

# EUS-guided pelvic drainage: A systematic review and meta-analysis

Banreet Singh Dhindsa<sup>1</sup>, Yassin Naga<sup>2</sup>, Syed Mohsin Saghir<sup>2</sup>, Amaninder Dhaliwal<sup>3</sup>, Daryl Ramai<sup>4</sup>, Chad Cross<sup>5</sup>, Shailender Singh<sup>1</sup>, Ishfaq Bhat<sup>1</sup>, Douglas G. Adler<sup>6</sup>

<sup>1</sup>Division of Gastroenterology and Hepatology, University of Nebraska Medical Center, 982000 Nebraska Medical Center, Omaha, NE, USA; <sup>2</sup>Department of Internal Medicine, University of Nevada, Las Vegas School of Medicine, Las Vegas, NV, USA; <sup>3</sup>Division of Gastroenterology and Hepatology, Moffitt Cancer Center, Tampa, FL, USA; <sup>4</sup>Department of Internal Medicine, The Brooklyn Hospital Center, Brooklyn, New York, USA; <sup>5</sup>Department of Biostatistics and Epidemiology, University of Nevada Las Vegas, Las Vegas, NV, USA; <sup>6</sup>Department of Gastroenterology and Hepatology, University of Utah, School of Medicine, Huntsman Cancer Center, Salt Lake City, Utah, USA

## ABSTRACT

**Background and Objectives:** EUS-guided pelvic abscess drainage (EUS-PAD) is a procedure that utilizes an echoendoscope to visualize an area of interest for needle insertion and placement of a stent, catheter, or both for drainage of the target abscess. The aim of this study was to perform a systematic review and meta-analysis for the safety and efficacy of EUS-PAD. **Materials and Methods:** We conducted a comprehensive search of several databases and conference proceedings including PubMed, EMBASE, Google Scholar, MEDLINE, SCOPUS, and Web of Science databases (earliest inception to February 2020). The primary outcomes for this study were the technical and clinical success of EUS-PAD. The secondary outcomes assessed for this study were adverse events of the procedure and subgroup analysis of individual adverse events. **Results:** Eight studies with a total of 135 patients combined were included in our analysis. The rate of technical success was 100% and the calculated pooled rate of clinical success was 92% (95% confidence interval [CI]: 87%, 98%;  $P = 0.31$ ;  $I^2 = 15\%$ ). The calculated pooled rate of adverse events was 9.4% ( $\pm 17.9\%$ ), with stent migration ( $5.5 \pm 18.06\%$ ) being the most common adverse event. **Conclusion:** EUS-PAD offers a viable alternative that can minimize the need for surgical intervention in the drainage of pelvic abscesses. EUS-PAD has also demonstrated long-term clinical success with an acceptable rate of complications.

**Key words:** abscess, drainage, EUS, meta-analysis, pelvic

## INTRODUCTION

Pelvic abscesses may arise from several etiologies including surgery (e.g., low anterior resection), perforation of pelvic viscera, diverticulitis, appendicitis, ischemic

colitis, inflammatory bowel disease, or from pelvic inflammatory disease, among other causes.<sup>[1,2]</sup> Pelvic abscesses are associated with significant morbidity

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** WKHLRPMedknow\_reprints@wolterskluwer.com

**How to cite this article:** Dhindsa BS, Naga Y, Saghir SM, Dhaliwal A, Ramai D, Cross C, et al. EUS-guided pelvic drainage: A systematic review and meta-analysis. *Endosc Ultrasound* 2021;10:185-90.

Access this article online	
<b>Quick Response Code:</b> 	<b>Website:</b> <a href="http://www.eusjournal.com">www.eusjournal.com</a>
	<b>DOI:</b> 10.4103/eus.eus_71_20

## Address for correspondence

Dr. Douglas G. Adler, University of Utah School of Medicine, Huntsman Cancer Center, 30 N 1900 E, Room 4R118, Salt Lake City, Utah 84132, USA. E-mail: douglas.adler@hsc.utah.edu

**Received:** 2020-05-29; **Accepted:** 2020-09-28; **Published online:** 2021-01-12

and mortality.<sup>[3]</sup> Management, per the Infectious Diseases Society of America and Surgical Infection Society, includes a combination of medical and surgical therapies, of which drainage of the abscess is of utmost importance to obtain source control.<sup>[4,5]</sup> Currently, computed tomography (CT)-guided percutaneous drainage (PCD) is the preferred method for drainage of pelvic abscesses.<sup>[5]</sup> Other modalities include ultrasound (US)-guided transrectal drainage and surgical drainage.

Limitations of PCD and US procedures include, but are not limited to, catheter dislodgment, patient discomfort, and limited access points of fluid drainage secondary to the complexity of pelvic anatomy.<sup>[1,6]</sup> EUS-guided pelvic abscess drainage (EUS-PAD) is an alternative minimally invasive procedure which can be used for drainage of pelvic abscesses. With EUS, one can usually target a pelvic abscess since most fluid collections are located close to the rectum and left colon.<sup>[7]</sup>

EUS-PAD was first described by Giovannini *et al.* in 2003.<sup>[8]</sup> The procedure utilizes an echoendoscope to visualize an area of interest for needle insertion and placement of a stent, catheter, or both for drainage of the target abscess.<sup>[6]</sup> With utilization of this procedure, patients can achieve shorter durations of hospital stay leading to lower costs and a bedside procedure can be performed in critically ill patients if necessary.<sup>[6]</sup>

The aim of this study was to perform a systematic review and meta-analysis for the safety and efficacy of EUS-PAD.

## METHODS

### *Data sources*

We performed a search of multiple databases including MEDLINE, EMBASE, Google Scholar, Cochrane, and Web of Science databases (earliest inception to February 2020). The literature search utilized a combination of keywords “EUS,” “endoscopic” and “ultrasound,” “pelvic,” “abscess,” and “drainage.” This search was carried out by two authors (BD and YN) who reviewed the titles and abstracts individually and excluded studies that did not meet the inclusion criteria. We conducted the search and narrowed down the final studies as per the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, as well as the Meta-Analysis of Observational Studies in Epidemiology guidelines to identify studies reporting on EUS-guided

drainage of pelvic abscesses [Supplementary Figure 1].<sup>[9]</sup> The bibliographic section of the selected articles, as well as the systematic and narrative articles on the topic, was manually searched for additional relevant articles.

### *Study selection*

We included studies that evaluated the clinical efficacy and adverse events of EUS-PAD. Studies were included as long as they provided data needed for the analysis. Exclusion criteria were as follows: (1) studies using other techniques of PAD other than EUS, (2) studies performed in the pediatric population (patient age <18 years) or among prisoners, (3) studies with <5 patients, and (4) studies not published in the English language.

We excluded multiple studies that reported on the same cohort. In case of overlapping cohorts, we included the most appropriate study.

### *Data abstraction and quality assessment*

Two authors independently assessed (BD and SS) and performed quality assessment independently, and any differences were resolved with the help of the third author (YN).

Data collection was recorded as number of reported events (*n*) out of the total number of patients (*N*) from each study. The collected data were treated akin to single group cohort studies, and therefore, we used the Newcastle–Ottawa scale (NOS) to assess the quality of studies.<sup>[10]</sup> This quality score is comprised of 3 categories and 8 questions, the details of which are provided in Supplementary Table 1.

### *Outcomes assessed*

The primary outcomes for this study were the technical and clinical success of EUS-PAD. The secondary outcomes assessed for this study include adverse events of the procedure and subgroup analysis of individual adverse events.

### *Definitions*

Technical success was defined as the successful access and drainage of the abscess via EUS. Clinical success was defined as symptom resolution with complete resolution of abscess on subsequent imaging performed 1–4 weeks after the procedure.

### *Statistical analysis*

We used meta-analysis techniques to calculate the pooled estimates for each outcome of interest following the

methods suggested by DerSimonian and Laird using the random-effects model where appropriate.<sup>[17]</sup> In several instances in the adverse event data, values of 0 occurred. In these instances, we avoided inadvertently adding positive bias to the outcomes by writing syntax to calculate weighted summary statistics. In this way, we preserved the integrity of the actual data values and avoided possible biases in reporting the outcomes. We assessed heterogeneity between study-specific estimates using Cochran's Q statistical test for heterogeneity and the  $I^2$  statistics.<sup>[18,19]</sup> In this, values of <30%, 30%–60%, 61%–75%, and >75% were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively.<sup>[20]</sup> Publication bias was ascertained qualitatively by visual inspection of funnel plot and quantitatively by the Luis Furuya-Kanamori (LFK) test; further, the extent of potential bias was ascertained utilizing the Doi plot.<sup>[21]</sup> Sensitivity analysis was conducted in instances of potential bias by recalculating all statistics after removal of studies leading to LFK asymmetry; if removal of the study impacted estimates, the study was removed from the final analysis. All meta-analyses were performed using MetaXL software (v. 5.3; EpiGear International, Sunrise Beach, Queensland, Australia). The weighted correlation was calculated using the <wt.cor> script in the "weight" package, with bootstrapped  $P$  values calculated with  $n = 10,000$  iterations, using R (v 3.6.1; Vienna, Austria). Finally, we estimated lower and upper confidence limits for clinical success using the Clopper–Pearson exact method implemented in the <PropCI> package, also using R.

## RESULTS

### *Search results and population characteristics*

From an initial group of 173 studies, 8 studies reported data regarding the use of EUS-PAD. Multiple studies with overlapping cohorts were found, and the most appropriate ones were included in the final analysis. The majority of the patient population were male (55.9%

reported in 7 studies), and the mean age mentioned in 7/8 studies was 54.22 years. Seventy percent of the abscesses were postsurgical and 30% of the abscesses were related to medical conditions, primarily diverticulitis. The mean abscess size was 63.32 mm, with abscesses being perirectal in 83.7% of the cases and pericolonic in the remainder of the cases.

Drainage was performed with double-pigtail plastic stents in 100 patients (74%) and lumen-apposing metal stent (LAMS) in 23 patients (17%). Twelve patients (9%) underwent needle aspiration only. Table 1 describes the characteristics of the included studies. The schematic diagram of study selection is illustrated in Supplementary Figure 1.

### *Characteristics and quality of included studies*

The analysis included 8 independent cohort studies, with a total of 135 patients. There were 2 multicenter studies, no population-based studies, and 6 single-center studies included in our final analysis. Two studies had more than 30 patients, 4 studies had more than 10 patients, and 2 studies had less than 10 patients. Seven studies were published in manuscript form, and one study was published in abstract form. All of the included studies had clear information reported on the technical and clinical success of EUS-PAD. Table 1 describes the characteristics of the included studies.

Quality assessment was performed with the help of the NOS scale. Seven studies were of good quality, and one study was of poor quality. The details of quality assessment are shown in Supplementary Table 1.

### *Meta-analysis outcomes*

#### *Primary outcomes*

The rate of technical success was 100% and the calculated pooled rate of clinical success was 92% (95% confidence interval [CI]: 87%, 98%;  $P = 0.31$ ;

**Table 1. Characteristics of the included studies**

Study name	Year	Country	Type of study	Single/multicenter	Manuscript or abstract	Number of patients	Mean age	Male	Female
Giovannini <i>et al.</i> <sup>[8]</sup>	2003	France	Prospective	Single center	Manuscript	12	67	9	3
Hadithi and Bruno <sup>[13]</sup>	2014	The Netherlands	Retrospective	Single center	Manuscript	8	55.5	6	2
Mudireddy <i>et al.</i> <sup>[16]</sup>	2018	USA	Retrospective	Multicenter	Manuscript	8	-	-	-
Poincloux <i>et al.</i> <sup>[15]</sup>	2017	France	Retrospective	Multicenter	Manuscript	37	61.4	20	17
Puri <i>et al.</i> <sup>[11]</sup>	2010	India	Retrospective	Single center	Manuscript	14	42	11	3
Ramesh-a <i>et al.</i> <sup>[12]</sup>	2013	USA	Retrospective	Single center	Manuscript	11	55.5	5	6
Ramesh-b <i>et al.</i> <sup>[12]</sup>	2013	USA	Retrospective	Single center	Manuscript	27	51	13	14
Ratone <i>et al.</i> <sup>[14]</sup>	2015	France	Retrospective	Single center	Manuscript	7	50	4	3
Manvar <i>et al.</i> <sup>[22]</sup>	2017	USA	Retrospective	Single center	abstract	11	51.36	3	8

$I^2 = 15\%$ ). Figure 1 shows the forest plot for clinical success of EUS-PAD.

### Secondary outcomes

The calculated pooled rate of adverse events was 9.4% ( $\pm 17.9\%$ ), with stent migration ( $5.5 \pm 18.06\%$ ) being the most common adverse event. Table 2 describes the adverse events in different studies.

### Validation of meta-analysis results

#### Sensitivity analysis

To assess whether any one study had a dominant effect on the meta-analysis, we excluded one study at a time and analyzed its effect on the main summary estimate. Based on this analysis, no single study significantly affected the outcome or the heterogeneity.

#### Heterogeneity

Based on Q statistics and  $I^2$  analysis for heterogeneity, low heterogeneity was noted in the analysis of clinical success of EUS-PAD.

#### Publication bias

Based on visual inspection of the funnel plot and the Doi plot, as well as quantitative measurement based on the LFK test, there was evidence of asymmetry and hence potential publication bias. Sensitivity analysis by removal of asymmetric studies revealed the impact of the possible

publication bias, but this did not lead to a statistical change in the calculated estimate or the conclusion of this meta-analysis. However, it should be noted that the ability to detect potential publication bias is limited.

## DISCUSSION

Our study demonstrates that EUS-PAD is an effective and minimally invasive treatment option for the management of pelvic abscesses. This meta-analysis shows that EUS-PAD has high technical and clinical success rates with low rates of adverse events.

The rate of technical success in our meta-analysis was 100%. The straightforward nature of the procedure allows it to be an effective alternative to more invasive approaches, such as image-guided PCD or surgery.<sup>[2]</sup> The clinical success rate of EUS-PAD, according to our analysis, was also high. Clinical success was related to technical success, indicating the importance of technically successful procedure. The etiology of the abscess also appeared to be a major determinant in treatment success. In a study by Ramesh *et al.*, diverticular abscesses had significantly lower treatment success rates than abscesses of other etiologies.<sup>[12]</sup> It is hypothesized that the often multiloculated and highly viscous nature of diverticular abscesses resulted in higher rates of treatment failure.<sup>[12]</sup>

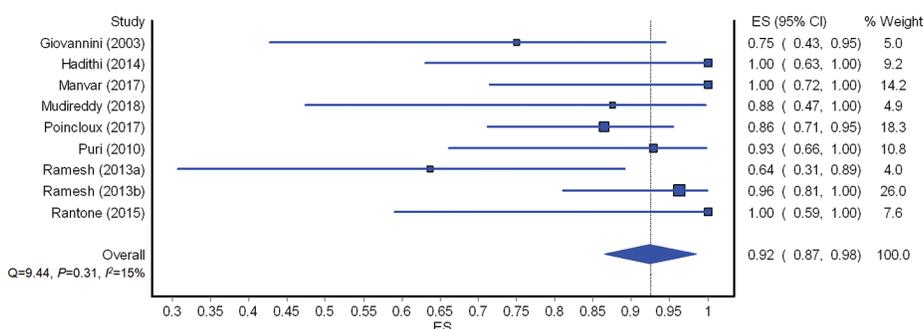


Figure 1. Forest plot showing clinical success of EUS-PAD

Table 2. Adverse events of EUS pancreatic drainage

Study name	Year	Total adverse events	Bleeding	Perforation	Abdominal pain	Stent migration	Others
Giovannini <i>et al.</i> <sup>[8]</sup>	2003	3	0	0	1	0	2
Hadithi and Bruno <sup>[13]</sup>	2014	6	0	0	0	6	1
Mudireddy <i>et al.</i> <sup>[16]</sup>	2018	-	-	-	-	-	-
Poincloux <i>et al.</i> <sup>[15]</sup>	2017	3	0	1	0	1	1
Puri <i>et al.</i> <sup>[11]</sup>	2010	1	0	0	0	0	1
Ramesh-a <i>et al.</i> <sup>[12]</sup>	2013	0	0	0	0	0	0
Ramesh-b <i>et al.</i> <sup>[12]</sup>	2013	0	0	0	0	0	0
Ratone <i>et al.</i> <sup>[14]</sup>	2015	0	0	0	0	0	0
Manvar <i>et al.</i> <sup>[22]</sup>	2017	0	0	0	0	0	0

Our study found an adverse event rate of 9.4%. This is comparable to outcomes of US/CT-guided PAD in which the adverse event rate ranges from 5.6% to 10%.<sup>[23-25]</sup> EUS provides accurate representations of the fluid collections, organs, and vessels, which allows for accurate transmural drainage while minimizing major complications, such as bleeding and perforation. In our meta-analysis, only one perforation was noted, and there were no cases of major bleeding. Perforation occurred, according to the study by Poincloux *et al.*, in a patient with a diverticular abscess.<sup>[15]</sup> This is consistent with the overall worse outcomes among patients with diverticular abscesses as noted by Ramesh *et al.*<sup>[12]</sup> Several minor complications, such as stent migration, abdominal pain, or rectal discomfort, also occurred. There were no procedure-related deaths.

EUS-PAD is performed by various and nonstandardized methods, such as needle aspiration, aspiration with or without tract dilation, and placement of plastic and/or LAMS.<sup>[11]</sup> Stents are utilized to maintain tract patency and to reduce the risk of premature tract closure. Stent placement is limited by the distance of the abscess to the rectal wall. If the distance is >20 mm, stent placement is often not technically feasible with currently available stents.<sup>[8,14]</sup> In the studies using double-pigtail plastic stents, one or two stents were placed. In the studies using LAMS, a single LAMS was placed. The decision to place one or two stents is determined by the operator and individualized to the patient's needs and clinical situation.<sup>[12,26]</sup> Historically, plastic stents were utilized. However, LAMS has been used in more recent studies.<sup>[15,16,22]</sup> Of the four patients treated with LAMS in the study by Poincloux *et al.*, one developed a recurrence; another with a diverticular abscess had a perforation.<sup>[15]</sup> Transrectal drainage catheters can also be utilized in conjunction with stenting to prevent obstruction for patients with larger abscesses (>8 cm).<sup>[12,26]</sup> However, these have been associated with rectal discomfort and are not clearly crucial for abscess resolution.<sup>[11,13,15]</sup>

Recurrence occurred in 6 patients (4%). Giovannini *et al.* and Puri *et al.* reported higher rates of recurrence in patients who only underwent aspiration without dilation or stenting. Three out of six patients who had recurrence underwent aspiration only. These authors hypothesized that further interventions, such as stenting and dilatation, could have reduced the likelihood of recurrence.<sup>[8,11]</sup> Overall, careful consideration should be taken with regard to the size, etiology, and maturity of

the abscess when considering stent placement. Smaller abscesses appear to be amenable to simple aspiration, whereas larger abscesses benefit from stent placement.

There were several limitations to this meta-analysis. The majority of the studies were retrospective in nature. Most of the studies were also undertaken in single centers with experienced advanced endoscopists, and the results may not be generalizable to the broader endoscopic community. Techniques utilized were individualized between different providers including the size, number, and methods in which stents were placed. Finally, no direct comparison was made to the other techniques used to drain pelvic abscesses (PCD or a surgical approach).

## CONCLUSION

EUS-PAD offers a viable alternative that can minimize the need for surgical intervention in the drainage of pelvic abscesses. It is best suited for unilocular abscesses with a mature wall that allows for the creation of a fistula to permit drainage.<sup>[2,8]</sup> Smaller abscesses < 4 cm can be usually treated without endoscopic intervention.<sup>[2]</sup> Considerations should be taken for abscesses of diverticular etiology as higher rates of complications were seen.<sup>[12]</sup> Finally, EUS-PAD should be strictly avoided in patients with ascites or if the abscess is >20 mm from the bowel lumen.<sup>[2]</sup> EUS-PAD has also demonstrated long-term clinical success with an acceptable rate of complications. However, more well-conducted randomized controlled trials are needed to establish its role as an alternative to imaging-guided abscess drainage.

### *Supplementary materials*

Supplementary information is linked to the online version of the paper on the *Endoscopic Ultrasound* website.

### *Financial support and sponsorship*

Nil.

### *Conflicts of interest*

There are no conflicts of interest.

## REFERENCES

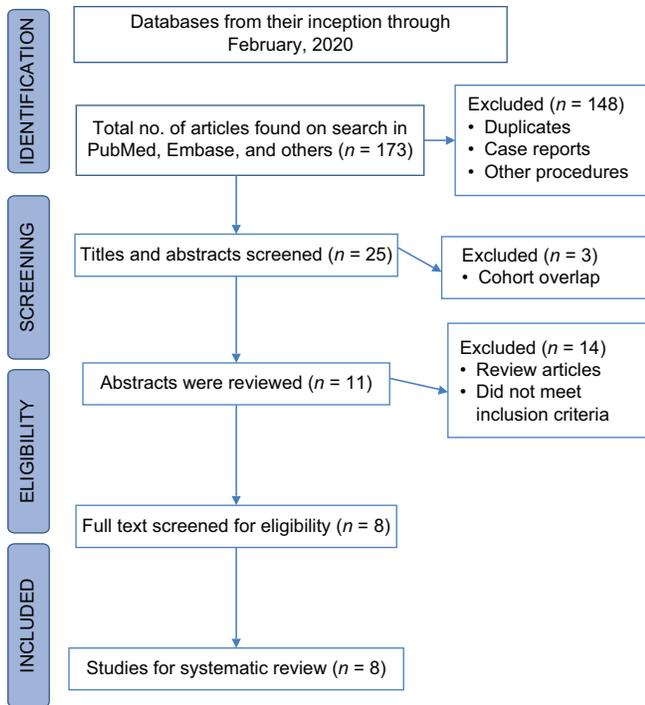
1. Dawod E, Nieto JM. Endoscopic ultrasound-guided drainage of pelvic, intra-abdominal, and mediastinal abscesses. In: *Interventional Endoscopic Ultrasound*. Cham: Springer; 2019. p. 177-88.
2. Mahadev S, Lee DS. Endoscopic ultrasound-guided drainage of pelvic

- fluid collections. *Gastrointest Endosc Clin N Am* 2017;27:727-39.
3. Granberg S, Gjelland K, Ekerhovd E. The management of pelvic abscess. *Best Pract Res Clin Obstet Gynaecol* 2009;23:667-78.
  4. Mazuski JE, Tessier JM, May AK, et al. The surgical infection society revised guidelines on the management of Intra-abdominal infection. *Surg Infect (Larchmt)* 2017;18:1-76.
  5. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: Guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Surg Infect (Larchmt)* 2010;11:79-109.
  6. Varadarajulu S. EUS-Guided Drainage of Pelvic Abscesses. Endosonography E-Book: Expert Consult; 2010.
  7. Prasad GA, Varadarajulu S. Endoscopic ultrasound-guided abscess drainage. *Gastrointest Endosc Clin N Am* 2012;22:281-90.
  8. Giovannini M, Bories E, Moutardier V, et al. Drainage of deep pelvic abscesses using therapeutic echo endoscopy. *Endoscopy* 2003;35:511-4.
  9. Moher D, Liberati A, Tetzlaff J, et al. Preferred reporting items for systematic reviews and meta-analyses: The PRISMA statement. *Ann Internal Med* 2009;151:264-9.
  10. Stang A. Critical evaluation of the Newcastle-Ottawa scale for the assessment of the quality of nonrandomized studies in meta-analyses. *Eur J Epidemiol* 2010;25:603-5.
  11. Puri R, Eloubeidi MA, Sud R, et al. Endoscopic ultrasound-guided drainage of pelvic abscess without fluoroscopy guidance. *J Gastroenterol Hepatol* 2010;25:1416-9.
  12. Ramesh J, Bang JY, Trevino J, et al. Comparison of outcomes between endoscopic ultrasound-guided transcolonic and transrectal drainage of abdominopelvic abscesses. *J Gastroenterol Hepatol* 2013;28:620-5.
  13. Hadithi M, Bruno MJ. Endoscopic ultrasound-guided drainage of pelvic abscess: A case series of 8 patients. *World J Gastrointest Endosc* 2014;6:373-8.
  14. Ratone JP, Bertrand J, Godat S, et al. Transrectal drainage of pelvic collections: Experience of a single center. *Endosc Ultrasound* 2016;5:108-10.
  15. Poincloux L, Caillol F, Allimant C, et al. Long-term outcome of endoscopic ultrasound-guided pelvic abscess drainage: A two-center series. *Endoscopy* 2017;49:484-90.
  16. Mudireddy PR, Sethi A, Siddiqui AA, et al. EUS-guided drainage of postsurgical fluid collections using lumen-apposing metal stents: A multicenter study. *Gastrointest Endosc* 2018;87:1256-62.
  17. DerSimonian R, Laird N. Meta-analysis in clinical trials. *Control Clin Trials* 1986;7:177-88.
  18. Higgins JP, Thompson SG, Deeks JJ, et al. Measuring inconsistency in meta-analyses. *BMJ* 2003;327:557-60.
  19. Kanwal F, White D. "Systematic reviews and meta-analyses" in clinical gastroenterology and hepatology. *Clin Gastroenterol Hepatol* 2012;10:1184-6.
  20. Guyatt GH, Oxman AD, Kunz R, et al. GRADE guidelines: 7. Rating the quality of evidence-inconsistency. *J Clin Epidemiol* 2011;64:1294-302.
  21. Furuya-Kanamori L, Barendregt JJ, Doi SAR. A new improved graphical and quantitative method for detecting bias in meta-analysis. *Int J Evid Based Healthc* 2018;16:195-203.
  22. Manvar A, Sachdev AH, Ho S, et al. Mo1259 EUS guided drainage of pelvic fluid collections with lumen-apposing metal stents. *Gastrointest Endosc* 2017;85:AB480.
  23. Akinci D, Ergun O, Topel Ç, et al. Pelvic abscess drainage: Outcome with factors affecting the clinical success. *Diagn Interv Radiol* 2018;24:146-52.
  24. Laganà D, Carrafiello G, Mangini M, et al. Image-guided percutaneous treatment of abdominal-pelvic abscesses: A 5-year experience. *Radiol Med* 2008;113:999-1007.
  25. Zhao N, Li Q, Cui J, et al. CT-guided special approaches of drainage for intraabdominal and pelvic abscesses: One single center's experience and review of literature. *Medicine (Baltimore)* 2018;97:e12905.
  26. Varadarajulu S, Drelichman ER. Effectiveness of EUS in drainage of pelvic abscesses in 25 consecutive patients (with video). *Gastrointest Endosc* 2009;70:1121-7.

**Supplementary Table 1. Quality assessment of the study with Newcastle-Ottawa Scale**

Study	Year	Number of patients	Newcastle-Ottawa Scale		
			Selection	Comparability	Outcome
Giovannini <i>et al.</i> <sup>[8]</sup>	2003	12	**	*	**
Puri <i>et al.</i> <sup>[11]</sup>	2010	14	***	*	***
Ramesh <i>et al.</i> <sup>[12]</sup>	2013	11	***	**	***
Hadithi and Bruno <sup>[13]</sup>	2014	35	**	*	***
Ratone <i>et al.</i> <sup>[14]</sup>	2015	7	**	*	***
Poincloux <i>et al.</i> <sup>[15]</sup>	2017	37	**	*	***
Manvar <i>et al.</i> <sup>[14]</sup>	2017	11	**	*	*
Mudireddy <i>et al.</i> <sup>[16]</sup>	2018	8	***	*	***

NOS score consists of 3 categories: 1) Selection-included 4 questions and maximum one star per question could be awarded 2) Comparability-included 1 question and maximum two stars could be awarded and, 3) Exposure- included 3 questions and maximum one star per question could be awarded. Good quality study was defined as 3 or 4 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome domain. Fair quality study was defined as 2 stars in selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in outcome domain. Poor quality study was defined as 0 or 1 star in selection domain and 0 stars in comparability domain and 0 or 1 star in outcome domain.



**Supplementary Figure 1.** Study selection process in accordance with preferred reporting items for systematic reviews and meta-analysis statement