Original Article

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Evaluation of Hepatectomy for Malignant Hepatic Tumor in Gastroenterology and Hepatology teaching hospital

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ABSTRACT

Background: The liver is an organ that is involved primarily or secondarily by vascular, metabolic, infectious, and malignant diseases. The liver tumor are divided into benign and malignant, mostly benign tumors are common, while malignant tumors are serious and increasing in incidence.**Objectives:** the study design to evaluate surgical treatment for patient with malignant liver tumor, in form of hepatic resection, and early post-operative complication. **Methods:**A prospective cross-sectional analytical study had been carried out in Gastroenterology and Hepatology Teaching Hospital/Medical City/ Baghdad/ Iraq.
The data collection phase extend over a period of 36 months from January/ 2015 to January/2018. The sample size was twenty patients, who are attends to hospital regardless to their gender or age. All patients reviewed by history, clinical examination, and investigations that including biochemical investigations in the form of liver function test, virology, and radiological evaluation in the form of ultra sound, CT scan and MRI prior to surgery.
Data were analyzed by (SPSS) version 23 to estimated frequency, percentage, Chi-square. In all cases p value < 0.05 was considered as statistically significant.
Results: twenty case of different types of hepatic resection recruited in the study, where, Most of them underwent hepatectomy in form of right hepatectomy, in less extent bisegmentectomy and segmentectomy, by different incision types at high percent we used J shape incision, followed by midline then Rt. Subcostal, the other type of incisions having the same proportion. Only 15% of the patients ended with post-operative bleeding, wound infection, death , while about 25% ended with bile leakage and about 45% needing blood transfusion, that nearly half of the population doesn't have complication and about one quarter have two complications and only 10% having three complications.
the collective number of complications showed significant statistical association with types of surgery **Conclusion:** Major hepatic resection is an accepted line of treatment for neoplastic tumors of the liver, in selected cases. Surgery should then be undertaken because of an expectation of increased survival. complete excision can be accomplished with low morbidity and mortality.
Keyword: Malignant liver tumor, Liver resection

Introduction:

The liver is an organ that is involved primarily or secondarily by vascular, metabolic, infectious, and malignant diseases. There are many classification used to help in diagnosis of liver lesions like, solid or cystic, single or multiple, cellular or mesenchymal, and benign or malignant lesions[1].
Liver tumors are divided into benign and malignant. Benign tumors are very common occurring in 9% of the population and usually are asymptomatic and discover accidentally on imaging, while malignant tumors are serious and increasing in incidence.[2]
The most common benign tumors are hemangioma, adenoma, and focal nodular hyperplasia[3]. The most common malignant tumors are hepatocellular carcinoma, then cholangiocarcinoma [4].

Hepatocellular carcinoma(HCC) is the most common primary malignant tumors in adults. 85% of all cases occur in chronic liver diseases and liver cirrhosis especially that associated with Hepatitis B and C virus infection.
Patients with HCC have bad prognosis, it is second leading cause of death in men and sixth in women [5]. HCC distribution varies according to age and geographical area, it affects people over age of (65) years, and nearly (80%) of all HCC occur in developing countries.
The incidence is high in Asia and Sub-Saharan Africa which reaches up to 80 per 100,000 per year in women and more than 110 per 100,000 per year in men. In developed countries the incidence tends to be low,

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nearly 6.8 per 100,000 per year in men and 2.2 per 100,000 per year in women. Many risk factors of HCC had been identified , but hepatitis B, hepatitis C, and alcohol are the main causes in the world.

Hepatitis B and C are responsible for 75%-80% of the total cases[6].

The mortality rate of HCC after hepatic resection ranges from (3.6%) to (19%) [7].

Secondary liver tumors (Metastatic neoplasms) are much more common malignant tumor of the liver. The relative proportion of primary to secondary tumor is 1:20 [8]. Primary colorectal cancer is the most common primary tumor metastasis to the liver [9]. Surgical excision of liver secondary is an effective therapy, and can prolong survival. Five year survival rate after liver resection, which differs in various countries(27- 49%) in the Western countries and (10- 46%) in the Far East countries.[10].

Hepatectomy for malignant liver tumor with expected good outcome depends primarily on early diagnosis and effective treatment because of most of patients with liver tumor (malignant) present very late. Screening to high risk groups like Hepatitis A, B,C, liver cirrhosis and hemochromatosis.

Classification

A: Histological classification of liver tumor:

**** Primary tumors:***

1.Epithelial tumors :
Benign : like Hepatocellular adenoma.
Malignant : like Hepatocellular carcinoma.

2.Non-epithelial tumors :
Benign : like Angiomyolipoma.
Malignant : Epithelioid hemangioendothelioma.

3.Miscellaneous tumors : like Solitary fibrous tumor.

4.Hematopoietic and lymphoid tumors.

****Secondary tumors:***

B:Clinical and pathological classification:

1.Benign tumors: like **Hepatic hemangioma, Focal nodular hyperplasia.**

2.Malignant tumors: like **Hepatocellular carcinoma, Intrahepatic cholangiocarcinoma.** [11,12].

Clinical manifestations:

Liver cancer may not cause any symptoms in early stages. Signs and symptoms appear when the tumor grows and leads to many symptoms like :

Abdominal pain , lump or mass, nausea and vomiting, early satiety, weight loss, malignant ascites, fatigue and weakness, hepatic encephalopathy [12].

Diagnosis: depend on,

1. History and physical exam., 2.Biochemical tests, 3.Hepatitis test, 4.Complete blood count, 5.Tumor markers tests, 6.Chest X-ray, 7.Ultrasound, 8.CT scan, 9.MRI, 10.Biopsy[13]

Stages of liver cancer:

1.Stage 0 (very early stage) : there is one tumor 2cm or less.

2.Stage A (early stage): there are up to three tumors, all are smaller than 3cm.

3.Stage B (intermediate stage): more than three tumors, at least one larger than 3cm.

4.Stage C (advanced stage) : the cancer grown into vessels of the liver and/ or lymph node involvement.

5.Stage D (end stage): the cancer grown into large blood vessels or spread to other parts of the body. [14]

Prognosis: It is depend on many factors such as **:**

1.Stage: stage 0 or A have more favorable prognosis.

2.Liver function: liver cirrhosis or hepatitis have poor prognosis.

3.Performance status and daily activities of patients.

4.Tumor characteristics: (multiple tumors, large vessels invasion, more than 5cm.)

5.Type of tumor: Fibrolamellar carcinoma has good prognosis. [15]

Treatments:

1.Surgery: depends on the stages of liver cancer, as one of following types:

A:Liver resection, or partial hepatectomy: it used to remove the tumor along with margin of healthy tissue around, In patients who has not cirrhosis and liver tissue remnant more than 20 %. [16]

***Remnant of liver tissue after hepatic resection**

Liver resection successful depend on the remnant livers ability to regenerate. If the liver remnant is less than 20% of original liver volume leading to post-resection liver failure[17].

***Types of liver resection (French classification)**

The types of liver resection includes:

1.**Right hepatectomy**: segment V, VI, VII, and VIII (+/- segment I).

2.**Extended Right or right trisectionectomy**: segment IV, V, VI, VII, and VIII.

3.**Left hepatoectomy**: segment II, III, and IV (+/- segment I).

4.**Extended Left or left trisectionectomy**: II, III, IV, V and VIII(+/- segment I).

5.**Right posterior sectionectomy** : segment VI and VII.

6.**Right anterior sectionectomy**: segment V and VIII.

7.**Left medial sectionectomy**: segment IV.

8.**Left lateral sectionectomy**: segment II and III. [18]

B:Liver transplant:

2.Transarterial chemoembolization:, **3.Ablation therapy :**, **4.Target therapy:** , **5.Radiation therapy:** [19]

Objectives:

1.To assess the early outcome of our surgical management for malignant hepatic tumor regarding complication and mortality in GIT center.

2.To evaluate of preoperative age, sex, presenting symptoms, incision type, liver segment resected, histopathology.

PATIENT AND METHOD

Type of the study :

A prospective cross sectional analytical study had been carried out in the GIT hospitals/ medical city/ Baghdad/ Iraq. over a period of 36 months from January/2015 to January/2018.

Study population :

The study population includes the patients referred to GIT hospital with hepatic tumor. All attendants are included regardless to their gender or age.

64 patients were diagnosed as a malignant liver tumor.Of them only 20 of 64 cases underwent hepatectomy.

The others either inoperable or refuse surgery or they lost during follow up.

Procedure of work :

We include in the study the patient treated surgically(hepatectomy), while the patient with other forms of treatment (chemo, radio, biopsy) were excluded from the study.

All patients reviewed by history, clinical examination, and investigations including biochemical investigations, radiological evaluation and anesthesia fitness.

All patients admitted to the hospital day or two before surgery .

All patient underwent surgery in an elective list after informed consent was obtained.

The targeted population underwent different incisions types **(bilateral subcostal**, **j shape, Mercedes, midline and Right subcostal**) and different type of surgery **(right hepatectomy, bisegmentectomy, segmentectomy)** had been implanted.

Postoperative evaluation of morbidity done, surgical outcome were evaluated.

Result:

Table 1: Distribution of studied population according to their presentation

presentation	Number	Percentage
Pain	**14**	**70.0**
Mass	**9**	**45.0**
Virology (positive)	**1**	**5.0**
Jaundice	**4**	**20.0**
Total		

Most of the patients presented with Pain, negative virology and for some extent some of them presented mass and jaundice.

Table 2: Distribution of studied population according to some of their liver function tests

	Mean	Std. Deviation	Range
TSB mg/dl	4.2400	8.36744	32.70
AFP ng/ml	205.7800	386.75037	1209.40
ALP iu/l	157.3000	110.56463	355.00
AST u/l	65.1500	39.24723	148.00
ALT u/l	66.3000	58.86836	201.00

Nearly all patient according to their mean presented with abnormal liver function test as shown in the table 2.

Figure 1:Distribution of patients according to the type of surgery.

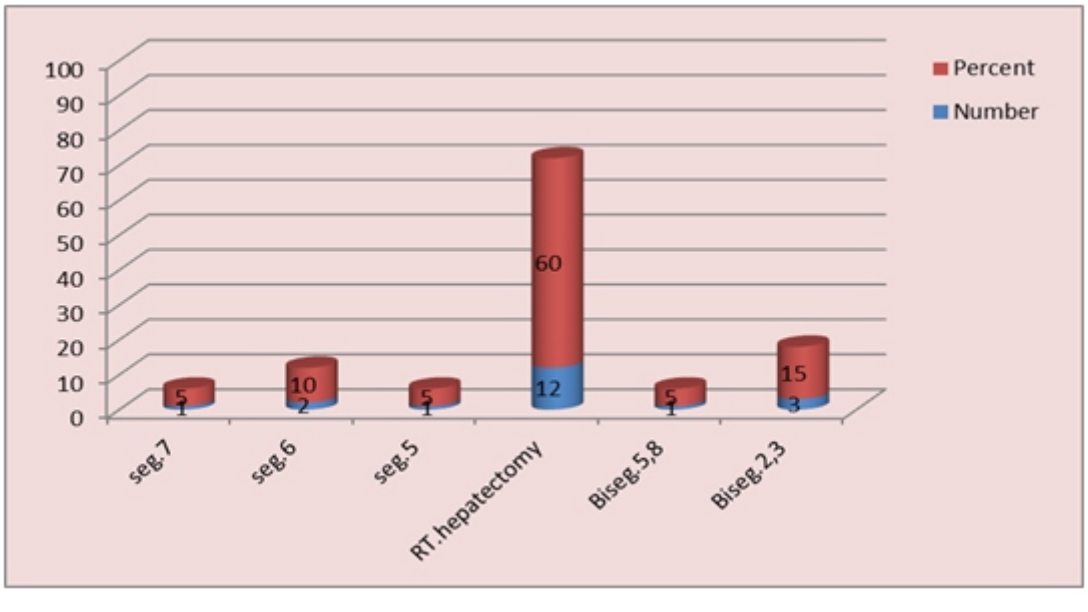
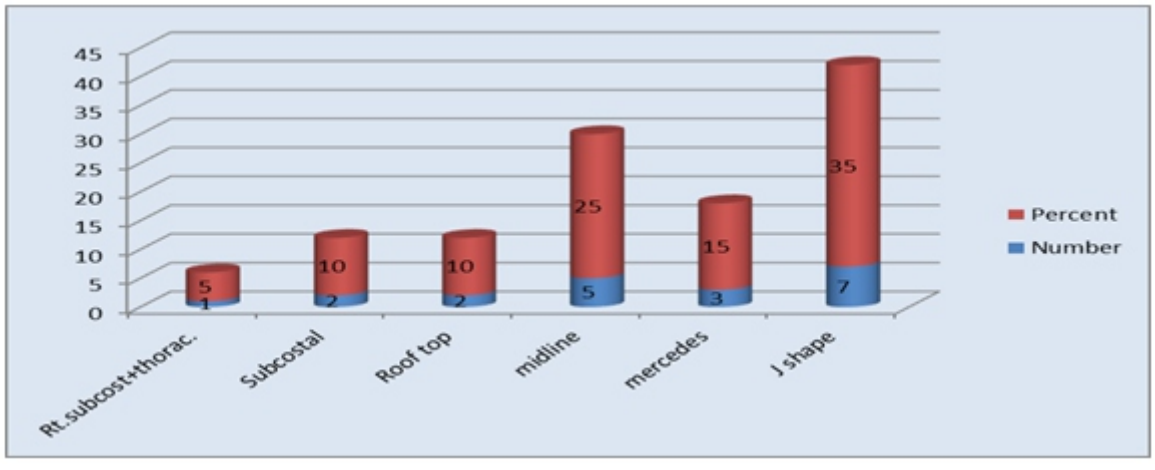


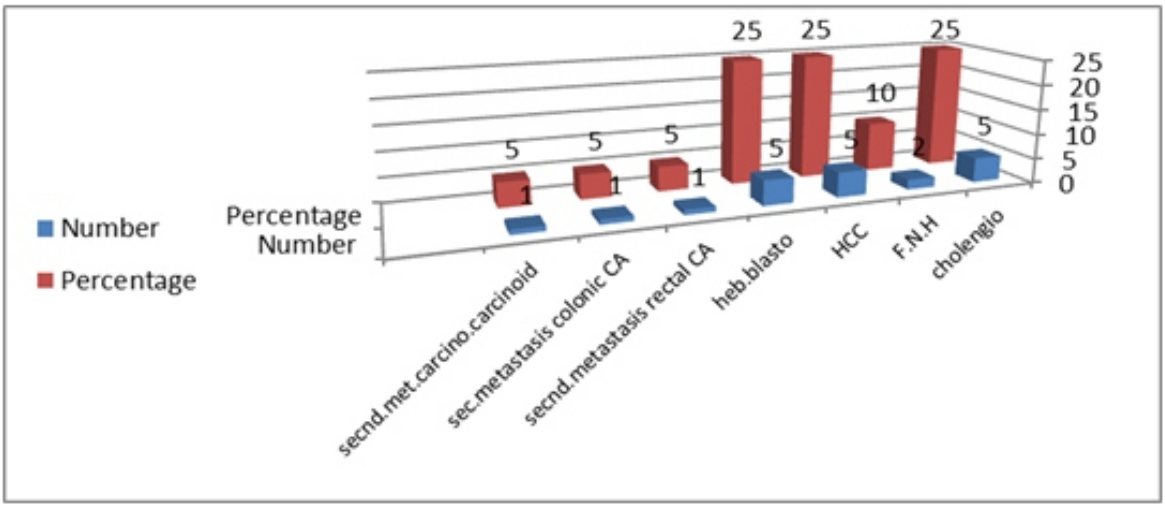
Figure one show different types of surgery and surgical procedure for the studied population.

Figure 2: Patients according to the types of incision



Most of the patients underwent into J shape incision, followed by Midline then Mercedes, the other two types of incision(roof top, subcostal) having the same proportion which was 10%, the last one was 5% as shown in **figure 2.**

Figure 3:Distribution of patients according to the histopathology



Table(3) :Distribution of patients according to the surgery complications

Post-operative complications	Number	Percentage
Postoperative bleeding	3	15.0
Blood transfusion	9	45.0
Post Op Bile leakage	5	25.0
Wound infection	3	15.0
Post-operative death	3	15.0

Only 15% of the patients ended with post-operative bleeding, wound infection and post-operative death , while about 25% ended with bile leakage and about 45% needing blood transfusion as seen in the **table 3**, while **figure four** showing that nearly half of the population doesn't having complication and about one quarter have two complications and only ten percent having three complications.

Figure 4:Distribution of patients according the number of overall post-operative complication developed $X2=0.135^{a}$ **P value-0.714**

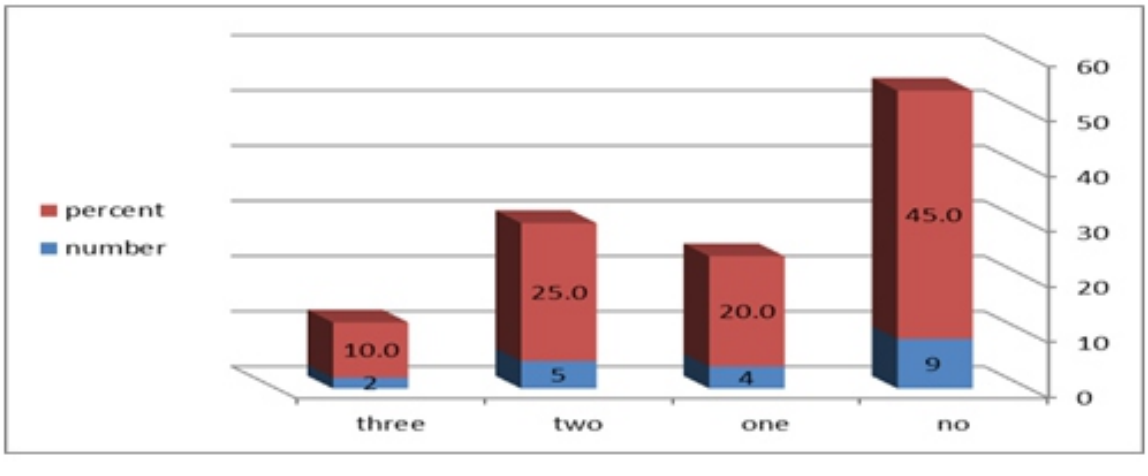
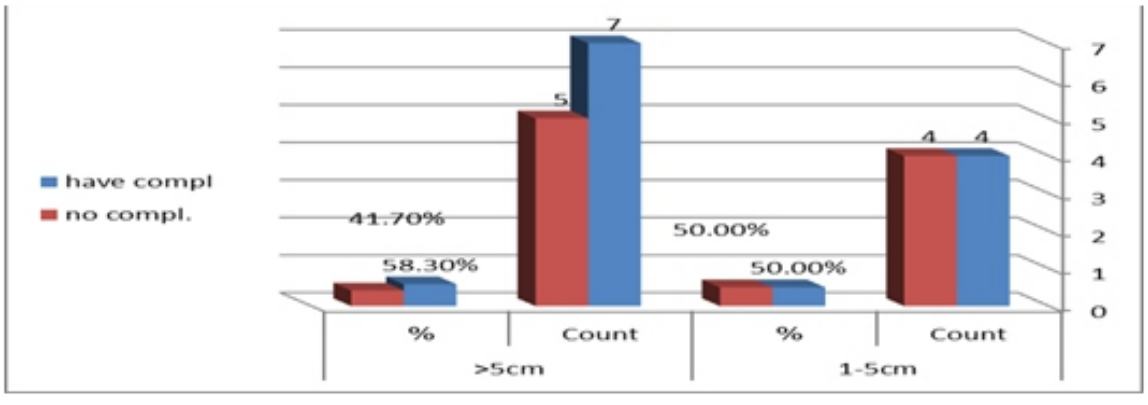


Figure 5:distribution of patient according to their tumor size and complication:

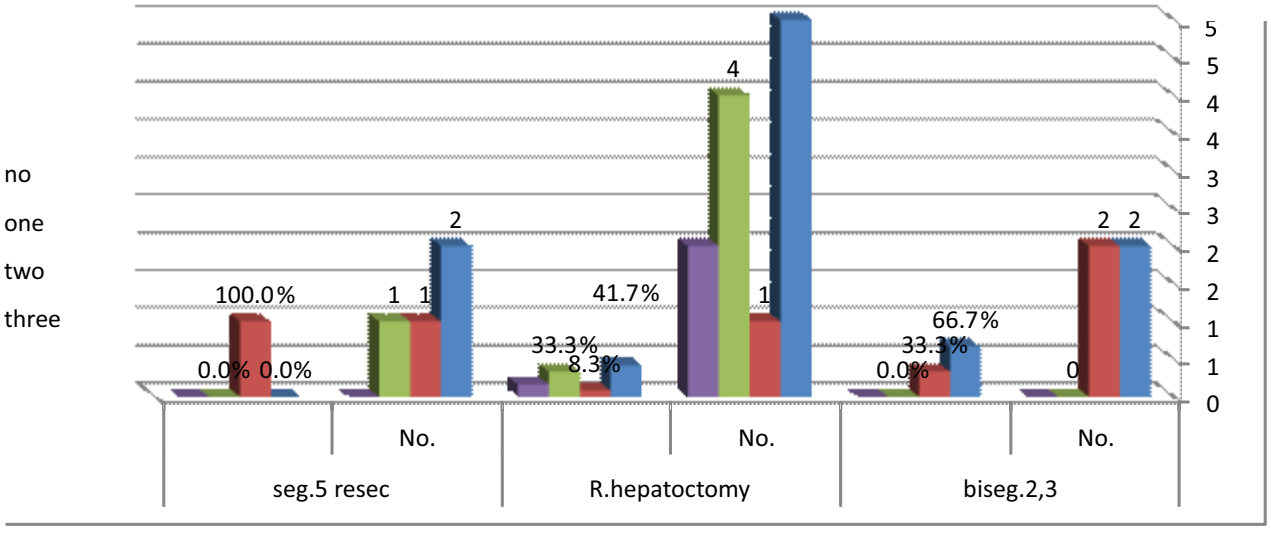


There was no significant statistical association between different types of surgeries and number of complications Fisher's Exact Test=1.798, P value=0.903

Table 4: Relationship of the types of surgery with development of complication during hospital stay

Type of surgery	Total patients	Jaundice	Post op. Bleeding	Post op. Bile leak	Post op. Death	Wound infection	Blood transfusion	Total of complication
RT. Hepatectomy	12	4 (33.3%)	3 (25%)	3 (25%)	2 (16.6%)	1 (8.3%)	5 (41.6%)	**18**
Bi,segmentectomy	4	0	0	1 (25%)	0	1 (25%)	1 (25%)	**3**
Segmentectomy	4	0	0	1 (25%)	1 (25%)	1 (25%)	3 (75%)	**6**
total	20	4 (20%)	3 (15%)	5 (25%)	3 (15%)	3 (15%)	9 (45%)	**27**
X2		4.569	2.356	0.364	1.781	1.105	3.420	
P. value		0.068	0.260	0.999	0.575	0.627	0.250	

Figure 6: Relationship between type of surgery and number of complications developed



F.E test=7.518. P value=0.056

Discission

Clinical presentation:

Liver cancer may not cause any symptoms in early stages, then signs and symptoms appear when the tumor grows . in current study the percentage of pain in liver cancer was 70%, and these result agree with study in China at 2015, which was 30-70% (Ye X, Lu D et al. at 2016) [20].

In this study jaundice present in 20% of cases, and the highest proportion were don't have jaundice(80%).These results agree with USA(2006) study which reported that the jaundice present in 19-40% of patient with hepatic cancer at the time of diagnosis.[21]

In present study the highest proportion of cases was with negative result and only 5% was with positive results. These results were lower than study conducted at 2006 by Perz JF et al., in which Hepatitis A virus and B virus are the most significant risk factors for HCC development, accounting about 10-20%.[22]

In this study, the percentage of abdominal mass was 45%, these results were lower than study in Egypt by Nanis S Holah[1], Dina S El-Azab et al. at 2015, which was 82.6% [23].

Postoperative complications:

In this study postoperative bleeding incidence was 15%, these results were higher than results of study in Italy at 2007, which was from 4.2 to 10% by Benzoni E. et al. [24].

This differences might be reflect to sample size and operative facilities .

Regarding operative bile leakage in current study was about one quarter of all patient (25%), these results were higher than results of study by Lee CC. et al. in Taiwan at 2005, which was ranged from 4 to 17%.[25]

Regarding postoperative wound infection in this study was 15%, which is nearly agree with study in Swiss at 2012 which were 12.8% by Takashi Kokudo et al.[26]

In this study postoperative blood transfusion was 45% of all patients and these result lower than results of study in Canada, which were 47.4% by Bennett S et AL..[27]

Regarding postoperative death (mortality rate) in current study was 15%, which was higher than results of study in Romania at 2012 by Dan RG, et al. (2.25%) [28].

.Types of hepatic resection :

Surgery of the liver is based on anatomic description of functional segments, which depends on organ's blood supply by hepatic artery and portal vein. The liver divided into eight functional segments. In current study about half patients were with right hepatectomy (60%), about 20% was Bisegmentectomy (II,III or V,VIII) , and 20% of those were with Segmentectomy resection (V or VI or VII) . Extent of liver resection depends on the number of resected segments.

The complication rate ranges 32% and mortality rate less than 1% in one resected segment, developing to 75% complication rate and 7.8% mortality rate in patients with resection of six segments. In patient with three or more resected segments, the mortality rate doubled from 3% to 6% when other problem of surgical procedure are associated . patients who are resection of less than three segments had no increasing in blood transfusion or death, while patients who are resected three or more segments leads to increase blood loss, blood transfusion, morbidity and mortality rate. This finding nearly the same as mentioned by Paes-Barbosa et al.[29].

Surgical incision in hepatic resection:

In present study, the highest proportion of surgical incision was among those patients with J-shape incision, which were 35%, and about one quarter of patients with midline incision, which were 25%. While the lowest proportion was among those with right subcostal incision, roof top incision were 10 % in equally. Mercedes incision were 15% and RT. Subcostal incision with thoracotomy was only in one patient 5%.

The incisions most commonly used have included a bilateral rooftop incision with or without vertical extension, J-shaped incision and L-shaped incision with or without left extension as mentioned by Chang SB, et al. [30].

The type of incision selected depends on many circumstances, like site, size of tumor and surgeon preference.

Distribution of patients according to histopathology:

In this study, about one quarter of patients (25%) were among those with intrahepatic cholengiocarcinoma, hepatoblastoma and hebatocellular carcenoma, while F.N.H were 10%. The lowest proportion were among those with secondary metastasis colonic carcinoma, secondary Carcinoid, and secondary metastasis rectal carcinoma, which were 5% in equally.

According to WHO, intrahepatic cholengiocarcinoma is the second most prevalent intrahepatic primary cancer.

Post-operative mortality rate in hepatic resection:

Despite advances in surgical technique and medical care, liver resection for liver cancer remains a high-risk major operation. The present study evaluated the postoperative mortality rate according to types of operation, which were highest proportion among those who were with right hepatectomy, with lowest proportion among those with other types of resection.2 out of 5 patients of cholangiocharcenoma were died, the cause is mainly cause is that cholangiocarcenoma need major hepatic resection with biliary duct excision, then biliary-enteric anastomosis, which is a major and carry high risk on the patients.

The total mortality rate for all types of surgeries was 15%. Recent studies reported perioperative mortality rates of 2.6% to 8.4%[31] for hepatocellular carcinoma patients undergoing major liver resection.

The definition of perioperative mortality in most studies was death in hospital or death within 30 days after the operation.

Conclusion:

Major hepatic resection is an accepted line of treatment for neoplastic tumors of the liver, in selected cases, as well as for benign disorders.

Where a patient is fit for surgery, has adequate liver function and the tumor is favorable, with accepted liver tissue remnant, resection should be considered, because of an expectation of increased survival. It is clear that patients who have disease confined to the liver that can be completely resected will benefit from an aggressive surgical approach. Continued research to help identify parameters for better selection of patients is ongoing.

Recommendation:

Hepatic resection in malignancy even its a major surgery, but in specialized centers, skilled surgeons, and with a good selection for patient will result in less complication and acceptable mortality.

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