted with caution in relation to the EUS training of the operator and viewed in light of pre-test probability. EUS operator should wisely report results according to EUS protocol.

Although this review shows that EUS is a valuable tool for gallbladder evaluation by emergency physicians, further studies should be undertaken to evaluate the diagnostic accuracy across a larger spread of EUS operators taking into account their EUS experience and its impact on EUS accuracy of use.

Acknowledgements

F.D.: review process, interpretation of data, and drafting of the article. P.G.: review process and interpretation of data. A.P., D.V., and X.B.: critical revision of the article. G.B.: methodology revision.

Conflicts of interest

X.B. declares a competing interest as an ultrasound teacher for GE (GE MEDICAL SYSTEMS ULTRASOUND) customers. For the remaining authors, there are no conflicts of interest.

References

1 Jain A, Mehta N, Secko M, Schechter J, Papanagnou D, Pandya S, Sinert R. History, physical examination, laboratory testing, and emergency department ultrasonography for the diagnosis of acute cholecystitis. *Acad Emerg Med* 2017; **24**:281–297.
2 Joshi G, Crawford KA, Hanna TN, Herr KD, Dahiya N, Menias CO. US of right upper quadrant pain in the emergency department: diagnosing beyond gallbladder and biliary disease. *Radiographics* 2018; **38**:766–793.
3 Krishnan M, Middleton W. Ultrasonographic evaluation of right upper quadrant pain in emergency departments. *Ultrasound Clin* 2011; **6**:149–161.
4 Fialkowski E, Halpin V, Whinney RR. Acute cholecystitis. *BMJ Clin Evid* 2008; **2008**:0411.
5 Kimura Y, Takada T, Kawarada Y, Nimura Y, Hirata K, Sekimoto M, *et al*. Definitions, pathophysiology, and epidemiology of acute cholangitis and cholecystitis: Tokyo Guidelines. *J Hepatobiliary Pancreat Surg* 2007; **14**:15–26.
6 Excoffier S, Poletti P-A, Brandstatter H. Douleurs abdominales aigues hautes: quelle imagerie? *Rev Med Suisse* 2013; **9**:1710.
7 Bortoff GA, Chen MY, Ott DJ, Wolfman NT, Routh WD. Gallbladder stones: imaging and intervention. *Radiographics* 2000; **20**:751–766.
8 Yarmish GM, Smith MP, Rosen MP, Baker ME, Blake MA, Cash BD, *et al*. ACR appropriateness criteria right upper quadrant pain. *J Am Coll Radiol* 2014; **11**:316–322.
9 American College of Emergency Physicians. ACEP emergency ultrasound guidelines – 2001. *Ann Emerg Med* 2001; **38**:470–481.
10 Blaivas M, Harwood RA, Lambert MJ. Decreasing length of stay with emergency ultrasound examination of the gallbladder. *Acad Emerg Med* 1999; **6**:1020–1023.
11 Ross M, Brown M, McLaughlin K, Atkinson P, Thompson J, Powelson S, *et al*. Emergency physician-performed ultrasound to diagnose cholelithiasis: a systematic review. *Acad Emerg Med* 2011; **18**:227–235.
12 Summers SM, Scruggs W, Menchine MD, Lahham S, Anderson C, Amr O, *et al*. A prospective evaluation of emergency department bedside ultrasonography for the detection of acute cholecystitis. *Ann Emerg Med* 2010; **56**:114–122.
13 Villar J, Summers SM, Menchine MD, Fox JC, Wang R. The absence of gallstones on point-of-care ultrasound rules out acute cholecystitis. *J Emerg Med* 2015; **49**:475–480.
14 The Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions [Internet]. 2020. Handbook-5-1.cochrane.org. https://handbook-5-1.cochrane.org/index.htm#chapter_6/6_2_1_8_grey_literature_databases.htm. Accessed October 13, 2019.
15 McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, Clifford T, *et al*; the PRISMA-DTA Group, Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. *JAMA* 2018; **319**:388–396.
16 Whiting PF, Rutjes AW, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, *et al*.; QUADAS-2 Group. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. *Ann Intern Med* 2011; **155**:529–536.
17 Cohen JF, Korevaar DA, Altman DG, Bruns DE, Gatsonis CA, Hooft L, *et al*. STARD 2015 guidelines for reporting diagnostic accuracy studies: explanation and elaboration. *BMJ Open* 2016; **6**:e012799.
18 Katirci Y, Soyuduru M, Başpinar I, Yurdakul MS, Demirtaş E, Ramadan H. Assessment of the usability of ultrasonography by emergency physicians in the diagnosis of acute cholecystitis. *Acta Med Mediterr* 2014; **30**:509–513.
19 Kendall JL, Shimp RJ. Performance and interpretation of focused right upper quadrant ultrasound by emergency physicians. *J Emerg Med* 2001; **21**:7–13.
20 Kozaci N, Avci M, Tulubas G, Ararat E, Karakoyun OF, Karaman C, *et al*. Role of emergency physician-performed ultrasound in the differential diagnosis of abdominal pain. *Hong Kong J Emerg Med* 2018; **27**:79–86.
21 Miller AH, Pepe PE, Brockman CR, Delaney KA. ED ultrasound in hepatobiliary disease. *J Emerg Med* 2006; **30**:69–74.
22 Rosen CL, Brown DF, Chang Y, Moore C, Averill NJ, Arkoff LJ, *et al*. Ultrasonography by emergency physicians in patients with suspected cholecystitis. *Am J Emerg Med* 2001; **19**:32–36.
23 Shekarchi B, Hejripour Rafsanjani SZ, Shekar Riz Fomani N, Chahardoli M. Emergency department bedside ultrasonography for diagnosis of acute cholecystitis; a diagnostic accuracy study. *Emerg (Tehran)* 2018; **6**:e11.
24 Torres-Macho J, Antón-Santos JM, García-Gutierrez I, de Castro-García M, Gámez-Díez S, de la Torre PG, *et al*.; Working Group of Clinical Ultrasound, Spanish Society of Internal Medicine. Initial accuracy of bedside ultrasound performed by emergency physicians for multiple indications after a short training period. *Am J Emerg Med* 2012; **30**:1943–1949.
25 Danse E, Annet L, Dragean C, Ghaddab M. *Echographie abdominale de l'adulte*. Montpellier: Sauramps Medical; 2017.
26 Shea JA, Berlin JA, Escarce JJ, Clarke JR, Kinosian BP, Cabana MD, *et al*. Revised estimates of diagnostic test sensitivity and specificity in suspected biliary tract disease. *Arch Intern Med* 1994; **154**:2573–2581.
27 Shah K, Wolfe RE. Hepatobiliary ultrasound. *Emerg Med Clin North Am* 2004; **22**:661–673, viii.
28 Macaskill P, Gatsonis C, Deeks J, Harbord R, Takwoingi Y. Chapter 10: analysing and presenting results. In: Higgins JPT, Green S, editors. *Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy*. 1st ed. Chichester, UK: The Cochrane Collaboration; 2010. pp. 97–165.