Communication from the ASGE Standards of Practice Committee

GUIDELINE

ASGE American Society for Gastrointestinal Endoscopy

American Society for Gastrointestinal Endoscopy guideline on management of post–liver transplant biliary strictures: methodology and review of evidence

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This document was reviewed and approved by the Governing Board of the American Society for Gastrointestinal Endoscopy.

This clinical practice guideline from the American Society for Gastrointestinal Endoscopy provides an evidence-based approach for strategies to manage biliary strictures in liver transplant recipients. This document was developed using the Grading of Recommendations Assessment, Development and Evaluation framework. The guideline addresses the role of ERCP versus percutaneous transhepatic biliary drainage and covered self-expandable metal stents (cSEMSs) versus multiple plastic stents for therapy of strictures, use of MRCP for diagnosing post-transplant biliary strictures, and administration of antibiotics versus no antibiotics during ERCP. In patients with post-transplant biliary strictures, we suggest ERCP as the initial intervention and cSEMSs as the preferred stent. In patients with unclear diagnosis or intermediate probability of a stricture, we suggest MRCP as the diagnostic modality. We suggest that antibiotics should be administered during ERCP when biliary drainage cannot be assured. (Gastrointest Endosc 2023;97:615-37.)

(footnotes appear on last page of article)

This guideline document was prepared by the Standards of Practice Committee of the American Society for Gastrointestinal Endoscopy using the best available scientific evidence and considering a multitude of variables including but not limited to adverse events, patients' values, and cost implications. The purpose of these guidelines is to provide the best practice recommendations that may help standardize patient care, improve patient outcomes, and reduce variability in practice.

We recognize that clinical decision-making is complex. Guidelines, therefore, are not a substitute for a clinician's judgment. Such judgements may, at times, seem contradictory to our guidance because of many factors that are impossible to fully consider by guideline developers. Any clinical decisions should be based on the clinician's experience, local expertise, resource availability, and patient values and preferences.

This document is not a rule and should not be construed as establishing a legal standard of care or as encouraging, advocating for, mandating, or discouraging any particular treatment. Our guidelines should not be used in support of medical complaints, legal proceedings, and/or litigation, because they were not designed for this purpose.

Bile duct strictures are a common adverse outcome of orthotopic liver transplantation and are associated with significant morbidity.[1] Managing post–liver transplant biliary strictures requires a multidisciplinary, evidence-based approach involving diagnostic imaging and invasive procedures. The American Society for Gastrointestinal Endoscopy (ASGE) Standards of Practice Committee have developed guidelines for management of biliary strictures after liver transplantation. These guidelines follow the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology. In formulating these guidelines, we conducted extensive literature reviews, including a formal systematic review of the literature and meta-analyses. To make all information

we collected and analyzed readily assessable, this guideline is presented in 2 documents. This document details guideline methodology including formulation of clinical questions, literature searches, data analyses, panel composition, evidence profiles, and other considerations like cost-effectiveness, patient preferences, and health equity. For each clinical question, this document includes outcomes of interest, pooled-effect estimates, and evidence that was considered by the panel in making final recommendations. The "Summary and Recommendations" is published separately and provides a summary of our findings and final recommendations.

METHODS

Formulation of clinical questions

This document was prepared by the Standards of Practice Committee of the ASGE and was conceptualized and conducted according to the GRADE framework.[2,3] Evidence was presented to a panel of experts representing various stakeholders including transplant surgery, transplant hepatology, and gastroenterology. A patient advocate was included on the panel to share patient values and preferences through lived experience. All panel members were required to disclose potential financial and intellectual conflicts of interest, which were addressed according to ASGE policies. In developing these recommendations, we took into consideration the certainty in the evidence, benefits and harms of different management options, feasibility, patient values and preferences, resources utilization, cost-effectiveness, and health equity. The final wording of the recommendations including direction and strength were approved by all members of the panel and the ASGE governing board. Stronger recommendations are stated as "we recommend," whereas conditional recommendations are indicated by "we suggest" based on the GRADE framework.[4]

This guideline addressed the following clinical questions using the GRADE format (Table 1):

1. In liver transplant recipients with a biliary stricture, should ERCP be used compared with percutaneous transhepatic biliary drainage (PTBD) as the initial therapy of choice for management of biliary strictures?
2. In patients with post-transplant biliary strictures, should covered self-expandable metal stents (cSEMSs) be used compared with multiple plastic stents (MPSs) as the initial therapy of choice for management of biliary strictures?
3. In liver transplant recipients with suspected biliary stricture, should MRCP be considered the preferred diagnostic modality?
4. In patients with post–liver transplant biliary strictures without cholangitis undergoing elective ERCP, should antibiotics be administered or not administered to reduce risk of infections?

Literature search and study selection criteria

To inform the guideline panel, comprehensive literature searches were performed by a medical librarian using Ovid MEDLINE, EMBASE, and Wiley Cochrane. The searches were limited to prospective and retrospective studies published in the English language and encompassed a time frame from inception to 2020. Case reports, case series with <10 patients, animal studies, conference posters, and abstracts were excluded. The searches were performed for each question, and specific search criteria were used.

For each patient/population, intervention, comparison, and outcomes (PICO) question, a literature search for existing systematic reviews and meta-analyses was also performed. If none was identified, full systematic reviews and meta-analyses (when possible) were conducted using the recommendations of the Preferred Reporting Items for Systematic reviews and Meta-Analyses criteria. Citations were imported into EndNote (Thompson Reuters, Philadelphia, Pa, USA), and duplicates were removed. The EndNote library was then uploaded into Covidence (www.covidence.org). Studies were first screened by title and abstract and then by full text by 2 independent reviewers (D.R.K. and S.K.A.), and all conflicts were resolved by consensus. When applicable, available systematic reviews and meta-analyses were updated based on literature review as described above.

Data extraction and statistical analysis

Data were extracted by 2 independent reviewers (D.R.K. and S.K.A.). The primary estimate of effect was based on a priori–identified outcomes of interest. Pooled analyses were performed for PICO questions 1, 2, and 4 and a meta-analysis for PICO question 3. Heterogeneity was assessed using the I^2 and Q statistic. Significant heterogeneity was defined as either $I^2 > 50\%$ or a significant P value (<.05) on the Q statistic. Random-effects models were used for analysis. Studies were weighted based on size. Publication bias was assessed using funnel plots. Statistical analyses were performed using Comprehensive Meta Analysis V3 (Biostat Inc, Englewood, NJ, USA).

Panel composition and conflict of interest management

A panel of stakeholders was assembled to review evidence and make recommendations. The panel consisted of lead authors (D.R.K. and S.K.A.), committee members with expertise in systematic reviews and meta-analyses (N.C.T. and M.D.), a transplant hepatologist with expertise in ERCP (M.E.H.), a transplant surgeon (S.C.), Standard of Practice committee members, and committee chair (B.J.Q.). A patient representative (T.T. [see Acknowledgments]) from an advocacy organization (National Organization for Transplant Enlightenment) was also included. A virtual meeting was convened on November 13, 2021.

All panel members were required to disclose potential financial and intellectual conflicts of interest, which were addressed according to ASGE policies set forth in the ASGE & Journal Policy for Managing Declared Conflicts

TABLE 1. Summary of population, intervention, comparator, and outcomes questions

Question no.	Population	Intervention	Comparator	Outcomes	Rating
1	Liver transplant recipients with post-transplant biliary strictures	ERCP	Percutaneous transhepatic biliary drainage	Technical success	Critical
				Adverse events	Critical
				Allograft failure	Critical
				Allograft rejection	Critical
				Acute mortality	Critical
				Readmission	Critical
				Length of stay	Critical
				Number of admissions	Critical
				Cost	Important
2	Liver transplant recipients with post-transplant biliary strictures undergoing ERCP	Fully-covered self-expandable metal stent	Multiple plastic stents	Stricture resolution	Critical
				Stricture recurrence	Critical
				Number of ERCPs	Critical
				Number of stents	Critical
				Treatment duration	Critical
				Adverse events	Critical
				Cost	Critical
3	Liver transplant recipients with suspected post-transplant biliary strictures	MRCP	ERCP	Sensitivity	Critical
				Specificity	Important
				Positive predictive value	Important
				Negative predictive value	Critical
				Accuracy	Important
4	Liver transplant recipients with post-transplant biliary strictures undergoing elective ERCP as outpatient	Periprocedural antibiotics	No antibiotics	Rater of infections	Critical
				Infections with antibiotics	Critical
				Adverse events	Critical
				Cost effectiveness	Important
				Survival	Critical

of Interest found at https://www.asge.org/docs/default-source/default-document-library/coi-full-policy-for-asge-and-publications_edd_2-10-20.pdf.

Certainty in evidence, outcomes, and definitions

The certainty in the body of evidence (or confidence in the estimated effects) was assessed using the GRADE framework as previously described (Table 2.)[5-7] Relevant clinical outcomes included all-cause mortality, allograft survival, technical success of procedure, and cost-effectiveness, among others.

Notably, this guideline is restricted to liver transplant recipients with unaltered foregut anatomy. Hence, the recommendations may not necessarily apply to patients with biliary-enteric anastomosis including Roux-en-Y surgical reconstruction for which other published evidence can be considered. Liver transplant recipients included patients with deceased, split, and living donor allografts. A summary of our final recommendations for management of patients with post–liver transplant biliary strictures is listed in Table 3.

External review

The guideline was reviewed by the *Gastrointestinal Endoscopy* Editorial Board and Governing Board and was made available for public comment on the ASGE website.

RESULTS

For each clinical question, we have summarized the results for a priori–identified outcomes of interest. Other considerations including cost-effectiveness, patient preferences and acceptability, and equity that are common to more than 1 question have also been summarized.

Question 1: In liver transplant recipients with biliary stricture, should ERCP be used compared with PTBD as the initial therapy of choice for management of biliary strictures?

Recommendation 1: In liver transplant recipients with a biliary stricture, the ASGE suggests ERCP over PTBD as the initial therapy for management of strictures (*conditional recommendation, very low quality of evidence*).

We performed a systematic review of published literature on this topic. We used Ovid MEDLINE and EMBASE for all studies published through December 2020. We used major search terms and subheadings including "liver transplant," "stenosis of bile duct," "bile duct stricture," "ERCP," and "percutaneous transhepatic biliary drainage" (Appendix 1, available online at www.giejournal.org). The systematic review (Fig. 1) was restricted to studies assessing outcomes with ERCP and PTBD as the first-line therapy

TABLE 2. Interpretation of the definitions of the strength of recommendation using the Grading of Recommendations Assessment, Development and Evaluation framework

Implications for	Strong recommendation	Conditional recommendation
Patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	Most individuals in this situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the test. Formal decision aids are not likely to be needed to help individual patients make decisions consistent with their values and preferences.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their values and preferences.
Policymakers	The recommendation can be adopted as policy in most situations. Compliance with this recommendation according to the guideline could be used as a quality criterion or performance indicator.	Policymaking will require substantial debate and involvement of various stakeholders.

Adapted from Andrews et al.[3]

TABLE 3. Summary of recommendations

Recommendation	Best practice advice	Strength of recommendation	Quality of evidence
In liver transplant recipients with a biliary stricture, the ASGE suggests ERCP over PTBD as initial therapy for management of strictures.	ERCP preferred if it is difficult for caregivers to manage percutaneous drains/catheters; risk of dislodgement of percutaneous drains/catheters; presence of multiple intrahepatic strictures in different hepatic lobes; lack of significant biliary dilation to facilitate percutaneous drainage. PTBD preferred if difficult endoscopic biliary access because of various reasons including altered anatomy or increased risk of adverse events from anesthesia.	Conditional recommendation	Very low
In liver transplant recipients with biliary strictures, the ASGE suggests covered self-expandable metal stents should be used instead of multiple plastic stents for initial therapy of extrahepatic biliary strictures.	Covered metal stents are most often used for extrahepatic biliary strictures, typically at the anastomosis. Cholangiographic findings, such as intrahepatic biliary strictures or anastomotic strictures just below the bifurcation, may preclude the use of covered metal stents.	Conditional recommendation	Low to moderate
In liver transplant recipients with suspected biliary stricture(s), the ASGE suggests use of MRCP as a diagnostic test.	MRCP is an acceptable diagnostic test for detecting post-transplant strictures. Individual clinical scenarios should dictate the utility of MRCP. In patients with a high pretest probability for a biliary stricture or cholangitis, proceeding directly to ERCP without a diagnostic MRCP is prudent.	Conditional recommendation	Moderate to high
In patients with post–liver transplant biliary strictures undergoing elective ERCP in whom complete biliary drainage is technically challenging to achieve (ischemic cholangiopathy, multiple strictures, failure of stenting), the ASGE suggests administration of periprocedural antibiotics over no antibiotics to reduce incidence of infectious adverse events.	An individualized approach for administering antibiotics based on each patient's unique biliary anatomy and clinical condition is prudent. Patients with inadequate drainage of the biliary tree because of strictures may benefit from preprocedural antibiotics. Otherwise, use of antibiotics should be discussed with the patient and transplant team before ERCP.	Conditional recommendation	Very low

ASGE, American Society for Gastrointestinal Endoscopy; *PTBD*, percutaneous transhepatic biliary drainage.

for liver transplant recipients with post-transplant strictures. Studies that selected ERCP or PTBD based on the presence of a Roux-en-Y biliary-enteric anastomosis were excluded. Only those studies in which patients could undergo ERCP or PTBD irrespective of foregut anatomy were included. Of note, endoscopic interventions such as sphincterotomy, dilation, or stenting were not subcategorized or analyzed separately and were all

Figure 1. Preferred Reporting Items for Systematic reviews and Meta-Analyses diagram showing the studies included in the systematic review evaluating initial therapy for post-transplant biliary strictures (patient/population, intervention, comparison, and outcomes question 1).

categorized within the ERCP arm. Similarly, PTBD included radiologic interventions like cholangioplasty, placement of external or internal–external drains, or stenting.

We identified 4 studies that met the inclusion and exclusion criteria.[1,8-10] All studies were retrospective single-center studies except 1, which was a multicenter retrospective analysis of a large database. Two studies were performed in the United States, 1 in Germany, and 1 in South Korea. Analysis was performed on a per-procedure instead of a per-patient basis.

In aggregate, 432 patients were analyzed, of which 275 underwent ERCP and 157 underwent PTBD as the initial therapy for post–liver transplant biliary strictures. In the Korean study,[9] the decision between ERCP or PTBD was based on the availability of an endoscopist. The study by Kohli et al[1] was a multicenter study that used a nationwide database and was restricted to hospitalized patients. Each study scored at least 7 on the Qumseya scale.[11] Considering all outcomes together, the overall quality of evidence was found to be very low. A summary of outcomes and their assessment can be seen in Table 4.

Success

For assessing success of the procedure, 2 studies were identified from the systematic review. The relative risk for success was 1.279 (95% confidence interval [CI], .27-2.33) for ERCP versus PTBD. However, there was no uniform definition of success between the 2 studies. Lee et al[9] defined success as the absence of fluoroscopic, clinical, and biochemical evidence of stricture and/or biliary obstruction along with a lack of subsequent procedures after stent removal. Heinemann et al[8] defined long-term success as a lack of any biliary intervention within 12 months of the last procedure.

Lee et al[9] reported a success rate of 60% with ERCP and 59% with PTBD ($P = .93$), whereas Heinemann et al[8] reported long-term success in 56% of patients undergoing ERCP and 29% with PTBD ($P = .06$, Fisher exact test). In assessing the certainty of evidence, we rated down evidence for lack of prospective studies and imprecision because of a small number of studies and patients and overall judged the quality of evidence to be very low (Fig. 2).

Adverse events

Two studies, by Kohli et al[1] and Lee et al,[9] reported the incidence of adverse events (AEs) after ERCP and PTBD in liver transplant recipients with post-transplant bile duct strictures. The relative risk for AEs was 1.12 (95% CI, .62-2.0). Lee et al[9] used standard definitions for postprocedure pancreatitis, significant bleeding requiring transfusion, and cholangitis. They reported overall procedure-related AEs in 24% of ERCP procedures and 23% of PTBD procedures ($P = .92$); although these values seemed to be high, no differences were found between the groups. Kohli et al[1] used the National Readmissions

TABLE 4. Evidence profiles for Question 1: Should liver transplant recipients with post-transplant biliary strictures undergo ERCP or PTBD as initial therapy?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	ERCP	PTBD	Relative (95% CI)	Absolute (95% CI)		
technical Success (assessed with: Long term f/u)												
2	observational studies	not serious[a]	not serious[b]	not serious	serious[c]	none[c]	63/110 (57.3%)	61/114 (53.5%)	**RR 1.28** (0.70 to 2.30)	**150 more per 1,000** (from 161 fewer to 696 more)	⨁◯◯◯ Very low	CRITICAL
Overall AE												
2	observational studies	not serious	not serious	not serious	serious[d]	none	68/188 (36.2%)	29/104 (27.9%)	**RR 1.12** (0.62 to 2.02)	**33 more per 1,000** (from 106 fewer to 284 more)	⨁◯◯◯ Very low	CRITICAL
Failure allograft												
1	observational studies	not serious	not serious	not serious	serious[d]	none	2/163 (1.2%)	4/43 (9.3%)	**OR 8.47** (1.47 to 48.60)	**372 more per 1,000** (from 38 more to 740 more)	⨁◯◯◯ Very low	CRITICAL
Rejection of allograft												
1	observational studies	not serious	not serious	not serious	serious[d]	none	24/163 (14.7%)	5/43 (11.6%)	**OR 0.74** (0.26 to 2.09)	**28 fewer per 1,000** (from 83 fewer to 99 more)	⨁◯◯◯ Very low	CRITICAL
Death during hospital stay												
1	observational studies	not serious	not serious	not serious	serious[e]	none	3/163 (1.8%)	1/43 (2.3%)	**OR 1.47** (0.15 to 14.60)	**11 more per 1,000** (from 20 fewer to 235 more)	⨁◯◯◯ Very low	CRITICAL
Readmission												
1	observational studies	not serious	not serious	not serious	serious[e]	none	56/163 (34.4%)	16/43 (37.2%)	**OR 0.98** (0.45 to 2.07)	**5 fewer per 1,000** (from 162 fewer to 179 more)	⨁◯◯◯ Very low	CRITICAL
Length of stay												
1	observational studies	not serious	not serious	not serious	serious[d]	none	Adjusted odds: 14.4 (3.7, 25.1)26.3 ± 22.5 for ERC vs 40.2 ± 37.4 for PTBD P= 0.008				⨁◯◯◯ Very low	CRITICAL
Number of interventions												
1	observational studies	not serious	not serious	not serious	serious[d]	none	Mean number of procedures 2.5+/-0.9 in ERCP vs 6.1+/-0.4 in PTBD (P<0.01)				⨁◯◯◯ Very low	CRITICAL
Cost												
0							No published studies comparing costs or cost-effectiveness				-	IMPORTANT

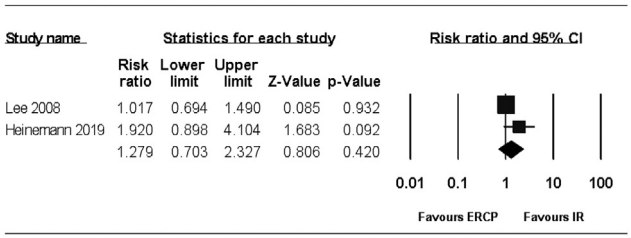
CI: confidence interval; **OR:** odds ratio; **RR:** risk ratio

Explanations

a. Qumseya scale 7,7,8,9
b. All studies show IR and ERCP have both successful
c. All 4 are retrospective studies including only 1 multicenter study
d. retrospective study
e. multicenter retrospective study of multiple community based hospitals

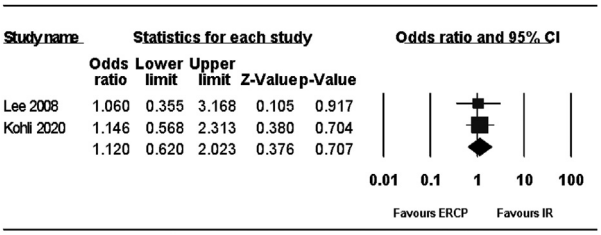
PTBD, Percutaneous transhepatic biliary drainage.

Database to identify the incidence of AEs using specific International Classification of Diseases 9th and 10th revision codes. In assessing the certainly of evidence, we rated down evidence for lack of prospective studies, imprecision because of small numbers of studies and patients, and overall judged the quality of evidence to be very low (Fig. 3).



N=2, RR 1.279 (0.703-2.327); I2=53.4%

Figure 2. Forest plot of the 2 studies evaluating the success of ERCP as compared with percutaneous transhepatic biliary drainage as the initial therapy for post-transplant biliary strictures showing no difference. n = 2, relative risk, 1.279 (95% confidence interval [CI], .703-2.327); I^2 = 53.4%.



N=2, RR 1.12 (0.62-2.023); I2=0%

Figure 3. Forest plot of the 2 studies evaluating the adverse events of ERCP as compared with percutaneous transhepatic biliary drainage as the initial therapy for post-transplant biliary strictures showing no difference. n = 2, relative risk, 1.12 (95% confidence interval [CI], .62-2.023); I^2 = 0%.

Allograft rejection and allograft failure

A single multicenter, retrospective study used the Nationwide Readmissions Database to assess outcomes in hospitalized liver transplant recipients from 2016 onward.[1] Of the 8300 liver transplant recipients meeting selection criteria, 554 patients had post–liver transplant strictures. The investigators identified outcomes including allograft rejection and failure using International Classification of Diseases 10th revision codes. Most patients were hospitalized in large, urban, private, not-for-profit teaching hospitals.

For the initial analysis, the primary exposure variable was the presence of post-transplant biliary stricture, whereas for the subsequent analysis, the primary exposure variable was procedure type. The multivariable model was then adjusted for potential confounding factors including demographics (age, sex), Charlson comorbidity index, liver-specific diseases (including chronic hepatitis B and C, malignant neoplasm of liver, nonalcoholic steatohepatitis, acute liver failure, hepatorenal syndrome, hepatopulmonary syndrome, primary biliary cholangitis, and autoimmune hepatitis), and other factors (solid tumor with or without metastasis, fluid and electrolyte disorder, and bed size).

On multivariate analysis, the adjusted odds of failure of liver allograft were 8.47 (95% CI, 1.47-48.6; P = .017) for PTBD versus ERCP. The odds of allograft rejection were similar between endoscopic and radiographic modalities. In assessing the certainty of evidence, we rated down evidence for lack of prospective studies and imprecision because of small sample size restricted to hospitalized patients and overall judged the quality of evidence to be very low.

Inpatient mortality and readmission

A single multicenter, retrospective study used the Nationwide Readmissions Database to assess outcomes in hospitalized liver transplant recipients.[1] The investigators defined readmission as a nonelective rehospitalization within 30 days of discharge in all patients who survived the hospitalization. These included patients who were discharged home, to skilled nursing facilities, or to long-term acute care hospitals. The readmission measure excluded those who died or had a December admission from the denominator because the Nationwide Readmissions Database does not track readmission between calendar years.

The rate of 30-day nonelective readmission was 38.4% for ERCP and 40% for PTBD arms. The rate of inpatient mortality was 1.8% with ERCP and 2.3% with PTBD. The adjusted odds of inpatient mortality and nonelective 30-day readmission were statistically similar among patients undergoing ERCP or PTBD. In assessing the certainty of evidence, we rated down evidence for lack of prospective studies and imprecision because of small sample size restricted to hospitalized patients and overall judged the quality of evidence to be very low.

Length of stay

The duration of hospitalization was 26.3 ± 22.5 days for the ERCP arm versus 40.2 ± 37.4 days for the PTBD arm (P = .008). The mean difference for PTBD versus ERCP was 14.4 (95% CI, 3.7-25.1).[1] In assessing the certainty of evidence, we rated down evidence for lack of prospective studies and imprecision because of small sample size restricted to hospitalized patients and overall judged the quality of evidence to be very low.

Number of interventions

One study from South Korea, by Lee et al,[9] reported the mean number of procedures performed to achieve clinical success. Lee et al defined success as the absence of radiographic clinical and biochemical evidence of stricture along with a lack of subsequent procedures after stent removal.

The mean number of procedures was 2.5 ± .9 in the ERCP group versus 6.1 ± .4 in the PTBD group (P < .01). Among patients undergoing PTBD, 181 additional procedures (mean, 3.0 ± .4) were performed because of external catheter problems such as leakage (14.9%, 27/181), retraction of catheter (29.8%, 54/181), decreased drainage (43.2%, 78/181), cholangitis (6.6%, 12/181), and other (5.5%, 10/181). The total duration of

the intervention for successful treatment was 5.3 ± .8 months for ERCP and 6.5 ± .7 months for PTBD (P = .31). In assessing the certainty of evidence, we rated down evidence for lack of prospective studies and imprecision because of small sample size restricted to a single study and overall judged the quality of evidence to be very low.

Other considerations

Cost. We did not find studies comparing costs or cost-effectiveness. One study restricted to hospitalized patients reported $179,179.3 ± 123,386.6 versus $257,058.7 ± 201,423.3 for ERCP versus PTBD.[1] The overall charge of hospitalization was lower for patients who underwent ERCP compared with PTBD. When published data are used for cost based on Current Procedural Terminology (CPT) codes, ERCP with sphincterotomy, balloon dilation, and stenting (CPT code 43274) results in $5028.52 as a facility payment for the hospital and $470.01 for the physician. ERCP with stent exchange, sphincterotomy, and balloon dilation (CPT code 43276) entails the same facility fee and a $489.20 physician fee. In comparison, CPT code 47556 for biliary endoscopy, percutaneous via T-tube or other tract, with dilation of biliary duct stricture(s) with stent results in a $3252 facility fee. Notably, the cost of the procedure may vary considerably based on local practice, use of anesthesia services, and reimbursement rates from individual insurance companies.

Location of stricture and technique. The panel members noted that although not specifically defined by each of the randomized controlled trials (RCTs), the location of the biliary stricture might necessitate placement of an MPS. For instance, stenoses at or just below the bifurcation would not allow a covered metal stent to bridge the stenosis without caging off 1 of the primary insertions. Moreover, there was no clear strategy regarding transpapillary or intraductal placement, the latter of which may decrease downward migration while increasing the difficulty of retrieval. In such instances, woven stents may be favored because laser cut stents may fracture or lose their native shape on retrieval.

Patient preferences and values. The patient advocate drew on personal experience and noted that ERCP was not associated with pain and was an easy procedure to undergo. The advocate also preferred to avoid PTBD because patients already have external drains out of the body. Also, the percutaneous drains may lead to scars and cosmetic disfigurement. Finally, the risk of leakage and discomfort at the drain site in already debilitated patients was deemed to be a disadvantage of PTBD.

Equity. The panel noted that patients undergoing PTBD will need additional follow-up care because percutaneous drains need to be flushed and patients and caregivers need to be educated about taking care of the drains. In assessing the certainty of evidence, we rated down evidence for lack of prospective studies and imprecision because of small sample size restricted to a single study and overall judged the quality of evidence to be very low. We found no studies reporting on patient values. Based on discussion with the patient advocate, the panel assumed that most patients would like to avoid the discomfort and risk of dislodgement associated with a percutaneous drain. Our literature search resulted in no studies to inform the outcome of mortality specifically because of post-transplant strictures

Discussion

Endoscopic and percutaneous drainage are both effective strategies in managing post–liver transplant biliary strictures. Although the therapeutic intent is similar, the technical approach is different. ERCP often requires general anesthesia and is typically performed in the prone position. It is also associated with a risk of post-ERCP pancreatitis. PTBD, on the other hand, can often be performed with moderate or deep sedation while the patient is lying supine and is typically associated with risks of bleeding and infection.

The patient advocate specifically mentioned concerns regarding the risk of dislodgment of the drain, need for careful handling of the drain, and cosmetic disfigurement because of scar formation. For these reasons as well as the need for more frequent interventions, the panel suggested ERCP as the preferred approach instead of PTBD. However, PTBD may be the appropriate initial intervention in patients with a surgically altered foregut in the setting of a Roux-en-Y gastrojejunostomy. A subset of critically ill patients with hemodynamic instability may not be ideal candidates for ERCP, and PTBD may be an acceptable alternative.

Question 2: In patients with post-transplant biliary strictures, should cSEMSs be used compared with MPSs as the initial therapy of choice for management of biliary strictures?

Recommendation 2: In liver transplant recipients with biliary strictures, the ASGE suggests cSEMSs should be used instead of MPSs for initial therapy of extrahepatic biliary strictures (*conditional recommendation, low to moderate quality of evidence*).

We performed a systematic review of the published literature on this topic. We used Ovid MEDLINE and EMBASE for all studies published through December 2020. We used major search terms and subheadings including "liver transplant," "ERCP," "stenosis," "bile duct," and "stent" (Appendix 2, available online at www.giejournal.org). The systematic review (Fig. 4) was restricted to studies assessing outcomes comparing the use of cSEMSs with MPSs as the first-line therapy for liver transplant recipients with post-transplant strictures. Notably, only those

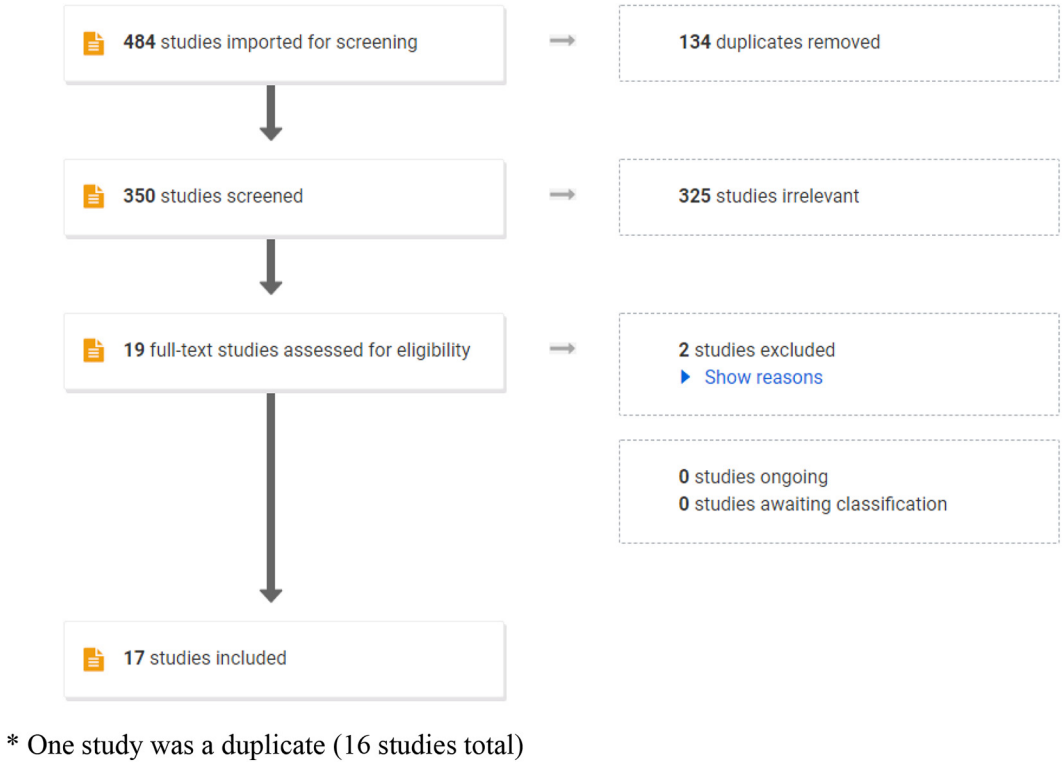


Figure 4. Preferred Reporting Items for Systematic reviews and Meta-Analyses diagram showing the studies included in the systematic review evaluating management of post-transplant biliary structures using covered metal stents or multiple plastic stents (patient/population, intervention, comparison, and outcomes question 2). One study was a duplicate (16 studies total).

studies in which patients could undergo either treatment irrespective of foregut anatomy were included.

We identified 16 studies that met the inclusion and exclusion criteria.[12-27] Of these 16, 4 were U.S.- and/or internationally based multicenter RCTs[14,16,20,22] and 6 were meta-analyses with or without novel retrospective data.[12,17-19,23,24] Of the 6 meta-analyses, 2 only evaluated 4 RCTs, whereas 4 only evaluated ≤3 RCTs, with some including retrospective data. The studies by Tringali et al[23] and Visconti et al[24] used similar methods, but the meta-analysis by Visconti et al evaluated more outcomes. Two retrospective studies published after these 2 RCTs were identified and found to have data and conclusions that did not differ from that presented in the RCTs.[13,15] Therefore, a decision was made to use the existing published analyses from Visconti et al.

In aggregate, 205 patients were analyzed within the 4 RCTs, of which 103 underwent cSEMS placement and 102 underwent MPS placement as the initial therapy for post–liver transplant biliary strictures. Follow-up was for at least 1 year for each of the studies,[14,20,22] except for Kaffes et al,[16] where the mean follow-up was over 1 year. Metallic indwelling time ranged between 3 and 6 months, whereas plastic stents were exchanged within a range of 6 to 16 weeks. Three studies noted stent removal within 12 months at stricture resolution, but the study by Tal et al[22] did not provide these data. Wallflex (8- to 10-mm caliber; Boston Scientific, Marlborough, Mass, USA) and Viabil (10-mm caliber; Taewoong, Gangseo-gu, Busan, South Korea) stents were evaluated with or without stricture balloon dilation at the discretion of the endoscopist. Although not always specifically noted, strictures were anastomotic duct to duct in location and not involving the intrahepatic ducts. Considering all outcomes together, the overall quality of evidence was found to be low to moderate. A summary of outcomes and their assessment can be seen in Table 5.

Stricture resolution

For assessing stricture resolution, all 4 RCTs were included with a total of 205 patients. All 4 studies were consistent with no statistically significant differences in the rate of stricture resolution when comparing cSEMSs and MPSs for biliary stricture resolution. Meta-analysis also did not demonstrate any significant differences between the groups with a risk difference of .01 (95% CI, –.08 to .10) and an I^2 of 12%. It was noted that plastic stents were exchanged through the point of resolution, whereas metal stents were removed after a defined period regardless of cholangiogram interpretation. In assessing the certainty of the evidence, we rated it down for imprecision (relatively low number of patients) and overall judged the quality of evidence to be moderate.

TABLE 5. Evidence profiles for Question 2: Should covered SEMSs or MPSs be used for management of post-transplant biliary strictures?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	SEMS	MPS	Relative (95% CI)	Absolute (95% CI)		
Stricture resolution												
4	randomised trials	not serious	not serious	not serious	serious[a]	none	103	102	-	MD **0.01 higher** (0.08 lower to 0.01 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Stricture Recurrence												
4	randomised trials	not serious	not serious	not serious	serious[a]	none	92	89	-	MD **0.013 higher** (0.03 lower to 0.28 higher)	⨁⨁⨁◯ Moderate	CRITICAL
Number of ERCPs												
4	randomised trials	not serious	serious[b]	not serious	serious[a]	none	103	102	-	MD **1.86 procedures fewer** (3.12 fewer to 0.6 fewer)	⨁⨁◯◯ Low	CRITICAL
Number of stents												
2	randomised trials	not serious	serious[a,c]	not serious	serious[a]	none	56	56	-	MD **10.63 stents/pt fewer** (20.82 fewer to 0.44 fewer)	⨁⨁◯◯ Low	CRITICAL
Treatment time												
4	randomised trials	not serious	serious	not serious	serious[a]	none	103	102	-	MD **105.07 days fewer** (202.38 fewer to 7.76 fewer)	⨁⨁◯◯ Low	CRITICAL
Adverse events												
2	randomised trials	not serious[d]	serious[d]	not serious	serious[a]	none	RD -0.10 [-0.65, -0.44] Total number of events with each group (42)				⨁⨁◯◯ Low	CRITICAL
Treatment Cost												
2	randomised trials	not serious	not serious	not serious	serious[a]	none	Covered avg cost 8288.50 SD 1959.39 Plastic avg cost 18580.00 SD 3514.32 P<0.001 IC 95%				⨁⨁⨁◯ Moderate	CRITICAL

CI: confidence interval; **MD:** mean difference

Explanations

a. Low number of patients
b. I2 =97%
c. I2=96%
d. I2=85%

SEMS, Self-expandable metal stent; *MPS*, multiple plastic stent.

Stricture recurrence

For assessing stricture recurrence, all 4 RCTs were included. However, not all patients were included because some did not have successful initial therapy, and as a result 181 patients were evaluated. Three studies demonstrated no significant difference between the groups, whereas Martins et al[20] favored MPSs. However, meta-analysis of the 4 studies revealed no significant difference between the groups, although a trend was noted favoring MPSs, with a risk difference of .13 (95% CI, –.03 to .28) and an I^2 of 52%. In assessing the certainty of the evidence, we rated down for imprecision (relatively low number of patients) and overall judged the quality of evidence to be moderate, because the I^2 of 52% was equivocal.

Number of ERCPs

For assessing the total number of ERCPs required for therapy, all 4 RCTs were included with a total of 205 patients evaluated. Three of 4 RCTs favored cSEMS,[14,16,20] whereas Tal et al[22] strongly favored cSEMSs. Meta-analysis of the 4 studies revealed a significant difference, with an average approaching 2 less procedures when using cSEMSs, specifically a mean difference of –1.86 (95% CI, –3.12 to –.06; I^2 = 97%). In assessing the certainty of evidence, we rated down for both imprecision (relatively low number of patients) and inconsistency (high I^2) and overall judged the quality of evidence to be low.

Number of stents. Only 2 RCTs involving 112 patients evaluated the overall number of stents used throughout stricture management. Both found a significant difference, favoring a lower number of stents per patient in the cSEMS group when compared with the MPS group, with an average of more than 10 fewer stents when using cSEMSs (mean difference, –10.63; 95% CI, –20.82 to –.44). In assessing the certainty of evidence, we rated down for both imprecision (relatively

low number of patients) and inconsistency (high I^2), overall judging the quality of evidence to be low.

Treatment time

All 4 RCTs evaluated the overall treatment time based on the number of days stents were indwelling, with a total number of 205 patients evaluated. Two of 4 RCTs favored cSEMSs and 2 trended toward shorter treatment duration with cSEMSs. Meta-analysis favored cSEMSs, with a significant difference of 105 fewer days compared with the MPS approach (mean difference, −105.07; 95% CI, −202.38 to −7.76; I^2 = 95%). In assessing the certainty of evidence, we rated down for both imprecision (relatively low number of patients) and inconsistency (high I^2) and overall judged the quality of evidence to be low.

Adverse events

There was variability among the RCTs when evaluating AEs, and only 2 provided sufficient data, focused on migration, for meta-analysis. Although Tal et al[22] trended toward a difference in AEs, mostly migration, favoring MPSs, Kaffes et al[16] demonstrated a significant difference favoring cSEMSs, with meta-analyses of the 2 favoring neither. All 4 studies mentioned migration, and in the remaining 2 studies there appears to be a higher frequency of downstream migration in the cSEMSs. However, it was noted that this was considered only a procedural finding rather than an AE if the stent was recovered on schedule and the stricture resolved. Indirect evidence has shown that cSEMSs can be associated with post-ERCP pancreatitis.[28] However, this was not reported in any of the RCTs. In assessing the certainty of evidence, we rated down for both imprecision (relatively low number of patients) and inconsistency (high I^2), overall judging the quality of evidence to be low.

Cost

Two RCTs compared the total cost between treatment strategies, which included facility fees, thereby incorporating the expense of the devices deployed.[16,20] Treatment with cSEMSs was less expensive than that with MPSs (average of $8288 and $19,580, respectively; $P < .01$). Of note, this meta-analysis included studies from 2 separate continents addressing the differences in healthcare systems. In assessing the certainty of evidence, we rated down for both imprecision (relatively low number of patients) and inconsistency (high I^2), overall judging the quality of evidence to be low.

Other considerations

Patient values. We found no studies reporting on patient values. Based on discussion with the patient advocate, the panel assumed that most patients would be indifferent to the type of stent placed but would favor shorter therapy, fewer procedures, and less expense.

Mortality. None of the 4 RCTs or any of the other 12 retrospective studies discussed patient death related to the strategy of stricture management.

Equity. The panel noted that individuals undergoing liver transplant have healthcare expenses typically covered by insurance or by government programs, with AEs requiring interventions such as ERCP usually managed at transplant centers with access to experienced endoscopists and both plastic and metal stents. This would suggest equity between treatment strategies.

Discussion

The panel members noted that although not specifically defined by each of the RCTs, the location of the biliary stricture might necessitate placement of MPSs. For instance, stenoses at or just below the bifurcation would not allow a covered metal stent to bridge the stenosis without obstructing 1 of the primary insertions. Moreover, there was no clear strategy regarding transpapillary or intraductal placement, the latter of which may decrease downward migration while increasing the difficulty of retrieval. In such instances, woven stents such as the Wallflex stent may be favored because laser cut stents may fracture or lose their native shape on retrieval.

Question 3: In liver transplant recipients with suspected biliary stricture, should MRCP be considered the preferred modality?

Recommendation 3: In liver transplant recipients with suspected biliary stricture, the ASGE suggests use of MRCP as a diagnostic test (*conditional recommendation, moderate to high quality of evidence*).

We performed a systematic review of the published literature on this topic. We used Ovid MEDLINE and EMBASE for all studies published through December 2020. We used major search terms and subheading including "liver transplant," "ERCP," "stenosis," "bile duct," and "MRCP" (Appendix 3, available online at www.giejournal.org). The systematic review (Fig. 5) was restricted to studies assessing the performance of MRCP in predicting biliary strictures in post–liver transplant patients using ERCP as the criterion standard. We identified 21 studies that met the inclusion and exclusion criteria, 13 of which were retrospective[29-41] and 8 of which were prospective.[42-49] Study scores ranged from 5 to 7 on the Qumseya scale with an average score of 6.14.

From these 21 studies, details of diagnostic performance characteristics of MRCP compared with ERCP for post-transplant biliary strictures were collected. We compared pooled sensitivity, specificity, positive and negative predictive values, and accuracy of MRCP compared with ERCP for post-transplant biliary stricture by meta-analyses. The diagnostic performance characteristics were extracted for MRCP compared with ERCP (control among

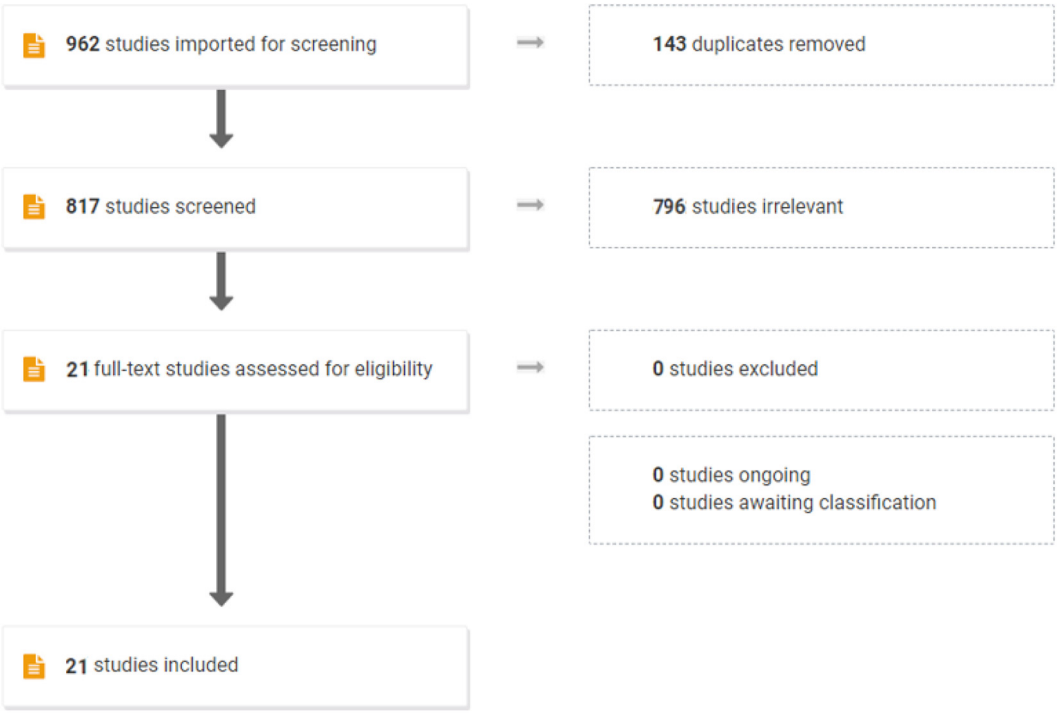


Figure 5. Preferred Reporting Items for Systematic reviews and Meta-Analyses diagram showing the studies included in the systematic review to evaluate the performance characteristics of MRCP in patients suspected to have post-transplant biliary strictures (patient/population, intervention, comparison, and outcomes question 3).

the included studies) as reported by these studies. When not directly reported, indirect calculations were performed using the reported diagnostic performance characteristics and prevalence. A priori random-effects meta-analysis (assuming a common effect of the diagnostic test across all studies) was performed examining diagnostic test accuracy using Comprehensive Meta-analysis V3 statistical software. The studies were weighted based on effect size and sample size. We assessed heterogeneity using the I^2 and Q statistic and publication bias by funnel plot. Any concern for publication bias based on funnel plot asymmetry was further evaluated by Egger's regression test. A summary of outcomes and their assessment can be seen in Table 6.

Sensitivity

For assessing sensitivity, 20 studies were found to have sufficient data for meta-analyses, involving an aggregate of 758 patients.[29-48] MRCP correctly diagnosed post-transplant biliary strictures at a rate of 94.9% (95% CI, 92.4-96.6) when compared with findings of subsequent ERCP (Fig. 6). Heterogeneity (I^2) was relatively low at 32.8%. Therefore, we did not rate down the level of evidence, resulting in a rating of high for quality of evidence. The funnel plot of standard error by logit event rate was suggestive of possible bias with a significant regression test and suggestive of a risk of publication bias (Fig. 7). We found no factors that would decrease the certainty of evidence.

Specificity

For assessing specificity, 20 studies were found to have sufficient data for meta-analyses, involving an aggregate of 758 patients.[29-48] ERCP confirmed suspected biliary strictures found by MRCP at a rate of 90.3% (95% CI, 84.7-94.0) (Fig. 8). Heterogeneity (I^2) was relatively high at 87.8%. Therefore, we rated down for inconsistency and rated the quality of evidence as moderate. The funnel plot of standard error by logit event rate was suggestive of possible bias with a significant regression test and suggestive of a possible risk of publication bias (Fig. 9). In assessing the certainty of the evidence, we rated down for inconsistency.

Positive predictive value

Sixteen studies were found to have sufficient data for a meta-analysis to evaluate positive predictive value, involving an aggregate of 584 patients.[29-31,33,35-38,40-43,45,46,48,49] Of those with strictures found on ERCP, MRCP truly diagnosed biliary strictures at a rate of 90.6% (95% CI, 85.6-93.9). Heterogeneity (I^2) was relatively high at 64.4% (Fig. 10). The funnel plot of standard error by logit event rate was suggestive of possible bias with a significant regression test and suggestive of publication bias (Fig. 11). In assessing the certainty of the evidence, we rated down for inconsistency.

Negative predictive value

Fourteen studies were found to have sufficient data for a meta-analysis to evaluate negative predictive value, involving

TABLE 6. Evidence profiles for Question 3: What are the test characteristics of MRCP for diagnosing post–liver transplant biliary strictures?

Sensitivity	0.95 (95% CI: 0.92 to 0.97)
Specificity	0.90 (95% CI: 0.85 to 0.94)

Prevalences	25%	50%	75%

Outcome	№ of studies (№ of patients)	Study design	Factors that may decrease certainty of evidence					Effect per 1,000 patients tested			Test accuracy CoE
			Risk of bias	Indirectness	Inconsistency	Imprecision	Publication bias	pre-test probability of25%	pre-test probability of50%	pre-test probability of75%	
True positives (patients with biliary strictures)	20 studies 878 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	not serious	not serious	none	237 (231 to 242)	475 (462 to 483)	712 (693 to 724)	⊕⊕⊕⊕ High
False negatives (patients incorrectly classified as not having biliary strictures)								13 (8 to 19)	25 (17 to 38)	38 (26 to 57)	
True negatives (patients without biliary strictures)	20 studies 878 patients	cross-sectional (cohort type accuracy study)	not serious	not serious	serious[a]	not serious	none	677 (635 to 705)	452 (424 to 470)	226 (212 to 235)	⊕⊕⊕◯ Moderate
False positives (patients incorrectly classified as having biliary strictures)								73 (45 to 115)	48 (30 to 76)	24 (15 to 38)	

Explanations

a. High I2

CI, Confidence interval.

an aggregate of 505 patients.[29,30,33,35-37,40-43,45,46,48,49] Of those without strictures found on ERCP, MRCP was consistent at a rate of 93.7% (95% CI, 86.2-97.2) (Fig. 12). Heterogeneity (I^2) was high at 81.2%. The funnel plot of standard error by logit event rate was suggestive of possible bias with a significant regression test and suggestive of publication bias (Fig. 13). In assessing the certainty of the evidence, we rated down for inconsistency.

Accuracy

For assessing accuracy, 12 studies were found to have sufficient data for meta-analyses, involving an aggregate of 508 patients.[29-31,36-38,40,42-45,48] MRCP was found to have an accuracy of 92.4% (95% CI, 89.0-94.6) (Fig. 14). Heterogeneity (I^2) was relatively low at 24.1%. The funnel plot of standard error by logit event rate was suggestive of possible bias with regression that is not significant and not suggestive of a possible risk of publication bias (Fig. 15).

Other considerations

We found no studies comparing the cost of managing post-transplant biliary strictures with and without diagnostic preprocedure MRCP. Although MRCP would undoubtedly incur cost, it is possible that the data provided may improve ERCP outcomes, decreasing the cost of unscheduled repeat procedures or associated testing.

We found no studies reporting on patient values. Based on discussion with the patient advocate, the panel assumed that most patients would not be against an MRCP if not contraindicated and recommended by the physician.

None of the studies discussed AEs of MRCP, although no morbidity or mortality is associated with this procedure because no intravenous contrast is required. The panel noted that individuals undergoing liver transplant have healthcare expenses typically covered by insurance or by government programs. Moreover, these individuals are typically managed at transplant centers with access to magnetic resonance imaging, suggesting no risk of inequity.

Discussion

The panel members noted that pretest probability and the clinical scenario should be taken into consideration

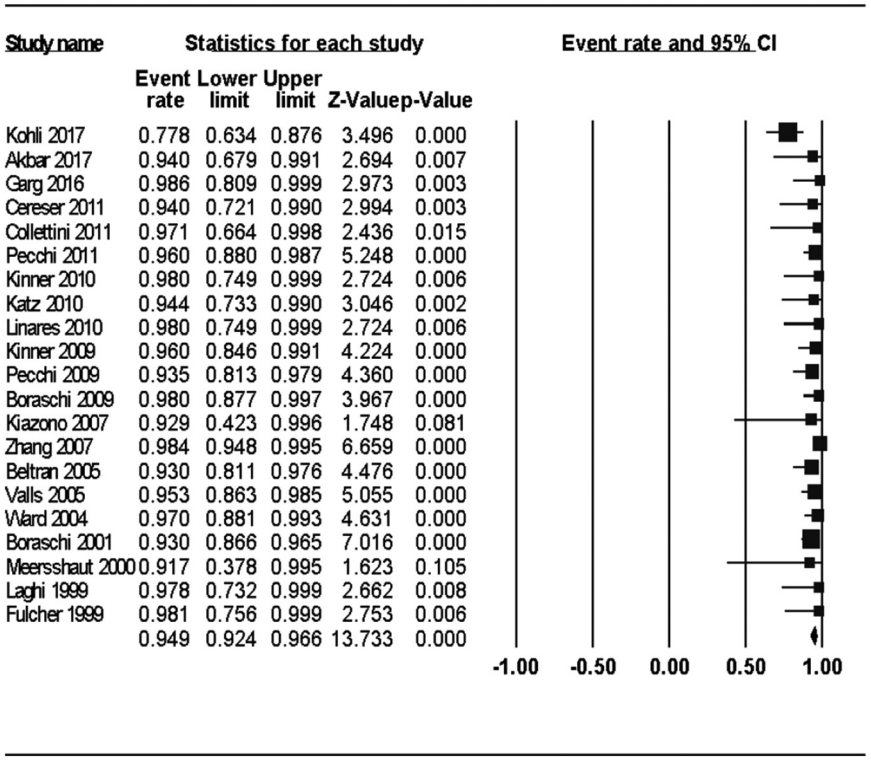


Figure 6. Forest plot of 20 studies assessing the sensitivity of MRCP to correctly diagnose post-transplant biliary strictures. *CI*, Confidence interval.

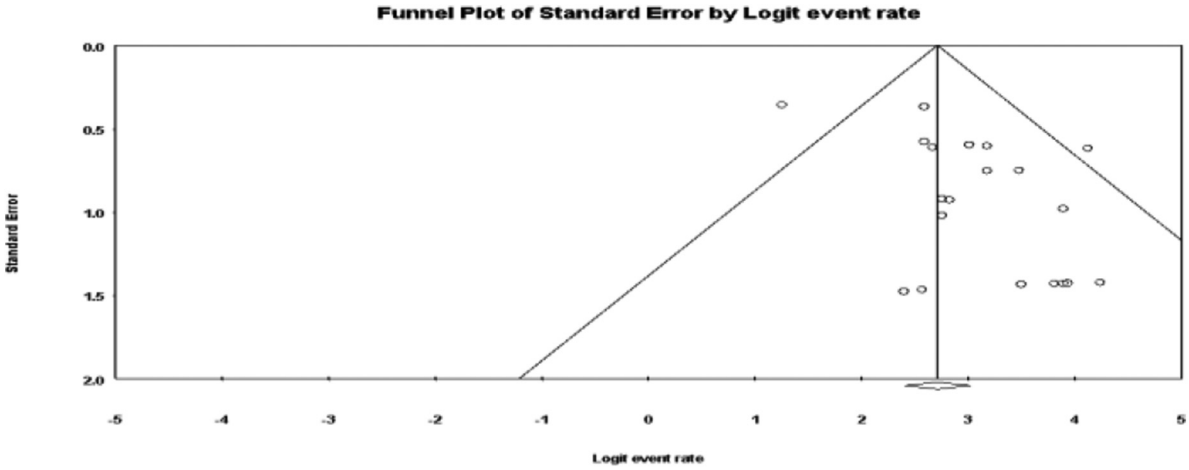


Figure 7. Funnel plot of 20 studies assessing the sensitivity of MRCP to correctly diagnose post-transplant biliary strictures suggesting risk of publication bias.

before organizing an MRCP because this may potentially delay an ERCP. For instance, if a post-transplant patient has a high bilirubin value with fever and positive blood cultures suggestive of cholangitis, performing an ERCP without a diagnostic MRCP would be prudent. Also, some individuals, in particular children, may require some level of sedation for MRCP, which would add potential risk and should be taken into consideration. The panel also recognized the critical nature of MRCP in the setting of complex anastomoses as with living donor recipients.

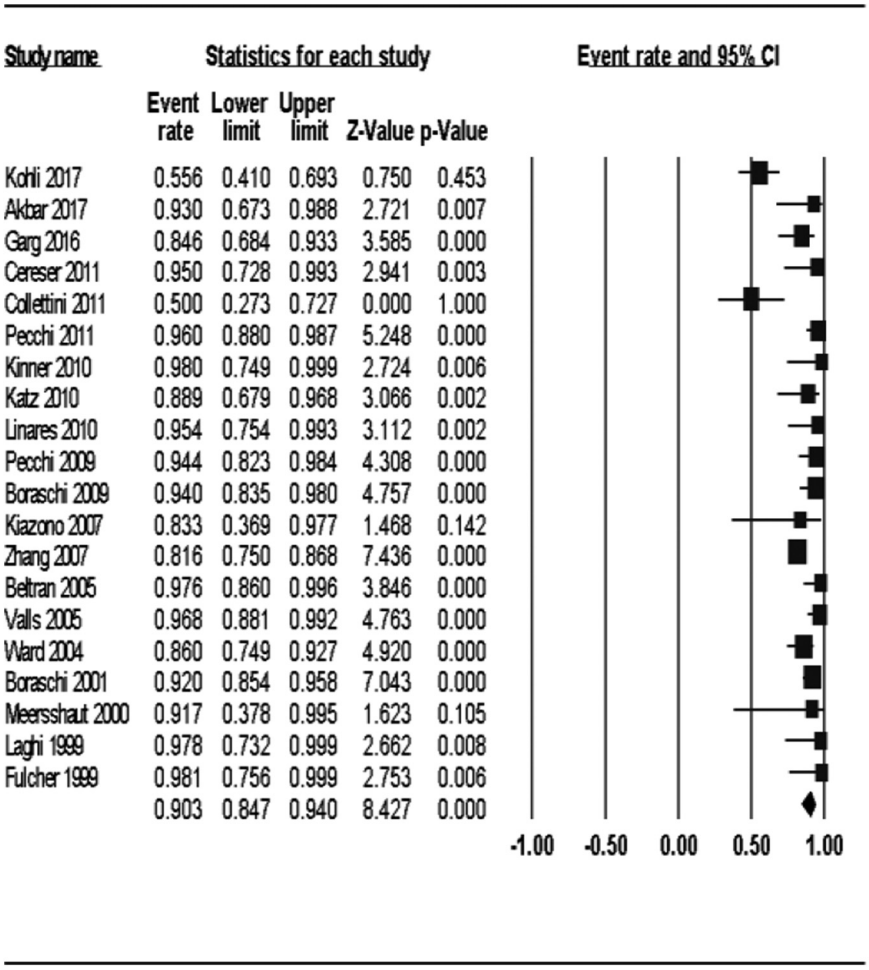


Figure 8. Forest plot of 20 studies assessing the specificity of MRCP to correctly diagnose post-transplant biliary strictures. *CI*, Confidence interval.

Question 4: In patients with post–liver transplant biliary strictures without cholangitis undergoing elective ERCP, should antibiotics be administered or not administered to reduce risk of infections?

Recommendation 4: In patients with post–liver transplant biliary strictures undergoing elective ERCP in whom complete biliary drainage is technically challenging to achieve (ie, ischemic cholangiopathy, multiple strictures, failure of stenting), the ASGE suggests administration of periprocedural antibiotics over no antibiotics to reduce incidence of infectious AEs (*conditional recommendation, very low quality of evidence*).

We performed a systematic review of the published literature on this topic. We used Ovid MEDLINE and EMBASE for all studies published through December 2020. We used major search terms and subheadings including "liver transplant," "stenosis of bile duct," "bile duct stricture," "ERCP," "antibiotics," and "infection" (Appendix 4, available online at www.giejournal.org).

The current ASGE guideline for antibiotic prophylaxis recommends administration of antibiotics in all liver transplant recipients undergoing ERCP.[50] Fluoroquinolones such as ciprofloxacin are typically administered periprocedurally and sometimes even after discharge of the patient. We conducted a systematic review (Fig. 16) of publications that compared the outcomes in liver transplant recipients with biliary strictures undergoing ERCP who received periprocedural antibiotics with those who did not receive antibiotics. Notably, patients with infection or cholangitis were excluded because there are clear guidelines that recommend administration of antibiotics.[51] Studies in which all patients received antibiotics during ERCP were also excluded because of the absence of a comparison arm. Infections were defined clinically and not based solely on the presence or absence of bacteremia. Of note, bacteremia occurs often during endoscopic procedures, including ERCP, although the incidence varies based on the type of procedure and therapy. This bacteremia is transient and not definitely associated with AEs.[51-53]

We identified 2 studies that met the inclusion and exclusion criteria.[54,55] Both studies were retrospective

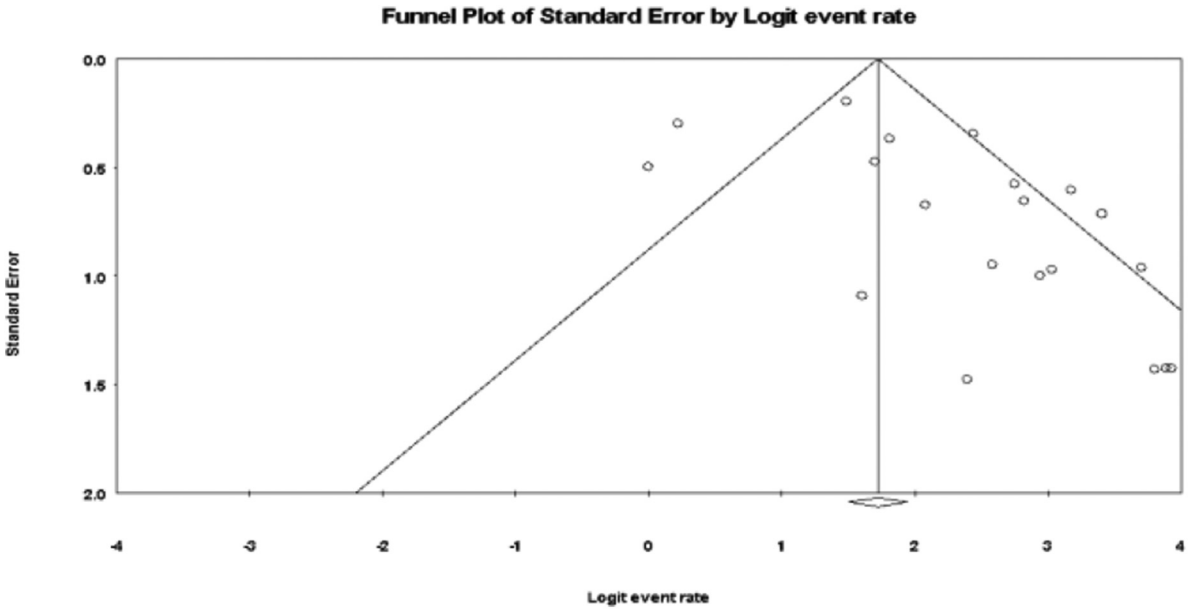


Figure 9. Funnel plot of 20 studies assessing the specificity of MRCP to correctly diagnose post-transplant biliary strictures suggesting risk of publication bias.

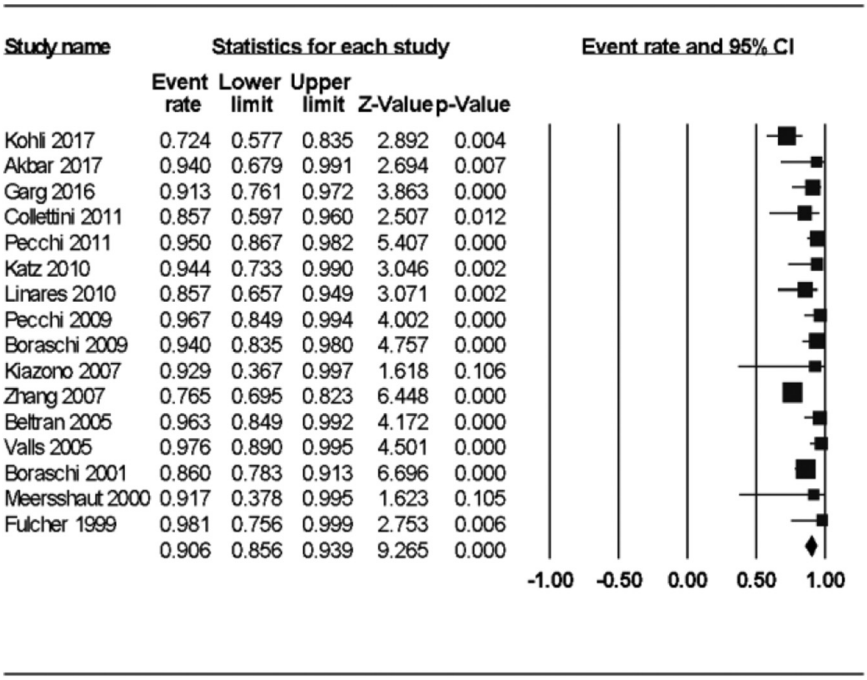


Figure 10. Forest plot of 16 studies assessing the positive predictive value of MRCP to truly diagnose post-transplant biliary strictures. *CI*, Confidence interval.

single-center studies carried out in university-based liver transplant centers in the United States. Analysis was performed on a per-procedure instead of a per-patient basis.

One study directly compared outcomes of antibiotic administration versus nonadministration in nonhospitalized liver transplant recipients undergoing ERCP.[55] Patients with cholangitis and inpatients (who could be getting antibiotics for unrelated reasons) were excluded. Notably, this study assessed for "clinically significant infections" and did not assess for asymptomatic bacteremia. The second study assessed the risk of infections and impact of antibiotics over time among all patients undergoing ERCP, irrespective of liver transplant status.[54] Data regarding liver transplant recipients undergoing ERCP was limited to a

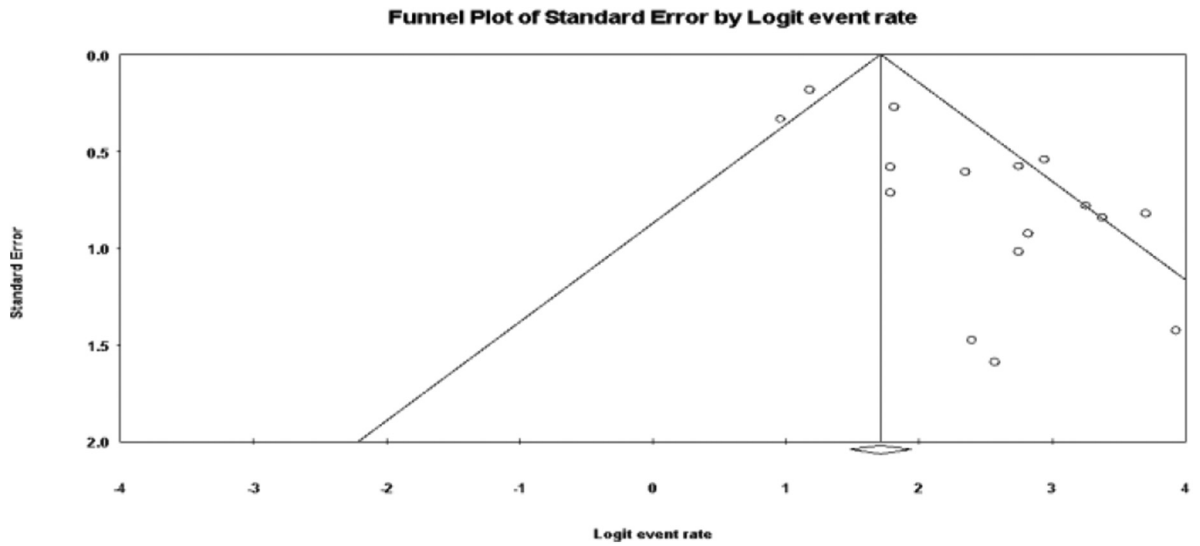


Figure 11. Funnel plot of 16 studies assessing the positive predictive value of MRCP to truly diagnose post-transplant biliary strictures suggesting risk of publication bias.

subgroup analysis. A summary of outcomes and their assessment can be seen in Table 7.

Rate of infection

Overall, 361 liver transplant recipients undergoing 959 ERCP procedures were assessed. The pooled incidence of infections was 1.1% (95% CI, .6-2.0; $I^2 = 0$ (Fig. 17).

Impact of antibiotics

Kohli et al[55] reported that clinically significant infections occurred in 1 of 89 patients who received antibiotics and in none of the 109 patients who did not receive antibiotics. Cotton et al[54] also noted that administration of antibiotics did not lower the risk of infections or adverse outcomes but did not provide exact data. Kohli et al postulated that the risk of infections in liver transplant recipients is finite but exceedingly small. The ability of antibiotics to further lower the risk of infectious AEs may thus be limited.

Adverse events

In our systematic review of published studies, we did not find any study that compared the incidence of AEs with administration of antibiotics versus not administering antibiotics in liver transplant recipients undergoing ERCP. Fluoroquinolones, such as ciprofloxacin, are most often prescribed during ERCP because of biliary excretion. Fluoroquinolones are associated with serious and nonserious AEs that should be discussed with the patient before the procedure as part of the informed consent process. The U.S. Food and Drug Administration has a black box warning because of increased risk of tendinitis and tendon rupture.[56]

Serious AEs include tendinitis, tendon rupture, peripheral neuropathy, central nervous system effects, and exacerbation of myasthenia gravis. This class of medications can also lead to prolongation of the QT interval and consequent arrhythmias, including torsade de pointes. These effects may be worsened in elderly patients who may be more susceptible to drug-associated effects on the QT interval.

Ciprofloxacin is a weak inhibitor of CYP3A4, which metabolizes tacrolimus.[57] Hence, ciprofloxacin can increase the serum concentration of tacrolimus. Tacrolimus trough levels may need to be monitored when weak CYP3A4 inhibitors are administered, especially in patients with reduced renal clearance.

Other considerations

In our systematic review of published studies, we did not find any study that assessed the cost-effectiveness of administering periprocedural antibiotics. Also, our literature search resulted in no studies to inform the outcome of mortality based on administration of antibiotics. We found no studies reporting on patient values.

Discussion

The need for antibiotics in immunosuppressed patients undergoing endoscopic interventions remains under investigation. Transient bacteremia often occurs during endoscopic interventions but is not associated with significant adverse outcomes. Over time, the number of indications for antibiotics during endoscopy has decreased. Although liver transplant recipients are immunosuppressed, the degree of immunosuppression decreases over time. Patients are more significantly immunosuppressed in the immediate post-transplant time period. The available data do not provide definite evidence to suggest that the risk of infections is high or that antibiotics can reduce this risk. In the absence of high-quality data, strong evidence-based

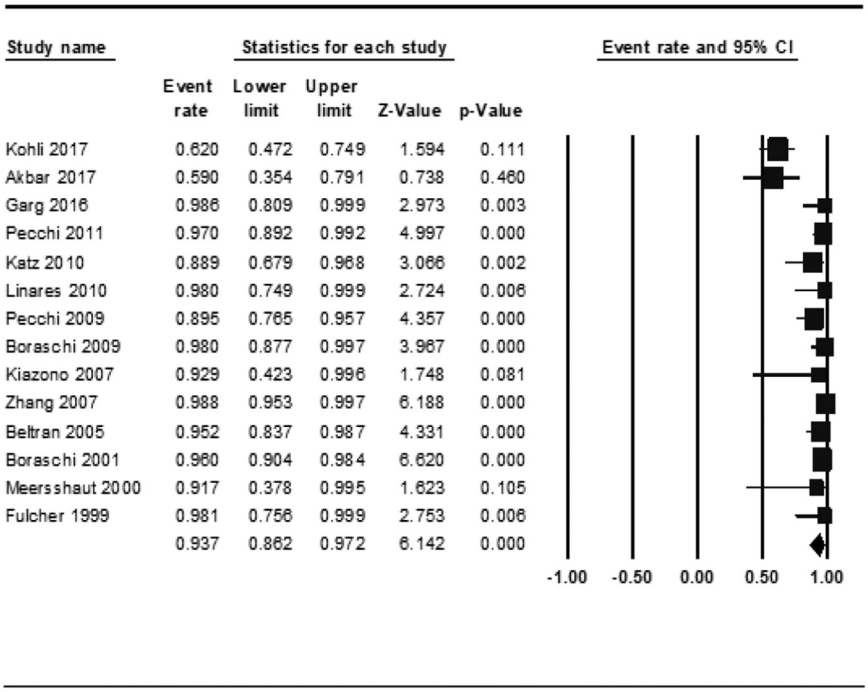


Figure 12. Forest plot of 14 studies assessing the negative predictive value of positive MRCP findings corresponding to post-transplant biliary strictures. *CI*, Confidence interval.

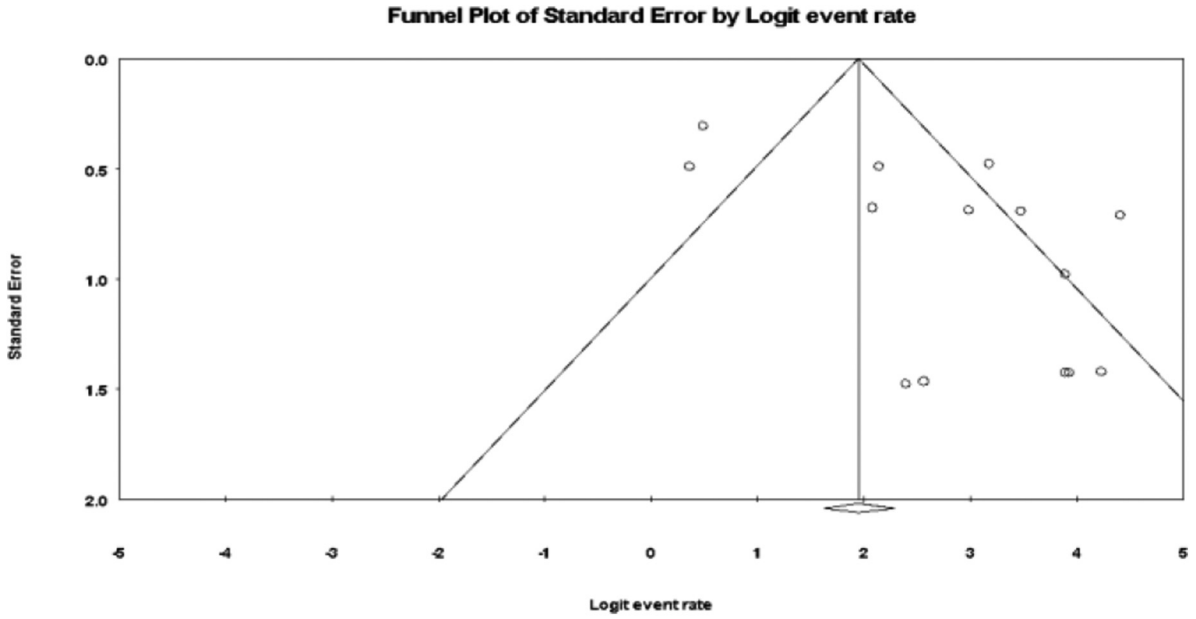


Figure 13. Funnel plot of 14 studies assessing the negative predictive value of positive MRCP findings corresponding to post-transplant biliary strictures suggesting risk of publication bias.

recommendations cannot be provided. We recommend an individualized approach for administering antibiotics based on each patient's unique biliary anatomy and clinical condition.

Hence, we continue to recommend administration of antibiotics in liver transplant recipients with cholangitis.[51] In patients at risk for having undrained ducts, antibiotics should be administered. These include patients with

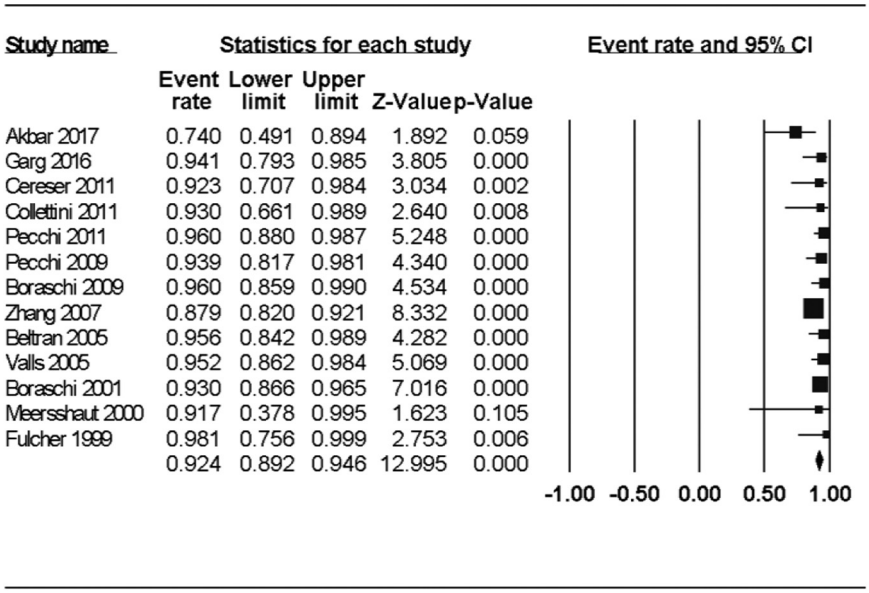


Figure 14. Forest plot of 13 studies assessing the accuracy MRCP findings corresponding to post-transplant biliary strictures. *CI*, Confidence interval.

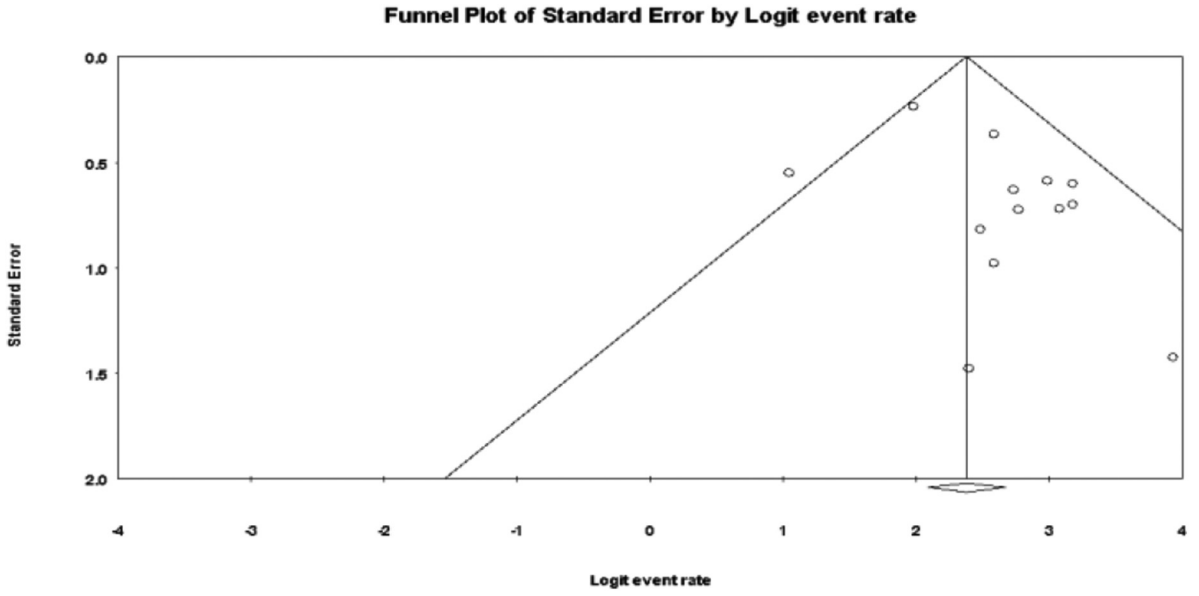


Figure 15. Funnel plot of 13 studies assessing the accuracy MRCP findings corresponding to post-transplant biliary strictures suggesting no publication bias.

stenosed intra- or extrahepatic ducts, ischemic cholangiopathy, multiple intrahepatic strictures, or patients in whom contrast was injected but stricture dilation or stent placement across a stricture was unsuccessful. In a subset of nonhospitalized liver transplant recipients undergoing elective ERCP in whom stricture resolution has been achieved and unimpeded contrast drainage can be visualized (eg, when initiating a stent-free trial after stricture resolution), antibiotics may or may not be administered. This decision should be individualized to a specific patient.

HEALTH DISPARITIES AND EQUITY

For each of the PICOs, the panel addressed feasibility and health equity, acknowledging that many patients

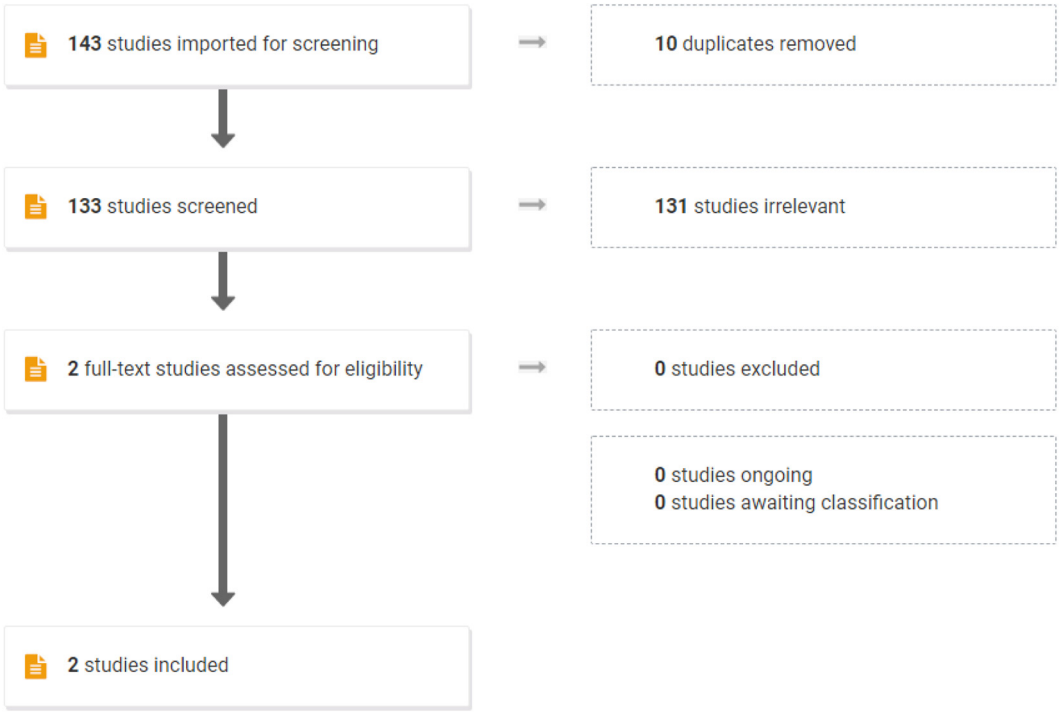


Figure 16. Preferred Reporting Items for Systematic reviews and Meta-Analyses diagram showing the studies included in the systematic review evaluating antibiotics in patients with post-transplant biliary strictures undergoing ERCP (patient/population, intervention, comparison, and outcomes question 4).

TABLE 7. Evidence profiles for Question 4: Should antibiotics be administered to individuals with post–liver transplant biliary strictures without cholangitis undergoing elective ERCP?

Certainty assessment							№ of patients		Effect		Certainty	Importance
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	antibiotics	no antibiotics	Relative (95% CI)	Absolute (95% CI)		
Rate of infection												
2	observational studies	not serious	not serious	not serious	serious[a]	none	Pooled incidence: event rate: 1.1% (0.6%-2.0%); I2=0. In both studies, administration of antibiotics was NOT associated with reduction in incidence of infections				⨁◯◯◯ Very low	CRITICAL
Infections with antibiotics												
1	observational studies	not serious	not serious	not serious	serious[b]	none	Infections WITH Antibiotics: 1/89 Infections withOUT antibiotics: 0/109				⨁◯◯◯ Very low	CRITICAL
AE												
0							data regarding adverse events of antibiotics in this setting are not known				-	CRITICAL
Cost effectiveness												
0							Data regarding cost and cost-effectiveness are not known.				-	IMPORTANT
Survival												
0							Impact of antibiotic administration on mortality is not known				-	CRITICAL

CI: confidence interval; **RR:** risk ratio

Explanations

a. In one study (Cotton), the study was not specifically focused on liver transplant patients. LT recipients were a subgroup
b. Low n

AE, Adverse event.

have limited access to high-quality medical care, and such differences among diverse socioeconomic and racial groups contribute to health disparities. Although out-of-pocket costs for patients needing management of biliary disease can vary considerably, pretransplant financial support is typically secured before transplant, whether it is through personal insurance or a government program, effectively addressing inequities based on socioeconomics.

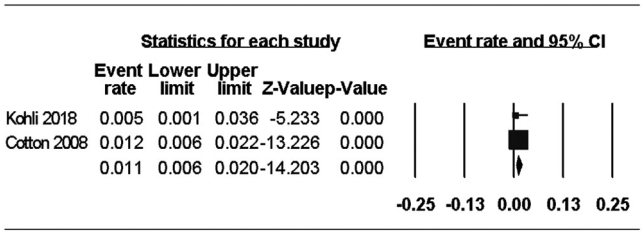


Figure 17. Pooled incidence of infections in liver transplant recipients undergoing ERCP. *CI*, Confidence interval.

DISCLOSURE

The following authors disclosed financial relationships: S. K. Amateau: Consultant for Olympus America Inc, Cook Medical LLC, Boston Scientific Corporation, Endo-Therapeutics, Hemostasis LLC, Heraeus Medical Components, LLC, Merit Medical Systems Inc, Steris Corporation, and Taewoong Medical; travel compensation from Olympus America Inc and Cook Medical LLC; food and beverage compensation from Olympus America Inc and Boston Scientific Corporation. D. R. Kohli: Grant support from Olympus Corporation of the Americas. N. Coelho-Prabhu: Consultant for Boston Scientific Corporation. S. E. Elhanafi: Travel compensation from Endogastric Solutions and Boston Scientific Corporation; food and beverage compensation from Endogastric Solutions, Boston Scientific Corporation, Merit Medical Systems, Inc, Salix Pharmaceuticals, and Intercept Pharmaceuticals. N. Forbes: Consultant and speaker for Boston Scientific Corporation and Pentax of America, Inc; research support from Pentax of America, Inc. L. L. Fujii-Lau: Food and beverage compensation from Pfizer Inc and AbbVie Inc. R. S. Kwon: Research support from AbbVie, Inc. J. D. Machicado: Speaker for Mauna Kea Technologies, Inc; food and beverage compensation from Abbott Laboratories. N. B. Marya: Consultant for and food and beverage compensation from Boston Scientific Corporation. W. Ruan: Grant support from Pfizer, Inc. S. G. Sheth: Food and beverage compensation from Takeda Pharmaceuticals USA, Inc. N. R. Thiruvengadam: Grant support from Boston Scientific Corporation. N. C. Thosani: Consultant for Boston Scientific Corporation, Covidien LP, and Pentax of America, Inc; travel compensation from Boston Scientific Corporation; food and beverage compensation from Boston Scientific Corporation, Covidien LP, Pentax of America, Inc, Erbe USA, Inc, and Ambu Inc; speaker for AbbVie Inc. B. J. Qumseya: Food and beverage compensation from Olympus America Inc. All other authors disclosed no financial relationships.

ACKNOWLEDGMENTS

We thank Tracy Thomas, a patient representative from the National Organization for Transplant Enlightenment, for participating in our panel and Robyn Rosasco (librarian) for assistance with searching for articles. We are also grateful to Dr Tiffany Chua, Dr Dennis Yang, and Dr Jonathan Cohen for their review of this document. This guideline was funded exclusively by the American Society for Gastrointestinal Endoscopy; no outside funding was received to support the development of this guideline.

GUIDELINE UPDATE

ASGE guidelines are reviewed for updates approximately every 5 years or in the event that new data may influence a recommendation. Updates follow the same ASGE guideline development process.

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Abbreviations: AE, adverse event; ASGE, American Society for Gastrointestinal Endoscopy; CI, confidence interval; CPT, Current Procedural Terminology; cSEMS, covered self-expandable metal stent; GRADE, Grading of Recommendations Assessment, Development and Evaluation; MPS, multiple plastic stent; PICO, patient/population, intervention, comparison, and outcomes; PTBD, percutaneous transhepatic biliary drainage; RCT, randomized controlled trial.

*Drs Amateau and Kohli contributed equally to this article.

Use your mobile device to scan this QR code and watch the author interview. Download a free QR code scanner by searching "QR Scanner" in your mobile device's app store.

0016-5107/$36.00
https://doi.org/10.1016/j.gie.2022.10.006

Received September 28, 2022. Accepted October 4, 2022.

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APPENDIX 1

Search strategies for patient/population, intervention, comparison, and outcomes question 1 data search terms

Database: Ovid MEDLINE ALL [1946 to Daily Update]
Number of Results: 855
Search Date: December 27, 2020
Limits: English
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver or hepatic).tw,kf.
2. (transplant* or graft* or allograft*).tw,kf.
3. 1 and 2
4. exp liver transplantation/
5. 3 or 4
6. exp bile ducts/
7. exp biliary tract diseases/
8. (bile duct* or biliary or hilar or peri?hilar or hilum or hilus).tw,kf.
9. or/6-8
10. exp constriction, pathologic/
11. (constriction or stricture* or stenosis or obstruction or occlusion or blockage).tw,kf.
12. 10 or 11
13. 9 and 12
14. exp cholestasis/
15. cholestasis.tw,kf.
16. ((bile duct* or biliary or hilar or peri?hilar or hilum or hilus or anastomotic or non-anastomic or nonanastomic) adj2 (stricture* or obstruction or occlusion or stenos?s or blockage)).tw,kf.
17. or/13-16
18. exp cholangiopancreatography, endoscopic retrograde/
19. exp stents/
20. exp prosthesis implantation/
21. exp prosthesis failure/ or exp prosthesis design/
22. * "Prostheses and Implants"/
23. *endoscopy/
24. "endoscopic retrograde cholangio?pancreatogra*". tw,kf.
25. ERCP.tw,kf.
26. ((endoscop* or ercp) and (stent* or prosthes* or endoprosthes*)).tw,kf.
27. or/18-26
28. exp drainage/
29. (percutaneous transhepatic biliary adj1 (drain* or stent*)).tw,kf.
30. ptdb.tw,kf.
31. drain*.tw,kf.
32. exp radiology, interventional/
33. interventional radiology.tw,kf.
34. exp radiotherapy/
35. (radiotherap* or irradiation or radiation).tw,kf.
36. radiotherapy.fs.
37. or/28-36
38. 5 and 17
39. 27 or 37
40. 38 and 39
41. limit 40 to english language
42. (addresses.pt. or biography.pt. or case reports.pt. or comment.pt. or directory.pt. or editorial.pt. or festschrift.pt. or interview.pt. or lectures.pt. or legal cases.pt. or legislation.pt. or letter.pt. or news.pt. or newspaper article.pt. or patient education handout.pt. or popular works.pt. or congresses.pt. or consensus development conference.pt. or consensus development conference, nih.pt. or practice guideline.pt.) not (exp animals/ not exp humans/)
43. 41 not 42

Database: Embase.com (Elsevier) [1947 to present]
Number of results: 928
Date run: December 27, 2020
Limits: English
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver OR hepatic):ti,ab,kw
2. (transplant* OR graft* OR allograft*):ti,ab,kw
3. #1 AND #2
4. 'liver transplantation'/exp
5. #3 OR #4
6. 'bile duct'/exp
7. 'biliary tract disease'/exp
8. ("bile duct*" OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
9. #6 OR #7 OR #8
10. 'stenosis, occlusion and obstruction'/exp
11. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
12. #10 OR #11
13. #9 AND #12
14. 'cholestasis'/exp
15. Cholestasis:ti,ab,kw
16. ("bile duct*" NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
17. (biliary NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
18. (hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
19. (peri?hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
20. (hilum NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
21. (hilus NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
22. (anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
23. (non-anastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw

24. (nonanastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
25. #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
26. 'endoscopic retrograde cholangiopancreatography'/exp
27. 'stent'/exp
28. 'prosthesis implantation'/exp
29. 'prosthesis complication'/exp OR 'prosthesis design'/exp
30. 'prostheses and orthoses'/de
31. 'endoscopy'/de
32. "endoscopic retrograde cholangio?pancreatogra*":ti,ab,kw
33. ERCP:ti,ab,kw
34. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw
35. #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34
36. 'drainage'/exp
37. ("percutaneous transhepatic biliary" NEAR/1 (drain* OR stent*)):ti,ab,kw
38. Ptdb:ti,ab,kw
39. ((internal NEAR/2 external) NEAR/2 drain*):ti,ab,kw
40. 'interventional radiology'/exp
41. (interventional NEAR/2 radiology):ti,ab,kw
42. 'radiotherapy'/exp
43. (radiotherap* OR irradiation OR radiation):ti,ab,kw
44. Radiotherapy:lnk
45. #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44
46. #5 AND #25
47. #35 OR #45
48. #46 AND #47
49. #48 AND english:la
50. ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [data papers]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [short survey]/lim OR 'animal cell'/de OR 'animal cell culture'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'clinical protocol'/de OR 'in vitro study'/de OR 'in vivo study'/de OR 'nonhuman'/de OR 'porcine model'/de OR 'practice guideline'/de OR 'case report'/de) NOT ('animals'/exp NOT 'humans'/exp)
51. #49 NOT #50

Database: Cochrane Library [Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL)] - Wiley
Number of results: 58
Date run: December 27, 2020
Limits: English

Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver OR hepatic):ti,ab,kw
2. (transplant* or graft* or allograft*):ti,ab,kw
3. #1 AND #2
4. [mh "liver transplantation"]
5. #3 OR #4
6. [mh "bile ducts"]
7. [mh "biliary tract diseases"]
8. (bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
9. #6 OR #7 OR #8
10. [mh "constriction, pathologic"]
11. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
12. #10 OR #11
13. #9 AND #12
14. [mh cholestasis]
15. Cholestasis:ti,ab,kw
16. ((bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus OR anastomotic OR non-anastomic OR nonanastomic) NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
17. #13 OR #14 OR #15 OR #16
18. [mh "cholangiopancreatography, endoscopic retrograde"]
19. [mh stents]
20. [mh "prosthesis implantation"]
21. [mh "prosthesis failure"] or [mh "prosthesis design"]
22. [mh "Prostheses and Implants"]
23. [mh "endoscopy"]
24. "endoscopic retrograde cholangio?pancreatogra*":ti,ab,kw
25. ERCP:ti,ab,kw
26. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw
27. #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
28. [mh drainage]
29. (percutaneous transhepatic biliary NEAR/1 (drain* OR stent*)):ti,ab,kw
30. Ptdb:ti,ab,kw
31. drain*:ti,ab,kw
32. [mh "radiology, interventional"]
33. interventional radiology:ti,ab,kw
34. [mh radiotherapy]
35. (radiotherap* OR irradiation OR radiation):ti,ab,kw
36. #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35
37. #5 AND #17
38. #27 OR #36
39. #37 AND #38

APPENDIX 2

Search strategies for patient/population, intervention, comparison, and outcomes question 2 data search terms

Database: Ovid MEDLINE ALL [1946 to Daily Update]
Number of Results: 279
Search Date: December 28, 2020
Limits: English
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver or hepatic).tw,kf.
2. (transplant* or graft* or allograft*).tw,kf.
3. 1 and 2
4. exp liver transplantation/
5. 3 or 4
6. exp bile ducts/
7. exp biliary tract diseases/
8. (bile duct* or biliary or hilar or peri?hilar or hilum or hilus).tw,kf.
9. or/6-8
10. exp constriction, pathologic/
11. (constriction or stricture* or stenos?s or obstruction or occlusion or blockage).tw,kf.
12. 10 or 11
13. 9 and 12
14. exp cholestasis/
15. cholestasis.tw,kf.
16. ((bile duct* or biliary or hilar or peri?hilar or hilum or hilus or anastomotic or non-anastomic or nonanastomic) adj2 (stricture* or obstruction or occlusion or stenos?s or blockage)).tw,kf.
17. or/13-16
18. exp cholangiopancreatography, endoscopic retrograde/
19. exp stents/
20. exp prosthesis implantation/
21. exp prosthesis failure/ or exp prosthesis design/
22. prostheses and implants/
23. endoscopy/
24. "endoscopic retrograde cholangio?pancreatogra*". tw,kf.
25. ERCP.tw,kf.
26. ((endoscop* or ercp) and (stent* or prosthes* or endoprosthes*)).tw,kf.
27. or/18-26
28. exp plastics/
29. exp stents/
30. 28 and 29
31. plastics.nm.
32. (plastic adj3 stent*).tw,kf.
33. ((10fr or 10-fr or "10 fr" or 7fr or 7-fr or "7 fr") and stent*).tw,kf.
34. or/28-33
35. exp self expandable metallic stents/
36. (metal* adj3 stent*).tw,kf.
37. ("fully?covered SEMS?" or FC?SEMS? or FCSEMS?).tw,kf.
38. (uncovered SEMS? or UCSEMS?).tw,kf.
39. or/35-38
40. (naso-biliary or nasobiliary or "naso biliary").tw,kf.
41. enbd.tw,kf.
42. 40 or 41
43. (sequential and (stent* or multi-stent* or multistent*)).tw,kf.
44. (standard adj3 (stent* or multi-stent* or multistent*)).tw,kf.
45. maximal stent*.tw,kf.
46. or/43-45
47. 5 and 17 and 27
48. 34 or 39 or 42 or 46
49. 47 and 48
50. limit 49 to english language
51. (addresses.pt. or biography.pt. or case reports.pt. or comment.pt. or directory.pt. or editorial.pt. or festschrift.pt. or interview.pt. or lectures.pt. or legal cases.pt. or legislation.pt. or letter.pt. or news.pt. or newspaper article.pt. or patient education handout.pt. or popular works.pt. or congresses.pt. or consensus development conference.pt. or consensus development conference, nih.pt. or practice guideline.pt.) not (exp animals/ not exp humans/)
52. 50 not 51

Database: Embase.com (Elsevier) [1947 to present]
Number of results: 165
Date run: December 28, 2020
Limits: English
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver OR hepatic):ti,ab,kw
2. (transplant* OR graft* OR allograft*):ti,ab,kw
3. #1 AND #2
4. 'liver transplantation'/exp
5. #3 OR #4
6. 'bile duct'/exp
7. 'biliary tract disease'/exp
8. ("bile duct*" OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
9. #6 OR #7 OR #8
10. 'stenosis, occlusion and obstruction'/exp
11. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
12. #10 OR #11
13. #9 AND #12
14. 'cholestasis'/exp
15. Cholestasis:ti,ab,kw
16. ("bile duct*" NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
17. (biliary NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw

18. (hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
19. (peri?hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
20. (hilum NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
21. (hilus NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
22. (anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
23. (non-anastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
24. (nonanastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
25. #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
26. 'endoscopic retrograde cholangiopancreatography'/exp
27. 'stent'/exp
28. 'prosthesis implantation'/exp
29. 'prosthesis complication'/exp OR 'prosthesis design'/exp
30. 'prostheses and orthoses'/de
31. 'endoscopy'/de
32. "endoscopic retrograde cholangio? pancreatogra*":ti,ab,kw
33. ERCP:ti,ab,kw
34. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw
35. #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34
36. 'plastic stent'/exp
37. Plastic*:tn
38. (plastic NEAR/3 stent*):ti,ab,kw
39. ((10fr OR 10-fr OR "10 fr" OR 7fr OR 7-fr OR "7 fr") AND stent*):ti,ab,kw
40. #36 OR #37 OR #38 OR #39
41. 'metal stent'/exp
42. (metal* NEAR/3 stent*):ti,ab,kw
43. ("fully?covered SEMS?" OR FC?SEMS? OR FCSEMS?):ti,ab,kw
44. (uncovered SEMS? OR UCSEMS?):ti,ab,kw
45. #41 OR #42 OR #43 OR #44
46. 'nasobiliary tube'/exp
47. (naso-biliary OR nasobiliary OR "naso biliary"):ti,ab,kw
48. Enbd:ti,ab,kw
49. #46 OR #47 OR #48
50. (sequential AND (stent* OR multi-stent* OR multistent*)):ti,ab,kw
51. (standard NEAR/3 (stent* OR multi-stent* OR multistent*)):ti,ab,kw
52. maximal stent*:ti,ab,kw
53. #50 OR #51 OR #52
54. #5 AND #25 AND #35
55. #40 OR #45 OR #49 OR #53
56. #54 AND #55
57. #56 AND english:la
58. ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [data papers]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [short survey]/lim OR 'animal cell'/de OR 'animal cell culture'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'clinical protocol'/de OR 'in vitro study'/de OR 'in vivo study'/de OR 'nonhuman'/de OR 'porcine model'/de OR 'practice guideline'/de OR 'case report'/de) NOT ('animals'/exp NOT 'humans'/exp)
59. #57 NOT #58

Database: Cochrane Library [Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL)] - Wiley
Number of results: 40
Date run: December 28, 2020
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver OR hepatic):ti,ab,kw
2. (transplant* or graft* or allograft*):ti,ab,kw
3. #1 AND #2
4. [mh "liver transplantation"]
5. #3 OR #4
6. [mh "bile ducts"]
7. [mh "biliary tract diseases"]
8. (bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
9. #6 OR #7 OR #8
10. [mh "constriction, pathologic"]
11. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
12. #10 OR #11
13. #9 AND #12
14. [mh cholestasis]
15. Cholestasis:ti,ab,kw
16. ((bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus OR anastomotic OR non-anastomic OR nonanastomic) NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
17. #13 OR #14 OR #15 OR #16
18. [mh "cholangiopancreatography, endoscopic retrograde"]
19. [mh stents]
20. [mh "prosthesis implantation"]
21. [mh "prosthesis failure"] or [mh "prosthesis design"]
22. [mh "Prostheses and Implants"]
23. [mh ^"endoscopy"]
24. "endoscopic retrograde cholangio? pancreatogra*":ti,ab,kw
25. ERCP:ti,ab,kw
26. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw

27. #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
28. [mh plastics]
29. [mh stents]
30. #28 AND #29
31. (plastic NEAR/3 stent*):ti,ab,kw
32. ("10fr "OR "10-fr" OR "10 fr" OR "7fr" OR "7-fr" OR "7 fr"):ti,ab,kw
33. #29 OR #30 OR #31 OR #32
34. [mh "self expandable metallic stents"]
35. (metal* NEAR/3 stent*):ti,ab,kw
36. ("fully?covered SEMS?" OR FC?SEMS? OR FCSEMS?):ti,ab,kw
37. (uncovered SEMS? OR UCSEMS?):ti,ab,kw
38. #34 OR #35 OR #36 OR #37
39. (naso-biliary OR nasobiliary OR "naso biliary"):ti,ab,kw
40. Enbd:ti,ab,kw
41. #39 OR #40
42. (sequential AND (stent* OR multi-stent* OR multistent*)):ti,ab,kw
43. (standard NEAR/3 (stent* OR multi-stent* OR multistent*)):ti,ab,kw
44. maximal stent*:ti,ab,kw
45. #42 OR #43 OR #44
46. #5 AND #17 AND #27
47. #33 OR #38 OR #41 OR #45
48. #46 AND #47

APPENDIX 3

Search strategies for patient/population, intervention, comparison, and outcomes question 3 data search terms

Database: Ovid MEDLINE ALL [1946 to Daily Update]
Number of Results: 244
Search Date: December 28, 2020
Limits: English, humans
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver or hepatic).tw,kf.
2. (transplant* or graft* or allograft*).tw,kf.
3. 1 and 2
4. exp liver transplantation/
5. 3 or 4
6. exp Liver/ or exp enzymes/
7. ((liver or hepatic) adj2 enzyme?).tw,kf.
8. ((liver or hepatic) adj3 function*).tw,kf.
9. (liver and (test* or diagnos*)).tw,kf. or exp Liver Function Test/
10. liver toxicity.tw,kf. or exp Liver Toxicity/
11. (hepatotoxicity or hepatotoxic or hepatotoxic$).tw,kf.
12. (ASAT or ALAT or SGPT or SGOT or GGT or AST or ALT).tw,kf.
13. ("Glutamic?Alanine Transaminase").tw,kf.
14. gamma Glutamyltransferase.tw,kf. or exp gamma-glutamyltransferase/ or gamma-Glutamyltransferase.nm. or gamma-glutamyltransferase, human.nm.
15. (Glutamyl Transpeptidase or GGTP or gamma?Glutamyl Transpeptidase or gammaglutamyltransferase).tw,kf.
16. ("Alanine?2?Oxoglutarate" or alanine transaminase).tw,kf. or Alanine Transaminase.nm.

or exp Alanine Aminotransferase/

17. aspartate aminotransferase?.tw,kf. or Aspartate Aminotransferases.nm.

or exp aspartate aminotransferases/

18. (aspartate apoaminotransferase or aspartate transaminase or "glutamic?oxaloacetic transaminase" or "L? aspartate?2?oxoglutarate aminotransferase" or "glutamate?aspartate transaminase").tw,kf.
19. (Aminotransferase or Alanine 2 Oxoglutarate Aminotransferase).tw,kf.
20. (alanine aminotransferase or "serum glutamic?oxaloacetic transaminase").tw,kf.
21. "Glutamic?Pyruvic Transaminase".tw,kf.
22. Alkaline phosphatase.tw,kf. or Alkaline Phosphatase.nm. or exp Alkaline Phosphatase/
23. or/6-22
24. exp bile ducts/
25. exp biliary tract diseases/
26. (bile duct* or biliary or hilar or peri?hilar or hilum or hilus).tw,kf.
27. or/24-26
28. exp constriction, pathologic/
29. (constriction or stricture* or stenos?s or obstruction or occlusion or blockage).tw,kf.
30. 28 or 29
31. 27 and 30
32. exp cholestasis/
33. cholestasis.tw,kf.
34. ((bile duct* or biliary or hilar or peri?hilar or hilum or hilus or anastomotic or non-anastomic or nonanastomic) adj2 (stricture* or obstruction or occlusion or stenos?s or blockage)).tw,kf.
35. or/31-34
36. exp cholangiopancreatography, endoscopic retrograde/
37. exp stents/
38. exp prosthesis implantation/
39. exp prosthesis failure/ or exp prosthesis design/
40. * "prostheses and implants"/
41. *endoscopy/
42. "endoscopic retrograde cholangio?pancreatogra*".tw,kf.
43. ERCP.tw,kf.
44. ((endoscop* or ercp) and (stent* or prosthes* or endoprosthes*)).tw,kf.
45. or/36-44
46. exp cholangiopancreatography, magnetic resonance/
47. "magnetic resonance cholangiopancreatography".tw,kf.
48. mrcp.tw,kf.
49. (MRI or NMRI or zeugmatogra* or ((computed or computerised or computerized or magneti* or MR or NMR or proton) adj5 (tomogra* or scan or scans or imaging or cholangiogra*))).tw,kf.
50. exp magnetic resonance imaging/
51. exp cholangiography/
52. (liver function test*).tw,kf.
53. exp liver function tests/
54. exp clinical enzyme tests/
55. or/46-54
56. exp Diagnosis/di
57. * diagnosis differential/
58. exp "Sensitivity and Specificity"/
59. * Reference Values/
60. * False Negative Reactions/
61. * False Positive Reactions/
62. exp Mass Screening/
63. or/56-62
64. diagnos$.tw.
65. (sensitivity or specificity).tw.
66. predictive value$.tw.
67. reference value$.tw.
68. ROC.tw.
69. likelihood ratio$.tw.
70. monitoring.tw.
71. or/64-70
72. or/63,71
73. 5 and 23 and 35
74. 45 or 52
75. 72 and 73 and 74
76. limit 75 to english language

77. (addresses.pt. or biography.pt. or case reports.pt. or comment.pt. or directory.pt. or editorial.pt. or festschrift.pt. or interview.pt. or lectures.pt. or legal cases.pt. or legislation.pt. or letter.pt. or news.pt. or newspaper article.pt. or patient education handout.pt. or popular works.pt. or congresses.pt. or consensus development conference.pt. or consensus development conference, nih.pt. or practice guideline.pt.) not (exp animals/ not exp humans/)
78. 76 not 77

Filter citation: van der Weijden T, Ijzermans CJ, Dinant GJ, et al. Identifying relevant diagnostic studies in MEDLINE. The diagnostic value of the erythrocyte sedimentation rate (ESR) and dipstick as an example. Fam Pract 1997;14:204-8.

Database: Embase.com (Elsevier) [1947 to present]
Number of results: 663
Date run: December 28, 2020
Limits: English, humans
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver OR hepatic):ti,ab,kw
2. (transplant* or graft* or allograft*):ti,ab,kw
3. #1 AND #2
4. [mh "liver transplantation"]
5. #3 OR #4
6. 'liver'/exp OR 'liver enzyme'/exp
7. (liver NEAR/2 enzyme?):ti,ab,kw
8. (hepatic NEAR/2 enzyme?):ti,ab,kw
9. (liver NEAR/3 function*):ti,ab,kw OR 'liver function'/exp
10. (hepatic NEAR/3 function*):ti,ab,kw
11. (liver and (test* or diagnos*)):ti,ab,kw OR 'liver function test'/exp
12. "liver toxicity":ti,ab,kw OR 'liver toxicity'/exp
13. (hepatotoxicity OR hepatotoxic OR hepatotoxic$):ti,ab,kw
14. (ASAT OR ALAT OR SGPT OR SGOT OR GGT OR AST OR ALT):ti,ab,kw
15. ("Glutamic?Alanine Transaminase"):ti,ab,kw
16. gamma Glutamyltransferase:ti,ab,kw OR 'gamma glutamyltransferase'/exp OR gamma-Glutamyltransferase:tn
17. (Glutamyl Transpeptidase OR GGTP OR gamma?Glutamyl Transpeptidase OR gammaglutamyltransferase):ti,ab,kw
18. ("Alanine?2?Oxoglutarate" OR alanine transaminase):ti,ab,kw OR Alanine Transaminase:tn OR 'alanine aminotransferase'/exp
19. aspartate aminotransferase?:ti,ab,kw OR Aspartate Aminotransferases:tn

OR 'aspartate aminotransferase'/exp

20. (aspartate apoaminotransferase OR aspartate transaminase OR "glutamic?oxaloacetic transaminase" OR "L?aspartate?2?oxoglutarate aminotransferase" OR "glutamate?aspartate transaminase"):ti,ab,kw
21. (Aminotransferase OR Alanine 2 Oxoglutarate Aminotransferase):ti,ab,kw
22. (alanine aminotransferase OR "serum glutamic?oxaloacetic transaminase"):ti,ab,kw
23. "Glutamic?Pyruvic Transaminase":ti,ab,kw
24. Alkaline phosphatase:ti,ab,kw OR Alkaline Phosphatase:tn OR 'alkaline phosphatase'/exp
25. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
26. 'bile duct'/exp
27. 'biliary tract disease'/exp
28. ("bile duct*" OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
29. #26 OR #27 OR #28
30. 'stenosis, occlusion and obstruction'/exp
31. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
32. #30 OR #31
33. #29 AND #32
34. 'cholestasis'/exp
35. Cholestasis:ti,ab,kw
36. ("bile duct*" NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
37. (biliary NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
38. (hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
39. (peri?hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
40. (hilum NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
41. (hilus NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
42. (anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
43. (non-anastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
44. (nonanastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
45. #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44
46. 'endoscopic retrograde cholangiopancreatography'/exp
47. 'stent'/exp
48. 'prosthesis implantation'/exp
49. 'prosthesis complication'/exp OR 'prosthesis design'/exp
50. 'prostheses and orthoses'/de
51. 'endoscopy'/de
52. "endoscopic retrograde cholangio?pancreatogra*":ti,ab,kw
53. ERCP:ti,ab,kw

54. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw
55. #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54
56. 'magnetic resonance cholangiopancreatography'/exp
57. "magnetic resonance cholangiopancreatography": ti,ab,kw
58. Mrcp:ti,ab,kw
59. (MRI OR NMRI OR zeugmatogra* OR ((computed OR computerised OR computerized OR magneti* OR MR OR NMR OR proton) NEAR/5 (tomogra* OR scan OR scans OR imaging OR cholangiogra*))):ti,ab,kw
60. 'nuclear magnetic resonance imaging'/exp
61. 'cholangiography'/exp
62. (liver function test*):ti,ab,kw
63. 'liver function test'/exp
64. 'enzyme assay'/exp
65. #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64
66. 'diagnosis'/exp
67. 'differential diagnosis'/de
68. 'sensitivity and specificity'/exp
69. 'reference value'/de
70. 'false negative result'/de
71. 'false positive result'/de
72. 'mass screening'/exp
73. #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72
74. diagnos$:ti,ab
75. (sensitivity OR specificity):ti,ab
76. predictive value$:ti,ab
77. reference value$:ti,ab
78. ROC:ti,ab
79. likelihood ratio$:ti,ab
80. monitoring:ti,ab
81. #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80
82. #73 OR #81
83. #5 AND #25 AND #45
84. #55 OR #65
85. #82 AND #83 AND #84
86. #85 AND english:la
87. ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [data papers]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [short survey]/lim OR 'animal cell'/de OR 'animal cell culture'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'clinical protocol'/de OR 'in vitro study'/de OR 'in vivo study'/de OR 'nonhuman'/de OR 'porcine model'/de OR 'practice guideline'/de OR 'case report'/de) NOT ('animals'/exp NOT 'humans'/exp)
88. #86 NOT #87

Database: Cochrane Library [Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL)] - Wiley

Number of results: 55

Date run: December 28, 2020

1. (liver OR hepatic):ti,ab,kw
2. (transplant* OR graft* OR allograft*):ti,ab,kw
3. #1 AND #2
4. [mh "liver transplantation"]
5. #3 OR #4
6. [mh Liver] OR [mh enzymes]
7. ((liver OR hepatic) NEAR/2 enzyme?):ti,ab,kw
8. ((liver OR hepatic) NEAR/3 function*):ti,ab,kw
9. (liver AND (test* OR diagnos*)):ti,ab,kw OR [mh "Liver Function Test"]
10. liver toxicity:ti,ab,kw OR [mh "Liver Toxicity"]
11. (hepatotoxicity OR hepatotoxic OR hepatotoxic$):ti,ab,kw
12. (ASAT OR ALAT OR SGPT OR SGOT OR GGT OR AST OR ALT):ti,ab,kw
13. ("Glutamic?Alanine Transaminase"):ti,ab,kw
14. gamma Glutamyltransferase:ti,ab,kw OR [mh "gamma-glutamyltransferase"]
15. (Glutamyl Transpeptidase OR GGTP OR gamma?Glutamyl Transpeptidase OR gammaglutamyltransferase):ti,ab,kw
16. ("Alanine?2?Oxoglutarate" OR alanine transaminase):ti,ab,kw OR [mh "Alanine Aminotransferase"]
17. aspartate aminotransferase?:ti,ab,kw OR [mh "aspartate aminotransferases"]
18. (aspartate apoaminotransferase OR aspartate transaminase OR "glutamic?oxaloacetic transaminase" OR "L?aspartate?2?oxoglutarate aminotransferase" OR "glutamate?aspartate transaminase"):ti,ab,kw
19. (Aminotransferase OR Alanine 2 Oxoglutarate Aminotransferase):ti,ab,kw
20. (alanine aminotransferase OR "serum glutamic?oxaloacetic transaminase"):ti,ab,kw
21. "Glutamic?Pyruvic Transaminase":ti,ab,kw
22. Alkaline phosphatase:ti,ab,kw OR [mh "Alkaline Phosphatase"]
23. #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22
24. [mh "bile ducts"]
25. [mh "biliary tract diseases"]
26. (bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
27. #24 OR #25 OR #26
28. [mh "constriction, pathologic"]
29. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
30. #28 OR #29
31. #27 AND #30
32. [mh cholestasis]
33. Cholestasis:ti,ab,kw
34. ((bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus OR anastomotic OR non-anastomic OR

nonanastomic) NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
35. #31 OR #32 OR #33 OR #34
36. [mh “cholangiopancreatography, endoscopic retrograde”]
37. [mh stents]
38. [mh “prosthesis implantation”]
39. [mh “prosthesis failure”] or [mh “prosthesis design”]
40. [mh "Prostheses and Implants"]
41. [mh ^“endoscopy”]
42. “endoscopic retrograde cholangio?pancreatogra* ":ti,ab,kw
43. ERCP:ti,ab,kw
44. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw
45. #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44
46. [mh “cholangiopancreatography, magnetic resonance”]
47. “magnetic resonance cholangiopancreatography": ti,ab,kw
48. Mrcp:ti,ab,kw
49. (MRI OR NMRI OR zeugmatogra* OR ((computed OR computerised OR computerized OR magneti* OR MR OR NMR OR proton) NEAR/5 (tomogra* OR scan OR scans OR imaging OR cholangiogra*))):ti,ab,kw
50. [mh “magnetic resonance imaging”]
51. [mh cholangiography]
52. (liver function test*):ti,ab,kw
53. [mh “liver function tests”]
54. [mh “clinical enzyme tests”]
55. #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54
56. #5 AND #23 AND #35
57. #45 OR #55
58. #56 AND #57

APPENDIX 4

Search strategies for patient/population, intervention, comparison, and outcomes question 4 data search terms

Database: Ovid MEDLINE ALL [1946 to Daily Update]
Number of Results: 24
Search Date: December 28, 2020
Limits: English, humans
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver or hepatic).tw,kf.
2. (transplant* or graft* or allograft*).tw,kf.
3. 1 and 2
4. exp liver transplantation/
5. 3 or 4
6. exp bile ducts/
7. exp biliary tract diseases/
8. (bile duct* or biliary or hilar or peri?hilar or hilum or hilus).tw,kf.
9. or/6-8
10. exp constriction, pathologic/
11. (constriction or stricture* or stenos?s or obstruction or occlusion or blockage).tw,kf.
12. 10 or 11
13. 9 and 12
14. exp cholestasis/
15. cholestasis.tw,kf.
16. ((bile duct* or biliary or hilar or peri?hilar or hilum or hilus or anastomotic or non-anastomic or nonanastomic) adj2 (stricture* or obstruction or occlusion or stenos?s or blockage)).tw,kf.
17. or/13-16
18. exp cholangiopancreatography, endoscopic retrograde/
19. exp stents/
20. exp prosthesis implantation/
21. exp prosthesis failure/ or exp prosthesis design/
22. prostheses and implants/
23. endoscopy/
24. "endoscopic retrograde cholangio?pancreatogra*".tw,kf.
25. ERCP.tw,kf.
26. ((endoscop* or ercp) and (stent* or prosthes* or endoprosthes*)).tw,kf.
27. or/18-26
28. exp Anti-Bacterial Agents/
29. (antibacterial* or anti-bacterial* or antibiotic* or bacterioci* or antimycobacterial* or anti-mycobacterial* or bacteremia).tw,kf.
30. 28 or 29
31. 5 and 17 and 27 and 30
32. limit 31 to english language
33. (addresses.pt. or biography.pt. or case reports.pt. or comment.pt. or directory.pt. or editorial.pt. or festschrift.pt. or interview.pt. or lectures.pt. or legal cases.pt. or legislation.pt. or letter.pt. or news.pt. or newspaper article.pt. or patient education handout.pt. or popular works.pt. or congresses.pt. or consensus development conference.pt. or consensus development conference, nih.pt. or practice guideline.pt.) not (exp animals/ not exp humans/)
34. 32 not 33

Database: Embase.com (Elsevier) [1947 to present]
Number of results: 116
Date run: December 28, 2020
Limits: English, humans
Excluded: Case reports, editorials, letters, comments, conference abstracts

1. (liver OR hepatic):ti,ab,kw
2. (transplant* OR graft* OR allograft*):ti,ab,kw
3. #1 AND #2
4. 'liver transplantation'/exp
5. #3 OR #4
6. 'bile duct'/exp
7. 'biliary tract disease'/exp
8. ("bile duct*" OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
9. #6 OR #7 OR #8
10. 'stenosis, occlusion and obstruction'/exp
11. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
12. #10 OR #11
13. #9 AND #12
14. 'cholestasis'/exp
15. Cholestasis:ti,ab,kw
16. ("bile duct*" NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
17. (biliary NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
18. (hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
19. (peri?hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
20. (hilum NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
21. (hilus NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
22. (anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
23. (non-anastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
24. (nonanastomic NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
25. #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24
26. 'endoscopic retrograde cholangiopancreatography'/exp
27. 'stent'/exp
28. 'prosthesis implantation'/exp
29. 'prosthesis complication'/exp OR 'prosthesis design'/exp

30. 'prostheses and orthoses'/de
31. 'endoscopy'/de
32. "endoscopic retrograde cholangio?pancreatogra*":ti,ab,kw
33. ERCP:ti,ab,kw
34. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw
35. #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34
36. 'antibiotic agent'/exp
37. (antibacterial* OR anti-bacterial* OR antibiotic* OR bacterioci* OR antimycobacterial* OR anti-mycobacterial* OR bacteremia):ti,ab,kw
38. #36 OR #37
39. #5 AND #25 AND #35 AND #38
40. #39 AND english:la
41. ([conference abstract]/lim OR [conference paper]/lim OR [conference review]/lim OR [data papers]/lim OR [editorial]/lim OR [erratum]/lim OR [letter]/lim OR [note]/lim OR [review]/lim OR [short survey]/lim OR 'animal cell'/de OR 'animal cell culture'/de OR 'animal experiment'/de OR 'animal model'/de OR 'animal tissue'/de OR 'clinical protocol'/de OR 'in vitro study'/de OR 'in vivo study'/de OR 'nonhuman'/de OR 'porcine model'/de OR 'practice guideline'/de OR 'case report'/de) NOT ('animals'/exp NOT 'humans'/exp)
42. #40 NOT #41

Database: Cochrane Library [Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL)] - Wiley
Number of results: 3
Date run: December 28, 2020

1. (liver OR hepatic):ti,ab,kw
2. (transplant* or graft* or allograft*):ti,ab,kw
3. #1 AND #2
4. [mh "liver transplantation"]
5. #3 OR #4
6. [mh "bile ducts"]
7. [mh "biliary tract diseases"]
8. (bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus):ti,ab,kw
9. #6 OR #7 OR #8
10. [mh "constriction, pathologic"]
11. (constriction OR stricture* OR stenos?s OR obstruction OR occlusion OR blockage):ti,ab,kw
12. #10 OR #11
13. #9 AND #12
14. [mh cholestasis]
15. Cholestasis:ti,ab,kw
16. ((bile duct* OR biliary OR hilar OR peri?hilar OR hilum OR hilus OR anastomotic OR non-anastomic OR nonanastomic) NEAR/2 (stricture* OR obstruction OR occlusion OR stenos?s OR blockage)):ti,ab,kw
17. #13 OR #14 OR #15 OR #16
18. [mh "cholangiopancreatography, endoscopic retrograde"]
19. [mh stents]
20. [mh "prosthesis implantation"]
21. [mh "prosthesis failure"] or [mh "prosthesis design"]
22. [mh "Prostheses and Implants"]
23. [mh "endoscopy"]
24. "endoscopic retrograde cholangio?pancreatogra*":ti,ab,kw
25. ERCP:ti,ab,kw
26. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw
27. #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26
28. [mh "Anti-Bacterial Agents"]
29. (antibacterial* OR anti-bacterial* OR antibiotic* OR bacterioci* OR antimycobacterial* OR anti-mycobacterial* OR bacteremia):ti,ab,kw
30. #28 OR #29
31. #5 AND #17 AND #27 AND #30