

Malignant Biliary Obstruction

Effective Date: August, 2022



Background

Malignant biliary obstruction can lead to jaundice, impair the quality of life and hepatic function of cancer patients,¹ and result in delays in treatment (e.g. chemotherapy). Symptoms may include fatigue, pruritis and nausea, however, malignant biliary obstruction is often asymptomatic until the disease is significantly advanced.² Biliary obstructions are typically classified by their location (proximal, distal or mid). Primary tumour infiltration (e.g. cholangiocarcinoma), compression by local extension of other tumours (e.g. hepatic, gallbladder, pancreatic cancers), or extrinsic compression by lymph node metastases are common causes for malignant biliary obstruction.^{3,4} Malignant biliary obstruction occurs frequently in these conditions. For example, 70% of pancreatic cancer patients have some degree of biliary obstruction at initial diagnosis.⁵ Furthermore, the presence of malignant biliary obstruction is typically associated with a poor 5-year survival rate of approximately 5%.⁵

Relief of the obstruction may lead to improved quality of life and extended survival.^{6,7} There are various treatment options available to relieve malignant biliary obstructions including surgical, endoscopic and percutaneous procedures. An external drain involves the insertion of a catheter extending from outside the body to the bile ducts, while an internal-external drain involves a catheter from outside the body to the bile duct and extending to the small intestine. Efficacy and appropriateness of treatment type depend on the patient and their expected prognosis, the site of obstruction and local expertise. The purpose of this guideline is to provide evidence-based recommendations on the management of malignant biliary obstruction. Whenever possible recommendations are evidence-based and when insufficient evidence exists provincial consensus has been used to guide practice.

Guideline Questions

1. What are the recommendations for the diagnostic workup for patients with malignant biliary obstruction?
2. What are the recommended treatment options for patients with malignant biliary obstruction?

Search Strategy

In August 2022, the pubmed database was searched for randomized clinical trials within the last 5 years with N>50 patients related to malignant biliary obstruction. Of the 12 studies identified, none were considered practice changing, and so the guideline was updated without revision.

Target Population

The recommendations in this guideline apply to the treatment of patients with neoplasms causing biliary obstruction. For primary management guidelines please see [here](#).

Recommendations

Suggested Diagnostic Work-Up

- An ultrasound should be performed to distinguish proximal/distal/mid location (see Figure 1). If the radiologist cannot clearly identify proximal/distal/mid location, a CT scan can be done. Proximal obstructions are located at or above the hilum, distal obstructions are located below the cystic duct, and mid obstructions are at the level of the cystic duct.
- Determine patient status and their expected prognosis.

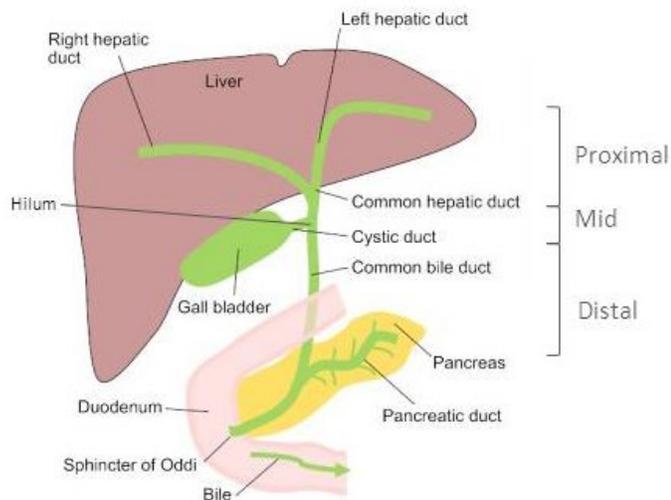


Figure 1. Approximate classification of biliary obstruction location (adapted from Zabron et al.¹¹)

Treatment

Factors affecting treatment include resectability, location of the obstruction, patient status, and clinical expertise. The goals of therapy are to improve quality of life (control or delay the onset of tumour-related symptoms) and if possible, prolong life.

- A multidisciplinary team should be consulted in the treatment of those suspected to have malignant biliary obstruction. The team should include medical oncologists, gastroenterologists, interventional radiologists and hepatobiliary surgeons.

Resectable:

1. Proximal resectable obstructions

- Early referral to a hepatobiliary surgeon is recommended to assess resectability prior to any instrumentation. If resection is entertained, a contrast enhanced MRI liver and magnetic resonance cholangiopancreatography (MRCP) are indicated, preferable before a drain is inserted because it is difficult to define the extent of biliary involvement once a stent has been placed. A percutaneous transhepatic cholangiogram (PTC) may assist in staging where noninvasive imaging is unable to clarify the proximal extent of disease. In the context of

primary biliary sclerosing cholangitis and concurrent suspected malignant obstruction, PTC is recommended for initial drainage and may be used to obtain brushings.

- The role of preoperative biliary drainage is controversial for hilar tumors. If a resection is planned, preoperative drainage may be considered to normalize coagulation status and to optimize liver function if an extensive liver resection is planned. A meta-analysis of 11 studies (10 retrospective and one prospective trials) investigating preoperative biliary drainage for hilar cholangiocarcinoma showed no difference in mortality (OR 0.70, 95% CI 0.41-1.19), however, a higher rate of postoperative complications (increased infection rates OR 2.17, 95% CI 1.24-3.80) was observed with preoperative drainage.¹² The potential benefit of preoperative drainage when remnant liver volume is <30% was shown in a retrospective study of patients with hilar cholangiocarcinoma who underwent hepatic resection (n=60).¹³ This study found preoperative drainage in those patients with preoperative future liver remnant volume of <30% was significantly associated with improved hepatic insufficiency and mortality rates, but this benefit was not apparent for patients with preoperative liver remnant volume predicted to be ≥30%. Ultimately, until more definitive data are available, the decision for preoperative drainage rests with the operating surgeon. Importantly, if pre-operative biliary drainage is considered, the drainage procedure should provide optimal preservation of the surgical field.
- If there is a delay to surgery (>1 week) or if drainage would improve the patient's condition, consider insertion of a percutaneous drain (e.g. external or internal/external drain). Endoscopic procedures for proximal obstructions are often technically difficult therefore percutaneous biliary drainage is strongly preferred.⁹ A retrospective study comparing percutaneous and endoscopic preoperative drainage in patients with hilar cholangiocarcinoma (n=101) found higher technical success rate (81% endoscopic group vs. 100% percutaneous group, p=0.20), significantly fewer infectious complications (48% endoscopic group vs. 9% percutaneous group, p<0.05) and significantly fewer additional drainage procedures (2.8 endoscopic group vs. 1.4 percutaneous group, P<0.01) with percutaneous preoperative drainage.¹⁴

2. Distal resectable obstructions

- Immediate surgery is preferred. A multicentre randomized trial for patients with resectable pancreatic cancer (n=202) compared preoperative endoscopic biliary drainage with plastic stents followed by surgery to surgery alone.¹⁵ This study found more serious complications in the preoperative drainage group (74% vs. 39%, respectively) and no difference in mortality rates. However, study limitations included a high failure rate and complication rate. This observation is confirmed by a meta-analysis focusing on preoperative drainage for distal obstructions which reported significantly increased infection rates with preoperative drainage compared with no drainage (p<0.0005) and no significant difference in mortality and morbidity.
- They identified 36 studies (including six randomized controlled trials) in their review and the majority of patients (67%) had endoscopic biliary drainage with plastic stents.
- If there is a delay to surgery (>1 week), consider insertion of an endoscopic plastic stent as a preoperative stent may help to normalize coagulation profile and improve nutritional status.

Endoscopic procedures are less invasive than percutaneous procedures and plastic stents are easily removed, however, they may require reintervention due to stent occlusion.

3. Mid resectable obstructions

- Early referral to a hepatobiliary surgeon is recommended to assess resectability. If resection is entertained, a contrast enhanced MRI liver and MRCP are indicated, preferable before biliary drainage is achieved, because it is difficult to define the extent of biliary involvement once a stent has been placed. A contrast enhanced CT of the chest, abdomen and pelvis should be considered, in addition to the MRI and MRCP, to identify metastatic disease.
- If there is a delay to surgery and decompression is needed an endoscopic approach or percutaneous transhepatic cholangiography (PTC) and drainage are viable options. Obstructions at this level require clinician expertise to determine the most appropriate approach to drainage.

Unresectable:

- In patients with unresectable or metastatic disease, biliary drainage can be used for palliation.⁹ The appropriate approach depends on the expected prognosis of the patient and the multidisciplinary team should be consulted.
- If imaging suggests intrahepatic duct dilatation and no extrahepatic duct involvement, then refer to interventional radiology. If extrahepatic duct dilatation then consider referral to gastroenterologist for endoscopic procedure. Additional imaging (e.g. MRI liver and MRCP) may be necessary to define the full extent of biliary involvement prior to stenting.
- There is a lack of evidence to recommend the use of prophylactic antibiotics. A Cochrane review from 2010 suggested that further research was required and there is not enough evidence to support prophylactic antibiotics with an ERCP.¹⁷ If biliary drainage fails to relieve the biliary obstruction then antibiotic administration could be considered.

4. Proximal unresectable obstructions

- Proximal obstructions are best managed with percutaneous biliary drainage. Treatment of these obstructions is dependent on life expectancy. We recognize that the determination of life expectancy is difficult and primarily dependent on the following factors: clinical status, metastatic disease, extent of local invasion, and use of palliative chemotherapy.
 - If life expectancy < 3 months, consider insertion of a percutaneous internal/external drain.
 - If life expectancy > 3 months, consider initial access via insertion of a percutaneous internal/external drain. Thereafter, consider insertion of a metal stent (via percutaneous or endoscopic approach) for patients with excellent performance status and whose condition markedly improved with the insertion of the internal/external drain. Metal stents have a life span of 6-12 months¹⁸⁻²⁰ which could mean repeat consult and insertion of another stent.

- A systematic review of the management of malignant hilar obstructions identified four studies (one randomized controlled trial and three retrospective studies) that compared endoscopic and percutaneous drainage with or without metal stent.²¹ Their results suggest initial percutaneous access is preferred because of higher therapeutic success, shorter time to reach desired drainage and negligible conversion rate. In particular, the review included a randomized controlled trial that compared endoscopic biliary drainage with a plastic stent to percutaneous biliary drainage.²² This study reported a significant difference in therapeutic success for initial percutaneous biliary drainage (89% percutaneous biliary drainage vs. 41% endoscopic biliary drainage, $p < 0.001$). The European Society of Gastrointestinal Endoscopy 2012 guideline suggests percutaneous drainage may be associated with fewer complications than the endoscopic approach and that the decision to perform endoscopic drainage be based on local expertise.⁹

5. Distal unresectable obstructions

- Refer to gastroenterologist for endoscopic drainage with insertion of a metal stent. Endoscopic retrograde cholangiopancreatography (ERCP) is the preferred treatment approach for distal unresectable obstructions as it is less invasive and has lower reported complication rates.⁸ A Cochrane systematic review compared surgery, metal endoscopic stents and plastic endoscopic stents for treatment of distal biliary obstruction in patients with inoperable pancreatic carcinoma.²³ The review included 29 studies and found endoscopic metal stents were associated with a lower risk of recurrent biliary obstruction (RR 0.48, 95% CI 0.38-0.62), but no differences in technical success, therapeutic success, or complications. They also noted that metal stents were reported to have significantly longer stent patency than plastic stents in several studies. The stent patency of metal and plastic stents were examined in a retrospective study of patients ($n=112$) with distal malignant biliary obstructions.²⁴ A significantly longer mean stent patency was reported for metal stents (278 days) compared to plastic stents (133 days) with no difference in total mean cost.
- If ERCP is unavailable or fails, then percutaneous biliary drainage should be considered to obtain palliative drainage. Definitive placement of a metallic stent can be achieved once the patient's condition has improved percutaneously or by a rendezvous procedure if internal access cannot be achieved percutaneously. A rendezvous procedure involves accessing the biliary tree percutaneously with placement of a guidewire to facilitate the completion of a challenging or failed ERCP.
- In select circumstances, such as failed ERCP, endoscopic ultrasound (EUS) guided biliary decompression can be considered. A randomized trial compared EUS-guided biliary drainage ($n=13$) after failed ERCP for distal malignant biliary obstructions with percutaneous drainage ($n=12$) and found similar outcomes for both procedures.²⁵ The advantage of EUS-guided biliary drainage is it can be performed in the same session as failed ERCP. A recent review of EUS-guided biliary drainage suggested that EUS-guided biliary drainage is a safe procedure that requires technical expertise and that back-up procedures, such as surgery or percutaneous

drainage, be available.²⁶ For EUS-guided choledocoduodenostomy, potential complications include peritonitis (4.0%), pneumoperitonitis (3.1%) and bleeding (2.7%).

- If an ERCP has been attempted and cannulation of the biliary tree was not successful, then an urgent referral for percutaneous drainage is indicated. Inoculation of an obstructed system with bowel flora can lead to biliary sepsis. For this reason, it is important to achieve biliary drainage as soon as possible after failed ERCP.

6. Mid unresectable obstructions.

- Endoscopic drainage or PTC are both viable options for biliary decompression. Obstructions at this level require clinician expertise to determine the most appropriate technique for drainage.

7. Role of surgical drainage

- As previously mentioned if the obstruction is determined to be unresectable then non-surgical treatment is preferred.²³ However, if unresectability is determined when the patient is already in the operating room surgical drainage can be performed. Surgical drainage is most relevant to distal obstructions as surgical drainage of proximal tumours is technically challenging. A meta-analysis conducted by Glazer et al.²⁷ identified five randomized controlled trails that compared immediate stent placement and surgical bypass for management of palliative malignant biliary obstruction. They concluded that patients who are good surgical candidates may benefit from surgical bypass as it was associated with lower risk of recurrence (RR 0.14, 95% CI 0.03-0.63; $p < 0.01$).

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Level of Evidence: 1a

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Level of Evidence: 1b

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Level of Evidence: 1a

Level	Description of Evidence
1a	Systematic reviews of randomized controlled trials
1b	Individual randomized controlled trials
1c	All or none randomized controlled trials
2a	Systematic reviews of cohort studies
2b	Individual cohort study or low quality randomized controlled trial
2c	Outcomes research
3a	Systematic review of case-control studies
3b	Individual case-control study
4	Case series
5	Expert opinion without explicit critical appraisal or based on physiology, bench research, or "first principles"

Development and Revision History

This guideline was reviewed and endorsed by the Alberta Provincial GI Tumour Team. Members include radiation oncologists, medical oncologists, urologists, nurses, pathologists, and pharmacists. Evidence was selected and reviewed by a working group comprised of members from the Alberta Provincial GI Tumour Team, external participants identified by the Working Group Lead, and a methodologist from the Guideline Resource Unit. A detailed description of the methodology followed during the guideline development process can be found in the [Guideline Resource Unit Handbook](#).

This guideline was originally developed in 2022.

Maintenance

A formal review of the guideline will be conducted in 2023. If critical new evidence is brought forward before that time, however, the guideline working group members will revise and update the document accordingly.

Abbreviations

AHS, Alberta Health Services; CCA, Cancer Care Alberta; CI, Confidence Interval; CT, Computed Tomography; ERCP, Endoscopic Retrograde Cholangiopancreatography; EUS, Endoscopic Ultrasound; MRCP, Magnetic Resonance Cholangiopancreatography; MRI, Magnetic Resonance Imaging; OR, Odds Ratio; PTC, Percutaneous Transhepatic Cholangiography; RR, Risk Ratio

Disclaimer

The recommendations contained in this guideline are a consensus of the Alberta Provincial GI Tumour Team and are a synthesis of currently accepted approaches to management, derived from a review of relevant scientific literature. Clinicians applying these guidelines should, in consultation with the patient, use independent medical judgment in the context of individual clinical circumstances to direct care.

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Conflict of Interest Statements

***Dr. Patricia Tang** reports Roche, Merck, Novartis, Pfizer, Incyte, and Apobiologix

Derek Tilley reports no conflicts.

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