MINIREVIEWS

Current role of palliative interventions in advanced pancreatic cancer

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Abstract

Pancreatic adenocarcinoma is the third leading cause of cancer death in the United States. Unfortunately, at diagnosis, most patients are not candidates for curative resection. Surgical palliation, a procedure performed with the intention of relieving symptoms or improving quality of life, comes to the forefront of management. This article reviews the palliative management of unresectable pancreatic cancer, including obstructive jaundice, duodenal obstruction and pain control with celiac plexus block. Although surgical bypasses for both biliary and duodenal obstructions usually achieve good technical success, they result in considerable perioperative morbidity and mortality, even when performed laparoscopically. The effectiveness of self-expanding metal stents for biliary drainage is excellent with low morbidity. Surgical gastrojejunostomy for duodenal obstruction appears to be best for patients with a life expectancy of greater than 2 mo while endoscopic stenting has been shown to be feasible with good symptom relief in those with a shorter life expectancy. Regardless of the palliative procedure performed, all physicians involved must be adequately trained in end of life management to ensure the best possible care for patients.

Key words: Surgical palliation; Duodenal obstruction; Hepatojejunostomy; Gastrojejunostomy; Endoscopic stenting; Malignant ascites; Celiac block; Palliative triangle; Pancreatic cancer; Obstructive jaundice

Core tip: Unfortunately, at the time of diagnosis most patients with pancreatic cancer are not candidates for curative resection. Surgical palliation, a procedure performed with the intention of relieving symptoms or improving quality of life, comes to the forefront of

management. The majority of palliative care focuses on three high burden symptoms: obstructive jaundice, duodenal obstruction and tumor-related pain. There exists a wide range of interventions including both operative and non-operative techniques. Regardless of the palliative procedure, all physicians involved must be adequately trained in end of life management to ensure the best possible care for patients.

PANCREATIC CANCER INTRODUCTION

The incidence of and number of deaths caused by pancreatic tumors have been slowly increasing. It is estimated that in 2018, 55440 new cases of pancreatic cancer will be diagnosed in the United States with a five-year survival of only 8.5%. Of newly diagnosed cancers, 29% will have regional spread and 52% will already be metastasized[1]. Patients with pancreatic cancer are often asymptomatic until the disease develops to an advanced stage and thus have a low cure rate. Surgery is the only curative treatment but only 20% of patients are suitable for a curative resection[2]. Therefore, surgeons must determine which patients have incurable disease, preoperatively or intraoperatively, and be well versed in surgical and nonsurgical options in regards to palliative care. Palliation for pancreatic cancer is often centered around three high burden symptoms: obstructive jaundice, duodenal obstruction and tumor-related pain.

GOALS OF PALLIATIVE INTERVENTION

Surgeons by necessity manage many patients at the end of life and have been at the forefront in the movement toward palliative care for decades. There exists a wide range of multidisciplinary treatments and a surgeon must consider which palliative intervention may aid in symptom relief from the advanced malignancy. Important factors to consider are the likelihood of symptom improvement, quality of life, pain control, and cost-effectiveness. The palliative phase of care should focus on reducing morbidity, mortality and duration of treatment. Symptom palliation may improve survival but it is not appropriate to select a procedure for that reason alone[3-6].

There have been a variety of definitions of palliative care put forth in the literature that has led to confusion in understanding the role of palliative operations. Historically, the term "palliative" has had an assortment of meanings. In an effort to help clarify the term the World Health Organization (WHO) has put forth a definition of palliative care as "the total active care of patients whose disease is not responsive to curative treatment". Control of pain, of other symptoms, and of psychological, social, and spiritual problems is paramount. The goal of palliative care is the achievement of the best quality of life for patients and their families[7]. While this definition broadly characterizes palliative, it does not illuminate the diverse goals of surgical palliation. Patients with advanced malignancy comprise a range of diverse clinical scenarios requiring surgery that it makes valid comparisons of outcomes difficult. Emphasis on maintaining an individualized approach is crucial as the same palliative procedure may have very different aims for each patient.

Surgical palliation is best defined as "the deliberate use of a procedure in a patient with incurable disease with the intention of relieving symptoms, minimizing patient distress, and improving quality of life"[4,5,7-9]. Palliative care is total care and not the opposite of a cure. Palliative decision-making should focus on attainable results that improve quality of life and symptom control for patients[8].

A customized approach requires effective communication between the patient, the family, and the surgeon. The palliative triangle has been put forth as a model to assist in the challenging clinical decision making when deliberating the most appropriate palliative surgical procedures[4,6]. The model was first created to explore high patient satisfaction after palliative operations even with poor rates of morbidity, mortality, and overall survival[4]. The palliative triangle enables the patient's symptoms, hopes, fears, beliefs, and psychological support to be considered with operative and non-operative options to craft a palliative intent agreed upon by all parties and thus fostering shared decision-making[4,5,8,9]. In a recent study including patients with pancreatic cancer, appropriate patient selection for palliative surgery was determined by the palliative triangle approach. Using this stratification there was improvement in symptom resolution, overall survival, 30-d morbidity and mortality compared to prior studies[9].

The intent behind the procedure is what transforms a palliative operation into a tool to accomplish a goal[3]. At the crux of palliative decision-making is quality not quantity of life. The foundation of palliative care is built upon the compassion a physician has for his terminally ill patient and is predicated on effective communication. The palliative triangle model can guide surgeons as they address and relieve the most common and debilitating symptoms of advanced pancreatic cancer: obstructive jaundice, duodenal obstruction and pain. A successful palliative intervention is one that provides durable symptom relief for a patient.

OBSTRUCTIVE JAUNDICE

Approximately half of newly diagnosed pancreatic

cancers occur within the head of the pancreas. Many of these patients present with jaundice, as the intra-pancreatic portion of the bile duct becomes obstructed by the mass[10]. The decrease excretion of bile acids into the duodenum results in pruritus and fat malabsorption that may increase risk of bleeding due to decreased absorption of fat soluble vitamin K and subsequently impaired synthesis of vitamin K dependent coagulation factors[11]. Patients require intervention as cholestasis can result in liver dysfunction and eventually failure. Interventions to decompress the obstructed bile duct include endoscopic stenting, percutaneous external drainage and operative biliary bypass.

Endoscopic stent placement

In patients who are diagnosed with unresectable disease at initial encounter, placement of an endoscopic biliary stent for biliary obstruction is the favored palliative intervention. Endoscopic stenting may also be the best definitive therapy for patients with poor performance status or short life expectancy. The procedure involves cannulation of the bile duct and guidewire placement. Then endoscopic retrograde cholangiography is performed typically with sphincterotomy, which facilitates the insertion of the prosthesis. Since the 1990s endoscopic technology has improved with randomized studies demonstrating that endoscopic stenting is feasible in over 90% of patients[12]. However, stents can become occluded resulting in cholangitis or pancreatitis. Stents can also migrate leading to the need for re-intervention[13].

Bliss *et al*[14] performed a retrospective analysis of unresected pancreatic cancer patients between 2007-2011 who received surgical bypass or endoscopic stenting for biliary obstruction. Among propensity score-matched patients mortality and readmission rates were similar. Patients in the endoscopic group had a lower median length of stay and cost. Also, those in the endoscopic group were more likely to be discharged home. However, 20.3% (63) of endoscopic compared to 4.5% (14) of surgical patients underwent reintervention, with endoscopic group having higher rate of obstructive complications including cholangitis, evidence of biliary obstruction, and acute pancreatitis[14].

Advances is stent development have resulted in several available endostents including plastic, uncovered or partially covered metal. Walter *et al*[15] performed a multicenter randomized trial to explore which stent enables successful and durable palliation of extrahepatic biliary obstruction: a plastic stent, an uncovered self-expanding metal stent (SEMS) or a partially covered SEMS. The study included 219 patients in The Netherlands from February 2008 through February 2013. Functional durability of uncovered stents was 288 d and for partially covered metal stents was 299 d. However, the durability for plastic stents was only 172 d. Median survival was 109 d overall, 80 d in patients with metastatic disease. When examining cost from initial

endoscopic retrograde cholangiography until 1 year later there was no significant difference between the SEMS arms and the plastic stents. Thus, Walter *et al*[16] determine that SEMS should be used for palliation of malignant extrahepatic biliary obstruction. Furthermore health-related quality of life (HRQoL) scores remained stable over time in SEMS arms, whereas HRQoL deteriorated over time in patients with a plastic stent[15,16]. Reduction in jaundice and pruritus was seen in both groups but SEMS endorsed significantly less fatigue, decrease in nausea and vomiting resulting in improved appetite.

Transhepatic biliary drainage

Percutaneous drainage is an alternative if endoscopic biliary stent placement is unsuccessful or technically not feasible. The placement of a transhepatic biliary catheter involves percutaneously entering the liver with a needle. Percutaneous access also allows for internal metal stent or drain placement once the guidewire is properly positioned. If an external drain is left additional procedures are common, including routine catheter changes, and major complications including hospitalization for catheter exchange due to malfunction or leakage. Despite this, percutaneous drain placement has been useful in significantly reducing pruritus[17]. New interventions such as endoscopic ultrasound (EUS)-guided biliary drainage are being explored as additional options for occasions when endoscopic retrograde cholangiography stent placement is unsuccessful[18].

Surgical biliary bypass

If unresectable disease is found during laparotomy, an open biliary-enteric bypass provides effective palliation of biliary obstruction. Also, if endoscopic or percutaneous palliation of jaundice is not feasible a palliative biliary bypass may be planned.

Open, laparoscopic and robotic techniques can be used to bypass malignant obstructions *via* anastomosis of bile duct to the duodenum or jejunum. Jejunal bypass is employed more frequently as cancer growth could dehisce or obstruct a duodenal anastomosis. A Roux-en-Y reconstruction is typical used as it reduces the risk of cholangitis from enteric reflux into the biliary tree[19].

The traditional biliary bypass is a Roux-en-Y choledochojejunostomy or hepaticojejunostomy. First a cholecystectomy is performed[19]. Then the common bile duct or hepatic duct is transected. The distal end of the bile duct is sutured closed. An approximately 40 cm to 60 cm in length roux limb is anastomosed end-to-side to a jejunal limb roughly 20 cm distal to the ligament of Treitz. The biliary-enteric anastomosis is created with interrupted 4-0 PDS or Vicryl suture or, if previous obstruction resulted in an enlarged duct the suture may be placed in a continuous fashion[20]. There are other options for creating a biliary enteric anastomosis, including using a side-to-side technique and a loop

hepaticojejunostomy (or choledochojejunostomy) can be performed. Patient anatomy, surgeon preference and operative modality all contribute.

The robotic system is emerging as a feasible and effective option for palliative biliary bypass. There are several unique advantages of the robotic system, which overcome the obstacles of conventional laparoscopic surgery such as improved visualization with a three-dimensional camera, increase dexterity with a platform that offers the seven degrees of movement as a human wrist does, and improved ergonomics[21]. A small study demonstrated robotic hepaticojejunostomy for advanced malignant biliary obstruction in nine patients, four with pancreatic head cancer. There were five patients who received Roux-en-Y hepaticojejunostomy and four patients who underwent double bypass. There was no procedure-related mortality[21]. The post-operative stay was 13.3 d. Future studies comparing laparoscopic and robotic approaches are needed.

DUODENAL OBSTRUCTION

Duodenal obstruction can be caused by duodenal invasion of pancreatic head tumors or pancreatic body tumors invading the doudeno-jejunal junction. Intestinal obstruction causes nausea, vomiting and poor oral intake, which can compromise quality of life and put patients at risk of dehydration and malnutrition. It has been estimated that 10%-25% of all patients with pancreatic cancer will develop symptomatic duodenal obstruction[22]. Rates as high as 38% have been reported in patients with pancreatic head adenocarcinoma[23]. Duodenal obstruction usually occurs late in the disease process. Traditional management was centered on open gastrojejunostomy (GJ). More recently minimally-invasive surgical GJ and endoscopic stenting have been introduced as alternatives.

Endoscopic stenting technique
Endoscopic stenting of the duodenum with SEMS is one option to relieve malignant obstruction. The stents are uncovered stents enabling them to lodge into the stricture and adjacent tissue. Metallic stent placement has been increasingly used as a minimally invasive method with the development of the through-the-scope stent placement (TTS) as opposed to earlier per-oral or percutaneous approach under fluoroscopic guidance. Once the stents are deployed they range from 18 to 12 mm in caliber and extend a length of 6 to 12 cm[24].

The procedure is performed under conscious seda-tion. An upper endoscope is employed to identify the stenosis. A guidewire is then inserted through the working channel of the endoscope and advanced distal to the obstruction. To permit adequate stent margin the stent length should enable 2 cm of overlap in both directions. Then, the SEMS system can be delivered over the guidewire and positioned so the undeployed stent covers the stenosis proportionately. Lastly, the stent is deployed and placement and luminal patency are verified endoscopically and fluoroscopically[25,26].

Patients with malignant duodenal obstruction may also have concurrent biliary obstruction. It is advised to place a biliary stent, as detailed above, before duodenal stenting in patients with existing or imminent biliary obstruction. If the duodenal stent is done prior, biliary stenting is very difficult so the biliary drainage must always precede the duodenal stent placement[27].

Endoscopic stenting indications and outcomes
Endoscopic stenting provides a therapeutic option for patients who are poor surgical candidates. Presence of carcinomatosis or malignant ascites would result in patients being at high-risk category for surgery. Furthermore, the patient's expected survival based on their disease course must be considered. In a multi-center study involving 176 patients with predominately pancreatic tumors obstructing the stomach and duodenum, stent deployment was technically successful in 173 patients. Oral intake was sustained for a median of 146 d in 84% of patients[28].

Mittal *et al*[29] compared outcomes for 16 patient who had open GJ, 14 patients who had laparoscopic GJ and 16 patients who underwent endoscopic stenting who were matched for age, sex, ASA grade and level of obstruction. Patients who underwent endoscopic stenting resumed oral intake the same day while it took 6 d in the open GJ group and 4 d in the laparoscopic GJ group ($P < 0.001$). The surgical groups had higher rate of complications (pneumonia, ileus, wound infection and sepsis) compared with the endoscopically treated group ($P = 0.016$). The length of stay after procedure was 2 d in the endoscopic stenting group, 7 d in laparoscopic GJ group and 10 d in the open GJ group[29].

Several studies have demonstrated a decrease in the time to tolerate oral intake, shorter length of stay after the procedure and lower complication rate for stented patients compared to surgical GJ[29,30]. Although similar survival rates have been described a small study in 2006 comparing enteral stent (24 patients) to open GJ (17 patients) found the 30 d mortality rate was decrease in the enteral stent group (16.6% *vs* 29.4%)[26].

Reinterventions have been shown to be higher after stent placement due to recurrent obstructive symptoms. Symptom recurrence is attributed to tumor ingrowth and stent migration[31]. Despite recurrence, additional duodenal stent placement has been shown to be feasible and effective[31,32]. Stent design continues to advance and covered stents were designed to mitigate tumor ingrowth, but were found to have a high rate of migration[33]. Now, partially covered stents are being investigated and outcomes may continue to improve. Furthermore, clinical trials are underway in patients with pancreatic cancer exploring if there is symptom

improvement with pyloric stent in addition to the duodenal stent[34].

Palliative GJ surgical technique

Traditionally, surgical GJ was performed for palliation of duodenal obstructions. The distal stomach is anastomosed to the jejunum in the antecolic approach. In the retrocolic approach a jejunal loop is positioned through the transverse colon mesentery.

An open approach begins with an incision in the upper midline of the abdomen. In an antecolic GJ a portion of the distal stomach is connected to a jejunal section located 15-20 cm distal to the ligament of Treitz. In a retrocolic GJ the transverse colon is raised cephalad to find an avascular section of mesentery to pass the jejunal loop through. A two-layer suture, single layer suture, or a stapled anastomosis can be performed depending on surgeon preferences. One option to decrease risk of bowel herniation is placement of sutures from mesentery to jejunum. Lastly, the midline incision is closed in the usual fashion[34,35]. GJ can also be performed laparoscopically or robotically.

As mentioned earlier, the robotic system is emerging as a feasible and effective option for palliative bypass. A small study performed double (hepaticojejunostomy, and GJ) in four patients with pancreatic head cancer. There was no procedure-related mortality[21]. The postoperative stay was 13.3 d. Future studies comparing laparoscopic and robotic approaches are needed.

Palliative GJ indications and outcomes

Surgical duodenal bypass procedures may be preferred in a patient population with relatively longer life expectancy, as they would benefit from the durability of surgical palliation. A multicenter randomized trial, the SUSTENT study, was conducted in The Netherlands and found long-term relief was better after GJ compared to stent placement in regards to food intake, major complications, recurrent obstructive symptoms, and reinterventions. Patients were observed for a period of two months following operation. The authors determined a palliative GJ is preferable in patients expected to live at least two months, but recommended stenting for patients with a life expectancy less than that[36]. Importantly, delayed gastric emptying is a common complication after GJ that can lead to prolonged hospitalization and time without oral intake.

One study from 1998 compared the short-term outcomes of open GJ (22 patients) to laparoscopic GJ (9 diagnosis-matched controls) for the palliation of gastric outlet obstruction caused by advanced pancreatic cancer. Mortality, overall morbidity, operating time, time to oral solid food intake, and survival were not significantly different between the 2 groups. However, estimated blood loss and hospital stay were significantly reduced in the laparoscopic group[37].

In 2004, Mittal *et al*[29] found the laparoscopic surgery correlated with a lower complications, a shorter

hospital stay, and a shorter time to tolerate a diet *vs* an open surgery. Increased laparoscopic training likely contributed to improvement in short-term outcomes in the laparoscopic group. Much of the literature has patient cohorts with a variety of malignancies and studies comparing open GJ and laparoscopic GJ in patients with only pancreatic cancer are sparse.

Prophylactic GJ

Even with thorough preoperative staging including three-dimensional imaging techniques, which have continued to improve over time, between 8% and 33% of patients, are found to be unresectable at the time of laparotomy[38]. There remains controversy over the best course when converting from a surgery with curative intent to a non-curative procedure for patients without duodenal obstruction symptoms pre-operatively.

In 1999, a prospective, randomized trial explored the need of prophylactic GJ in unresectable pancreatic cancer discovered at time of surgery. Eighty-seven patients with no evidence of intestinal obstruction were randomized to receive either a GJ or no GJ. Performing a GJ did not influence morbidity, mortality or length of hospital stay. No patients experienced late gastric outlet obstruction in the GJ group, but 19% of patients in the no-GJ group required subsequent bypass for gastric outlet obstruction[39]. Thus, the authors recommended prophylactic GJ in all patients found to be unresectable at laparotomy.

In another randomized study from 2003, 65 patients with unresectable periampullary cancer discovered at laparotomy were randomized to double bypass or hepaticojejunostomy only. Gastric outlet obstruction developed in (5.5%) who underwent double bypass as compared (41.4%) treated with hepaticojejunostomy alone. The postoperative hospital stay, morbidity, and survival between the two groups were not significantly different. The authors concluded that the most appropriate palliative surgery would include prophylactic GJ completed at the time of hepaticojejunostomy in all patients to minimize the risk of postoperative gastric outlet obstruction[40]. The trial was terminated early due to the superiority of the double bypass.

More recently, studies have shown increased morbidity and mortality among patients who receive a palliative procedure at the time of laparotomy. Spanheimer *et al*[41]'s retrospective study published in 2014 found duodenal bypass compared to laparotomy only did not decrease the future need for intervention of gastric outlet obstruction in the cohort examined. Insulander *et al*[42]'s retrospective observational cohort study from 2016 demonstrated longer overall survival in patients who received chemotherapy after laparotomy alone versus laparotomy with double bypass. This may be reflective of the improvement in chemotherapy options for pancreatic cancer in the past several years. Each patient is unique and most recent data suggests that surgical bypass procedures should be performed

only in selected patients.

MALIGNANT ASCITES

Peritoneal carcinomatosis, which is one of the most frequently encountered modes of metastasis in pancreatic cancer, can result in symptomatic ascites[43]. Conventional modalities for managing malignant ascites include sodium restricted diets, diuretic therapy and serial paracentesis[44]. Paracentesis is used most frequently. Fischer described a simple technique of inserting a 14-gauge needle with a catheter into the peritoneal cavity enabling multiple liters to be drained[45]. However, symptom resolution is usually less than 72 h. Newer therapies are being investigated such as radical cytoreductive surgery combined with intraperitoneal chemotherapy with hyperthermia (known as HIPEC)[44]. Even in patients who are not candidates for cytoreductive surgery, hyperthermic intraperitoneal perfusion chemotherapy *via* a catheter placed by minimal invasive laparoscopic approach has been shown as a valuable treatment. A multi-institutional analysis in fifty-two patients with a variety of primary tumors demonstrated resolved ascites in 94% of patients using laparoscopic HIPEC. Mean hospital stay was 2.3 d with a median survival of 14 wk. Postoperative complications consisted of two minor wound infections and one deep vein thrombosis. Laparoscopic HIPEC has been well demonstrated as an effective intervention to palliate malignant ascites[44,46].

TUMOR RELATED PAIN

Approximately 75% of patients will present with abdominal or back pain[47]. Location of tumor is crucial in determining presenting symptoms as patients with pancreatic head tumors tend to have jaundice but those with tumors in the body or tail tend to have abdominal pain[48]. Tumor can invade into mesenteric or celiac nerve plexus which may result in the classic epigastric pain. Most cancer related pain is treated by pharmacological oral treatments. The WHO put forth an analgesic ladder, with a progressive administration of non-opioids then adding opioids in increasing strength as needed. Managing pain as best as possible is of upmost importance since uncontrolled pain has been correlated with depression and decrease quality of life[49]. Additional modalities must be considered to adequate control pain.

Celiac plexus block

The celiac plexus is a nerve cluster in proximity to the celiac artery. Parasympathetic nerves to the viscera are located here in addition to pancreatic nociceptive fibers[50]. The block is chemical, usually consisting of ethanol or local anesthetic. The procedure can also be performed open, laparoscopically, percutaneously, endoscopically or thoracoscopically[51].

For patients with unresectable disease at presentation EUS-guided celiac plexus neurolysis is preferred. The neurolytic agent is injected around the celiac trunk using a linear-array echo endoscope. Celiac plexus neurolysis can also be performed during diagnostic EUS. Diagnostic EUS has been shown to result in improved pain relief and prevent progressive increases in opioid use[51]. Safety may be improved with EUS since color Doppler enables real-time visualization of blood vessels surrounding the gastric lumen can be imaged as opposed to traditional percutaneous technique[52].

Celiac plexus block can be performed intra-operatively by a laparoscopic or open approach for patients found to have unresectable disease at laparotomy. The laparoscopic approach is performed under ultrasound guidance and the probe has a small channel to guide the needle directly. In the open technique, the non-dominant hand is placed on the aorta, with index and middle finger on either side. Then moving inferiorly the first branch encountered is the celiac trunk. The retroperitoneum is then infiltrated with a spinal needle[20].

Randomized controlled trials of patients with pancreatic cancer showed significant pain reduction with regional neurolysis of celiac plexus and provides an adjunct for pain control[52]. A meta-analysis of 302 patients in randomized trials compared systemic opiate therapy with neurolytic celiac plexus block and found lower pain scores at 2, 4, and 8 wk after randomization for patients who underwent celiac plexus block, along with less systemic opiate use and constipation[53]. Adverse events reported include transient diarrhea and 20%-42% of patients can have transient orthostatic hypotension due to vasodilation[54].

PALLIATIVE CHEMOTHERAPY

For patients with advanced malignancy, a procedure that offers quicker recovery can lead to earlier palliative systemic or local therapy, and to an improved quality of life. Palliative chemotherapy has demonstrated a survival benefit and improved quality of life in patients with unresectable disease[55]. Gemcitabine monotherapy has been the standard in patients with metastatic pancreatic cancer. With new combination chemotherapy, such as nab-paclitaxel plus gemcitabine, demonstrating increased overall and progression free survival any factors leading to delay in chemotherapy may be detrimental[56].

CONCLUSION

Pancreatic cancer is an extremely aggressive disease with a five-year survival of only 8.5%. When a curable operation is not possible, treatment decisions should focus on reducing morbidity and improving quality of life. The success of a palliative treatment to provide durable symptom resolution should be at the forefront

of the discussion among physicians, patients and their families.

Palliative treatment of obstructive jaundice, duodenal obstruction and pain should be promptly addressed. The role of surgical palliation has evolved over the past several decades as there have been advances in non-operative palliative interventions. Although surgical bypasses for both biliary and duodenal obstructions usually achieve good technical success, they result in considerable perioperative morbidity and mortality, even when performed laparoscopically. The effectiveness of SEMS for biliary drainage is excellent with low morbidity and demonstrate reduction in jaundice and pruritus. Surgical GJ for duodenal obstruction appears to be best for patients with a life expectancy of greater than 2 mo while endoscopic stenting has been shown to be feasible with relief of nausea and emesis in those with a shorter life expectancy. Regional neurolysis of celiac plexus can serve as an adjunct for better tumor-related pain control. Regardless of the palliative procedure performed, all physicians involved must be adequately trained in end of life management to ensure appropriate and compassionate care for patients.

REFERENCES

1 **National Cancer Institute**. SEER Cancer Stat Facts: Pancreatic Cancer. Available from: URL: https://seer.cancer.gov/statfacts/html/pancreas.html

2 **Gillen S**, Schuster T, Meyer Zum Büschenfelde C, Friess H, Kleeff J. Preoperative/neoadjuvant therapy in pancreatic cancer: a systematic review and meta-analysis of response and resection percentages. *PLoS Med* 2010; **7**: e1000267 [PMID: 20422030 DOI: 10.1371/journal.pmed.1000267]

3 **Thomay AA**, Jaques DP, Miner TJ. Surgical palliation: getting back to our roots. *Surg Clin North Am* 2009; **89**: 27-41, vii-viii [PMID: 19186229 DOI: 10.1016/j.suc.2008.10.005]

4 **Miner TJ**, Jaques DP, Shriver CD. A prospective evaluation of patients undergoing surgery for the palliation of an advanced malignancy. *Ann Surg Oncol* 2002; **9**: 696-703 [PMID: 12167585 DOI: 10.1007/BF02574487]

5 **Miner TJ**, Jaques DP, Tavaf-Motamen H, Shriver CD. Decision making on surgical palliation based on patient outcome data. *Am J Surg* 1999; **177**: 150-154 [PMID: 10204560 DOI: 10.1016/S0002-9610(98)00323-7]

6 **Miner TJ**, Brennan MF, Jaques DP. A prospective, symptom related, outcomes analysis of 1022 palliative procedures for advanced cancer. *Ann Surg* 2004; **240**: 719-26; discussion 726-7 [PMID: 15383799 DOI: 10.1097/01.sla.0000141707.09312.dd]

7 **Miner TJ**, Jaques DP, Karpeh MS, Brennan MF. Defining palliative surgery in patients receiving noncurative resections for gastric cancer. *J Am Coll Surg* 2004; **198**: 1013-1021 [PMID: 15194084 DOI: 10.1016/j.jamcollsurg.2004.02.007]

8 **Miner TJ**. Communication as a core skill of palliative surgical care. *Anesthesiol Clin* 2012; **30**: 47-58 [PMID: 22405432 DOI: 10.1016/j.anclin.2011.11.004]

9 **Miner TJ**, Cohen J, Charpentier K, McPhillips J, Marvell L, Cioffi WG. The palliative triangle: improved patient selection and outcomes associated with palliative operations. *Arch Surg* 2011; **146**: 517-522 [PMID: 21576604 DOI: 10.1001/archsurg.2011.92]

10 **Huggett MT**, Pereira SP. Diagnosing and managing pancreatic cancer. *Practitioner* 2011; **255**: 21-25, 2-3 [PMID: 21932502]

11 **O'Brien DP**, Shearer MJ, Waldron RP, Horgan PG, Given HF. The extent of vitamin K deficiency in patients with cholestatic jaundice: a preliminary communication. *J R Soc Med* 1994; **87**: 320-322 [PMID: 8046700]

12 **Moss AC**, Morris E, Mac Mathuna P. Palliative biliary stents for obstructing pancreatic carcinoma. *Cochrane Database Syst Rev* 2006; **(2)**: CD004200 [PMID: 16625598 DOI: 10.1002/14651858.CD004200.pub2]

13 **Costamagna G**, Pandolfi M. Endoscopic stenting for biliary and pancreatic malignancies. *J Clin Gastroenterol* 2004; **38**: 59-67 [PMID: 14679329 DOI: 10.1097/00004836-200401000-00013]

14 **Bliss LA**, Eskander MF, Kent TS, Watkins AA, de Geus SW, Storino A, Ng SC, Callery MP, Moser AJ, Tseng JF. Early surgical bypass versus endoscopic stent placement in pancreatic cancer. *HPB* (Oxford) 2016; **18**: 671-677 [PMID: 27485061 DOI: 10.1016/j.hpb.2016.05.008]

15 **Walter D**, van Boeckel PG, Groenen MJ, Weusten BL, Witteman BJ, Tan G, Brink MA, Nicolai J, Tan AC, Alderliesten J, Venneman NG, Laleman W, Jansen JM, Bodelier A, Wolters FL, van der Waaij LA, Breumelhof R, Peters FT, Scheffer RC, Leenders M, Hirdes MM, Steyerberg EW, Vleggaar FP, Siersema PD. Cost Efficacy of Metal Stents for Palliation of Extrahepatic Bile Duct Obstruction in a Randomized Controlled Trial. *Gastroenterology* 2015; **149**: 130-138 [PMID: 25790742 DOI: 10.1053/j.gastro.2015.03.012]

16 **Walter D**, van Boeckel PG, Groenen MJ, Weusten BL, Witteman BJ, Tan G, Brink MA, Nicolai J, Tan AC, Alderliesten J, Venneman NG, Laleman W, Jansen JM, Bodelier A, Wolters FL, van der Waaij LA, Breumelhof R, Peters FT, Scheffer RC, Steyerberg EW, May AM, Leenders M, Hirdes MM, Vleggaar FP, Siersema PD. Higher quality of life after metal stent placement compared with plastic stent placement for malignant extrahepatic bile duct obstruction: a randomized controlled trial. *Eur J Gastroenterol Hepatol* 2017; **29**: 231-237 [PMID: 27741030 DOI: 10.1097/MEG.0000000000000762]

17 **Robson PC**, Heffernan N, Gonen M, Thornton R, Brody LA, Holmes R, Brown KT, Covey AM, Fleischer D, Getrajdman GI, Jarnagin W, Sofocleous C, Blumgart L, D'Angelica M. Prospective study of outcomes after percutaneous biliary drainage for malignant biliary obstruction. *Ann Surg Oncol* 2010; **17**: 2303-2311 [PMID: 20358300 DOI: 10.1245/s10434-010-1045-9]

18 **Khashab MA**, Valeshabad AK, Modayil R, Widmer J, Saxena P, Idrees M, Iqbal S, Kalloo AN, Stavropoulos SN. EUS-guided biliary drainage by using a standardized approach for malignant biliary obstruction: rendezvous versus direct transluminal techniques (with videos). *Gastrointest Endosc* 2013; **78**: 734-741 [PMID: 23886353 DOI: 10.1016/j.gie.2013.05.013]

19 **Teitelbaum EN**. Laparoscopic bypass for pancreatic cancer. In: Twelfth ed. 2017: 1578-1582

20 **Conrad C**, Lillemoe KD. Surgical palliation of pancreatic cancer. *Cancer J* 2012; **18**: 577-583 [PMID: 23187845 DOI: 10.1097/PPO.0b013e3182797dfe]

21 **Lai EC**, Tang CN. Robot-assisted laparoscopic hepaticojejunostomy for advanced malignant biliary obstruction. *Asian J Surg* 2015; **38**: 210-213 [PMID: 25797562 DOI: 10.1016/j.asjsur.2015.01.010]

22 **Nakakura EK**, Warren RS. Palliative care for patients with advanced pancreatic and biliary cancers. *Surg Oncol* 2007; **16**: 293-297 [PMID: 17855076 DOI: 10.1016/j.suronc.2007.08.003]

23 **Shah A**, Fehmi A, Savides TJ. Increased rates of duodenal obstruction in pancreatic cancer patients receiving modern medical management. *Dig Dis Sci* 2014; **59**: 2294-2298 [PMID: 24781163 DOI: 10.1007/s10620-014-3170-y]

24 **Maire F**, Sauvanet A. Palliation of biliary and duodenal obstruction in patients with unresectable pancreatic cancer: endoscopy or surgery? *J Visc Surg* 2013; **150**: S27-S31 [PMID: 23597937 DOI: 10.1016/j.jviscsurg.2013.03.005]

25 **Gaidos JK**, Draganov PV. Treatment of malignant gastric outlet obstruction with endoscopically placed self-expandable metal stents. *World J Gastroenterol* 2009; **15**: 4365-4371 [PMID: 19764086 DOI: 10.3748/wjg.15.4365]

26 **Espinel J**, Sanz O, Vivas S, Jorquera F, Muñoz F, Olcoz JL, Pinedo E. Malignant gastrointestinal obstruction: endoscopic stenting versus surgical palliation. *Surg Endosc* 2006; **20**: 1083-1087 [PMID: 16703436 DOI: 10.1007/s00464-005-0354-8]

27 **Kim KO**, Kim TN, Lee HC. Effectiveness of combined biliary and duodenal stenting in patients with malignant biliary and duodenal obstruction. *Scand J Gastroenterol* 2012; **47**: 962-967 [PMID: 22571283 DOI: 10.3109/00365521.2012.677956]

28 **Telford JJ**, Carr-Locke DL, Baron TH, Tringali A, Parsons WG, Gabbrielli A, Costamagna G. Palliation of patients with malignant gastric outlet obstruction with the enteral Wallstent: outcomes from a multicenter study. *Gastrointest Endosc* 2004; **60**: 916-920 [PMID: 15605006 DOI: 10.1016/S0016-5107(04)02228-X]

29 **Mittal A**, Windsor J, Woodfield J, Casey P, Lane M. Matched study of three methods for palliation of malignant pyloroduodenal obstruction. *Br J Surg* 2004; **91**: 205-209 [PMID: 14760669 DOI: 10.1002/bjs.4396]

30 **Nagaraja V**, Eslick GD, Cox MR. Endoscopic stenting versus operative gastrojejunostomy for malignant gastric outlet obstruction-a systematic review and meta-analysis of randomized and non-randomized trials. *J Gastrointest Oncol* 2014; **5**: 92-98 [PMID: 24772336 DOI: 10.3978/j.issn.2078-6891.2014.016]

31 **Siddiqui A**, Spechler SJ, Huerta S. Surgical bypass versus endoscopic stenting for malignant gastroduodenal obstruction: a decision analysis. *Dig Dis Sci* 2007; **52**: 276-281 [PMID: 17160470 DOI: 10.1007/s10620-006-9536-z]

32 **Uemura S**, Iwashita T, Iwata K, Mukai T, Osada S, Sekino T, Adachi T, Kawai M, Yasuda I, Shimizu M. Endoscopic duodenal stent versus surgical gastrojejunostomy for gastric outlet obstruction in patients with advanced pancreatic cancer. *Pancreatology* 2018; **pii**: S1424-3903(18)30082-6 [PMID: 29753623 DOI: 10.1016/j.pan.2018.04.015]

33 **Park KB**, Do YS, Kang WK, Choo SW, Han YH, Suh SW, Lee SJ, Park KS, Choo IW. Malignant obstruction of gastric outlet and duodenum: palliation with flexible covered metallic stents. *Radiology* 2001; **219**: 679-683 [PMID: 11376254 DOI: 10.1148/radiology.219.3.r01jn21679]

34 **Dua K**. Comparison of Duodenal Stenting vs. transplyloric and Duodenal stenting for malignant obstruction. [accessed 2018 May 15]. In: ClinicalTrials.gov [Internet]. Bethesda (MD): U.S. National Library of Medicine. Available from: URL: http://clinicaltrials.gov/show/ NCT03125148 ClinicalTrials.gov Identifier: NCT03125148

35 **Townsend CM**, Evers BM. Atlas of General Surgical Techniques E-Book. London: Elsevier, 2014; Chapter 32: 334-344

36 **Jeurnink SM**, Steyerberg EW, van Hooft JE, van Eijck CH, Schwartz MP, Vleggaar FP, Kuipers EJ, Siersema PD; Dutch SUSTENT Study Group. Surgical gastrojejunostomy or endoscopic stent placement for the palliation of malignant gastric outlet obstruction (SUSTENT study): a multicenter randomized trial. *Gastrointest Endosc* 2010; **71**: 490-499 [PMID: 20003966 DOI: 10.1016/j.gie.2009.09.042]

37 **Bergamaschi R**, Mårvik R, Thoresen JE, Ystgaard B, Johnsen G, Myrvold HE. Open versus laparoscopic gastrojejunostomy for palliation in advanced pancreatic cancer. *Surg Laparosc Endosc* 1998; **8**: 92-96 [PMID: 9566559 DOI: 10.1097/00019509-1998040 00-00002]

38 **Mayo SC**, Austin DF, Sheppard BC, Mori M, Shipley DK, Billingsley KG. Evolving preoperative evaluation of patients with pancreatic cancer: does laparoscopy have a role in the current era? *J Am Coll Surg* 2009; **208**: 87-95 [PMID: 19228509 DOI: 10.1016/j.jamcollsurg.2008.10.014]

39 **Lillemoe KD**, Cameron JL, Hardacre JM, Sohn TA, Sauter PK, Coleman J, Pitt HA, Yeo CJ. Is prophylactic gastrojejunostomy indicated for unresectable periampullary cancer? A prospective randomized trial. *Ann Surg* 1999; **230**: 322-328; discussion 328-330 [PMID: 10493479 DOI: 10.1097/00000658-199909000-00005]

40 **Van Heek NT**, De Castro SM, van Eijck CH, van Geenen RC, Hesselink EJ, Breslau PJ, Tran TC, Kazemier G, Visser MR, Busch OR, Obertop H, Gouma DJ. The need for a prophylactic gastrojejunostomy for unresectable periampullary cancer: a prospective randomized multicenter trial with special focus on assessment of quality of life. *Ann Surg* 2003; **238**: 894-902; discussion 902-905 [PMID: 14631226 DOI: 10.1097/01.sla.0000098617.21801.95]

41 **Spanheimer PM**, Cyr AR, Liao J, Johlin FC, Hoshi H, Howe JR, Mezhir JJ. Complications and survival associated with operative procedures in patients with unresectable pancreatic head adenocarcinoma. *J Surg Oncol* 2014; **109**: 697-701 [PMID: 24395080 DOI: 10.1002/jso.23560]

42 **Insulander J**, Sanjeevi S, Haghighi M, Ivanics T, Analatos A, Lundell L, Del Chiaro M, Andrén-Sandberg Å, Ansorge C. Prognosis following surgical bypass compared with laparotomy alone in unresectable pancreatic adenocarcinoma. *Br J Surg* 2016; **103**: 1200-1208 [PMID: 27250937 DOI: 10.1002/bjs.10190]

43 **Sadeghi B**, Arvieux C, Glehen O, Beaujard AC, Rivoire M, Baulieux J, Fontaumard E, Brachet A, Caillot JL, Faure JL, Porcheron J, Peix JL, François Y, Vignal J, Gilly FN. Peritoneal carcinomatosis from non-gynecologic malignancies: results of the EVOCAPE 1 multicentric prospective study. *Cancer* 2000; **88**: 358-363 [PMID: 10640968 DOI: 10.1002/(SICI)1097-0142(20000115)88:23.0.CO;2-O]

44 **Sangisetty SL**, Miner TJ. Malignant ascites: A review of prognostic factors, pathophysiology and therapeutic measures. *World J Gastrointest Surg* 2012; **4**: 87-95 [PMID: 22590662 DOI: 10.4240/wjgs.v4.i4.87]

45 **Fischer DS**. Abdominal paracentesis for malignant ascites. *Arch Intern Med* 1979; **139**: 235 [PMID: 434979 DOI: 10.1001/archinte.139.2.235]

46 **Valle M**, Van der Speeten K, Garofalo A. Laparoscopic hyperthermic intraperitoneal peroperative chemotherapy (HIPEC) in the management of refractory malignant ascites: A multi-institutional retrospective analysis in 52 patients. *J Surg Oncol* 2009; **100**: 331-334 [PMID: 19697441 DOI: 10.1002/jso.21321]

47 **Grahm AL**, Andrén-Sandberg A. Prospective evaluation of pain in exocrine pancreatic cancer. *Digestion* 1997; **58**: 542-549 [PMID: 9438600 DOI: 10.1159/000201499]

48 **Watanabe I**, Sasaki S, Konishi M, Nakagohri T, Inoue K, Oda T, Kinoshita T. Onset symptoms and tumor locations as prognostic factors of pancreatic cancer. *Pancreas* 2004; **28**: 160-165 [PMID: 15028948 DOI: 10.1097/00006676-200403000-00007]

49 **Kelsen DP**, Portenoy RK, Thaler HT, Niedzwiecki D, Passik SD, Tao Y, Banks W, Brennan MF, Foley KM. Pain and depression in patients with newly diagnosed pancreas cancer. *J Clin Oncol* 1995; **13**: 748-755 [PMID: 7884435 DOI: 10.1200/JCO.1995.13.3.748]

50 **Moore JC**, Adler DG. Celiac plexus neurolysis for pain relief in pancreatic cancer. *J Support Oncol* 2009; **7**: 83-87, 90 [PMID: 19507453]

51 **Wyse JM**, Carone M, Paquin SC, Usatii M, Sahai AV. Randomized, double-blind, controlled trial of early endoscopic ultrasound-guided celiac plexus neurolysis to prevent pain progression in patients with newly diagnosed, painful, inoperable pancreatic cancer. *J Clin Oncol* 2011; **29**: 3541-3546 [PMID: 21844506 DOI: 10.1200/JCO.2010.32.2750]

52 **Minaga K**, Takenaka M, Kamata K, Yoshikawa T, Nakai A, Omoto S, Miyata T, Yamao K, Imai H, Sakamoto H, Kitano M, Kudo M. Alleviating Pancreatic Cancer-Associated Pain Using Endoscopic Ultrasound-Guided Neurolysis. *Cancers* (Basel) 2018; **10**: pii: E50 [PMID: 29462851 DOI: 10.3390/cancers10020050]

53 **Yan BM**, Myers RP. Neurolytic celiac plexus block for pain control in unresectable pancreatic cancer. *Am J Gastroenterol* 2007; **102**: 430-438 [PMID: 17100960 DOI: 10.1111/j.1572-0241.2006.00967.x]

54 **Zhong W**, Yu Z, Zeng JX, Lin Y, Yu T, Min XH, Yuan YH, Chen QK. Celiac plexus block for treatment of pain associated with pancreatic cancer: a meta-analysis. *Pain Pract* 2014; **14**: 43-51 [PMID: 23682788 DOI: 10.1111/papr.12083]

55 **Glimelius B**, Hoffman K, Sjödén PO, Jacobsson G, Sellström H, Enander LK, Linné T, Svensson C. Chemotherapy improves

survival and quality of life in advanced pancreatic and biliary cancer. *Ann Oncol* 1996; **7**: 593-600 [PMID: 8879373 DOI: 10.1093/oxfordjournals.annonc.a010676]

56   **Von Hoff DD**, Ervin T, Arena FP, Chiorean EG, Infante J, Moore M, Seay T, Tjulandin SA, Ma WW, Saleh MN, Harris M, Reni M, Dowden S, Laheru D, Bahary N, Ramanathan RK, Tabernero J, Hidalgo M, Goldstein D, Van Cutsem E, Wei X, Iglesias J, Renschler MF. Increased survival in pancreatic cancer with nab-paclitaxel plus gemcitabine. *N Engl J Med* 2013; **369**: 1691-1703 [PMID: 24131140 DOI: 10.1056/NEJMoa1304369]

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