Adverse events with lumen-apposing metal stents in endoscopic gallbladder drainage: A systematic review and meta-analysis

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ABSTRACT

Background: Lumen-apposing metal stents (LAMS) are rapidly being used in endoscopic interventional drainage procedures and have started to replace the self-expanding metal stents (SEMSs). Its use in gallbladder drainage (GBD) is limited by lack of good-quality studies, and data are scarce on its safety. Methods: We conducted a comprehensive search of multiple electronic databases and conference proceedings including PubMed, Embase, and Web of Science databases (from inception through July 2018) to identify studies that reported on the use of LAMS in GBD. The outcomes measured were the pooled rates of all adverse events (AEs), pooled rates of early AEs and pooled rates of delayed AEs.

Results: A total of 8 studies (393 patients) were included. The pooled rate of all AEs was 12.7% (95% CI 8.4-18.7, F = 7.7) compared to 17.5% (95% CI 10.2-28.2, F = 65.1) with other SEMS, P = 0.39. The rate of early AEs with LAMS in endoscopic ultrasound-GBD (EUS-GBD) was 6.5% (95% CI 4.2-10, F = 1.2), and the rate of delayed AEs was 8.3% (95% CI 5.8-11.9, F = 4.8). The rate of recurrent cholecystitis and/or cholangitis was 4.6% (95% CI 2.6-9.5, F = 0) and the pooled rate of death was 5% (95% CI 2.6-9.5, F = 36.4). Conclusion: We report an overall AE rate of 13% with LAMS in EUS-GBD. Early AE risk appears to be 6.5% and delayed AE risk appears to be 8%. Our results are analyzed out of good-quality studies, with minimal to zero heterogeneity.

Key words: Adverse events, gallbladder drainage, lumen-apposing metal stents, self-expanding metal stents

INTRODUCTION

Lumen-apposing metal stents (LAMS) were first introduced in 2012 and made widely clinically...
available in 2015. The different LAMS commercially available for use are the AXIOS stent (by Xlumena Inc., Mountain View, CA, USA); the Niti-S SPAXUS and NAGI stents (by Taewoong-Medical Co., Ilsan, Korea); the AIX stent (by Leufen Medical, Aachen, Germany); and the brachiocephalic fistula (BCF) stent (by Hanaro MRI Tech). All are made of nitinol wire and fully covered with silicon. The shape of a LAMS is designed to keep the target object (pseudocyst, walled-off necrosis, etc.) closely apposed to the gastrointestinal (GI) lumen. They are now widely employed in many clinical settings, including the treatment of benign luminal GI strictures, endoscopic drainage of pancreatic fluid collections, endoscopic gallbladder drainage (E-GBD), and endoscopic gastrojejunostomy.

Like any other advanced endoscopic intervention, the use of LAMS carries risks of adverse events (AEs). Early recognition of AEs is critical to minimize morbidity and mortality. These AEs can be immediate during the stent deployment or delayed. Data are limited regarding the safety of LAMS when used to provide E-GBD. The reported results are highly varied as the current literature consists of many small retrospective case series. Recently published qualitative and quantitative reviews are limited by inclusion of these small studies. Small and low-quality studies add to the heterogeneity and negatively impact the overall reliability of the results. Despite the limited data on the safety of LAMS, there has been clinical adoption of this stent globally in setting where a LAMS is used, and studies have suggested that it can be safely used in an outpatient setting.

We conducted this meta-analysis, using only good-quality studies, to better understand and quantify the AE rates with the use of LAMS in GBD.

METHODS

Search strategy
We conducted a comprehensive search of several databases and conference proceedings including PubMed, Embase, and Web of Science databases (earliest inception to July 2018). We followed the preferred reporting items for systematic reviews and meta-analyses guidelines, by using predefined protocol, to identify studies reporting the use of LAMS in GBD. An experienced medical librarian using inputs from the study authors helped with the literature search.

Keywords used in the search included a combination of “lumen-apposing metal stent,” “AXIOS stent,” “SPAXUS stent,” “NAGI stent,” “NITI-S stent,” “AIX stent,” “BCF stent,” “endoscopic ultrasound guided,” and “gall-bladder drainage.” The search was restricted to studies in human subjects and published in English language in peer-reviewed journals. Three authors (M.B., S.M., A.R.) 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 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) use of LAMS in GBD and (2) data on AEs attributed to LAMS. Studies irrespective of the reason for GBD, the size of LAMS, the commercial type of LAMS, geography, and abstract/manuscript status were included as long as they provided data needed for the analysis.

Following were our exclusion criteria: (1) studies that provided no data on AEs attributed to LAMS, (2) studies that reported on self-expanding metal stents (SEMSs) that were not lumen apposing, and (3) <30 patients in the study cohort.

In case of multiple publications from the same cohort, data from the most recent and/or most appropriate comprehensive report were included. In our search process, we encountered two such studies, one by Jang et al. and other by Irani et al.

Data abstraction and quality assessment
Data on study-related outcomes in the individual studies were abstracted onto a standardized form by at least 2 authors (M. B., S. M.) independently, and 3 authors (M. B., S. M., G. R.) did the quality scoring independently.

Using a scale modified from the Newcastle–Ottawa scale for cohort studies assessed the quality of included studies. This quality score consisted of
6 questions: representative of the average adult in the community (1 point for population-based studies, 0.5 point for multicenter studies; 0 point for a single-center hospital-based study); large cohort size (1 point if >30 patients, 0.5 point if between 15 and 30 patients, 0 point if <15 patients); information on overall AEs (1 point if reported; 0 point if not reported); information on subtypes of AEs (1 point if reported, 0 point if not reported); type of article write-up (1 point if original manuscript, 0.5 point if abstract); and attrition rate (1 point if all patients were accounted for, 0.5 point if <50% patients lost to follow-up, 0 point if >50% patients lost to follow-up). A score of ≥5, 3–4, and <3 was considered suggestive of high-quality, medium-quality, and low-quality study, respectively.

Outcomes assessed
The primary analysis focused on assessing the pooled rate of overall AEs in EUS-GBD with LAMS. The pooled rate of AE in EUS-GBD with other SEMS was used as a comparator.

Our secondary analysis focused on calculating the following in EUS-GBD with LAMS:
1. Pooled rates of early AE; with further classification into bleeding, bile leak, stent occlusion, perforation, and stent migration
2. Pooled rates of delayed AE; with further classification of the delayed AEs into bleeding, bile leak, stent occlusion, and stent migration
3. Pooled rates of recurrent cholecystitis and/or cholangitis and death, and
4. Pooled rates of technical success and clinical success.

Definitions
Majority of studies defined AEs as any procedure, drain or stent-related event. Studies did not mention any predetermined criterion to define bile leak, perforation, stent occlusion, and stent migration. These were considered as AEs even if the patient suffered no clinical symptoms out of the event. Bleeding was defined as significant if requiring blood product transfusion, endoscopic therapy, and radiologic or surgical interventions. AEs reported within the first 2 weeks of EUS-guided LAMS placement were considered early, and the ones reported after 2 weeks of intervention were considered delayed.

Technical success was defined as the ability to place a transmural LAMS into the gallbladder and/or the bile duct as determined by the flow of bile and/or pus. Clinical success was defined as the resolution of symptoms, laboratory abnormalities, and/or radiologic abnormalities. There was variability in the laboratory resolution cutoff among studies, with majority defining it as a decrease in bilirubin levels to <10% of initial levels and/or <50% of initial levels with resolution of clinical symptoms.

Statistical analysis
We used meta-analysis techniques to calculate the pooled estimates in each case following the methods suggested by DerSimonian and Laird using the random effects model.[13] When the incidence of an outcome was zero in a study, a correction of 0.01 was added to the number of incident cases before statistical analysis.[14] We assessed heterogeneity between study-specific estimates using two methods, the Cochran Q statistical test for heterogeneity and the $I^2$ statistic.[15,16] In this, values of <30%, 30%–60%, 61%–75%, and >75% were suggestive of low, moderate, substantial, and considerable heterogeneity, respectively.[17] Since random effects model estimates an average effect, we also calculated the 95% prediction interval, which deals with the dispersion of the effects.[18] Publication bias was ascertained, qualitatively, by visual inspection of funnel plot, and quantitatively, by the Egger test.[20]

All analyses were performed using comprehensive meta-analysis software, version 3 (BioStat, Englewood, NJ, USA).

RESULTS

Search results and population characteristics
From an initial total of 658 citations identified using our search strategy, our search of the database resulted in 36 studies that met our inclusion criteria. Of these, 18 studies were excluded because they had <30 patients in their study cohort and 10 studies were excluded because of other methods and/or routes used to drain the gallbladder. A total of 8 studies were included in the final analysis. All studies used the AXIOS stent except one study that used the Spaxus stent.[23] The schematic diagram of study selection is illustrated in Figure 1. Table 1 describes the study and population characteristics.

Majority of the population consisted of males (37%–65%), with an age range of 25–93 years.
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**Table 1. Study and population characteristics**

| Study                          | Most common clinical indication | Male % | Age (years) | Procedure Time (min) | Stent     | Follow-up period (days) | Total n | All adverse events | Success | Technical | Clinical | Study quality |
|-------------------------------|---------------------------------|--------|-------------|--------------------|-----------|------------------------|---------|-------------------|---------|-----------|----------|---------------|
| Kunda et al., 2016, USA[23]   | Malignancy                      | 54     | 49-93       | 11 to 65           | HA & CA  | 151+/−145              | 57      | 8                 | 56      | 54/56     | High     |               |
| Anderloni et al., 2018, Italy[21] | Malignancy                      | 54     | 71.3+/−12.4 | 10 to 104          | HA       | 18-411                 | 35      | 5                 | 32/34   | 30/32     | Medium   |               |
| Walter et al., 2016, Netherlands[24] | Acute Cholecystitis            | 37     | NR          | NR                 | CA       | 298+/−82               | 30      | 4                 | 27      | 26/27     | High     |               |
| Irani et al., 2017, USA[11]   | Acute Cholecystitis            | 64     | 25-87       | 18 to 52           | HA & CA  | 1-621                  | 45      | 6                 | 44      | 43/44     | High     |               |
| Dollhopf et al., 2017, Germany[5] | Acute Cholecystitis            | 48     | mean 75+/−11| 8 to 60            | HA       | 201+/−226              | 75      | 5                 | 74      | 71/74     | High     |               |
| Teoh et al., 2018, China[25]  | Acute Cholecystitis and Malignancy | 56   | 68+/−13     | NR                 | Spaxus   | 29-38                  | 36      | 0                 | 32      | 29/32     | High     |               |
| Teoh et al., 2017, China/Spain[26] | Acute Cholecystitis            | 51     | 82.7+/−7.9  | NR                 | HA & CA  | 450.7+/−343            | 59      | 8                 | 57      | 53        | High     |               |
| Garcia-Alonso et al., 2018, Spain[22] | Multiple indications          | 65     | 57.9-83.6   | NR                 | HA & CA  | 31-246.5               | 56      | 11                | NR      | NR        | Medium   |               |

NR: Not reported, AE: Adverse events; HA: Hot-AIYOS, CA: Cold-AIYOS. (Table 1. Study and population characteristics)

Procedure time was reported in the range of 8–104 min. Acute cholecystitis and/or malignancy was the clinical indication for EUS-GBD. Period of follow-up ranged from 1 day to 411 days.

Characteristics and quality of included studies

Table 1 describes the study and population characteristics. None of the studies were population based. Six studies[5,11,23-26] were multicenter based and the rest 2[21,22] were from single center. All studies had more than or equal to 30 patients. All studies reported on the overall AEs but were variable in the subtypes. One study by Garcia-Alonso et al.[22] reported only on stent migration and gastrointestinal bleeding. All studies except two by Anderloni et al. and Teoh et al.[21,23] were full manuscripts and all studies had adequate follow up of their study population. Overall, 6 studies[5,11,23-26] were considered to be of high quality and the rest 2[21,22] were of medium quality. None were of low quality. The study by Walter et al.[24] was a prospectively designed study [Supplement Table 1 Study quality assessment].

Adverse events in EUS-gallbladder drainage with lumen-apposing metal stents

The rate of all AEs with LAMS in EUS-GBD (8 studies,[5,11,23-26] 393 patients, 47 events) was 12.7% (95% CI 8.4-18.7, \(I^2 = 7.7\)), as compared to 17.5% (95% CI 10.2-28.2, \(I^2 = 65.1\)) with the use of other SEMS (6 studies,[27-32] 154 patients), without any statistical significance to the difference, \(P = 0.39\) [Figure 2].

Rates of AE subtypes are as given below:
- Bleeding: 4.2% (95% CI 2.2-7.9, \(F = 31.8\))
- Bile leak: 2.4% (95% CI 1.1-5.1, \(F = 0\))
- Stent occlusion: 5.2% (95% CI 3.8-7.3, \(F = 0\))
- Perforation: 2.3% (95% CI 1.1-4.7, \(F = 0\))
- Stent migration: 3.2% (95% CI 1.8-5.8, \(F = 0\)).

[forest plots: Supplement Figure 1, 4, 7, 8, 9].
Rates of early AE subtypes are as given below:
- Bleeding: 2.6% (95% CI 0.9-7.2, $I^2 = 47.1$)
- Bile leak: 1.3% (95% CI 0.5-3.3, $I^2 = 0$)
- Stent occlusion: No events
- Perforation: 2.3% (95% CI 1.1-4.7, $I^2 = 0$)

Procedure and/or lumen-apposing metal stents-related early adverse events

The rate of all early AE with LAMS in EUS-GBD (8 studies, 393 patients, 19 events) was 6.5% (95% CI 4.2-10, $F = 1.2$) [Figure 3].
Stent migration: 1.5% (95% CI 0.6-3.5, $I^2 = 0$).

[forest plots: Supplement Figure 2, 5, 8, 10].

Lumen-apposing metal stents-related delayed adverse events; recurrent cholecystitis and/or cholangitis; death

The rate of all delayed AE with LAMS in EUS-GBD (8 studies, [5,11,21-26] 393 patients, 28 events) was 8.3% (95% CI 5.8-11.9, $I^2 = 4.8$) [Figure 4].

Rates of delayed AE subtypes are as given below:

• Bleeding: 2% (95% CI 0.9-4.1, $I^2 = 0$)
• Bile leak: 1.9% (95% CI 0.8-4.3, $I^2 = 0$)
• Stent occlusion: 5.2% (95% CI 3.8-7.6, $I^2 = 0$)
• Stent migration: 3% (95% CI 1.5-5.8, $I^2 = 0$).

[forest plots: Supplement Figure 3, 6, 7, 11].

The rate of recurrent cholecystitis and/or cholangitis (6 studies, [5,11,22,24-26] 301 patients, 11 events) was 4.6% (95% CI 2.6-8.0, $I^2 = 0$) [Supplement Figure 12].

The rate of death (7 studies, [5,11,21,23-26] 337 patients, 15 events) was 5% (95% CI 2.6-9.5, $I^2 = 36.4$) [Supplement Figure 13]. All adverse events reported are summarized in Table 2 and all pooled results are summarized in Table 3. Forest plots for all adverse event sub-types are given in supplementary material.

Technical success and clinical success

The rates of technical success and clinical success with LAMS in EUS-GBD (8 studies, [5,11,21-26] 393 patients) were 94.9% (95% CI 90.8-97.3, $I^2 = 25.5$) and 94.6% (95% CI 91.4-96.7, $I^2 = 0$), respectively [forest plots: Supplement Figure 14 and 15].

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. 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 ($I^2 < 30$) to no ($I^2 = 0$) heterogeneity was noted in the analyses of the primary and secondary outcomes of LAMS in EUS-GBD.

Publication bias

Based on visual inspection of the funnel plot as well as quantitative measurement that used the Egger regression test, there was no evidence of publication bias [Supplement Figure 16 - funnel plot].

Table 2. Breakdown of adverse events

| Study                        | Total n | All ae | Early Adverse-events | Delayed Adverse-events | Recurrent Cholecystitis/ Cholangitis | Death |
|------------------------------|---------|--------|----------------------|------------------------|--------------------------------------|-------|
| Kunda et al., 2016           | 57      | 8      | 4                    | 0                      | 2                                   | 1     |
| Anderloni et al., 2018       | 35      | 5      | 0                    | 0                      | 0                                   | 0     |
| Walter et al., 2016          | 30      | 4      | 0                    | 0                      | 0                                   | 0     |
| Irani et al., 2017           | 45      | 6      | 2                    | 1                      | 0                                   | 0     |
| Dollhopf et al., 2017        | 75      | 5      | 3                    | 1                      | 0                                   | 0     |
| Teoh et al., 2018            | 36      | 0      | 0                    | 0                      | 0                                   | 0     |
| Teoh et al., 2017            | 59      | 8      | 3                    | 0                      | 0                                   | 0     |
| Garcia-Alonso et al., 2018   | 56      | 11     | 7                    | NR                     | NR                                  | 4     |

NR: not reported, AE: adverse events; HA: Hot-AXIOS, CA: Cold-AXIOS
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Table 3. EUS-GBD with LAMS: Summary of all results

| Group                  | Overall  | Early    | Delayed  |
|------------------------|----------|----------|----------|
|                        | (95% CI, P%) | (95% CI, P%) | (95% CI, P%) |
| Adverse events         | 12.7 (8.4-18.7, 7.7) | 6.5 (4.2-10.1, 1.2) | 8.3 (5.8-11.9, 4.8) |
| Bleeding               | 4.2 (2.2-7.9, 31.8) | 2.6 (0.9-7.2, 47.1) | 2% (0.9-4.1, 0) |
| Bile leak              | 2.4 (1.1-5.1, 0) | 1.3 (0.5-3.3, 0) | 1.9% (0.8-4.3, 0) |
| Stent occlusion        | 5.2 (3-8.7, 0) | No events | 5.2% (3-8.7, 0) |
| Perforation            | 2.3 (1.1-4.7, 0) | 2.3 (1.1-4.7, 0) | Not reported |
| Stent migration        | 3.2 (1.8-5.8, 0) | 1.5 (0.6-3.5, 0) | 3% (1.5-5.8, 0) |
| Cholecystitis          | 4.6 (2.6-8.0, 0) | - | - |
| Death                  | 5 (2.6-9.5, 36.4) | - | - |
| Technical success      | 94.9 (90.8-97.3, 25.5) | - | - |
| Clinical success       | 94.6 (91.4-96.7, 0) | - | - |

DISCUSSION

Our meta-analysis is the first study to report pooled data from good-quality studies, avoiding small case studies and reports, on the AEs of LAMS in GBD. We report an overall AEs rate of 13% with LAMS as compared to 17.5% with other SEMS, with no statistical significance. The early AE rate was 6.5%, and the delayed AE rate was 8%.

The calculated early versus delayed rates for bleeding (2.6% vs 2%), bile leak (1.3% vs 1.9%), and stent migration (1.5% vs 3%) were comparable. The calculated risk of perforation was 2.3% that was reported only as an early AE. The calculated rate of stent occlusion was 5.2% that was reported only as a delayed AE. The rate of cholecystitis and/or cholangitis was 4.6%, and the rate of death was 5%. Our calculated rate of death needs to be interpreted with caution. Majority of studies reported death as the end outcome and were mostly related to the underlying disease process. None of the reported death events were related to the procedure and/or the use of LAMS. The calculated technical success was 94.9% and clinical success was 94.6%.

Why do this study and how do our results compare with other recently published similar studies? At the time this study was generated, at least four other systematic reviews were published on similar topic. These are studies by Han et al.,[33] Manta et al.,[34] Kalva et al.[35] and Jain et al.[36] All studies, including our study, were consistent in the reporting of calculated technical success (93.86%–95%) and clinical success (92.48%–93%) rates. Nevertheless, our study differs significantly from these studies in the calculation and reporting of the AEs. The study by Jain et al.[36] was a qualitative review without a quantitative pooling of results. Manta et al.[34] did not report the pooled rates of AEs. Kalva et al.[35] included the BONA-AL stent (Standard Sci Tech Inc, Seoul, Korea) in their analysis, which technically does not generate lumen-apposing force and hence is not considered a LAMS. Han et al.[33] studied the use of LAMS in pancreatic fluid collections and GBD. They reported a pooled AE rate of 17.1% with LAMS in EUS-GBD without any mention of heterogeneity and/or validation statistics for their meta-analysis. All these studies were severely limited by the inclusion of multiple small studies.

The strengths of our review are as follows: systematic literature search with well-defined inclusion criteria, carefully excluding small studies, case reports and redundant studies, inclusion of high quality studies, detailed extraction of clinically useful data in terms of early and delayed AEs attributed to LAMS, rigorous evaluation of study quality, overall low to zero heterogeneity, and statistics to establish and/or refute the validity of the results of our meta-analysis.

There were few limitations to this study and are the ones expected with any meta-analysis. The included studies were not entirely representative of the general population and community practice. The studies did not uniformly follow the severity of AEs grading according to the lexicon of endoscopic AEs. The data itself were derived from a patient group with high morbidity and/or mortality and were not able to stratify our results based on patient performance characteristics. Paucity of data limited our ability to analyze the events with respect to the commercial type of stent used. More large-scale studies are needed to better compare the safety profiles of the different types of LAMS, along with cost-effectiveness. However, this estimate is still the best available estimate that may be used in counseling patients undergoing GBD with LAMS.
CONCLUSION

In conclusion, our estimated risk of LAMS-related AE with EUS-GBD is 13%, which is the lowest reported in literature thus far. The rate of early AE is 6.5%, and the risk of delayed AE is 8%. There was low to no heterogeneity in our analysis.

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

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Conflicts of interest
There are no conflicts of interest.

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SUPPLEMENT MATERIALS

Supplement Figure 1. Forest plot - overall bleeding

Supplement Figure 2. Forest plot - early bleeding

Supplement Figure 3. Forest plot - delayed bleeding
### Meta Analysis

**Supplement Figure 4.** Forest plot - overall bile leak

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al[23]     | 0.009      | 0.001       | 0.123       |
| Anderloni et al[21] | 0.014      | 0.001       | 0.187       |
| Walter et al[24]    | 0.016      | 0.001       | 0.211       |
| Irani et al[31]     | 0.044      | 0.011       | 0.161       |
| Dollhopf et al[38]  | 0.007      | 0.000       | 0.097       |
| Teoh et al[39]      | 0.014      | 0.001       | 0.182       |
| Teoh et al[39]      | 0.034      | 0.008       | 0.126       |
|                     | 0.024      | 0.011       | 0.061       |

### Meta Analysis

**Supplement Figure 5.** Forest plot - early bile leak

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al[23]     | 0.009      | 0.001       | 0.123       |
| Anderloni et al[21] | 0.014      | 0.001       | 0.187       |
| Walter et al[24]    | 0.016      | 0.001       | 0.211       |
| Irani et al[31]     | 0.022      | 0.003       | 0.142       |
| Dollhopf et al[38]  | 0.007      | 0.000       | 0.097       |
| Teoh et al[39]      | 0.014      | 0.001       | 0.182       |
| Teoh et al[39]      | 0.008      | 0.001       | 0.120       |
|                     | 0.013      | 0.005       | 0.033       |

### Meta Analysis

**Supplement Figure 6.** Forest plot - delayed bile leak

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al[23]     | 0.009      | 0.001       | 0.123       |
| Anderloni et al[21] | 0.014      | 0.001       | 0.187       |
| Walter et al[24]    | 0.016      | 0.001       | 0.211       |
| Irani et al[31]     | 0.022      | 0.003       | 0.142       |
| Dollhopf et al[38]  | 0.007      | 0.000       | 0.097       |
| Teoh et al[39]      | 0.014      | 0.001       | 0.182       |
| Teoh et al[39]      | 0.034      | 0.008       | 0.126       |
|                     | 0.019      | 0.008       | 0.043       |
### Supplement Figure 7. Forest plot - stent occlusion (all delayed)

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al.[23]   | 0.070      | 0.027       | 0.173       |
| Anderloni et al.[21] | 0.086      | 0.028       | 0.234       |
| Walter et al.[24]  | 0.067      | 0.017       | 0.231       |
| Irani et al.[21]   | 0.044      | 0.011       | 0.161       |
| Dollhopf et al.[26] | 0.007      | 0.000       | 0.097       |
| Teoh et al.[27]    | 0.014      | 0.001       | 0.182       |
| Teoh et al.[28]    | 0.017      | 0.002       | 0.111       |
|                   | 0.052      | 0.030       | 0.087       |

### Supplement Figure 8. Forest plot - perforation (all early)

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al.[23]   | 0.035      | 0.009       | 0.130       |
| Anderloni et al.[21]| 0.014      | 0.001       | 0.187       |
| Walter et al.[24]  | 0.016      | 0.001       | 0.211       |
| Irani et al.[21]   | 0.011      | 0.001       | 0.151       |
| Dollhopf et al.[26] | 0.013      | 0.002       | 0.089       |
| Teoh et al.[27]    | 0.014      | 0.001       | 0.182       |
| Teoh et al.[28]    | 0.034      | 0.008       | 0.126       |
|                   | 0.023      | 0.011       | 0.047       |

### Supplement Figure 9. Forest plot - overall stent migration

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al.[23]   | 0.018      | 0.002       | 0.114       |
| Anderloni et al.[21]| 0.029      | 0.004       | 0.177       |
| Walter et al.[24]  | 0.016      | 0.001       | 0.211       |
| Irani et al.[21]   | 0.011      | 0.001       | 0.151       |
| Dollhopf et al.[26] | 0.027      | 0.007       | 0.100       |
| Teoh et al.[27]    | 0.014      | 0.001       | 0.182       |
| Teoh et al.[28]    | 0.017      | 0.002       | 0.111       |
| Garcia-Alonso et al.[29] | 0.071  | 0.027 | 0.175       |
|                   | 0.032      | 0.018       | 0.058       |
Supplement Figure 10. Forest plot - early stent migration

Supplement Figure 11. Forest plot - delayed stent migration

Supplement Figure 12. Forest plot - recurrent cholangitis
### Supplement Figure 13. Forest plot - death

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al[20]     | 0.035      | 0.009       | 0.130       |
| Anderloni et al[21] | 0.029      | 0.004       | 0.177       |
| Walter et al[22]    | 0.167      | 0.071       | 0.343       |
| Irani et al[23]     | 0.022      | 0.003       | 0.142       |
| Dollhopf et al[24]  | 0.040      | 0.013       | 0.117       |
| Teoh et al[25]      | 0.014      | 0.001       | 0.182       |
| Teoh et al[26]      | 0.051      | 0.016       | 0.146       |
|                     | 0.050      | 0.026       | 0.095       |

### Supplement Figure 14. Forest plot - technical success

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al[20]     | 0.982      | 0.886       | 0.998       |
| Anderloni et al[21] | 0.941      | 0.793       | 0.985       |
| Walter et al[22]    | 0.900      | 0.732       | 0.967       |
| Irani et al[23]     | 0.978      | 0.858       | 0.997       |
| Dollhopf et al[24]  | 0.987      | 0.911       | 0.998       |
| Teoh et al[25]      | 0.689      | 0.739       | 0.958       |
| Teoh et al[26]      | 0.966      | 0.874       | 0.992       |
|                     | 0.949      | 0.908       | 0.973       |

### Supplement Figure 15. Forest plot - clinical success

| Study name          | Event rate | Lower limit | Upper limit |
|---------------------|------------|-------------|-------------|
| Kunda et al[20]     | 0.964      | 0.868       | 0.991       |
| Anderloni et al[21] | 0.938      | 0.782       | 0.984       |
| Walter et al[22]    | 0.963      | 0.779       | 0.995       |
| Irani et al[23]     | 0.977      | 0.856       | 0.997       |
| Dollhopf et al[24]  | 0.959      | 0.882       | 0.987       |
| Teoh et al[25]      | 0.906      | 0.746       | 0.969       |
| Teoh et al[26]      | 0.930      | 0.827       | 0.973       |
|                     | 0.946      | 0.914       | 0.967       |
### Supplementary Table 1. Study quality assessment

| QUESTION                                      | SCORING SCHEME | Kunda et al., 2016\(^{(23)}\) | Anderloni et al., 2018\(^{(21)}\) | Walter et al., 2016\(^{(24)}\) | Irani et al., 2017\(^{(11)}\) | Dollhopf et al., 2017\(^{(5)}\) | Teoh et al., 2018\(^{(25)}\) | Teoh et al., 2017\(^{(26)}\) | Garcia-Alonso et al., 2018\(^{(22)}\) |
|-----------------------------------------------|-----------------|-------------------------------|-----------------------------------|---------------------------------|---------------------------------|---------------------------------|-------------------------------|--------------------------|-------------------------------|
| Representative of the average adult in the community | 1 point: population-based studies, 0.5 point: multicenter studies, 0 point: single-center hospital-based study | 0.5 | 1 | 0 | 1 | 1 | 1 | 1 | 0 |
| Cohort size                                   | 1 point: >30 patients 0.5 point: 30-15 patients 0 point: <15 patients | 1 | 1 | 0.5 | 1 | 1 | 1 | 1 | 1 |
| Information on overall adverse events         | 1 point: reported with clarity 0 point: not reported | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| Information on adverse event sub-types        | 1 point: reported with clarity 0 point: not reported | 1 | 1 | 1 | 1 | 1 | 1 | 0.5 | 0.5 |
| Type of article write up                      | 1 point: original manuscript 0.5 point: abstract | 1 | 0.5 | 1 | 1 | 1 | 0.5 | 1 | 1 |
| Attrition rate                                | 1 point: all patients accounted for 0.5 point: <50% not accounted for 0 point: >50% not accounted for | 1 | 1 | 1 | 1 | 1 | 1 | 1 | 1 |
| **TOTAL (maximum=6; high >5; medium 5-3; low<3)** | | **5.5** | **4.5** | **5** | **5.5** | **5.5** | **5** | **5** | **4.5** |

**Supplement Figure 16.** Funnel plot – all studies