Equipment and techniques for optimizing diagnostic efficacy after endoscopic ultrasound-guided tissue acquisition from solid pancreatic and abdominal masses

Ph.D. Thesis Booklet

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1.Introduction

5.1.1. Pancreatic cancer and endoscopic ultrasound

Pancreatic cancer is one of the most common and deadly gastrointestinal cancers currently. If a pancreatic mass is detected and needs pathological assessment before resection is considered, endoscopic ultrasound (EUS)-guided tissue acquisition is performed under sedation, either fine-needle aspiration (FNA) or biopsy (FNB). The tissue is then processed for pathology.

5.1.2. Diagnostic adequacy

Approximately 14% of samples are inadequate for histology, and 8% for cytology. Resampling exposes the patient to risk of delayed diagnosis and complications (e.g. bleeding, pancreatitis).

Different equipment and techniques have been evaluated to improve the diagnostic performance and adequacy of the sample. Contrast-enhanced EUS (CEH-EUS) may improve targeting of the lesion, yielding samples that contain relevant tissues rather than necrotic/fibrotic parts of the mass. Different processing methods for cytology, such as conventional smear (CS) or liquid-based cytology (LBC), may improve diagnostic performance.

5.1.3. Implementation of results

Improving the technical guidelines for EUS-guided tissue acquisition will optimize the sampling procedure for patients, sparing them re-interventions and maximizing adequacy and diagnostic rates.

2. Objectives

2.1. Study I. – Comparing CEH-EUS to conventional EUS for tissue acquisition from solid pancreatic masses

This study aimed to assess the diagnostic adequacy and accuracy parameters of EUS-guided tissue acquisition when using CEH-EUS during the procedure, as compared to conventional EUS.

2.2. Study II. – Comparing CS to LBC, and their combination, for EUS-guided tissue acquisition from abdominal masses

This study aimed to compare primarily the diagnostic accuracy and secondarily the diagnostic adequacy of

EUS-guided tissue acquisition when using CS versus LBC, with an additional comparison to the combination of methods.

3.Methods

3.1. Study I.

Five databases were searched in November 2023 (PubMed, Embase, Central, Scopus, Web of Science). Studies were eligible for inclusion in random effects meta-analysis if comparing CEH-EUS to conventional EUS and reporting diagnostic adequacy, accuracy and safety. Both randomized trials (RCTs) and non-randomized studies were included. Selection was performed by two individuals in parallel, as was the data extraction. Odds ratios (OR) and Risk Ratios (RR) with 95% confidence intervals (CI) were calculated. Heterogeneity was quantified using the i^2 parameter. Risk of bias was assessed using Risk of Bias tool for randomized controlled trials (RoB2) and the Risk of Bias in Non-Randomized Studies of Interventions (ROBINS-I), by two independent investigators, conflicts were resolved by discussion. Level of evidence was assessed using the GRADE approach.

3.2. Study II.

Three databases (Medline, via Pubmed, Embase and Central) were searched on November 17th, 2024. Studies were included if they compared CS, LBC and their combination for the assessment of samples taken by EUS-guided tissue acquisition from abdominal masses. To be eligible for inclusion, studies needed to have performed both CS and LBC in their study, studies reporting on only one of the two were not eligible for inclusion. Due to the sparse data, studies evaluating the combination were included regardless of if they reported single test results. Selection was performed by two independent investigators, as was the data extraction. Any disagreements were resolved by discussion. Diagnostic parameters of sensitivity, specificity, accuracy and inadequacy were extracted and analyzed by meta-analysis. Instead of the usual bivariate approach for diagnostic analysis, a simple proportional meta-analysis was conducted, due to the high specificity found. The methodological quality of included papers was assessed using the Quality in Diagnostic Accuracy Studies tool version 2 (QUADAS-2).

4.Results

4.1. Study I.

3858 records were identified, of which nine studies (1160 patients) were included. The OR for an adequate sample was 1.467 (CI: 0.850–2.533) overall, in the RCT subgroup 0.902 (CI: 0.541–1.505), in the non-randomized subgroup 2.396 (CI: 0.916–6.264), with significant subgroup difference. For diagnostic accuracy, the OR was 1.326 (CI: 0.890–1977), in the RCT subgroup 0.997 (CI: 0.593–1.977), for non-randomized studies 1.928 (CI: 1.096–3.393), with a significant subgroup difference ($p = 0.0467$). For technical failures and adverse events, no differences were observed. For most outcomes, risk of bias was “low” to “some concerns”, mostly moderate for non-randomized studies. The level of evidence for the RCT subgroup of diagnostic adequacy was moderate, others low to very low.

4.2. Study II

16 studies including 2128 patients were included in the review. For pancreatic masses, we found a sensitivity of 0.714 (CI: 0.629 – 0.787, I2: 82%) for CS, 0.747 (CI: 0.643 – 0.828, I2: 84.1%) for LBC, and 0.862 (CI: 0.824 – 0.893, I2: 52.7%) for the combination. The subgroup analysis comparing the two methods to each other was not significant. The subgroup analysis comparing CS/LBC to the combination was significant (p=0.001). For abdominal masses we found a sensitivity of 0.763 (CI: 0.679 – 0.830, I2: 86.5%) for CS, 0.736 (CI: 0.656 – 0.802, I2: 81.8%) for LBC, and 0.880 (CI: 0.840 – 0.912, I2: 69.1%) for the combination. Subgroup analysis comparing individual methods was not significant, that comparing conventional smear/LBC to the combination was significant (p=0.001/p=0.006). Specificity was 100% in nearly all studies. In abdominal masses, combining the two methods produced a much lower rate of inadequate samples 1.5% (CI: 0-36.2, I2: 33.6%) than CS – 4.8% (CI: 3.2-7.1, I2: 24.5%) – or LBC – 4.9% (CI: 1.5-14.9, I2: 91.9%) – alone. While this was a significant subgroup difference

comparing conventional smear to the combination of methods (p=0.063), the very wide confidence intervals render the results hypothesis generating.

5. Conclusions

CEH-EUS likely does not improve diagnostic adequacy or accuracy. The combination of LBC and CS significantly improves sensitivity and reduces the rate of inadequate samples.

6. Bibliography

-Publications related to the thesis:

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