A meta-analysis and systematic review of percutaneous catheter drainage in treating infected pancreatitis necrosis

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Abstract
Background: In the current meta-analysis, we focus on the exploration of percutaneous catheter drainage (PCD) in terms of its overall safety as well as efficacy in the treatment of infected pancreatitis necrosis based on qualified studies.

Methods: The following electronic databases were searched to identify eligible studies through the use of index words updated to May 2018: PubMed, Cochrane, and Embase. Relative risk (RR) or mean difference (MD) along with 95% confidence interval (95% CI) were utilized for the main outcomes.

Results: A total of 622 patients in the PCD group and 650 patients in the control group from 13 studies were included in the present meta-analysis. The aggregated results indicated that the incidence of bleeding was decreased significantly (RR: 0.42, 95% CI: 0.25–0.70) in the PCD group as compared with the control group. In addition, PCD decreased the mortality (RR: 0.76, 95% CI: 0.41–1.42), hospital duration (SMD: −0.22, 95% CI: −0.77 to −0.33), duration in intensive care unit (ICU) (SMD: −0.13, 95% CI: −0.30 to −0.04), pancreatic fistula (RR: 0.73, 95% CI: 0.46–1.17), and organ failure (RR: 0.91, 95% CI: 0.45–1.82) in comparison with the control group, but without statistical significance.

Conclusion: Our findings provide evidence for the treatment effect of PCD in the decrease of bleeding, mortality, duration in hospital and ICU, pancreatic fistula, organ failure as compared with the surgical treatment. In conclusion, further studies based on high-quality RCTs with larger sample size and long-term follow-ups are warranted for the confirmation of PCD efficacy in treating infected pancreatitis necrosis.

Abbreviations: CI = confidence interval, MD = mean difference, OR = odds ratio, PCD = percutaneous catheter drainage, RR = relative risk, VARD = video-assisted restroperitoneal debridement.

Keywords: inguinal hernias, laparoscopic, lichtenstein, meta-analysis

1. Introduction

Acute pancreatitis is commonly diagnosed gastrointestinal disorder disease, which contributes to about 2,700,000 inpatients annually and costs more than 2.5 billion dollars for outpatients in the United States.\textsuperscript{11} Necrotizing pancreatitis has been reported to account for 10% to 15% patients harboring acute pancreatitis, with or without infection.\textsuperscript{12} It is acknowledged to be manageable for sterile pancreatic necrosis, while infected pancreatitis necrosis is associated with varying mortality rate of 20% to 30% and leading to 40% if accompanied with organ failure.\textsuperscript{13,41} The traditional treatment for infected pancreatitis necrosis is open necrosectomy that contribute to the removal of necrotic tissue as well as the drainage of infected compartments. In addition, open necrosectomy may lead to various complications with as high as 11% to 39% in the mortality rate.\textsuperscript{12–37} In the past decades, minimally invasive technique has been analyzed among several published studies. The minimally invasive techniques currently include the following approaches: endoscopic necrosectomy, video-assisted restroperitoneal debridement (VARD), minimally invasive necrosectomy, and percutaneous catheter drainage (PCD).\textsuperscript{8–10} PCD has been regarded as the least invasive procedure in treating infected pancreatitis necrosis, with reduced infected fluid under pressure and the infection level, stable symptoms, and less complications.\textsuperscript{11} Hence, we conducted the current meta-analysis based on qualified studies to explore the overall effectiveness of PCD in terms of treating infected pancreatitis necrosis.

2. Methods

2.1. Search strategy and study collection

A wide electronic search of the following databases, such as the PubMed, Embase, and Cochrane, was performed to identify eligible studies concerning PCD vs surgical treatment for infected pancreatitis necrosis updated to May 2018. We also searched other associated publications as well as reference lists. Studies
were screened separately by 2 investigators; any difference was resolved through the aid of 3rd party to reach a consensus.

### 2.2. Study selection and criteria

Studies were required to be included based on the following inclusion criteria: clinical study that analyzed the efficacy of PCD in the treatment of infected pancreatitis necrosis; the included patients were diagnosed with infected pancreatitis necrosis; the 2 groups were treated with PCD and surgical treatment respectively; the outcomes included one of the following parameters: mortality, duration in hospital and ICU, bleeding, pancreatic fistula, organ failure.

Studies should be excluded if the following exclusion criteria were met: repeat publications, or shared content and results; economic analysis, expert comment, theoretical research, meta-analysis, systematic review, case report, conference report; and irrelevant outcomes.

Two authors screened and checked separately to identify eligible studies according to predefined criteria; any disagreements were settled through the discussion with a 3rd author.

### 2.3. Statistical extraction and evaluation

The analyses data from eligible studies were collected by 2 reviewers, including basic information and main outcomes. Basic information included the following parameters: the name of author, the year of publication, the study design, the treatment method, the sample size, the gender, the age. Furthermore, clinical outcomes included duration in hospital and ICU, mortality, bleeding, pancreatic fistula, as well as organ failure. The above-mentioned evaluation process was separately conducted by 2 investigators; any arising differences were settled by general consensus.

### 2.4. Statistics analysis

The meta-analysis was conducted through the use of the STATA 10.0 (College station, TX). Heterogeneity of the trial results was assessed with the I² tests value and P-value to select ideal analysis model (random-effect model or fixed-effect model): I² > 50% and Chi-squared test P < .05 reflected a high heterogeneity and random-effects model was utilized; I² ≤ 50% and Chi-squared test P > .05 reflected an acceptable heterogeneity data with the assessment of fixed-effects model. For the continuous variables, they were analyzed by mean difference (MD) and expressed as the mean ± standard deviation. We calculated and presented the categorical data as percentages and analyzed the data through the use of odds ratio (OR) or relative risk (RR). OR and its 95% CI were used to analyze all the risk factors. Mortality, bleeding, pancreatic fistula, and organ failure were analyzed by RR and 95% CI. Duration in hospital and ICU were also under the evaluation with the use of MD and 95% CI.

### 3. Results

#### 3.1. Study characteristics

Through the search of indexes, a total of 1219 publications were included. After title and abstract screening, 1135 publications were then excluded, thus 84 publications were left for further assessment. During full-text screening, 71 publications were excluded due to: case report (5), diagnosis study (8), has nonclinical outcomes (30), theoretical research, or review (28). Therefore, a final total of 13 studies[8,12–23] that included 15 compared groups were presented in the meta-analysis, of which 622 patients were evaluated in the PCD group and 650 in the control group (Fig. 1).

Table 1 revealed the major characteristics of studies. The study design included retrospective or prospective cohort study, clinical study, and randomized controlled trial. The therapy of PCD group contained PCD, minimally invasive PCD, and image-guide PCD. The therapy of control group contained surgical necrosectomy, video-assisted retroperitoneal debridement, conservative treatment, and open laparotomy. The current study contained patients with mean age of above 40, and other information such as sample, gender, and APACHE II score.

#### 3.2. Mortality

Twelve trials with a total of 605 and 633 patients that were evaluated respectively in PCD and control group provided the data about the mortality. On basis of the I² tests value (I² = 58.0%) and Chi-squared test P-value (P = .003), random effect model was used to analyze the mortality. The pooled results revealed that there was no remarkable difference in mortality between the 2 study groups (RR: 0.76, 95% CI: 0.41–1.42, Fig. 2).

#### 3.3. Length of hospital stay

Six trials with a total of 372 and 266 patients that were evaluated respectively in PCD group and control group provided the data about the length of hospital stay. I² tests value (I² = 88.2%) and Chi-squared test P-value (P = .000) were calculated with random effect model to analyze the length of hospital stay. The aggregated results revealed no significant difference of the length of hospital stay when comparing the 2 study groups (SMD: −0.22, 95% CI: −0.77 to −0.33, Fig. 3).

#### 3.4. Length of ICU stay

Six trials with a total of 372 and 266 patients that were evaluated respectively in PCD group and control group provided the data about the length of ICU stay. According to the I² tests value (I² = 0.8%) and Chi-squared test P-value (P = .418), fixed effect model was applied to analyze the length of ICU stay. The aggregated results revealed no remarkable difference when comparing the 2 study groups in the length of ICU stay (SMD: −0.13, 95% CI: −0.30 to −0.04, Fig. 4).

#### 3.5. Pancreatic fistula

Four trials with a total of 286 and 148 patients that were evaluated respectively in PCD group and control group provided the data about the pancreatic fistula. I² tests value (I² = 0.0%) and Chi-squared test P-value (P = .875) were calculated with fixed effect model to analyze the pancreatic fistula. According to pooled results, no significant difference was observed in the pancreatic fistula when comparing the 2 study groups (RR: 0.73, 95% CI: 0.46–1.17, Fig. 5).

#### 3.6. Bleeding

Seven trials with a total of 395 and 441 patients that were evaluated respectively in PCD group and control group provided the data
about the bleeding. $I^2$ tests value ($I^2 = 16.4\%$) and Chi-squared test $P$-value ($P = .301$) with the use of fixed effect model to analyze the bleeding. Based on the pooled results, the bleeding incidence was significantly decreased in the PCD group in comparison of the control group (RR: 0.42, 95% CI: 0.25–0.70, Fig. 6).

3.7. Organ failure

Eight trials with a total of 251 and 477 patients that were evaluated respectively in PCD group and control group provided the data about the organ failure. $I^2$ tests value ($I^2 = 87.4\%$) and Chi-squared test $P$-value ($P = .000$) with the use of random effect model to analyze the organ failure. Based on the pooled results, there was no significant difference between the 2 groups in terms of the organ failure (RR: 0.91, 95% CI: 0.45–1.82, Fig. 7).

3.8. Quality assessment and potential bias

On the basis of the predefined criteria, a total of 13 publications were analyzed in the current systematic review. We applied the
Table 1
The major characteristics of the qualified studies in more detail.

| Study     | Publication year | Study design                | Study period    | Sample size | MI-TLIF | O-TLIF | Pathology                                                                 |
|-----------|------------------|-----------------------------|-----------------|-------------|---------|--------|---------------------------------------------------------------------------|
| Tian      | 2014             | Prospective observational study | 2010–2011      | 30          | 31      | Symptomatic degenerative disease of the lumbosacral spine (L2-S1)         |
| Sulaiman  | 2014             | Prospective observational study | 2009–2012      | 57          | 11      | Degenerative spondylolisthesis                                            |
| Singh     | 2014             | Retrospective observational study | 2008–2010      | 33          | 33      | Lumbar degenerative disc disease (DDD), degenerative spondylolisthesis, or spinal stenosis |
| Parker    | 2014             | Prospective observational study | Not report      | 50          | 50      | Lumbar spondylolisthesis                                                 |
| Gu        | 2014             | Prospective observational study | 2010–2011      | 44          | 38      | Two-level lumbar degenerative disease                                    |
| Terman    | 2014             | Retrospective observational study | 2007–2011      | 53          | 21      | Lumbar DDD, herniated disc, listhesis, stenosis                          |
| Zhang     | 2014             | Retrospective observational study | 2014–2017      | 48          | 50      | Single-level lumbar instability or degenerative disk disease             |
| Kulkarmi  | 2016             | Prospective observational study | 2011–2013      | 36          | 25      | Back and leg pain secondary to degenerative disease                      |
| Serban    | 2017             | Prospective randomized study  | 2011–2015      | 40          | 40      | Symptomatic with low back pain plus radicular pain and/or neurogenic claudication |
| Wu        | 2018             | Retrospective observational study | 2010–2015      | 79          | 88      | grade I or II single segmental spondylolisthesis                         |

Figure 2. Forest plot showing the mortality of percutaneous catheter drainage vs surgical treatment.

Figure 3. Forest plot showing the length of hospital stay of percutaneous catheter drainage versus surgical treatment.

Figure 4. Forest plot showing the length of intensive care unit stay of percutaneous catheter drainage versus surgical treatment.
Mazumdar and Begg rank test, Egger test, as well as funnel plot to further check the potential bias and quality of studies. The funnel plot for log RR in mortality was remarkably symmetrical, indicating there was no significant publication bias (Fig. 8). Additionally, evidential symmetry was observed through the assessment of Mazumdar and Begg rank test ($Z = 1.64, P = .101$). Additionally, no remarkable publication bias was indicated from the results of the Egger test ($P = .143$).

### 4. Discussion

Several meta-analyses as well as systematic reviews have been published, regarding the effect of PCD in terms of treating infected pancreatitis necrosis. Reports supported by Ke et al. found that about 55.3% patients suffered from organ failure before PCD. About as high as 56.2% patients gained beneficial treatment effects with PCD alone and 38.5% should seek extra surgical intervention after PCD. Fistula commonly occurred as one of the complications affecting 25.1% patients with a mortality rate of 18% in general (104 out of 577). It is considered as an efficient as well as alternative method in treating patients harboring infected pancreatitis necrosis with intervention of PCD alone. Aggregated reports have revealed that the negative parameters include multiple organ failures that occur before PCD treatment. No strong evidence has been showed the superior effect of large catheters in draining necrotic tissue. Nevertheless, difficulty exists in terms of determining single prognostic factor for the extent of multi-morbid individuals. Cirocchi et al. found that, when comparing open necrosectomy (ON) surgery with minimally invasive necrosectomy (MIN) for the therapy of infected necrosis of acute pancreatitis, superior treatment effect of MIN was observed with regards to the following outcomes: new-onset diabetes (OR, 0.32; 95% CI: 0.12–0.88), incisional hernias (OR, 0.23; 95% CI: 0.06–0.90), incidence of multiple organ failure (OR, 0.16; 95% CI: 0.06–0.39), as well as for the use of pancreatic enzymes (OR, 0.005; 95% CI: 0.04–0.57). In addition, there were no remarkable difference concerning the intraabdominal bleeding (OR, 0.79; 95% CI: 0.41–1.50), multiple systemic complications (OR, 0.34; 95% CI: 0.01–8.60), pancreatic fistula (OR, 0.66; 95% CI: 0.30–1.46), mortality rate (OR, 0.43; 95% CI: 0.18–1.05), surgical reintervention for further necrosectomy (OR, 0.16; 95% CI: 0.00–3.07), surgical reintervention for postoperative complications (OR, 0.50; 95% CI: 0.23–1.08), and
enterocutaneous perforation or fistula of visceral organs (OR, 0.52; 95% CI: 0.27–1.00).

To our knowledge, however, several limitations exited that should not be ignored in the present meta-analysis, including: retrospective researches in most studies; different selection criteria for patients in various trials and studies; various surgical technique in different trials; we used pooled data for analyses with unavailable individual data, which limited for more comprehensive analyses.

Given the overall results of our analysis, the present study offers moderate evidence to prove the beneficial effect of PCD in decreasing the incidence of bleeding, mortality, duration in hospital and ICU, pancreatic fistula, and organ failure. While no significant differences were observed between PCD and surgical treatment. Therefore, additional high-quality RCTs with larger sample size and longer follow-ups are in great need for the confirmation of PCD efficacy in treating infected pancreatic necrosis.

Author contributions

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