Systematic Review and Meta-Analysis

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Fine needle biopsy is superior to fine needle aspiration in endoscopic ultrasound guided sampling of pancreatic masses

A meta-analysis of randomized controlled trials

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Abstract

Background: The comparison between endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) and EUS guided fine needle biopsy (FNB) in sampling pancreatic masses is still controversial.

Methods: A systematic search was conducted in PubMed and Web of Science to identify all relevant randomized controlled trials (RCTs). Odds ratios (OR) and 95% confidence intervals (95% CI) were calculated for dichotomous outcomes of interest (specimen adequacy, diagnostic accuracy, complications, and technical success), while mean difference (MD) and 95% CI were pooled for continuous variables (number of needle passes required for diagnosis).

Results: Eleven RCTs were identified with a total of 694 EUS-FNA cases and 688 EUS-FNB cases. Compared with EUS-FNA, EUS-FNB had a better specimen adequacy (OR: 1.83, 95% CI: 1.27–2.64), higher diagnostic accuracy (OR: 1.62, 95% CI: 1.17–2.26), and fewer number of needle passes (MD: 0.69, 95% CI: 1.18 to 0.20). No significant difference was found in complications (OR: 1.01, 95% CI: 0.27–3.78) and technical success (OR: 0.13, 95% CI: 0.02–1.07).

Conclusion: EUS-FNB is superior to EUS-FNA in sampling pancreatic masses.

Abbreviations: CI = confidence interval, EUS = endoscopic ultrasound, FNA = fine needle aspiration, FNB = fine needle biopsy, MD = mean difference, OR = odds ratios, RCT = randomized controlled trial, RR = relative risk.

Keywords: endoscopic ultrasound, fine needle aspiration, fine needle biopsy, meta-analysis, pancreatic masses

1. Introduction

Pancreatic cancer is characterized by a poor prognosis, with an overall 5-year survival rate of 5% to 6% and a median survival of 3 to 5 months after diagnosis of metastatic disease.[1] Thus, rapid and accurate pathological diagnosis of pancreatic masses is important to direct subsequent clinical management. Currently, endoscopic ultrasound (EUS) guided fine needle aspiration (FNA) is the standard method for tissue diagnosis of pancreatic masses, with a reported sensitivity of 85% to 95%, specificity of 95% to 98% and diagnostic accuracy of 78% to 95%.[2,3] The diagnostic failures are usually caused by inadequate samples, inexperience of the endoscopist, and necrotic, or fibrotic tumors in which viable cells are difficult to obtain.[4] Recently, a new core biopsy needle, which is equipped with a side opening and a reverse bevel, has been developed to improve the sample quality. Sampling with this new needle is referred as EUS guided fine needle biopsy (EUS-FNB). Several randomized controlled trials (RCTs) have compared EUS-FNA and EUS-FNB in sampling pancreatic masses, but reached inconsistent results. The meta-analysis by Wang et al[5] found that EUS-FNB showed a comparable accuracy to EUS-FNA in diagnosing pancreatic masses. However, it ignored several newly published studies, especially the large-scale RCT by Chen et al,[6] in which EUS-FNB showed a higher accuracy than EUS-FNA in diagnosing pancreatic masses. Thus, we conducted an update meta-analysis of RCTs to compare the efficacy and safety of EUS-FNA and EUS-FNB in sampling pancreatic masses.

2. Methods

2.1. Search strategy

The databases of PubMed and Web of Science were searched for relevant studies published up to October 28, 2017, using the key words including: "endoscopic ultrasound," "EUS," "fine needle aspiration," "EUS-FNA," "fine needle biopsy," "core biopsy," "EUS-FNB," "pancreas," and "pancreatic". Studies in languages other than English or Chinese were excluded. Moreover, we also

Editor: Okasha Hussein.

HL and WL contributed equally to this study.

Funding: None.

The authors have no conflicts of interest to disclose.

Supplemental Digital Content is available for this article.

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Medicine (2018) 97:13(e0207)

Received: 6 December 2017 / Received in final form: 23 January 2018 / Accepted: 27 February 2018

http://dx.doi.org/10.1097/MD.0000000000010207

reviewed the references of related studies, reviews and meta-analyses for undetected studies. This study was approved by the ethics committee of The Central Hospital of Enshi Autonomous Prefecture.

2.2. Study selection and exclusion

All the studies were reviewed independently by 2 investigators. Studies were included if they satisfied the following criteria: patients with the presence of pancreatic masses revealed by computed tomography (CT) and/or magnetic resonance imaging (MRI) and/or EUS; RCTs; compared EUS-FNA and EUS-FNB in sampling pancreatic masses; included at least one of the following as outcome measures: diagnostic adequacy, diagnostic accuracy, mean number of needle passes required for diagnosis, adverse events or complications, and technical success. The exclusion criteria were as follows: reviews, case-reports, pediactric or animal studies, non-RCTs, and studies without full-text or sufficient data.

2.3. Data extraction and quality assessment

The following information was extracted from each included study: authors, publication year, area, study duration, number of cases, sampling type (EUS-FNA or EUS-FNB), needle size, age, mass size, suction method, sample examination, follow-up for final diagnosis, diagnostic adequacy, diagnostic accuracy, mean number of needle passes required for diagnosis, adverse events or complications, and technical success. The quality of included studies was assessed using the Cochrane collaboration's tool for assessing the risk of bias, with the following domains: random sequence generation, allocation concealment, binding of participants and personnel, binding of outcomes assessment, incomplete outcome data, and selective reports.[7] Any disagreement in data abstraction and quality evaluation was solved by discussion.

2.4. Statistical analysis

All data analyses were realized with Review Manager 5.2 (RevMan, The Nordic Cochrane Center, The Cochrane Collaboration, 2012). For dichotomous data, odds ratios (OR) with 95% confidence intervals (CI) were used to report the risk estimates following the Mantel-Haenszel method.[8] For continuous data, mean differences (MD) and 95% CI were adopted by the method of Inverse Variance. The heterogeneity between studies was estimated by Q test and I^2 statistic. $I^2>50\%$ represented substantial heterogeneity, and a random-effects analysis was conducted. Otherwise, a fixed-effects model was used. Egger's test was used to detect publication bias. All tests were sided with a significance level of 0.05.

3. Results

3.1. Characteristics of included studies

Finally, 11 studies were included into this meta-analysis, with a total of 694 cases for EUS-FNA and 688 cases for EUS-FNB.[6,9,10–18] The characteristics of included studies were listed in Table 1. In FNA, the needle sizes were 22G (n=10) and 25G (n=3), and the most common needle was EchoTip of Cook Medical (n=8), followed by Expect of Boston Scientific (n=2), and EZShot2 of Olympus (n=1) (Table S1, http://links.lww.com/

Table 1

Characteristics of included studies.

Study	Area	Duration	Cases (M/F)	Type	Needle size (cases)	Age, years	Mass size, mm	Suction method	Sample examination	Follow-up for final diagnosis
Bang[9]	USA	2011.06–2011.09	56 (31/25)	FNA	22G (n=28)	65.4±11.1	33.7±7.2	None	Histology, immunohistochemistry or special staining	–
				FNB	22G (n=28)	65.0±15.4	32.5±9.0	10 mL syringe for 20 seconds		
Hucl et al[10]	India	2011.03–2012.07	69 (37/22)	FNA	22G (n=69)	51.7±13.6	41.9±17.0	10 mL syringe	Histopathology, immunohistochemistry	≥6 months
				FNB	22G (n=69)					
Lee et al[11]	Korea	2012.01–2013.05	116 (73/43)	FNA	22G (n=30); 25G (n=28)	63.1±10.6	36.5 (17.0–74.0)	10 mL syringe	Cytology, histology, immunohistochemistry	≥6 months
				FNB	22G (n=34); 25G (n=24)	66.7±12.7	36.5 (15.0–100.0)			
Strand et al[12]	USA	2011.11–2012.09	32 (13/19)	FNA	22G (n=32)	67.8±13.3	–	10 mL syringe for 30 seconds	Histology, cytology	–
				FNB	22G (n=32)					
Vanbiervliet [13]	USA	2012.01–2012.10	80 (49/31)	FNA	22G (n=80)	67.1±11.1	33.9±10.8	10 mL syringe for 20 seconds	Histology, immunohistochemistry, cytology	≥12 months
				FNB	22G (n=80)					
Alatawi et al[14]	France	2012.04–2013.03	100 (63/37)	FNA	22G (n=50)	68.0±11.2	33±2.7	10 mL syringe	Histology, cytology, immunohistochemistry or specific staining	≥12 months
				FNB	22G (n=50)	67.8±13.1	32±5.1			
Aadam et al[15]	USA	2013.01–2014.05	73	FNA	22/25G (n=37)	–	–	10 mL syringe	Histology, cytology	–
				FNB	19/22/25G (n=36)	–	–	Stylet		
Kamata et al[17]	Japan	2013.04–2013.09	214 (112/102)	FNA	25G (n=108)	67 (34–89)	27.9±14.4	Stylet	Histology, cytology, immunohistochemistry	≥12 months
				FNB	25G (n=106)	68 (43–90)	29.3±15.6			
Bang et al[16]	USA	–	46 (28/18)	FNA	22G (n=46)	67.9±14.7	29±8	–	Histology, cytology, immunohistochemistry	232 days (mean)
				FNB	22G (n=46)			–		
Chen et al[17]	China	2014.12–2016.01	249	FNA	22G (n=126)	–	–	Stylet + 5 mL syringe	Histology, cytology	≥48 weeks
				FNB	22G (n=123)	–	–			
Noh et al[18]	Korea	2013.07–2015.02	60 (35/25)	FNA	22G (n=60)	61.6±10.0	31±8	Stylet + 10 mL syringe	Histology, cytology	–
				FNB	22G (n=60)			–		

F=female, FNA=fine needle aspiration, FNB=fine needle biopsy, G=gauge, M=male.

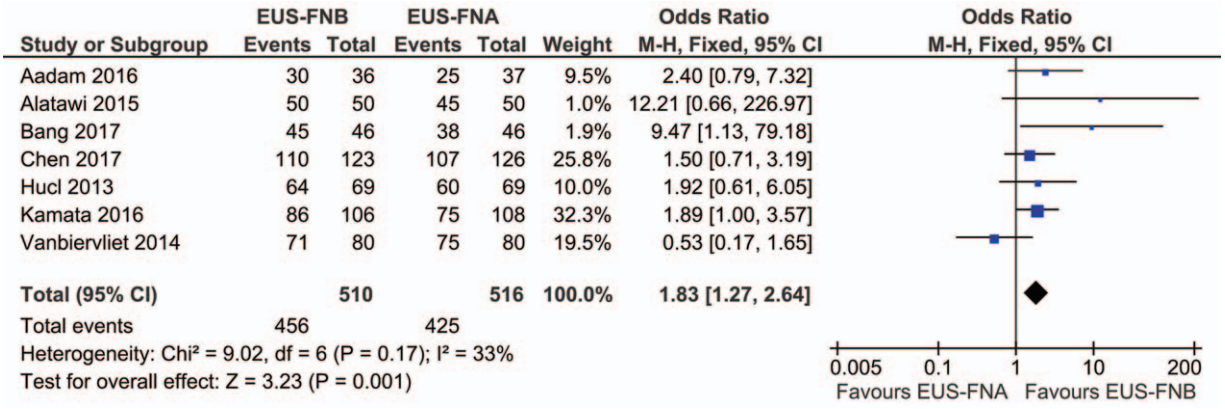

Figure 1. Forrest plot for specimen adequacy between FNA and FNB in sampling pancreatic masses. FNA = fine needle aspiration, FNB = fine needle biopsy.

MD/C179). In FNB, the needle sizes were 19G (n = 1), 22G (n = 10), and 25G (n = 3), and the most common needle was Echotip Procore of Cook Medical (n = 9), followed by Acquire of Boston Scientific (n = 1) and ProCore of Wilson-Cook Medical (n = 1). Most studies used a syringe or stylet for sample suction. Five studies (Hucl et al, Strand et al, Vanbiervliet et al, Bang et al, and Noh et al) used both needles in all patients, while the other 6 studies used either FNA or FNB in each patient. More than half of the studies applied rapid on-site evaluation which could ascertain sample adequacy for further analysis. The final diagnosis was based on histology, cytology and immunohistochemistry. Seven studies also had a follow-up of at least 6 months for the final diagnosis. In quality assessment, all included studies were at low risk of selection bias, detection bias, attrition bias and reporting bias, but at high risk of performance bias as no endoscopist was blinded to the type of needle in use (Figure S1, http://links.lww.com/MD/C179).

3.2. Specimen adequacy

Seven studies compared the specimen adequacy between FNA and FNB (Fig. 1). FNB had a better specimen adequacy than FNA in sampling pancreatic masses (OR: 1.83, 95% CI: 1.27–2.64; $I^2 = 33\%$). Egger's test detected no significant publication bias ($P = .294$).

3.3. Diagnostic accuracy

Ten studies compared the diagnostic accuracy between FNA and FNB (Fig. 2). FNB showed a higher accuracy than FNA in diagnosing pancreatic masses (OR: 1.62, 95% CI: 1.17–2.26; $I^2 = 17\%$). In the 7 studies with a follow-up of at least 6 months, FNB also showed a higher accuracy (OR: 1.73, 95% CI: 1.21–2.48; $I^2 = 5\%$). Egger's test detected no significant publication bias ($P = .644$).

3.4. Number of needle passes required for diagnosis

Five studies compared the mean number of needle passes required for diagnosis between FNA and FNB (Fig. 3). FNB had a fewer number of needle passes than FNA in sampling pancreatic masses (MD: −0.69, 95% CI: −1.18 to −0.20; $I^2 = 92\%$). Egger's test detected no significant publication bias ($P = .838$).

3.5. Complications

Ten studies compared the complications between FNA and FNB (Fig. 4). The 2 groups showed no significant difference in the

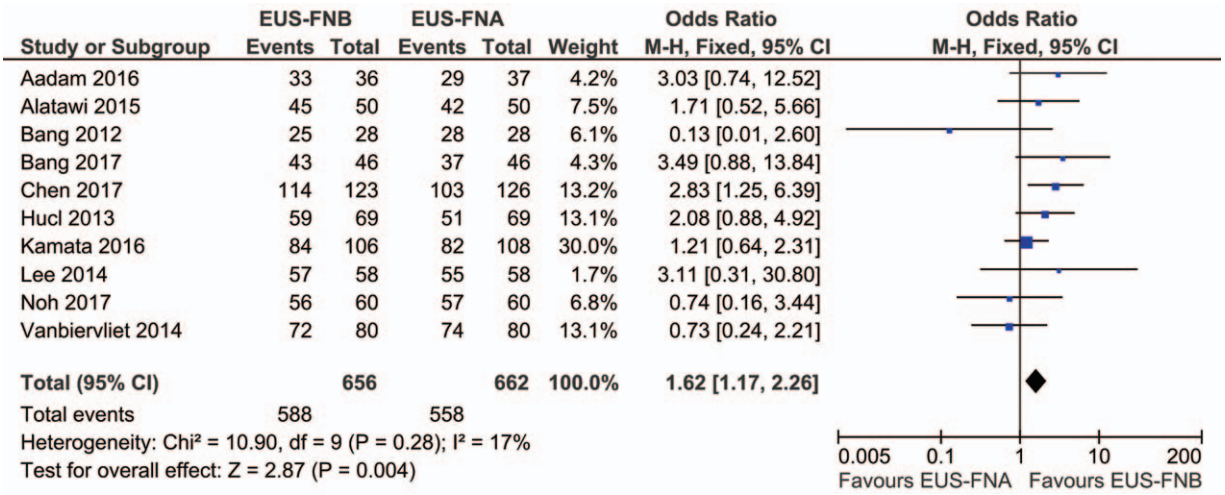

Figure 2. Forrest plot for diagnostic accuracy between FNA and FNB in sampling pancreatic masses. FNA = fine needle aspiration, FNB = fine needle biopsy.

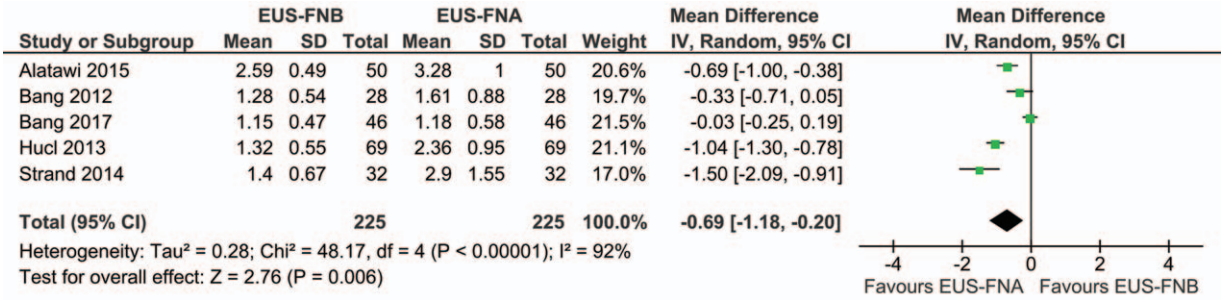

Figure 3. Forrest plot for number of needle passes required for diagnosis between FNA and FNB in sampling pancreatic masses. FNA = fine needle aspiration, FNB = fine needle biopsy.

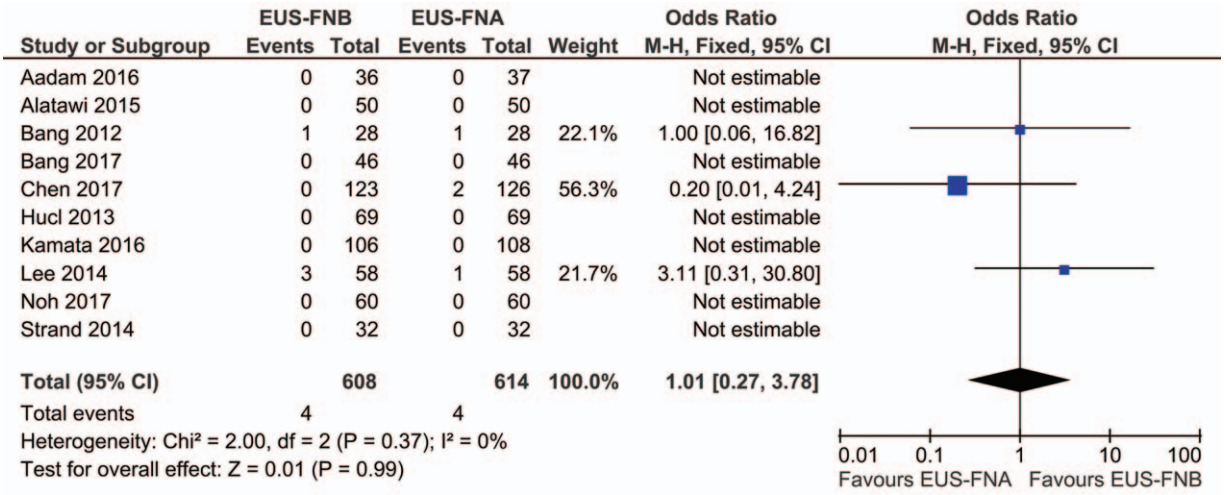

Figure 4. Forrest plot for complications between FNA and FNB in sampling pancreatic masses. FNA = fine needle aspiration, FNB = fine needle biopsy.

incidence of complications (OR: 1.01, 95% CI: 0.27–3.78; $I^2 = 0\%$).

3.6. Technical success

Nine studies compared the technical success between FNA and FNB (Fig. 5). The 2 groups showed no significant difference in the rate of technical success (OR: 0.13, 95% CI: 0.02–1.07; $I^2 = 0\%$).

4. Discussion

Currently, EUS-FNA is considered to be the gold standard for EUS-guided sampling of pancreatic masses. However, it still has

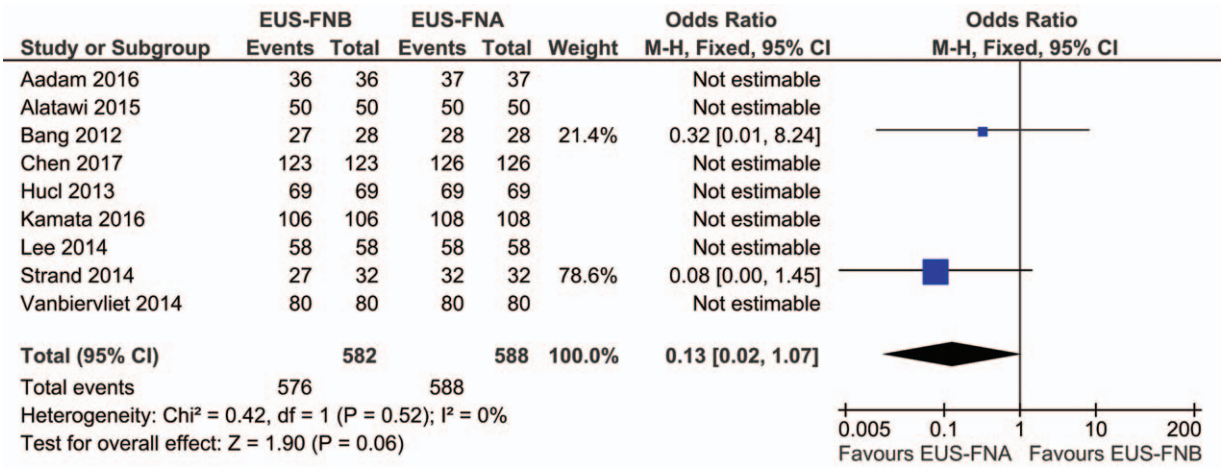

Figure 5. Forrest plot for technical success between FNA and FNB in sampling pancreatic masses. FNA = fine needle aspiration, FNB = fine needle biopsy.

several limitations. First of all, EUS-FNA samples relatively a small amount of tissue specimens, and unable to provide core tissue with preserved architecture which is essential for histological diagnosis of pancreatic masses. For example, cytological analysis alone may not diagnose certain neoplasms like stromal cell tumors, lymphomas, and well-differentiated adenocarcinomas.[19] To obtain more specimens for an accurate diagnosis, it is inevitable to increase the number of needle passes which can lead to an increasing risk of adverse events. Moreover, the success of EUS-FUA is also greatly influenced by the presence of an on-site histopathologist or cytopathologists, as well as an experienced endoscopist.

In order to overcome some of these limitations and to improve diagnostic accuracy, EUS-FNB was developed to promote the collection of core tissue. Compared with FNA, FNB was characterized by a core trap which could reduce the number of needle passes required to establish a diagnosis, particularly a histological diagnosis. In our meta-analysis, we also found FNB group required fewer needle passes and obtained more specimen than FNA group. This might explain the higher diagnostic accuracy in FNB group. In the aspects of complications and technical success, no significant difference was found between the 2 groups. In general, EUS-FNB showed superiority to EUS-FNA in sampling pancreatic masses.

The recent meta-analysis by Khan et al[20] compared EUS-FNA and EUS-FNB in the diagnostic yield and the value of onsite cytopathological assessment. No significant difference was found in diagnostic adequacy (RR: 0.99, 95% CI: 0.95–1.03; n = 12), as well as for pancreatic lesions (RR: 0.99, 95% CI: 0.90–1.08; n = 9). Another recent meta-analysis by Wang et al[5] compared EUS-FNA and EUS-FNB in sampling pancreatic masses, and the diagnostic accuracy was comparable in FNA and FNB group (RR: 0.72, 95% CI: 0.49–1.07; n = 7). However, there was a trend toward FNB showing a higher diagnostic accuracy in sampling pancreatic masses than FNB. We thought this might contribute to the limited number of included studies, and the diagnostic accuracy might be different between FNA and FNB. After including 3 newly published studies, we found a higher diagnostic accuracy in EUS-FNB. Thus, we conducted this meta-analysis, and wanted the finding to be a reference for clinical practice in the future.

Several limitations in this study also need to be considered. First, all studies were at high risk of performance bias. Second, there was obvious heterogeneity in the meta-analyses of needle passes which might be caused by limited number of included studies. Third, the needles in Aadam et al study were not in the same size between the FNA and FNB groups.

Author cntributions

Data curation: H. Li.
Formal analysis: Q. Zhou.
Methodology: B. Fan., H. Li., W. Li.
Software: W. Li.
Writing – original draft: H. Li, Q. Zhou.
Writing – review & editing: H. Li.

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