# The diagnostic accuracy of CT and MRI for the detection of lymph node metastases in gallbladder cancer

Lohman, E. A. J. de Savornin; de Bitter, T. J. J.; van Laarhoven, C. J. H. M.; Hermans, J. J.; de Haas, R. J.; de Reuver, P. R.

*Published in:*
European Journal of Radiology

*DOI:*
10.1016/j.ejrad.2018.11.034



*Publication date:*
2019

European Journal of Radiology 110 (2019) 156–162

Contents lists available at ScienceDirect

European Journal of Radiology

journal homepage: www.elsevier.com/locate/ejrad

Research article

# The diagnostic accuracy of CT and MRI for the detection of lymph node metastases in gallbladder cancer: A systematic review and meta-analysis

E.A.J. de Savornin Lohman[a,*], T.J.J. de Bitter[b], C.J.H.M. van Laarhoven[a], J.J. Hermans[c], R.J. de Haas[d], P.R. de Reuver[a]

[a] Department of Surgery, Radboud University Medical Centre, Nijmegen, P.O. Box 9101, 6500HB, the Netherlands
[b] Department of Pathology, Radboud University Medical Centre, Nijmegen, P.O. Box 9101, 6500HB, the Netherlands
[c] Department of Radiology and Nuclear Medicine, Radboud University Medical Centre, Nijmegen, the Netherlands
[d] Department of Radiology, University of Groningen, University Medical Centre Groningen, Groningen, P.O. Box 30.001, 97700 RB, the Netherlands

ARTICLE INFO

*Keywords:*
Gallbladder cancer
Pre-operative staging
CT
MRI
Lymph node metastases

ABSTRACT

*Background:* Lymph node metastases (LNM) are an ominous prognostic factor in gallbladder cancer (GBC) and, when present, should preclude surgery. However, uncertainty remains regarding the optimal imaging modality for pre-operative detection of LNM and international guidelines vary in their recommendations. The purpose of this study was to systematically review the diagnostic accuracy of computed tomography (CT) versus magnetic resonance imaging (MRI) in the detection of LNM of GBC.

*Methods:* A literature search of studies published until November 2017 concerning the diagnostic accuracy of CT or MRI regarding the detection of LNM in GBC was performed. Data extraction and risk of bias assessment was performed independently by two reviewers. The sensitivity of CT and MRI in the detection of LNM was reviewed. Additionally, estimated summary sensitivity, specificity and diagnostic accuracy of MRI were calculated in a patient based meta-analysis.

*Results:* Nine studies including 292 patients were included for narrative synthesis and 5 studies including 158 patients were selected for meta-analysis. Sensitivity of CT ranged from 0.25 to 0.93. Estimated summary diagnostic accuracy parameters of MRI were as follows: sensitivity 0.75 (95% CI 0.6 – 0.85), specificity 0.83 (95% CI 0.74 – 0.90), LR + 4.52 (95% CI 2.55–6.48) and LR- 0.3 (95% CI 0.15 – 0.45). Small (< 10 mm) LNM were most frequently undetected on pre-operative imaging. Due to a lack of data, no subgroup analysis comparing the diagnostic accuracy of CT versus MRI could be performed.

*Conclusion:* The value of current imaging strategies for the pre-operative assessment of nodal status in GBC remains unclear, especially regarding the detection of small LNM. Additional research is warranted in order to establish uniformity in international guidelines, improve pre-operative nodal staging and to prevent futile surgery.

## 1. Introduction

Gallbladder cancer (GBC) is the fifth most prevalent malignancy of the gastrointestinal tract worldwide. [1,2] Due to an asymptomatic course in early stages and a propensity for aggressive local growth, most gallbladder cancers are only diagnosed in an advanced stage. Outcomes are poor with reported 5-year survival rates ranging from 10 to 20% [3]. Radical excision currently remains the only curative treatment option. However, only 20–30 % of pre-operatively diagnosed patients are candidates for resection [4].

Prognosis after surgery is primarily determined by tumour- and lymph node stage; one-year survival rate after radical resection in T3 tumours drops from 50% to 2% when distant lymph nodes (outside of the hepatoduodenal ligament) are involved. [5] Once the tumour has metastasised to the periaortic, pericaval, superior mesenteric and celiac lymph nodes, resection does not appear to increase survival and surgery is deemed futile [6]. Adequate pre-operative detection of lymph node metastases (LNM) is therefore of vital importance to adequately select surgical candidates and to prevent surgery-related morbidity and mortality.

Agarwal et al. [7] analysed 60 patients with irresectable gallbladder cancer and found that 4 (7%) patients were irresectable due to pre-operatively undetected distant LNM. Other studies show that up to 50% of locally advanced gallbladder tumours appear to be irresectable

* Corresponding author.
*E-mail address:* elise.desavorninlohman@radboudumc.nl (E.A.J. de Savornin Lohman).

https://doi.org/10.1016/j.ejrad.2018.11.034
Received 15 October 2018; Received in revised form 25 November 2018; Accepted 27 November 2018
0720-048X/ 

during exploratory laparotomy due to undetected lymph node or peritoneal metastases [8]. Recently, staging laparoscopy has been incorporated into clinical practice in order to determine the resectability of gallbladder cancer before committing to exploratory laparotomy. However, a study [8] found that among 314 patients who were deemed resectable after pre-operative CT imaging and staging laparoscopy, 47 (15%) ultimately were irresectable due to nonlocoregional LNM. Clearly, better pre-operative radiological detection of nonlocoregional lymph nodes in addition to staging laparoscopy is paramount in order to prevent redundant surgery in gallbladder cancer patients. However, it is unclear which is the optimal imaging modality with the highest diagnostic accuracy.

Currently, computed tomography (CT) is the most widely used imaging modality for pre-operative staging. [5] However, the reported sensitivity of CT for the detection of LNM is only around 24% [9]. Evidence suggests that magnetic resonance imaging (MRI) might outperform CT with a sensitivity of up to 80% for nodal metastases and 100% for liver invasion [10]. Additionally, opposed to CT, MRI does not rely on the use of ionizing radiation, using magnetic stimulation of hydrogen atoms to depict the targeted tissue. MRI is especially useful for creating highly detailed images of soft tissues since these contain a high amount of hydrogen atoms. Although availability of MRI is less compared to CT, it is increasingly being used in clinical practice due to a better safety profile, suspected superior diagnostic performance and increasing availability.

The aim of the current systematic review is to determine the diagnostic accuracy of CT and MRI in the detection of LNM in order to define the optimal pre-operative imaging strategy in patients with gallbladder carcinoma.

## 2. Methods

### 2.1. Study selection

All prospective and retrospective cross-sectional studies analysing the diagnostic accuracy of CT and MRI in the detection of LNM of gallbladder cancer were considered eligible. Studies were included for narrative review if the following additional criteria were met: (a) all patients were > 18 years of age, (b) histopathological analysis or follow-up imaging was available as a reference standard, (c) sufficient data was reported in order to extract the number of true positive and false negative results of CT and/or MRI in the detection of lymph node metastases, regardless of level of reporting.

For the meta-analysis, studies reporting anything other than the patient as unit of analysis were excluded since data from varying levels of reporting (for example patient versus lymph node versus regional) cannot be pooled. Only studies reporting patient-level data reporting true positives, true negatives, false positives and false negatives in a manner that sensitivity and specificity could be reconstructed were included for meta-analysis. Case-control studies were excluded due to a high risk of bias. There were no restrictions based on publication status. Studies reporting results in any language but English, Dutch or German were excluded. When cohort overlap was suspected, the study with the smallest number of participants was excluded.

### 2.2. Search strategy

A systematic literature search was conducted in the databases of MEDLINE (8th of November, 2017) and EMBASE (10th of November, 2017). The search was performed including terms for ''gallbladder cancer'', ''Magnetic Resonance Imaging'' and ''Computed Tomography'' (full search strategy is provided in Appendix A in Supplementary Materials, Tables A1 &A2). Additionally, the references of all included studies and major meta-analyses were searched for additional studies not included in the results of electronic searches. Online clinical trial registries such as ISRCTN (www.isrctn.com) and ClinicalTrials.gov (www.clinicaltrials.gov) were searched as an additional source for related studies. This study was carried out in accordance with the protocol as registered in PROSPERO (record ID 83752).

### 2.3. Data extraction

One reviewer (E.S.L.) screened titles and abstracts of records retrieved by the electronic searches for eligibility. A second reviewer (T.B.) assessed the accuracy of decision making on a random sample of 20%. Full text of the studies possibly meeting inclusion criteria was obtained. Two independent reviewers (E.S.L. and T.B.) applied the inclusion criteria to the full records. Any disagreement in study selection was resolved by discussion or arbitration by a third reviewer (P.R.). When not enough information was provided in order to assess eligibility of the study for inclusion, the study authors were contacted with a request for additional information.

Data was extracted into Review Manager version 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) by two independent reviewers using a standardized data extraction form. The following data was extracted for all studies included for review: year of publication, country of publication, study design (e.g. retrospective cohort study, prospective cohort study, randomised controlled trial), full text publication or abstract, inclusion and exclusion criteria, number of participants, participant age and gender, years of experience and expertise of assessors, MRI/CT characteristics, reference standard characteristics and sensitivity for the detection of LNM.

Additionally, for studies included for meta-analyses the following additional data was extracted: number of true positives (TP), true negatives (TN), false positives (FP) and false negatives (FN) and diagnostic criteria and cut-off values / version of TNM staging used.

When raw data on diagnostic accuracy was not available, study authors were contacted in order to obtain additional data. Any differences were resolved by discussion or by input from a third reviewer (P.R.).

### 2.4. Assessment of methodological quality

Using a modified version of the QUADAS-2 assessment-tool [11], study design characteristics were extracted and analysed by two independent reviewers (E.S.L. and T.B.) to assess methodological quality. Any discrepancies were resolved by means of discussion and consensus. When discrepancies persisted, a third author (P.R.) was requested for additional input in order to reach consensus. See Appendix B in Supplementary Materials provides the criteria used to classify responses (yes, no or unclear) to each of the QUADAS-2 checklist items.

### 2.5. Statistical analysis and data synthesis

For each study included in the meta-analysis, data was extracted to generate 2 × 2 contingency tables displaying true-positives, true-negatives, false positives and false negatives. Patients with N0 nodal status were regarded as disease negative and patients with either N1 or N2 nodal status were disease positive. True positives were defined as cases in which patients were categorised as having disease by both the index- and reference test. False positives were defined as patients categorised as having disease by the index test but categorised as not having disease by the reference standard. True negatives were patients categorised as not having disease by the index- and reference test. False negatives were defined as patients categorised as not having disease by the index test and having disease by the reference standard. Forest plots were constructed for all included studies displaying sensitivity, specificity and the corresponding 95% confidence interval for both index tests. Summary sensitivity and specificity of MRI were also plotted on a ROC curve. Since a common implicit cut-off value for test positivity is to be expected, estimates of pooled sensitivity and specificity were calculated by fitting a bivariate random effects model. A P-value of < 0.05

was considered statistically significant. All analyses were conducted using Review Manager 5.3 and R 3.6 statistical package (R Core Team (2016). R, R Foundation for Statistical Computing, Vienna, Austria)

### 2.6. Assessment of reporting bias

To date, no formal tool for the assessment of reporting bias in diagnostic accuracy studies exists. However, we highlighted possible sources of detection, selection and reporting bias and consequently excised caution in the interpretation of results.

### 2.7. Heterogeneity exploration

Due to the nature of diagnostic accuracy studies, heterogeneity is expected to be present. [12] We planned to conduct a sensitivity analysis exploring the influence of the following characteristics on sensitivity and specificity; year of publication, experience of assessor (defined as ≤ 5 or > 5 years of experience), type of MRI/CT (single-slice vs. multi-slice, 1.5 vs. 3 T), study design (prospective vs. retrospective), full text publications versus abstracts, age of participants, type of reference standard, version of TNM-staging used and use of contrast agents. However, due to the small sample of included studies, we did not conduct any sensitivity analyses.

## 3. Results

### 3.1. Search strategy and study selection

A flowchart of the selection process is provided in Fig. 1. Our search strategy identified 1612 records in MEDLINE, 2665 in EMBASE and 0 in the Cochrane Library of Diagnostic Test Accuracy Studies. A handsearch of references from these studies and reviews did not yield any additional records. After removal of duplicates, the titles and abstracts of 3777 records were screened for relevance and 117 studies were selected for full text evaluation. A total of 108 studies were excluded after full-text assessment for the following reasons: narrative review/editorial/comment (N = 48); no full text available (N = 24); not addressing the research question (N = 10); not reporting data in such a way that sensitivity for LNM detection can be calculated (i.e. not all patients received verification by a reference test or not reporting data for GBC separately) (N = 19) or other reasons (N = 7). Five studies reported patient-level data and were included for meta-analysis. An additional four studies provided sensitivity data for CT or MRI, and were included for narrative synthesis.

The studies that met our inclusion criteria for meta-analysis or narrative review are described in Table 1.

### 3.2. Studies included for meta-analysis

Five studies were included for meta analysis. Four investigated the diagnostic accuracy of MRI [13–16] in 138 participants and one investigated the diagnostic accuracy of CT [17] in 20 participants. All except one [16] were of retrospective design. None of the studies directly compared the diagnostic accuracy of CT with MRI. All except one [17] only included patients in which either curative or palliative surgery was performed, arguing the need for histopathological analysis of the final resection specimen as a reference standard. One study [17] chose to include irresectable patients, using a combination of percutaneous biopsy and autopsy results as an alternative reference standard. Another MRI study [13] excluded patients in which CT imaging was considered to be diagnostic for tumour stage. Criteria for lymph node positivity were reported in 3 out of 5 studies. The prevalence of node-positive disease ranged from 33% [16] to 72% [15] with a median of 54% (IQR 43–68%).

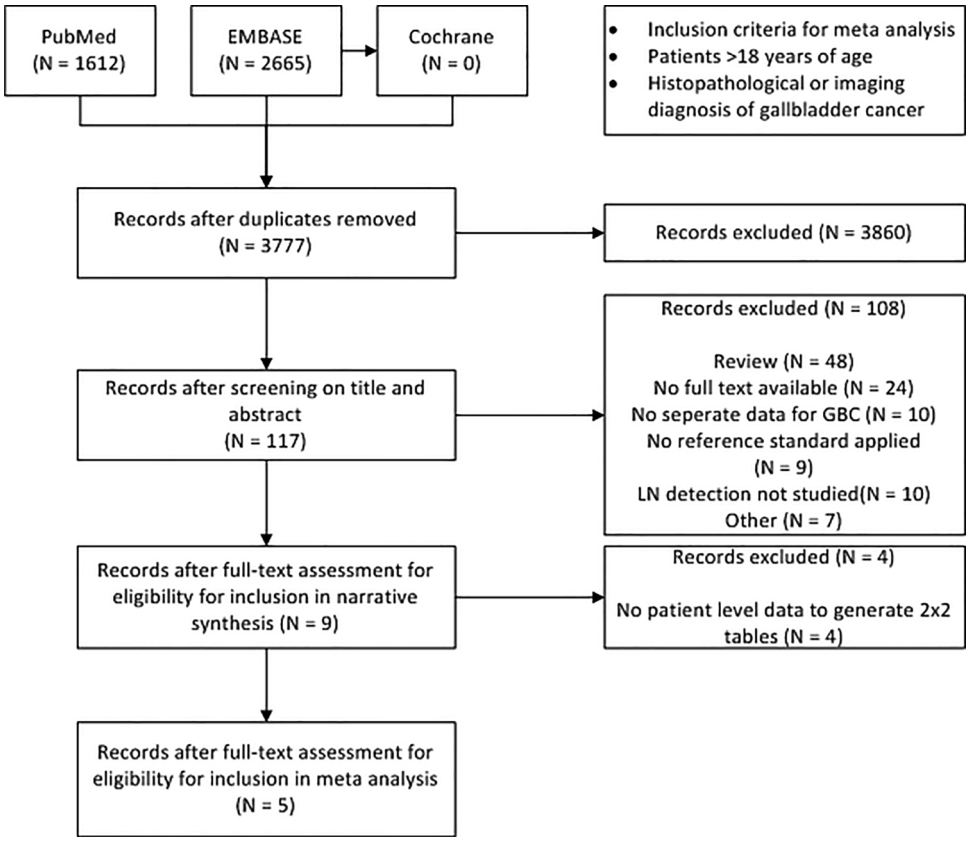


**Fig. 1.** Study selection flowchart.

**Table 1**
Characteristics of included studies.

| Basic study and patient characteristics | | | | | | |
|---|---|---|---|---|---|---|
| Authors | Year of publication | Number of participans | Age, mean | Study design | Reference standard | Modality |
| Engels et al. | 1989 | 20 | Unknown | Retrospective cohort | Surgical findings, autopsy, FNA biopsy results | CT |
| Kalra et al. | 2006 | 20 | 50 | Prospective cohort | Surgical findings, histopathology | CT |
| Kaza et al. | 2006 | 15 | 52 | Prospective cohort | Surgical findings, histopathology | MRI |
| Kim et al. | 2002 | 18 | 57 | Retrospective cohort | Surgical findings, histopathology | MRI |
| Kim et al. | 2015 | 86 | 65 | Retrospective cohort | Surgical findings, histopathology | MRI |
| Ohtani et al. | 1996 | 59 | 65 | Retrospective cohort | Surgical findings, histopathology | CT |
| Oikarinen et al. | 1993 | 37 | 69 | Retrospective cohort | Histopathology, FNA biopsy results, follow-up imaging results | CT |
| Schwartz et al. | 2002 | 19 | 68 | Retrospective cohort | Surgical findings, histopathology | MRI |
| Tseng et al. | 2002 | 18 | Unknown | Retrospective cohort | Surgical findings | MRI |

### 3.3. Additional studies included for narrative review

Four studies could not be included for meta-analysis but did meet our eligibility criteria for narrative review. Three studies [18–20] investigated CT in 116 participants and one study [21] investigated MRI in 18 participants for the detection of LNM. All studies except one [20] were retrospective in nature. Three studies [18,20,21] chose to exclude patients in whom no surgical and/or histopathological analysis of a resection specimen was available as a reference standard. One study [19] did not exclude irresectable patients, but chose to compare preoperative imaging findings to a combination of follow-up imaging and fine-needle biopsy results. None of the studies excluded patients based on age, gender or tumour stage. Three studies [18–20] used a cut-off value of a diameter > 10 mm as criterion for lymph-node positivity. One study [21] did not describe diagnostic criteria.

### 3.4. Methodological quality

An overview of the methodological quality of included studies as assessed by QUADAS-2 is provided in Fig. 2. Additionally, scores on each individual QUADAS-2 item for all included studies are displayed in Appendix C in Supplementary Materials. As illustrated, there is a substantial amount of underreporting in the included studies, resulting in many "unclear" judgements and consequently diminishing the quality of the data.

## 4. Findings

### 4.1. Sensitivity of CT and MRI in the detection of LNM

Five studies investigated the diagnostic accuracy of MRI in 156 participants and four studies investigated the diagnostic accuracy of CT in 136 participants. In Fig. 3, an overview of the sensitivity of CT and MRI in the detection of lymph node metastases is displayed. Results from all studies are shown, including studies not reporting patient level data. As demonstrated, sensitivity of both modalities varied greatly, ranging from 0.25 to 0.93. Of note, all studies in which the size of the false negative lymph nodes was reported [15–17,20] stated that all missed LNM were < 10 mm in size.

### 4.2. Accuracy of MRI and CT for the detection of LNM in gallbladder cancer

A Forest Plot of sensitivity and specificity of MRI and CT for nodal staging from individual studies is displayed in Fig. 4. Our search identified only one study which investigated the diagnostic accuracy of CT and reported data on patient level [17]. In this study, 20 patients with gallbladder cancer were included and the respective sensitivity and specificity of CT were 0.93 (95% CI 0.66–1.00) and 1.00 (95% CI 0.54–1.00). The negative likelihood ratio including 95% confidence interval was 0.07 (0.01 - 0.47). No false positives were reported in this study; therefore, the positive likelihood ratio could not be calculated.

The sensitivity of MRI ranged from 57% to 92%. Specificity ranged from 78% to 100%. The estimated summary sensitivity and specificity

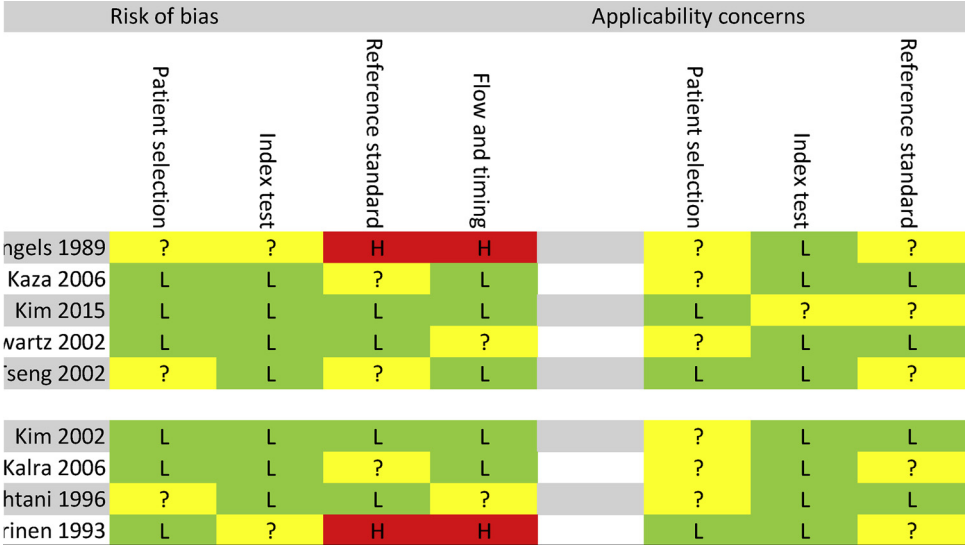


**Fig. 2.** Risk of bias assessment according to QUADAS2. Abbreviations: L = low, H = high,? = unknown.

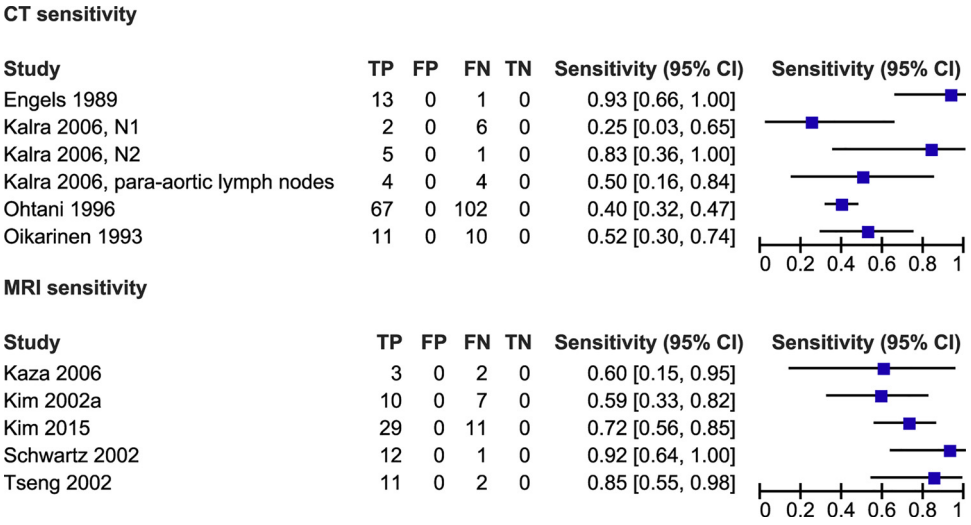


**Fig. 3.** Forest plot of reported sensitivity of all included studies.

values (Fig. 5) including 95% confidence intervals were 0.75 (0.60 - 0.85) and 0.83 (0.74 - 0.90), respectively. The pooled positive likelihood ratio was 4.52 (95% CI 2.55 to 6.48), and the pooled negative likelihood ratio was 0.30 (95% CI 0.15 to 0.45).

The assessors in the study by Kim et al. [13] did not perform consensus readings. Instead, diagnostic accuracy data was reported from the separate readings of both assessors. We chose to incorporate the readings of both assessors into our model as separate studies. We also attempted to conduct two sensitivity analyses, incorporating only the data from either one of the assessors. However, not enough data was available and a summary ROC point could not be estimated. Fig. 5 displays a summary ROC point for the diagnostic accuracy of MRI as well as individual accuracy estimates of all included studies.

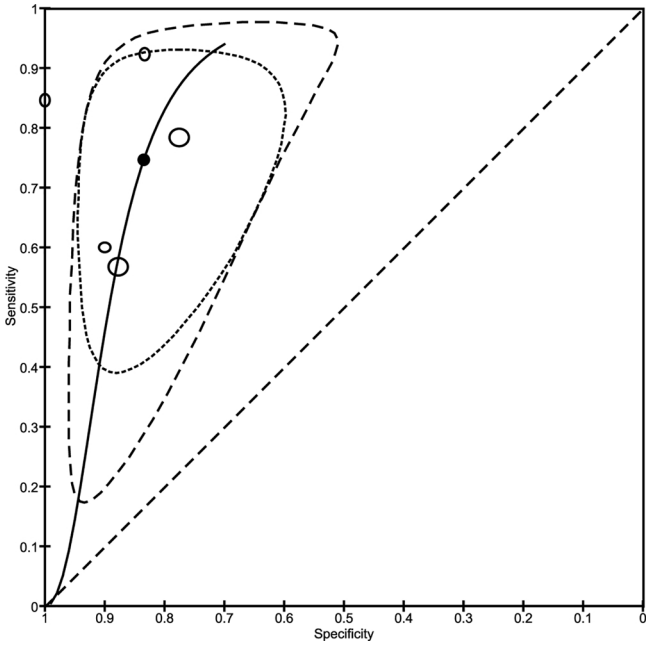


**Fig. 5.** Summary receiver operating characteristic (SROC) curve of the diagnostic accuracy of MRI.

## 5. Discussion

Pre-operative staging of gallbladder cancer still presents a significant clinical challenge. The presence of LNM, especially in non-locoregional sites (i.e. outside of the hepatoduodenal ligament) is associated with a poor prognosis. [22] Pre-operative detection of LNM in gallbladder cancer is essential in order to determine the treatment approach, prevent unnecessary surgery and establish prognosis.

Five studies investigating the diagnostic accuracy of CT or MRI met our inclusion criteria for meta-analysis. An additional 4 studies were included for narrative review. Based on these studies, the estimated summary sensitivity of MRI for detection of LNM was 0.75. Sensitivity of CT could not be pooled as only one study was included, but the sensitivity of CT ranged from 0.25 to 0.93 in the studies included for narrative review.

Currently, substantial controversy exists regarding the optimal pre-operative imaging strategy for gallbladder cancer. The guideline from the European Society of Medical Oncology (ESMO) [23] states that all patients should receive pre-operative MRI since within the literature superior sensitivity of MRI compared to CT has been reported for the staging of various tumours [24,25], but other guidelines [5,26] state that not enough evidence is available to support this approach. Our

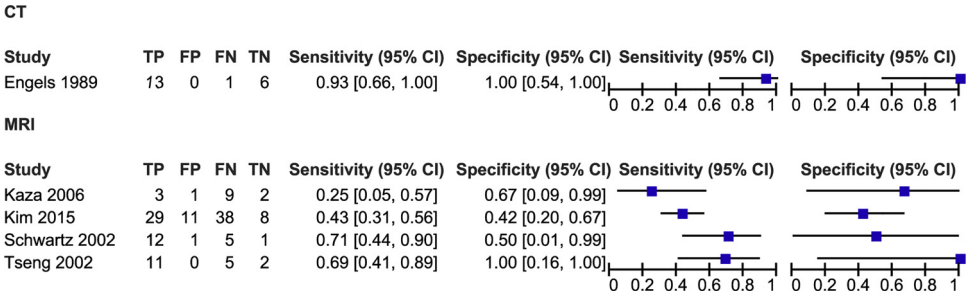


**Fig. 4.** Forest plot of reported sensitivity and specificity of studies included in the meta-analysis.

findings confirm this notion and no difference between CT and MRI could be demonstrated. Significant heterogeneity was found in reported sensitivity and specificity, patient population characteristics, and reference standards.

Almost all studies (with the exception of two [16,20]) were retrospective case series in which the criteria for additional MRI were not clearly outlined. In current clinical practice virtually all patients receive CT-imaging; additional MRI is only conducted when deemed necessary by the treating physician; for example when liver involvement cannot be clearly outlined on CT imaging. This may result in selection bias as only those patients with ambiguous CT results will receive an additional pre-operative MRI. Furthermore, a variety of reference standards was used for the verification of imaging results. Most studies only included resectable patients and chose to use histopathological analysis of the resection specimen as the reference standard. However, some studies also included inoperable patients and used follow-up imaging or biopsy results to verify imaging results. Evidently, arguments supporting the validity of both strategies can be made. On the one hand, surgical exploration and histopathological analysis remain the gold standard for the verification of imaging results. On the other hand, this is obviously not possible in patients not undergoing surgery and excluding irresectable patients might result in significant selection bias, as more patients with irresectable e.g. locally advanced tumours are more likely have positive distant LNM [27]. Thus, the use of an alternate reference standard like adequate follow-up imaging can provide valuable additional information.

The materials and scanning protocols used in the included studies differed significantly. Notably, slice thickness of the CT and MRI scanners varied considerably. As nodal size is the most important characteristic used for LNM detection which is obviously influenced by slice thickness, up-to-date imaging devices with smaller slice thickness may detect LNM more accurately. Furthermore, most studies stated that metastatic lymph nodes missed on pre-operative imaging were usually smaller than 10 mm in size. Newer imaging devices with a higher resolution or techniques like diffusion-weighted MRI or MRI using nano-sized contrast particles have demonstrated promising results in other hepatobiliary malignancies [28–30]and could more accurately detect LNM.

This systematic review and meta-analysis has several limitations that need to be considered. First and foremost, the number of included studies was limited, resulting in a paucity of data available for meta-analysis. Diagnostic accuracy data for CT could not be pooled since only one study was included and MRI and CT could not be compared. Although we planned to conduct sensitivity analyses in order to identify sources of heterogeneity, the limited quantity of data made this impossible. Second, there was considerable heterogeneity regarding patient characteristics, test characteristics and reference standards used. Some of the studies were published before 2000 and might have been conducted using out-of-date imaging techniques. Finally, the quality of the studies was rated as unclear on many aspects due to serious underreporting regarding methodology and patient selection. This is an important cause of concern and should be taken into consideration when interpreting the results.

## 6. Conclusions

Our systematic review and meta-analysis show significant uncertainty regarding the optimal imaging strategy for the pre-operative detection of LNM in GBC. Current clinical practice involves standard pre-operative imaging by CT and additional MRI only in case of inconclusive CT results regarding pre-operative staging. Although a potential superior diagnostic accuracy of MRI has been reported, this is not supported by our results. Both CT and MRI demonstrate varying sensitivity and seem to be unreliable for the detection of LNM < 10 mm in size as demonstrated by the finding that in the studies included in this review all false negative lymph nodes were < 10 mm in size. More advanced pre-operative imaging techniques and better knowledge of metastatic lymph node imaging characteristics are needed to improve the pre-operative detection of LNM in gallbladder cancer and prevent unnecessary surgery-related morbidity and mortality.

## Funding sources

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

## Declaration of interests

None of the authors have any actual or potential conflicts of interest to declare in relation to this article.

## Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.ejrad.2018.11.034.

## References

[1] C. Are, et al., Global epidemiological trends and variations in the burden of gallbladder cancer, J. Surg. Oncol. 115 (5) (2017) 580–590.
[2] R. Hundal, E.A. Shaffer, Gallbladder cancer: epidemiology and outcome, Clin. Epidemiol. 6 (2014) 99–109.
[3] P. Cubertafond, A. Gainant, G. Cucchiaro, Surgical treatment of 724 carcinomas of the gallbladder. Results of the French Surgical Association Survey, Ann. Surg. 219 (3) (1994) 275–280.
[4] A. Duffy, et al., Gallbladder cancer (GBC): 10-year experience at Memorial Sloan-Kettering cancer centre (MSKCC), J. Surg. Oncol. 98 (7) (2008) 485–489.
[5] Aloia, T.A., et al., Gallbladder cancer: expert consensus statement. HPB (Oxford), 2015. 17(8): p. 681-690.
[6] H. Wakabayashi, et al., Analysis of prognostic factors after surgery for stage III and IV gallbladder cancer, Eur. J. Surg. Oncol. 30 (8) (2004) 842–846.
[7] Agarwal, A.K., R. Kalayarasan, and A. Javed, Role of staging laparoscopy in gall bladder cancer: Analysis of 406 patients. Hpb, 2012. 14: p. 17-18.
[8] C. Pilgrim, V. Usatoff, P.M. Evans, A review of the surgical strategies for the management of gallbladder carcinoma based on T stage and growth type of the tumour, Eur. J. Surg. Oncol. 35 (9) (2009) 903–907.
[9] H. Petrowsky, et al., Impact of integrated positron emission tomography and computed tomography on staging and management of gallbladder cancer and cholangiocarcinoma, J. Hepatol. 45 (1) (2006) 43–50.
[10] L. Zhong, L. Li, Q.Y. Yao, Preoperative evaluation of pancreaticobiliary tumor using MR multi-imaging techniques, World J. Gastroenterol. 11 (24) (2005) 3756–3761.
[11] P.F. Whiting, et al., QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies, Ann. Intern. Med. 155 (8) (2011) 529–536.
[12] M.M. Leeflang, Systematic reviews and meta-analyses of diagnostic test accuracy, Clin. Microbiol. Infect. 20 (2) (2014) 105–113.
[13] S.J. Kim, et al., Preoperative staging of gallbladder carcinoma using biliary MR imaging, J. Magn. Reson. Imaging 41 (2) (2015) 314–321.
[14] L.H. Schwartz, et al., Gallbladder carcinoma: findings at MR imaging with MR cholangiopancreatography, J. Comput. Assist. Tomogr. 26 (3) (2002) 405–410.
[15] J.H. Tseng, et al., Diagnosis and staging of gallbladder carcinoma. Evaluation with dynamic MR imaging, Clin. Imaging 26 (3) (2002) 177–182.
[16] R.K. Kaza, et al., Evaluation of gall bladder carcinoma with dynamic magnetic resonance imaging and magnetic resonance cholangiopancreatography, Australas. Radiol. 50 (3) (2006) 212–217.
[17] J.T. Engels, D.M. Balfe, J.K. Lee, Biliary carcinoma: CT evaluation of extrahepatic spread, Radiology 172 (1) (1989) 35–40.
[18] T. Ohtani, et al., Spread of gallbladder carcinoma: CT evaluation with pathologic correlation, Abdom. Imaging 21 (3) (1996) 195–201.
[19] H. Oikarinen, et al., Radiological findings in cases of gallbladder carcinoma, Eur. J. Radiol. 17 (3) (1993) 179–183.
[20] N. Kalra, et al., MDCT in the staging of gallbladder carcinoma, AJR Am. J. Roentgenol. 186 (3) (2006) 758–762.
[21] J.H. Kim, et al., Preoperative evaluation of gallbladder carcinoma: efficacy of combined use of MR imaging, MR cholangiography, and contrast-enhanced dual-phase three-dimensional MR angiography, J. Magn. Reson. Imaging 16 (6) (2002) 676–684.
[22] S. Miyakawa, et al., Biliary tract cancer treatment: 5,584 results from the Biliary Tract Cancer Statistics Registry from 1998 to 2004 in Japan, J. Hepatobiliary. Surg. 16 (1) (2009) 1–7.
[23] J.W. Valle, et al., Biliary cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up, Ann. Oncol. 27 (Suppl. 5) (2016) v28–v37.
[24] B. Liu, S. Gao, S. Li, A comprehensive comparison of ct, MRI, positron emission tomography or positron emission tomography/CT, and diffusion weighted imaging-mri for detecting the lymph nodes metastases in patients with cervical cancer: a meta-analysis based on 67 studies, Gynecol. Obstet. Invest. 82 (3) (2017) 209–222.

[25] G.P. Schmidt, et al., Whole-body magnetic resonance imaging and positron emission tomography-computed tomography in oncology, Top. Magn. Reson. Imaging 18 (3) (2007) 193–202.
[26] I.K. Nederland, Galweg- en Galblaascarcinoom 2.0, (2010).
[27] Y. Shirai, et al., Assessment of lymph node status in gallbladder cancer: location, number, or ratio of positive nodes, World J. Surg. Oncol. 10 (2012) 87.
[28] J.K. Kim, et al., Feasibility of diffusion-weighted imaging in the differentiation of metastatic from nonmetastatic lymph nodes: early experience, J. Magn. Reson. Imaging 28 (3) (2008) 714–719.
[29] I. Ryoo, et al., Gadobutrol-enhanced, three-dimensional, dynamic MR imaging with MR cholangiography for the preoperative evaluation of bile duct cancer, Invest. Radiol. 45 (4) (2010) 217–224.
[30] H.Y. Sun, et al., Gadoxetic acid-enhanced MRI with MR cholangiography for the preoperative evaluation of bile duct cancer, J. Magn. Reson. Imaging 38 (1) (2013) 138–147.