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

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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.)

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 judgments 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 I² and Q statistic. Significant heterogeneity was defined as either I² > 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.
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). 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.
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...
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. 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, the decision between ERCP or PTBD was based on the availability of an endoscopist. The study by Kohli et al 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. 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], 1.07-2.33) for ERCP versus PTBD. However, there was no uniform definition of success between the 2 studies. Lee et al 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 defined long-term success as a lack of any biliary intervention within 12 months of the last procedure.

Lee et al reported a success rate of 60% with ERCP and 59% with PTBD (P = .93), whereas Heinemann et al 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 and Lee et al, 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, 1.02-2.0). Lee et al 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 used the National Readmissions...
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).

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

<table>
<thead>
<tr>
<th>Event</th>
<th>No. of patients</th>
<th>Effect</th>
<th>Certainty</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ERCP</td>
<td>PTBD</td>
<td>Relative (95% CI)</td>
</tr>
<tr>
<td>Technical Success (assessed with: Long term follow-up)</td>
<td>2 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Overall AE</td>
<td>2 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Failure allograft</td>
<td>1 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Rejection of allograft</td>
<td>1 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Death during hospital stay</td>
<td>1 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Readmission</td>
<td>1 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Length of stay</td>
<td>1 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Number of interventions</td>
<td>1 observational studies</td>
<td>not serious</td>
<td>not serious</td>
</tr>
<tr>
<td>Cost</td>
<td>0</td>
<td>No published studies comparing costs or cost-effectiveness</td>
<td>IMPORTANT</td>
</tr>
</tbody>
</table>

PTBD, Percutaneous transhepatic biliary drainage.
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. 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 strictures, 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. 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). 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, 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

<table>
<thead>
<tr>
<th>Study name</th>
<th>Statistics for each study</th>
<th>Risk ratio and 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lee 2008</td>
<td>1.017 0.994 1.940 0.985 0.932</td>
<td>0.01 0.1 1 10 100</td>
</tr>
<tr>
<td>Kort 2020</td>
<td>1.120 0.520 2.025 0.378 0.707</td>
<td>0.01 0.1 1 10 100</td>
</tr>
</tbody>
</table>

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], 0.703-2.327); I2 = 53.4%.

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], 0.62-2.023); I2 = 0%.

www.giejournal.org
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 impreci-
sion 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. The overall charge of
reported $179,179.3/C6

effectiveness. One study restricted to hospitalized patients
months for ERCP and 6.5
/C6

Management of post-
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 effec-
tive strategies in managing post–liver transplant biliary
strictures. Although the therapeutic intent is similar, the
technical approach is different. ERCP often requires gen-
eral 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 per-
formed 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 sug-
gested 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 pa-
tients with hemodynamic instability may not be ideal can-
didates 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 recommen-
dation, low to moderate quality of evidence).

We performed a systematic review of the published
literature on this topic. We used Ovid MEDLINE and EM-
BASE 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 recip-
ients with post-transplant strictures. Notably, only those
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 RCTs14,16,20,22 and 6 were meta-analyses with or without novel retrospective data.12,17,19,25,24 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 al23 and Visconti et al24 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 al22 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 I² 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.

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* One study was a duplicate (16 studies total)
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\(^\text{20}\) favored MPSs. However, meta-analysis of the 4 studies revealed no significant difference between the groups, although a trend was noted favoring MPSSs, 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\(^\text{14,16,20}\), whereas Tal et al\(^\text{22}\) 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 \(I^2\)) and overall judged the quality of evidence to be low.
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.\(^2\) trended toward a difference in AEs, mostly migration, favoring MPSs, Kaffes et al.\(^1\) 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.\(^5\) 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 stenosis 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.

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**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
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. 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 possible risk of publication bias (Fig. 7). In assessing the certainty of the evidence, we rated down for inconsistency.

### Specificity
For assessing specificity, 20 studies were found to have sufficient data for meta-analyses, involving an aggregate of 758 patients. 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. 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 a possible risk 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...
an aggregate of 505 patients. 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. 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.
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.
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).

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.51 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 8. Forest plot of 20 studies assessing the specificity of MRCP to correctly 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. 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. Data regarding liver transplant recipients undergoing ERCP was limited to a
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; I² = 0 (Fig. 17).

Impact of antibiotics
Kohli et al55 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 al54 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
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.\textsuperscript{51} In patients at risk for having undrained ducts, antibiotics should be administered. These include patients with
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...
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 Taekeda Pharmaceuticals USA Inc. N. R. Thiruvengadam: Grant support from Boston Scientific Corporation. N. C. Thosani: Consultant for Boston Scientific Corporation, Coviden LP, and Pentax of America, Inc; travel compensation from Boston Scientific Corporation; food and beverage compensation from Boston Scientific Corporation, Coviden 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.

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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.

REFERENCES


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www.giejournal.org Volume 97, No. 4 : 2023 GASTROINTESTINAL ENDOSCOPY 637
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-anastomotic or nonanastomotic) adj2 (stricture* or obstruction or occlusion or stenosis 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/"
25. ERCP.tw,kf.
26. ((endoscop* or ercp) and (stent* or prosth* 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 stenosis OR obstruction OR occlusion OR blockage):ti,ab,kw
12. #10 OR #11
13. #9 AND #12
14. ‘cholestatic’/exp
15. Cholestasis:ti,ab,kw
16. (‘bile duct*’ NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
17. (biliary NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
18. (hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
19. (peri?hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
20. (hilum NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
21. (hilus NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
22. (anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
23. (non-anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw

Management of post–liver transplant biliary strictures: review of the evidence
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:lnk
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 ilus):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 stenosis? 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 ilus OR anastomotic OR non-anastomotic OR non-anastomotic) NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis? OR blockage)):ti,ab,kw
17. #13 OR #14 OR #15 OR #16
18. [mh “choangiopancreatography, 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 choangio?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 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-anastomotic or non-anastomotic) adj2 (stricture* or obstruction or occlusion or stenosis 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/
  25. ERCP.tw,kf.
  26. ((endoscop* or ercp) and (stent* or prosthesis* 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.
  38. (uncovered SEMS? or UCSEMS?).tw,kf.
  39. or/35-38
  40. (nasal-biliary or nasobiliary or "nasal biliary").tw,kf.
  41. endbr.tw,kf.
  42. 40 or 41
  43. ((sequential and (stent* or multi-stent* or multi-stent*)).
tw,kf.
  44. (standard adj3 (stent* or multi-stent* or multi-stent*)).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 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 stenosis 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 stenosis OR blockage)):ti,ab,kw
  17. (biliary NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
18. (hilar NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
19. (perihilary NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
20. (hilum NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
21. (hilus NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
22. (anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
23. (non-anastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
24. (nonanastomotic NEAR/2 (stricture* OR obstruction OR occlusion OR stenosis 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":ti,ab,kw
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 cholangiopancreatography":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. (nasobiliary OR nasobiliary OR "naso biliary"):ti,ab,kw
48. Endbd: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 hils):ti,ab,kw
9. #6 OR #7 OR #8
10. [mh "constriction, pathologic"]
11. (constriction OR stenosis 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 hils):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 cholangiopancreatography":ti,ab,kw
25. ERCP:ti,ab,kw
26. ((endoscop* OR ercp) AND (stent* OR prosthes* OR endoprosthes*)):ti,ab,kw

Management of post-liver transplant biliary strictures: review of the evidence
Management of post-liver transplant biliary strictures: review of the evidence

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.
14. gamma Glutamyltransferase.tw,kf. or exp gamma-glutamyltransferase/ or gamma-Glutamyltransferase.nm.
15. (Glutamyl Transpeptidase or GGTP or gamma?Glutamyl Transpeptidase or gammaglutamyltransferase).tw,kf.
17. or exp Alanine Aminotransferase/
18. aspartate aminotransferase?.tw,kf. or Aspartate Aminotransferases.nm.
19. or exp aspartate aminotransferases/
21. (Aminotransferase or Alanine 2 Oxoglutarate Aminotransferase).tw,kf.
22. (alanine aminotransferase or “serum glutamic?oxaloacetic transaminase”).tw,kf.
24. Alkaline phosphatase.tw,kf. or Alkaline Phosphatase.nm. or exp Alkaline Phosphatase/
25. or/6-22
26. exp bile ducts/
27. exp biliary or hilar or peri?hilar or hilum or hilus).tw,kf.
28. or/24-26
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-anastomotic) adj2 (structure* 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 choanal?opancreatogra*".tw,kf.
43. ERCP.tw,kf.
44. ((endoscop* or ercp) and (stent* or prosthes* or endoprotheties*)).tw,kf.
45. or/56-64
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 choanal?iography*)).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

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 hepatoxic 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 Alamine 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?2oxoglutarate 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 Phosphatasia: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’*:ti,ab,kw 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*:ti,ab,kw OR occlusion OR occlusion OR obstruction):ti,ab,kw
32. #30 OR #31
33. #29 AND #32
34. ’cholestasis’/exp
35. Cholestasis:ti,ab,kw
36. (#29 AND #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44
37. (biliary NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw OR blockage)):ti,ab,kw
38. (hilar NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw OR blockage)):ti,ab,kw
39. (peri?hilar NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw OR blockage)):ti,ab,kw
40. (hilum NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw OR blockage)):ti,ab,kw
41. (hilus NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw OR blockage)):ti,ab,kw
42. (anastomotic NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw OR blockage)):ti,ab,kw
43. (non-anastomotic NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw OR blockage)):ti,ab,kw
44. (anastomotic NEAR/2 (stricture*:ti,ab,kw OR occlusion OR stenosis*:ti,ab,kw 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 prosthesis* 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)*ti,ab,kw
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

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 ALT 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 GGT OR gamma?Glutamyl Transpeptidase OR gamma?glutamyltransferase):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 stenosis 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-anastomotic OR
nonanastomic) NEAR/2 (stricture* OR obstruction OR occlusion OR stenoses 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 cholangiopancreatography*”:ti,ab,kw
43. ERCP:ti,ab,kw
44. ((endoscop* OR ercp) AND (stent* OR prosthesis* OR endoprostheses*)):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 stenoses 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-anastomotic or nonanastomotic) adj2 (striction* or obstruction or occlusion or stenosis 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 cholangiopancreatogra*".tw,kf.
25. ERCP.tw,kf.
26. ((endoscopy or ercp) and (stent* or prosthesis* or endoprosthesis*)).tw,kf.
27. or/18-26
28. exp Anti-Bacterial Agents/
29. (antibacterial* or anti-bacterial* or antibiotic* or bacteriocin* 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 stenoses 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 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
17. (biliary NEAR/2 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
18. (hilar NEAR/2 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
19. (peri*hilar NEAR/2 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
20. (hilum NEAR/2 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
21. (hilus NEAR/2 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
22. (anastomotic NEAR/2 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
23. (non-anastomotic NEAR/2 (striction* OR obstruction OR occlusion OR stenosis OR blockage)):ti,ab,kw
24. (nonanastomotic NEAR/2 (striction* OR obstruction OR occlusion OR stenosis 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. 'sten*t'/exp
28. 'prosthesis implantation'/exp
29. 'prosthesis complication'/exp OR 'prosthesis design'/exp
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30. “prostheses and orthoses”/de
31. “endoscopy”/de
32. “endoscopic retrograde cholangiopancreatogra*”: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 bacterioc* OR antimycobacterial* OR anti-mycobacterial* OR bacteremia):ti,ab,kw
38. #36 OR #37
39. #5 AND #17 AND #27 AND #30 AND #38
40. #39 AND english:la
41. ([conference abstract]/lim OR [conference paper]/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-anastomotic OR nonanastomotic) 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 bacterioc* OR antimycobacterial* OR anti-mycobacterial* OR bacteremia):ti,ab,kw
30. #28 OR #29
31. #5 AND #17 AND #27 AND #30