The role of laparoscopy and laparoscopic ultrasound in the preoperative staging of pancreatico-biliary cancers: a meta-analysis

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CRD summary
The review concluded that staging laparoscopy offered significant benefit to patients with resectable pancreatico-biliary cancers in avoiding non-therapeutic laparotomy and should be adopted in routine clinical practice in a judicious algorithm. Weaknesses in the review process and analyses mean that these conclusions should be interpreted cautiously.

Authors' objectives
To assess the effect of preoperative staging using staging laparoscopy (SL) with or without laparoscopic ultrasound (LUS) on the surgical management of of pancreatico-biliary cancers.

Searching
Literature was searched using PubMed and the related articles function in PubMed (31 June 2009). Search terms were reported. There were no language restrictions. Bibliographies of identified articles were screened for additional studies.

Study selection
Studies that assessed the effect of preoperative staging using SL with or without LUS (SL/LUS) on the surgical management of patients with potentially resectable pancreatic/peripancreatic cancers (PPC) and proximal-biliary cancers (PBC) were eligible for inclusion. Gall bladder cancers and hilar and intrahepatic cholangiocarcinomas were included.

Included studies were required to use surgical evaluation as the reference standard for staging, except when laparoscopy detected obvious metastatic lesions (usually biopsy proven) or locally advanced disease, or confirmed benign pathology or absence of disease, that prevented surgical exploration.

The authors did not state how many reviewers screened studies for inclusion.

Assessment of study quality
Methodological quality of included studies was assessed using Standards for Reporting of Diagnostic Accuracy (STARD) guidelines for the reporting of test accuracy studies. No further details of quality assessment were reported. The authors appeared to have used STARD to derive a summary quality score.

The authors did not state how many reviewers performed the quality assessment.

Data extraction
Data were extracted to calculate the sensitivity, specificity and diagnostic odds ratios (DORs), with 95% confidence intervals (CIs), of SL/LUS to change management in patients with potentially resectable PPC and PBC and the overall diagnostic yield of laparoscopic examination. Data were extracted to calculate the sensitivity, specificity and diagnostic odds ratios of SL/LUS to detect liver metastases, peritoneal deposits, locally advanced disease (invasion into adjacent vessels or organs) and lymph node lesions.

Two reviewers independently extracted data. Any disagreements were resolved by discussion with a third reviewer.

Methods of synthesis
Summary Receiver Operator Characteristic (SROC) curves were estimated using the Moses-Shapiro-Littenberg model weighted by sample size. Results were compared to the hierarchical SROC model.

Summary diagnostic odds ratios, with 95% CIs, were calculated for the odds of having unresectable disease given a
positive laparoscopy compared to a negative laparoscopy.

Sensitivity analyses were performed for inclusion of studies with more than 100 successful laparoscopies and inclusion of studies with STARD scores of at least 18.

Subgroup analyses were performed to assess diagnostic accuracy of SL/LUS for liver metastases, peritoneal metastases and local/vascular invasion.

Between-study heterogeneity was assessed using Cochran’s Q-test based on a $\chi^2$ distribution and quantified using the $I^2$ statistic. Meta-regression analysis was performed to explore sources of heterogeneity (such as year of publication, sample size, use of LUS and study quality).

Results of the review

Twenty-nine studies (n=3,305 participants) were included in the review. A total of 2,827 patients with PPC and 478 patients with PBC deemed potentially resectable on pre-operative staging were included in the analyses. STARD scores ranged from 5 to 20.

**Pancreatic/peripancreatic cancers (PPC):** The overall yield of SL/LUS for PPC was 25% (95% CI 24 to 27) with a pooled diagnostic odds ratio of 104 (95% CI 48 to 227). Use of SL/LUS improved the resection rate from 61% to 80%. The overall specificity for detecting inoperable disease were 64% (95% CI 61% to 66%) and 99% (95% CI 99% to 100%) with significant between-study heterogeneity in all data sets. Subgroup analyses showed sensitivities for detection of liver lesions (88%, 95% CI 83% to 92%) and peritoneal lesions (92%, 95% CI 84% to 96%). Sensitivity for detection of local invasion was low (58%, 95% CI 51% to 65%).

**Proximal biliary cancers (PBC):** The overall yield of SL/LUS for PBC was 47% (95% CI 42% to 52%) with a pooled diagnostic odds ratio of 61 (95% CI 19 to 189). Use of SL/LUS increased the curative resection rate from 27% to 50%. Overall sensitivity and specificity of SL/LUS in detecting inoperable disease were 63% (95% CI 58% to 68%) and 100% (95% CI 97% to 100%) with significant between-study heterogeneity for sensitivity. Subgroup analyses showed sensitivities for the detection of liver lesions (83%, 95% CI 69% to 92%) and peritoneal lesions (93%, 95% CI 81% to 99%). Sensitivity for detection of local invasion was low (34%, 95% CI 22% to 47%).

Sensitivity analyses that included only high-quality studies (STARD score ≥18) showed no significant improvement in test performance for PPC or PBC. Restriction to studies that employed LUS increased sensitivity and diagnostic odds ratio in PPC, but did not affect test performance in PBC. There were insufficient studies with more than 100 participants to conduct sensitivity analyses based on sample size. Meta-regression did not reveal any cause for the observed heterogeneity between studies.

Additional data were reported for laparoscopy related complications.

Authors’ conclusions

SL offered significant benefit to patients with resectable pancreatico-biliary cancers in avoiding non-therapeutic laparotomy and should be adopted in routine clinical practice in a judicious algorithm.

CRD commentary

The review stated a clear research objective. Inclusion criteria could have been presented more clearly. In particular, limited details were provided of how diagnoses were confirmed in patients who did not undergo surgery. No language restrictions were applied to the literature search, which minimised the risk of language bias. The limited number of sources searched raised a possibility that relevant articles were missed. The data extraction process included measures to minimise error and/or bias; it was unclear whether similar measures were used throughout the review process. The methodological quality of included studies was assessed based on the STARD guideline for reporting of test accuracy studies rather than a quality assessment tool and no details of the quality assessment were provided beyond an overall score, so it was not possible to adequately assess the reliability of individual study results. A large number of summary estimates of test performance were presented, but these are of questionable value given the presence of significant heterogeneity in most cases. Reporting of the details of individual included studies was limited.
Overall, the authors conclusions reflected the data presented, but should be viewed cautiously because of limitations in the review process and analyses.

**Implications of the review for practice and research**

**Practice:** The authors stated that SL appeared to be beneficial for patients with pancreatic and biliary cancers for detection of peritoneal disease and small surface liver metastasis below the threshold of other imaging modalities. They further stated that SL should be adopted in routine clinical practice and algorithms designed for its judicious use.

**Research:** The authors did not state any recommendations for future research.

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