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<td>Kawakubo, Kazumichi; Kawakami, Hiroshi; Kuwatani, Masaki; Haba, Shin; Kudo, Taiki; Abe, Yoko; Kawahata, Shuhei; Onodera, Manabu; Ehira, Nobuyuki; Eto, Kazunori; Sakamoto, Naoya</td>
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<tr>
<td>Citation</td>
<td>Gut and Liver, 8(3), 329-332</td>
</tr>
<tr>
<td>Issue Date</td>
<td>2014-05</td>
</tr>
<tr>
<td>Doc URL</td>
<td><a href="http://hdl.handle.net/2115/56536">http://hdl.handle.net/2115/56536</a></td>
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<tr>
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**Hokkaido University Collection of Scholarly and Academic Papers: HUSCAP**
Safety and Utility of Single-Session Endoscopic Ultrasonography and Endoscopic Retrograde Cholangiopancreatography for the Evaluation of Pancreatobiliary Diseases

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Endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) are essential for diagnosing and treating pancreatobiliary diseases. Single-session EUS and ERCP are considered to be essential in reducing the duration of hospital stays; however, complications are a primary concern. The aim of this study was to evaluate the safety and efficacy of single-session EUS and ERCP. Sixty-eight patients underwent single-session EUS and ERCP at a tertiary referral center between June 2008 and December 2012. We retrospectively reviewed patient data from a prospectively maintained EUS-ERCP database and evaluated the procedural characteristics and complications. Thirty-eight patients (56%) underwent diagnostic EUS, and 30 patients (44%) underwent EUS fine-needle aspiration, which had an overall accuracy of 100%. Sixty patients (89%) underwent therapeutic ERCP, whereas the remaining eight procedures were diagnostic. Thirteen patients underwent biliary stone extraction, and 48 underwent biliary drainage. The median total procedural time was 75 minutes. Complications were observed in seven patients (10%). Six complications were post-ERCP pancreatitis, which were resolved using conservative management. One patient developed Mallory-Weiss syndrome, which required endoscopic hemostasis. No sedation-related cardiopulmonary complications were observed. Single-session EUS and ERCP provided accurate diagnosis and effective management with a minimal complication rate.

Key Words: Endoscopic retrograde cholangiopancreatography; Endoscopic ultrasound; Single-session procedure

INTRODUCTION

Both endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP) are required to evaluate patients with pancreatobiliary diseases. ERCP is a well-established technique to evaluate and manage biliary obstructions, but it carries a risk of complications, such as post-ERCP pancreatitis, bleeding, and perforation. Therefore, ERCP is reserved mainly for therapeutic indications. EUS is a less-invasive modality and has high accuracy for diagnosing pancreatobiliary diseases such as biliary stones and pancreatic tumors. These two procedures can be performed during a single session under same anesthesia, but concern regarding their safety has been raised due to complications. However, a single session results in a reduction in hospital stay and avoidance of repeated sedation as compared to multiple sessions. Previous studies only evaluate the utility of single-session EUS and ERCP in a single setting. Therefore, we performed a retrospective analysis of patients with pancreatobiliary diseases who underwent single-session EUS and ERCP to evaluate their safety and efficacy in a variable setting.

CASE REPORT

We retrospectively reviewed data from a prospectively maintained database of patients who underwent single-session EUS with/without fine-needle aspiration (FNA) and ERCP at Hokkaido University Hospital between July 2008 and December 2012. The collected data included age, sex, indications for the procedure, primary diseases, endoscopic and clinical outcomes, procedural complications, and pathological findings if observed. This study was approved by the Institutional Review Board.
of Hokkaido University Hospital and was registered with the University Hospital Medical Information Network-Clinical Trial Registry (UMIN-CTR; number, UMIN000008409).

Written informed consent was obtained from all patients before the procedures. Combined EUS and ERCP were performed under conscious sedation using intravenous midazolam with fentanyl. Before 2009, EUS was performed with a radial echoendoscope (GF-UM2000 or GF-UE260; Olympus Medical Systems Co., Tokyo, Japan). After introduction of the linear echoendoscope (GF-UCT240-AL5; Olympus Medical Systems Co.) to our institution, we used either type of echoendoscope at the discretion of the endoscopist. Patients also underwent EUS-guided FNA (EchoTip Ultra, Cook-Japan, Tokyo, Japan; or Expect, Boston Scientific Japan, Tokyo, Japan) with rapid on-site cytology evaluation if necessary. Subsequent ERCP-related procedures were performed following EUS during the same session using a duodenoscope (JF-240, TJF-240, or TJF-260V; Olympus Medical Systems Co.). In patients who were using antithrombotic or antiplatelet agents, each procedure was performed according to the Japanese guidelines. After the procedure, patients were monitored at an inpatient unit in the same way as those who underwent ERCP alone. Procedural-related complications were classified and graded according to consensus criteria. A total of 1,519 ERCP and 1,559 EUS procedures were performed respectively at our institution. Among them, 68 patients (mean age, 69 years; 38 males and 30 females) underwent EUS and ERCP in a single session and were included in this study (Table 1). Diagnostic EUS was performed in 38 patients (linear EUS in 14 and radial EUS in 24) with a median procedure time of 32 minutes. EUS-FNA was performed in 30 patients (44%) (Table 2). The sensitivity and specificity of EUS-FNA for malignancy were 100% and 100%. Choledocholithiasis was confirmed in all patients with acute cholangitis. Bile duct cannulation following EUS was successful in all but one patient. Sixty patients underwent therapeutic ERCP, whereas the remaining eight were diagnostic procedures. Thirteen patients underwent endoscopic

<table>
<thead>
<tr>
<th>Table 1. Patient Characteristics</th>
<th>Value</th>
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<tbody>
<tr>
<td>No. of patients</td>
<td>68</td>
</tr>
<tr>
<td>Age, yr</td>
<td>69 (62–76)</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>38/30</td>
</tr>
<tr>
<td>Indications for EUS</td>
<td></td>
</tr>
<tr>
<td>Indeterminate biliary stricture</td>
<td>46</td>
</tr>
<tr>
<td>Acute cholangitis</td>
<td>20</td>
</tr>
<tr>
<td>Other</td>
<td>2</td>
</tr>
<tr>
<td>Laboratory data</td>
<td></td>
</tr>
<tr>
<td>WBC/mL</td>
<td>5,200 (1,925–7,200)</td>
</tr>
<tr>
<td>CRP, mg/dL</td>
<td>0.5 (0.08–2.9)</td>
</tr>
<tr>
<td>Total bilirubin, mg/dL</td>
<td>1.6 (1.0–5.9)</td>
</tr>
<tr>
<td>Amylase, IU/mL</td>
<td>59 (42–86)</td>
</tr>
<tr>
<td>Final diagnosis</td>
<td></td>
</tr>
<tr>
<td>Pancreatic cancer</td>
<td>17</td>
</tr>
<tr>
<td>Bile duct cancer</td>
<td>11</td>
</tr>
<tr>
<td>Gallbladder cancer</td>
<td>9</td>
</tr>
<tr>
<td>Ampullary cancer</td>
<td>2</td>
</tr>
<tr>
<td>Lymph node metastasis</td>
<td>3</td>
</tr>
<tr>
<td>Pancreatic neuroendocrine tumor</td>
<td>1</td>
</tr>
<tr>
<td>Intraductal papillary mucinous neoplasm</td>
<td>1</td>
</tr>
<tr>
<td>Autoimmune pancreatitis</td>
<td>3</td>
</tr>
<tr>
<td>Choledocholithiasis</td>
<td>19</td>
</tr>
<tr>
<td>Benign biliary stricture</td>
<td>2</td>
</tr>
</tbody>
</table>

Data are presented as number or median (interquartile range). EUS, endoscopic ultrasonography; WBC, white blood cells; CRP, C-reactive protein.

<table>
<thead>
<tr>
<th>Table 2. Characteristics of the Procedures</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total procedure time, min</td>
<td>75 (53–88)</td>
</tr>
<tr>
<td>Diagnostic EUS</td>
<td>38 (56)</td>
</tr>
<tr>
<td>Linear/radial</td>
<td>14/24</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>32 (18–41)</td>
</tr>
<tr>
<td>EUS-FNA</td>
<td>30 (44)</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>40 (26–49)</td>
</tr>
<tr>
<td>Puncture site (pancreas/lymph node/bile duct)</td>
<td>13/2/1</td>
</tr>
<tr>
<td>Needle (19/22/25 gauge)</td>
<td>3/23/4</td>
</tr>
<tr>
<td>Sensitivity, %</td>
<td>100</td>
</tr>
<tr>
<td>Specificity, %</td>
<td>100</td>
</tr>
<tr>
<td>Accuracy, %</td>
<td>100</td>
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<tr>
<td>ERCP</td>
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</tr>
<tr>
<td>Diagnostic/therapeutic</td>
<td>8/60</td>
</tr>
<tr>
<td>Biliary cannulation failure</td>
<td>1</td>
</tr>
<tr>
<td>Biliary stenting</td>
<td>48 (71)</td>
</tr>
<tr>
<td>Plastic stent/ENBD/SEMS</td>
<td>11/25/12</td>
</tr>
<tr>
<td>Stone extraction</td>
<td>13 (19)</td>
</tr>
<tr>
<td>Sphincterotomy</td>
<td>25 (37)</td>
</tr>
<tr>
<td>Procedure time, min</td>
<td>34 (24–44)</td>
</tr>
<tr>
<td>Sedative/analgesic agents</td>
<td></td>
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<tr>
<td>Midazolam, mg</td>
<td>10 (8–13)</td>
</tr>
<tr>
<td>Fentanyl, μg</td>
<td>150 (100–200)</td>
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<tr>
<td>Complications</td>
<td>7 (10)</td>
</tr>
<tr>
<td>Post-ERCP pancreatitis (mild/moderate/severe)</td>
<td>6 (3/2/1)</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>0</td>
</tr>
<tr>
<td>Perforation</td>
<td>0</td>
</tr>
<tr>
<td>Mallory-Weiss syndrome</td>
<td>1</td>
</tr>
</tbody>
</table>

Data are presented as number (%) or median (interquartile range). EUS, endoscopic ultrasonography; EUS-FNA, EUS-guided fine-needle aspiration; ERCP, endoscopic retrograde cholangiopancreatography; ENBD, endoscopic nasobiliary drainage; SEMS, self-expandable metallic stent.
sphincterotomy followed by stone extraction, whereas six pa-
tients underwent plastic stent placement due to severe cholan-
gitis or were taking antithrombotic agents. Biliary drainage was
performed using self-expandable metallic stents in 12 patients,
plastic stents in 11, and nasobiliary drainage in 25.

Seven complications (10.3%; 95% confidence interval, 3.1
to 17.5) were observed. Six were post-ERCP pancreatitis. One
patient with bile duct carcinoma who underwent EUS-FNA for
lymph node and endoscopic nasobiliary drainage placement for
obstructive jaundice developed severe pancreatitis. Three pa-
tients were mild, and two patients were moderate, according to
the consensus criteria. All patients resolved with conservative
management. One patient developed Mallory-Weiss syndrome
1 day after the single-session procedure, which required endo-
scopic hemostasis. No severe cardiopulmonary complications or
deaths related to the combined procedure were observed.

**DISCUSSION**

We revealed that single-session EUS and ERCP were both
safe and effective for managing pancreatobiliary disorder in a
variable setting. The combined procedure facilitated appropriate
patient management without severe complications and could be
considered a standard treatment that reduces hospital stay and
avoids unnecessary sedation.

It was necessary but sometimes difficult to distinguish be-
tween malignant and benign originating lesions in patients with
biliary obstructions. EUS has greater sensitivity for detecting
small pancreatic tumors or preoperative staging than computed
tomography, and improves the diagnosis of indeterminate bile
duct strictures without EUS-FNA. Therefore, identifying unre-
sectable malignant tumors by EUS in patients with a biliary ob-
struction may require a metallic stent rather than a plastic stent
due to the longer patency. Furthermore, if the presence of a
biliary stent interferes with preoperative staging of a pancreatic
head tumor by EUS, EUS should be performed before ERCP to
avoid unnecessary laparotomies. In this study, three patients
who did not have tumors following the EUS examination were
diagnosed with a benign biliary stricture, and were managed
successfully. Ascuncce et al. also reported that benign biliary
strictures can be diagnosed and managed successfully by single-
session EUS-ERCP without FNA.

EUS-FNA has great sensitivity for detecting malignancy in
not only pancreatic tumors, but also biliary strictures. Ident-
ifying a malignancy by EUS-FNA eliminates the need for bili-
ary brushing, the sensitivity of which is inferior to that of EUS-
FNA. Furthermore, because preoperative biliary drainage is not
necessary in patients with obstructive jaundice who undergo a
Whipple resection, positive cytology could avoid unnecessary
biliary stenting. Ross et al. reported that the combination of
EUS-FNA with ERCP for evaluation of patients with obstructive
jaundice from presumed pancreatic malignancy provides ac-
curate tissue diagnosis and biliary drainage. In this study, EUS-
FNA was performed in 30 patients; malignancy was detected in
all malignant diseases. Three patients without malignancy were
diagnosed with autoimmune pancreatitis and successfully man-
gaged with steroid therapy. Furthermore, EUS-FNA immediately
after biliary stent placement was associated with a high rate
of inconclusive cytology; thus, EUS-FNA should be performed
before ERCP for a correct diagnosis. In patients with indeter-
minate biliary stricture, single-session EUS and ERCP would be
the most reasonable.

EUS is superior to other modalities for detecting biliary stones
and can avoid unnecessary ERCP in patients with suspected
biliary stone or biliary pancreatitis. Fabri et al. reported
that single-session EUS and ERCP in patients at low risk of bili-
ary stones is safe and effective with reduced procedural time
and costs compared to performance in separate sessions. In our
study, 13 patients underwent EUS and ERCP with sphinctero-
tomy and stone extraction without complications, whereas the re-
main ing patients with severe cholangitis and/or those who were
taking antithrombotic agents underwent placement of a biliary
stent without sphincterotomy. One of the concerns regarding a
single-session procedure is total procedural time. However,
Benjaminov et al. reported that separate EUS and ERCP sessions
for symptomatic choledocholithiasis expose the patient to a higher
risk of cholangitis as compared to a single-session procedure.
Stone extraction in a single session is reasonable considering its
safety and decreased hospital stay. Therefore, single-session EUS
and ERCP would be the most useful for patients with cholangitis
in whom choledocholithiasis could not be confirmed by other
imaging modalities.

The advantage of single-session EUS and ERCP as com-
pared to a separate session is expedited patient management,
shortening of the hospital stay, reduced cost and avoidance of
repeated sedation. The major disadvantages of these proce-
dures are the long procedural time and the increase in intestinal
gas volume. However, previous studies of single-session EUS
and ERCP reported no severe complications. We observed
six cases of post-ERCP pancreatitis, all of which resolved with
conservative management. However, post-ERCP pancreatitis
is an inherent complication of ERCP and was not attributed to
the single-session procedure. We had experienced one Mallory-
Weiss syndrome, which was also one of the complications of
upper endoscopy. Iles-Shih et al. reported the safety of single-
session EUS and ERCP in elderly patients, with no more adverse
events than in nonelderly patients. Therefore, this disadvantage
does not preclude performance of both procedures in a single
session, considering their efficacy.

Our study had some limitations. First, it was of a retrospective
design conducted at a single center. Second, a single-session
procedure can be performed only by endoscopists experienced
in both EUS and ERCP. A single-session procedure is not the
standard. Third, we did not compare hospital stay duration and
the cost of a single-session procedure with those of separate sessions. Fourth, we could not evaluate the patients who could avoid unnecessary ERCP.

Our results show that single-session EUS and ERCP were safe and useful for management of pancreatobiliary diseases. However, development of a new therapeutic endoscope, using which both EUS and ERCP can be performed in a single-session without scope exchange, is necessary for the widespread acceptance of this combined procedure.

CONFLICTS OF INTEREST

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

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