Effect of pancreatic mass size on clinical outcomes of endoscopic ultrasound-guided fine-needle aspiration

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Abstract

Background: Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) has a high diagnostic accuracy for pancreatic diseases. However, the effect of mass size on diagnostic accuracy has yet to be determined, especially for small pancreatic lesions. We aimed to determine the effect of pancreatic mass size on diagnostic yield of EUS-FNA.

Methods: We searched the database in Hokkaido University Hospital between May 2008 and December 2016 and identified solid pancreatic lesions examined by EUS-FNA. All lesions were stratified into five groups based on mass sizes: Groups A (<10mm), B (10-20mm), C (20-30mm), D (30-40mm) and E (40mm≤). The sensitivity, specificity, diagnostic accuracy and adverse event rate were retrospectively evaluated.

Results: We analyzed a total of 788 solid pancreatic lesions in 761 patients. The patients included 440 males (57.8%) with a mean age of 65.7 years. The sensitivities in Groups A (n=36), B (n=223), C (n=304), D (n=147) and E (n=78) were 89.3%, 95.0%, 97.4%, 98.5% and 98.7%, respectively, and they significantly increased as the mass size increased (P<0.01, chi-squared test for trend). The diagnostic accuracies were 91.7%,

96.4%, 97.7%, 98.6% and 98.7%, respectively, and they also significantly increased as the mass size increased (P=0.03). Multivariate analysis showed that pancreatic mass size was associated with diagnostic accuracy. The adverse event rates were not significantly different between the five groups.

Conclusions: The sensitivities and diagnostic accuracies of EUS-FNA for solid pancreatic lesions are higher for lesions of 10 mm or more in size and they are strongly correlated with mass size.

Keywords: Endoscopic ultrasonography, Endoscopic ultrasonography fine-needle aspiration, Pancreatic tumor

Introduction

Endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) was first reported by Vilmann et al. [1] in 1992 and has become the most widely utilized technique for pathological diagnosis and staging of various malignancies. However, the diagnostic yields of EUS-FNA for solid pancreatic neoplasms vary depending on the period and institution. It has been reported that sensitivities range from 64% to 95%, specificities range from 75% to 100% and diagnostic accuracies range from 78% to 95% [2]. The diagnostic yield of EUS-FNA is dependent on a number of factors including lesion location [3], availability of a cytologist for rapid onsite evaluation (ROSE) [4], skill and experience of an endosonographer [5], size and type of the needle selected for tissue acquisition [6], and presence of chronic pancreatitis [7]. Lesion size is also considered to be a determinant of diagnostic yield, but it has not been verified in detail. Some studies have shown that the sensitivity and diagnostic accuracy of EUS-FNA for a solid pancreatic lesion were strongly correlated with lesion size [3,8,9], namely, that the larger the mass size was, the higher the sensitivity was. However, other studies showed no relationship between pancreatic mass size and performance of

EUS-FNA [10,11]. There were several limitations in each previous study. First, the number of cases was small, especially cases with lesions of < 10 mm in size. Second, pancreatic masses were divided into only a few groups. Third, the diagnostic yields of EUS-FNA were not evaluated by multivariate analysis. Fourth, the overall diagnostic yields of EUS-FNA itself were relatively low.

The aim of the current study was to determine whether the size of a solid pancreatic lesion affects the diagnostic yield and accuracy of EUS-FNA.

Materials and Methods

Study design

This was a retrospective cohort study conducted at Hokkaido University Hospital, a tertiary referral center. We searched the database in Hokkaido University Hospital for patients who underwent EUS-FNA of pancreatic masses at the first session between May 2008 and December 2016 and identified them for this study. The exclusion criteria were 1) patients who had purely cystic lesions of the pancreas or pseudocysts, 2) use of new type needles for histological core tissue and 3) refusal for

enrollment into this study by the patients or their families. The available cohort was stratified into five groups based on pancreatic mass sizes determined by the greatest diameters measured by ultrasonography, computed tomography, magnetic resonance imaging and EUS (all patients having undergone two or more imaging tests): Group A (< 10 mm), Group B (10-20 mm), Group C (20-30 mm), Group D (30-40 mm) and Group E (40 mm ≤). The classification was based on previous reports [9-11] with patients being divided into 5 groups of 10-mm ranges.

The study was approved by the Institutional Review Board of Hokkaido University Hospital (017-0002).

EUS-FNA procedure

EUS-FNA was performed under conscious sedation with fentanyl and midazolam. A linear array echoendoscope (GF-UCT240-AL5 or GF-UCT260, Olympus Medical Systems Co., Tokyo, Japan) was used with the standard station approach. When a pancreatic mass was identified, cross-sectional size measurements including measurement of greatest dimensions were performed. Avoiding intervening vessels, we

punctured the mass via the gastric or duodenal wall using a standard FNA needle (Expect™, Boston Scientific Japan, Tokyo, Japan; Echotip®, Cook Japan, Tokyo, Japan) with a size of 19-, 22- or 25-gauge. At the beginning, the endosonographer schemed to use the 22-gauge FNA needle. However, if the 22-gauge FNA needle was difficult to use because of the size of and location of the target mass, the 25-gauge FNA needle was selected. On the other hand, if the 19-gauge FNA needle was relatively easy to use, the 19-gauge FNA needle was selected. The final decision of diameter of FNA needle was made by the endosonographer.

Preparation of a specimen for on-site analysis

On-site Diff-Quik staining (Kokusai Shiyaku, Kobe, Japan) was immediately performed by a cytopathologist to ascertain sample adequacy and provide a preliminary diagnosis. The numbers of punctures were determined by such on-site evaluations for adequacy and diagnosis. When pancreatic lesions were difficult for trainees or fellows to puncture, experts finally performed EUS-FNA until the samples obtained were adequate for histological assessment using ROSE. In a few cases, although adequate

samples were not obtained, the procedure was not completed due to the risk of complications or a plateau of the clinical outcome as previously reported [12] at the discretion of the endosonographer (maximum: 8 passes). Alcohol-treated smears were also prepared for Papanicolaou staining. The method of cell block was not used in our institution.

Preparation for histological analysis

The EUS-FNA specimens were also put into formalin containers at the same time as on-site evaluations. Thereafter, the specimens were embedded in paraffin and sectioned for histopathological analysis with hematoxylin and eosin (H&E) staining. All specimens were classified as benign, malignant, or indeterminate by a histopathologist. Carcinoma, neuroendocrine tumor (NET), solid pseudopapillary neoplasm (SPN), lymphoma and malignant melanoma were defined as malignant and the others were defined as benign in the present study. Since target lesions were non-diagnostic with H&E staining alone, even when an adequate specimen was available, immunohistochemical analyses were performed for accurate diagnosis.

Clinical diagnostic methodology of benignancy and malignancy used for final diagnosis

In this study, malignant diseases were ultimately diagnosed on the basis of (1) autopsy after death, (2) histopathological analyses of surgically resected or core biopsy specimens from the pancreatic mass, or (3) radiological or clinical data indicating evidence of disease progression. Namely, in the cases with the mass growth or new metastatic lesions after 6 months, they were diagnosed having a malignant disease. Most low-grade NETs do not change in size for some years. Therefore, NET was diagnosed on the basis of (1) histopathological analyses of surgically resected or core biopsy specimens from the pancreatic mass or (2) immunohistochemical analyses of EUS-FNA specimens with immunohistochemical staining positive for chromogranin A or synaptophysin [13]. Benign diseases were diagnosed on the basis of (1) histopathological analyses of surgically resected specimens of the pancreatic mass or (2) no change, decrease or improvement in the clinical course for more than 6 months. Diagnosis of autoimmune pancreatitis (AIP) needed to fulfill the international

consensus diagnostic criteria [14] and to show no existence of any tumor cell by EUS-FNA.

In the case of indeterminate EUS-FNA results in histological analysis in lesions with the final diagnosis of malignancy, the EUS-FNA results were defined as incorrect. On the other hand, in lesions with the final diagnosis of benignancy, the EUS-FNA results were defined as correct..

Outcome measures

The primary outcomes of the present study were the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy of EUS-FNA in each group. The secondary outcomes were the sensitivity, specificity, PPV, NPV, diagnostic accuracy of EUS-FNA according to the location of the lesion and the puncture route, the number of passes and adverse events. Adverse events were graded according to the severity grading system of the American Society for Gastrointestinal Endoscopy lexicon [15]. Factors affecting diagnostic accuracy were evaluated by multivariate analysis using variables of pancreatic location (Ph, Pb or Pt),

puncture route (transgastric or transduodenal), pancreatic mass size (Group A, B, C, D or E), final diagnosis (pancreatic adenocarcinoma, neuroendocrine tumor or other tumor), and parenchyma (chronic pancreatitis or none).

Statistical analysis

Statistical analysis was performed using GraphPad Prism software 7.0 (GraphPad Software Inc., San Diego, CA) and the free software EZR [16]. Results are shown as means (SD) for quantitative variables, medians (range) for nonparametric variables, and percentages for categorical variables. Intra-group comparisons of patient, procedural characteristics, sensitivity, specificity, positive and negative predictive value, diagnostic accuracy, and adverse events were done using Fisher's exact test. The Kruskal-Wallis test was conducted to compare median values of the number of FNA passes among all groups. The Cochran-Armitage test (chi-squared test for trend) was performed to examine for increasing or decreasing trends in sensitivity, specificity, positive and negative predictive value and diagnostic accuracy with pancreatic mass size. Results of multivariate analysis were evaluated using logistic regression analysis.

Results

By a search of the database, 1268 lesions in 1128 patients examined by EUS-FNA for a pathological diagnosis were identified. Of the 1268 lesions, 480 lesions ware excluded and 788 solid pancreatic lesions in 761 patients were finally analyzed in the present study (Fig. 1). Two hundred sixty-one lesions could be evaluated by both EUS-FNA specimens and surgically resected or core biopsy specimens. Of these, one lesion could be evaluated also by autopsy after death. On the other hand, 527 lesions were evaluated by EUS-FNA specimens and clinical course. All pancreatic lesions were immediately evaluated using on-site analysis at EUS-FNA.

Baseline characteristics

The patients included 440 males and 321 females with a mean age of 65.7 (± 11.8) years. The EUS-FNA specimens were diagnosed in histological analysis as malignant for 664 lesions, benign for 98 lesions, and indeterminate for 26 lesions. The intermediate lesions in EUS-FNA specimens were clinically classified as malignant in

15 lesions and benign in 11 lesions. The final diagnoses were malignant for 685 lesions and benign for 103 lesions. The details of the final diagnosis of malignancy were based on histopathological analyses of surgically resected or core biopsy specimens in 257 lesions (including autopsy after death in 1 lesion), radiological or clinical data in 401 lesions, and immunohistochemical analyses confirmed by EUS-FNA specimens in 27 lesions. The details of the final diagnosis of benignancy were based on histopathological analyses of surgically resected specimens in 4 lesions and clinical data in 99 lesions.

There was a significant difference in location of the mass between five groups as shown in Table 1. In Group A (< 10 mm), there were 36 lesions in 34 patients. The patients in Group A included 11 males and 23 females with a mean age of 61.5 (± 12.4) years, and the mean mass diameter was 8.0 (± 1.7) (range 3.5-9.9) mm. As shown in Table 2, the final diagnoses in Group A were NET in 19 lesions (including 3 lesions of insulinoma), adenocarcinoma in 6 lesions (including 1 lesion of metastasis from gastric cancer), autoimmune pancreatitis in 3 lesions, clear cell carcinoma in 1 lesion, malignant melanoma in 1 lesion and other benign masses in 5 lesions.

Primary and secondary outcomes

The overall sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and diagnostic accuracy were 96.9%, 100%, 100%, 97.3% and 83.2%, respectively. The sensitivities in Groups A, B, C, D and E were 89.3%, 95.0%, 97.4%, 98.5% and 98.7%, respectively, and they significantly increased as the mass size increased (*P* value < 0.01). The diagnostic accuracies in Groups A, B, C, D and E were 91.7%, 96.4%, 97.7%, 98.6% and 98.7%, respectively, and they also significantly increased as the mass size increased (*P* value = 0.03). However, NPVs were not significantly different between the five groups (*P* value = 0.66) (Table 3). As shown in Table 4, diseases of false negative were NET in 2 lesions and metastatic pancreatic tumor from renal cancer in 1 lesion. The sensitivities, specificities, PPV, NPV and diagnostic accuracies in each of the mass locations (Ph, Pb and Pt) and in each of the puncture routes (transgastric and transduodenal routes) are shown in Table 5. The sensitivities, NPV and diagnostic accuracies were not significantly different among the three locations or between transgastric and transduodenal routes (*P* value > 0.05).

There was a significant difference between the five groups in the diameter of the

FNA needle used (*P* value < 0.01). The median number of passes was also significantly different among the five groups: Group A, 3 (range, 1-5); Group B, 3 (range, 1-8); Group C, 3 (range, 1-8); Group D, 2 (range, 1-11); Group E, 2 (range, 1-6) (*P* value = 0.04) (Table 6).

According to the results of multivariate analysis of the accuracy of EUS-FNA, compared with group A, the odds ratios in group C and group D were significantly increased and the odds ratios in group B and group E tended to be increased as shown in Table 7. On the other hand, mass location, puncture route, final diagnosis, and parenchymal condition were not significant factors for yields of EUS-FNA.

The rate of adverse events in all patients was 2.2%. The rates of adverse events in Groups A, B, C, D and E were 2.8%, 2.2%, 1.3%, 3.4% and 2.6%, respectively, and there was no significant difference between the five groups (*P* value = 0.51). The details of adverse events are shown in Table 7. Pancreatitis (mild in 7 patients and severe in 3 patients) was the most frequent in all groups. There were no procedure-related deaths.

Discussion

The current study revealed that the sensitivity and diagnostic accuracy of EUS-FNA significantly increase as pancreatic mass size increases. This study is the first study in which many cases with a lesion of less than 10 mm in size were included and in which diagnostic yield of EUS-FNA was evaluated by detailed multivariate analysis.

Early detection and diagnosis of a small pancreatic lesion are clinically important because the survival time of a patient with small pancreatic cancer (< 10 mm) is significantly longer than that of a patient with a larger one (≥ 10 mm) [17]. In addition, early diagnosis of pancreatic NET, even if the mass size is smaller than 10 mm, is also recommended for clinical benefit [18]. EUS is the most effective modality for detection of a small pancreatic mass because of its high image resolution [19] and EUS-FNA is the most efficacious for pathological diagnosis of a pancreatic lesion because of its accuracy and safety [3,10,11]. In the present study, each pancreatic mass size was measured by two or more imaging modalities for precision, and the correlation between yield of EUS-FNA and pancreatic mass size would therefore have been accurately evaluated.

Some studies have shown the performance of EUS-FNA in relation to pancreatic mass size [8] [20]. Siddiqui et al. [9] showed that the sensitivity and diagnostic accuracy of EUS-FNA for solid pancreatic tumors were strongly correlated with tumor size and that the sensitivity and diagnostic accuracy significantly decreased for tumors smaller than 1cm. Haba et al. [3] reported that the sensitivity and diagnostic accuracy for pancreatic tumors of 10 mm or larger were higher than those for pancreatic tumors smaller than 10 mm as well as for tumors with the threshold size of 20 mm.

On the other hand, Uehara et al. [10] showed that EUS-FNA was accurate for evaluation of suspected pancreatic malignancy regardless of its size. In tumors smaller than 10 mm, the sensitivity, specificity, PPV, NPV and diagnostic accuracy were 100%, 90%, 93%, 100% and 96%, respectively. The values were very high; however, their study had limitations of a small number of cases (n=23), deviation to malignancies and lack of details of both final diagnoses and lesion locations.

Ramesh et al. [11] reported that there was no correlation between sensitivity or diagnostic accuracy and pancreatic mass size. In their study, lesions were divided into four groups: Group A (≤ 10 mm), Group B (11-20 mm), Group C (21-40 mm) and

Group D (> 40 mm). The sensitivities in the four groups were 73.3%, 87.4%, 87.8% and 78.5%, respectively, and diagnostic accuracies were 73.3%, 86.6%, 88.1% and 81.6%, respectively. The sensitivity and diagnostic accuracy in Group D were lower than those in Group B and Group C, and the mean number of passes in Group D was more than the mean numbers in the other groups. The difference between their results and our results would be caused by the difference in characteristics of large masses. Eighty percent of the large masses in our study were adenocarcinoma, while only 37% of the large masses in their study were adenocarcinoma [11]. Meanwhile, the overall sensitivities and diagnostic accuracy itself were relatively low in their results. The sensitivities and diagnostic accuracy even in group A (< 10 mm) in our results were about 90%; therefore, the technical aspect of EUS-FNA itself might have caused the differences.

It is controversial whether the location of the lesion affects the diagnosis yield of EUS-FNA. Haba et al. [3] showed that the diagnostic accuracies in the Pb and Pt lesion were significantly higher than that in the Ph lesion. On the other hand, Sakamoto et al. [21] and Turner et al. [22] showed that no association was found between the location of the mass and diagnosis yield as well as in the current study. Although the difference

would be caused by the kinds of used needles, further studies are necessary to solve it.

In the current study, there were significant differences in the diameter of the FNA needle used and the median number of passes among the five groups. Madhoun et al. [6] indicated that diagnostic accuracy of EUS-FNA was not improved by a large-bore needle. However, the yields of EUS-FNA with more large-bore needles in groups including patients with large masses were improved in our study (Group B, C, D and E). That means large mass size has a good effect on the yields. Iglesias-Garcia et al. [23] showed that ROSE had a positive effect on the diagnostic accuracy of EUS-FNA. Moreover, in a recent meta-analysis, Matynla et al. [24] showed that ROSE was an effective modifier on the relationship between needle passes and per-case adequacy for EUS-FNA of solid pancreatic lesions. Our data totally indicate that large mass size and ROSE is very efficacious for reduction of needle passes and for improvement of diagnostic yield.

There was no significant difference in the rate of adverse events among the five groups in our study, although O'Toole et al. [25] showed that the size of a lesion was a predictor of adverse events. A recent meta-analysis of the results of 31 prospective

studies showed a cumulative FNA-related adverse event rate of 1.72% similar to that in the present study [26].

There are several limitations in the present study. First, this study was a retrospective study. Second, this study was performed in a single center. Third, all of the pancreatic masses were not analyzed by surgically resected or core biopsy specimens. NETs would sometimes be unchanged for more than 6 months; therefore, some final diagnoses were based on immunohistochemical analyses of EUS-FNA specimens.

In conclusion, we showed by detailed statistical analysis that the sensitivity and diagnostic accuracy of EUS-FNA are strongly correlate with pancreatic mass size.

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Tables

Table 1 Characteristics of all patients

	N = 788					
Age, mean (SD), years	65.7 (11.8)					
Sex (male : female)	440 : 321					
Lesion location, n (%)						
Head	440 (55.8)					
Body	222 (28.2)					
Tail	126 (16.0)					
	Group A (n=36)	B (n=223)	C (n=304)	D (n=147)	E (n=78)	Total
Location, n (%)						*P* value < 0.01
Head	13 (36)	120 (54)	190 (62)	94 (64)	23 (30)	440 (56)
Body	16 (45)	73 (33)	78 (26)	29 (20)	26 (33)	222 (28)
Tail	7 (19)	30 (13)	36 (12)	24 (16)	29 (37)	126 (16)
Final diagnosis, n (%)						*P* value < 0.01
Adenocarcinoma (primary)	5 (13.9)	143 (64.1)	248 (81.6)	127 (86.4)	63 (80.8)	586 (74.3)
Neuroendocrine tumor	19 (52.8)	26 (11.7)	8(2.6)	5 (3.4)	7 (9.0)	65 (8.2)
Metastatic pancreatic tumor	4 (11.1)	7 (3.1)	10 (3.3)	0	3 (3.8)	24 (3.0)
Autoimmune pancreatitis	3 (8.3)	12 (5.4)	20 (6.6)	8 (5.4)	1 (1.3)	44 (5.6)
Solid pseudopapillary neoplasm	0	3 (1.3)	4 (1.3)	1 (0.7)	3 (3.8)	11 (1.4)
Other benign tumor	5 (13.9)	32 (14.4)	14 (4.6)	6 (4.1)	1(1.3)	58 (7.4)

Fisher's exact test

Table 2 Characteristics of patients with a pancreatic mass smaller than 10 mm (Group A)

	N = 36	
Age, mean (SD), years	61.5 (12.4)	
Sex (male : female)	11 : 23	
Maximum diameter of tumor, median (range), mm	8.5 (3.5 - 9.9)	
Lesion location, n (%)		
Head	13	(36.1)
Body	16	(44.4)
Tail	7	(19.4)
Number of passes, mean (SD)	2.8	(1.2)
Final diagnosis, n (%)		
Adenocarcinoma (primary)	5	(13.9)
Neuroendocrine tumor	19	(52.8)
Metastatic pancreatic tumor	4	(11.1)
Autoimmune pancreatitis	3	(8.3)
Other benign tumor	5	(13.9)
Primary disease of metastatic pancreatic tumor, n		
Gastric cancer	1	
Renal cancer	1	
Multiple myeloma	1	
Malignant melanoma	1	

Table 3 Yields of EUS-FNA in groups classified by mass size

	Group A	B	C	D	E	*P* value
Sensitivity (%)	89.3	95.0	97.4	98.5	98.7	<0.01
Specificity (%)	100	100	100	100	100	1
Positive predictive value (%)	100	100	100	100	100	1
Negative predictive value (%)	72.7	84.9	83.3	87.5	66.7	0.66
Diagnostic accuracy (%)	91.7	96.4	97.7	98.6	98.7	0.03

Cochran-Armitage test (chi-squared test for trend)

Table 4 Yields of EUS-FNA in group A (< 10 mm)

	N = 36
True positive	25
False negative	0
True negative	8
False negative	3
Diseases of false negative, n	
Neuroendocrine tumor	2
Metastatic pancreatic tumor (renal cancer)	1

Table 5 Yields of EUS-FNA in groups classified by mass location and puncture route

Location	Ph (n=440)	Pb (n=220)	Pt (n=126)	*P* value
Sensitivity (%)	95.8	98.0	98.1	0.15
Specificity (%)	100	100	100	1
Positive predictive value (%)	100	100	100	1
Negative predictive value (%)	78.7	85.2	91.3	0.37
Diagnostic accuracy (%)	96.4	98.2	98.4	0.36

Puncture route	Transgastric (n=386)	Transduodenal (n=402)	*P* value
Sensitivity (%)	97.7	95.9	0.28
Specificity (%)	100	100	1
Positive predictive value (%)	100	100	1
Negative predictive value (%)	84.9	80.6	0.64
Diagnostic accuracy (%)	97.9	96.5	0.28

Fisher's exact test

Table 6 Numbers of passes and diameters of fine-needle aspiration needles used

	Group A (n=36)	B (n=223)	C (n=304)	D (n=147)	E (n=78)	*P* value
Number of passes, median (range)						
	3 (1-5)	3 (1-8)	3 (1-8)	2 (1-11)	2 (1-6)	0.04[#]
Diameter of FNA needle						
	(n=40)	(n=251)	(n=315)	(n=152)	(n=84)	< 0.01[##]
19	1 (2.5)	20 (8.0)	26 (8.3)	12 (7.9)	20 (23.8)	
22	29 (72.5)	181 (72.1)	232 (73.7)	115 (75.7)	52 (61.9)	
25	10 (25.0)	50 (19.9)	57 (18.1)	25 (16.4)	12 (14.3)	

[#]Kruskal-Wallis test, [##]Fisher's exact test

Table 7 Multivariate analysis of factors affecting the accuracy of EUS-FNA

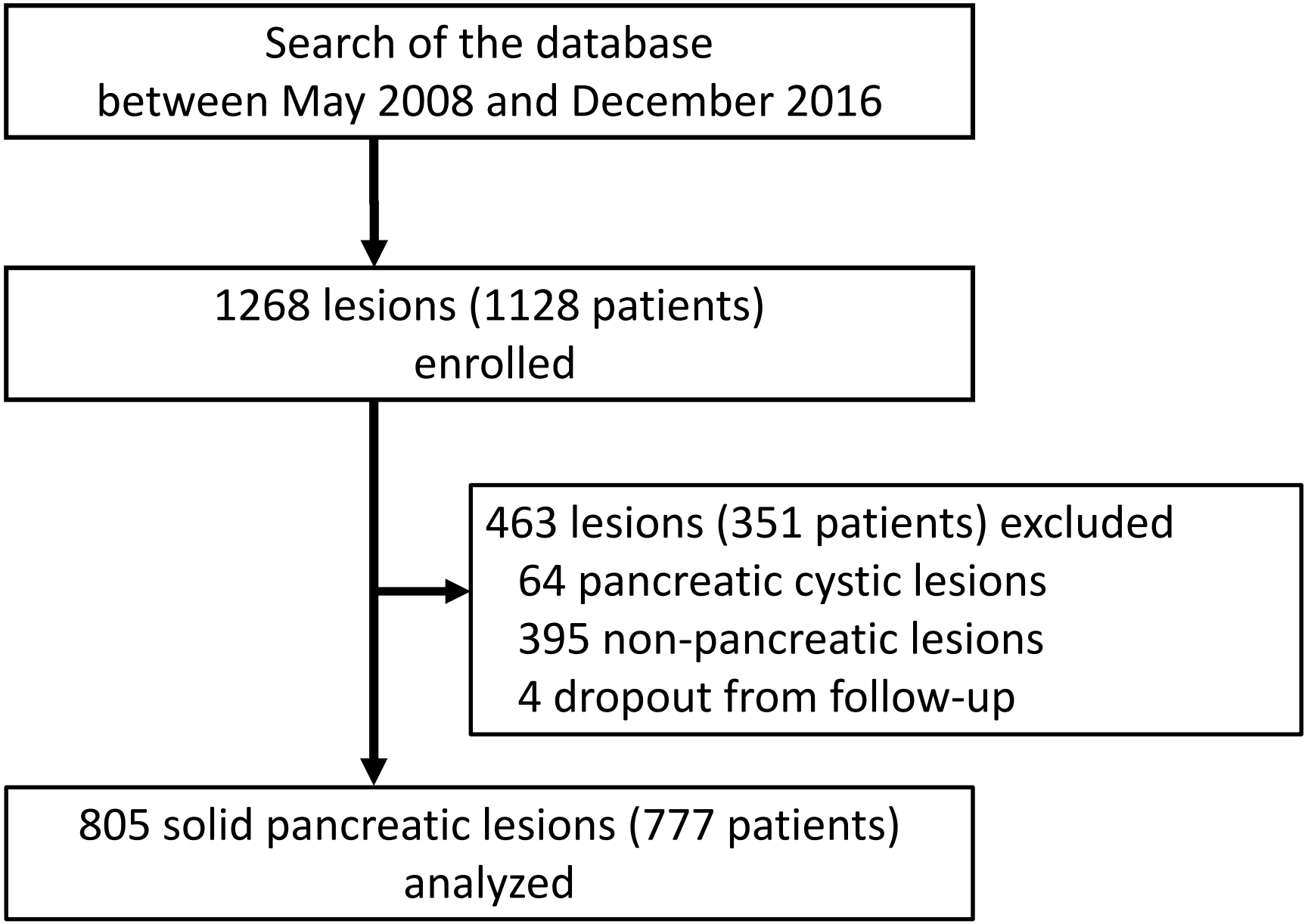
	Odds ratio	95% CI	*P* value
Mass location			
Ph	1		
Pb	2.54	0.58 – 11.2	0.22
Pt	2.27	0.35 – 14.6	0.39
Puncture route			
Transgastric	1		
Transduodenal	1.00	1.00 – 1.00	0.92
Mass size			
Group A (<10 mm)	1		
Group B (10-20 mm)	3.31	0.72 – 15.1	0.12
Group C (20-30 mm)	6.93	1.38 – 34.8	0.02
Group D (30-40 mm)	12.3	1.65 – 91.1	0.01
Group E (40 mm≤)	9.77	0.84 – 113	0.07
Final diagnosis			
Adenocarcinoma (primary)	1		
Neuroendocrine tumor	1.93	0.36 – 10.5	0.45
Other tumor	1.77	0.42 – 7.23	0.43
Parenchymal condition			
No chronic pancreatitis	1		
Chronic pancreatitis	1.26	0.14 – 11.8	0.84

Logistic regression analysis

Table 8 Adverse events in groups classified by mass size

	Group A (n=36)	B (n=223)	C (n=304)	D (n=147)	E (n=78)	*P* value
Adverse event, n (%)						
	1 (2.8)	5 (2.2)	4 (1.3)	5 (3.4)	2 (2.6)	0.51
Severe/Moderate/Mild, n						
	1/0/0	2/0/3	0/2/2	1/0/4	0/2/0	
pancreatitis, n	1	4	2	3	0	
bleeding, n	0	0	0	2	0	
perforation, n	0	1	1	0	0	
peritonitis, n	0	0	0	0	1	
infection, n	0	0	1	0	1	

Fisher's exact test


Search of the database
between May 2008 and December 2016
1268 lesions (1128 patients)
enrolled
463 lesions (351 patients) excluded
64 pancreatic cystic lesions
395 non-pancreatic lesions
4 dropout from follow-up
805 solid pancreatic lesions (777 patients)
analyzed