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Research

Morbidity and Mortality of Major Hepatectomies in A Resource-Limited Country

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1. Abstract

1.1. Introduction

A major hepatectomy is defined as the resection of at least three liver segments. Most often carried out as part of the treatment of a malignant liver tumor, it still causes significant morbidity and mortality.

1.2. Objective

To report the morbidity and survival of patients who underwent major hepatectomy in the hepatobiliary surgery unit of the Tengandogo University Hospital Center.

1.3. Methods

A retrospective study was conducted over 83 months. Data of interest including patient epidemiology, diagnostics, type of surgery, postoperative outcomes and prognostic factors were studied.

1.4. Results

Major hepatectomies were carried out in 38 patients, 27 of whom were male. There was an annual average of 4.75 major hepatectomies, representing 64.4% of liver resections performed. Major hepatectomy was performed in 28 patients (73.6%) for hepatocellular carcinoma. With respect to laterality, the procedure was a right hepatectomy in 30 patients (79%). Complications were noted in 36.8% of cases. Overall survival was 39.4% with a mean survival time of 19.2 months. Ten patients (26.3%) died within 90 days. The factors influencing survival were tumor size ≥ 15 cm ($p = 0.0023$), operating time ≥ five hours ($p = 0.0011$), a Child-Pugh B score ($p = 0.0113$) and AFP ≥ 200 ng/ml ($p= 0.0206$). Conclusion: Due to delays to diagnosis, major hepatectomy is relatively common in Burkina Faso. Improving diagnostic tools and algorithms, strengthening the technical platform and training surgical teams could help improve patient outcomes. Major hepatectomy remains a challenge, which resource-limited countries can perform provided there is rigorous selection and postoperative monitoring of patients.

2. Introduction

Major hepatectomy consists of resection of at least three liver segments [1]. It has evolved considerably since the first resection carried out in 1952 [2,3]. This development was based on increasingly precise indications. Indeed, the contribution of medical imaging has been immense, particularly with new high-performance modalities such as computed tomography (CT), magnetic resonance imaging (MRI) and positron emission tomography (PET) scan. Furthermore, the advent of artificial intelligence has opened up the possibility of preoperative reconstruction and the development of interventional radiology provides an indispensable complement to surgical procedures [2]. Surgical care has also benefited from performance improvement and strengthening of equipment both in surgery and in intensive care [4,5]. All these advances make it possible to operate on a larger number of patients who have recently been deemed inoperable by performing major hepatectomies or extended hepatectomies involving more than three segments. In Europe the mortality of major hepatectomies is less than 10.4% with morbidity rates of 29% [6-8]. The dominant causes of morbidity include hemorrhage, bile leaks and liver failure which occurs when the volume and/or quality of the remaining parenchyma is insufficient for essential metabolic functions [4]. Despite this significant morbidity and mortality, overall survival after major hepatectomy was 90% at 1 year, 67% at 3 years and 48% at 5 years in expert liver surgery centers in France and Germany in 2020 [9,10]. Studies have identified poor prognostic factors including high

Child-Pugh score, alpha-fetoprotein level and tumor size, as well as long intra-operative times and the type of intervention [11,12]. In Burkina Faso, liver surgery has been common practice since 2015 and major hepatectomies are increasingly being performed in the country. The aim of our study was to report the morbidity and mortality of patients after major hepatectomy in the hepato-bilio-pancreatic surgery unit of the Tengandogo University Hospital. The findings of this analysis could inform targeted interventions to improve performance and patient outcomes following major hepatectomy.

3. Methods

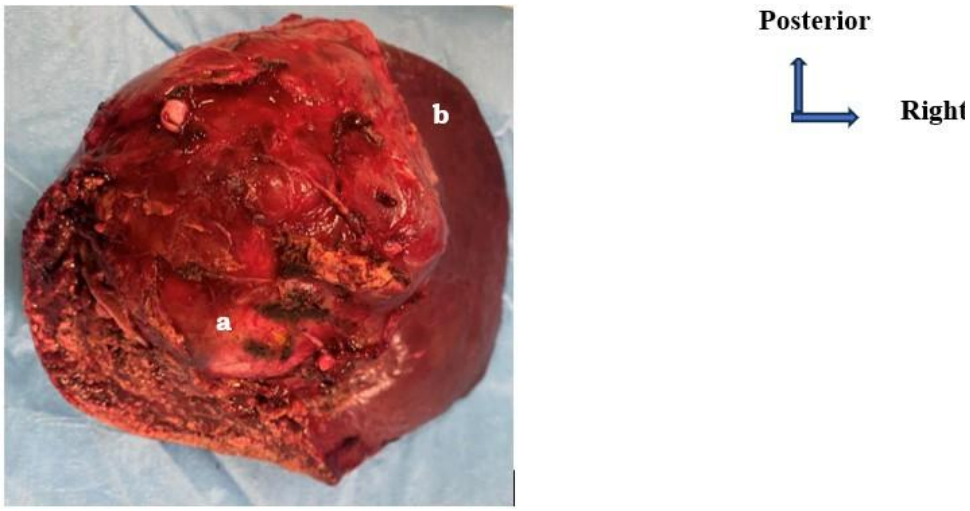
The authors conduced a retrospective cohort study with descriptive and analytical aims. Data collection was retrospective over a period of eight years from January 1, 2015 to December 31, 2022. The study population consisted of all patients treated in the hepatobiliary and pancreatic surgery unit of the Tengandogo University Hospital Center. This hospital is one of the 4 university hospitals in the capital of Burkina Faso (Ouagadougou). It has a capacity of 600 beds. Thirty-eight patients who underwent major hepatectomy were included. The parameters studied were age, sex, date of diagnosis, location of the tumor, size of the tumor, histological type, Child-Pugh classification, procedure performed, post-operative outcomes, and factors associated with morbidity and mortality. The data collected were entered and processed using Epi Info software version 7.2.2.6 then exported to SPSS software for analysis according to the themes previously defined. Variables were described using the mean and survival was estimated by the Kaplan Meier method. For the analysis, a Cox model was used to determine the factors in univariate analysis. Thus, the variables associated with death in univariate analysis with a significance level less than 0.20 were included in the multivariate model. In multivariate analysis, associated variables with a significance level less than 0.05 were taken into account in the final model.

4. Results

Over the eight-year period, 759 cases of liver tumors were evaluated in hepato-biliary and pancreatic surgery consultations. Liver resection was performed in 59 patients (8%). A major hepatectomy was indicated and performed in 38 cases (64.4%). The average age of the patients was 48.7 ± 13.2 years with extremes of nine and 69 years. There were 27 male subjects (71%) and the sex ratio was 2.45. Chief complaints for the initial consultation included pain in the right hypochondrium in 20 cases (52.6%), an abdominal mass in 10 cases (26.3%) and epigastric pain in three cases (7.9%). Five patients had been referred for a liver nodule discovered incidentally as part of follow-up for hepatitis virus infection (13.1%). Twenty-six (26) patients (68.4%) had cirrhosis of viral origin. Of these, viral hepatitis B was identified in 20 cases (77%), viral hepatitis C in four cases and co-infection with hepatitis B and C in two cases. There was a history of colon cancer in two (2) cases. The diagnosis of liver tumor was made for 36 patients (95%) based on imaging and alpha-fetoprotein levels. In three cases (5%) a liver biopsy was performed. The average size of the tumors on preoperative imaging (CT and MRI) was 14.3 cm with extremes of three and 20 cm. The tumor was located in the right liver in 30 patients (79%) and in the left liver in five patients (13%). The location was central in three patients (8%). Right hepatectomy was performed in 30 patients (78.9%). Four patients underwent primerly a portal vein right branch surgical ligation. Table I illustrates the different types of hepatectomies performed. Figures 1 and 2 illustrates an operative view and the surgical specimen of a right hepatectomy. Intraoperative complications included injuries of the inferior vena cava in three patients (8%) and right hepatic vein in two patients (5%). These vascular injuries were repaired immediately using a 5/0 non-absorbable suture. A histological examination of the surgical specimen was carried out in all cases. The histological type of tumors is summarized in Table II. Figure 3, 4 and 5 illustrate a histological section of a Hepatocellular carcinoma found in 73.6% of cases. Postoperative complications occurred in 14 patients (36.8%), including liver failure in six patients (42.7%), bile leak in three patients (21.4%), post-operative hemorrhage in three patients (21.4%) and pleural effusion in two patients (14.2%). Intraoperative blood transfusion was performed in 30 patients (79%). Ten patients died within 90 days of major hepatectomy. The mortality rate was 26.3%. The average survival time was 19.2 months with extremes of 4 days and 80 months. The 1-year, 3-year, and 5-year survival rate was respectively; 60.9, 35.5 and 35.5%. Fifteen patients survived after major liver resection. Overall survival was 39.5%. Survivals at one, three and five years are illustrated in Figures 6a, 6b and 6c respectively. In univariate analysis, the statistically significant factors linked to mortality were a tumor size ≥ 15 cm ($p = 0.0023$), operative time ≥ 5 hours ($p = 0.0011$), a Child-Pugh B score ($p = 0.0113$) and an AFP level ≥ 200 ng/ml ($p=0.0263$). Table III summarizes the relationship between mortality and risk factors.

In multivariate analysis, there were no statistically significant associations between Child-Pugh B score ($p=0.0642$), AFP level ($p=0.2539$) and death. However, a statistically significant association was found between tumor size and mortality ($p=0.0430$).

Figure 1: Operative view after right hepatectomy
1a. Remaining left liver
.1b. Right hepatectomy compartment with drain



.**Figure 2**: Inferior view of operative specimen of right hepatectomy
2a. Tumor
2b. Healthy liver

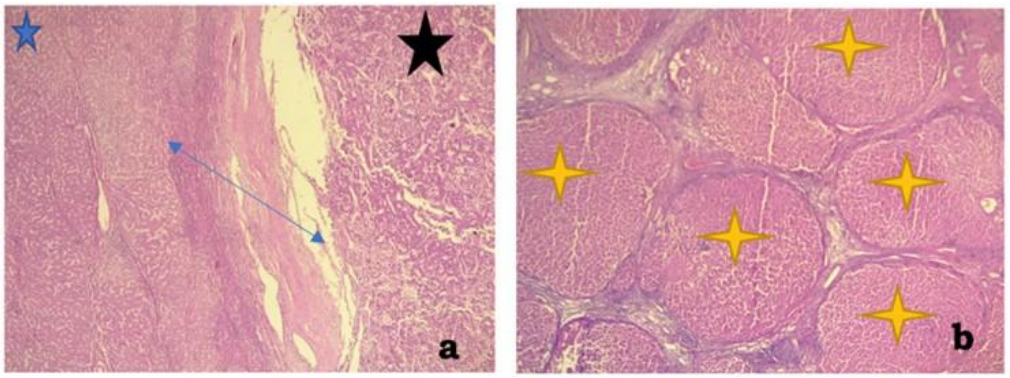


Figure 3: Histological section of a hepatocellular carcinoma and Histological sample stained with hematein-eosin (magnification 10x).
3a. Tumor proliferation (black star) circumscribed by a fibrous capsule (blue arrow) is observed, separating it from the non-tumorous liver parenchyma (small blue star).
3b. Non-tumorous liver parenchyma composed of cirrhotic nodules (yellow stars).

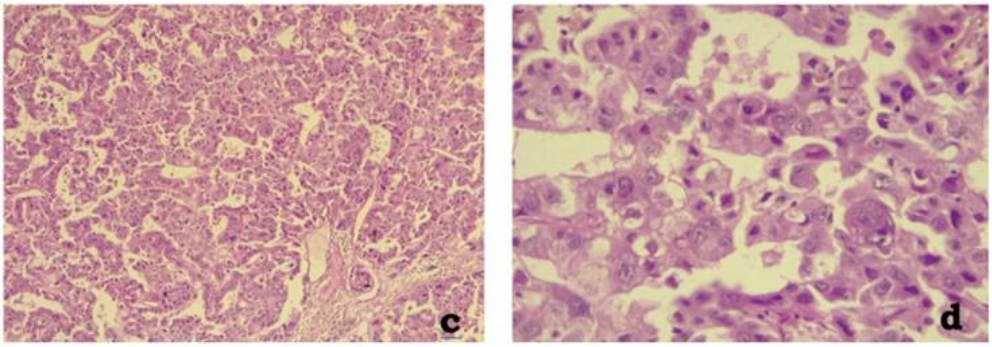


Figure 4: Histological sample stained with hematein-eosin showing tumor proliferation, made of sections of several rows of cells sometimes conjoined.

4c. Magnification 100x

4d. Magnification 400x

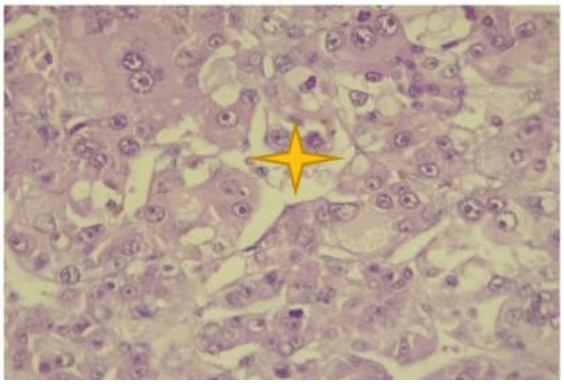
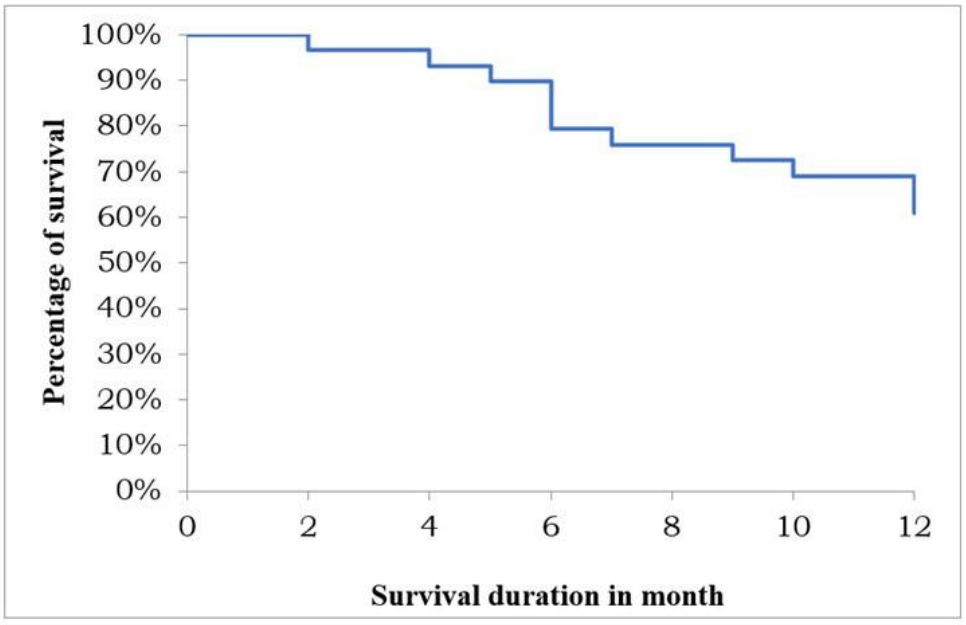


Figure 5: Histological sample stained with hematein-eosin (magnification 400x) showing cellular details. Large cells with slightly eosinophilic cytoplasm. The nuclei are large, with irregular contours and a central nucleolus. There are intranuclear vacuoles (yellow star).



.**Figure 6a**: One-year Kaplan Meier survival curve

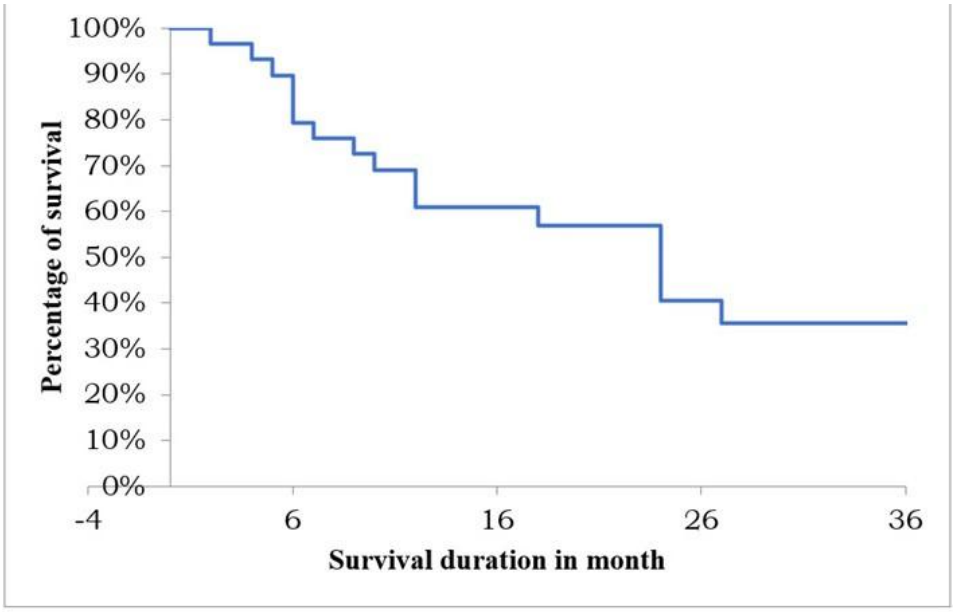


Figure 6b: Three-year Kaplan Meier survival curve.

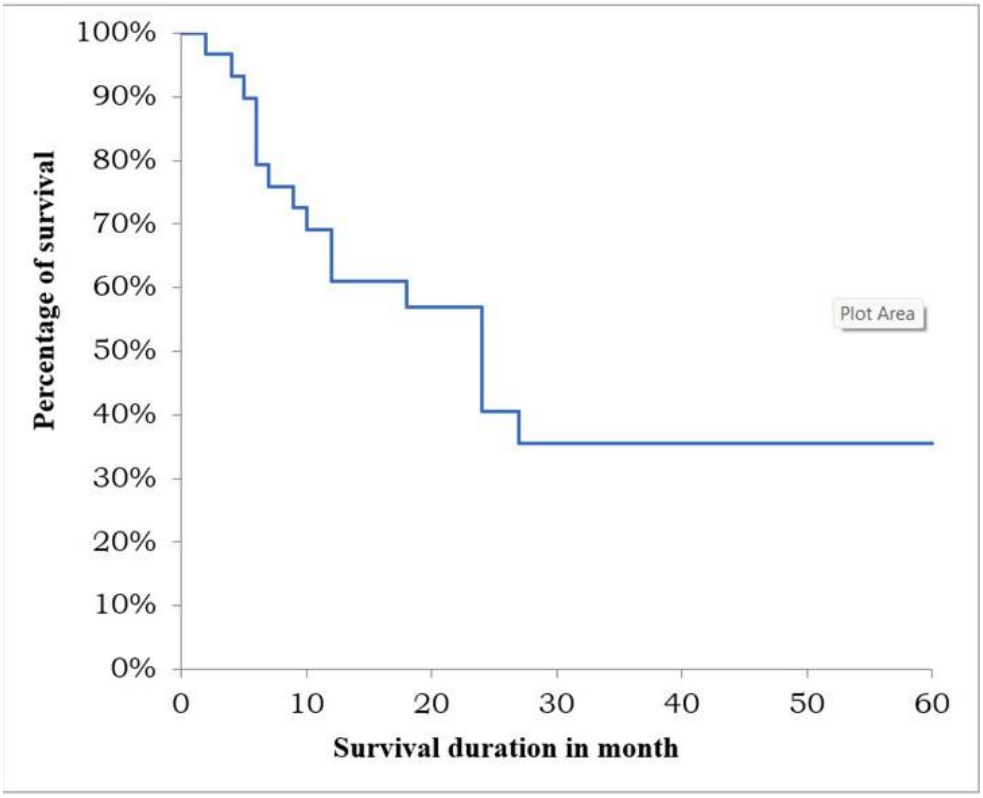


Figure 6c: Five-year Kaplan Meier survival curve.

Table I: Different types of interventions performed on our patients.

Types of hepatectomy	Frequency	(%)
Right hepatectomy	30	78.9
Left hepatectomy	4	10.5
Central hepatectomy	3	7.8
Extended Left hepatectomy	1	2.6
Total	38	100

Table II: Distribution of patients following diagnosis (n= 38).

Diagnosis	Frequency	(%)
Hepatocellular carcinoma	28	73.6
Hemangioma	5	13.1
Cholangiocarcinoma	2	5.2
Colorectal cancer metastasis	2	5.2
Stromal and epithelial tumor	1	2.6
Total	38	100

Table III: Mortality disaggregated by risk factors.

Risk factors	Mortality		RR [IC at 95%]	p value
	Yes (%)	No (%)		
Tumor size				
< 15 cm	3 (25.00)	9 (75.00)	1	
≥ 15 cm	18 (78.26)	5 (21.74)	0.29 [0.13-0.67]	0.0023
Duration of operation				
< 5 hours	17 (85.00)	3 (15.00)	1	
≥ 5 hours	6 (33.33)	12 (66.67)	0,23 [0.08-0.67]	0.0011
Child-Pugh Score				
A	12 (46.15)	14 (53.85)	1	
B	10 (90.91)	1 (9.09)	1.92 [1.77-45.71]	0.0113
AFP Level				
< 200 ng/mL	14 (50.00)	14 (50.00)	1	
≥ 200 ng/mL	9 (90.00)	1 (10.00)	0.20 [0.05-0.84]	0.0263
Albumin				
≥ 35 g/L	18 (54.55)	15 (45.45)	1	
< 35 g/L	5 (100.00)	0 (0.00)	-	0.0527

5. Discussion

Only 8% of liver tumors seen in consultation were resectable. Of these, a major hepatectomy was indicated in 64.4% of cases. In a nationwide analysis in Germany, Krautz C reported 57% of major hepatectomies [9]. In surgical practice in Burkina Faso, major hepatectomies are frequently indicated due to delays in diagnosis that result in large tumor size at time of presentation which make minor hepatectomies and parenchymal-sparing approaches difficult. Hepatocellular carcinoma was found in 73.6% of patients included in this analysis. According to Brustia R [15], major hepatectomies were performed in a single-center cohort study in France for liver metastases in 55.7% of cases, hepatocellular carcinoma in 17.5% of cases, and cholangiocarcinoma in 8.6% of cases. The predominance of hepatocellular carcinoma in the study setting is due to the fact that hepatitis B constitutes a pandemic disease in Burkina Faso and throughout the sub-Saharan zone. Tumors occurring in a cirrhotic liver caused by viral hepatitis B are most often asymptomatic. Based on guidelines for surveillance of patients with a known diagnosis of hepatitis, patients carrying the hepatitis B or C virus should be subject to regular monitoring to enable early detection of liver nodules. However, it must be recognized that there are difficulties in monitoring the disease and insufficient awareness among practitioners in Burkina Faso. Indeed, the majority of patients (60.5%) included in this analysis sought consultation at a late stage following symptom onset of abdominal pain. Unlike Chin KM in Singapore [16] who found an average tumor size of 7.5 cm, imaging (CT and MRI) in our series found an average tumor size of 14.31 cm which, in the case of resectable tumors, most often requires a major hepatectomy. The demographic profile of patients included in this analysis was composed predominantly of young subjects with an average age of 48.7 years. The same observation was made by other African authors who found an average age of 45 years [3,13]. With a generally young African population, and hepatitis B infection which remains a pandemic despite the introduction of vaccination programs against hepatitis B, maternal-fetal infections are still frequently observed which leads to early cirrhosis then to hepatocellular carcinoma around the age of 35. On the other hand, Kemper M [14] in Germany

and Chin KM [16] in Singapore reported a mean age of 64 and 59 years, respectively. Like Kemper M [14] in Germany who reported 73.6% right hepatectomies in their series of major hepatectomies, we performed 79% right hepatectomies. No clear and convincing explanation has been found for the predominance of liver lesions on the right. The experience acquired gradually due to the multiple training courses carried out by the members of our team in hospital Paul Brousse (France), has made it possible to have zero intraoperative mortality and prompt control of intraoperative complications despite the significant challenges of the procedure. However, in our study post-operative complications were observed in 14 patients, placing the morbidity rate at 36.8%. This morbidity, while close to the rates reported by other teams between 26-46% [10,17,18], could be reduced. The complications observed were mainly related to the volume and quality of the remaining liver. Specifically with regard to liver failure, prevention requires optimal preoperative preparation of patients including carrying out a volumetry of the future liver remnant, which makes it possible to assess the adequacy of the post-hepatectomy liver remnant to meet the physiological needs of the patient after hepatectomy. This preparation also requires meticulous screening of patients in order to identify whether they are eligible for a surgical procedure of this magnitude, and to conduct adequate risk stratification. During preoperative evaluation, a diagnosis of cirrhosis must be made and characterized by its progressive stage based on tools such as the Child-Pugh classification score. When the evaluation of the function of the future remaining liver is unsatisfactory, portal venous obstruction can be considered to improve it. This procedure is currently recommended percutaneously guided by radiology unlike our practice which consisted of performing four surgical ligations which nevertheless gave satisfactory results. The development of interventional radiology in Burkina Faso could improve our results. During surgery, the dosage of indocyanine green clearance after injection is also a good indicator of liver failure. In addition, at the same time, careful hemostasis and bilistasis of the section is also the best way to avoid bleeding and bile leakage. Furthermore, the use of the ultrasound dissection, which we do not have, permits better control of intraoperative bleeding. In the context of Burkina Faso, intermittent pedicle clamping is used to adapt to the state of the parenchyma to avoid excessively prolonged ischemia of the remaining cirrhotic liver. The overall 90-day mortality in our study was 26.3%. This high mortality was mainly due to the occurrence of postoperative liver failure and related to the large size of the tumors in a cirrhotic liver. In these circumstances the only option for salvage is transplantation, which does not exist in Burkina Faso. Lower mortality rates of 10.5 and 21% respectively were reported by Krautz C [9] in Germany and Baumgartner R [18] in Sweden. Many poor prognostic factors have been identified [20]. Among these factors, our study revealed associations between Child-Pugh B score (p=0.0113), AFP level ≥ 200 ng/mL (p=0.0263), tumor size ≥ 15 cm (P =0.014), operative time ≥ 5 hours (p=0.0011) and mortality. These factors indicate an advanced tumor process which leads to a challenging procedure with poor associated prognosis.

Despite major hepatectomy sometimes performed outside of standard resectability criteria, delays to diagnosis, and delays to treatment due to lack of financial means, we found an overall survival of 39.5%. Faucher M [4] as well as Kong QY [19] found an overall survival of 50.25%. These figures show that post-operative survival of major hepatectomies outside of transplantation remains low worldwide and that liver resection in malignant tumors remains a wait-and-see treatment before transplantation. Due to the culture of team spirit that reigns within the hepato-bilio-pancreatic surgery unit of the Tengandogo University Hospital the results are encouraging. This team brings together hepatobiliary and pancreatic surgeons, anesthesiologists and intensive care specialists, hepato-gastro-enterologists, pathologists and radiologists participate in the diagnosis and treatment of liver and pancreas diseases. However, the capabilities of local surgical teams in the performance of safe and effective liver resection need to be improved by strengthening the material resources and technical capacities of these actors. Raising awareness among patients and caregivers about early diagnosis would also make it possible to obtain better operative outcomes. Further, efforts to initiate liver transplantation programs within Burkina Faso should continue to be developed.

6. Conclusion

Despite significant resource limitations, major hepatectomies are performed in Burkina Faso. The prognosis after liver resection remains poor. However, numerous steps can be taken to improve in morbidity and mortality following liver resection in resource-limited settings including enhanced control of clinical, biological and histological factors. Liver resection and liver transplantation must be promoted in Burkina Faso due to the high frequency of cirrhosis caused by viral hepatitis. Specialized training for all members of the multidisciplinary surgical team, improvement of equipment and material resources, early detection of liver tumors and the continuation of multidisciplinary consultation meetings during post-operative follow-up can improve the prognosis following major hepatectomy.

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