Evaluation and Management of Malignant Biliary Obstruction

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KEYWORDS

• Biliary malignancies • Malignant obstructive jaundice • Surgical palliative care • Futility of care • Difficult conversation

KEY POINTS

- Conditions causing malignant biliary obstruction evolve silently and appear often at advanced stages.
- Imaging has optimized staging and decompression.
- Endoluminal techniques have replaced, when available, surgical procedures for palliation.
- Supportive and palliative care often are not available.

INTRODUCTION AND HISTORICAL PERSPECTIVE

Surgical intervention was the only option for the management of patients affected by malignant biliary obstruction (MBO), both for curative intent and for symptom management, for decades. Even in the most optimal presentation, midterm survival was mediocre at best, and long-term survival anecdotal. Realism and decency guided the management of this subset of aggressive cancers by surgical pioneers until the 1970s. Surgical palliation was piloted by intraoperative staging and symptom management because curative intention rarely was attainable. Currently, palliation still is the main philosophy for the management of many patients given the advanced stage at presentation and associated limited life expectancy.

The evolution of death perception over the past 50 years in the United States and the rise of sophisticated and aggressive care has affected the role of palliative care

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as a valid, equivalent, therapeutic modality for patients affected with deadly conditions. Arguably, society at large benefited from the progress of knowledge, technology, and innovation through the development of aggressive care, occupying a preponderant therapeutic place. This is an industrialized world statement, solipsistic, focused on a small subset of humanity. Most people do not, and never may, have access to the technology described in this article.

The normative concept of life prolongation as the only valid option over patients' choice and quality of life has relegated palliative care to a set of second order measures, with an associated semantic focused on failure and abandonment. The almost singular focus on aggressive care appears to be shifting gradually as increased attention and discussion focuses on patient-centric care. The patient, rather than the medical or scientific community, as definer of beneficial and nonbeneficial therapy is assuming a larger role in the scientific and lay literature. One of the most approachable examples from recent literature is *Being Mortal* by Dr Atul Gawande, a multi-award winning book on the topic of quality of life when quantity no longer is available.[1]

The curability, life expectancy, and quality of life of patients affected by MBO have improved and the once surgical only option has become a complex multimodal catalog of options dedicated to cure and also to improving the symptoms of noncurable patients with longer survival.

The patient's choice is regaining a place that technology has suppressed for a few decades, because the value of life at any cost was, and still might be, the only metric used to gauge efficacy of medical interventions. The multimodal options available in MBO are valid only for the fortunate few who live in a supportive health care system, operationally, financially, and socially. For the others, the immense majority, outcomes might not have changed. Multidisciplinary management requires access to care and there is no causality between level of industrialization and development and universal access to care.

TWO ERAS OF MANAGEMENT

This article is not a systematic review of MBO but a narrative one, because only articles in English and French were reviewed. The literature reviewed is time sensitive and can be separated in 2 different eras, still overlapping, depending on the geographic site of practice of the investigators. The first era starts when surgical intervention was the only option for diagnosis and symptom management; sometimes cure was attainable. The natural history was rapid progression to death within a few months. This still is the decision tree used in many areas of the world. The second era started with the appearance of multimodal therapies and the prospect for improved survival, if not cure. The consequence, intended or not, of this second era of management, has been a transition from individual, patient-centered care toward a focus on aggregated, population-based outcomes (eg, overall survival and progression-free survival). Similarly, the insidious shift in focus from the patient as the center of care and ultimate arbiter of a "good outcome" to a time of aggregate survival also is seen in the language. Cancer patients now can be classified as survivors or not.[2] The corollary is the ranking of the therapeutic options and the race for life at any cost, because only days or weeks count. When population-based outcomes take primacy in determining the benefits of treatment, this also introduces the risk to more vulnerable populations, such as the elderly, who may not experience the same benefits extrapolated from clinical trials of predominantly younger patients.[3] Clear advances of this second era are the development and refinement of alternate modes of technical palliation that certainly have contributed to the improved symptomatic management of this population.[4,5]

APPROACH TO THE JAUNDICE PATIENT

Jaundice is a rare clinical sign in the adult population. In a 2-year study of a family practice patients' cohort, 277 patients of 186,814 (approximately 0.15%) adults older than 45 developed at least 1 episode of jaundice[6]; 33% had bile duct stones, 12% had pancreatic cancer, 5% had cholangiocarcinoma, 10% had another malignancy, and 9% had liver disease. Almost one-quarter, 22%, did not have a record of the diagnosis. As illustrated by these data, the critical need to rule out malignancy as a cause of jaundice not always is appreciated. Furthermore, the urgency of securing a diagnosis is paramount given the aggressive biology of these malignancies.[7] Disparities in access to advanced care, such as endoscopic retrograde cholangiopancreatography (ERCP) in some geographic areas of the United States, and for some ethnic groups also contribute to health care disparities seen in patients with jaundice and the associated underlying malignancies.

By either extrinsic compression or intrinsic formation, the resultant jaundice from biliary obstruction is often the initial presenting sign of several hepato-pancreaticobiliary malignancies, as in the classic presentation of jaundice in pancreatic head adenocarcinoma and cholangiocarcinoma. Data from the American Cancer Society published in 2020 reported that pancreatic ductal adenocarcinoma is the fourth leading cause of cancer death in the United States despite its relatively low incidence of approximately 57,600 cases yearly and 47.050 deaths.[8] Approximately 80% of these patients presented with biliary obstruction, typically located at the head of the pancreas or at the uncinate process. As one of the deadliest cancers, the survival rate for patients with advanced pancreatic cancer across all genders and races is approximately 3% at 5 years.[9] Cholangiocarcinoma, although less prevalent, also is a deadly disease; 42,030 cases and 31,780 deaths were reported in 2020.[8] Classified by anatomic location—intrahepatic, perihilar, or distal—cholangiocarcinoma rarely is diagnosed at an early stage. It has an incidence of 1.6 per 100,000 people each year in the United States. Several studies have shown, however, an increased incidence of cholangiocarcinoma over the past decade. The 5-year survival rate for cholangiocarcinoma diagnosed at an advanced stage is approximately 2%.[10]

Although patient history and physical examination are required elements toward making a diagnosis of benign or MBO, advanced imaging and the pathologic evaluation of tissue are mandatory when a malignancy is suspected (discussed later). Classic painless jaundice, the pathognomonic sign of pancreatic head adenocarcinoma, often is associated with nonspecific signs secondary to the systemic effects of biliary retention, including pruritus, dark urine, and discolored stools, which almost always are present.[11] Important signs for the diagnosis and the prognosis of patients with suspected pancreatic cancer are the presence of unintentional weight loss and new-onset diabetes in an older adult; these findings should be identified as paraneoplastic syndromes associated with pancreatic cancer.[12] Similarly, depression and fatigue may precede the diagnosis.[13] Elevated conjugated bilirubin and alkaline phosphatase are common but nondiagnostic for malignancy. The tumor markers commonly evaluated in patients with biliary obstruction have variable sensitivity and specificity for malignancy. For instance, carbohydrate antigen 19-9 (CA 19-9) greater than 37 U/mL has a sensitivity of 70% to 86% and specificity of 8% to 90% for MBO whereas carcinoembryonic antigen has a sensitivity of 33% to 68% and a specificity of 75% to 95% for cholangiocarcinoma.[14–16] Recent studies show several other potential tumor markers, including PAM4, glypican 1, KRAS mutations, and microRNAs (miRNAs) used in the early diagnosis of pancreatic cancer. Elevated levels of miR-143 and

miR-30e have a reported sensitivity of 83% and a specificity of 96% for identifying pancreatic cancer.[17]

DIAGNOSIS AND STAGING

The second era of evaluation and management of MBO is characterized by advanced imaging. Although an exhaustive review of pancreaticobiliary imaging is beyond the scope of this article, several key imaging modalities now are used routinely to evaluate patients with MBO. Transabdominal ultrasonography (TAUS) or screening computed tomography (CT) guides the need for further imaging. In many instances, when the findings of these initial imaging studies raise suspicion for a malignant cause of biliary obstruction, referral often is made to a tertiary center where several modalities using various CT scan protocols or magnetic resonance imaging (MRI) or magnetic resonance cholangiopancreatography are used in conjunction with endoluminal procedures to identify lesions, obtain tissue for biopsy, and perform biliary decompression with ERCP. In patients without endoluminal access for biliary decompression or following unsuccessful attempt at endoscopic decompression, percutaneous catheterization of the biliary system by interventional radiology often is required. In a recent systematic review, Toft and colleagues[18] compared sensitivities, specificities, and diagnostic accuracy of several modalities for the diagnosis of pancreatic adenocarcinomas. Sensitivities range from 88% for TAUS to 93% for MRI. Specificity was highest with TAUS at 94% compared with CT with 87%. Finally, accuracy ranged from 89% for CT and endoscopic ultrasound (EUS) to 90% and 91% for MRI and TAUS, respectively.[18]

Confirmation of the diagnosis of malignancy requires pathologic evaluation of tissue, typically obtained through nonsurgical techniques. The combination of EUS and fine-needle aspiration has a high accuracy (93%) for diagnosing pancreatic adenocarcinoma.[19] Mallery and colleagues[20] reported the equivalence of accuracy between EUS, CT scan–guided and surgically obtained biopsies.

TECHNICAL INTERVENTIONS FOR MALIGNANT BILIARY OBSTRUCTION

Surgical Approach

When only surgical procedures were available for evaluation and management of MBO (first era), the techniques dedicated to palliation included cholecystogastrostomy, hepaticojejunostomy, cholecystojejunostomy, and choledochoduodenostomy.[21,22] More recently, Saldinger and colleagues[23] described 2 approaches to palliation of MBO in patients with hilar cholangiocarcinoma. Patients diagnosed with unresectable tumors preoperatively are offered percutaneous drainage whereas those determined to be unresectable intraoperatively undergo biliointestinal bypass. Palliative surgery proportionally has decreased with the advent of improved preoperative imaging and interventional procedures. **Fig. 1** shows an algorithm with currently available therapy options to help guide treatment of symptomatic relief of MBO.

Endoluminal and Percutaneous Therapies

The major procedural change in the management of MBO is the shift from open surgical procedures to percutaneous and endoluminal interventions, at the end of the 1970s.[24] The time when laparotomy was required for staging and palliative bypass largely has passed. Endoluminal and percutaneous techniques have variable indications, most commonly intrahepatic or distal biliary obstructions, and have a place in the diagnosis and in preoperative and palliative management.[25] Endoscopic biliary drainage (EBD) modalities via dilation of strictures or stent placement across tumors,

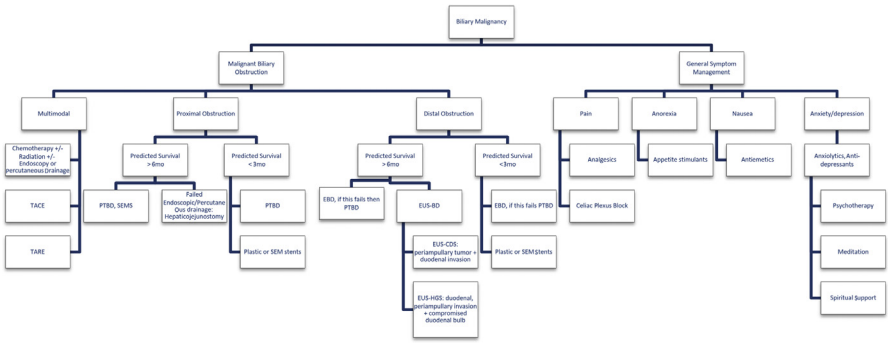

Fig. 1. Palliative treatment algorithm for biliary malignancy. TACE, transarterial chemoembolization; TARE, transarterial radioembolization.

have been used primarily for biliary decompression in patients with obstructive jaundice to relieve symptoms, such as severe itching or biliary sepsis, mainly from distally located tumors. Intrahepatic tumors more often are treated initially with percutaneous access of the biliary tree due to anatomic limitations that prevent successful endoscopic intervention. The timing and approach to managing MBO are critical. The following questions must be addressed clearly to avoid inappropriate use of endoluminal or percutaneous therapies: (1) Has a diagnosis of MBO been established? (2) Is the tumor resectable? and (3) Is the patient a surgical candidate? Failure to successfully answer these questions prior to intervention can have disastrous and life-limiting consequences. For example, if a tissue diagnosis of malignancy has not been obtained prior to endoluminal or percutaneous biliary intervention, obtaining a satisfactory biopsy can be difficult/impossible, particularly if a stent has been placed. Without biopsy confirmation of malignancy, cancer-directed therapies, if otherwise indicated, may not be offered. The accuracy of diagnostic imaging also can be impacted negatively by the placement of a stent or other biliary drainage (BD) procedure. For those patients who may be considered for surgical resection in the future, perioperative complications, in particular infectious complications, are increased in patients who have undergone preoperative biliary decompression.[25,26]

Stents commonly are used for unresectable tumors. In patients with unresectable disease, EBD with stent placement has shown to be less morbid than surgical intervention while providing similar relief of symptoms and survival. The primary outcomes measured in the setting of unresectable disease are survival and stent patency rather than actual palliative outcomes, such as symptomatic relief or quality of life. Consequently, the optimal endoscopic and/or endoluminal approach to palliation of MBO is largely unstudied.

The most common types of stents utilized in patients with MBO are plastic and self-expanding metal stents (SEMSs). Drug-eluting SEMSs are coated most commonly with chemotherapeutic agents, such as paclitaxel, gemcitabine, or sorafenib.[27–29] SEMSs are recommended for patients with predicted survival of greater than 3 months and Bismuth-Corlette classification type II-IV, with tumor involvement of the confluence, bifurcation of the right and/or left hepatic ducts or multifocal disease involvement. Plastic stents typically are recommended as temporary drainage option for cholangitis, in cases of undetermined treatment plan, or when predicted survival is less than 3 months.[30] Published data support use of SEMSs over plastic stents due higher clinical success rates (77%), higher long-term patency rates (median 5.4 months), and reduced need for secondary procedures. Park and colleagues[31]

reviewed the efficacy of various stents for palliation of MBO and reported that SEMss (covered and uncovered) were superior to plastic ones in terms of recurrent biliary obstruction. Due to the short median survival associated with MBO, in patients with unresectable disease, in many cases, SEMSs may provide lifetime patency and reduction of future endoscopic interventions.[32–34] Covered SEMSs have been shown to have increased patency rates (up to 85.7% at 12 months) compared with uncovered SEMSs, likely due to decreased tumor ingrowth across the interstices and the margins of the stent. Moole and colleagues[35] compared covered and uncovered stents and did not find any differences in survival, overall adverse events, or patency rates between these 2 types of stents. Some investigators argue that the benefits of covered SEMSs do not outweigh their increased costs.

A growing body of literature also has sought to determine the optimal technique for stent placement for MBO. Transmural stenting refers to EUS-guided BD (EUS-BD) and is a lesser-known endoscopic treatment option for MBO. This intervention is not widely available due to limited access to the device utilized and the need for specialized training in EUS-BD specifically.[36] EUS-BD includes choledochoduodenostomy stent (CDS) and hepaticogastrostomy stent (HGS). EUS-CDS scenting is considered for patients with distal biliary obstruction and periampullary tumor infiltration with distal duodenal invasion. EUS-HGS is considered for patients with distal biliary obstruction and duodenal bulb invasion (i.e. gastric outlet obstruction), periampullary duodenal invasion with compromised duodenal bulb, or surgically altered anatomy.[36] EUS-CDS and EUS-HGS utilize a lumen apposing metallic stent (LAMS) for drainage. Two recent systematic reviews and meta-analyses comparing LAMSs to SEMSs reported comparable rates of technical feasibility (in excess of 90%), complications (17.1% vs 18.3%, respectively), and reintervention (10.9% vs 13.9%, respectively).[37,38] Within the EUS-BD groups, there was no difference in stent patency rate between EUS-CDS and HGS.[36] Additionally, multiple reviews comparing EUS-BD versus ERCP-BD for the management of MBO have found equivalent efficacy of these 2 procedures, with some reviews reporting lower complications in the EUS-BD group (eg, post-ERCP pancreatitis and stent dysfunction) and shorter hospital stay (4 d vs 5 d).[39–44] Because EUS-guided procedures require creation of a temporary fistula, however, risk of bile leak is of major concern despite an approximately 5% complication rate.[45]

Stent occlusion is a significant issue in patients with MBO managed with stent placement and is important particularly in the palliative setting because repeat interventions associated with stent can have an adverse impact on quality of life, particularly for patients with limited life expectancy. As a result, various investigators have sought to identify techniques that can improve stent patency. Some investigators have reported a potential role for drug-eluting SEMSs to prevent direct tumor ingrowth and thereby increase patency rate.[33,46] In contrast, a recent review by Mohan and colleagues[47] found comparable overall survival and stent patency as well as complications between drug-eluting and covered metal stents.

Zhu and colleagues[48] reported on a multicenter trial of irradiation stents Iodine 125 (I^{125}) versus conventional metal stents for MBO. Compared with SEMSs, irradiation stents have lower rates of occlusions (9% vs 15%, respectively, at 90 days; 16% vs 27%, respectively, at 180 days; and 21% vs 33%, respectively, at 360 days). Survival in patients treated with irradiation stents was longer: median survival was 202 days versus 140 days respectively compared with SEMs.[48] Intraluminal brachytherapy and biliary stenting were compared with stenting alone by Xu and colleagues[49] in a systematic review and meta-analysis of 12 studies representing 641 patients. They found that the combination of brachytherapy and stenting was superior to stenting

alone in terms of stent occlusion and mean survival with comparable complications and efficacy of normalization of liver function studies. The combination of intraductal radiofrequency ablation (RFA) plus stenting in MBO caused by cholangiocarcinoma recently was reviewed by Cha and colleagues[50] They found that overall survival was improved with RFA with stent insertion versus stenting alone. No difference in duration of stent patency was found between the 2 groups. Similar to the findings combining intraductal RFA plus stenting, the combination of high intensity focused ultrasound with stenting is associated with improved stent patency and overall survival in patients with MBO.[51] The current literature largely is based on pooled analyses of several studies, and key issues, such as the learning curve required to successfully administer these advanced techniques as well as how they should be incorporated in treatment algorithms, are lacking.

Due to the issues related to stenting for MBO, some investigators have advocated for ablative procedures for biliary malignancies, primarily cholangiocarcinoma, prestent or poststent placement. For example, Laquiμre and colleagues[52] reported on a small series of patients with unresectable extrahepatic cholangiocarcinoma treated with endoscopic biliary RFA. The reported that this procedure had an acceptable safety profile with no adverse events or biliary fistula. Yang and colleagues[28] recently reported on 75 patients with unresectable extrahepatic cholangiocarcinoma treated with endoscopic RFA either with or without a novel 5-fluorouracil compound. They found a median overall survival of 16 months in the RFA plus chemotherapy group compared with 11 months in the RFA-alone group ($P<.001$). Karnofsky performance scale scores also were significantly higher in the combined treatment group at 9 months and 12 months, postoperatively. Recent reviews have confirmed the findings of these studies, showing improved stent patency and overall survival in this particularly challenging patient population, and note that the ideal treatment approach remains unclear owing to the novelty of these techniques and lack of widespread availability of the equipment and expertise required.[29,30]

SURGICAL VERSUS ENDOLUMINAL OR PERCUTANEOUS INTERVENTIONS

The choice of surgical versus endoluminal or percutaneous intervention for MBO is dependent on several factors, including morbidity and mortality of the procedure and length of hospitalization. The risks of palliative procedures are well known and have a significant impact, particularly in patients with limited life expectancy. Additionally, the time required to recover from an intervention also can have a negative impact on patient quality of life. Surgical bypass has a lower rate of recurrent biliary obstruction compared with endoscopic stent placement: 3.1% versus 28.7%, respectively, with a risk ratio of 0.14 in 1 study.[53] A 2-fold increase in total number of hospital days from the index procedure until death has been reported in patients undergoing stenting compared with surgical bypass due to the need for repeat procedures, including stent replacement or ultimate need for percutaneous BD (PTBD). Despite the superiority of surgical bypass in terms of lower rate of recurrent biliary obstruction, overall survival and rates of major morbidity and mortality are comparable to stenting alone. Significant complications are associated, however, with these palliative surgical interventions and include gastrointestinal bleeding, wound infections, gastrointestinal obstruction, pulmonary embolism, and stroke. Up to 50% of patients treated for MBO eventually require an intervention for gastric outlet obstruction; therefore, some investigators advocate performing simultaneous enteric bypass during surgical biliary bypass.[53] Robust evidence comparing surgery versus PTBD is not available. Current recommendations are surgical bypass with concomitant gastric emptying procedure if

life expectancy is at least 6 months. SEMSs are recommended if life expectancy is less than 4 months; however, for those with expected survival of 4-6 months there is no clear recommendation regarding stent type.[53]

THE ROLE OF PALLIATIVE CARE

The choice of placing supportive and palliative care first is deliberate and responds to the often poor prognosis of both pancreatic adenocarcinoma and cholangiocarcinoma, the 2 primary causes of MBO. The definition of palliative care according to the World Health Organization is "an approach that improves the quality of life of patients and their families facing the problem associated with life-threatening illness, through the prevention and relief of suffering by means of early identification and impeccable assessment and treatment of pain and other problems, physical, psychosocial and spiritual.[54] Therefore, it is expected that a multidisciplinary approach to patient-centered care is more likely to deliver the necessary holistic palliative care that these patients and families need.

In both eras of MBO management, the need for palliative care has been apparent. In the first era, curative intent rarely was an option; therefore, optimal methods to prepare patients and family for an inevitable death had to be initiated at the time of the diagnosis of incurability. Choices were limited, guided only by the aggressivity of the condition. In the second era, medical and technological advancement supported patients, their families, and the medical team and created a bridge to safer and less morbid means of MBO management. Additionally, advances in imaging and surgical techniques and perioperative care improved surgeons' ability to select patients for surgical intervention, both palliative and those with curative intent. A growing body of literature characterizes the benefits of palliative care in patients with advanced malignancies, in general, and in MBO, specifically.[55–58] In addition to the benefits of palliative care for symptom management, the importance of clear communication and prognostic awareness is paramount. A recent review by Laryionava and Winkler[59] found that eliciting patient preferences enabled advance care planning, avoided overtreatment at end of life, and helped ensure that patients received goal-concordant care. Particularly in the setting of the aggressive malignancies associated with MBO, understanding patient preferences for balancing the trade-off between quantity of life and quality of life is crucial.[60] Additionally, as choices become nonbinary: life, death, or survival with the disease, the central role of patient-centered decision-making is key and the challenge for providers is to resist portraying treatment options in these binary terms. This mode of thinking—la pensée unique—is a 1980 derivative of the economic thinking, "there is no alternative," that has affected not only oncology but also other modalities of aggressive care, especially critical care.[61] Coincident with the medical and technological advances seen between the 2 eras of MBO management has been a shift from the well-intentioned, if paternalistic, approach to medical decision making toward shared decision-making models. The essence of the trust between surgeons and patients is the disclosure of attainable goals, allowing for an informed decision. The discussion about attainable goals can be mediated through the utilization of scenarios, best case/worst case, as illustrated in Kruser and colleagues,[62] to assist in the definition of choices. Although autonomy is elevated as a primary ethical value in bioethics in the United States, choices of nonaggressive care often are questioned and challenged by medical teams, revealing cultural differences between patients and physicians.[63,64] It also is during this second era that the role of palliative care in cancer care has been recognized.[55] Despite that most major oncology professional societies and cancer care guidelines call for the integration of palliative care with routine cancer care, an

integrated model of care still is far distant in all but the largest cancer centers.[65,66] Beesley and colleagues[67] used the term, *tsunami*, to describe unmet supportive care needs in patients with pancreatic and ampullary cancers. They found that 96% of those survey reported having some palliative care needs. Only 59% of patients with unresectable disease, however, accessed palliative care services compared with 27% for those with resectable tumors.

SUMMARY

MBO is an ominous sign and warrants prompt evaluation and management. The options for management depend on the location of the obstruction and on the tumor histology. Unfortunately, in a majority of cases, MBO portends poor prognosis. Technical considerations regarding the optimal management for biliary decompression tend to dominate the initial treatment decision making. These considerations must not be prioritized, however, to the exclusion of other significant needs of the patient and their family for aggressive symptom management (beyond addressing jaundice) and early initiation of goals of care discussions. The surgeon must be prepared to provide the full spectrum of palliative treatment required in these cases: surgical biliary and/or enteric bypass, referral for endoscopic or percutaneous biliary interventions, multidisciplinary coordinated care with medical and radiation oncology, and medical management for the symptoms seen most commonly, including tumor-related pain, nausea and vomiting, and fatigue.[68,69]

There is little doubt that advances in procedural interventions and systemic therapies will continue to improve for patients with MBO, just as seen between the first and second eras. These advances will come through properly designed studies, ideally that include a representative sample of those affected by these tumors. The need for holistic patient care, from the time of diagnosis to end of life, is essential. Those providers charged with caring for patients with MBO must remain vigilant against the temptation to measure that which is easy to measure (eg, bilirubin levels, overall survival, and progression-free survival) while minimizing the outcomes most important to the patient; it cannot be assumed that clinical markers and patient outcomes are equivalent. Early integration of palliative care, either through utilization of dedicated departments or, more importantly, by institutional initiative to develop a multidisciplinary primary palliative care, offers one of the surest ways to ensure that patient care stays patient focused.

CLINICS CARE POINTS

- Palliation is the main philosophy in management of advanced stage malignant biliary obstruction due to its associated limited life expectancy and our duty to serve the patient's goals.
- Patients' needs matter and need to be heard and understood by the medical team.
- When population-based outcomes take precedence over patient-centered care, we risk making generalizations that do not apply or best-serve the patient, particularly those from vulnerable populations.
- Although autonomy is elevated as a primary ethical value in bioethics, choices of nonaggressive care are often questioned and challenged by medical teams.
- Studies show that a holistic patient-focused palliative care approach best improves the quality of life of patients and their families; balancing the trade-off of quantity of life and quality of life is crucial.

DISCLOSURE

The authors have nothing to disclose.

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