Diagnostic accuracy of endoscopic ultrasound-guided fine-needle aspiration for solid pancreatic lesion: a systematic review

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CRD summary
The review concluded that endoscopic ultrasound-guided fine-needle aspiration had excellent sensitivity and specificity for pancreatic malignancy and rapid onsite evaluation by a cytopathologist or an endosonographer could improve accuracy. The authors’ conclusions reflect the data presented except that there did not appear to be sufficient evidence to support improvements arising from rapid onsite evaluation.

Authors' objectives
To assess the accuracy of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) for diagnosis of pancreatic cancer.

Searching
MEDLINE was searched from January 2002 to January 2012. Search terms were reported. Other databases searched included Science Direct, EBSCO and Springer link. Bibliographies of included articles were screened for additional studies. Only publications in English were included.

Study selection
Prospective or retrospective studies that assessed the diagnostic performance of endoscopic ultrasound-guided fine-needle aspiration in patients with suspected pancreatic cancer were eligible for inclusion. Studies were required to use histopathology as the reference standard to confirm diagnosis; in patients who did not undergo surgery, clinical and morphological (imaging) follow-up for a minimum of six months was accepted. Included studies had to report sufficient data to derive absolute numbers of true positive, false negative, false positive and true negative test results.

Studies were required to exclude patients with cystic lesions or other malignancies (such as cholangiocarcinoma, duodenal adenocarcinoma and periampullary adenocarcinoma).

Included studies were conducted in Europe, USA, Japan and Australia. Ultrasound-guided fine-needle aspiration samples were histology, cytology or a combination of both.

Two reviewers independently assessed studies for inclusion.

Assessment of study quality
The methodological quality of included studies was assessed using the STARD reporting guideline for test accuracy studies. Components assessed included: clinical and demographic characteristics; a consecutive series of participants; prospective study; the reference standard and its rationale; technical specifications of materials and methods; reporting distribution of severity of disease; blinding; and reporting how indeterminate and missing test results were handled.

Two reviewers independently assessed study quality.

Data extraction
Data were extracted on absolute numbers of true positive, false negative, false positive and true negative test results and used to calculate sensitivity and specificity, positive and negative likelihood ratios and diagnostic odds ratio (DOR), with 95% confidence intervals (CI).

Non-diagnostic specimens were classified as false negative where malignancy was confirmed histopathologically and true negative where a benign diagnosis was ultimately established.

Two reviewers independently extracted data.

Methods of synthesis
Pooled estimates of sensitivity and specificity, positive and negative likelihood ratios and diagnostic odds ratio, with 95% CI, were calculated using a random-effects model.

Statistical heterogeneity was assessed using the $X^2$ test and quantified using the $I^2$ statistic.

A summary receiver operating characteristic (SROC) curve was generated using the Moses and Littenberg model. Meta-regression was used to assess the effects of potential sources of heterogeneity (study design, use of rapid on-site evaluation, prevalence of malignancy, sample size, year of publication, cytology versus biopsy for ultrasound-guided fine-needle aspiration sample, needle size and fixative system) on overall accuracy as indicated by DOR.

**Results of the review**

Fifteen studies (1,860 participants, range 42 to 231) were included in the review. Eleven studies had a prospective design and nine of these enrolled participants consecutively. One study used histopathology alone as the reference standard; the other studies used an alternative reference standard comprised of clinical and imaging follow-up. None of the studies reported blinding.

Pooled estimates of sensitivity and specificity were 92% (95% CI 91 to 93) and 96% (95% CI 93 to 98; high statistical heterogeneity $I^2$>50%). Pooled positive and negative likelihood ratios were 14.24 (95% CI 7.78 to 26.07; $I^2$=32.5%) and 0.09 (95% CI 0.07 to 0.13; $I^2$=70.1%). The pooled DOR was 168.28 (95% CI 94.07 to 301.02; $I^2$=5.6%).

None of the variables included in the meta-regression analysis were significant.

Subgroup analyses of studies with and without rapid on-site evaluation gave sensitivities of 95% (95% CI 93 to 96; $I^2$=0; six studies) and 89% (95% CI 86 to 91%; $I^2$=69.3%; nine studies).

**Authors’ conclusions**

Endoscopic ultrasound-guided fine-needle aspiration had excellent sensitivity and specificity for diagnosis of malignancy in solid pancreatic lesions. Rapid onsite evaluation by a cytopathologist or an endosonographer could help improve the accuracy of the test.

**CRD commentary**

The article reported a clearly stated research objective that was fully defined by appropriate inclusion criteria. Various sources were searched for relevant studies. The restriction to studies in English may have resulted in the omission of relevant data. The review process included measures to minimise error and bias. The authors reported an assessment of the methodological quality of included studies but this was based on the STARD statement (a reporting guideline rather than a tool for assessing methodological quality). Therefore it was not possible to adequately assess the extent to which methodological weaknesses in the included studies may have affected the results of the review.

The meta-analytic methods were adequate but a hierarchical or bivariate SROC model may have been more appropriate for the heterogeneous data set presented.

The authors' conclusions reflect the data presented exception that there did not appear to be sufficient evidence to support the idea that rapid onsite evaluation by a cytopathologist or an endosonographer can improve test accuracy.

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

**Practice:** The authors stated that because of the risk of complications for patients with tumour in the body or tail of the pancreas, endoscopic ultrasound-guided fine-needle aspiration should be conducted with caution.

**Research:** The authors stated that high quality trials were needed.

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