EUS-guided biliary drainage: A systematic review and meta-analysis

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ABSTRACT

ERCP is the current procedure of choice for patients with jaundice caused by biliary obstruction. EUS-guided biliary drainage (EUS-BD) has emerged as an alternative to ERCP in patients requiring biliary drainage. The aim of the study was to conduct a systematic review and meta-analysis to report the overall efficacy and safety of EUS-BD. We conducted a comprehensive search of several databases including PubMed, EMBASE, Web of Science, Google Scholar, and LILACS databases (earliest inception to June 2018) to identify studies that reported EUS-BD in patients. The primary outcome was to look at the technical and clinical success of the procedure. The secondary analysis focused on calculating the pooled rate of re-interventions and all adverse-events, along with the commonly reported adverse-event subtypes. Twenty-three studies reporting on 1437 patients were identified undergoing 1444 procedures. Majority of the patient population were male (53.86%), with an average age of 67.22 years. The pooled technical success rates and clinical success rates were 91.5% (95% confidence interval [CI]: 87.7–94.2, \(I^2=76.5\)) and 87% (95% CI: 82.3–90.6, \(I^2=72.4\)), respectively. The total adverse event rates were 17.9% (95% CI: 14.3–22.2, \(I^2=69.1\)). Subgroup analysis of three major individual adverse events was bile leak: 4.1% (2.7–6.2, \(I^2=46.7\)), stent migration: 3.9% (2.5–6.2, \(I^2=43.5\)), and infection: 3.8% (2.8–5.1, \(I^2=0\)). Substantial heterogeneity was noted in the analysis. EUS-BD has high technical and clinical success rate and hence a very effective procedure. Concerns about publication bias exist. Careful consideration should be given to the adverse events and weighing the risks and benefits of the alternative nonsurgical/surgical approaches.

Key words: Biliary drainage, Biliary obstruction, ERCP, EUS guided, jaundice

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INTRODUCTION

ERCP is the current procedure of choice for patients with jaundice caused by biliary obstruction. It has a high success rate and a low major adverse event rate.\(^1\) Failure of ERCP can be secondary to surgically altered anatomy, inaccessible papilla due to malignancy, or (rarely) cannulation failure. Percutaneous drainage has historically been the treatment of choice in patients with failed ERCP.

EUS-biliary drainage (BD) was first described by Giovannini in 2001.\(^2\) Since then, EUS-BD has emerged as an alternative to ERCP in patients requiring BD. Various studies have reported high technical success associated with EUS-BD.

The aim of this study was to evaluate the technical success, clinical success, and adverse events of EUS-BD.

METHODS

Search strategy

We conducted a comprehensive search of several databases and conference proceedings including PubMed, EMBASE, Web of Science, Google Scholar, and LILACS databases (earliest inception to June 2018). We followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, using a predefined protocol, to identify studies reporting EUS-guided BD. An experienced medical librarian using inputs from the study authors helped with the literature search.

Keywords used in search included a combination of “Endoscopic ultrasound,” “EUS,” “biliary,” “drainage,” and “complications.” The search was restricted to studies in human subjects and published in the English language in peer-reviewed journals. Two authors (BSD and HSM) independently reviewed the title and abstract of studies identified in primary search and excluded studies that did not address the research question, based on prespecified exclusion and inclusion criteria. The full text of the remaining articles was reviewed to determine whether it contained relevant information. Any discrepancy in article selection was resolved by consensus and in discussion with a coauthor.

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

In this meta-analysis, we included cohort studies that met the following criteria: (1) EUS-BD (2) information on adverse events, (3) information on subcategories of adverse events, (4) technical success rate, and (5) clinical success rate. Studies irrespective of the geography and abstract/manuscript status were included as long as they provided data needed for the analysis.

We excluded the studies that (1) provided insufficient data to allow the estimation of adverse events and (2) insufficient data on the subcategories of adverse events.

In case of multiple publications from the same cohort, data from the most recent comprehensive report were included. We did not encounter any such study in our analysis.

Data abstraction and quality assessment

Data on study-related outcomes in the individual studies were abstracted onto a standardized form by at least two authors (BSD and HSM) independently, and two authors (BSD and HSM) did the quality scoring independently.

Using a scale modified from the Newcastle-Ottawa scale for cohort studies assessed the quality of the included studies.\(^3\) This quality score consisted of three categories: (1) selection – included four questions and maximum one star per question could be awarded (2) comparability – included one question and maximum two stars could be awarded, and (3) exposure – included three questions and maximum one star per question could be awarded. Good-quality study was defined as 3 or 4 stars in the selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in the outcome domain. Fair-quality study was defined as 2 stars in the selection domain and 1 or 2 stars in comparability domain and 2 or 3 stars in the outcome domain. Poor-quality study was defined as 0 or 1 star in the selection domain and 0 stars in comparability domain and 0 or 1 star in the outcome domain.

Quality assessment for randomized controlled trials (RCTs) was done with Jadad-Oxford scale. A maximum of 5 points could be given to a study on the basis of randomization, blinding, and withdrawals from the study. A score of ≤2 was defined as a poor-quality study.
Outcomes assessed
The primary analysis of this study focused on calculating the pooled rate of overall technical success and clinical success in EUS-BD.

Our secondary analysis focused on calculating the pooled rate of re-interventions and all adverse events, along with the commonly reported adverse-event subtypes (pneumoperitoneum, infection, bleeding, bile leak, and stent migration).

Statistical analysis
We used meta-analysis techniques to calculate the pooled estimated in each case following the methods suggested by DerSimonian and Laird using the random-effect model, and our application can be seen to fit within their general approach (where the effect is measured by the probability of risk). When the incidence of an outcome was zero in a study, a correction of 0.5 was added to the number of incident cases before the statistical analysis. We assessed heterogeneity between study-specific estimates using two methods: Cochrane’s Q statistics and I² statistics. In this, values of <30%, 30%–60%, 61%–75%, and >75% were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively. Publication bias was ascertained qualitatively by visual inspection of funnel plot and quantitatively by the Egger test. When publication bias was present, further statistics using the fail-Safe N test and Duval and Tweedie’s “Trim and Fill test” was used to ascertain the impact of the bias. Three levels of impact were reported based on the concordance between the reported results and the actual estimate if there was no bias. The impact was reported as minimal if both versions were estimated to be the same; modest if effect size changed substantially, but the final finding would still remain the same; and severe if the basic final conclusion of the analysis is threatened by the bias.

All analyses were performed using Comprehensive Meta-Analysis software, version 3 (BioStat, Englewood, NJ, USA).

RESULTS

Search results and population characteristics
From a total of 761 citations identified by our search criteria, 47 studies reported the use of EUS-BD.

The schematic diagram of the study selection is illustrated in Supplementary Figure 1.

Table 1 describes the study characteristics. Majority of the patient population were males (53.86%), with an average age of 67.22 years. The indications for the EUS-BD included malignant obstructive jaundice, cholangitis, bile leak, and other benign causes. In the majority of studies, technical success was defined as successful deployment of the stent and clinical success was defined as a reduction in serum total bilirubin by 50% at 1 week or <3 mg/dL at 2 weeks after the procedure.

The type of intervention during the EUS was through transgastric (29.5%), transduodenal (34.34%), and other techniques (19.8%). One of the studies did not mention the technique used, so the above numbers exclude that study.

Characteristics and quality of the included studies
Table 1 describes the characteristics of the included studies.

The meta-analysis included 20 independent cohort studies and 3 RCTs with a total of 1437 patients.

None of the studies were population based. Ten studies were multicenter based, and the rest were from single center. Thirteen studies had more than 40 patients, 3 studies had 30–40 patients, and 7 studies had <30 patients. All of the included studies had clear information reported on the technical success, clinical success, and adverse-event rates, including the subcategory of the adverse events. All the studies were published in the original manuscript form. Overall, 18 studies were considered to be of high quality and rest 5 were considered medium quality. None were of low quality.

Supplementary Table 1 details the study quality assessment.

Technical success and clinical success
The calculated pooled rate of technical success was 91.5% (95% confidence interval [CI]: 87.7–94.2, F² = 76.5).

The calculated pooled rate of clinical success was 87% (95% CI: 82.3–90.6, F² = 72.4).

Figures 1 and 2 show the forest plot for technical and clinical success, respectively.
### Table 1. Study description and clinical outcomes

| Study year | Study type | Single center or multicenter | Abstract or manuscript | Cohort/case control/RCT | Number of patients | Mean age |
|------------|------------|------------------------------|------------------------|--------------------------|--------------------|---------|
| 2019       | Prospective | Multicenter                  | Manuscript             | RCT                      | 47                 | 73      |
| 2018       | Prospective | Single                       | Manuscript             | RCT                      | 14                 | 66.8    |
| 2018       | Prospective | Multicenter                  | Manuscript             | Cohort                   | 19                 | 70.6    |
| 2016       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 35                 | 81      |
| 2016       | Prospective | Single                       | Manuscript             | Cohort                   | 52                 | 68      |
| 2015       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 121                | 65.5    |
| 2015       | Prospective | Single                       | Manuscript             | Cohort                   | 94                 | 67      |
| 2014       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 104                | 66.7    |
| 2015       | Prospective | Single                       | Manuscript             | RCT                      | 49                 | 66      |
| 2013       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 234                | 67.3    |
| 2015       | Prospective | Single                       | Manuscript             | Cohort                   | 21                 | 67.4    |
| 2014       | Prospective | Single                       | Manuscript             | Cohort                   | 27                 | 67      |
| 2015       | Retrospective | Single                       | Manuscript             | Cohort                   | 101                | 70.8    |
| 2014       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 68                 | NA      |
| 2013       | Prospective | Single                       | Manuscript             | Cohort                   | 64                 | 72      |
| 2014       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 45                 | 64.9    |
| 2013       | Retrospective | Single                       | Manuscript             | Cohort                   | 25                 | 59.9    |
| 2013       | Retrospective | Single                       | Manuscript             | Cohort                   | 35                 | 53.4    |
| 2013       | Retrospective | Single                       | Manuscript             | Cohort                   | 35                 | 66.1    |
| 2013       | Retrospective | Single                       | Manuscript             | Cohort                   | 21                 | 62.8    |
| 2012       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 125                | 69.03   |
| 2012       | Retrospective | Multicenter                  | Manuscript             | Cohort                   | 13                 | 68.8    |
| 2011       | Retrospective | Single                       | Manuscript             | Cohort                   | 88                 | 65      |

| Males | Females | Total number of procedures | Technical success | Clinical success | Total adverse effects | Pneumoperitoneum | Infection | Bleeding | Bile leak |
|-------|---------|-----------------------------|-------------------|------------------|-----------------------|-----------------|-----------|----------|-----------|
| 24    | 23      | 54                          | 46                | 46               | 10                    | 0               | 3         | 0        | 1         |
| 9     | 5       | 14                          | 13                | 13               | 2                     | 0               | 0         | 0        | 0         |
| 12    | 7       | 19                          | 19                | 18               | 7                     | 1               | 2         | 0        | 0         |
| 16    | 19      | 35                          | 32                | 31               | 9                     | 0               | 2         | 2        | 0         |
| 27    | 25      | 52                          | 50                | 40               | 5                     | 0               | 1         | 4        | 0         |
| 70    | 51      | 121                         | 112               | 93               | 20                    | 1               | 7         | 2        | 3         |
| 45    | 49      | 94                          | 80                | 79               | 15                    | 0               | 2         | 1        | 0         |
| 58    | 46      | 104                         | 97                | 93               | 9                     | 0               | 1         | 2        | 2         |
| 25    | 24      | 49                          | 46                | 39               | 8                     | 0               | 1         | 4        | 1         |
| 119   | 115     | 234                         | 207               | NA               | 81                    | 12              | 8         | 26       | 27        |
| 12    | 9       | 21                          | 20                | 19               | 2                     | 0               | 0         | 0        | 1         |
| 13    | 14      | 27                          | 27                | 26               | 5                     | 3               | 0         | 1        | 0         |
| 58    | 43      | 101                         | 99                | 93               | 12                    | 2               | 3         | 1        | 5         |
| 34    | 34      | 68                          | 65                | 65               | 14                    | 0               | 5         | 1        | 4         |
| 35    | 29      | 64                          | 61                | NA               | 12                    | 1               | 1         | 2        | 5         |
| 28    | 17      | 45                          | 41                | 39               | 4                     | 1               | 1         | 0        | 0         |
| 13    | 12      | 25                          | 23                | 23               | 5                     | 0               | 1         | 0        | 4         |
| 22    | 13      | 35                          | 34                | 34               | 12                    | 2               | 0         | 0        | 2         |
| 18    | 17      | 35                          | 33                | 32               | 4                     | 1               | 1         | 0        | 0         |
| 11    | 10      | 21                          | 20                | 19               | 2                     | 1               | 0         | 0        | 1         |
| 71    | 54      | 125                         | 84                | 79               | 29                    | 0               | 1         | 6        | 0         |
| 9     | 4       | 13                          | 12                | 11               | 5                     | 0               | 2         | 0        | 0         |
| 45    | 43      | 88                          | 62                | 62               | 6                     | 1               | 1         | 1        | 1         |

RCT: Randomized controlled trial, NA: Not available
Re-intervention and adverse events
The calculated pooled rate of re-intervention was 6.5% (95% CI: 3.8–10.8, $F = 69.3$) [Figure 3].

The calculated pooled rate of adverse events was 17.9% (95% CI: 14.3–22.2, $F = 69.1$) [Figure 4].

All results along with the adverse-event subtypes are summarized in Supplementary Figures 2-6.

At this stage, the authors decided to conduct a subgroup analysis on the data to explore reasons for the observed heterogeneity. Studies were subgrouped based on the study center (single center vs. multicenter) and study type (prospective vs. retrospective; RCT vs. observational). The observed heterogeneity was not explained by this subgrouping. We were not able to subgroup and combine the studies based on the approach to BD (gastric vs. duodenal) due to the fact that the majority of the studies used a combination of these approaches.

Validation of meta-analysis results
Sensitivity analysis
To assess whether anyone 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. In this analysis, no single study significantly affected the outcome or the heterogeneity.

Heterogeneity
Based on Q statistics and $F$ analysis for heterogeneity, substantial heterogeneity ($F = 69.1$) was noted in the analysis of all adverse events, none ($F = 0$) with infection, moderate ($F = 46.7$) with bile leak, moderate ($F = 41.8$) with bleeding, low with pneumo-peritoneum ($F = 2$), and moderate with stent migration ($F = 43.5$).

Substantial heterogeneity ($F = 76.5$) was noted with the analysis of technical success and clinical success ($F = 72.4$).
Publication bias
Based on the visual inspection of the funnel plot [Supplementary Figure 7] as well as the quantitative measurement that used the Egger regression test, there was evidence of publication bias. Further statistics using the fail-Safe N test and Duval and Tweedie’s “Trim and Fill” test revealed the impact of the possible publication bias to be minimal and not to change the calculated estimate or the conclusion of this meta-analysis.

DISCUSSION
Based on the meta-analysis of EUS-guided gallbladder drainage done in 1437 patients from 23 studies, we report a pooled technical success rate of 91.5%, a pooled clinical success rate of 87%, and a pooled adverse event rate of 17.9%.

ERCP remains the preferred procedure for providing internal BD. EUS-BD is utilized in patients who need biliary decompression when ERCP has either failed or is technically not feasible due to an inaccessible papilla and/or surgically altered anatomy and/or malignancy. The reported success and safety of EUS-BD have been variable across many studies. We report a pooled technical success rate of 91.5% with EUS-BD, and our calculated rate is on par with the currently reported values in literature, although with a heterogeneity percentage of 76.5%, which may be due to one or more of the following reasons: (1) different techniques to access routes the gallbladder, including hepatogastrostomy (EUS-HG), cholecystostomy, choledochoduodenostomy (EUS-CDD), and other techniques; (2) use of different modalities of drainage, such as plastic stents, metal stents, lumen-apposing metal stents, nasobiliary drainage tubes, and a combination of these; and (3) the steep learning curve with the use of EUS in BD with accumulating experience. In the study by Vila et al.,[32] endoscopists with >500 EUS procedures had higher success rates than endoscopists who had performed fewer than 500 EUS procedures.

We report a clinical success rate of 87% with EUS-BD. Clinical success has also been variable across many studies, with reported clinical success in the range of...
63.2%–76.9%.[16,17,32,34] Other studies have shown clinical success in the range of 84%–97%.[13,14,18,19,22-25,27,31,33] In the majority of studies,[13-15,18,19,22-25,27-34] clinical success has been closely related to technical success, indicating the importance of a successful procedure. A recent randomized controlled trial by Park et al.[13] compared EUS- and ERCP-guided BD and showed no significant difference in technical and clinical success, with similar adverse events. However, it was a single-center study with a small population size.

Our analysis of the adverse events demonstrated an overall pooled rate of 17.9%. The most commonly reported adverse events were biliary leak and infection. The pooled rate of biliary leaks was 4%, and the pooled rate of infection and stent migration was 3.8%. Our reported rates of the adverse events with EUS-BD are the key findings of this analysis, as studies vary widely in the reported rates of adverse events with EUS-BD. A recently published meta-analysis of studies[38] reporting on EUS-guided CDD reported an overall pooled adverse event rate of 14.5% with EUS-CDD and 20.9% with EUS-HG.[35] The overall adverse events were higher as compared to ERCP, which are reported to be 9.8% as per Enochsson et al.[1]

Our analysis of the subgroups, based on the study type (prospective vs. retrospective) and study center (single vs. multi), showed comparable technical success and clinical success rates in EUS-BD. We, however, noticed a reduction in the heterogeneity \( I^2 \) values with prospectively done studies as compared to the retrospective ones, suggesting that this could be one another contributing factor to our overall observed heterogeneity. We noted that the pooled rate of adverse events reported from multicenter studies was statistically higher when compared to single-center studies (28% vs. 14%, \( P = 0.02 \)). The pooled re-intervention rate was numerically higher with multicenter-based studies as compared to single-center ones (11% vs. 4%, \( P = 0.07 \)) and approached statistical significance.

The strengths of this review are as follows: systematic literature search with well-defined inclusion criteria, carefully excluding redundant studies, detailed extraction
of adverse events, their subcategories, technical success,
and clinical success information.

There are limitations to this study. The included studies
were not entirely representative of the general population
and community practice, with most studies being
performed in tertiary-care referral centers. Our pooled
rates were limited by heterogeneity. Although our subgroup
analysis did not ascertain the cause for the observed
heterogeneity, we believe that the most likely reason is the
route of access to BD. Patient-related characteristics such
as age, smoking, previous attempts and procedures, the
stage of malignancy, and performance characteristics could
influence the calculated rates. However, this estimate is the
best available that summarizes the overall clinical outcomes
with EUS-BD that is being rapidly adopted across centers
around the world.

CONCLUSION

EUS-BD is a safe alternative option in cases where ERCP
fails and in future may become an alternative to ERCP
for BD. However, more well-conducted RCTs are needed
to establish its role as an alternative to ERCP.

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

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Conflicts of interest
There are no conflicts of interest.

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Databases from their inception through February, 2019

Total no. of articles found on search in Pubmed, Embase and others (n = 605)

Titles and abstracts screened (n = 115)

- Excluded (n = 31)
  - Duplicates
  - Case reports
  - Not in English

Abstracts were reviewed (n = 84)

- Excluded (n = 41)
  - Not in English
  - Numbers not mentioned
  - Procedures done for other indications

Full text screened for eligibility (n = 43)

- Excluded (n = 19)
  - Cohort overlap
  - Number incomplete

Studies for systematic review (n = 24)

**Supplementary Table 1. Study quality assessment**

| Author      | Study type | Cohort case-control | Year | Number of patients | Newcastle-Ottawa Scale |
|-------------|------------|---------------------|------|--------------------|------------------------|
| Tsuchiya    | Prospective| Cohort              | 2017 | 19                 | ***                    |
| Kahaleh     | Retrospective| Cohort             | 2016 | 35                 | ***                    |
| Tyberg      | Prospective| Cohort              | 2016 | 52                 | **                     |
| Khhashab    | Retrospective| Cohort            | 2016 | 121                | ***                    |
| Will        | Prospective| Cohort              | 2015 | 94                 | ***                    |
| Dhir        | Retrospective| Cohort            | 2015 | 104                | ***                    |
| Gupta       | Retrospective| Cohort            | 2014 | 234                | ***                    |
| Weillert    | Prospective| Cohort              | 2014 | 21                 | ***                    |
| Song        | Prospective| Cohort              | 2014 | 27                 | **                     |
| Poincloux   | Retrospective| Cohort         | 2013 | 64                 | ***                    |
| Dhir        | Retrospective| Cohort            | 2013 | 68                 | ***                    |
| Kawakubo    | Retrospective| Cohort            | 2013 | 25                 | ***                    |
| Park        | Prospective| Cohort              | 2013 | 45                 | ***                    |
| Bapaye      | Retrospective| Cohort            | 2013 | 35                 | ***                    |
| Dhir        | Retrospective| Cohort            | 2013 | 35                 | ***                    |
| Khhashab    | Retrospective| Cohort            | 2013 | 21                 | ***                    |
| Prachayakul | Retrospective| Cohort           | 2012 | 125                | ***                    |
| Vila        | Retrospective| Cohort            | 2012 | 13                 | ***                    |
| Kim         | Retrospective| Cohort            | 2011 | 66                 | **                     |
| Shah        | Retrospective| Cohort            | 2013 | 68                 | ***                    |

*Jadad-Oxford score for RCT*:

| Author | Study type | Cohort case-control | Year | Number of patients | Jadad-Oxford score |
|--------|------------|---------------------|------|--------------------|-------------------|
| Minaga | Prospective| RCT                | 2019 | 47                 | 2 | 1 | 1 |
| Park   | Prospective| RCT                | 2018 | 14                 | 2 | 0 | 1 |
| Artifon| Prospective| RCT                | 2015 | 49                 | 2 | 0 | 1 |

*meaning: number of stars awarded to each criteria based on the quality of bias. RCT: Randomized controlled trial*

**Supplementary Figure 1.** Preferred Reporting items for Systematic Reviews and Meta-Analyses flow diagram of the study selection
Supplementary Figure 2. Bile leak
Supplementary Figure 3. Bleeding

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Park,2018           | 0.036      | 0.002       | 0.384       |
| Tsuchiya,2017       | 0.026      | 0.002       | 0.210       |
| Kahuleh,2016        | 0.057      | 0.014       | 0.202       |
| Tyberg,2016         | 0.077      | 0.029       | 0.188       |
| Khashab,2016        | 0.017      | 0.004       | 0.064       |
| Wilt,2015           | 0.011      | 0.001       | 0.072       |
| Dhir,2015           | 0.019      | 0.005       | 0.074       |
| Arifon,2015         | 0.082      | 0.031       | 0.196       |
| Gupta,2014          | 0.111      | 0.077       | 0.158       |
| Weilert,2014        | 0.024      | 0.001       | 0.287       |
| Song,2014           | 0.037      | 0.005       | 0.221       |
| Pintoub,2014        | 0.010      | 0.001       | 0.067       |
| Dhir,2013a          | 0.015      | 0.002       | 0.097       |
| Kawakubo,2013       | 0.031      | 0.008       | 0.117       |
| Park,2013           | 0.011      | 0.001       | 0.154       |
| Bapaye,2013         | 0.020      | 0.001       | 0.251       |
| Dhir,2013b          | 0.014      | 0.001       | 0.191       |
| Khashab,2013        | 0.014      | 0.001       | 0.191       |
| Prachayakul,2013    | 0.024      | 0.001       | 0.287       |
| Vila,2012           | 0.046      | 0.022       | 0.103       |
| Kim,2012            | 0.038      | 0.002       | 0.403       |
| Shah,2011           | 0.011      | 0.002       | 0.076       |
| Minaga,2019a        | 0.024      | 0.001       | 0.287       |
| Minaga,2019b        | 0.026      | 0.002       | 0.310       |

Supplementary Figure 3. Bleeding
Supplementary Figure 4. Pneumoperitoneum
Supplementary Figure 5. Stent migration
Supplementary Figure 6. Infection

Supplementary Figure 7. Funnel plot