Minimally Invasive Drainage Versus Open Surgical Debridement for Severe Acute Pancreatitis: a Meta-Analysis and Systemic Review

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Abstract: Objective This study compared the treatment outcomes between minimally invasive drainage (MID) and open surgical debridement (OSD) for severe acute pancreatitis (SAP). Methods Reviewers manually searched PubMed/MEDLINE, China National Knowledge Infrastructure database, WANFANG database, and China Biology Medicine database for studies reporting on the use of MID and OSD for treating SAP. All publications from inception to January 2021 were considered. Randomized control trials (RCTs) with SAP diagnoses made based on the 2019 WSES guidelines for the management of SAP, wherein the included SAP patients underwent MID or OSD treatment were included in this study. A PRISMA recommended tool was used for assessing the risk of bias of the included RCTs. Results In all, 1050 publications were identified. However, after applying the inclusion and exclusion criteria, 12 RCTs including 1167 patients who received OSDs (n = 501) and MIDs (n = 666) were considered eligible. The META-analysis indicated that compared with OSD, MID showed a decrease in the mortality (fixed-effects model: OR = 0.41, 95% CI: 0.31–0.54) and morbidity rate with regard to multiple organ dysfunction syndrome, MODS (fixed-effects model: OR=0.25, 95% CI: 0.14–0.45). Conclusions Compared with OSD, MID is an effective measure to treat SAP. MID can significantly decrease the mortality rate and the incidence of MODS and improve patient outcomes in SAP.

1. Introduction

Severe acute pancreatitis (SAP) is one of the most common and most fatal gastrointestinal diseases worldwide requiring emergency hospitalization. SAP is a serious condition with rapid progression and a high mortality rate. Patients diagnosed with SAP usually manifest nausea, vomiting, and abdominal pain. If the patients do not receive appropriate treatment at an early stage, SAP usually progresses into multiple organ dysfunction syndrome, drastically deteriorating the life of quality of patients [1,2]. As per the revised Atlanta classification[3], acute pancreatitis (AP) can be classified into mild AP, moderate AP, and severe AP depending on the severity. Most AP cases are mild, wherein the patients can be discharged quickly without any major treatment[4,5]. The morbidity rate of SAP among all pancreatitis patients is 20% to 30% and its cause-specific mortality is 10%-35% [6,7,8]. Discharging the ascites, wiping out the necrotic tissue, and controlling infection effectively and in a timely manner can improve the outcomes of SAP patients or even shorten their hospitalization duration [9]. The serious characteristics associated with SAP are the reason why it is considered one of the most challenging conditions in the emergency department [10]. Buchler et al [11] reported that SAP patients diagnosed with infectious pancreatic necrosis are highly vulnerable patients, and surgical treatment as early as possible is recommended to these patients. Open surgical debridement (OSD) is a type of traditional surgical treatment for SAP, but it is associated with a higher morbidity and mortality rate [12,13]. Clinically, minimally invasive drainage (MID) includes percutaneous submucosal dissection (ESD), percutaneous catheter drainage (PCD), and minimal

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incision surgery (MIS) [13,14] Many studies have indicated that MID can be successfully and safely used for the treatment of SAP [15]. However, currently there is no study comparing MID and OSD with regard to SAP treatment[16]. Thus, we aim to conduct a meta-analysis to explore the differences between MID and OSD in terms of SAP treatment, and provide some references for clinicians dealing with SAP.

2. Methods

This meta-analysis was constructed according to the PRISMA checklist.

2.1 Eligibility Criteria

Studies meeting the following criteria were included in the analysis: 1) RCTs; 2) SAP diagnosis as per the 2019 WSES guidelines [5]; 3) patient age >18 years; and 4) MID or OSD as a treatment measure. No restrictions were placed on race or nationality. The following studies were excluded: 1) reviews, case reports, and expert reviews; 2) animal studies; 3) *in vitro* studies; 4) repeat publications or data duplication; and 5) non-SAP studies. Interventions included MID (ESD, PCD, and MIS) and OSD. In some cases, patients were first treated with MID, but later treated via OSD laterally; these patients were included in the MID group.

2.2 Search Strategy

Two reviewers independently searched the PubMed/MEDLINE, China National Knowledge Infrastructure database, WANFANG database, and China Biology Medicine database for RCTs wherein MID or OSD was used to treat SAP patients via manual search. The RCTs comparing between MID and OSD with regard to SAP treatment were shortlisted. Further, the studies were filtered for the publication year and all studies published until January 2021 were included. The search keywords were “severe pancreatitis”, “MID”, “severe acute pancreatitis”, “severe necrotized pancreatitis”, “OSD”, “random allocation”, “random”, “randomly”, and “randomized”. We searched for articles in all languages, and the articles were translated when necessary. We also searched for some relevant references in the articles; the retrieval was constructed by the free words and the subject words plus the free words. The titles and abstracts were searched for the abovementioned keywords using the following search operators: “Minimally Invasive Drainage” OR “Open Surgical Debridement” OR “severe acute pancreatitis”.

2.3 Data Extraction

Researchers extracted data from articles by reading the titles and abstracts, then screened the studies that met the eligibility criteria, and constructed an Excel sheet named “Data extraction archive”. The following data were recorded: general information (author, publishing date, language, nationality, and research type); quality data (allocation concealment, blinding method, and follow-up); intervention data (treatments and control measures); outcome data (death and MODS); and all measurements recorded in the original studies.

2.4 Outcomes

In the enrolled studies, one or two of the following main research indicators must be included: (1) primary endpoint: mortality; (2) secondary endpoint: MODS as a morbidity. We use odds ratios (OR) and 95% confidence intervals (CIs) to assess the outcome quantitatively.

2.5 Statistical Analyses

This meta-analysis is based on binary-continuous method. The outcome measures were evaluated by ORs and 95% CIs. We used Stata SE to analysis the collected data. The I^2 statistic was applied for the analysis owing to the heterogeneity. P values less than 0.05 or I^2 value higher than 50% indicated heterogeneity, and its origin was taken into consideration. Following this, if the heterogeneity still existed, a random effect model was adopted for analysis. In contrast a fixed-effect model was adopted when the P value was greater than 0.05 or the I^2 value was not more

than 50%. The stability of this meta-analysis was evaluated by eliminating any of the studies successively. We drew a forest plot and risk of bias plot using STATA SE (Version 15). The funnel plot and the sensitivity analysis (publication bias) were also acquired using STATA SE (Version 15).

3. Results

We identified 1050 references, including 245 from PubMed/MEDLINE, 221 from CNKI, 171 from WANFANG, 148 from CBM, and 265 from EMBASE. The deadline for the publication date was set for January 31, 2021. Following this, the study selection was carried out based on the eligibility criteria and the duplicate studies were removed in this process. After reading the title and abstract, 1038 articles were excluded according to the exclusion criteria. Finally, 1167 subjects of 12 studies that met the inclusion criteria were selected for further analysis. The screened flow chart is as follows (Fig.1). The basic characteristics of the patients enrolled in the study can be seen in Table 1.

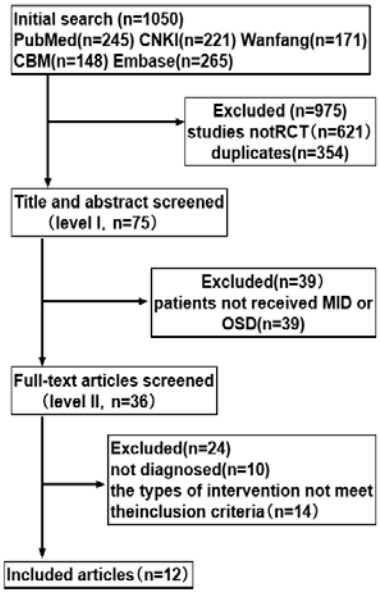


Fig.1 Flowchart of the Study Selection Process

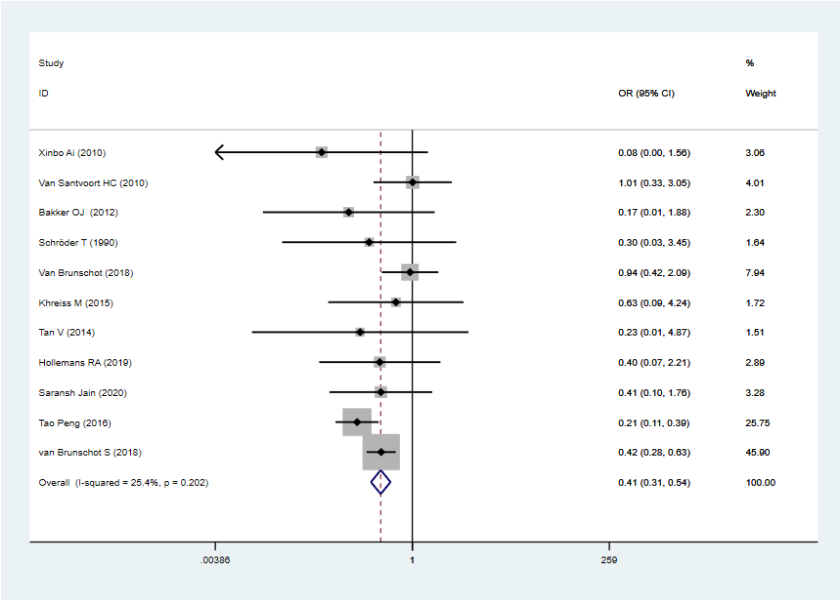
Table 1 Characteristic of Enrolled Studies

Author	Year	Country	Language	Study design	Intervention	Number of patients	Deaths	Number of MODS
Xinbo Ai[18]	2010	China	English	RCT	MID	13	0	1
					OSD	16	5	3
Peng Tao[19]	2016	China	Chinese	RCT	MID(PCD)	212	40	Not Mentioned
					OSD	61	32	Not Mentioned
Van Santvoort HC[14]	2010	Holland	English	RCT	MID	43	8	5
					OSD	45	7	18
Bakker OJ[20]	2012	Holland	English	RCT	MID	10	1	0
					OSD	10	4	5
Schröder T[21]	1990	Finland	English	RCT	MID	10	1	Not Mentioned
					OSD	11	3	Not Mentioned
Khreiss M[23]	2015	USA	English	RCT	MID(ESD)	20	2	Not Mentioned
					OSD	20	3	Not Mentioned

Kumar N[24]	2014	USA	English	RCT	MID(ESD)	12	Not Mentioned	0
					OSD	12	Not Mentioned	5
Tan V[25]	2014	France	English	RCT	MID(ESD)	11	0	2
					OSD	21	3	5
Hollemans RA[26]	2019	Holland	English	RCT	MID	35	2	0
					OSD	38	5	1
Saransh Jain[27]	2020	India	English	RCT	MID(PCD)	41	7	7
					OSD	12	4	4
van Brunschot S[28]	2018	Holland	English	RCT	MID(ESD) OSD	208 208	57 99	Not Mentioned
Van Brunschot[22]	2018	Holland	English	RCT	MID(ESD) OSD	51 47	22 21	4 11

3.1 Effect of Mid and Osd on the Mortality of Sap Patients

In all, 11 studies reported on the mortality rates of patients; among the 1143 SAP patients included in these studies, 654 and 489 underwent MID treatment and OSD, respectively. In the MID and OSD groups, 140 and 186 deaths were reported, respectively. The combined statistics were calculated for determining heterogeneity using the fixed-effects model, and the result was found to be homogenous (Chi square value: 13.41, I^2 value: 25.4%, P value: 0.202). According to the results of the combined analysis of references, compared to the OSD group, the MID group showed significant decrease in the mortality of SAP patients (OR: 0.41, 95% CI: 0.31–0.54, Z: 6.31, P: 0.000; Figure 2). We constructed a funnel plot to determine if there was publication bias (Fig. 3). However, we cannot judge the plot symmetry with bare eyes. Accordingly, as per the results of Begg's funnel, we concluded that the studies we selected have no publication bias ($z = 1.56$, $P = 0.119$; $z < 1.96$, $P > 0.05$). The funnel plot illustrates the bias of this research is mild because the funnel plot is symmetric (Fig. 3).



(Fig.2. Effect of MID and OSD on the mortality of SAP patients forest plot)

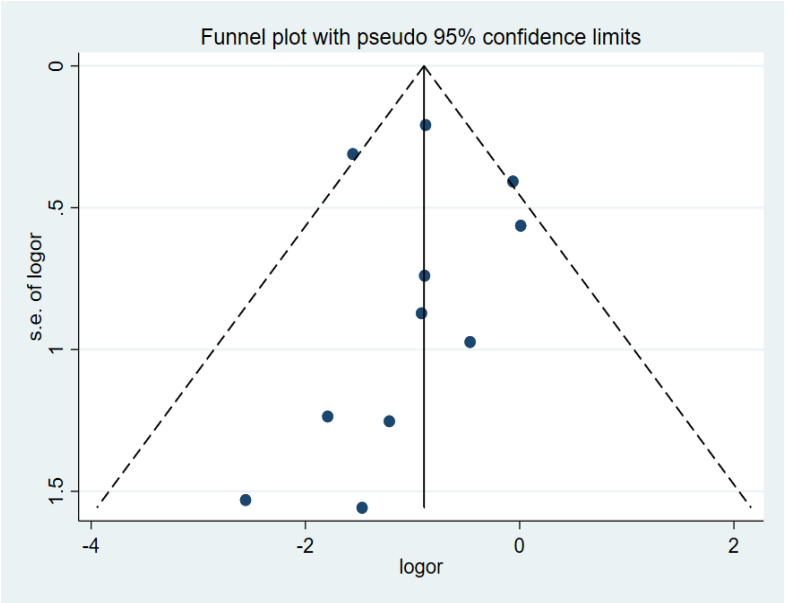


Fig.3 : a Funnel Plot to Determine the Effects of Mid and Osd on the Mortality of Sap Patients

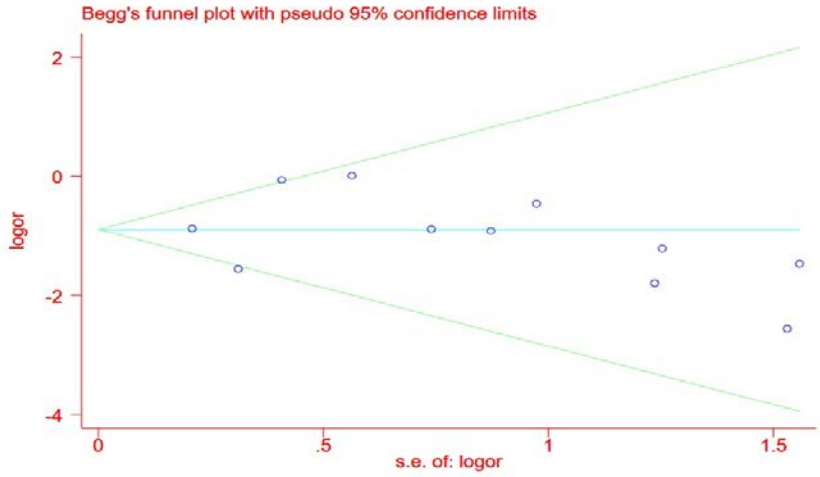


Fig.4 : Funnel Plot for the Predictive Value of Effects of Mid and Osd on the Mortality of Sap Patients

3.2 Effect of Mid and Osd in Terms of Mods Morbidity in Sap Patients

Further, 8 studies in our analysis were associated with morbidities. Of the 417 patients included in these 8 studies, 216 patients underwent MID treatment and 201 patients underwent OSD treatment. The number of patients with MODS in the MID group was 19 and that in the OSD group was 52. The combined statistics calculated using the fixed-effects model for the heterogeneity test indicated homogenous results (Chi squared value: 4.14, I^2 value: 0.0%, P value: 0.764). The combined analysis indicated that compared with the OSD group, the MID group showed significantly decreased MODS morbidity of SAP patients (combined OR: 0.25, 95% CI: 0.14–0.45, Z: 4.65, P: 0.000, Figure 5). The funnel plot illustrates that the bias of this research is mild because the funnel plot is symmetric (Figure 6).

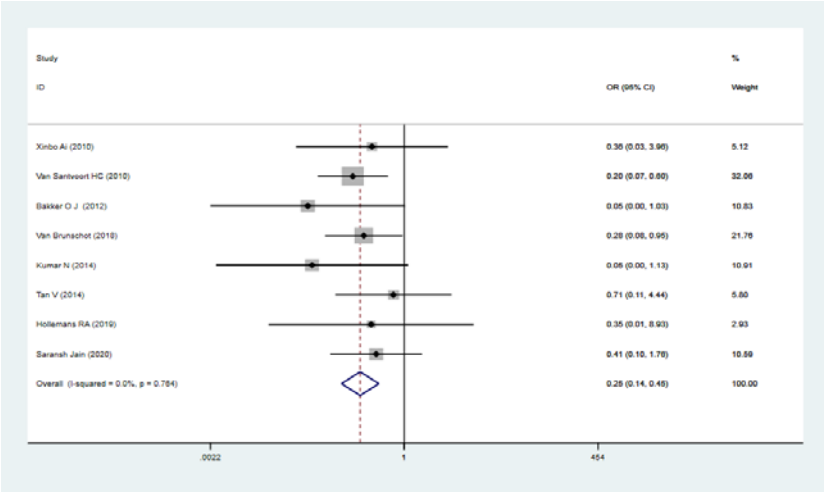


Fig.5 : Effect of Mid and Osd on the Mods Morbidity in Sap Patients: Forest Plot

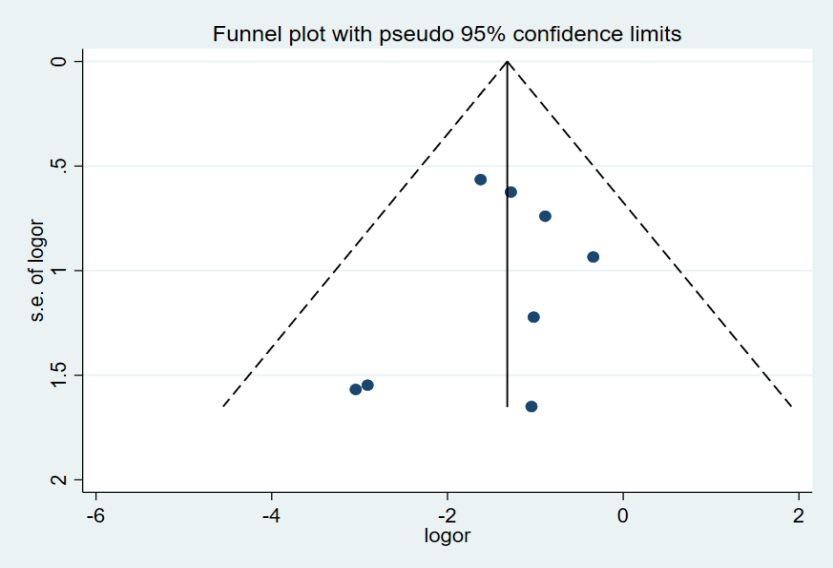


Fig.6 : a Funnel Plot of the Effect of Mid and Osd on Mods Morbidity in Sap Patients

4. Discussion

This meta-analysis indicated that compared with the OSD, MID is a safe and effective way to salvage patients suffering from SAP. We included 12 studies in our analysis with the aim to compare between MID and OSD for treating SAP. Our statistical analyses showed that the number of deaths in the MID group was lower (140/654) than that in the OSD group (186/489). The number of patients with MODS in the MID group was 19 (n = 216) and that in the OSD group was 52 (n = 201). Obviously, these results indicate that the MID is a much safer and more effective treatment measure compared with OSD in SAP patients.

The studies using MID in our analysis mainly included the ESD and PCD. Although minimally invasive surgery is very welcomed, MID has not yet become the gold standard for the treatment of SAP given that there are few studies reporting on its superiority to OSD. Our meta-analysis can provide some evidence showing that MID is superior to OSD. Thus, we believe our findings will significantly contribute to the effective management of SAP in the future.

However, there are several limitations to this study. First, we found that the number of the RCTs aiming at assessing a minimal invasive method was not sufficient. Further, for the RCT, aiming at assessing the minimal invasive method, the sample size was not enough. Second, when we searched the databases, we found that there were few meta-analyses comparing between MID and OSD for SAP treatment. Before this meta-analysis, most of the studies we searched had some bias in field of

methodology, as they involved not only RCTs but also some retrospective studies.

5. Conclusion

According to the evidence reported in the current analysis, compared with OSD, MID can dramatically decrease the mortality rate and reduce the morbidity of MODS in SAP patients. However, further high-quality, multi-center studies with a large sample size are required to provide more solid data foundation to support the clinical application of our findings.

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