Diagnostic Use of Endoscopic Retrograde Cholangiopancreatography for Pancreatic Duct Injury in Trauma Patients

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ABSTRACT: Background: Trauma patients diagnosed with pancreatic duct injury (PDI) have a high complication rate and prolonged hospital stay. The role of endoscopic retrograde cholangiopancreatography (ERCP) in the diagnosis of PDI remains unclear. During the last decade, our trauma unit incorporated ERCP into the management protocol for suspected PDI cases. Objectives: To determine whether ERCP is a sensitive tool to detect PDI. Methods: This retrospective trauma patient series study assessed the diagnostic yield of ERCP in trauma cases with suspected PDI on computed tomography (CT) or intraoperatively. Between 1 January 2004 and 31 December 2011, 13 patients admitted to our medical center underwent ERCP for suspected PDI. Patient demographics, mechanism of injury, Injury Severity Score (ISS), time from injury to ERCP, and ERCP-related complications were documented and assessed. Results: Of the 13 patients included in the analysis, 8 stable patients with suspected PDI on CT had no leak from the main pancreatic duct on ERCP. Two of them underwent surgery for suspected pancreatic transection. ERCP confirmed a main pancreatic duct leak in three patients. Two patients underwent ERCP for suspected PDI after “damage control” surgery. No leak from the pancreatic ducts was diagnosed. No pancreas-related complications or ERCP-related complications were observed. Conclusions: ERCP is a sensitive and relatively safe tool for the diagnosis of PDI, and its use might prevent unnecessary surgical interventions in selected trauma cases. KEY WORDS: pancreatic duct injury (PDI), endoscopic retrograde cholangiopancreatography (ERCP), trauma management

Injury to the pancreas occurs in approximately 3% to 12% of patients with abdominal trauma [1-3]. The management of traumatic pancreatic duct injury is determined by diagnostic visualization of the pancreatic duct. Numerous publications report relatively high rates of delay in traumatic PDI diagnosis, which results in increased morbidity and mortality [4-6]. Controversy regarding the diagnostic modality of choice to detect PDI in trauma patients still exists. The management dilemma stems mainly from lack of evidence comparing the safety and efficacy of the different approaches [6-8]. Endoscopic retrograde cholangiopancreatography (ERCP) and stenting of the biliary tree or the pancreatic duct is a well-established practice for the treatment of patients with biliary and pancreatic pathologies such as obstructive jaundice, biliary pancreatitis and iatrogenic biliary duct injuries [8-10]. A few reports indicate the use of ERCP for the diagnosis of PDI in an acute trauma setting as well as after a delay since the traumatic injury [11]. However, several studies have reported complications following ERCP in patients with major trauma and have questioned the diagnostic usefulness weighed against the risk of complications [4-8]. The objective of this study was to describe the sensitivity of detection, the complication rate and the prognosis of abdominal trauma patients receiving treatment according to our trauma unit management protocol for suspected pancreatic injury.

PATIENTS AND METHODS
We performed a retrospective trauma case series analysis of all patients admitted to our medical center between 1 January 2004 and 31 December 2011 who underwent ERCP for suspected PDI. Inclusion in the study was regardless of the trauma mechanism (blunt or penetrating) or the initial method of management (laparotomy vs. expectant management). This study was approved by our Institutional Review Board. Patient demographics, mechanism of injury, Injury Severity Score (ISS), time from injury to ERCP, and either pancreas-related or ERCP-related complications were documented.

TREATMENT
The primary management protocol was conducted strictly according to the Advanced Trauma Life Support guidelines...
of the American College of Surgeons. Every patient with suspected PDI was treated according to our pancreatic trauma in-hospital management protocol [Figure 1]. Patients were assigned to surgery according to their injury and hemodynamic condition. A “damage control” approach was used for patients who developed coagulopathy, hypothermia and metabolic acidosis during surgery, followed by a staged laparotomy.

A computed tomography (CT) scan was done in all stable patients with suspected abdominal trauma, followed by ERCP if PDI was suspected. ERCP was performed by an attending gastroenterologist in the operating room or intensive care unit, using either sedation or general anesthesia.

Figure 1. Flow chart for managing patients with suspected pancreatic injury

- Abdominal trauma
  - Abdominal CT
    - Stable
      - ERCP
        - CT findings
          - Not done
            - Pancreatic hematoma
            - Pancreatic laceration
            - Pancreatic transection
          - Indication for ERCP
            - CT
            - Pancreatic hematoma
          - Treatment
            - Damage control laparotomy
            - Distal pancreatectomy
            - Explorative laparotomy
            - Observation
          - ERCP findings
            - Main pancreatic duct leak
            - No leak
            - Tertiary duct leak
    - Stable
      - OR
    - OR
      - ERCP
        - Follow-up
          - Main pancreatic duct leak
          - Tertiary pancreatic duct leak
          - Papillotomy stent

Table 1. Patient baseline characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Value</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>24.1 ± 20.4</td>
<td></td>
</tr>
<tr>
<td>Injury Severity Score</td>
<td>22.0 ± 14.0</td>
<td></td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>5</td>
<td>38.5%</td>
</tr>
<tr>
<td>Male</td>
<td>8</td>
<td>61.5%</td>
</tr>
<tr>
<td>Trauma mechanism</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blunt</td>
<td>11</td>
<td>84.6%</td>
</tr>
<tr>
<td>Penetrating</td>
<td>2</td>
<td>15.4%</td>
</tr>
<tr>
<td>CT findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not done</td>
<td>2</td>
<td>15.3%</td>
</tr>
<tr>
<td>Pancreatic hematoma</td>
<td>6</td>
<td>46.2%</td>
</tr>
<tr>
<td>Pancreatic laceration</td>
<td>4</td>
<td>30.8%</td>
</tr>
<tr>
<td>Pancreatic transection</td>
<td>1</td>
<td>7.7%</td>
</tr>
<tr>
<td>Indication for ERCP</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CT</td>
<td>11</td>
<td>84.6%</td>
</tr>
<tr>
<td>Pancreatic hematoma</td>
<td>2</td>
<td>15.4%</td>
</tr>
<tr>
<td>Treatment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Damage control laparotomy</td>
<td>2</td>
<td>15.4%</td>
</tr>
<tr>
<td>Distal pancreatectomy</td>
<td>3</td>
<td>23.0%</td>
</tr>
<tr>
<td>Explorative laparotomy</td>
<td>2</td>
<td>15.4%</td>
</tr>
<tr>
<td>Observation</td>
<td>6</td>
<td>46.2%</td>
</tr>
<tr>
<td>ERCP findings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Main pancreatic duct leak</td>
<td>3</td>
<td>23.1%</td>
</tr>
<tr>
<td>No leak</td>
<td>9</td>
<td>69.2%</td>
</tr>
<tr>
<td>Tertiary duct leak</td>
<td>1</td>
<td>7.7%</td>
</tr>
</tbody>
</table>

ERCP = endoscopic retrograde cholangiopancreatography

CT CRITERIA FOR PANCREATIC INJURY

Specific signs of pancreatic injuries on CT scans were based on the American Association for the Surgery of Trauma system of pancreatic injury scoring and included fractures or lacerations of the pancreas, edema or hematoma of the pancreatic parenchyma, active hemorrhage from the pancreas, and blood collections between the parenchyma and the splenic vein [12].

RESULTS

Thirteen patients with suspected PDI underwent ERCP at our medical center between 1 January 2004 and 31 December 2011. Patient characteristics are presented in Table 1. The mean patient age was 24.1 ± 20.4 years. Eight of them were male (61.5%). Mean ISS was 22.0 ± 14.0. The mechanism of injury was blunt in 11 patients (84.6%) and penetrating in 2 (15.3%).

DIAGNOSTIC COMPARISON OF CT AND ERCP

Patient stratification by CT diagnosis, ERCP findings, and treatment are presented in Table 2. Of the 13 patients, 11 had pancreatic injury located distal to the superior mesenteric vessels. Eight patients with CT-proven pancreatic injuries had no leak from the main pancreatic duct on ERCP. Six of them were managed expectantly and two underwent laparotomy due to a suspected major laceration of the pancreas on CT. One of these two underwent intraoperative ERCP that demonstrated a tertiary pancreatic duct leakage, and a closed peripancreatic vacuum drainage.
was placed; the patient developed a low output pancreatic discharge that resolved spontaneously after 16 days. Laparotomy in the second patient revealed no pancreatic laceration but a large peripancreatic hematoma. ERCP performed on the first day after laparotomy did not reveal PDI. No complications were noted during the postoperative course in both patients. No pancreas-related complications were observed in the remaining patients.

ERCP detected a leak from the main pancreatic duct in three other patients with a CT-proven pancreatic injury. A distal pancreatectomy was performed 3 to 18 hours following injury. No pancreas-related morbidity was observed following surgery, regardless of the time since injury.

Two additional patients had a non-expanding peripancreatic hematoma that was not explored on the initial 'damage control' laparotomy. ERCP was performed (bedside in one and before staged laparotomy in the other) after hemodynamic stability and coagulopathy correction were achieved. No leak from the pancreatic duct was diagnosed and peripancreatic drainage was obtained during the staged laparotomy. These two patients did not have any pancreas-related complications.

None of the patients in the study developed ERCP-related complications or died during the follow-up period. CT was indicative for pancreatic injury in 11 patients, but only 3 (27%) of them had evidence of main pancreatic duct laceration on ERCP. Patients with normal ERCP findings were discharged after an in-hospital follow-up period of 2 ± 5 days.

**DISCUSSION**

Our study describes 13 trauma cases of suspected PDI (by CT or laparotomy) who underwent confirmatory diagnostic ERCP. Our findings suggest that ERCP is a more sensitive diagnostic tool for PDI, compared with CT or laparotomy. For example, only one of six patients who were initially diagnosed with pancreatic hematoma on CT had a confirmed PDI on ERCP (16.7%). ERCP ruled out 50% (2 of 4) false positive CT-diagnosed pancreatic lacerations. Finally, ERCP ruled out PDI in a patient initially diagnosed with a pancreatic transection on CT. No ERCP-related complications were reported in any of the patients in the study.

Traumatic pancreatic injuries are associated with high morbidity and mortality rates, especially when PDI is undiagnosed [4-7,11,13]. Failure to recognize major ductal injury remains a key element in poor outcome due to pancreatic injury [14].

Smego et al. [15] emphasized the importance of intraoperatively assessing the magnitude of the pancreatic injury. In their study, performing distal resection for suspected ductal injury resulted in significantly reduced mortality and morbidity rates. In contrast, a multicenter study of 83 patients who underwent distal pancreatectomy for trauma demonstrated an overall complication rate of 46.2% and a 14% occurrence rate of pancreatic fistulas [6].

Patton et al. [16] addressed the operative management of pancreatic injuries in 134 patients, 124 of whom survived 12 hours. Thirty-seven injuries were proximal (to the right of the superior mesenteric vessels) and 87 were distal. All proximal injuries were managed by drainage alone. Patients with a high suspicion of distal ductal injury underwent distal pancreatectomy and drainage. Thirty-seven percent of the distal pancreatic injuries were treated with closed suction drainage alone. Pancreatic morbidity was 11% in 37 proximal injuries treated with drainage alone. In the subgroup of patients with distal pancreatic injury and indeterminate ductal status, the complication rate was similar whether drainage alone (27%) or distal resection (33%) was used ($P = 0.60$). Overall, the incidence of pancreatic fistulas was 15%, almost all of which closed spontaneously. According to the data of Patton and colleagues [16], most proximal pancreatic injuries can be treated by drainage alone. Our study presents similar results where six of eight patients with a CT-proven pancreatic injury and no leak from the main pancreatic duct on ERCP were managed expectantly and discharged home without complications.

The role of CT in the diagnosis of pancreatic injury was widely addressed in the American Association for the Surgery of Trauma multicenter study [6]. Twenty centers enrolled 206 patients. The sensitivity of the 16-slice CT for pancreatic injury was 60%, compared to only 47% for the 64-slice CT. For pancreatic ductal injury, sensitivities were 54% for the 16-slice CT and 52% for the 64-slice CT. They confirmed that CT of the abdomen greatly improved the diagnosis of isolated abdominal injuries in stable trauma patients but has a limited role in the diagnosis of pancreatic injury.

ERCP is considered a relatively safe procedure compared to laparotomy in the setting of multiple trauma or an isolated retroperitoneal trauma. However, the role of ERCP in trauma is still debated. ERCP is currently performed more frequently for pancreatic injury following abdominal trauma [11].

Several authors have emphasized the usefulness of ERCP in the management of pancreatic injury [11,14,16-18]. In the study by Duchesne and team [17], ERCP was used essentially to stage patients in initial evaluations. Patients with confirmed ductal injuries undergoing laparotomy as well as those with an intact ductal system were managed conservatively. Rogers et al. [11] reported on 26 patients undergoing ERCP 19 days after injury on average. Nine of them underwent definitive endoscopic treatment of their pancreatic injuries, including pancreatic sphincterotomy or ductal stenting, or both.

We found that ERCP can downstage the severity of injury initially diagnosed by CT or laparotomy. Therefore, ERCP may assist in eliminating unnecessary surgery on one hand or anticipating surgery on the other. Moreover, intraoperative ERCP can also lead to a change in the operative strategy [6]. For example, two patients with pancreatic trauma...
underwent ERCP on the operating table that ruled out PDI, thus eliminating unnecessary pancreatic exploration. To the best of our knowledge, no studies have been published on ERCP performed in an acute setting after ‘damage control’ laparotomy. We did not observe any ERCP-related complications in our patients.

Our study has several limitations. The main limitation was the small number of suspected PDI trauma patients, which prevented us from performing a comparative randomized control trial to assess ERCP sensitivity, adverse events and prognosis. Second, validity of our results was obtained only for the management protocol of our medical center, and we cannot assess its relative efficacy compared to other management protocols. Still, patients were treated by a team of surgeons and gastroenterologists, enabling a team approach based on the accumulated experience learned from each case.

CONCLUSIONS
ERCP is a safe and supportive diagnostic tool in the management of patients with pancreatic injuries. It can be performed safely with minimal morbidity, avoiding unnecessary pancreatic exploration. We believe that ERCP should be considered among the preferred procedures for selected patients with suspected pancreatic duct injury. Future studies are warranted to identify patients who would benefit most from diagnostic ERCP. Also, comparative studies of suspected PDI trauma management protocols, with and without the use of diagnostic ERCP, might contribute to our evaluation of the role of ERCP in this setting.

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References

Molecular analysis of gastric cancer identifies subtypes associated with distinct clinical outcomes

Gastric cancer, a leading cause of cancer-related deaths, is a heterogeneous disease. Cristescu et al. attempted to establish clinically relevant molecular subtypes that would encompass this heterogeneity and provide useful clinical information. The authors used gene expression data to describe four molecular subtypes linked to distinct patterns of molecular alterations, disease progression and prognosis. The mesenchymal-like type includes diffuse-subtype tumors with the worst prognosis, the tendency to occur at an earlier age, and the highest recurrence frequency (63%) of the four subtypes. Microsatellite-unstable tumors are hyper-mutated intestinal-subtype tumors occurring in the antrum; these have the best overall prognosis and the lowest frequency of recurrence (22%) of the four subtypes. The tumor protein 53 (TP53)-active and TP53-inactive types include patients with intermediate prognosis and recurrence rates (with respect to the other two subtypes), with the TP53-active group showing better prognosis. They describe key molecular alterations in each of the four subtypes using targeted sequencing and genome-wide copy number microarrays and validated these subtypes in independent cohorts in order to provide a consistent and unified framework for further clinical and preclinical translational research.

Eitan Israeli