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Wang, R; Hu, P; Kong, QZ; Li, Z.

Corresponding author:

Zhen Li

qilulizhen@sdu.edu.cn

Author Affiliation:

Qilu Hospital of Shandong University.

ADMINISTRATIVE INFORMATION**Support** - NA.**Review Stage at time of this submission** - Preliminary searches.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202490047**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 11 September 2024 and was last updated on 11 September 2024.**INTRODUCTION**

Review question / Objective P: Patients with pancreatic walled off necrosis (WON) undergoing endoscopic ultrasound (EUS)-guided drainage using lumen-apposing metal stents.

I: endoscopic ultrasound (EUS)-guided drainage with immediate direct endoscopic necrosectomy (DEN).

C: endoscopic ultrasound (EUS)-guided drainage without immediate direct endoscopic necrosectomy (DEN) and undergo endoscopic necrosectomy if the condition does not improve.

O: Primary outcome is the overall clinical success; Secondary outcomes are mean number of required necrosectomy sessions, the need for additional percutaneous drainage, adverse events, mortality rate, and technical success.

Condition being studied Acute pancreatitis is one of the most common gastroenterology diagnoses which brings great pain and cost. According to the revised Atlanta classification, walled-off necrosis

(WON) is defined as a mature and encapsulated collection of necrotic tissue with a well defined inflammatory wall, and is observed after four weeks of the onset of acute pancreatitis.

EUS-guided drainage has become a first-line treatment. Because it avoids the risks of pancreatic fistula and exo/endocrine insufficiency, gives better quality of life, lower complications and shorter hospital stay. After placement of metal/plastic stents, patients usually remove necrotic material through endoscopy approach, that is, direct endoscopic necrosectomy (DEN). Due to potentially lethal adverse events, such as bleeding, perforation, and peritonitis, DEN is usually delayed for several days after EUS-guided drainage. This strategy is known as "the step-up approach." However, it has been reported that DEN immediately after EUS-guided drainage can shorten the treatment duration without increasing adverse events. Especially with the development of dedicated lumen-apposing metal stent (LAMS), its large diameter of endoprosthesis can promote better drainage of necrotic contents. This can reduce the number of interventions or need for

necrosectomy. This meta-analysis aimed to compare the immediate versus on-demand DEN approach of EUS for WON drainage.

METHODS

Participant or population Patients with pancreatic walled off necrosis (WON) undergoing endoscopic ultrasound (EUS)-guided drainage using lumen-apposing metal stents.

Intervention Endoscopic ultrasound (EUS)-guided drainage with immediate direct endoscopic necrosectomy (DEN).

Comparator Endoscopic ultrasound (EUS)-guided drainage without immediate direct endoscopic necrosectomy (DEN) and undergo endoscopic necrosectomy if the condition does not improve.

Study designs to be included Full text published articles, including prospective and retrospective studies and randomised controlled trials (RCTs) will be considered for this meta-analysis. Any conference abstract provided complete information of our primary and secondary outcomes on the topic will be considered.

Eligibility criteria NA.

Information sources PubMed/MEDLINE, Embase, Web of Science and Cochrane Library. For any missing data, corresponding authors will be contacted to provide us with missing information on the topic.

Main outcome(s) Primary outcome is the overall clinical success; Secondary outcomes are mean number of required necrosectomy sessions, the need for additional percutaneous drainage, adverse events, mortality rate, and technical success.

Quality assessment / Risk of bias analysis We will assess the risk of bias (RoB) in included studies by using the Cochrane Collaboration's tool and the Newcastle-Ottawa Scale (NOS).

Strategy of data synthesis We will utilize the risk ratio (RR) to combine dichotomous outcomes, and for continuous outcomes, we will employ mean difference (MD) along with a 95% confidence interval (CI). In the absence of heterogeneity, we will employ the random-effects model to calculate pooled-effect estimates. When there is significant heterogeneity, we will employ the random-effects model.

Cochran Q test will be used to calculate heterogeneity using I^2 metric. I^2 values $\geq 50\%$ will indicate significant heterogeneity. For all the tests (except for heterogeneity), we will consider a two-tailed probability value <0.05 as statistically significant.

Subgroup analysis NA.

Sensitivity analysis Sensitivity analysis will be carried out through the exclusion method. Each study was excluded separately, and by observing the changes of the combined results, we can evaluate whether the original meta-analysis results have significant changes due to the influence of some studies.

Country(ies) involved China.

Keywords walled-off necrosis, direct endoscopic necrosectomy, endoscopic ultrasound-guided drainage.

Contributions of each author

Author 1 - Rui Wang.

Email: rui-wang@mail.sdu.edu.cn

Author 2 - Ping Hu.

Author 3 - Qingzhou Kong.

Author 4 - Zhen Li.