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Endoscopic Versus Laparoscopic Treatment for Pancreatic Pseudocysts

A Systematic Review and Meta-analysis

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Objective: The aim of the study was to evaluate the efficacy and safety of endoscopic treatment for pancreatic pseudocysts (PPCs) compared with laparoscopic treatment.

Methods: The Embase, Medline, Cochrane Library, Web of Science databases, China National Knowledge Infrastructure Chinese citation database, and WANFANG database were systematically searched to identify all comparative trials investigating endoscopic versus laparoscopic treatment for PPC. The main outcome measures included treatment success rate, adverse events, recurrence rate, operation time, intraoperative blood loss, and hospital stay.

Results: Six studies with 301 participants were included. The results suggested that there was no difference in rates of treatment success (odds ratio [OR], 0.90; 95% confidence interval [CI], 0.40–2.01; $P = 0.79$), adverse events (OR, 0.80, 95% CI, 0.38–1.70; $P = 0.57$), or recurrence (OR, 0.55, 95% CI, 0.22−1.40; $P = 0.21$) between endoscopic and laparoscopic treatments. However, the endoscopic group exhibited reduced operation time (weighted mean difference [WMD], −67.11; 95% CI, −77.27 to −56.96; $P < 0.001$), intraoperative blood loss (WMD, −65.23; 95% CI, −103.38 to −27.08; $P < 0.001$), and hospital stay (WMD, −2.45; 95% CI, −4.74 to −0.16; $P = 0.04$).

Conclusions: Endoscopic treatment might be suitable for PPC patients.

Key Words: endoscopy, laparoscopy, pancreatic pseudocyst, meta-analysis

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Pancreatic pseudocyst (PPC) is a collection of pancreatic enzyme–rich fluid originating in or around the pancreas that is enclosed by granulation with/without fibrous tissue lacking epithelial lining.[1] It is known that PPC is a common complication of

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acute or chronic pancreatitis and pancreatic trauma that typically forms 4 weeks after the initial injury.[2,3] The main symptoms of PPC are abdominal pain (76%–94%), early satiety, nausea, vomiting (50%), and weight loss (20%–51%).[4,5] Usually, PPC is more common in chronic pancreatitis than in acute pancreatitis. Existing studies show that the prevalence of PPC in acute pancreatitis ranges from 6% to 18.5%, whereas in chronic pancreatitis, the rate is 20% to 40%.[4–6] Moreover, advances in radiological techniques have in part led to an increase in the diagnosis of PPC and a better characterization of the associated complications.

Previous studies have indicated that appropriate treatment should be given to PPC patients with complicated cases, such as bleeding, infection, and obstruction of the gastric or biliary outlet.[7,8] Open surgery has gradually become a remedial treatment method for PPC, but it is always associated with large trauma, bleeding, and long hospital days. At present, minimally invasive drainage is becoming a preferred approach because it is less invasive than open surgery and has a high long-term success rate.[7,9] Three different minimally invasive strategies for PPC are available: endoscopic drainage; laparoscopic drainage; and percutaneous catheter drainage. Percutaneous catheter drainage of PPC is rarely performed because of the high risk of morbidity and mortality; according to some clinical studies, it should be performed only when there is an acute pseudocyst in patients in physiological exhaustion with no operative condition.[3,9,10] Endoscopic drainage can be operated mainly by 2 means: when PPC is communicated to the main pancreatic duct, the stent is placed in the pancreatic duct for better drainage by endoscopic retrograde cholangiopancreatography; when endoscopic ultrasonography (EUS) shows adhesion of the PPC to the stomach or duodenal wall, transmural drainage is performed through the stomach or duodenal wall. Laparoscopy is performed through a single entrance, such as the umbilical, and is an innovative approach that allows for accomplishing the operation with no need for an additional incision. Laparoscopic drainage of PPC is also available in 2 main ways: when the pseudocyst is close to the stomach, pseudocyst-gastric anastomosis is performed; when the pseudocyst is far from stomach, pseudocyst-jejunostomy is suitable.

Currently, there have been meta-analyses comparing surgical treatment for PPC with endoscopic drainage.[11–14] However, no meta-analysis has compared endoscopic drainage and laparoscopic drainage; thus, we conducted this study to summarize and analyze the difference between endoscopic drainage and laparoscopic drainage treatment in PPC patients, including treatment success, adverse events, recurrence, operation time, intraoperative blood loss, and hospital stay.

MATERIALS AND METHODS

This meta-analysis was conducted in accordance with the preferred reporting items for systematic review and meta-analysis protocols guidelines[15] and was registered in International prospective register of systematic reviews International Prospective Register

of Systematic Reviews (http://www.crd.york.ac.uk/prospero/) with the registration number CRD42020164595.

Search Strategy

A systematic search of the Embase, Medline, Cochrane Library, and Web of Science databases was performed by 2 authors (Y.C. and W.H.) separately until March 10, 2020, without language restriction. In particular, the China National Knowledge Infrastructure Chinese citation database and WANFANG database were searched for Chinese studies. The titles and abstracts of all retrieved studies were first examined to select articles with a relevant subject. The full texts of these articles were then judged on the basis of relevance in the next phase. Any disagreement was determined by the third author (A.Y.).

The relevant search terms were as follows: (pancreatic pseudocyst OR pancreatic collections OR pancreatic fluid collections) AND (endoscope OR endoscopy OR endosonographic OR laparoscope OR laparoscopy OR laparoscopic). References of relevant studies were also screened to gather further potential trials.

Inclusion and Exclusion Criteria

Studies comparing endoscopic and laparoscopic treatment for PPC patients were included. The full text of studies should be available. Patients with other diseases combined were excluded, such as pancreatic cystic tumors or pancreatic cancer. Studies including patients with walled-off necrosis (WON) were also rejected. Year of publication, number of participants, and study type were not restricted.

Data Collection

A special data extraction form was predefined, and the collected information was as follows: author, publication year, country, characteristics of patients, study type, information needed for quality assessment, and outcomes. Outcome measures included treatment success rate, adverse events, operation time, intraoperative blood loss, length of hospital stay, and recurrence rate. When the required data were not reported, authors were contacted by e-mail to evaluate whether studies report on the same patient clientele and to gather additional data. In case of multiple publications of 1 study, the main article was included, but all of the articles were read and included for data extraction to gather all available information. Two investigators (Y.C. and W.H.) independently extracted all relevant data, and any disagreement was resolved by the judgment of a third reviewer (A.Y.).

Quality Assessment

The Cochrane Collaboration's tool for assessing risk of bias was used to assess the methodological quality of randomized controlled trials (RCTs).[16] The Newcastle-Ottawa Quality Assessment Scale[17] for cohort studies was used to assess the methodological quality of retrospective or prospective comparable trials.

Statistical Analysis

If appropriate comparisons were available, a meta-analysis was conducted. Otherwise, a descriptive review of the identified evidence was performed. Dichotomous outcomes were evaluated
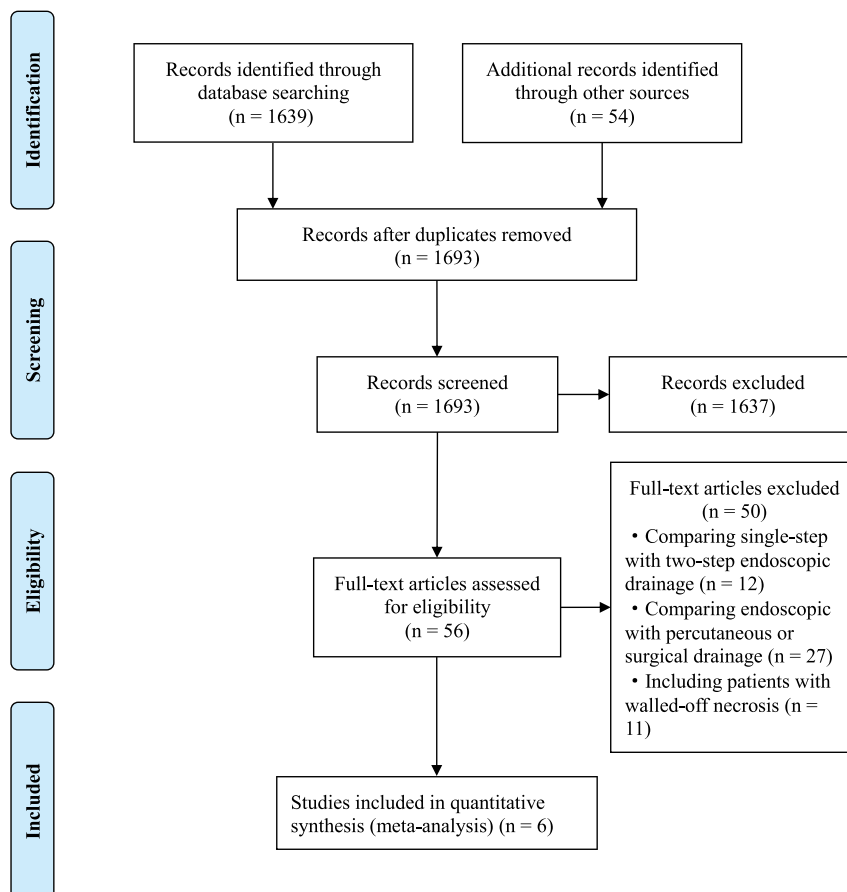

FIGURE 1. Flow diagram of the selection process.

TABLE 1. Basic Information of the Included Studies

No.	Source	Country	Study Type	Characteristics of Endoscopic Drainage	Characteristics of Laparoscopic Drainage	Success	Follow-up
1	Li and Qin[24] (2008)	China	Retrospective comparative trial	Transgastric or trans duodenal drainage (8); 1 or 2 double-pigtail stents (4); needle knife (2)	Cyst-gastrostomy (7); cyst-jejunostomy (2)	Not mentioned	Range, 6–28 mo
2	Melman et al[25] (2009)	United States	Retrospective comparative trial	1 or 2 transgastric stents (45)	Cyst-gastrostomy or cyst-jejunostomy (16)	Symptom or cyst resolution at the last clinical follow-up assessment and could include multiple attempts at or methods of intervention.	Mean, 9.5 (range, 1–40) mo
3	Wang[23] (2016)	China	Retrospective comparative trial	Transgastric drainage (19); transduodenal drainage (7)	Laparoscopic cyst-jejunostomy (14); laparoscopic cyst-gastrostomy (8)	The clinical symptoms completely disappeared after the drainage, with PPC disappearing thoroughly after 3 mo of treatment.	>6 mo
4	Ma[21] (2017)	China	Retrospective comparative trial	Transgastric drainage or transduodenal drainage (2)	Laparoscopic cyst open drainage (10); laparoscopic cystic resection (4); laparoscopic cyst-gastric anastomosis (3); laparoscopic cyst-jejunum anastomosis (2)	After treatment, the clinical symptoms were significantly reduced and reviewed results of CT or B-mode ultrasound suggest that the cyst had thoroughly disappeared without obvious liquid accumulation or the clinical symptoms were reduced, and the reviewed result suggest the diameter of PPC reduced to half of the previous.	>3 d
5	Mai et al[22] (2017)	China	Retrospective comparative trial	Pancreatic tube stent (36); operation with EUS guided (18); operation without EUS guided (9)	Laparoscopic cyst-gastric anastomosis or laparoscopic cyst-jejunum anastomosis (48)	PPC was not confirmed in CT or color Doppler ultrasound in abdomen with the clinical symptoms of PPC were completely disappeared after a month of treatment.	1 d, 1 mo, 6 mo
6	Redwan et al[20] (2017)	Egypt	Prospective comparative trial	1 or 2 transgastric stent or transduodenal stent/ pancreatic tube stent (35)	Laparoscopic pancreatic cyst-gastrostomy (2); laparoscopic pancreatic cyst-jejunostomy (Roux-en-Y, 2)	Clinical or radiographic cyst resolution at the last clinical follow-up assessment.	15 d, 1 mo, 3 mo, 6 mo, and yearly thereafter

CT indicates computed tomography.

TABLE 2. Patient Demographic Data and Present Conditions of the Included Studies

No.	Source	Patient No.	Patient Male/Total, n	Age, Mean (SD), y	Pseudocyst Size, Mean (SD), cm	Cause	Pseudocyst Position	Adverse Events
1	Li and Qin[24] (2008)	21	E: NM/14 L: NM/7	47 (9)	8.7 (4)	NM	NM	E: total 3, 1 bleeding, 1 stent migration, 1 pancreatitis L: total 1, 1 infection
2	Melman et al[25] (2009)	61	E: 26/45 L: 10/16 $P > 0.05$	E: 51.8 (1.9) L: 46.5 (3.6) $P > 0.05$	E: 9.1 (0.4) L: 10.4 (0.5) $P > 0.05$	E: 23 gallstones L: 8 gallstones	NM	E: total 7, 2 bleeding, 3 reintervention, 2 gastric perforation L: total 4, 2 bleeding
3	Wang[23] (2016)	48	E: 19/26 L: 16/22 $P > 0.05$	E: 49.12 (9.53) L: 47.83 (7.26) $P > 0.05$	E: 8.51 (4.32) L: 8.64 (4.20) $P > 0.05$	E: 24 gallstones L: 20 gallstones	E: 8 head, 18 body or tail L: 7 head, 15 body or tail	E: total 3, 2 infection, 1 stent occlusion L: total 2, 2 infection
4	Ma[21] (2017)	21	E: 1/2 L: 8/19	E: 38.5 (17.5) L: 44.6 (17.5) $P > 0.05$	E: 9.5 (7.8) L: 7.5 (4.2)	E: 1 traumatic pancreatitis, 1 other L: 10 acute pancreatitis, 3 chronic pancreatitis, 6 other	E: 1 neck, 1 tail L: 1 head, 1 neck, 8 body, 9 tail	E: total 0 L: total 5, 2 infection, 3 fistula
5	Mai et al[22] (2017)	111	E: NM/63 L: NM/48	$P > 0.05$	$P > 0.05$	NM	E: 24 head, 39 body or tail L: 19 head, 29 body or tail	E: total 5, 2 bleeding, 1 infection, 2 pancreatitis L: total 4, 4 infection
6	Redwan et al[20] (2017)	39	E: 20/35 L: 2/4 $P > 0.05$	E: 49.2 (3.8) L: 51.8 (1.9) $P > 0.05$	E: 10.3 (0.7) L: 10.1 (0.8) $P > 0.05$	E: 20 gallstones, 9 traumatic, 6 unspecified L: 1 gallstone, 3 traumatic	NM	E: total 3 L: total 1

E indicates endoscopy group; L, laparoscopy group; NM, not mentioned; SD, standard deviation.

based on event rates using a pooled odds ratio (OR). For continuous variables, a weighted mean difference (WMD) was calculated. The results are reported with 95% confidence intervals (CIs).

Heterogeneity among studies was tested using Q and I^2 statistics. The heterogeneity was regarded as significant if $P < 0.10$ for Q statistics or $I^2 \geq 25\%$, and meta-analysis was performed using the random-effects model. Otherwise, the fixed-effects model was adopted. Egger linear regression test and Begg rank correlation test were used to assess the possibility of publication bias. The level of $P < 0.05$ was regarded to be significantly different unless otherwise specified. Statistical analysis was performed using STATA (Version 11; Stata Corp, College Station, Tex) and Review Manager 5.3 (Cochrane Collaboration, Copenhagen, Denmark).

RESULTS

Description of Included Studies

A total of 1693 publications were identified, and 1637 of them were excluded after title and abstract screening. After full-text assessment, 50 studies were excluded (12 studies comparing single-step with two-step endoscopic drainage, 27 studies comparing endoscopic with percutaneous or surgical drainage, and 11 studies including patients with WON). Finally, 6 studies were selected, including 5 retrospective comparative trials and 1 prospective comparative trial.[18–23] The flow diagram is shown in Figure 1. The included studies were published between 2008

TABLE 3. Methodological Quality of the Included Studies Evaluated by the Newcastle-Ottawa Scale

No.	Author (Year)	Selection	Comparability	Outcome/Exposure	Total Score
1	Li and Qin[24] (2008)	★★★	★★	★★★	8
2	Melman et al[25] (2009)	★★★	★★	★★★	8
3	Wang[23] (2016)	★★★	★★	★★★	8
4	Ma[21] (2017)	★★★	★★	★★	7
5	Mai et al[22] (2017)	★★★	★★	★★★	8
6	Redwan et al[20] (2017)	★★★★	★★	★★★	9

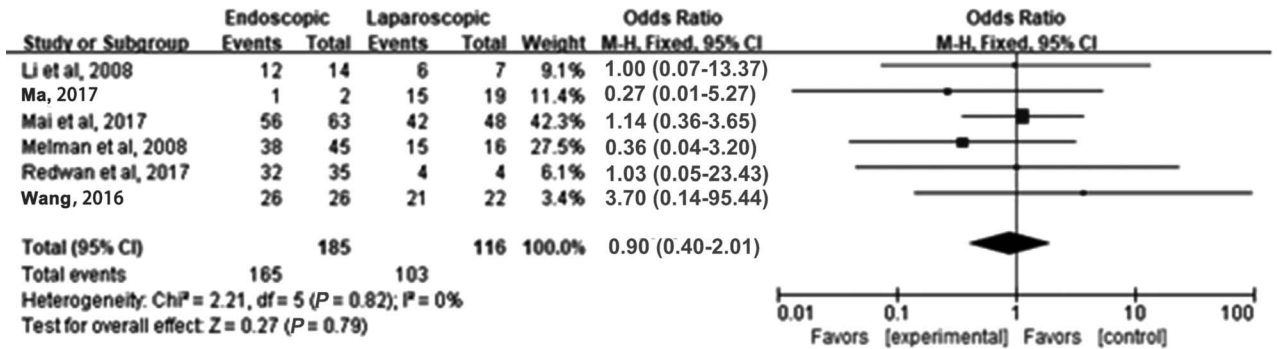Three to 4 stars in a category are good.

FIGURE 2. Forest plot showing meta-analysis of treatment success. M-H, Mantel-Haenszel.

and 2017. Four studies were from China, 1 from the United States, and 1 from Egypt. Detailed information regarding the operation of endoscopic/laparoscopic drainage and the definition of treatment success are presented in Table 1. The patient demographic data and disease conditions of the included studies are shown in Table 2. These 6 trials included 301 patients in total, of which 185 were in the endoscopy group and 116 were in the surgical group.

Quality Assessment of Included Studies

All of the included studies belonged to prospective or retrospective comparative studies; thus, the Newcastle-Ottawa Quality Assessment Scale for Cohort Studies was used. The mean score of the included studies was 8 stars, ranging from 7 to 9 stars, and they were all rated high quality. Five studies were not assigned a score because they were retrospective studies; the follow-up duration of 1 study was not clear, and thus, it was also not assigned a score. The results of the quality assessment are shown in Table 3.

Outcome Measures

All 6 studies reported data on treatment success. Treatment success rates ranged from 50% to 100% in endoscopy groups and from 78.9% to 100% in laparoscopic groups. Overall treatment success rates were 89.2% (165 of 185) and 88.8% (103 of 116), respectively. Heterogeneity was examined with $P = 0.82$ and $I^2 = 0\%$; thus, the fixed-effects model was adopted for combined analysis. Pooled analyses revealed that there was no difference in treatment success rates between the 2 groups (OR, 0.90; 95% CI, 0.40–2.01; $P = 0.79$). The results are shown in

Figure 2. Begg test and Egger test were also conducted, and publication bias was not found ($P = 0.452$ and 0.752, respectively).

All 6 studies reported data on adverse events. The overall adverse event rate was 11.35% (21 of 185) in the endoscopy group and 14.66% (17 of 116) in the laparoscopy group. Bleeding was the most common adverse event in the endoscopy group (5 of 185, 2.70%), whereas in the laparoscopy group, it was infection (9 of 116, 7.76%). Adverse event rates ranged from 0% to 21.4% in the endoscopy group and from 8.3% to 26.3% in the laparoscopy group. Heterogeneity was examined with $P = 0.90$ and $I^2 = 0\%$; thus, the fixed-effects model was adopted for combined analysis. The results suggested that there was no significant difference between the 2 groups (OR, 0.80; 95% CI, 0.38–1.70; $P = 0.57$). The results are shown in Figure 3. Begg test and Egger test were also conducted, and publication bias was not found ($P = 1.000$ and 0.847, respectively).

Three studies reported the data of operation time. Heterogeneity was examined with $P = 0.18$ and $I^2 = 42\%$; thus, the random-effects model was adopted. The results revealed that the operation time of the endoscopy group was significantly less than that of the laparoscopy group (WMD, −67.11; 95% CI, −77.27 to −56.96; $P < 0.001$). The results are shown in Figure 4. Begg test and Egger test were also conducted, and publication bias was not found ($P = 1.000$ and 0.581, respectively).

Three studies reported blood loss data. Heterogeneity was examined with $P < 0.001$ and $I^2 = 98\%$; thus, the random-effects model was adopted. Pooled analyses revealed that the blood loss of the endoscopy group was significantly less than that of the laparoscopy group (WMD, −65.23; 95% CI, −103.38 to −27.08; $P < 0.001$). The results are shown in Figure 5. Begg test
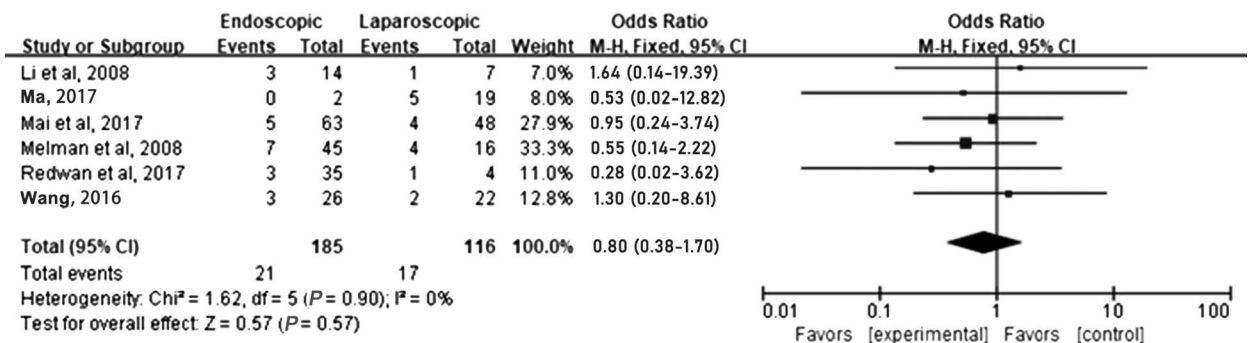

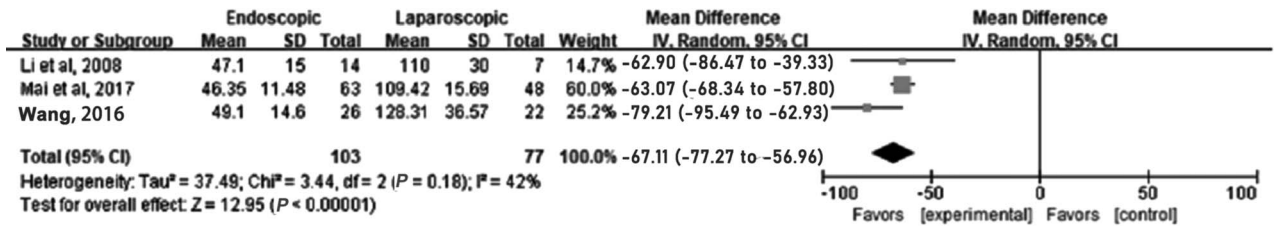**FIGURE 3.** Forest plot showing meta-analysis of adverse events.

FIGURE 4. Forest plot showing meta-analysis of operation time.

and Egger test were also conducted, and publication bias was not found ($P = 1.000$ and 0.629, respectively).

Four studies reported data on the length of hospital stay. Heterogeneity was examined with $P = 0.004$ and $I^2 = 78\%$; thus, the random-effects model was adopted for combined analysis. Comparison between groups demonstrated that endoscopic drainage was associated with a shorter length of hospital stay (WMD, -2.45; 95% CI, -4.74 to -0.16; $P = 0.04$). The results are shown in Figure 6. Begg test and Egger test were also conducted, and publication bias was not found ($P = 0.734$ and 0.540, respectively).

Five studies reported data on recurrence. Heterogeneity was examined with $P = 0.83$ and $I^2 = 0\%$; thus, the fixed-effects model was adopted for combined analysis. Pooled analyses revealed that there was no difference in recurrence rates between the 2 groups (OR, 0.55; 95% CI, 0.22–1.40; $P = 0.21$). The results are shown in Figure 7. Begg test and Egger test were also conducted, and publication bias was not found ($P = 1.000$ and 0.777, respectively).

DISCUSSION

This study is the first meta-analysis comparing endoscopic and laparoscopic treatment for PPC. The results suggested that there was no difference in the rate of treatment success, adverse events, or recurrence between endoscopic and laparoscopic treatment, but the operation time, intraoperative blood loss, and hospital stay of endoscopic treatment were significantly less than those of laparoscopic treatment, indicating that endoscopy had certain advantages in PPC treatment.

Endoscopic drainage for PPC has been a hot topic in recent years, but the indications for endoscopic treatment for PPC have not been unified. For mature PPC with a diameter of more than 6 centimeters that compresses the gastrointestinal wall, it is generally believed that endoscopic drainage is a suitable treatment. Currently, some experts believe that endoscopic treatment of PPC is one of the methods with the least damage to patients. Studies have shown that the success rate of stent implantation by endoscopic retrograde cholangiopancreatography is more than 75%, and the success rate of transgastric or duodenal drainage guided by EUS is more than 90%.[24] However, it has been reported that

the complication rate of endoscopic therapy can be up to 5% to 19%, mainly manifesting as hemorrhage and recurrence.[21] Furthermore, some studies have indicated that endoscopy does not apply to patients with coagulation dysfunction with multiple PPCs.[25]

Laparoscopy is an innovative approach accomplishing the operation with no additional wounds. The incidence of complications and therapeutic effect can be the same as endoscopic treatment.[26] Performing better than traditional open surgery, laparoscopic drainage reduces the surgical mortality and cyst recurrence rate and has less trauma and faster recovery.[13] Moreover, laparoscopic drainage can remove more necrotic tissue in the cyst while exploring the cyst wall structure than endoscopic drainage. However, abdominal contamination, incomplete anastomosis, and gastric perforation in laparoscopic drainage limit the application of laparoscopy to some extent.

Our research showed that there were differences in the prognostic indicators of endoscopic and laparoscopic drainage of PPC. Endoscopic treatment was superior to laparoscopic treatment in terms of reduced operation time, intraoperative blood loss, and hospital stay. The operation time of endoscopic treatment is shorter than that of laparoscopic treatment, which might be due to the fact that no sewing operation is performed. Thus, the hospital stay is shorter, which could be improved with the development of better hemostatic equipment and excellent suturing.[27] Endoscopic ultrasound guidance might be one of the reasons why endoscopic drainage causes less blood loss.[28,29] Operation in the digestive tract also avoids many important blood vessels and nerves located in the abdomen.[30] Moreover, the application of laparoscopic treatment of PPC might not be as mature as endoscopy.[27]

Meta-analyses[11,12,14] and clinical studies[31,32] have focused on comparing traditional surgery and endoscopy. The conclusions of these studies suggested that there is no significant difference in the recurrence rate or incidence of adverse events,[14,18,32] but endoscopic treatment was completed with a shorter length of hospital stay in all 5 studies. One study suggested that endoscopic drainage resulted in a significant reduction in blood loss, operation time, opioid demand, and length of hospital stay compared with traditional open surgery and laparoscopic drainage, whereas
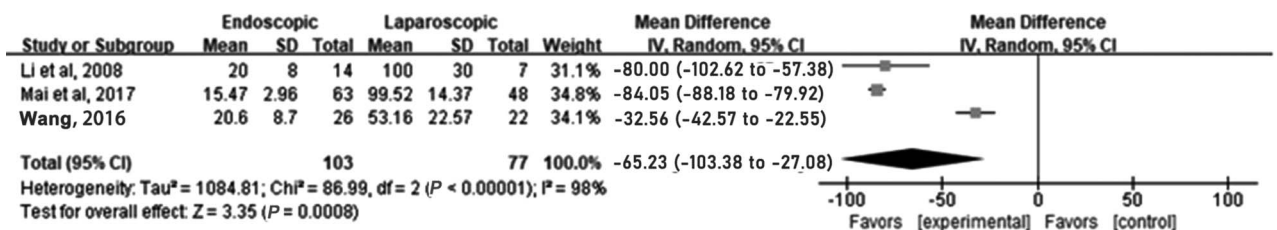

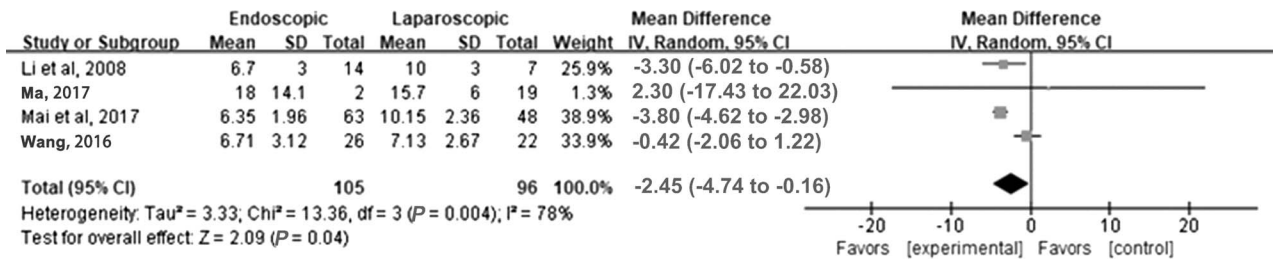**FIGURE 5.** Forest plot showing meta-analysis of blood loss.

FIGURE 6. Forest plot showing meta-analysis of length of hospital stay.

laparoscopy is comparable with traditional open surgery with regard to the success rate.[18] The results of our study are consistent with the previously mentioned conclusions. Some authors have reported on the routine exchange of stents every 6 to 8 weeks as long as the PPC remained unresolved completely.[33] We also found that the patients involved in the analysis might need 2 or more procedures to achieve completely successful endoscopic drainage, as 13.3% (6 of 45) of patients who underwent endoscopic drainage in the study by Melman et al[25] and 28.6% (4 of 14) of patients who underwent endoscopic drainage in the study by Li et al[24] underwent 2 endoscopic drainage procedures. Although endoscopic drainage has advantages of less blood loss, a shorter hospital stay, and less operation time than laparoscopic drainage, there also exists a drawback of endoscopic drainage in the risk of stent exchange. The endoscopic operation procedure can be clarified in future studies. Furthermore, some authors suggest that laparoscopy may have a distinct advantage over endoscopic drainage in dealing with PPC containing significant debris because of the larger size of the stoma that is created.[34]

According to the scientific and rigorous retrieval methods and procedures, the inclusion and exclusion criteria were clarified in our meta-analysis, and the incorporated studies were evaluated objectively. Statistical methods were used to analyze the data to reduce the occurrence of bias. However, this study also has some limitations. First, only 1 RCT study[35] was found, but we did not include it in the analysis because its patients included both PPC and WON without distinguishing between them. Finally, we included patients with only PPC because the choice of surgical procedure could not exclude the influence of differences in disease and the subjective choice of patients on the analysis results. There was no indication of publication bias, but most of the studies included in this analysis were retrospective studies, which cannot provide all of the indicators needed to evaluate the surgical

program; thus, publication bias may exist to some extent. Second, the overall sample size was limited, and the lack of long-term follow-up led to dissatisfaction with the lasting response to treatment. Third, we could not certify that the severity of PPC was comparable when treated by laparoscopic or endoscopic drainage; thus, we could not exclude the possibility that patients undergoing laparoscopic drainage were in a more complicated condition. Moreover, there was a large difference between domestic and foreign studies in the selection of outcome indicators. Finally, different medical institutions may have differences in procedures, such as different instruments and equipment, different skilled operators, and different medical levels, which might bring heterogeneity.

CONCLUSIONS

To our knowledge, this report is the first meta-analysis comparing endoscopic and laparoscopic treatment of PPC. The evidence from this research did not show that endoscopic treatment was superior to laparoscopic treatment in terms of the rate of treatment success, adverse events, and recurrence. However, considering its improvements in operation time, intraoperative blood loss, and hospital stay, endoscopic treatment might be the better treatment approach for patients with PPC than laparoscopic treatment. In any case, a patient-specific approach taking into account patient preferences should be considered, and treatment should be determined by a multidisciplinary team of therapeutic endoscopists, interventional radiologists, and pancreatic surgeons. In the future, high-quality prospective RCTs should be conducted to provide clear evidence for the treatment of PPC.
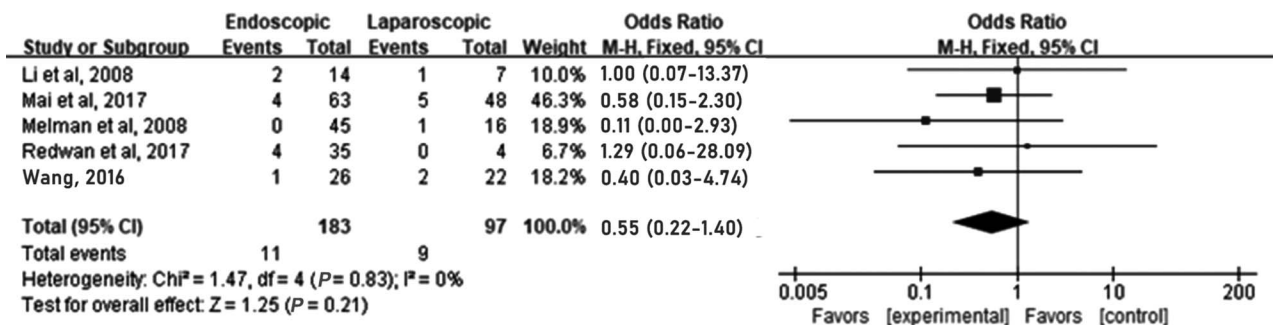

FIGURE 7. Forest plot showing meta-analysis of recurrence.

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