Usefulness of Routine Plain CT the Day After an Interventional EUS Procedure

Aya Kiyanagi1,2, Toshio Fujisawa1, Shigeto Ishii1, Ko Tomishima1, Yusuke Takasaki1, Akinori Suzuki1, Mako Ushio1, Sho Takahashi1, Wataru Yamagata1, Yoshihiro Okawa1, Kazushige Ochiai1, Hiroaki Saito1, Hiroyuki Isayama1

1Department of Gastroenterology, Graduate School of Medicine, Juntendo University, Tokyo, 2Department of Gastroenterology, Obihiro Daiichi Hospital, Hokkaido, Japan

Abstract

Background: Interventional endoscopic ultrasound-guided procedures (I-EUS) are widely accepted as salvage procedures in ERCP-failed cases, and to drain fluid collected in the abdominal cavity. Although I-EUS has a relatively high incidence of complications and is severe/fatal in some cases, no follow-up strategy has been established. In our institution, plain computed tomography (P-CT) is performed routinely the day after I-EUS. In this study, we evaluated the usefulness of routine P-CT the day after I-EUS, as a follow-up method, and propose an algorithm.

Methods: We retrospectively reviewed 81 patients who underwent I-EUS and evaluated the usefulness of P-CT, abdominal X-ray, laboratory data, and symptoms as a follow-up method. An adverse event (AE) was defined as an event requiring any treatment.

Results: Technical success, clinical success, and AE rates were 96.3%, 90.1%, and 18.9%, respectively. In total, 30 patients had abnormal findings among the follow-up methods: 6 cases underwent additional procedures, 8 underwent medical treatments, and 16 were observed. The sensitivity, specificity, and accuracy for detecting AEs were assessed based on P-CT (85.7%, 100%, and 97.5%), X-ray (7.1%, 100%, and 83.5%), laboratory data (71.4%, 83.0%, and 81.0%), and symptoms (92.9%, 86.2%, and 87.3%). The sensitivity and accuracy of the latter two items were as high as those for X-ray, but specificity was lower than those for X-ray and P-CT.

Conclusions: Routine P-CT the day after I-EUS was useful for detecting complications and deciding to perform an invasive salvage procedure. Symptoms and laboratory data were useful to supplement routine P-CT.

Keywords: Adverse event, algorithm, interventional EUS, plain CT, stent migration.

INTRODUCTION

Interventional endoscopic ultrasound-guided procedures (I-EUS) have become widely accepted and various procedures...
have been reported. EUS-guided biliary drainage (EUS-BD), including EUS-hepaticogastrostomy (HGS) and EUS-choledochoduodenostomy (CDS), are effective treatments for patients in whom endoscopic retrograde cholangiopancreatography (ERCP) failed, or was difficult.[1,3] The main reasons for this are failed biliary cannulation, surgically altered anatomy, and gastric obstruction. These techniques are recognized as salvage therapy for ERCP, with acceptable technical success and complication rates. The EUS-guided rendezvous (EUS-RV) technique is used for failed biliary/pancreatic cannulation[1,3] EUS-guided pancreatic drainage (EUS-PD) is also used as a salvage procedure for patients who require pancreatic ductal drainage and cases of failed/difficult ERP.[4] EUS-guided abscess drainage (EUS-AD) and EUS-guided pancreatic cystic drainage (EUS-PCD) are drainage methods for abdominal abscesses, walled-off necrosis after acute pancreatitis, and pancreatic pseudo cysts.[7,8] EUS-guided antegrade procedures (EUS-AG) include the management of biliary stones and strictures in surgically altered anatomy patients.[9]

Many studies have reported high technical and clinical success rates for these procedures, but the complication rate associated with some of them is high. For example, the complication rate of EUS-BD is approximately 20%, including severe cases that require surgery or are lethal.[10] EUS-guided drainage involves placing stents between organs with no adhesions. Therefore, severe complications, such as peritonitis and perforations, can occur.

Abdominal X-rays are typically taken as follow-up the day after an ERCP session. We consider that an abdominal X-ray is insufficient after I-EUS because it lacks three-dimensional information and fluid collection imagery. In our institution, we routinely take plain CT (P-CT) the day after an I-EUS procedure. P-CT provides more information than a simple abdominal X-ray. P-CT has enabled us to detect complications during the early phase, evaluate the location for a stent, and determine whether the drainage is working. No study has described follow-up methods after I-EUS. Some I-EUS guidelines are available, but no follow-up method has been recommended.[11] In this study, we evaluated the usefulness of routine P-CT the day after I-EUS as a follow-up method, and propose an algorithm.

METHODS

Patients
This was a single-center, retrospective study performed at Juntendo University Hospital, between March 2017 and February 2019. The objective was to evaluate the usefulness of a P-CT scan taken the day after an I-EUS procedure. Patients were excluded from analyses if they met any of the following criteria: insufficient data or information regarding the patient’s status, previous CT showing abnormal findings that were difficult to evaluate, or any other reason decided by the authors. An immediate enhanced CT scan was performed if the patient had severe symptoms, high fever >38.5°C, abdominal pain (poor response to pain reliever), or symptoms suggesting a procedure (decided by a physician). The protocol of the present study was approved by the institutional review board of our hospital on April 18, 2019 (No. 19-022).

Procedures
I-EUS includes EUS-BD, HGS, hepaticojejunostomy (HJS), and CDS, EUS-AG, EUS-GBD, EUS-RV, EUS-PD, EUS-PCD, and EUS-AD. Both abdominal X-rays and P-CT are routinely taken the day after I-EUS at Juntendo University Hospital.

The convex-type echoendoscope and EUS systems used in this study were the EG-580UT and SU-1 (Fujifilm Corp., Tokyo, Japan). All procedures were performed with patients in the prone position and sedated with pethidine hydrochloride and midazolam. Propofol was added if needed. A 19-G EUS-FNA needle (EZ Shot 3; Olympus Medical Systems, Tokyo, Japan. or Expect Flex; Boston Scientific Japan, Tokyo, Japan) was used. A guidewire (0.025-inch, angled type Visiglide2; Olympus Medical Systems, Tokyo, Japan) was inserted after successfully puncturing the bile duct, pancreatic duct, or cystic cavity. In 53 cases of the double guidewire technique, a double lumen catheter was used for the 0.025- and 0.035-inch guidewires (uneven catheter; Piolax Medical Devices Inc., Kanagawa, Japan), and other guidewire types (0.025 and 0.035 inches, angled type Revowave; Piolax Medical Devices) were employed. The fistula dilation devices used in this study were a bougie dilator (7 Fr ES dilator; Zeon Medical Co., Ltd., Tokyo, Japan), a cautery dilator (6 Fr Cysto-gastro-set; ENDO-FLEX, Voerde, Germany), and a balloon dilator (4 or 6 mm REN; Kaneka Medix Corp., Osaka, Japan) in combination as necessary. Covered self-expandable metallic stents (partially or fully covered) or plastic stents were placed as needed.

Definitions
Technical success was defined as stents that were placed adequately or achieved the aims of the procedure. Clinical success was defined as improved symptoms with normal laboratory data. The definitions of symptoms are as follows: severe abdominal pain (poor response to pain reliever), moderate abdominal pain (required pain reliever), mild abdominal pain (pain reliever not required),
high fever (>38.5°C), and fever (37°C < body temperature < 38.5°C).

The findings of abnormal P-CT and abdominal X-ray were defined as increase of ascites, fluid collection, free air, stent displacement, acute pancreatitis, mediastinitis, cholecystitis and cholangitis. CT findings that had been presented before procedure were excluded.

The abnormal laboratory data were defined as WBC >12000/μl, CRP >5 mg/dl, AST >200 U/L, total bilirubin >4 mg/dl, amylase >200 U/L.

Adverse events (AEs) were defined as conditions that required additional treatment, including invasive treatment, prolonged fasting, or administration of antibiotics. Treatments for AEs were classified into three categories: 1) required an additional procedure (RAP), 2) conservative management, 3) observation, and 4) no follow up. An elective procedure for the RAP cases was defined as an additional procedure requiring more than 3 days after I-EUS, and conservative management was defined as prolonged fasting and intravenous antibiotic administration for more than 3 days. Observation was defined as additional physical examinations and laboratory tests without any additional treatment.

Evaluations
The endpoint of this study was the detectability of AEs by routine P-CT during the I-EUS follow-up. Medical records, including laboratory data and symptoms, abdominal X-ray, and P-CT were retrospectively reviewed. P-CT and abdominal X-rays were taken routinely the day after the procedure. Laboratory data were checked 1 day before, the next day, and 2 weeks after the procedure. Symptoms were evaluated before and after the procedure.

We analyzed sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of each evaluating modality for detecting the AEs.

RESULTS

In total, 81 patients who underwent I-EUS during the study period were screened, and two patients were excluded: one patient did not undergo P-CT and another patient did not perform I-EUS due to ascites. Finally, 79 cases were enrolled and their records were reviewed: 54 biliary I-EUS (34 EUS-HGS/HJS, 13 EUS-AG, 2 EUS-CD, 2 EUS-GBD, and 3 EUS-RV), 20 pancreatic I-EUS (12 EUS-PD and 8 PCD), and 5 other I-EUS (EUS-AD) cases. Table 1 lists the baseline patient characteristics, including primary diseases and reasons for selecting the procedures.

Table 1 lists the I-EUS results: total technical success, clinical success and AE rates were 96.3%, 90.1%, and 19.0%, respectively. The technical success rate of EUS-AG was relatively low, and all failed cases were puncture failures due to an invisible/undilated bile duct.

In total, 30 of the 79 patients had findings suggesting an AE by P-CT, abdominal X-ray, abnormal laboratory data, and/or abnormal symptoms after the I-EUS procedure [Table 3]. We classified these cases into the four categories previously defined in the methods section: RAP, conservative management, observation, and no follow-up. The first two categories were defined as AEs (14 cases, 17.7%) related to the I-EUS procedure.
The diagnostic ability of routine P-CT for detecting the AEs was analyzed and compared with abdominal X-rays, symptoms, and abnormal laboratory data. P-CT, symptoms, and abnormal laboratory data were effective for detecting AEs, but abdominal X-rays were not [Table 4]. Sensitivity, specificity, PPV, NPV, and accuracy of the diagnostic items were calculated and are listed in Table 5. Accuracy of AE detection was highest for P-CT, high for both symptoms and abnormal laboratory data, and lowest for abdominal X-ray.

Four patients needed an immediate procedure to manage their AEs, including two cases of stents moving toward the abdominal cavity, with a <20 mm length of the protruding portion in the stomach, as detected by P-CT the next day. This situation was considered life-threatening stent migration. We immediately performed an endoscopic stent anchoring procedure to prevent migration. The procedure is called the “ClipFlap technique” and involves performing endoscopic clipping on the metallic stent wall as a newly made flap.[12] Abdominal X-ray did not reveal the dislocation of stents, and only CT revealed the relationship between the gastric wall and the stent.

Biliary peritonitis after EUS-GBD with migration of the plastic stent into the abdominal cavity required additional drainage of the gallbladder and peritoneal cavity, which has been reported previously.[13] The next day a CT revealed that the stent had migrated and a large volume of ascites was present; however, the abdominal X-ray revealed only an elevated right diaphragm and no dislocated stent. Acute cholangitis required additional biliary drainage and the other case required immediate additional procedures.

Elective drainage procedures were performed in two cases with mild peritonitis due to biliary and pancreatic leakage. A follow-up CT 2 days after the initial P-CT revealed an increase in the volume of ascites, so we performed additional drainage procedures 4 days after the initial I-EUS procedure.

Eight cases received conservative management, including prolonged administration of antibiotics and fasting. These cases revealed some abnormal P-CT findings, symptoms, and abnormal laboratory data, but did not require an additional procedure to improve their status. In this category, one case of aspiration pneumonia died 1 week after the procedure because of the lack of effectiveness of the antibiotics. The other AEs were mediastinitis, pancreatitis, pancreatic leakage, biliary peritonitis, and suspicion of localized peritonitis. All of these cases were diagnosed by P-CT findings and a CT was taken after a few days to evaluate the medical treatment. The five cases of mediastinitis, pancreatitis, pancreatic leakage, and biliary peritonitis improved after conservative treatment, which was continued. Two cases of suspicious peritonitis were encountered because of moderate abdominal pain with remarkable laboratory data, but the P-CT was normal. These cases were suspected to be localized peritonitis due to the small amount of bile leakage, and their findings improved after a few days of medical treatment.

The remaining 16 cases had abnormal laboratory data and symptoms, but the CT and X-rays did not suggest conditions requiring treatment. They were observed for a few days and recovered without any additional treatment.

Figure 1 presents a case of life-threatening stent migration [case no. 2 in Table 3]. EUS-HGS was performed for obstructive jaundice due to advanced gastric cancer because of a pyloric obstruction [Figure 1a]. The procedure
was successful and the length of the protruding stent in the stomach was about 20 mm [Figure 1b]. An abdominal X-ray the day after the procedure revealed no migration of the stent [Figure 1c], but the routine P-CT revealed a life-threatening stent migration into the abdominal cavity [Figure 1d]. An endoscopic examination was performed urgently, and the length of the stent in the stomach was about 60 mm [Figure 1e]. Then, we performed the “ClipFlap” anchoring[13] and “Crisscross” anchoring techniques[14] previously reported [Figure 1f]. In this case, no symptoms were observed, and the laboratory data improved compared with the day before the procedure.

The abdominal X-ray did not indicate that the stent was dislocated, and only P-CT detected the life-threatening
stent migration. This was an extremely useful case of routine P-CT after I-EUS to avoid a severe complication.

Other useful P-CT findings included the detection of fluid collection or free air in the abdominal cavity. One case underwent EUS-PD for failed passage of a stricture due to chronic pancreatitis [case no. 5 in Table 3][Supplementary Figure 1a]. An abdominal X-ray image taken the next day revealed no abnormal findings or stent migration [Supplementary Figure 1b]. However, this patient had a high fever, mild abdominal pain, and an elevated white blood cell count and C-reactive protein the next morning. The P-CT revealed fluid collection in the dorsum of the stomach, which was considered pancreatic leakage [Supplementary Figure 1c]. We managed this patient conservatively with fasting and administered antibiotics. A contrast CT image taken after 3 days of conservative treatment revealed an increased volume of fluid [Supplementary Figure 2a]. Additional EUS-guided abscess drainage was performed and was effective for improving the symptoms [Supplementary Figure 2b and c].

Five cases of bile and pancreatic leakage were observed: two required additional drainage and three improved after prolonged fasting and antibiotic administration. The CT findings the day after the procedure and a few days after medical treatment helped in decision-making. Routine CT was useful for evaluating medical treatment and avoiding unnecessary invasive treatment.

**DISCUSSION**

Routine P-CT the day after the procedure for the follow-up of interventional EUS was useful to detect complications and determine the best management plan. All cases with abnormal CT findings received treatment including additional invasive procedures. Symptoms were also a strong factor determining treatment, but half of the symptomatic patients did not receive treatment. Symptoms are very important, but CT findings were more objective after the procedure. Routine CT may be useful to determine the need to perform additional procedures, improve the patient’s status earlier, and yield a better clinical outcome and a shorter hospital stay.

No standard follow-up methods have been established for pancreato-biliary endoscopy. In Japan, checking vital signs, blood examinations, and plain X-rays are standard the day following ERCP-related procedures, but no follow-up methods have been reported for EUS-related interventional procedures.[3] In the EUS-BD clinical practice guidelines, P-CT is described as a useful follow-up tool to detect AEs but it is not recommended because of lack of evidence.[3] After ERCP, simple abdominal X-ray may reveal a dislocated stent, remnant contrast medium in the bile duct, or free air. However, locating the stents was difficult after interventional EUS. The sensitivity of abdominal X-ray for detecting complications was very low compared with abdominal P-CT (7.1% vs. 85.7%), as was accuracy (83.5% vs. 97.5%). The sensitivity of detection is the most important factor for managing a complication.

Other items used to evaluate complications include symptoms and a blood examination, and these were able to detect complications. In particular, the sensitivity of symptoms was high, but specificity was not. These findings indicate that symptoms are not objective and are influenced by the procedure and the characteristics of each patient. Additionally, cases of life-threatening migration did not exhibit any specific symptoms. The results of the blood examination influenced the decision for treatment, but invasive treatment could not be performed without abnormal CT findings. Symptoms and blood examinations in combination with CT may provide adequate information to make a treatment decision, but symptoms and/or abnormal blood findings alone did not help determine an invasive treatment. Performing a CT scan when a patient is symptomatic or has abnormal blood findings may be an option at follow-up, but this could delay important treatment decisions.

Contrast-enhanced CT reveals more information, and is available for cases with severe symptoms, but this is more invasive than P-CT. Both procedures can identify stent migration to other organs and can detect risky cases of migration. One problem with routine P-CT is increased radiation exposure. Another problem is a shortage of CT examination machines, making it difficult to use CT routinely. However, the benefits of P-CT appear to outweigh the invasiveness and/or difficulty of performing a CT scan.

Some limitations of this study should be considered. It was a single-center study without a large number of cases,

### Table 5: Diagnostic ability of evaluation items for adverse events after interventional EUS

| Item                        | Sensitivity (%) | Specificity (%) | PPV (%) | NPV (%) | Accuracy (%) |
|-----------------------------|----------------|-----------------|---------|---------|--------------|
| Abnormal CT findings        | 85.7           | 100             | 100     | 97.0    | 97.5         |
| Abnormal X-ray findings     | 7.1            | 100             | 100     | 83.3    | 83.5         |
| Abnormal laboratory data    | 71.4           | 83.0            | 47.6    | 93.1    | 81.0         |
| Symptoms                    | 92.9           | 86.2            | 59.1    | 98.2    | 87.3         |
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and the data were reviewed retrospectively. The doctor who read the P-CT scans was not blinded, and a single gastroenterologist performed all diagnoses. Symptoms were difficult to review retrospectively from the medical chart.

Figure 2 presents our proposed follow-up algorithm after interventional EUS. Patients with severe symptoms should undergo contrast-enhanced CT immediately. Other patients should receive routine P-CT. Patients without any symptoms, abnormal laboratory data, or abnormal P-CT findings do not need to be followed up and can be permitted to eat. Patients with mild symptoms and/or abnormal laboratory data should be observed using physical and blood examinations. For patients with abnormal P-CT findings, it will be necessary to decide whether conservative treatment will be sufficient or whether additional procedures are necessary. Possible findings indicating additional procedures include stent dislocation, suspicion of perforation, ascites suggesting leakage (pancreatic and bile juice), cholangitis with bile duct dilation, pancreatitis with dilation of the pancreatic duct, and any findings requiring a procedure as decided by the doctors.

In conclusion, performing a routine P-CT scan instead of an abdominal X-ray the day after interventional EUS was useful to detect complications and making decisions about whether to perform an invasive salvage procedure. Dislocation of the stent and fluid corrections were difficult to detect based on an abdominal X-ray. We propose performing a P-CT scan routinely 1 day after an interventional EUS procedure for patients without severe symptoms, high fever >38.5°C, abdominal pain (poor response to pain reliever), or symptoms suggesting a procedural requirement for contrast-enhanced CT. However, a prospective controlled study including several institutions will be required to evaluate our proposed follow-up algorithm for interventional EUS.

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Conflicts of interest
There are no conflicts of interest.

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Supplementary Figure 1: Pancreatic leakage after endosonography-guided pancreatic ductal drainage (EUS-PD) (a) X-ray image of the EUS-PD procedure for a chronic pancreatitis patient (b) Abdominal X-ray image with no abnormal findings the day after the procedure (c) Routine plain CT image the day after the EUS-PD procedure revealed fluid collection in the dorsum of the stomach.

Supplementary Figure 2: A case with pancreatic leakage after EUS-PD a few days later (a) Contrast CT image after 3 days of conservative treatment. Fluid volume increased. (b) EUS image of EUS-guided puncture of an abscess developing from pancreatic leakage. (c) EUS-guided abscess drainage.