# Endoscopic or Percutaneous Biliary Drainage for Gallbladder Cancer: A Randomized Trial and Quality of Life Assessment

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***Background & Aims:*** **Patients with carcinoma of the gallbladder (GBC) and obstructive jaundice are usually not amenable to curative resection. Effective palliation by biliary decompression is the goal of treatment. Endoscopic stenting (ES) and percutaneous transhepatic biliary drainage (PTBD) can provide biliary decompression. We compared unilateral PTBD and ES in patients with a hilar block caused by GBC and assessed their quality of life (QOL).** ***Methods:*** **Consecutive patients with GBC not suitable for curative resection with Bismuth type 2 or 3 block were randomized to either PTBD or ES with a 10F plastic stent. Technical success, successful drainage, early cholangitis, complications, procedure-related mortality, 30-day mortality, survival, and QOL before and 1 and 3 months after stenting were compared between the 2 groups. All patients were followed up until death.** ***Results:*** **Fifty-four patients were randomized to PTBD or ES (27 each). Successful drainage was better in the PTBD group (89% vs 41%; $P < .001$). Early cholangitis was significantly higher in the ES group (48% vs 11%; $P = .002$). Procedure-related (4% vs 8%) and 30-day mortality (4% vs 8%) and median survival were similar (60 days in both; $P = .71$). Although the World Health Organization–Quality of Life 1- and 3-month physical and psychological scores were better after PTBD, the difference was not significant. The European Organization for Research and Treatment of Cancer (EORTC)–Quality of Life Questionnaire 30 global health status at 3 months was significantly better after PTBD (75 vs 30.5, $P = .02$). The EORTC symptom scores improved in both groups, but only fatigue was significantly better after PTBD.** ***Conclusions:*** **PTBD provides better biliary drainage and has lower complication rates in patients with GBC and hilar block.**

Gallbladder cancer (GBC) is one of the most common abdominal malignancies worldwide. It has a very high incidence in Chile, Japan, and India.[1,2] In the United States the incidence of GBC is 1.2 per 100,000, with 2800 deaths per year.[3] GBC is the most common cause of malignant hilar biliary obstruction. Jaundice caused by biliary obstruction is the presenting feature in 30%–60% of patients with GBC.[4] The usual cause of biliary obstruction is direct infiltration of the common hepatic duct by the tumor.[4] Most patients with GBC and obstructive jaundice are not amenable to a curative surgical resection,[4,5] and hence, effective palliation is the goal of treatment. Although surgical bilioenteric bypass has been the traditional palliative approach, it is associated with substantial morbidity and mortality.[5] Nonoperative alternatives in the form of percutaneous and endoscopic drainage have been used to provide effective biliary drainage.[6–10] It has been shown that even if only 30% of the liver parenchyma is drained, it provides adequate palliation to relieve the jaundice and associated pruritus.[11,12] Therefore, unilateral drainage of one lobe of the liver might be sufficient to palliate the jaundice and pruritus and improve the quality of life (QOL).[12–16] A few trials have shown that endoscopic drainage is better than percutaneous drainage in patients with lower bile duct obstruction caused by pancreatic and periampullary cancers.[17,18] However, in patients with malignant hilar obstruction (Bismuth types 2 and 3), endoscopic drainage is associated with a higher incidence of cholangitis, and the success rate varies from 40%–80%.[13,14] On the other hand, percutaneous drainage might be associated with complications such as biliary leak and bleeding. There is no published randomized controlled trial comparing endoscopic and percutaneous drainage in patients with only malignant hilar obstruction. Hence, we did a randomized prospective trial comparing percutaneous and endoscopic biliary drainage in patients with hilar biliary obstruction caused by GBC in terms of successful drainage and QOL after the drainage.

## Patients and Methods

Consecutive patients with obstructive jaundice caused by GBC presenting to the outpatient departments of Gastrointestinal Surgery and Gastroenterology at the All India Institute of Medical Sciences were evaluated. The diagnosis of obstructive jaundice was established on the basis of liver chemistry (increased serum bilirubin and alkaline phosphatase levels) and an abdominal ultrasonography (US) showing dilated intrahepatic radicles. The diagnosis of GBC was made if a mass was seen arising from the gallbladder on a dual phase, contrast-enhanced computed tomography scan (CECT) of the abdomen.[4] Histologic and/or cytologic confirmation of malignancy was done whenever possible by a fine-needle aspiration cytology/trucut biopsy. The site of biliary obstruction was classified according to the Bismuth-Corlette classification on the basis of

*Abbreviations used in this paper:* CECT, contrast-enhanced computed tomography; EORTC QLQ, European Organization for Research and Treatment of Cancer Quality of Life Questionnaire; ES, endoscopic stenting; GBC, gallbladder cancer; PTBD, percutaneous transhepatic biliary drainage; US, ultrasonography; WHO-QOL, World Health Organization–Quality of Life.


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the preprocedural investigations that included US, CECT, and magnetic resonance cholangiopancreatography.[19] The final differentiation between types 2 and 3 blocks was based on the findings noted during the biliary intervention, ie, endoscopic or percutaneous.

### *Inclusion Criteria*

Patients with GBC and hilar block (Bismuth type 2 or 3 block) not suitable for curative resection with 1 or more of the following criteria were included: (1) jaundice with serum bilirubin >10 mg/dL, (2) pruritus, and (3) cholangitis.

### *Exclusion Criteria*

Patients with 1 or more of the following were excluded from the study: (1) patients with resectable cancer as judged on imaging studies, (2) patients with a poor performance status: Karnofsky index <60,[20] (3) Bismuth type 1 or 4 block, (4) uncontrolled ascites, (5) duodenal obstruction, and (6) patients who opted for insertion of a metal stent.

### *Sample Size Calculation*

The number of patients to be included in each group was calculated to be 91 on the basis of the assumption that percutaneous drainage would be better than endoscopic drainage by 20% in terms of successful drainage. The sample size was calculated for a power of 80% and alpha error of 0.05. However, we could enroll 54 patients during the stipulated study period of 2 years. The reason for lesser numbers was exclusion of patients as a result of the predetermined exclusion criteria. However, the power of the study was 96% on reverse calculation for intention-to-treat analysis.

### *Study Design: Randomized Controlled Trial*

The trial is registered at www.ClinicalTrials.gov (NCT00409864) and was approved by the institutional ethics committee, and patients were included after informed consent. The random numbers were computer-generated. The patients were randomized by using the sealed envelope technique into 2 groups: group A, percutaneous transhepatic biliary drainage (PTBD) and group B, endoscopic stenting (ES).

### *Preprocedural Preparation*

The baseline investigations obtained included hemoglobin, blood cell counts, blood urea, serum creatinine, serum electrolytes, blood sugar, liver chemistry, and prothrombin time.[21] A chest x-ray and an electrocardiogram were also obtained. All patients received injectable prophylactic antibiotic (cefoperazone + sulbactam 1 g) for 72 hours starting 2 hours before the procedure. Patients were kept nil by mouth for 8 hours before the procedure and were well-hydrated with intravenous fluids. The procedure was performed under conscious sedation (midazolam and pentazocine).

### *Procedure*

**Percutaneous transhepatic biliary drainage.**[21] *Approach.* Either a right- or left-sided approach was used for PTBD. Patients with extensive right-sided disease and/or right lobe atrophy with sparing of the left lobe were subjected to a left-sided approach and vice-versa. For type 2 blocks either the right anterior or left system was chosen (left was chosen if the left lobe of the liver was not atrophied). For type 3a blocks (right secondary confluence involved), a left-sided drainage was done, whereas for type 3b blocks, a right-sided drainage was done.

*Technique.* An anterior subxiphoid approach was used for the left duct, whereas a right lateral approach was used for the right duct. The procedure was done under ultrasound guidance, and the skin entry was through the intercostal space below the costophrenic angle. Once entry was gained to a suitable duct, the standard Seldinger technique was used to place a guidewire in the biliary system. The tract was dilated, and after crossing the obstruction with a hydrophilic guidewire (Terumo; Terumo Inc, Tokyo, Japan), a ring biliary 8F catheter (Cook Medical, Bloomington, IN) was placed to provide internal-external drainage. In a subsequent session (done 1–2 days later), a 10F straight plastic stent (polyurethane) was placed in the biliary system through a sheath across the obstruction to provide internal drainage. A standard 8F pigtail drainage catheter was placed just proximal to the stent to maintain access to the ductal system for 1–2 days after internalization. This was done to facilitate flushing of the system to prevent clogging of the stent and to facilitate further intervention, if the stent should block or migrate. A cholangiogram study was done through the external drainage catheter to ensure good stent function, and then it was removed, leaving the tract to heal.

*Endoscopic stenting.*[22] Endoscopic retrograde cholangiography was performed with a therapeutic duodenoscope (TJF 160; Olympus, Tokyo, Japan), and a standard sphincterotome was used for cannulation of the bile duct. A hydrophilic guidewire (Terumo, 0.032-inch diameter; Terumo Inc, or Jag wire 0.035-inch diameter; Boston Scientific Microvasive, Natick, MA) was used to cross the malignant stricture. After crossing the stricture, bile was aspirated, and then a limited cholangiogram was done. A small-size sphincterotomy was done to facilitate the passage of the stent. A 10F straight plastic stent was inserted across the stricture.

*Crossover procedures.* If a patient had a failed insertion of the stent by either procedure, he or she was considered for the other technique. These patients were included in the crossover group for per protocol analysis.

### *Outcome Measures*

The primary outcome measures were successful drainage and QOL. Successful drainage was defined as reduction in bilirubin to <50% of the pretreatment value within 7 days after drainage. The secondary outcome measures included early and late complications, procedure-related mortality, 30-day mortality, stent patency time, and survival. The early and late complications were defined as those occurring within 30 days and after 30 days of stent placement, respectively. Early cholangitis was defined as cholangitis occurring during the first 7 days after the procedure as evidenced by fever, leukocytosis with worsening biochemical parameters. A procedure-related mortality was defined as death directly related to complications of the procedure. The duration of stent patency was defined as the period of time from stent insertion to stent occlusion. The stent was considered to be occluded when patients had abnormal/worsening biochemical parameters and/or cholangitis. It was confirmed by biliary dilatation in the drained lobe on US.

**Quality of Life assessment.** The World Health Organization (WHO)–QOL BREF-26 and European Organization