Retrospective Study

Comparison of treatment modalities in pancreatic pseudocyst: A population based study

Yanting Wang, Yazan Abu Omar, Rohit Agrawal, Zimu Gong

Abstract

BACKGROUND
Current therapeutic techniques for pancreatic pseudocyst include surgical management with a laparoscopic approach or an open surgical procedure, percutaneous catheter drainage and endoscopic drainage. Yet it remains controversial whether different treatment approaches affect inpatient outcome.

AIM
To investigate inpatient outcome of different treatment approaches in treating pancreatic pseudocyst.

METHODS
Here we conducted a retrospective analysis of pancreatic pseudocyst-associated hospitalizations using the Healthcare Cost and Utilization Project-Nationwide Inpatient Sample. International Classification of Diseases 10 clinical modification and procedure codes are used.

RESULTS
A total of 7060 patients meeting the above criteria were identified. Our study revealed laparoscopic approach associated with the lowest rate of red blood cell transfusion ($P < 0.001$), and it had lower short-term complications including acute renal failure ($P = 0.01$), urinary tract infection ($P = 0.01$), sepsis ($P < 0.001$) and acute respiratory failure ($P = 0.01$). Laparoscopic surgical approach associated with the shortest mean length of stay ($P = 0.009$), and it had the lowest total charge ($P = 0.03$). All three modalities have similar inpatient mortality ($P = 0.28$). The study also revealed that percutaneous drainage associated with more emergent admission ($P < 0.001$), rural hospital performs the most open surgical drainage ($P < 0.001$) and patients who received laparoscopic drainage are more likely to be discharged home ($P < 0.001$).
CONCLUSION
Laparoscopic drainage of pancreatic pseudocysts associated with the least short-term complications and had better outcomes comparing to percutaneous and open surgical drainage from 2016 National Inpatient Sample database.

Key words: Pancreatic pseudocyst; Acute pancreatitis; Drainage; Epidemiology; Inpatient outcome

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Core tip: Pancreatic pseudocyst, the rare clinical entity poses a significant challenge in management given its rarity and lack of evidence suggesting the best managing approach. Most common procedures performed for those patients included open surgical drainage, laparoscopic drainage, radiology guided drainage, and endoscopic drainage. It remains unclear how different treatment modalities affect the outcome of patients with pancreatic pseudocyst. In the present study, we utilized the national inpatient sample to investigate the inpatient outcome of patients who underwent various procedures and provided practical information for clinicians.

INTRODUCTION
Pancreatic pseudocysts are defined as encapsulated, mature fluid collections that usually occur outside the pancreas, although they may be partly or entirely intrapancreatic. Pancreatic pseudocyst is one of the four types of pancreatic fluid collections, which also include acute peripancreatic fluid collection, acute necrotic collection and walled off necrosis and pancreatic pseudocyst according to Atlanta classification[1]. Pancreatic pseudocyst have a well-defined wall with minimal or no necrosis, making it different from the other three types of pancreatic fluid collection[2]. Pseudocysts are more commonly associated with acute pancreatitis or pancreatic trauma and typically form after four weeks since the initial insult[3]. However, they also occur in approximately 20%-40% patients with chronic pancreatitis[4]. Spontaneous resolution of pancreatic pseudocysts is not uncommon, therefore selected patients can be managed conservatively as watchful monitoring[5]. The most common indications for the decompression of the pseudocyst by include abdominal pain, nausea and vomiting, superimposed infection, or gastric outlet or biliary tract obstruction[6]. Treatment options include endoscopy-guided drainage, radiology-guided percutaneous drainage and surgical drainage with either laparoscopic or open surgical approach. However, the best methods for draining a pancreatic pseudocyst remains controversial. It was established historically that open surgery was the standard initial management for pancreatic pseudocysts, yet higher complication rates have been reported in previous studies[7]. With continued progression of medical technology, much less invasive options including laparoscopic, percutaneous and endoscopic drainage were increasingly reported. Previous study by Morton et al[8] in 2004 from NIS data from 1997 through 2001 using International Classification of Diseases (ICD)-9 diagnosis and procedure codes compared percutaneous with surgical drainage of pancreatic pseudocysts. The study showed that surgical approach is associated with shorter length of stay and decreased inpatient mortality, while percutaneous drainage had a higher rate of complications. However, the difference between laparoscopic approach and open surgical approach was not illustrated. With the advantage of ICD-10 codes, we are now able to differentiate the two different surgical modalities. Our study aim to examine population-based outcomes among different treatment options for pancreatic pseudocysts, namely, laparoscopic drainage, open surgical drainage and radiology-guided percutaneous drainage.
MATERIALS AND METHODS

Data source
The National Inpatient Sample (NIS) is an inpatient database maintained by the Agency for Healthcare Research and Quality (AHRQ). It updates annually the information on nearly 8 million inpatient stays from as many as around 1000 hospitals. The database represents a 20% sample of all hospital discharges in the United States, stratified by geographic region, size of the hospital, urban versus rural location, and teaching versus non-teaching status\[9\]. The data from this retrospective cohort study is obtained from 2016 National Inpatient Sample (NIS) and it represents of the entire population of the United States Supplementary material.

Study population
Cases of this study were discerned by ICD, Tenth Revision (ICD-10) diagnosis code for pancreatic pseudocyst, K863, and by procedure code 0F9G40Z, 0F9G4ZZ, 0F9G4ZX for laparoscopic drainage, codes 0F9G00Z, 0F9G0ZX, 0F9G0ZZ for open surgical drainage and codes 0F9G30Z, 0F9G3ZX, 0F9G3ZZ for radiology-guided percutaneous drainage of pancreatic pseudocysts. No specific ICD-10 procedure code was established for endoscopic drainage during the year 2016.

Patients with the age of greater than 18 years and with a status of non-pregnant were selected. Cases that had more than one of the above procedure codes were excluded, given the concern that if surgically drained patients have had prior percutaneous drainage, the adverse events may be overestimated from the previous percutaneous drainage, as illustrated by the previous study by Morton et al\[8\].

Patient characteristics and outcome variables
Patient age, gender, race, admission type, hospital type, primary payer and comorbidities were examined. Charlson Comorbidity Index\[10\] (0-3, with 3 indicating greatest comorbidity) was calculated for each patient based on ICD-10 diagnosis codes, which permit risk stratification by a general severity of illness scale. Specific accompanying ICD-10 diagnosis codes included acute pancreatitis (K85x), chronic pancreatitis (K860, K861) and acute on chronic pancreatitis.

Patient outcomes after either laparoscopic drainage, open surgical drainage or percutaneous drainage were examined. We assessed outcomes including inpatient procedures, complication rates, length of stay (LOS), total charges, and inpatient mortality. Complications analyzed were pulmonary embolism, acute deep vein thrombosis, acute renal failure, urinary tract infection, pneumonia, sepsis, acute hepatic failure, acute respiratory failure, heart failure exacerbation, intraabdominal abscess and cardiac arrest. Inpatient procedures assessed were transfusion of red blood cell, fresh frozen plasma, platelet and mechanical ventilation.

Statistical analysis
Chi-square analysis was used to compare procedure related adverse event rates and inpatient mortality. Mann-Whitney U test was used to compare length of stay among patient who received different procedures. Data analysis was performed using R programming software. P < 0.05 was considered statistically significant.

RESULTS

Demographics and comorbidities
A total of 7060 cases of pancreatic pseudocysts were identified in the NIS in 2016, including 702 patients who underwent drainage procedures. Of these, 248 (35.33%) patients underwent laparoscopic drainage, 107 (15.24%) with open surgical drainage and 347 (49.43%) patients with percutaneous drainage.

There is no significant difference of age distribution, gender or race among patients who underwent different drainage procedures. No difference was noted about the chronic pancreatitis type (acute vs chronic vs acute on chronic) among the three drainage methods (Table 1). Neither Charlson Comorbidity Index nor specific comorbidities (Table 2) was of statistically significant difference among patients receiving different drainages.

Compared to patients with elective admission, those admitted through the emergency department are more likely to receive percutaneous drainage (53.4% vs 25.0%, risk ratio 2.04, 95%CI: 1.45-2.85). All types of hospital perform more percutaneous drainage (urban teaching 47.6%, urban non-teaching 60% and rural hospital 50%), yet rural hospitals perform more open surgical drainage (38.9%) (Table 1).
### Table 1 Baseline characteristics of the study cohort, n (%)

|                | Percutaneous | Laparoscopic | Open Surgical | P value |
|----------------|--------------|--------------|---------------|---------|
| **n**          | 347          | 248          | 107           |         |
| **Age**        |              |              |               |         |
| 18-35          | 56 (16.1)    | 33 (13.3)    | 13 (12.1)     | 0.64    |
| 36-60          | 175 (50.4)   | 137 (55.2)   | 55 (51.4)     |         |
| 60 +           | 116 (33.4)   | 78 (31.5)    | 39 (36.4)     |         |
| **Sex**        |              |              |               | 0.15    |
| Male           | 220 (63.4)   | 158 (63.7)   | 66 (61.7)     |         |
| Female         | 126 (36.3)   | 90 (36.3)    | 41 (38.3)     |         |
| **Race**       |              |              |               | 0.53    |
| White          | 224 (64.6)   | 169 (68.1)   | 70 (65.4)     |         |
| Black          | 50 (14.4)    | 28 (11.3)    | 15 (14.0)     |         |
| Hispanic       | 39 (11.2)    | 20 (8.1)     | 14 (13.1)     |         |
| Asian-Pacific Islander | 9 (2.6) | 3 (1.2) | 2 (1.9) | |
| Other          | 14 (4.0)     | 13 (5.2)     | 2 (1.9)       |         |
| **Admission type** |         |              |               | < 0.001 |
| Emergency      | 318 (53.4)   | 212 (35.6)   | 65 (10.9)     |         |
| Non-emergency  | 26 (25.0)    | 36 (34.6)    | 42 (40.4)     |         |
| **Hospital type** |         |              |               | < 0.001 |
| Urban teaching | 280 (47.6)   | 227 (38.6)   | 81 (13.8)     |         |
| Urban non-teaching | 58 (60.4) | 19 (19.8) | 19 (19.8) | |
| Rural          | 9 (50)       | 2 (11.1)     | 7 (38.9)      |         |
| **Primary payer** |         |              |               | 0.42    |
| Medicare       | 111 (32.0)   | 62 (25.0)    | 35 (32.7)     |         |
| Medicaid       | 71 (20.5)    | 57 (23.0)    | 24 (22.4)     |         |
| Private        | 121 (34.9)   | 103 (41.5)   | 36 (33.6)     |         |
| Other          | 44 (12.7)    | 26 (10.5)    | 12 (11.2)     |         |
| **Pancreatitis type** |     |              |               | 0.06    |
| Acute          | 164 (47.3)   | 89 (35.9)    | 35 (32.7)     |         |
| Acute on chronic | 84 (24.2) | 71 (28.6) | 25 (23.4) | |
| Chronic        | 38 (11.0)    | 36 (14.5)    | 17 (15.9)     |         |
| **Charlson Comorbidity index** | | | | 0.77 |
| 0              | 126 (36.3)   | 103 (41.5)   | 45 (42.1)     |         |
| 1-2            | 189 (54.5)   | 123 (49.6)   | 56 (52.3)     |         |
| 3-4            | 30 (8.6)     | 21 (8.5)     | 6 (5.6)       |         |
| ≥ 5            | 2 (0.6)      | 1 (0.4)      | 0 (0.0)       |         |

### Treatments and outcomes

Laparoscopic approach associated with the lowest rate of red blood cells transfusion (P < 0.001), whereas percutaneous drainage had higher risk for acute renal failure (P = 0.01), urinary tract infection (P = 0.01), sepsis (P < 0.001) and acute respiratory failure (P = 0.01) (Table 3). Laparoscopic surgical approach associated with the shortest mean length of stay (7 d vs 11 d with open surgical approach vs 9 d of percutaneous drainage, P = 0.009). In patients discharged alive, those received laparoscopic drainage and surgical drainage are more likely to be discharged home (70.6% and 64.8%), compared to those received percutaneous drainage (49.4%, P < 0.001). Laparoscopic drainage associated with the lowest total charge (121008 vs 165378 with open surgical vs 184240 with percutaneous drainage, P = 0.03). All three modalities have similar inpatient mortality (P = 0.28) (Table 4). Multivariate analysis was performed which also demonstrated that laparoscopic drainage associated with shorter length of hospital stay (P = 0.001) and lower total charge (P = 0.017) comparing to non-laparoscopic drainage (Table 5).
Table 2  Specific comorbidities of the study cohort, n (%)

|                                | Percutaneous | Laparoscopic | Surgical | P value |
|--------------------------------|--------------|--------------|----------|---------|
| Acute myocardial infarction    | 15 (4.3)     | 8 (3.2)      | 5 (4.7)  | 0.74    |
| Congestive heart failure       | 31 (8.9)     | 19 (7.7)     | 4 (3.7)  | 0.21    |
| Peripheral vascular disease    | 15 (4.3)     | 7 (2.8)      | 3 (2.8)  | 0.56    |
| Cerebrovascular disease        | 6 (1.7)      | 3 (1.2)      | 1 (0.9)  | 0.78    |
| Dementia                       | 2 (0.6)      | 3 (1.2)      | 0 (0.0)  | 0.42    |
| Chronic obstructive pulmonary disease | 58 (16.7) | 43 (17.3)   | 16 (15.0) | 0.86   |
| Rheumatoid disease             | 11 (3.2)     | 3 (1.2)      | 0 (0.0)  | 0.07    |
| Peptic ulcer disease           | 10 (2.9)     | 13 (5.2)     | 3 (2.8)  | 0.28    |
| Mild liver disease             | 52 (15.0)    | 36 (14.5)    | 9 (8.4)  | 0.21    |
| Diabetes without complications | 105 (30.3)   | 61 (24.6)    | 32 (29.9) | 0.29   |
| Diabetes with complications    | 12 (3.5)     | 11 (4.4)     | 5 (4.7)  | 0.77    |
| Hemiplegia or paraplegia       | 3 (0.9)      | 0 (0.0)      | 0 (0.0)  | 0.21    |
| Renal disease                  | 33 (9.5)     | 24 (9.7)     | 4 (3.7)  | 0.14    |
| Cancer (any malignancy)        | 15 (4.3)     | 6 (2.4)      | 4 (3.7)  | 0.46    |
| Moderate or severe liver disease | 10 (2.9) | 17 (6.9)    | 7 (6.5)  | 0.06    |
| Metastatic solid tumour        | 6 (1.7)      | 2 (0.8)      | 0 (0.0)  | 0.28    |
| AIDS/HIV                       | 2 (0.6)      | 1 (0.4)      | 0 (0.0)  | 0.72    |

DISCUSSION

This study compared different approaches for pancreatic pseudocyst drainage using a nationwide, population-based database. The NIS is a large, carefully designed database which provided an opportunity to investigate the in-hospital outcome of this rare yet not fully understood condition. With the advantage of ICD-10, we are the first study that is able to precisely define radiology guided percutaneous drainage and differentiate laparoscopic and open surgical approach. Despite similar clinical baseline, different treatment modalities are clearly associated with different complication profiles as well as clinical outcome. Our study provided practical information for clinicians when choosing a certain treatment modality for patients.

The study found that laparoscopic drainage of pancreatic pseudocysts associated with the least short-term complications comparing to percutaneous and open surgical drainage, including acute renal failure, urinary tract infection, sepsis and acute respiratory failure. While it was reported that surgical approach is associated with higher mortality and longer length of hospital stay, it remains unclear if the less invasive and more precise laparoscopic approach will provide clinical benefit compared to open approach. In this study, the mean length of stay of patients who underwent laparoscopic drainage was 4 d less than open surgical approach and 2 d less than percutaneous drainage. With the shorter length of stay, lower hospitalization cost, and least post-operative complications, we believe laparoscopic drainage is the most cost-effective modality among the three.

Percutaneous drainage is associated with the highest rate of developing acute respiratory failure and sepsis. It is possible that patients in this group had inadequate pseudocyst drainage leading to superimposed infection, causing prolonged sepsis. Likewise, percutaneous drainage is usually performed under sedation without endotracheal intubation and this predisposes patients to aspiration and pulmonary complications including acute respiratory failure. Moreover, comparing to laparoscopic drainage, patients receiving open surgical drainage are more prone to have acute blood loss during the surgery thus have a higher rate of red blood cell transfusion.

The study also demonstrates that patients with emergent admission received more percutaneous drainage followed by laparoscopic drainage. Controversies still exists regarding the best modality in emergent settings. Further studies need to be conducted to illustrate it. We also found that rural hospitals adhere to more traditional modality and performed more open surgical drainage. The drainage approach is not influenced by the type of pancreatitis, whether it is acute, chronic or acute on chronic. Also, Charlson Comorbidity Index and specific comorbidities are both similar among patients receiving different drainages, indicating that the
Table 3  Procedure related complications, n (%)

| Complications               | Percutaneous | Laparoscopic | Open surgical | P value |
|-----------------------------|--------------|--------------|---------------|---------|
|                             | n = 347     | n = 248      | n = 107       |         |
| Transfusion of RBC          | 39 (11.2)   | 7 (2.8)      | 20 (18.7)     | < 0.001* |
| Transfusion of FFP          | 4 (1.2)     | 4 (1.6)      | 4 (3.7)       | 0.19    |
| Transfusion of Platelet     | 2 (0.6)     | 0 (0.0)      | 0 (0.0)       | 0.36    |
| Mechanical ventilation     | 37 (10.7)   | 18 (7.3)     | 12 (11.2)     | 0.31    |
| Pulmonary embolism          | 11 (3.2)    | 5 (2.0)      | 2 (1.9)       | 0.60    |
| Acute deep vein thrombosis  | 3 (0.9)     | 3 (1.2)      | 0 (0.0)       | 0.52    |
| Acute renal failure         | 84 (24.2)   | 49 (19.8)    | 12 (11.2)     | 0.01*   |
| Urinary tract infection     | 34 (9.8)    | 12 (4.8)     | 2 (1.9)       | 0.01*   |
| Pneumonia                   | 21 (6.1)    | 8 (3.2)      | 6 (5.6)       | 0.28    |
| Sepsis                      | 109 (31.4)  | 34 (13.7)    | 23 (21.5)     | < 0.001* |
| Acute hepatic failure       | 5 (1.4)     | 6 (2.4)      | 1 (0.9)       | 0.53    |
| Acute respiratory failure   | 60 (17.3)   | 24 (9.7)     | 9 (8.4)       | 0.01*   |
| Exacerbation of heart failure | 19 (5.5)   | 13 (5.2)     | 2 (1.9)       | 0.30    |
| Cardiac arrest              | 5 (1.4)     | 3 (1.2)      | 0 (0.0)       | 0.47    |
| Intraabdominal abscess      | 34 (9.8)    | 14 (5.6)     | 8 (7.5)       | 0.18    |

*P < 0.05. RBC: Red blood cell; FFP: Fresh frozen plasma.

difference in post-procedure complications is unlikely to be related to patients’ underlying comorbidities.

Our study is limited by its retrospective nature and the limitation of ICD-10 in which the procedure code for endoscopic drainage is not established until 2017. Also, long term outcome is not available in the NIS database. Further studies especially randomized clinical trials should be conducted to determine the best treatment modality.
Table 4  Inpatient outcome of the study cohort, n (%)

|                      | Percutaneous | Laparoscopic | Surgical | P value |
|----------------------|--------------|--------------|----------|---------|
|                      | n = 347      | n = 248      | n = 107  |         |
| Length of stay, median | 9            | 7            | 11       | 0.009*** |
| Total charge, mean    | 184240       | 121008       | 165378   | 0.03*** |
| Disposition, home     | 166 (49.4)   | 173 (70.6)   | 68 (64.8)| < 0.001*** |
| Inpatient mortality   | 11 (3.2)     | 3 (1.2)      | 2 (1.9)  | 0.28    |

*P < 0.05.

Table 5  Multivariable regression of length of stay and total charge

|                      | Standardized coefficient for length of stay | P value | Standardized coefficient for total charge | P value |
|----------------------|---------------------------------------------|---------|-------------------------------------------|---------|
| Type of pancreatitis |                                             |         |                                           |         |
| Acute pancreatitis   | Reference                                   | Reference | Reference | Reference |         |
| Chronic pancreatitis | -0.197                                      | < 0.001 | -0.172                                   | < 0.001 |
| Acute on chronic pancreatitis | -0.130                          | < 0.001 | -0.148                                   | 0.001   |
| Hospital type        |                                             |         |                                           |         |
| Urban teaching       | Reference                                   | Reference | Reference | Reference |         |
| Urban non-teaching   | -0.054                                      | 0.19    | 0.09                                      | 0.82    |
| Rural                | -0.044                                      | 0.291   | -0.046                                   | 0.277   |
| Drainage type        |                                             |         |                                           |         |
| Laparoscopic         | Reference                                   | Reference | Reference | Reference |         |
| Non-laparoscopic     | 0.135                                       | 0.001   | 0.102                                     | 0.017   |

ARTICLE HIGHLIGHTS

Research background
Current therapeutic techniques for pancreatic pseudocyst include surgical management with a laparoscopic approach or an open surgical procedure, percutaneous catheter drainage and endoscopic drainage.

Research motivation
The best therapeutic technique for pancreatic pseudocyst remains controversial. We are motivated to investigate whether different treatment approaches affect inpatient outcome.

Research objectives
The objectives of this study are to investigate inpatient outcome of different treatment approaches in treating pancreatic pseudocyst.

Research methods
Here we conducted a retrospective analysis of pancreatic pseudocyst-associated hospitalizations using the Healthcare Cost and Utilization Project-Nationwide Inpatient Sample. International Classification of Diseases (ICD)-10 clinical modification and procedure codes are used.

Research results
A total of 7060 patients meeting the above criteria were identified. Our study revealed laparoscopic approach associated with the lowest rate of RBC transfusion (P < 0.001), and it had lower short-term complications including acute renal failure (P = 0.01), urinary tract infection (P = 0.01), sepsis (P < 0.001) and acute respiratory failure (P = 0.01). Laparoscopic surgical approach associated with the shortest mean length of stay (P = 0.009), and it had the lowest total charge (P = 0.03). All three modalities have similar inpatient mortality (P = 0.28). The study also revealed that percutaneous drainage associated with more emergent admission (P < 0.001), rural hospital performs the most open surgical drainage (P < 0.001) and patients who received laparoscopic drainage are more likely to be discharged home (P < 0.001).

Research conclusions
The study found that laparoscopic drainage of pancreatic pseudocysts associated with the least short-term complications and had better outcomes comparing to percutaneous and open surgical drainage from 2016 National Inpatient Sample (NIS) database. Laparoscopic surgical approach
associated with the shortest mean length of stay. With the shorter length of stay, lower hospitalization cost, and least post-operative complications, we believe laparoscopic drainage is the most cost-effective modality among the three.

**Research perspectives**

Our study is limited by its retrospective nature and the limitation of ICD-10 in which the procedure code for endoscopic drainage is not established until 2017. Also, long term outcome is not available in the NIS database. Further studies especially randomized clinical trials should be conducted to determine the best treatment modality.

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