

Severe Bleeding and Perforation Are Rare Complications of Endoscopic Ultrasound-Guided Fine Needle Aspiration for Pancreatic Masses: An Analysis of 3,090 Patients from 212 Hospitals

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Background/Aims: Endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is useful for the pathological diagnosis of pancreatic masses, but patients are susceptible to severe bleeding and perforation. Because the incidence and severity of these complications have not been fully evaluated. **Methods:** We aimed to evaluate severe bleeding and perforation after EUS-FNA for pancreatic masses using large-scale data derived from a Japanese nationwide administrative database. **Results:** In total, 3,090 consecutive patients from 212 low- to high-volume hospitals were analyzed. Severe bleeding requiring transfusion or endoscopic treatment occurred in seven patients (0.23%), and no perforation was observed. No patient mortality was recorded within 30 days of EUS-FNA. The rate of severe bleeding in low-volume hospitals was significantly higher than that in medium- and high-volume hospitals (0.48% vs 0.10%, $p=0.045$). **Conclusions:** Severe bleeding and perforation following EUS-FNA for pancreatic masses are rare, and the procedure is safe. (*Gut Liver* 2014;8:215-218)

Key Words: Hemorrhage; Perforation; Endoscopic ultrasound-guided fine needle aspiration; Pancreas

INTRODUCTION

Endoscopic ultrasound (EUS) is an established procedure for morphologic evaluation of pancreatic masses,¹ and EUS-guided fine needle aspiration (EUS-FNA) permits cytological and histological examinations.²⁻⁴ Despite the high diagnostic accuracy of EUS-FNA in pancreatic masses, the procedure requires echoen-

doscope insertion and needle penetration through the gastrointestinal mucosa into the pancreas, and bleeding and perforation after EUS-FNA cannot be completely avoided.⁵

One systematic review of EUS-FNA reported the incidence of severe bleeding and perforation after the procedure was 0.10% and 0.01%.⁶ However, the studies in that review were based on the results of EUS-FNA performed by a single or a few endosonographers in high-volume centers and may underestimate the complication rate. Furthermore, there was a discrepancy in the complication rates between retrospective and prospective studies, implying a publication bias; and a large sample size is needed to evaluate rare events. Here we report a retrospective study of data from a Japanese national administrative database (Diagnosis Procedure Combination [DPC] database) to evaluate the incidence of severe bleeding and perforation after EUS-FNA for pancreatic masses.

MATERIALS AND METHODS

The DPC database records admission/discharge abstracts, administrative claims, and implementation of intervention procedures.^{7,8} The primary diagnoses and complications during hospitalization are recorded using International Classification of Diseases and Related Health Problems 10th Revision (ICD-10) codes, supplemented by text in Japanese. The database contains detailed medical information, patients' age and sex, length of hospital stay, discharge status including in-hospital death, and medications including drugs and intervention/surgical procedures indexed by Japanese original codes. This study was approved by the review board of The University of Tokyo Hospital

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who waived the requirement for patient informed consent because of the anonymous nature of the data.

We extracted data on consecutive patients who underwent EUS-FNA (indexed by the Japanese original code) for pancreatic masses and were discharged between 1 July 2010 and 31 October 2011. We identified pancreatic masses as targeted lesions of EUS-FNA by screening for potential lesions using the ICD-10 codes (C25.0-25.4, C25.7-25.9) and verified the diagnoses by notes recorded in Japanese. We converted each ICD-10 code of comorbidity into a score and calculated a Charlson Comorbidity Index.⁹ Hospitals were divided into academic and nonacademic, and into low-, medium-, or high-volume classes, by dividing total patients undergoing EUS-FNA annually into tertiles. Severe bleeding was identified from records of red blood cell (RBC) transfusion, endoscopic treatment, or vascular embolization for gastrointestinal bleeding with/without the records of intraperitoneal bleeding (K66.1), or upper gastrointestinal bleeding (K92.2). Perforation was identified from the ICD-10 codes indicating perforation of the stomach and duodenum: K25.1, 25.2, 26.1, and 26.2. Data for bleeding or perforation that occurred more than three days after the initial EUS-FNA procedure were excluded to separate bleeding associated with the procedure from other conditions requiring the same treatment.

We calculated descriptive statistics with IBM SPSS version 19.0 (IBM Co., Armonk, NY, USA). The incidence of complications between groups was compared using Fisher exact test. A *p*-value <0.05 was considered significant.

RESULTS

We found 3,090 patients who had undergone the EUS-FNA procedure for pancreatic masses in 72 academic and 140 non-academic hospitals. Over half of patients were male, with a median age of 67 (Table 1).

Seven patients (0.23%) required RBC transfusion, endoscopic treatment or vascular embolization. Of these seven patients, four targeted lesions were at the pancreatic tail and two at the pancreatic head (Table 2). The incidence of severe bleeding did not differ significantly between the masses of the pancreatic head and body-tail (0.17% vs 0.31%, *p*=0.689). Severe bleeding was observed in five (0.48%) patients in low-volume hospitals, one (0.10%) in a medium-volume, and one (0.10%) in a high-volume hospital. The incidence of severe bleeding was significantly higher (*p*=0.045) in low-volume hospitals than in medium- and high-volume hospitals. The incidence of severe bleeding was similar in academic and nonacademic hospitals (0.22% vs 0.23%, *p*=1.000).

Severe bleeding requiring RBC transfusion within three days of EUS-FNA occurred in three patients (0.10%). All RBC transfusion was performed within 24 hours of EUS-FNA. Endoscopic treatments for intestinal bleeding within 3 days were performed in four patients (0.13%) who did not require RBC transfusion.

The time between EUS-FNA and endoscopic treatment was <24 hours in 3 patients (75%), 24 to 48 hours in 0, and 48 to 72 hours in 1 patient (25%). No vascular embolization was performed.

No patient was recorded with perforation, indicated by the ICD-10 codes of perforation of the gastrointestinal tract. No patient died from bleeding and perforation after EUS-FNA patients in hospital within 30 days of the procedure.

Twenty-six patients (0.84%) were receiving antithrombotic drugs before and after the EUS-FNA procedure. Fourteen patients were receiving low-dose aspirin, six were receiving warfarin, three icosapentate, and one clopidogrel. One patient received low-dose aspirin/cilostazol, and one patient received low-dose aspirin/sarpogrelate. One patient (no. 6, Table 2) who was receiving icosapentate suffered severe bleeding, but the incidence of severe bleeding in patients receiving antithrombotic drugs did not differ significantly from that in patients who were not receiving antithrombotic drugs (0.20% vs 3.8%, *p*=0.057%).

DISCUSSION

Here, we found severe bleeding and perforation after the

Table 1. Characteristics of 3,090 Patients Who Underwent Endoscopic Ultrasound-Guided Fine Needle Aspiration for Pancreatic Masses

Characteristic	Value
Age, yr	67.4±10.4
Sex	
Male	1,745 (56.5)
Female	1,345 (43.5)
Location of lesions	
Head of the pancreas	1,201 (38.9)
Body-tail of the pancreas	1,300 (42.1)
Unavailable	589 (19.1)
Charlson Comorbidity Index	
2	1,212 (39.2)
3-4	1,081 (35.0)
≥5	797 (25.8)
Hospital volume	
Low-volume (≤18/yr)	1,031 (33.4)
Medium-volume (19-36/yr)	1,031 (33.4)
High-volume (≥37/yr)	1,028 (33.3)
Hospital type	
Academic	1,813 (58.7)
Nonacademic	1,277 (41.3)

Age is reported as the mean and standard deviation. Other variables are reported as the number and proportion (%). The Charlson Comorbidity Index was determined based on Quan's algorithm.⁹ Hospital volume was defined based on the number of patients undergoing endoscopic ultrasound-guided fine needle aspiration for pancreatic masses annually in each hospital.

Table 2. Patients Who Developed Severe Bleeding after Endoscopic Ultrasound-Guided Fine Needle Aspiration for Pancreatic Masses (n=7)

No.	<50	50-65	>65	Sex	Location of mass	Hospital volume	Hospital type	RBC transfusion	Endoscopic procedure
1	√			Male	Tail of the pancreas	Low	Academic	√	
2	√			Female	Tail of the pancreas	Low	Nonacademic	√	
3		√		Male	Head of the pancreas	High	Academic		√
4		√		Female	Tail of the pancreas	Low	Nonacademic		√
5			√	Male	Tail of the pancreas	Low	Academic		√
6			√	Male	Head of the pancreas	Low	Nonacademic		√
7			√	Male	Unavailable	Medium	Academic	√	

RBC, red blood cell.

EUS-FNA procedure were rare and no patients died from internal bleeding within 30 days of the procedure. Although these complications are potentially life-threatening,^{5,6} the results of the present study provide a robust estimation of complication incidence.

In most Japanese hospitals, EUS-FNA is completed as an inpatient procedure, and the DPC database covers about 7 million patients in 1,000 Japanese hospitals. Given that the database includes most patients who underwent EUS-FNA in Japan between 1 July 2010 and 30 June 2011, we are confident the present study provides a robust estimate of the risk of complications following the EUS-FNA procedure. The incidence of complications was similar to that previously reported.⁶

However, the incidence of severe bleeding in low-volume hospitals was 5-fold higher than in medium- and high-volume hospitals ($p=0.045$). This result supports previous studies showing the procedure administration may require a learning curve to reduce complications incidence.¹⁰

A further consideration is that an increasing number of patients are given antithrombotic drugs. Several drugs have prophylactic effects against cardiovascular and cerebrovascular diseases,¹¹ and the risk of those diseases may increase if antithrombotic drugs are stopped.^{12,13} However, the present study cannot confirm the safety of EUS-FNA for patients receiving antithrombotic drugs, because the sample size of effected patients was small. We are unaware of a consensus on how patients receiving antithrombotic drugs should be managed in during the EUS-FNA procedures,^{14,15} and a prospective randomized controlled trial to evaluate the safety of EUS-FNA for patients on antithrombotic drugs is needed.

There are some limitations to the present study. Several important clinical data (such as the size of needles, the number of passes, the detailed EUS findings of the targeted pancreatic masses and the experience of endosonographers) were unavailable from the DPC database.¹⁰ Bleeding requiring RBC transfusion and endoscopic treatment may not be a consequence of the EUS-FNA, leading to an overestimation of the incidence of severe bleeding after this procedure. Furthermore, since the DPC database is an inpatient administrative database, those patients

could not be identified who took antithrombotic agents regularly and discontinued these medications prior to admission for preparation of EUS-FNA. However, we consider these limitations do not affect the validity of the study.

In conclusion, we found severe bleeding and perforation requiring additional treatment were rare complications after EUS-FNA for pancreatic masses, and we conclude that EUS-FNA is a safe diagnostic procedure.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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