Non-Surgical Biliary Drainage on Biliary Obstruction Due to Malignancy

Evy Yunihastuti, LA Lesmana**, Ari Fahrial Syam***, Irsan Hasan**, Karmel Tambunan*****

*Department of Internal Medicine, Medical Faculty University of Indonesia
**Division of Hepatology, Department of Internal Medicine,
Medical Faculty, University of Indonesia
***Division of Gastroenterology, Department of Internal Medicine,
Medical Faculty, University of Indonesia
****Division of Hematology and Medical Oncology, Department of Internal Medicine, Medical Faculty,
University of Indonesia

ABSTRACT

Surgery is still the golden standard of curative therapy for malignant biliary obstruction, but only 10-20% of cases considered resectable. Therefore, palliative therapy to relieve pain, cholestasis, and biliary obstruction, is the main treatment for most patients. The development of percutaneous transhepatic biliary drainage and endoscopic biliary drainage had brought about minimally invasive treatment for malignant biliary obstruction, which had lower morbidity and mortality than surgical drainage. The choice of drainage technique depends on type of tumor , site of obstruction, also the available expert and instrumentation.

Key words: *malignant biliary obstruction, percutaneous transhepatic biliary drainage, therapeutic endoscopic retrograde cholangiopancreatography*

INTRODUCTION

Biliary obstruction is an emergency biliary and liver emergency that requires careful, precise and comprehensive treatment from internists, surgeons and radiologists.[1,2] Biliary obstruction can be caused by various malignancies, such as cholangiocarcinoma, pancreatic carcinoma, carcinoma of the bile duct, malignancies in the liver and duodenum, as well as metastases of colon carcinoma. [1,3]

In developed nations, billiopancreatic malignancy is the fifth largest cause of death due to cancer after lung cancer, colorectal cancer, breast cancer, and prostate cancer.[4] Pancreatic carcinoma itself is the fourth largest cause of death due to cancer in the United States.[5,6] Even though biliary malignancy is less commonly found, its mortality rate is still high – almost 4000 deaths annually.[6]

From the year 1994 to 1998, periampula tumor was the most common cause of biliary obstruction out of 62 reported cases (54.8%) at the surgery department of dr. Cipto Mangunkusumo National Public Hospital – Referral Center. From 1999 to 2000, periampula caused 58% of all reported cases of biliary obstruction.[7]

Biliary obstruction due to malignancy was once known as surgical jaundice, since the gold standard for therapy was by surgical means.[3,6,8] However, since most patients came in advanced stages, only 10-20% of cases could still undergo curative therapy by means of surgery.[5,8,9] Thus, most patients receive palliative therapy.[9]

At first, drainage using bilio-digestive anastomosis was more commonly used to eliminate biliary obstruction. However, palliative surgical therapy is often correlated with a high mortality rate (15-30%) and morbidity rate (20-60%).(9) Other reports mention a post-surgical mortality rate of 30-65% for patients with biliary obstruction due to malignancy.[10]

Development of minimally invasive therapy in the past two decades has brought dramatic changes in modern

medicine. Minimally invasive therapy has been accepted and has been widely used in various organs. So far, it is most widely applied in the hepatobiliary system.[11] The high rate of mortality and morbidity in surgical palliative therapy has also stimulated the introduction of minimally invasive therapy in cases of biliary obstruction due to malignancy. Since the introduction of percutaneous transhepatic drainage in the year 1962, there has been much development in palliative therapy of biliary obstruction due to malignancy.[12-14] A widely used technique is the Percutaneous Transhepatic Biliary Drainage (PTBD) and Endoscopic Biliary Drainage (EBD).[3,11,15]

BILIARY OBSTRUCTION DUE TO MALIGNANCY

Biliary obstruction is caused by blockage of one or more bile ducts that dispenses bile from the liver to the gallbladder, or from the gallbladder to the duodenum. Symptoms of biliary obstruction are related to bile flow obstruction and increased serum bilirubin. The patient may suffer from pruritus, yellowish eyes and skin (jaundice), brownish (tea-like) urine, acholic feces, cholangitis, even liver failure.[5]

Diagnosis of biliary obstruction is established based on anamnesis and physical examination, increased liver function (transaminase, alkaline phosphatase, and bilirubin), as well as ultrasonographic findings of intra and extra-hepatic biliary tracts. Ultrasound examination could also assist approximation of the location of obstruction. Enlargement of the common bile duct and gallbladder indicate obstruction at the distal, while enlargement of the intra-hepatic bile duct without enlargement of the common bile duct indicate obstruction at the proximal of the common hepatic duct.[16]

Table 1. The cause of biliary obstruction due to malignancy, based on location.[16]

Proximal	Distal
Cholangiocarcinoma	Carcinoma of the pancreas
Adenopathy	Cholangiocarcinoma
Carcinoma of the gallbladder	Adenopathy
Hepatoma	Carcinoma of the ampulla
	Carcinoma of the duodenum

Carcinoma of the gallbladder is the most common biliary tract malignancy. Over 50% of patients with gallbladder carcinoma are found with distant metastasis at the time of the initial diagnosis. The patient's prognosis is poor, with a median life expectancy of 3 more months. Only 14% survive the first year.[17]

Patients with cholangiocarcinoma have better prognosis, with a median life expectancy of 18-30 months with surgery and 5 months without. If the cholangiocarcinoma is located at the distal, the survival rate is even better – over 50% for the first 3 years, with a median life expectancy of 24 months.[8,17]

Carcinoma of the pancreas is the most common malignancy at the distal (70%). The rest comprise of distal cholangiocarcinoma, adenocarcinoma of the duodenum, and adenocarcinoma of the ampulla.[6] Prognosis of carcinoma of the pancreas, with a 5 year survival rate of 3% and a median life expectancy of 3-4 months.[18]

Palliative therapy of biliary obstruction due to malignancy is aimed at alleviation of pain symptoms, cholestasis, biliary obstruction, and improving the patient's quality of life. Thus, palliative therapy should have minimal morbidity rate and should be able to relieve the patient of pain and biliary obstruction as well as its consequences.[5,9]

NON-OPERATIVE BILIARY DRAINAGE

Biliary drainage was first introduced by Glenn, et al in the year 1962, who placed a catheter for external drainage after percutaneous transhepatic cholangiography. At the time, the catheter was inserted percutaneously for 5 days to prevent intraperitoneal leakage of the bile, which is the main complication of the examination.[3,12-14]

Such external drainage has the disadvantage of disturbing the patient, who has to carry a bag containing the fluid that comes out of the external catheter. Furthermore, the use of an external drainage also results in electrolyte loss and other metabolic disturbances.[3,15]

To prevent these problems, the internal drainage with an internal-external catheter was invented. The transhepatic catheter with a side hole was placed above and below the point of obstruction down to the duodenum, so that the bile flows through the catheter into the duodenum. This kind of catheter must be routinely replaced every 3 months to prevent obstruction. This kind of catheter also has several disadvantages, such as having the patient constantly reminded of his or her illness, difficulty maintaining, and it is often a potential source of infection. Since then, the internal catheter has developed and became widely used.[3]

General indication for biliary drainage in cases of malignant biliary obstruction is jaundice accompanied with cholangitis, sepsis, pruritus, as well as nausea and vomiting which could cause dehydration and malnutrition.

Biliary drainage is also often performed prior to surgery. The catheter, placed in the extra-hepatic bile duct, could assist the surgeon in making the anastomosis.[3,19] On the other hand, since pre-operative drainage increases post-surgical morbidity and mortality rate, such therapy should undergo careful consideration and should only be indicated if the patient shows signs of acute cholangitis, severe obstructive jaundice, or there are plans for other neo-adjuvant therapy.[3,20]

PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE

Percutaneous transhepatic biliary drainage is performed in two steps, percutaneous transhepatic cholangiography (PTC), followed by insertion of the catheter assisted by fluoroscopy or ultrasonography.[12,21]

Indication and Contraindication

PTC is indicated for palliative drainage in biliary obstruction due to malignancy with high risk for surgery and difficulty to perform endoscopic drainage, as well as for pre-operative drainage to improve the patient's general condition.[2,4,19] Suda, et al has also used the technique for nutritional support.[22]

This procedure is contraindicated for patients who are uncooperative, those with coagulation disturbance, and severe cholangitis. Patients with widespread hepatic metastasis are not advised to undergo this procedure since drainage is not very successful and there is a greater possibility for complication. Ascites is also a contraindication, since it facilitates the development of peritonitis.[12]

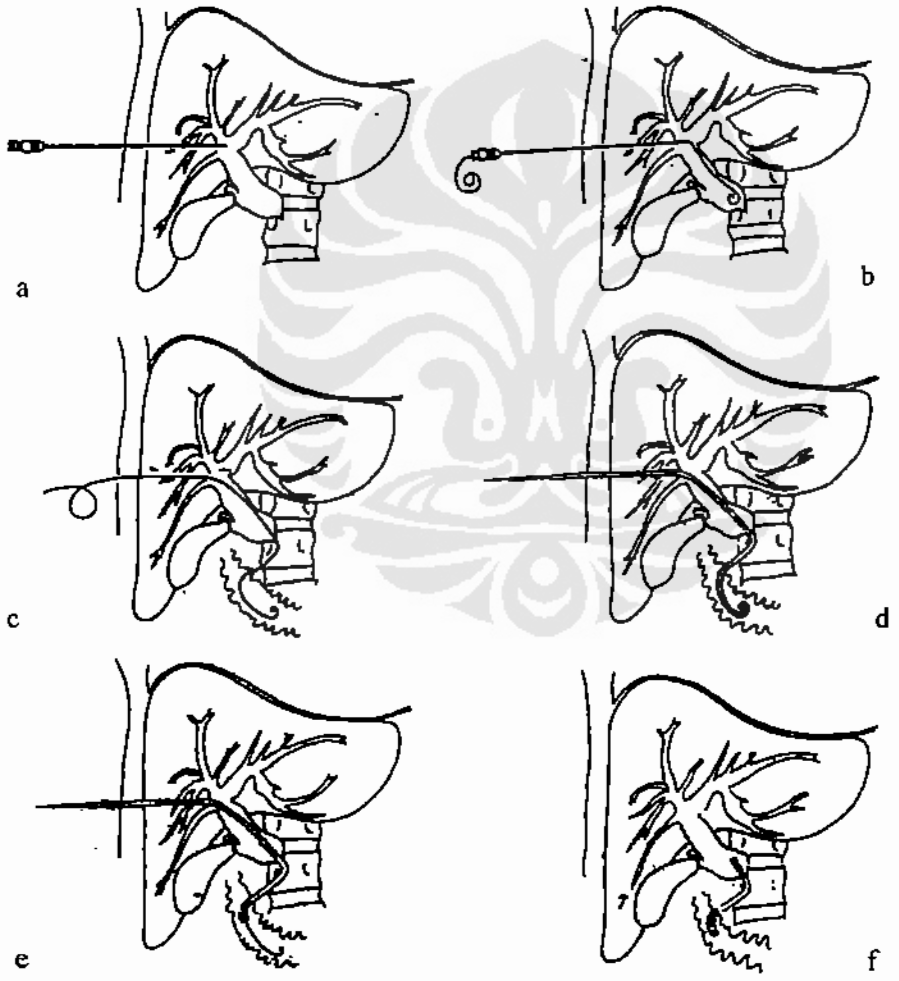


Figure 1. Steps of percutaneous transhepatic biliary drainage
a. Diagnostic percutaneous transhepatic cholangiography
b-d. Biliary drainage using an extemal catheter or a combination of external and internal catheters
e,f. Internal drainage using endoprothesis

DOMETA®

Domperidone 10 mg

Efektif untuk : *(1)

- Pengobatan Dispepsia yang disertai masa pengosongan lambung yang lambat
- Refluks gastroesofagus
- Anoreksia nervosa
- Gastroparesis
- Anti emetik pasca pembedahan
- Penderita yang mendapat kemoterapi

Dengan Aksi ganda :

Sentral :

- Menghambat impuls muntah di CTZ

Perifer :

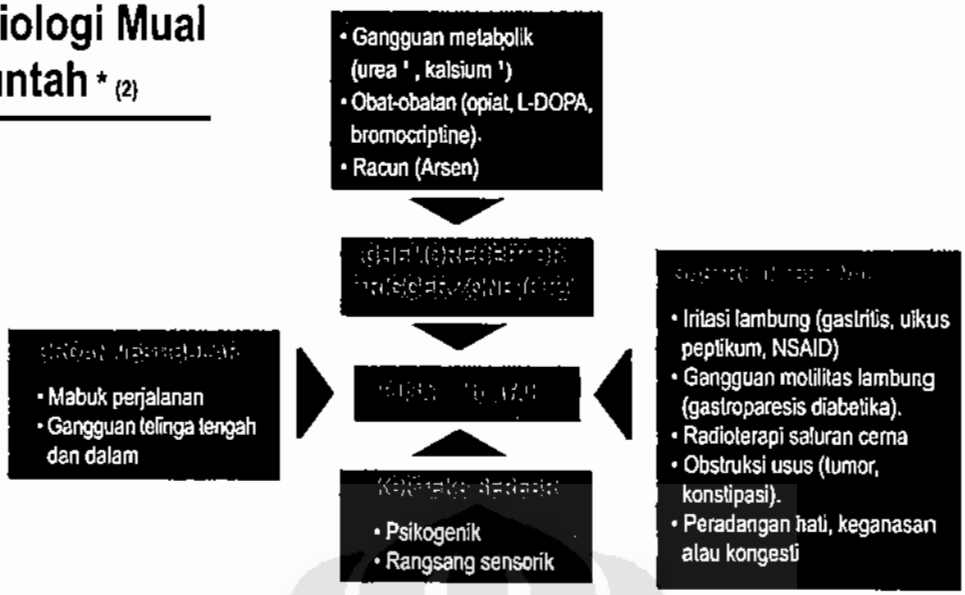
- Memperbaiki kontraksi sfingter esofagus inferior
- Mempercepat pengo - songan lambung
- Memperbaiki aktivitas peristaltik antro duodenum.

PT. IKAPHARMINDO PUTRAMAS
PHARMACEUTICAL LABORATORIES
JAKARTA - INDONESIA

DOMETA®

Domperidone 10 mg

Patofisiologi Mual dan Muntah * (2)



KOMPOSISI :

Tiap tablet salut selaput mengandung :

• Domperidon maleat 12.73 mg setara dengan Domperidon 10 mg.

FARMAKOLOGI :

Domperidon merupakan antagonist dopamin dengan khasiat antiemetik. Domperidon tidak dapat menembus sawar darah otak, pada pemberian domperidon terutama pada orang dewasa, efek samping ekstrapiramidal sangat jarang, tetapi domperidon dapat merangsang pelepasan prolaktin dari hipofise. Efek anti emetik dapat disebabkan oleh kombinasi efek perifer (gastrokinetik) dengan antagonis terhadap reseptor dopamin di daerah pemicu reseptor kimia (chemoreceptor trigger zone), yang terletak diluar sawar darah otak di area postrema.

INDIKASI :

Untuk pengobatan mual dan muntah akut yang disebabkan oleh berbagai penyebab pada orang dewasa.
Pengobatan mual muntah yang disebabkan L-dopa dan bromocriptine
Untuk pengobatan gejala dispepsia fungsional.

DOSIS :

Dosis dan lama pemberian tergantung dari berat dan lamanya gejala.
Untuk pengobatan mual, muntah.
Dewasa (termasuk lanjut usia) : 10 - 20 mg dengan interval waktu 4 - 8 jam.
Anak-anak : 0.4 mg/kg dengan interval waktu 4 - 8 jam.
Untuk pengobatan gejala dispepsia fungsional.
• Dewasa (termasuk lanjut usia) : 10 - 20 mg 3 kali/hari sebelum makan sebelum tidur malam (10 - 20 mg) tergantung respons klinik.

EFEK SAMPING :

Hypersensitif terhadap domperidon. Domperidon tidak boleh digunakan jika serangan motilitas lambung dapat membahayakan, seperti pendarahan, obstruksi mekanik, atau perforasi gastro intestinal. Domperidon juga dikontraindikasikan pada pasien dengan prolaktinoma tumor hipofise yang mengeluarkan prolaktin.

INTERAKSI OBAT :

Domperidon dapat diberikan bersamaan dengan :
• Obat-obat neurologik, yang efeknya tidak menyebabkan potensiasi.
• Obat-obat antagonis dopaminergik (bromocriptine, L-dopa) dimana efek perifer yang tidak diinginkan seperti gangguan pencernaan, mual dan muntah dapat ditekan tanpa menghalangi khasiat sentralnya.

KEMASAN : Dus 10 strip @ 10 tablet salut selaput. No. Reg. : DKL 9909314917A1

*Referensi :
* (1) Malagelada J. ; Drug Treatment of Gastric Motility Disorders ; Role of Domperidone. Clinician (1985). 3/8 : 9 - 15.
* (2).Clayton M. ; Management of chronic nausea. Medical Progress 1997 October ; 31 - 33.

Untuk informasi lebih lanjut hubungi : PT. IKAPHARMINDO PUTRAMAS Pharmaceutical Laboratories Jl. Cideng Barat No. 78 Jakarta Pusat Indonesia 1015 Tlp. (62 - 21) 3522

Technique and Instrumentation

Routine preparations include prophylaxis antibiotics, examination of bleeding and clotting time, premedications, sterilization, and informed consent.[11,12] The patient should fast at least 6 hours prior to the procedure.[2]

Procedure

We must first identify an easy to reach duct in the right or left hepatic lobe. Assisted by fluoroscopy, the horizontal section of the right hepatic duct is easily reached. To access the spot, the syringe should be inserted from the right lateral.[2,21] Guided by an ultrasound, the syringe may be inserted from other directions. To avoid the possibility of transpleural laceration, accidental removal of the catheter, or bending of the catheter in the space between the liver and the abdominal wall, it is advisable to insert the syringe from the anterior towards the left lobe. In addition, anterior insertion provides more comfort for the patient.[21] This method is also performed if there is stricture in the left hepatic duct.[23] An 18-22 gauge syringe needle should be inserted while the patient holds his or her breath.

The next step is ultrasound or fluoroscopy guided percutaneous transhepatic cholangiography. After the syringe is inserted at the proper position, the bile is aspirated, and then the contrast is injected and fluoroscopy and radiography are conducted in several positions.

After a cholangiogram is performed, the guiding shaft is inserted into the bile duct from the needle. A pig-tail catheter with several side outlets is inserted through the guiding shaft into the bile duct. The shaft can then be removed. If an external catheter is being used, the catheter is then stitched on the skin for fixation and a three-way stopcock is placed.

Post-insertion care of an external catheter include irrigation using 15-20 ml of physiologic alkaline fluid twice daily, measurement of excreted bile fluid, and monitoring of bilirubin and alkaline phosphatase levels. In addition, routine check of electrolyte levels and abdominal x-ray to determine catheter position should be performed.[21]

Success Rate

Current reports demonstrate that percutaneous transhepatic biliary drainage is an effective method for biliary drainage in cases of biliary obstruction due to malignancy. Ferrucci, et al, reported a success rate of 93.5% in 62 patients for drainage using this technique.[21] Hamlin, et al, reported a success rate of 97%.[25] Sirinek, et al, even reported an initial success rate of up to 98% in 221 patients.[26] Percutaneous transhepatic biliary drainage of the left love in the 89 patients reported by Kaufman, et al, achieved a success rate of 92%.[23]

Reduction of bilirubin to normal occurs in 22.5% cases reported by Ferrucci, et al, while 50% of patients experience reduction of bilirubin up to 10 mg. This reduction of bilirubin occurs within an average of 11.2 days following the procedure.[14,21]

Complication

Even though the success rate is high, percutaneous transhepatic biliary drainage often creates minor as well as major complications (21-69%). Minor complications in question are complications that only require medical management, correction of the position of the catheter, or without specific therapy. Major complications include those that require radiological or surgical intervention, blood transfusion, or those that are fatal.[25]

Table 2. Major and minor complications of percutaneous transhepatic biliary drainage [21,25-27]

Complication	Hamlin, et al	Ferrucci et al	Sirinek, et al	Carrasco, et al
Minor				
Haemobillia	16	DU	DU	7
Fever	14	DU	DU	DU
Leukocytosis	12	DU	DU	DU
Cholangitis	DU	14.5	48.9	47
Hypotension	7.6	DU	DU	DU
Catheter obstruction	DU	DU	DU	14
Bile leakage	DU	DU	6.1	16
Accidental catheter removal	3.4	DU	DU	18
Others	1.7	4.8	DU	DU
Major				
Bleeding	1.7	3.2	8.1	DU
Septic shock/ subphrenic abscess	1.7	1.6	2	DU
Peritonitis	2.6	DU	DU	DU
Arteriovenous/ biliopleural fistula	0.8	DU	DU	2.5
Others	DU	DU	DU	0.6

DU: Data Unavailable

Mueller and McPherson divided the complications of transhepatic biliary drainage into acute and late-onset complications, as seen in Table 3.

Death occurs in 15-32% of patients that undergo this procedure. Death may be due to accidental removal of

the catheter, causing peritonitis and sepsis (44%), post-procedural sepsis (33%), bile hypersecretion (11%), and formation of a biliopleural fistula after catheter removal (11%).[4,25,27] Bleeding has also been reported as a cause of post-procedural death.[25]

Table 3. Acute and late-onset complications of percutaneous transhepatic biliary drainage.[14,28]

Complication	Mueller, et al (%)	McPherson, et al (%)
Acute		
Bleeding	5.0	DU
Sepsis	3.7	DU
Fever	11.1	DU
Haemobillia	9.5	5.4
Intraperitoneal bile leakage	DU	8.1
Abdominal discomfort	DU	81
Bowel perforation	DU	2.7
Late onset		
Cholangitis/bacteremia	20.7	27
Catheter leakage	4.2	DU
Catheter bending	5.8	10.8
Intrahepatic abscess	DU	5.4
Drainage obstruction	3.7	DU

DU: Data Unavailable

ALTERNATIVE PERCUTANEOUS PROCEDURES

- Drainage with percutaneous cholecystography

  This procedure is useful for obstructions below the level of the cystic duct. It can be conducted if transhepatic biliary drainage fails, but it is only temporary. The technique is not very different from percutaneous transhepatic biliary drainage.[12]
- Drainage with percutaneous transjejenal procedure

  In this procedure, the catheter is inserted percutaneously through a previously constructed biliojejunal Roux-en-Y anastomosis towards the biliary duct. This procedure is performed to keep the endoprothesis in place for a long period of time.[12,29]

ENDOSCOPIC BILIARY DRAINAGE

External and internal biliary drainage may be performed using endoscopy. External drainage is performed using the nasobiliary tube, while internal drainage is performed using endoprothesis.

The first nasobiliary drainage was introduced by Nagai in the year 1976. Two years afterwards (1978), Soehendra, Cotton, and Huibregtse placed the first bilioduodenal endoprothesis using endoscopy.[30,31]

Indication and Contraindication

Endoscopic biliary drainage is the chief palliative therapy in biliary obstruction due to malignancy in patients with old age, or those with contraindications for surgical procedures. This procedures is also indicated as pre-surgical drainage in cases where resection could still be performed to reduce the mortality rate due to surgical procedures.[30,32]

This procedure could not be performed on patients with manifestations of blood coagulation disturbances or uncooperative patients.[30,33]

Preparation

Routine preparations include prophylaxis antibiotics, examination of bleeding and clotting time, premedications, sterilization, and informed consent.[11,12] The patient should fast at least 6 hours prior to the procedure.[11,12]

ENDOSCOPIC NASOBILIARY DRAINAGE

This technique is performed using a size 5-7 Fr nasobiliary tube with Endoscopic Retrograde Cholangiopancreatography (ERCP).[2,34]

Technique

After ERCP canulation and contrast injection, a sphincterotomy is performed to facilitate catheter insertion. The papilla vateri is cut with an electric current

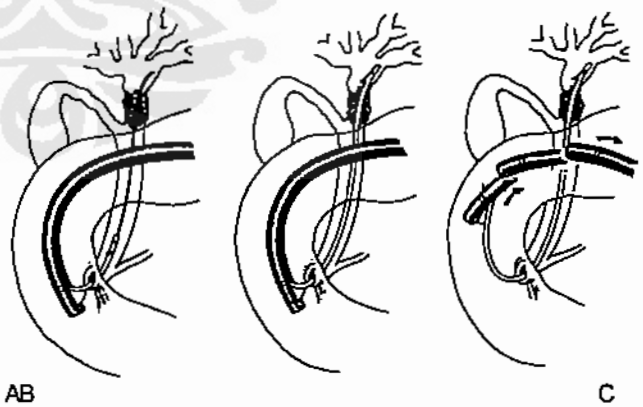


Figure 2. Nasobiliary drainage insertion on a tumor located at the bifurcation (Klatksin type I).[34] A. A guide wire and size 10 Fr nasobiliary tube is shoved through the common biliary duct after the sphincterotomy. B. The nasobiliary is shoved through the obstructed area, while the guide wire is removed. C. The endoscope is removed.

wire, thus enlarging the mouth of the papilla vateri.[2,34,35] A guide wire is then inserted into the collecting duct. The nasobiliary tube is inserted into the collecting duct through the guide wire. After its tip is located at the proximal (common hepatic duct/intrahepatic duct), the guide wire is removed. The spade is then removed while the nasobiliary tube is inserted further to prevent accidental removal. The proximal tip of the nasobiliary tube is replaced from the mouth to the nostrils with a hook, or is attached to a common nasogastric tube until it is position like a nasogastric tube and is fixated on the face. The bile is collected in a sterile plastic bag.[2,34]

Usage of the nasobiliary tube facilitates periodic cholangiography without repeated endoscopy.[34]

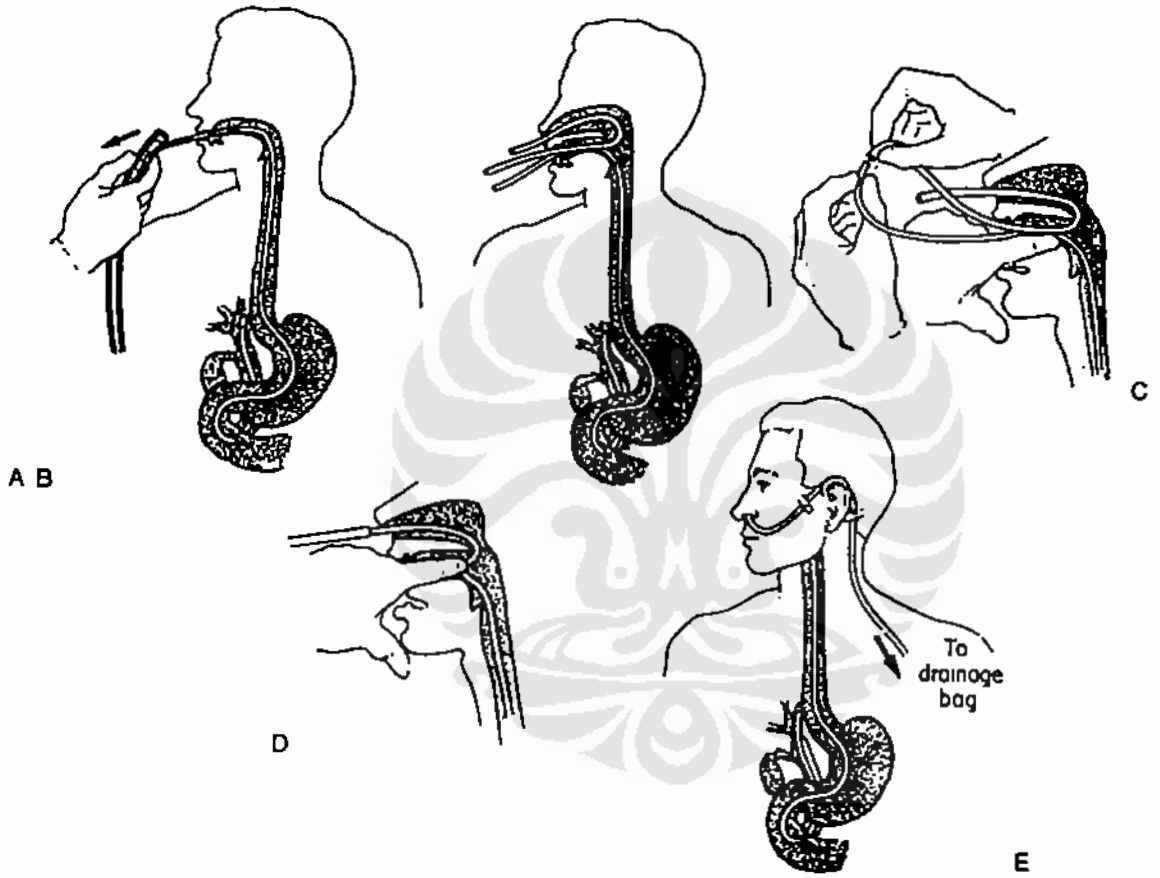


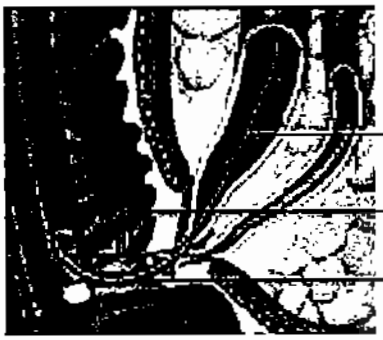
Figure 3. Endoscopic insertion of the nasobiliary tube[34]

A. The endoscope is removed. B. The nasopharyngeal tube is inserted through the nostril through the pharynx, and then extracted through. C. The proximal part of the nasobiliary tube is attached to the nasoparyngeal tube. D. Both tubes are reinserted to the mouth while the tube is extracted through the nostril. E. The proximal portion of the nasobiliary tube is attached to the drainage bag.

ENDOSCOPIC INTERNAL DRAINAGE (ENDOPROTHESIS)

Technique

Similar to insertion of the nasobiliary tube, after ERCP canulation, contrast injection and sphincterotomy (if necessary), the guide wire is inserted into the collecting duct. A biliary stent/endoprothesis that fits the patient's common bile duct is then inserted through the wire with the endoscope. After the endoprothesis is inserted into the common bile duct with its distal tip out side the papilla vateri, the guide wire is removed, leaving the endoprothesis at the site of obstruction.[2,4,30-33,37]



Freeman ML et al, 1996

Figure 4. Standard sphincterotomy/papillotomy. The sphincter of the papilla vateri is cut using an electrocauter that passes through the papillotome. The cauter is directed towards the base of the papilla.[36]

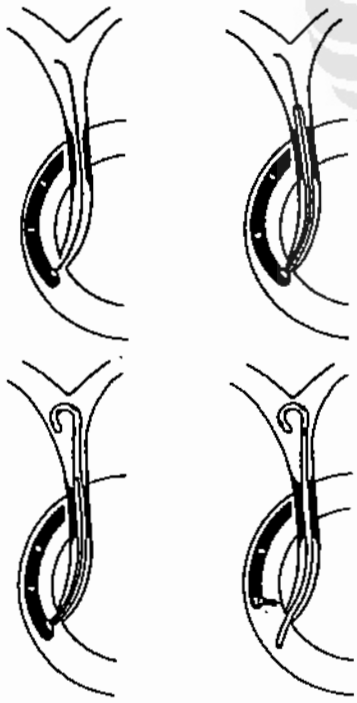


Figure 5. Schematic illustration of endoscopic insertion of an endoprothesis.[30]

Success Rate

The technique for endoscopic insertion of endoprothesis demonstrates a high success rate (84-92%) for cases of tumor at the periampula, distal, or the pancreas; and is able to eliminate jaundice in more than 80-97% of patients.[4,37-39] The mortality rate for the first 30 days ranges from 4-22%.[4] The success rate for several kinds of cancer as seen in Table 3.

Complication

Initial complications occurring within 1 week after the insertion of an endoprothesis is mostly due to the sphincterotomy performed or the endoprothesis itself.[4,30,32]

Complications due to the sphincterotomy procedure reported by Huibregtse, et al occur in 6-8% of all cases, including bleeding, pancreatitis, and perforation of the duodenum or biliary duct as seen in Table 3.[4,32] Marquiles, et al reported that sphincterotomy increases the possibility of acute complications. Acute complications of endoprothesis insertion occur in 8.3% patients that undergo sphincterotomy and in only 1.2% of patients that do not undergo sphincterotomy.[40] The possibility of bleeding is greater in patients with portal vein obstruction and varices due to extension of pancreatic tumor as reported as Cvertkovski, et al.[41]

The most significant acute complication due to endoprothesis is acute cholangitis. Even though prophylactic antibiotics have been administered prior to the procedure and the endoprothesis and other instruments have been disinfected, contamination of bacteria from the mouth and bowel during the procedure cannot be avoided. Such bacterial contamination would cause cholangitis in the case of incomplete biliary drainage. This explains why cholangitis more often complicates tumors at the bifurcatio (19%), since adequate drainage at this site is more difficult.[4,32] To deal with this problem, obstruction at the bifurcatio is managed by inserting two endoprothesis simultaneously. The success rate for drainage in the case where two endoprothesis are placed simultaneously is better than if only one endoprothesis is inserted (88.6% compared to 76.9%), thus reducing the complication of cholangitis (8.8% compared to 16.6%).[42] The incidence of cholangitis also increases with multiple attempts to insert the endoprothesis.[4]

The main complication that could occur later on is obstruction of the endoprothesis, which occurs in 21-36% of cases, reported by Huibregtse, et al.[4] Retrospective studies found cases of endoprothesis obstruction in 10-30% cases, while random prospective studies found a higher rate of 21-52% with a total incidence of 42%.

Table 4. The outcome of endoscopic endoprothesis insertion in biliopancreatic cancer (Amsterdam).[4,32]

	Ampulla	Pancreas	Gallbladder	Bifurcatio
Drainage success rate (%)	96	90	86	84
Bilirubin				
Reduced (%)	98	97	94	87
Normal (%) within 30 days	96	94	84	68
Mortality				
Due to the procedure (%)	0	2	2	6
Within 30 days (%)	2	9.5	20	23
Median life expectancy (in months)	13.5	5	4.5	3

Table 5. Initial complication of endoprothesis in the first week.[4,32]

Complication	Incidence rate (%)		
Due to sphincterotomy			
Bleeding	1-2		
Pancreatitis	0-1		
Perforation	0-1		
Due to endoprothesis			
Acute cholecystitis	0-1		
Obstruction	1-2		
Acute cholangitis	7-19	Ampulla	7
		Pancreas	8
		Gallbladder	12
		Bifurcatio	1
Mortality due to the procedure		0-6	

The average time span for the endoprothesis to function prior to obstruction is 4.9 months (ranging from 1.4 to 9.2 months).[43] Other complications such as acute cholecystitis, endoprothesis migration and perforation is rarely found. Cholecystitis may be due to stenosis of the cystic duct, which occurs slowly, accompanied by continuous infection caused by the endoprothesis. Duodenal stenosis, which is commonly found, is not an actual complication of this procedure, but instead is due to rapid growth of the tumor.[4,30,33]

Preventing Endoprothesis Obstruction

Bile sediment is the substance that plays the greatest role in obstructing the endoprothesis. It contains bilirubinic calcium crystals, palmitic calcium, cholesterol, protein, and bacteria.[3,43,44] Bacteria encourages bile sedimentation, possibly due to the great number of bacteria that adheres t the biofilm and bacterial enzymes such as beta-glucoronidase, which is active in the bile. Bacteria found in the endoprothesis include *Escherichia coli, Klebsiella oxytoca, Klebsiella pneumonia, Enterobacter cloa-*

Table 6. Late onset complications of endoprothesis insertion.[4,32]

Complications	Incidence rate (%)		
Obstruction	21-36		
Acute cholecystitis	0-1		
Endoprothesis dislocation	0-1		
Perforation	1-2		
Duodenal stenosis	2-23	Ampulla	23
		Pancreas	7.5
		Gallbladder	5
		Bifurcation	5
Death	Rare		

cae, Citrobacter freundii, Pseudomonas aeruginosa (gram negative), *Enterokokus sp, Streptokokus sp, Clostridium sp* (gram positive).[4,43,45] Duodenal reflux also enhances obstruction of the endoprothesis.[4]

Many methods to prevent endoprothesis blockage are still under trial.

Diameter of The Endoprothesis

This is the most widely accepted method to delay endoprothesis obstruction. Siegel, et al, reported delayed obstruction in the use of size 12 French endoprothesis compared to 10 French.[43] Pereira, et al reported similar findings in a comparison between the use of 11,5 French and 10 French endoprothesis, while Coene compared size 10 French and 7 French endoprothesis.[4,46] Nevertheless, current techniques only allow the use of a size 12 French endoprothesis, limited by the size of the duodenoscope.[43] To avoid this, self-expanding metal stents (SEMS) with the ability to expand up to size 30 French was introduced. SEMS have been proven to remain functional twice as long compared to conventional plastic endoprothesis. Obstruction occurs after 8 to 12 months due to tumor growth between and at the tip of the endoprothesis. Unfortunately, SEMS is permanent, is irreplaceable, and is more expensive.[43,46,48-49]

Type and Design of The Endoprothesis

Available endoprothesis are made of various materials, including plastics (polyethylene, polyurethane, Teflon, vivatan) and metal.[44] Plastic endoprotheses is cheaper and could be easily replaced, while metal endoprotheses are difficult to replace.[44,47] Since bacteria are suspected to adhere by hydrophobic interaction, Costamagna, et al tried to use a hydromer-coated polyurethane endoprothesis, and compared it to the standard polyurethane endoprothesis. Even though the comparison did not demonstrate statistically significant findings, the coated endoprothesis function for a longer period of time (103 days compared to 68 days).[46,50] The vivatan endoprothesis, with its smoother surface, is also considered to delay obstruction.[44] Pig-tails and side openings are also supposed to delay obstruction.[4,44]

Regular Endoprothesis Replacement

Most endoscopy experts recommend regular replacement of the endoprothesis every 4 months prior to obstruction, especially in high-risk patients, which are those with prior history of endoprothesis obstruction.[44]

Endoprothesis Cleansing

Several researchers tried endoprothesis cleansing as an alternative to endoprothesis replacement. This is made possible by the stent retriever invented by Soehendra, and the snare-over wire technique. However, the benefits are minimal and there is the risk of biliary sepsis.[44]

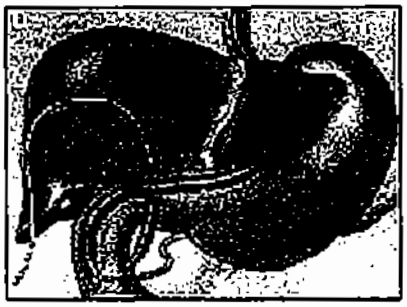
Oral Antibiotics and Bile Salts

Most current clinical trials in preventing endoprothesis obstruction use a combination of bile salts, such as ursodeoxycholic acid or rowachol, to improve bile flow with antibiotics. Among these studies, only one study using ursodeoxycholic acid and norfloxacin has demonstrated significant benefits.[44,47,51]

COMBINATION OF PERCUTANEOUS AND ENDOSCOPIC TRANSHEPATIC BILIARY DRAINAGE

The main cause of failure in internal endoscopic drainage is obstruction at the duodenum and failure of the canule to pass through the common bile duct or to pass through the stricture. In such cases, a combination of the percutaneous rendezvous and endoscopic technique may be performed.[4,32,52] In this procedure, the guide wire is inserted percutaneously through the stricture area and

is then removed through an endoscope. The catheter and endoprothesis is then inserted through the endoscope.[4]



Freeman ML et al, 1996

Figure 6. Endoprothesis insertion using a combination of percutaneus transhepatic biliary drainage and endoscopic biliary drainage[36]

MRCP-GUIDED ENDOPROTHESIS INSERTION

Another alternative technique is by inserting the endoprothesis guided by Magnetic Resonance Cholangiopancreatography (MRCP). This technique can be used if endoscopic insertion fails. This technique also reduces the incidence of cholangitis up to 6%.[53]

Choice of Drainage Technique

The choice between surgical or non-surgical drainage is still controversial. In general, for patients with a life expectancy of less than 6 month, non-surgical drainage seems to be more favorable. But for patients with a longer life expectancy, palliative surgical treatment is more advantageous.[19]

Which technique to chose usually depends on the availability of expert and instrumentation at each institution.[3,11,19] Beyer III, et al, proposed an algorithm based on the site of obstruction, hemostasis function, and dilatation of the biliary duct, as seen in Illustration 8.[11]

The latest recommendation from American Society for Gastrointestinal Endoscopy prefers the endoscopic biliary drainage as the first choice, followed by a second endoscopic trial, followed by other techniques such as the PTBD, or a combination of both efforts, or surgical drainage if all else fails.[54,55]

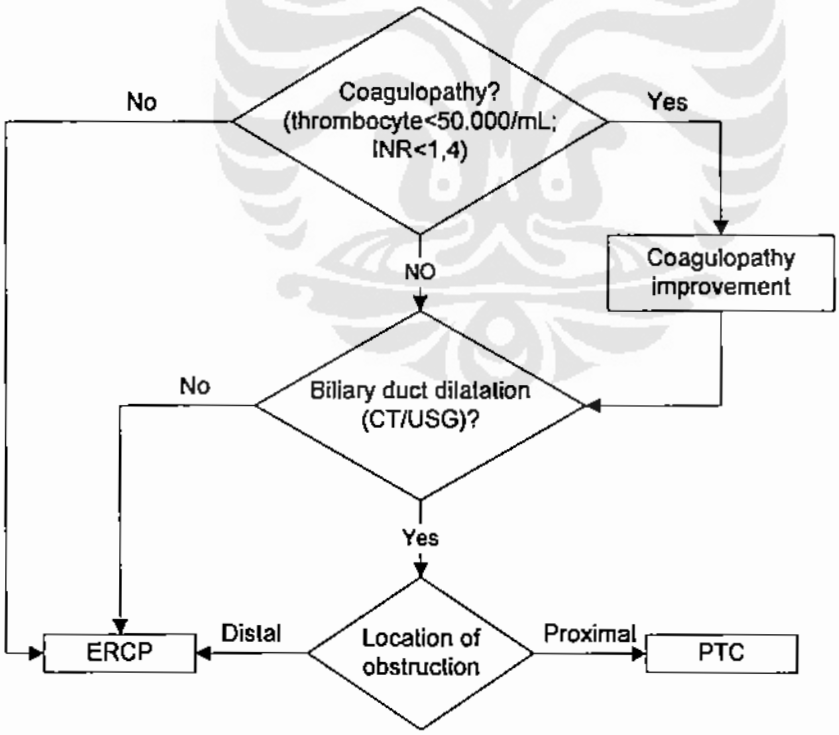


Figure 7. Choice of non-operative technique to reach the biliary system.[11]

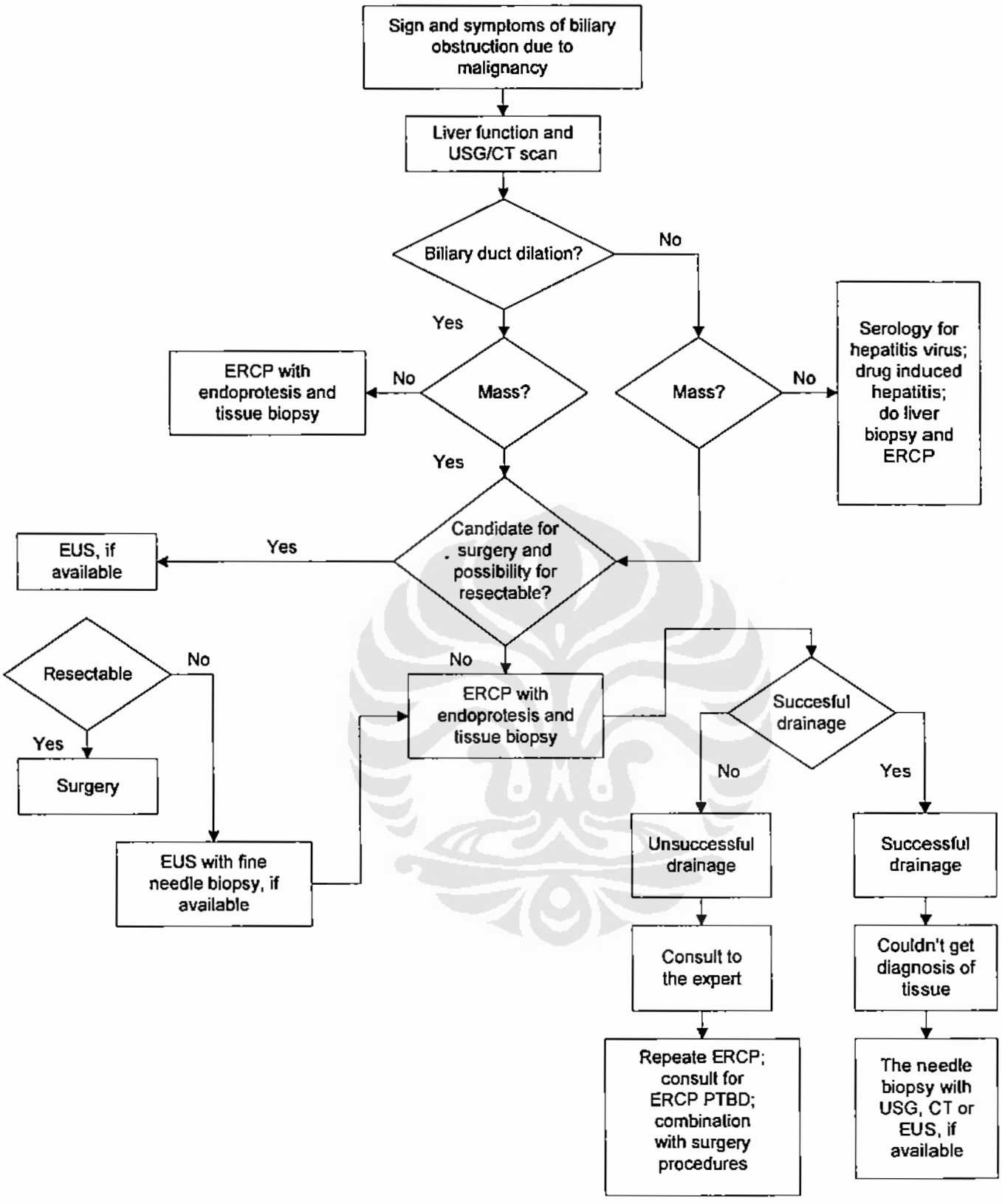


Figure 8. The algorithm for the therapeutic approach towards biliarly obstruction due to malignancy.[54]

CONCLUSION

1. Management of biliary obstruction due to malignancy requires cooperation between the internist, surgeon, and radiologist.
2. Non-surgical biliary drainage is the chosen palliative treatment for biliary obstruction due to malignancy with a life expectancy of less than six months, since it has a lower rate of complication than surgical drainage.
3. The choice for non-surgical drainage technique depends on the type of tumor, location of obstruction, and the availability of experts and instrumentation.

REFERENCES

1. Finsinger RL. Integrating medical and surgical treatments in gastrointestinal, genitourinary and biliary obstruction in patients with cancer. Hematol Oncol Clin North Am 1996; 10: 173-88.
2. Simadibrata M. Penatalaksanaan intervensional ikterus obstruktif di bidang penyakit dalam. Dalam: Kumpulan Makalah Temu Ilmiah Bedah Digestif; 4-5 Mei 2001: Jakarta. Jakarta: Subbag Bedah Digestif Bag. Bedah Digestif FKUI/RSUPNCM; 2001.
3. Shapiro MC. Management of malignant biliary obstruction: nonoperative and palliative techniques. Oncology 1995; 9: 493-504.
4. Coene PPLO. Endoscopic biliary stenting. Mechanisms and possible solutions of the clogging phenomenon [thesis]. Amsterdam: University of Amsterdam; 1990.
5. Molinari M, Helton WS, Espat NJ. Palliative strategies for locally advanced unresectable and metastatic pancreatic cancer. Surg Clin North Am 2001; 3: 651-66.
6. Martin RF, Rossi RL. Multidisciplinary considerations for patients with cancer of the pancreas or biliary tract. Surg Clin North Am 2000; 80: 709-29.
7. Lalisang TJM. Penanganan bedah ikterus obstruksi. Dalam: Kumpulan Makalah Temu Ilmiah Bedah Digestif; 4-5 Mei 2001; Jakarta. Jakarta: Subbag Bedah Digestif Bag. Bedah Digestif FKUI/RSUPNCM; 2001.
8. Sherlock S, Dooley J. Diseases of the liver and biliary system, 10th ed. Oxford: Blackwell Science Ltd; 1997.
9. Van den Bosch RP, Van der Schelling GP, Klinkenbijl JHG, Mulder PGH, Van Blankenstein M, Jeekel J. Guidelines for the application of surgery and endoprotheses in the palliation of obstructive jaundice in advanced cancer of the pancreas. Ann Surg 1994; 219: 18-24.
10. Povoski SP, Karpeh Jr MS, Conlon KC, Blumgart LH, Brennan MF. Association of preoperative biliary drainage with postoperative outcome following pancreaticoduodenectomy. Ann Surg 1999; 230: 131-42.
11. Beyer III JA, Delcore R, Cheung LY. Nonoperative treatment of biliary tract disease. Arch Surg 1998; 133: 1172-6.
12. Lameris JS. Ultrasound-guided percutaneous transhepatic cholangiography and drainage in malignant biliary disease. In: Lygidakis NJ, Tytgat GNJ, eds. Hepatobiliary and pancreatic malignancies, 1st ed. New York: Thieme Medical Publishers Inc; 1989. p. 115-24.
13. Rajiman I, Wallace S, Ajani J. Management of malignant biliary obstruction: nonoperative and palliative techniques. The shapiro article reviewed. Oncology 1995; 9: 499-500.
14. McPherson GAD, Benjamin IS, Habib NA, Bowley NK, Blumgart LH. Percutaneous transhepatic drainage in obstructive jaundice: advantages and problems. Br J Surg 1982; 69: 261-4.
15. Smith AC, Dowsett JR, Russel RCG, Hatfield ARW, Cotton PB. Stent or surgery for the palliation of malignant biliary obstruction: is the choice clear now? Lancet 1994; 344: 1655-60.
16. Rossi RL, Traverso LW, Pimentel F. Malignant obstructive jaundice: evaluation and management. Surg Clin North Am 1996; 76: 67-70
17. Custis K, Brown C, El Younis CM. Common biliary tract disorders. Clinics in Fam Practice 2000; 2: 141-54.
18. Williams SR. Pancreatic cancer. In: Djulbegovic B, Sullian DM, eds. Decicion making in oncology. Evidence-based management. New York: Churchill Livingstone; 1997. p.187-92.
19. Gobien RF, Stanley JH, Soucek CD, Anderson MC, Vujic I, Gobien BS. Routine preoperative biliary drainage: effect on management of obstructive jaundice. Radiology 1984; 152: 353-6.
20. Povoski SP, Karpeh Jr MS, Conlon KC, Blumgart LH, Brennan MF. Association of preoperative biliary drainage with postoperative outcome following pancreaticoduodenectomy. Ann Surg 1999; 230: 131-42.
21. Ferrucci JT, Mueller PR, Harbin WP. Percutaneous transhepatic biliary drainage. Technique, results, and applications. Radiology 1980; 135: 1-13.
22. Suda T, Ozawa T, Aoyagi Y, Mori S, Watanabe M, Tsukada Y, et al. Nutritional support through percutaneous transhepatic internal drainage route in common bile duct cancer. J Gastroenterol Hepatol 1994; 9: 524-6.
23. Kaufman SL, Kadir S, Mitchell SE, Kinnison ML, Chang R. Left lobe of the liver: percutaneous biliary drainage. Radiology 1989; 170: 191-4.
24. Weber J. Percutaneous transhepatic biliary drainage (PTBD). In: Lygidakis NJ, Tytgat GNJ, eds. Hepatobiliary and pancreatic malignancies, 1st ed. New York: Thieme Medical Publishers Inc, 1989. p. 125-35.
25. Hamlin JA, Friedman M, Stein MG, Bray JF. Percutaneous biliary drainage: complications of 118 concecutive catheterizations. Radiology 1986; 158: 199-202.
26. Sirinek KR, Levine BA. Percutaneous transhepatic cholangiography and biliry decompression. Invasive, diagnostic, and therapeutic procedures with too high price? Arch Surg 1989; 124: 885-8.
27. Carrasco CH, Zornova J, Bechtel WJ. Malignant biliary obstruction: complications of percutaneous biliary drainage. Radiology 1984; 152: 343-6.
28. Mueller PR, vanSonnenberg E, Ferrucci JT. Percutaneous biliary drainage; technical and catheter related problems in 200 procedures. AJR 1982; 138: 17-23.
29. McPherson SJ, Gibson RN, Colier NA, Speer TG, Sherson ND. Percuteneous transjejunal biliary intervention: 10-year experience with axxess via roux-en-y loops. Radiology 1998; 206: 665-72.
30. Grimm H, Sochendra N. Endoscopic biliary drainage (Hamburg). In: Lygidakis NJ, Tytgat GNJ, eds. Hepatobiliary and pancreatic malignancies, 1st ed. New York: Thieme Medical Publishers Inc; 1989. p. 418-25.
31. Marks WM, Freeny PC, Ball TJ, Gannan RM. Endoscopic retrograde biliary drainage. Radiology 1984; 152: 357-60.

32. Huibregtse K, Tytgat GN. Endoscopic biliary drainage (Amsterdam). In: Lygidakis NJ, Tytgat GNJ, eds. Hepatobiliary and pancreatic malignancies, 1st ed. New York: Thieme Medical Publishers Inc; 1989. p. 426-39.
33. ASGE guidelines. The role of ERCP in diseases of the biliary tract and pancreas. Gastrointest Endosc 1999; 50: 915-20.
34. Siegel JG. Endoscopic retrograde cholangiopancreatography, technique, diagnosis, and therapy. New York: Raven Press; 1992.
35. Lesmana LA. Endoscopic retrograde cholangiopcanreatography (ERCP) diagnostik dan terapeutik pada ikterus bedah. Simposium sehari penatalaksanaan ikterus; 14 Sept 1991; Palembang. Palembang: Fakultas Kedokteran Universitas Sriwijaya;1991.
36. Freeman ML, Nelson DB, Sherman S, Haber GB, Herman ME, Dorsher PJ, et al. Complications of endoscopic biliary sphincterotomy. N Eng J Med 1996; 335: 909-18.
37. Das A, Sivak MV. Endoscopic palliation for inoperable pancreatic cancer. Cancer Control 2000; 7: 452-7.
38. Speer G, Cotton PB, Russel CRG, Mason RR, Hatfield ARW, Leung JWC. Randomised trial of endoscopic versus percutaneous stent insertion in malignant obstructive jaundice. Lancet 1987; 2: 57-62.
39. Rubin J, Jowell PS. Predictive factors for survival of patients with inoperable malignant distal biliary strictures: a practical management guideline. Gastrointest Endosc 1998; 48: 441-2.
40. Marguiles C, Siqueira ES, Silverman WB, Lin XS, Martin JA, Rabinovitz M, et al. The effect of endoscopic sphincterotomy on acute and chronic complications of biliary endoprotheses. Gastrointest Endosc 1999; 49: 716-9.
41. Cvetkoski B, Kurtz RC. Hemobilia in advanced pacreatic cancer with portal vein obstruction and metal endobiliary stent: a case report. Gastrointest Endosc 1999; 50: 420-2.
42. Sherman S. Endoscopic drainage of malignant hilar obstruction: is one biliary stent enough or should we work to place two? Gastrointest Endosc 2001; 53: 681-4.
43. Libby ED, Leung JW. Prevention on biliary stent clogging: a clinical review. Am J Gastroenterol 1996; 91: 1301-8.
44. ASGE guidelines. Technology status evaluation report: biliary stents. Update May 1999. Gastrointest Endosc 1999; 50; 938-42.
45. Moesch C, Sautereau D, Cessot F, Berry P, Mounier M, Gainant A. Physicochemical and bacteriological analysis of the contents of occluded biliary endoprotheses. Hepatology 1991; 14: 1142-6.
46. Faigel DO. Preventing biliary stents occlusion. Gastrointest Endosc 2000; 51: 104-7.
47. Pereira-Lima JC, Jakobs R, Maier M, Benz C, Kohler B, Riemann JF. Endoscopic biliary stenting for the palliation if pancreatic cancer: results, survival predictive factors, and comparison if 10-french with 11.5-french gauge stents. Am J Gastroenterol 1996; 91: 2179-84.
48. Reed Jr DN, Vitale GC. Interventional endoscopic retrograde cholangiopancreaticography and endoscopic surgery. Surg Clin North Am 2000; 80: 1171-201.
49. Mallery S, Van Dam J. Advances in diagnostic and therapeutic endoscopy. Med Clin North Am 2000; 84: 1059-83.
50. Costamagna G, Mutignani M, Rotondano G, Cipolletta L, Ghezzo L, Foco A, et al. Hydrophilic hydromer-coated polyurethane stents versus uncoated stents in malignant biliary obstruction: a randomized trial. Gastrointest Endosc 2000; 51: 8-11.
51. Barrioz T, Ingrand P, Besson I, de Ledinghen , Silvain C, Beauchant M. Randomised trial of prevention of biliary stent occlusion by ursodeoxycholic acid plus norfloxacin. Lancet 1994; 344: 581-2.
52. Dowsett JF, Vaira D, Hatfield ARW, Cairns SR, Polydorou A, Frost R, et al. Endoscopic biliary therapy using the combined percutaneous and endoscopic technique. Gastroenterology 1989; 96: 1180-6.
53. Hintze RE, Abou-Rebyeh H, Adler A, Veltzke-Schlieker W, Felix R, Wiedenmann B. Magnetic resonance cholangiopancreaticography-guided unilateral endoscopic stent placement for klatskin tumors. Gastrointest Endosc 2001; 53: 40-6.
54. Eisen GM, Dominitz JA, Faigel DO, Goldstein JL, Kalloo AN, Petersen BT, et al. Guidelines. An annotated algorithmic approach to malignant biliary obstruction. Gastrointest Endosc 2001; 53: 651-666
55. Choudari CP, Sherman S, Fogel EL, Phillips S, Kochel A, Flueckiger J, et al. Success of ERCP at a referral center after a previously unsuccessful attempt. Gastrointest Endosc 2000; 52: 478-83.