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PERIOPERATIVE OUTCOMES AMONG PATIENTS UNDERGOING OPEN BILIARY BYPASS SURGERY FOR MALIGNANT BILIARY OBSTRUCTION IN A LOW RESOURCE SETTING: A MULTI-CENTER PROSPECTIVE COHORT STUDY

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A RESEARCH THESIS SUBMITTED TO DEPARTMENT OF SURGERY COLLEGE OF MEDICINE AND HEALTH SCIENCES, ADDIS ABABA UNIVERSITY IN PARTIAL FULFILLMENT OF THE REQUIREMENTS FOR THE SUB-SPECIALITY CERTIFICATE IN HEPATOPANCREATICOBILIARY SURGERY.

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The full title of the research project	PERIOPERATIVE OUTCOMES AMONG PATIENTS UNDERGOING OPEN BILIARY BYPASS SURGERY FOR MALIGNANT BILIARY OBSTRUCTION IN A LOW RESOURCE SETTING: A MULTI-CENTER PROSPECTIVE COHORT STUDY
Study Period	From July 1, 2022 – June 30, 2023
Study Area	Tertiary hospitals in Addis Ababa <ul style="list-style-type: none"> • Tikur Anbessa Specialized Hospital • Yekatit-12 Comprehensive Specialized Hospital • Menelik II Hospital • Addis Hiwot General Hospital • Amin General Hospital • Lancet General Hospital
Budget	79,654

DECLARATION

This is to certify that the research thesis entitled “perioperative outcomes among patients undergoing open biliary bypass surgery for malignant biliary obstruction in a low resource setting: a multi-centre prospective cohort”; submitted as partial fulfillment of sub-specialty certificate in Hepatopancreaticobiliary Surgery, Addis Ababa University, is a record of my original work and has not been submitted to any other institution for any purpose. The references used for this thesis are properly cited and the assistance I received has been duly acknowledged.

Yoseph Solomon Bezabih

Name of the candidate

Date

APPROVAL OF THESIS FOR DEFENSE

I hereby certify that I have supervised, read and evaluated this research thesis titled “Perioperative outcomes among patients undergoing open biliary bypass surgery for malignant biliary obstruction in a low resource setting: a multi-centre prospective cohort” by Yoseph Solomon under my guidance. I recommended the thesis for oral defense.

Advisor’s name

Signature

Date

1. Dr. Shimelis Nigussie

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Acronyms and Abbreviations:

ASA: American Society of Anesthesiologists

AVAC: Ampulla of Vater Cancer

BTC: Biliary Tract Cancers

CA 19-9: Carbohydrate antigen 19-9

CEA: Carcinoembryonic antigen

COPD: Chronic obstructive pulmonary disease

CRP: C-reactive protein

HCCA: Hilar Cholangiocarcinoma

DCCA: Distal Cholangiocarcinoma

DCA: Duodenal Cancer

DM: Diabetes mellitus

EBDC: Extrahepatic Bile Duct Cholangiocarcinoma

GBCA: Gall Bladder Cancer

IBDC: Intrahepatic Bile Duct Cholangiocarcinoma

MBO: Malignant Biliary Tract Obstructions

PACA: Periapillary Carcinoma

PDAC: Pancreatic Duct Adenocarcinoma

PHT: Pancreatic Head Tumor

GLOBOCAN: The global cancer observatory

SPSS: Statistical Package of Social Sciences

Abstract

Introduction: Obstructive jaundice is the most common symptom of malignant diseases of the extrahepatic biliary system and necessitates either non-operative or operative biliary bypass. Because of percutaneous and endoscopic approaches, the use of palliative surgical procedures has decreased in recent years. However, in resource-limited situations, open biliary bypasses remain a viable option. This study aimed to identify factors associated with adverse perioperative outcomes following open biliary bypass.

Methods: From June 2022 to May 2023, 69 patients underwent open biliary bypass for malignant biliary obstruction. Postoperative morbidity and mortality within 30 days of surgery were assessed. A Kaplan-Meier was used for categorical variables, and a log-rank test was used to determine the statistically significant difference between variables. A Cox regression analysis was conducted to identify factors associated to time to develop complications.

Results: The hazard of developing complications among those with preoperative cholangitis was 2.49 times higher than those without preoperative cholangitis (HR 2.49, 95% CI [1.06, 5.84]). For every hour increment in the length of surgery, the hazard of getting complications increased by 2.47 times (HR 2.47, 95% CI [1.28, 4.77]). As serum bilirubin increased by 1mg/dl, the hazard of developing complications increased by 14% (HR 1.14, 95% CI [1.03, 1.17]).

Conclusion: Patients who had long operation times, preoperative cholangitis, and elevated total bilirubin levels are at increased risk for poor perioperative outcomes. Clinicians may use these results to optimize these patients to decrease their elevated risk of serious morbidity and mortality.

Key Words: Malignant biliary obstruction, Open biliary bypass, Perioperative outcomes.

1. Introduction

1.1. Background of the study

Malignant tumors of the biliary tree, the pancreas, and the periampullary region frequently obstruct the bile duct, which can result in crippling symptoms and raise the risk of eventual surgery. The causes of Malignant Biliary Obstruction (MBO) can be divided into intrahepatic and extrahepatic depending on where the obstruction is located. Some of the pathologies that cause intrahepatic blockage of the bile duct are intrahepatic cholangiocarcinoma (ICC) and hepatocellular cancer (HCC). Extrahepatic biliary obstruction can be caused by several different conditions, including hilar and distal cholangiocarcinomas, gallbladder, periampullary, duodenal, and pancreatic head tumors.

Even though BTC are still uncommon, their detections are becoming more frequent. It is unclear if this is a true indication of an increase in incidence or a result of more accurate techniques for biliary tree imaging in obstructive jaundice [1]. Annually, 7500 new cases of biliary tract cancers (BTC) are identified in the US; 5000 of these cases are gallbladder cancers (GBCA), while another 2000–3000 cases are bile duct cancers [2]. According to estimates from the global cancer observatory (GLOBOCAN), there were 5,454 (0.49%) new cases of GC in Africa in 2020. 4,249 people were estimated to have died from GC in the same year, making up 0.60% of all cancer-related deaths. Based on data from the Addis Ababa Cancer Registry, GLOBOCAN estimated that in 2020, there were 370 (0.48%) new cases of GC and 338 (0.65%) deaths from GC [3].

Considering these dismal statistics, the goal with early-stage disease is to move promptly to therapy, specifically to reach surgical resection, as this is the only treatment option that offers a possibility of recovery (A). However, most of the cases are incurable at diagnosis and is handled in a palliative manner. Palliative therapy, in contrast, places a strong emphasis on symptom relief and delaying the progression of the disease. Typically, the first step in this procedure is to remove the obstruction and get the serum bilirubin level back to normal [4].

Although initial surgical bypass results showing low rates of recurrent jaundice (2–5%), the procedure itself has a sizable risk of postoperative morbidity and mortality, up to 24%

in certain trials [5]. Recently, several high-volume hospitals reported noticeably lower death rates, as low as 1-2 percent. On the other hand, perioperative morbidity is still a common occurrence [6]. This study will try to highlight on the outcomes of patients who underwent open biliary bypass for MBO, and the factors associated with poor perioperative outcome in a low resource setting.

1.2. Statement of the problem

Failure of detection of tumors at an early stage makes management of MBO difficult. Despite notable advancements in diagnostic techniques, only 20% of individuals with MBO were discovered to have a resectable tumor at presentation because of their invasiveness and delayed symptom onset. The management approaches for patients with MBO are primarily based on whether the mass is amenable to surgical resection or not. Pancreatoduodenectomy is the primary therapy option for distal MBO that can be surgically removed, whereas surgical palliative biliary bypass and percutaneous or endoscopic stenting are the primary alternatives for MBO that cannot be surgically removed. Both curative and palliative surgical techniques have been associated with a considerable risk of perioperative morbidity and mortality. Several high-volume centers recently reported considerably lower mortality rates, as low as 1% to 2%. This was accomplished by identifying variables associated with poor perioperative outcomes. However, postoperative morbidity is still a common occurrence [6].

Finding high-risk patients is the first step in developing specific interventions to optimize perioperative outcomes. High-level evidence is required to identify preoperative risk factors and customize therapies to minimize unfavorable perioperative outcomes, which is scarce throughout Ethiopia and Africa in general. The low prevalence of biliary tract malignancies, the paucity of high-level evidence generated by the few surgically handled cases, the heterogeneity of surgical techniques, and the lack of experience in managing such patients make this effort difficult.

1.3. Significance of the study

Measurement of clinically relevant outcomes provides healthcare practitioners with the knowledge they need to enhance their practice and decision-making by improving preoperative evaluation, optimization, and patient and operation selection. The study will give insights into the perioperative outcomes and associated variables for patients who received palliative biliary bypass at several hospitals in Addis Ababa, Ethiopia. Additionally, the analysis that is offered in this study aims to close any knowledge gaps and provide useful data for MBO research that will be conducted in the future.

2. Literature Review

Jaundice can be caused by pre-hepatic, intra-hepatic, or post-hepatic pathologies. A serum bilirubin level in adults normally is less than 1 mg/dL (17micromole/liter). A comprehensive clinical examination, however, cannot detect jaundice unless the serum bilirubin is twice the upper normal limit or greater than 2 mg/dL (34micromole/liter) [7]. Post-hepatic jaundice, often referred to as obstructive jaundice, is defined by a partial or complete obstruction of the biliary duct between the liver and duodenum, which limits the flow of bile. The majority of this hyperbilirubinemia is conjugated [8].

According to a recent estimate from North American Surveillance, Epidemiology, and End Results (SEER) database the frequency of pancreaticobiliary cancers are increasing. In 2019, there were an estimated 89,248 people living with pancreatic cancer in the United States. According to the same estimate, gallbladder cancer, the most common extra-hepatic biliary tree malignancy, was projected to have 12,778 cases in 2019 [9].

According to a Tanzanian study on the etiology and outcome of OJ, out of 116 patients, 58.6% had MBO, with pancreatic head carcinoma being the most common tumor in the malignant group followed by extrahepatic cholangiocarcinoma and gallbladder cancer. Male to female ratios of 1:1.4 were seen, indicating that MBO was more common in women. The mean age of patients with malignant causes was 58.64 ± 24.14 years (range 44-78 years) [10]. Another study from Nigeria indicated that 76% of cases of obstructive

jaundice had a malignant origin, with pancreatic head tumors were the most common. All the patients had advanced disease, and the causes of the cancer were readily apparent. They all underwent bypass surgery and/or had biopsies, but none of them had a curative resection [11].

According to a study done in Ethiopia, MBO was the major cause in 31.9% of cases of extrahepatic biliary tract obstruction. The study found that 32.4% and 29.7% of the MBO patients were in their sixth and seventh decades of life respectively. In contrast to earlier investigations, 70% of the patients with MBO in this study were male. According to the same study, duodenal adenocarcinoma and distal cholangiocarcinoma accounted for 24.3% and 8.1%, respectively, of all MBO causes, while pancreatic head tumor accounted for 51.4% of all MBO causes. In this study, a palliative cholecystojejunostomy with Braun's anastomosis was performed on 60% of MBO patients [12].

A study of the literature indicates that several pre-operative factors do increase the risk of mortality in persons with MBO. Age 50, an increasing ASA class, low levels of blood albumin, jaundice, ascites, and coexisting comorbidities like DM, COPD, heart failure, and hypertension are a few of them. Age has been shown to be an accurate predictor of mortality, increasing steadily for each decade after age 50. Although postoperative complications, length of postoperative hospital stay, and 30-day mortality were similar in those under and over 75, the older adult group had a higher postoperative ICU admission rate [13]. Other factors that have a substantial impact on survival include pain, the presence of metastasis, and the levels of leukocytes, CRP, CEA, and CA19-9 [14].

According to multiple studies, a higher ASA class has been linked to higher rates of morbidity and mortality for a variety of surgical procedures, including palliative biliary bypasses for MBO [15]. Low albumin levels (<3.5 g/dl) in MBO patients may be a secondary symptom of cancer-related cachexia or long-term poor nutritional status. Palliative biliary bypass procedures for MBO in patients with hypoalbuminemia are associated with higher postoperative morbidity and mortality rates. Ascites was also found to be related to less desirable outcomes. This is most likely a result of overall nutritional deficiencies and poor liver function [16].

Long operative time, organ space infection, pneumonia, septic shock, unplanned intubation, renal failure, and myocardial infarction were among the perioperative and postoperative factors that increase the chance of mortality. In several investigations, the mortality rate following operative procedures ranged from 3% to 10% [6]. Studies have suggested that the duration of the procedure is a factor that is associated with increased postoperative mortality. Inadequate experience, technical problems, and intraoperative complications are only a few of the many factors prolonging the procedure [17].

The need for intraoperative transfusion and the amount of intraoperative blood loss were other independent risk factors found to be associated with high morbidity and mortality rates. Blood transfusions are known to have immunosuppressive effect that may affect wound healing, cancer metastases and recurrence. (18)

Other complication that are common with operative interventions for MBO included stroke, deep venous thrombosis, sepsis, superficial surgical site infection, deep surgical site infection, organ/space surgical site infection, pneumonia, pulmonary embolism, progressive renal insufficiency and acute renal failure. (19)

3. Objective

3.1. General Objective

- ✓ To assess incidence and factors associated with poor perioperative outcome in patients with MBO who are managed with palliative open biliary bypass at selected Hospitals, Ethiopia from Sep to Feb 2023.

3.2. Specific Objectives

- ✓ To assess the clinical pattern of patients admitted for surgical management of MBO.
- ✓ To assess the incidence of poor perioperative outcome following palliative biliary bypass for MBO.
- ✓ To identify factors associated with adverse perioperative outcome in patients who undergo palliative biliary bypass for MBO.

4. Material and Methods

4.1. Study design, period, and setting.

This multi-centre prospective cohort study was conducted at six tertiary hospitals (Tikur Anbessa, Yekatit-12, Menelik II, Addis Hiwot, Lancet, and Amin General Hospitals) in Addis Ababa, Ethiopia. The study was carried out between June 2022 and May 2023. All patients who were hospitalized in the surgical departments of the hospitals and underwent open biliary bypass during the study period were sequentially recruited into the study.

4.2. Eligibility

All adults (age > 18) who underwent open surgical bypass at the mentioned hospitals during the study period were included. The study excluded patients who refused to give consent to participate.

4.3. Study procedure and follow-up.

All the surgical bypass procedures were done by hepatobiliary surgery fellows and experienced hepatobiliary surgeons. Baseline data were collected from each patient at the time of admission for surgery, including patient characteristics, age, gender, history of weight loss, comorbidity, Eastern Cooperative Oncology Group (ECOG) performance status [18], and American Society of Anesthesiologists (ASA) physical status [19]. Follow-up visits were done at the discretion of the operating surgeon, and every three days, telephone interviews were done after discharge to look for the outcome of interest.

4.4. Outcome measures

The primary outcome measure was the presence of 30-day morbidity and mortality, which was measured according to Clavien-Dindo grading [20].

4.5. Statistical analysis

The statistical analysis was carried out using STATA software version 14.2. Descriptive statistics were computed, utilising the mean and standard deviation for normally distributed data, while the median with Inter Quartile Range (IQR) was used for non-normally distributed data. Kaplan-Meier curve analysis and the log-rank test were performed for each independent variable. A Cox regression analysis was conducted to assess the association

between the independent and outcome variables, and statistical significance was determined at a significance level of $p < 0.05$. The association was quantified using Hazard Ratio (HR) along with its corresponding confidence interval. Lastly, the final parsimonious model was constructed using the stepwise backward elimination method.

4.6. Ethical consideration

The study was conducted in the Department of General Surgery's Hepatopancreaticobiliary Division with approval from the Addis Ababa University Institutional Review Board. All study participants gave written informed consent.

5. Results

Between June 2022 and May 2023, 69 patients with malignant biliary obstruction underwent palliative open biliary bypass at three private and three public tertiary care hospitals in Addis Ababa, Ethiopia. The mean (\pm SD) age at surgery was 55.13 years (\pm 13.98). Among the study participants 38 (55.07%) were male and 31 (44.92%) were female. Comorbidities were present among 20 (28.98%) of the study's participants. The most frequent comorbidities were hypertension (HTN) and diabetes mellitus (DM), which were reported in 9 (13.04%) and 8 (11.59%) patients, respectively. Based on the American Society of Anesthesiologists (ASA) physical state classification, 60 (86.96%) patients were classified as class-1, 7 (10.14%) patients as class-2, and 2 (2.89) patients as class -3. According to the Eastern Cooperative Oncology Group (ECOG) performance status grading, 45 patients (65.22%) had a performance status of 0 and 24 (34.78%) had a performance status of 1. (Table 1)

The leading cause of malignant biliary obstruction was pancreatic head mass, accounting for 38 (55.07%) cases. The second common preoperative diagnosis was periampullary mass, accounting for 17 (24.64%) cases. Nineteen (27.5%) patients in this cohort were diagnosed with preoperative cholangitis and were admitted for intravenous antibiotics prior to their bypass surgery. Except for one patient, all the study participants had yellowish discolouration of the eyes. Among the patients, 56 (81.2%) experienced abdominal pain, 43 (62.3%) weight loss, and 30 (43.5%) suffered appetite loss. Thirty-seven (53.6%) patients noticed a change in the colour of their urine, and 24 (34.8%) patients reported a change in the colour of their stool. Thirty-five (50.7%) patients complained of having

pruritus. Nineteen (27.5%) patients reported Gastric Outlet Obstruction (GOO) symptoms, such as vomiting and early satiety. (Table 1)

Variables		Frequency	Percentage
Sex	Male	38	55.07
	Female	31	44.92
Comorbidity	Hypertension	9	13.04
	Diabetes Mellitus	8	11.59
	Heart disease	2	2.89
	Asthma	1	1.44
American Society of Anesthesiologists (ASA)	Class 1	7	10.14
	Class 2	60	86.95
	Class 3	2	2.89
Eastern Cooperative Oncology Group (ECOG) performance status	Grade 0	45	65.21
	Grade 1	24	34.78
Preoperative cholangitis	Yes	19	27.53
	No	50	72.46
Preoperative diagnosis	Pancreatic head mass	38	55.07
	Periampullary mass	17	24.64
	Hilar cholangiocarcinoma	6	8.70
	Gallbladder cancer	4	5.80
	Distal Cholangiocarcinoma	3	4.35
	Pyloroduodenal mass	1	1.45

Table 1: Characteristics of patients who had open biliary bypass for malignant biliary obstruction (n= 69)

At admission, a complete blood count, bilirubin, albumin, the International Normalisation Ratio (INR), and creatinine were all measured as baseline laboratory tests. Only 12 (17.39%) patients had their Carbohydrate Antigen (CA) 19-9 levels determined. At presentation, the median (IQR) total bilirubin level was 15.5 mg/dl (7.2–21.4 mg/dl); the median (IQR) direct bilirubin level was 8.6 mg/dl (4.5–13.1 mg/dl); and the median (IQR) level of Alkaline Phosphatase (ALP) was 712 U/L (493–1008 U/L). Forty-five (65.22%) of the study's participants had hypoalbuminemia, and among those, eight had severe hypoalbuminemia. Among the study participants, 10 (14.49%) had preoperative INR > 1.5 and 3 (4.30%) had creatinine > 1.2 mg/dL. White Blood Cell (WBC) count was found to be < 4000/ μ l in 4 (5.80%) and > 11,000/ μ l in 13 (18.84%) patients.

Out of the total patients, the initial intent of surgery was palliative in 61 (88.41%) and was curative in the remaining patients. Only 2 (2.89%) patients received preoperative biliary stenting. The most commonly performed procedure to bypass biliary obstruction was Roux-en-Y Hepaticojejunostomy. This was followed by cholecystojejunostomy with Braun's anastomosis, performed on 29 (42.02%) patients. Gastric bypass surgery was performed on 49 (71.01%) patients. Among those who underwent gastric bypass, 31 (63.27%) received gastrojejunostomy to address established gastric outlet obstruction (GOO), while 18 (36.73%) patients underwent the procedure as a prophylactic measure. Segment III bypass was performed on 8 (11.59%) patients, and only two (2.89%) patients had undergone endoscopic stenting prior to surgery. (Table 2)

Variables		Frequency	Percentage
Initial intent of surgery	Palliative	61	88.41
	Curative	8	11.59
Type of procedure	Roux-en-Y Hepaticojejunostomy with gastrojejunostomy	23	33.33
	Roux-en-Y Hepaticojejunostomy	9	13.04
	Cholecystojejunostomy with Braun anastomosis + gastrojejunostomy	26	37.70
	Cholecystojejunostomy with Braun anastomosis	3	4.34
	Segment III bypass	8	11.59
Gastrojejunostomy *	For established GOO	31	63.27
	For prophylaxis	18	36.73

Table 2: Distribution of palliative surgical procedure performed (n=69). * The total number of patients who underwent gastrojejunostomy was 49.

The most common reason for inoperability was locally advanced disease, which was found among 61 (88.40%) patients. Five (7.24%) patients underwent palliation as they were deemed unfit for definitive surgery due to their significant hypoalbuminemia. Additional features of inoperability: ascites: 22 (31.88%), lymph node involvement: 21 (30.43%), liver nodules: 13 (18.84%), and peritoneal disease: 3 (4.34%) were documented. Tissue biopsies were taken from 25 patients (36.20%); six were from lymph nodes, six were from gallbladder masses, five were from liver nodules, five were from pancreatic masses, and three were from peritoneal nodules. Only 2 (2.89%) patients needed intraoperative transfusions. The length of the procedure ranged (IQR) from 120 minutes to 180 minutes, with a median of 150 minutes.

There were 28 perioperative complications in 23 (33.3%) patients, defined as Clavien Dindo class ≥ 2 , and the overall time at risk was 488 days. Among the study participants, the incidence rate of perioperative complications was 4.7. Five (7.24%) of the study participants had unplanned postoperative ICU admissions, and all died within 30 days following surgery. Of the five perioperative deaths, one happened after a hepaticojejunostomy, two after a cholecystojejunostomy, and two after a segment three bypass. Two (2.90%) patients suffered an anastomotic leak, one from a gastrojejunostomy and the other from a biliary anastomosis. The median (IQR) postoperative hospital stay was nine days (7-11 days). (Table 3)

Postoperative Complications		Percentage
Hospital acquired pneumonia	3	4.35
Wound infection	3	4.35
Acute kidney injury/renal insufficiency	3	4.35
Gastrointestinal bleeding	2	2.90
Sepsis	2	2.90
Leak from biliary anastomosis	1	1.45
Leak from gastrojejunostomy	1	1.45
Intra-abdominal collection	2	2.90
Urinary tract infection	1	1.45
Unplanned ICU admission	5	7.25
Death	5	7.25

Table 3: Proportion of postoperative complication among patients who had biliary bypass for malignant biliary bypass (n= 69)

In the Kaplan-Meier curve analysis, a statistically significant difference was observed in the perioperative outcome between patients who experienced perioperative cholangitis and those who did not (Figure 1). Cox regression analysis was conducted for every presumed variable, and three variables were found to be statistically significant. The hazard of developing complications among those with preoperative cholangitis was 2.49 times higher than those without cholangitis (HR 2.49, 95% CI [1.06, 5.84]). For every hour increment in the length of surgery, the hazard of getting a complication increases by 2.47 times (HR 2.47, 95% CI [1.28, 4.77]). As the value of bilirubin increases by 1 mg/dl, the hazard of developing complications increases by 14% (HR 1.14, 95% CI [1.03, 1.17]). (Table 4)

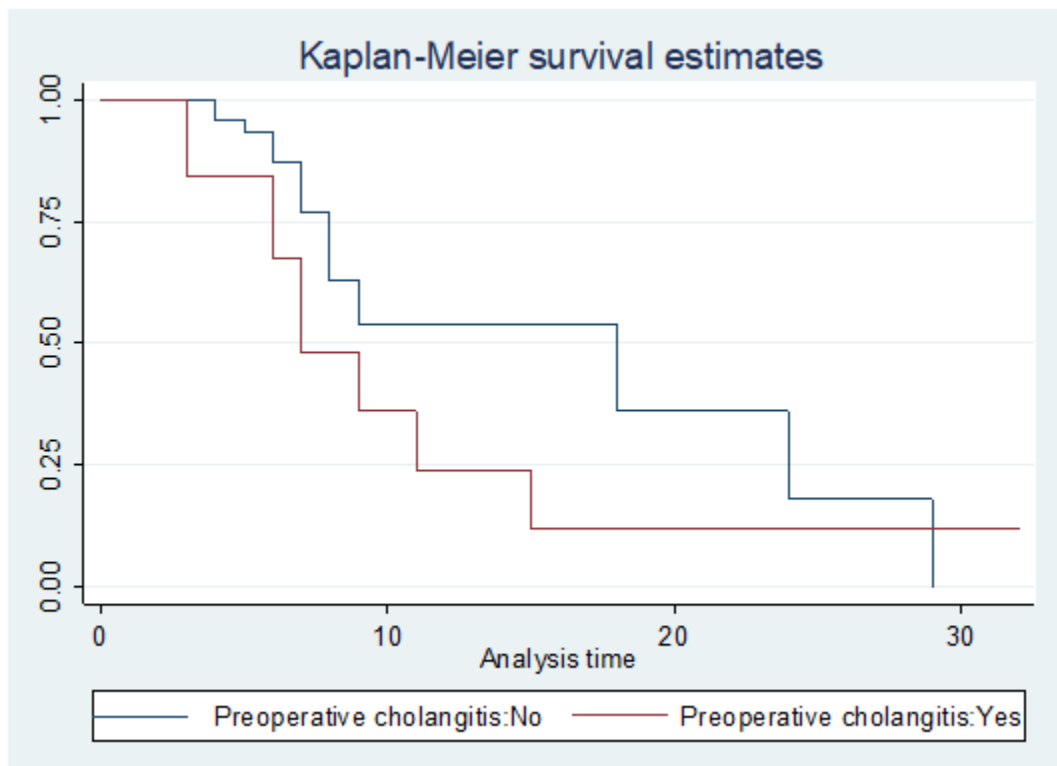


Figure 1: Kaplan-Meier survival estimates of perioperative outcomes after open biliary bypass for patients with malignant biliary obstruction with reference to cholangitis.

Variables	Hazard Ratio (HR)	[95% Confidence Interval]	p-value
Preoperative Cholangitis	2.49	[1.06, 5.84]	0.035
Length of the Procedure	2.47	[1.28, 4.77]	0.007
Total Bilirubin	1.14	[1.03, 1.17]	0.048

Table 4: Multivariable cox regression analysis of factors associated with time to complication development among patients who had open biliary bypass for malignant biliary obstruction.

6. Discussion

Palliation of malignant biliary obstruction by surgery, endoscopy, or percutaneous method is required in patients who presented with obstructive jaundice due to an inoperable malignancy or in those whose malignancy was discovered to be unresectable during surgical exploration [21]. Because both endoscopic and percutaneous treatment modalities are mostly scarce in a resource-limited setting, open biliary bypass is the surgical procedure that is most frequently used to palliate malignant biliary obstruction [22]. Despite being the most widely used operation to relieve malignant biliary obstruction in low-resource settings, its short- and long-term postoperative outcomes are poorly investigated. We prospectively evaluated the perioperative outcomes in a cohort of patients with malignant biliary obstruction who underwent palliative biliary bypass.

The mean age of patients with malignant biliary obstruction in our study was 55.13 years (± 13.98), which is lower than most global reports [23, 24]. Consistent with other studies [24, 25], our study has a slight male predominance. As with most regional and international studies, our study also shows that the most common cause of malignant biliary obstruction is pancreatic adenocarcinoma, followed by periampullary tumours accounting for 55.07% and 24.64% of the cases, respectively [22, 26, 27]. In our study, Roux-en-Y Hepaticojejunostomy was performed the most to palliate jaundice, followed by cholecystojejunostomy with Braun's anastomosis. In most literature, the most frequently used procedures to palliate distal obstructions are cholecystojejunostomy and hepaticojejunostomy, which have been replaced by endoscopic and percutaneous procedures in recent years [28, 29].

In our cohort, 31 patients presented with established Gastric Outlet Obstruction (GOO) and underwent gastrojejunostomy. The presence of GOO at presentation was not significantly associated with a poor perioperative outcome in our study. In other studies, advanced pancreatico-biliary malignancies that result in GOO are associated with a reduced length of survival [30]. This may be the case, as other studies, in contrast to our investigation, have examined the long-term effects of GOO on survival. Another 18 patients underwent a gastrojejunostomy for prophylactic treatment. In 1999, the Johns Hopkins group conducted a randomised controlled trial and found that prophylactic gastrojejunostomy significantly lowers the incidence of late gastric outlet obstruction [31]. In one Cochrane review, the proportion of patients who developed long-term gastric outlet obstruction was significantly lower in the prophylactic gastrojejunostomy group compared with no gastrojejunostomy group. However, there was no evidence of a difference in overall survival, perioperative mortality or morbidity, quality of life, or hospital stay [32]. Previously, there were disagreements regarding the role of prophylactic gastrojejunostomy during biliary bypass surgery [33, 34]. However, prophylactic gastrojejunostomy has been recommended by recent prospective multicentre studies as well as systematic Cochrane reviews [32, 35-37].

The main finding of this study was the association between preoperative cholangitis, higher bilirubin levels, and longer operation times with adverse perioperative outcomes. The existence of preoperative cholangitis was found to be one of the significant factors for the development of poor perioperative outcomes. This finding was supported by a recent study from Massachusetts General Hospital, which shows a significant difference in the primary outcome of two-year all-cause mortality from the time of pancreaticoduodenectomy between cholangitis and no cholangitis comparison arms [38].

In this study, time to develop poor perioperative outcomes was found to be statistically associated with increasing total bilirubin levels. In alignment with our study, in a pooled analysis of 291 patients, Kullmann F. et al. observed that increased bilirubin had a significant association with lower overall survival [39]. Contrary to our finding, in a retrospective cohort study of 304 patients with pancreatic head mass who underwent pancreaticoduodenectomy in Turkey, the level of bilirubin did not substantially correlate with a poor postoperative outcome [40]. This could be because of the differences in the primary outcome of interest and the nature of the varied study approaches. Furthermore,

comparing our findings was challenging because most outcome studies were carried out after definitive treatment rather than palliative surgery.

Out of the 69 patients in our study, 5 (7.24%) died, which is greater than most reports from high-volume centres. In most of the literature, mortality following open biliary bypass ranged from 0-7% [14, 28]. All the patients who died had unplanned admissions to the ICU. This may be because there are inadequate rescue mechanisms in our institutions when major complications arise. According to our data, two individuals experienced anastomotic leaks, and another two experienced intra-abdominal collections following the surgery. Patients with acute abdominal pain must be carefully and promptly evaluated for intra-abdominal complications such as anastomotic leaks and collections in the early postoperative days following open surgical biliary bypass [41].

7. Limitations

Even though the study was conducted using a prospective design, there are some limitations that need to be addressed. The heterogeneous nature of the disease and the procedure make it difficult to compare outcomes. Important laboratory variables, such as the Carcinoma Embryonic Antigen (CEA) and CA 19-9, were not identified since they were not frequently determined in our group. These variables might have had a relationship with the study's primary outcome.

8. Conclusion

Selecting patients for open biliary bypass based on rigorous criteria is usually difficult in a resource-constrained situation where there are few endoscopic and minimally invasive approaches to managing malignant biliary obstruction. Surgeons in low-resource settings should develop a consensus guideline to improve perioperative outcomes through effective patient selection and preoperative optimisation in high-risk patients. According to our research, it is vital to consider the hazards of preoperative cholangitis and elevated bilirubin levels when considering open biliary bypass in patients with malignant biliary obstruction. The fact that every patient admitted to the ICU died in our study might demonstrate the failure to rescue, which is the occurrence of death following a severe but theoretically avoidable complication. The failure-to-rescue rate should, therefore, be reduced by strengthening the capacity of high dependency and intensive care units of hospitals in resource-limited settings.

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