Surgical management of hepatocellular carcinoma (laparoscopic vs. open techniques)

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Abstract: Laparoscopic approach in management of HCC has been progressively developed along the past two decades. Liver surgery was one of the last frontiers reached by minimally invasive surgery. Surgical technique and equipment evolved to overcome technical limitations, making laparoscopic liver resections (LLR) safe and feasible. Surgeons developed skills in a stepwise approach, beginning with low complexity operations for benign diseases and reaching high-complexity surgeries for malignant cases and living donor organ harvesting. In this study, a comparison between laparoscopic approach and open approach was done to compare short-term results. This study was conducted on 100 patients with hepatocellular carcinoma. 50 patients (50%) were treated by laparoscopic approach (Group A) while the other 50 patients (50%) were treated by open approach (Group B). All cases were classified to be CHILD grade A with median MELD score in laparoscopic group was 8.96±1.72 ranging from 6 to 14 while in open group the mean MELD sore was 8.2±1.42 ranging from 6 to 11. The difference was statistically not significant (P<0.254). The mean operative time in open group was 158.15±35.9 minutes, while the laparoscopic group mean time was 130.4±38.1 minutes with statistically significant difference between the 2 groups (P<0.001) with decreased operative time in the laparoscopic group. The mean blood loss in open group was 390±193.7 ml while the laparoscopic group mean blood loss was 386 ±371.1ml with no statistically significant difference relations between the 2 groups (P= 0.671), with conversion rate of (10%) happened in 5 cases. The mean hospital stay in open group was 5.9±0.88 days ranging from 3-7 days, while the laparoscopic group was 3.74±.85 days ranging from 2-5 days with highly statistically positive correlation difference between 2 groups (P< 0.001). Also the drain was removed in the laparoscopic group earlier showing highly statistical difference between two groups (P< 0.001). The most frequent complication was postoperative ascites and which was seen in 35 (70%) cases in the open group and in 23 (46%) cases in laparoscopic group with highly significant difference between both groups with much more lower incidence in laparoscopic group (P<0.004). There was a case of histologically proved port site metastasis in laparoscopic group at the right subcostal port where the specimen is extracted with percentage of (2%) (P=1.00). Hepatocellular carcinoma was found in all patients in both groups. There were 42 patients moderate differentiation (84%) in laparoscopic group, with mean resection margin of 8.1±2.2 mm while moderately-differentiated in 41 (82%) patients (82%) in open group with mean resection margin 7.62±2.28 mm with no statistical significance (P=0.132). Recurrence occurred in 2 patients (4%) in Group A and 1 patient (2 %) in Group B while mortality occurred in only one patient (3.05%) in the open group in the laparoscopic group, the 1-year survival was 98 %, while in the open group was (96 %) (P=1.00). In the laparoscopic group, the 1-year survival was 98 %, while in the open group was (96%) (P=1.00).

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1. Introduction

Hepatocellular carcinoma (HCC) is the most common primary hepatic malignancy ranking sixth in the world among all malignancies and becoming the third cause of death due to cancer. Incidence has increased all over the world **(Waller et al., 2015).**

Egypt has one of the highest prevalence of HCC where it contributes up to 70.48% of all primary liver tumors. The increased incidence of HCC in Egypt is attributed to the increased prevalence of hepatitis B and hepatitis C also there has been improvements in screening and diagnostic tools leading to earlier detection of HCC **(Holas et al., 2015).**

Liver resection is the preferable initial treatment option for solitary or limited multifocal HCCs with no extra hepatic spread. The mortality and morbidity of liver resection have significantly decreased in the last two decades because of improvements in patient evaluation, surgical technique, and perioperative care. Resection is the ideal treatment, as it allows for complete removal and pathological confirmation of lesions. However, it is more invasive than other loco regional therapies such as Trans arterial chemoembolization, tumor ablative therapy, and radiation therapy **(Otsuka et al., 2016).**

Nowadays, the mortality rate of most liver resections has been brought down to below 5% and blood transfusion rates to between 6.2%and 49%

(Chowdhury, 2010).

Due to improved laparoscopic instruments and increasing experience with laparoscopic and liver surgery, the technical difficulty of laparoscopic liver resection (LLR) is slowly being overcome. An increasing number of reports on LLR have documented outcomes comparable to those of open liver resection. LLR is currently expanding its application in terms of indications and extent of resection **(Yoon et al., 2009).**

Nonetheless, there have been only a few reports on LLR for hepatocellular carcinoma (HCC). Although some reports have shown encouraging oncologic results, LLR for HCC is still challenging for both surgeons and patients, because most HCCs are associated with underlying liver diseases such as chronic hepatitis and liver cirrhosis. Moreover, the application of LLR to HCC has also been limited by tumor location. Most reported cases have had peripheral lesions located in the anterolateral segments (segments 2, 3, 4b, 5, and 6). More recently, the limitation of LLR according to lesion location is being gradually overcome. LLR for lesions located in the posterosuperior segments (Couinaud segment 1, 4a, 7, and 8) has been reported on by some surgeons who have great expertise. Since the first successful right posterior sectionectomy for HCC in 2003. **(Yoon et al., 2009)**

Laparoscopy has been used extensively and continues to improve as a surgical option. Laparoscopic liver resection (LLR), a minimally invasive treatment for liver cancer, is now increasingly performed worldwide. **(Otsuka et al., 2016)**

Regular post treatment follow up with imaging studies and serum tumor markers every 3 to 6 months in the first 2 years; thereafter, regular checkups at individualized intervals. **(Yu, 2016)**

Aim of the Work

The aim of the work is to compare between open surgical management and laparoscopic surgical management of hepatocellular carcinoma regarding preoperative assessment, operative management and details and postoperative course and complications.

2. Patients and Methods

This study is retro- prospective randomized controlled trial (RCT), which involved 100 patients with hepatic tumors (with Child A classification fit for surgical intervention) at National Hepatology Tropical medicine Research Institute (NHTMRI) and their data collected during period from June 2017 until January 2019. The patients were divided into 2 groups, Group A (50 patients) managed with laparoscopic (resection or ablation) technique and Group B (50 patients) managed with open surgical management (resection and ablation) technique.

Inclusion criteria

1) Tumor site: located in segments II, III, IVb, V, and VI.

2) Child-Pugh class A.

3) American Society of Anesthesiologists (ASA) status I and II patients.

Exclusion criteria

1) Tumor thrombus in the portal vein, hepatic vein, IVC.

or bile duct or invasion of the surrounding tissues.

2) Rupture or bleeding of the tumor.

3) Distant metastasis.

4) one of tumor nodules > 3 cm or more than 3 nodules.

All Patients were subjected to:

1. Complete patient history including personal history, present illness history, family history and past medical history.
2. General and local examinations.
3. Laboratory investigations.
4. Radiological investigations.
5. Counseling and Informed consent signing.

Statistical analysis

Data collected throughout history, basic clinical examination, laboratory investigations and outcome measures coded, entered and analyzed using Microsoft Excel software. Data were then imported into Statistical Package for the Social Sciences (SPSS version 20.0) **(**Statistical Package for the Social Sciences) software for analysis. According to the type of data qualitative represent as number and percentage, quantitative continues group represent by mean ± SD, the following tests were used to test differences for significance difference and association of qualitative variable by Chi square test (X^2) OR Fisher. Differences between quantitative paired by paired t multiple groups by ANOVA. P value was set at <0.05 for significant results & <0.001 for high significant result.

3. Results

This study involved 100 patients with hepatic focal lesions. All the patients included in this study had hepatic focal lesions the patients randomly divided into 2 groups, Group A (50 patients (50%)) managed with laparoscopic technique. And Group B (50 patients (50 %)) managed with open technique.

Preoperative data

Table (1) illustrated that the Mean age ±SD in laparoscopic group was 60.4 ±5.9 ranged between 47-78years while in open group was 56.9 ±6.7ranged between 43-74years with no statistical significant difference between two groups (P =0.223).

Table (1): Difference in age between both groups.

Age in years	*Mean age ±SD*	*Range*	P-value
Group A (n=50)	60.4 ±5.9	47-78	0.223
Group B (n=50)	56.9 ±6.7	43-74	

Regarding the gender, There was 30 males (60%) and 20 females (40%) in the laparoscopic group and 26 males (52%) and 24 females (48%) in the open group. The difference was not significant.

In terms of smoking, 24patients (48%) were nonsmokers and 26 patients (52%) were smokers in the laparoscopic group while there 25patients (50%) were nonsmokers and 25 patients (50%) were smokers found in the open group.

There were no patients in each group showing negative viral markers. 58 patients (98%) had Hepatitis C virus (50 in group A and 48 in group B) while only two patients (2%) had both hepatitis B & C virus. The difference was not significant

However, in regards to the past history of medical diseases rather than hepatitis, in the laparoscopic group 11patients (22%) had associated hypertension, 13patients (26%) had diabetes mellitus while in the open group 8patients (16%) had associated hypertension, 14patients (28%) had diabetes mellitus and 8 patients (16%) had both combined hypertension and diabetes mellitus in each group.

Table (2): Shows the demographic data among the patients included in the study.

		Group A (n=50)	*Group B (n=50)*	X2	
		N (%)	*N (%)*	xxxx	*P-value*
Gender	*Male*	30 (60)	26 (52)		0.718
	Female	20 (40)	24 (48)		
Smoking	*Non smoker*	24(48)	25(50)		0.675
	Smoker	26 (52)	25 (50)		
Co-Morbidity	*Non*	18 (36)	20 (40)		0.457
	HTN	11 (22)	8(16)		
	DM	13 (26)	14 (28)		
	Others	8(16)	8(16)		
viral markers	*HCV positive*	100	96		
	Combined C & B	0	4		

Preoperative investigations

Table (3): Shows the preoperative investigations among the patients included in the study. By comparing the means of laboratory results between both groups, no significant differences could be found.

	Group A (n=50)		*Group B (n=50)*		*P*
	Mean	*SD*	*Mean*	*SD*	*value*
AST	77.5	35.9	75.6	43.9	0.426
ALT	67.6	34.7	64.8	36.2	0.872
T. BIL	1.1	0.37	0.94	0.32	0.167
ALB	3.5	0.43	3.62	0.4	0.294
ALP	102.5	46.8	119.5	44.3	0.077
INR	1.2	0.13	1.14	0.12	0.345
CREAT	0.83	0.23	0.81	0.18	0.075
HB	13.2	1.2	13.15	1.9	0.679
TLC	5.4	1.8	6.39	1.91	0.08
PLT	124.56	39.15	145.7	61.9	0.098

The median Alpha fetoprotein level in laparoscopic group was 62.6 ng/ml ranging between 4.1-978 ng/ml, while the median level in open group was 53 (ng/ml), ranging between 2 and 1602 (ng/ml), and showing no statistical significant difference between both groups.

Table (4): Preoperative Alfa feto-protein levels in both groups.

	Group A (n=50)		*Group B (n=50)*		*Man whitney test*	*P-value*
	Median	*Range*	*Median*	*Range*		
AFP	62.5	4.1 - 978	53	2-1602	-.807	0.482

Preoperative status of the patients

All the patients included in both groups of this study were classified to be CHILD grade A. MELD score among the patients included in the study. The mean MELD score in laparoscopic group was 8.96±1.72 ranging from 6 to 14 while in open group the mean MELD sore was 8.2 ±1.42 ranging from 6 to 11. There were no statistically significant differences (P<0.254).

Table (5): The following table shows the largest tumor size and the overall tumor burden which were insignificant between two groups.

	Group A (n=50)	***Group B (n=50)***	
	Mean ± SD	*Mean ± SD*	***P-value***
tumor size	2.3 ±.46	2.35 ±.47	**0.627**
Overall tumor burden	**2.3 ±.47**	**2.31 ±.47**	**0.857**

Intraoperative Data:

The mean operative time in open group was 158.15 ±35.9 minutes, while the laparoscopic group mean time was 130.4 ±38.1 minutes with statistically significant difference between the 2 groups, (P< 0.001) with decreased operative time in the laparoscopic group.

The mean blood loss in open group was 390 ±193.7 ml while the laparoscopic group mean blood loss was 386 ±371.1 ml with no statistically significant difference relations between the 2 groups, (P= 0.671). Ten cases (20%) only needed intraoperative blood transfusion in laparoscopic group compared with 10 cases (20%) in open group. 15 cases (30%) showed no need for plasma transfusion in laparoscopic group compared with only 13cases (26%) in open group.

Table (6): Difference of intraoperative data between both groups.

	Group A (n=50)	***Group B (n=50)***	
	Mean ± SD	*Mean ± SD*	***P-value***
Operative time (min)	130.4 ±38.1	158.15 ± 35.9	**0.001**
Blood loss (ml)	**386 ± 371**	**390 ± 193.7**	**0.671**

Table (7): Required transfusions in both groups.

		Group A (n=50)	***Group B (n=50)***	
		N (%)	*N (%)*	***P value***
Blood Transfusion	*No*	40 (80)	40 (80)	**1.00**
	Yes	10(20)	10(20)	
Plasma Transfusion	*No*	15 (30)	13(26)	**0.198**
	Yes	35 (70)	37 (74)	

There were 5cases converted from laparoscopic to open technique with percentage of 10% of group A. Intraoperative bleeding occurred in 2 cases (4%) in the laparoscopic group and converted to open technique, also another case (6%) was converted due to difficult localization by laparoscopic intraoperative ultrasound probe.

HCC was the main indication in both groups. Among Group A, 49 patients (98%) had non-anatomical wedge resection while the remaining 1 patient had anatomical resection in form of segmentectomy in one patient (2%). Among group B, 49 patients (98%) had non-anatomical wedge resection while the remaining 1 patient had anatomical resection

in form of segmentectomy in one patient (2%). All cases within laparoscopic group underwent intraoperative ultrasonography. Five cases in open group needed intraoperative ultrasonography. No statistically significance (P=1).

Table (8): Operative details in both groups.

Resection type	***Group A (n=50)***		***Group B (n=50)***		***P – value***
	N	*%*	*N*	*%*	
Non anatomical	49	98	49	98	
Anatomical	1	2	1	2	**1.00**

Postoperative Data:

As regarding *the hospital stay*, the mean hospital stay in open group was 5.9±.88 days ranging from 3-7 days, while the laparoscopic group was 3.74±.85 days ranging from 2-5 days with highly statistically positive correlation difference between 2 groups (P< 0.001). Also the drain was removed in the laparoscopic group earlier showing highly statistical difference between two groups (P< 0.001).

Table (8): The following table shows the postoperative data of the patients included in the study.

	Group A (n=50)		**Group B (n=50)**		***P-value***
	Mean ± SD	*Range*	*Mean ±SD*	*Range*	
Hospital stay (days)	3.74±.85	2-5	5.9±.88	3-7	**<0.001**
Drain removal (days)	2.9±0.97	2-5	4.31±1.1	3-7	**<0.001**

As shown in table (9), the most frequent complication was postoperative ascites and which was seen in 35 (70%) cases in the open group and in 23 (46%) cases in laparoscopic group with highly significant difference between both groups with much more lower incidence in laparoscopic group (P<0.004). It was recorded that the complications occurred all over the both groups in relation to the technique of resection which was more in open than laparoscopic resection but without statistically significant.

Table (9): Postoperative complications in both groups.

	Group A (n=50)	*Group B (n=50)*	*P-value*
	N (%)	*N (%)*	
Bleeding	1 (2)	0 (0)	0.053
Ascites	23 (46)	35 (70)	0.004
Wound infection	3 (6)	6 (12)	0.613
Liver failure	0	0	1
Pulmonary complication	0	0	1
Port site metastasis	1 (2)	0 (0)	1.00
Incisional Hernia	1 (2)	2 (4)	
BILE LEAK/STRICTURE	0	0	
Mortality	0	0	

There was a case of histologically proved *port site metastasis* in laparoscopic group at the right subcostal port where the specimen is extracted with percentage of (2%) (P=1.00).

Histopathological Data:

All cases of HCC in open group were histologically divided into well differentiated HCC in 6 cases (12%) of them and moderately differentiated in 42cases (84%) and another 2 cases (4%) of poorly differentiated. In the laparoscopic group, there were 7 (14%) cases of well differentiation, moderate differentiation in 41 (82%) case and poor differentiation in 2 (4%) case and all cases had clear surgical margins with mean resection margin of 8.1±2.2 mm in laparoscopic group while 7.62±2.28 mm in open group. There were no cases of benign liver tumors.

Table (10): Distribution of histopathological data of liver tumors cases in both groups.

	Group A (n=50)	*Group B (n=50)*	*P-value*
	N (%)	*N (%)*	
Hepatocellular carcinoma	50 (100)	50 (100)	1
Benign adenoma	0 (0)	0 (0)	

Table (11): Histopathological finding in hepatocellular carcinoma cases in both groups.

		Group A (n=50)	*Group B (n=50)*	*P-value*
		N (%)	*N (%)*	
Histopathology	Hepatocellular carcinoma	50(100)	50(100)	0.596
Histological Grade	Well differentiated	6 (12)	7 (14)	0.470
	Moderately differentiated	42 (84)	41 (82)	
	Poorly differentiated	2 (4)	2 (4)	
Resection Margins (MM)	Mean ±SD	8.1±2.2	7.62±2.28	0.132
	Range	5-16	5-16	

Follow up:

Table (12): Showed the level of AFP at the one year follow up between two groups had no difference and no statistically significance.

		Group A (n=50)	***Group B (n=50)***	***P- value***
		N (%)	*N (%)*	
AFP 3months	*Declining*	48 (96)	**48 (96)**	**1.00**
AFP 6 months	*Declining*	49(98)	**48 (96)**	
AFP 9 months	*Declining*	43 (86)	**45 (90)**	
AFP 12 months	***Declining***	**48 (96)**	**45 (90)**	

Table (13): Shows the frequency of overall recurrence in both groups either recurrence at operative site or de novo lesions over the 12 months follow up detected by triphasic CT, had been occurred in 2 patients (4%) in laparoscopic group while occurred in 4patients (8%) in open group with no statistically significance.

Item		***Group A (n=50)***	***Group B (n=50)***	***P – value***
		N (%)	N (%)	
CT3 months	*Recurrence at operative site*	2(4)	1 (2)	**0.391**
	Negative	48(96)	49(98)	
CT6 months	*Recurrence at operative site*	0	0	**0**
	Negative	50(100)	50(100)	
CT9 months	*Recurrence at operative site*	0	0	**kk**
	De novo lesions	4(8)	4(8)	
	Negative	46(88)	46(92)	
CT12 months	*Recurrence at operative site*	0	1(2)	
	De novo lesions	1(2)	3(6)	
	Negative	49(98)	47 (94)	

	P value
Log Rank (Mantel-Cox)	0.935

Mortality

Table (14): Showed that over the 12 months follow up, only 2 patient had been died (3.05%) in the open group with no statistical significance.

	Group A	*Group B*	*P-value*
Mortality 1 year	N (%)	N (%)	1.00
	1 (2)	2(4)	

	P value
Log Rank (Mantel-Cox)	0.325

4. Discussion

Hepatocellular carcinoma constitutes one of the most frequently encountered malignant tumors while it is accounted for as one of the leading causes of cancer-related deaths worldwide. Although liver transplantation would suggest the optimal treatment option for these patients in early stages, in an era of increasing HCC incidence as well as organ shortage such option is not viable in a large scale **(Bruix and Sherman, 2011).**

As a result, alternative and more easily accessible curative treatment options such as resection and percutaneous ablation are adopted. Although initially confronted with skepticism and restraint by hepatobiliary surgeons during the last 15 years, laparoscopic liver surgery is currently considered a safe and effective approach to the management of surgical liver diseases in the hands of trained surgeons with experience in hepatobiliary and laparoscopic surgery **(Buell et al., 2008).**

Various new studies document that LLR for HCC offers benefits equivalent to other forms of minimally invasive surgery over OLR. Less pain as well as shorter length of stay is included among these benefits.

Moreover, these studies find comparable differences in terms of morbidity and mortality between laparoscopic procedures and open surgery, both achieving adequate oncologic results **(Felli et al., 2015).**

With the refinements in laparoscopic instruments and accumulated experience with open liver surgery and laparoscopic surgery for various liver resections, LLR has become a common method of treatment for HCC. Nonetheless, LLR remains challenging because it requires adequate handling of bleeding and important structures **(Chen et al., 2017).**

In this study, a comparison between laparoscopic management and open management was done to compare short-term results between laparoscopic and open procedures. This study focused on perioperative period of patients undergoing minor liver resection and assessing its results if going in line with literature.

This study was conducted on 100 patients with hepatic focal lesions for whom patients randomly divided into 2 groups, Group A (50 patients (50%)) managed with laparoscopic technique. And Group B (50 patients (50 %)) managed with open technique.

In this study, both groups were homogeneous with regard to age, sex, etiology of liver cirrhosis, the presence of associated medical conditions, laboratory results and AFP levels. No significant differences were found between both groups regarding demographic data.

In the laparoscopic group, mean age was 60.4 ranged between 47-78 years, while in open group was 56.9 ranged between 43-74years with no statistical difference between the two groups (P<0.223).

Similar to a meta-analysis done on 550 patients by **Xiong et al., (2012)** which included nine studies showed no statistical significant difference in the mean age of LLR and OLR groups **(Xiong et al., 2012).**

In our work, There was 30 males (60%) and 20 females (40%) in the laparoscopic group and 26 males (52%) and 24 females (48%) in the open group. The difference was not significant between two groups going along with a meta-analysis done on 4 comparative studies by **Twaji et al., (2014),** had showed no significance in sex between both groups **(Twaji et al., 2014).**

There were no patients in each group showing negative viral markers. The difference was not significant. 98 patients (98%) had Hepatitis C virus (50 in group A and 48 in group B) while only two patients (2%) had both hepatitis B & C virus. The difference was not significant.

Egypt has the highest prevalence of HCV in the world (14.7%) **(Elghannam et al., 2017).** HCV-4 is a continuing epidemic in Egypt **(Zayed et al., 2017)**, ranging from 6% to more than 40% in different regions whereas 30–60% of the infected patients develop chronic liver disease and a substantial percentage develops cirrhosis or even hepatocellular carcinoma **(Omar et al., 2017).**

Concerning our study, the mean MELD score in laparoscopic group was 8.96±1.72 ranging from 6 to

14 while in open group the mean MELD sore was 8.2 ±1.42 ranging from 6 to 11. There were no statistically significant differences (P<0.254). In a study done by **Teh et al., (2007)** had shown that the MELD score can be used to determine which patients with cirrhosis are at low risk of mortality after hepatic resection for HCC. Several other reports have concluded that patients with a higher MELD score are at increased risk of mortality or morbidity after surgery **(Nicoll, 2012).**

In this current study, the median Alpha fetoprotein level in laparoscopic group was 62.6 ng/ml ranging between 4.1-978 ng/ml, while the median level in open group was 53 ng/ml, ranging between 2-1602 ng/ml, showing no statistical significant difference between both groups.

Serum AFP levels are useful for diagnosing recurrence and predicting prognosis in HCC patients who have undergone hepatic resection. High serum AFP levels occur in 60-70% of HCC patients; however, serum AFP levels remain in the normal range in 15- 30% of HCC patients. AFP plays an important role in the regulation of both oncogenic and ontogenetic growth. Apparently, AFP is not only a diagnostic marker, but is also a growth factor that promotes tumor progression, as supported by reports that higher serum AFP is associated with increased mortality **(Toro et al., 2014).**

The sensitivity of intra-operative ultrasonography (IOUS) for detecting small HCC was 98-99%, which was superior to the sensitivities of preoperative ultrasound, angiography and computed tomography **(Nagasue et al, 1989).**

The mean operative time in open group was 158.15 ±35.9 minutes, while the laparoscopic group mean time was 130.4 ±38.1 minutes with statistically significant difference between the 2 groups, (P< 0.001) with decreased operative time in the laparoscopic group.

Similar results of significantly shorter operative time in the LLR group when compared to the OLR group were found in the a lot of different recent comparative studies as ***Leong et al., (2015)*** (250.43 min vs. 349.90 min, P <0.001), ***Chen et al., (2017)*** (200 vs. 220min, P<0.001), ***Untereiner et al., (2016)*** (185 vs. 250 P <0.001), ***Yoon et al., (2015)*** (207 vs. 225 min, P <0.001) and Lai et al., (2016) (120 vs. 160 min, P< 0.05).

On the contrary of our result which was supported by previous mentioned studies, other respectable studies showed significantly longer operative time in the laparoscopic group. This is stated in different studies comparing laparoscopic versus open minor liver resection as ***Jiang et al., (2016)*** (200 vs. 160 min, P<0.15), ***Takahara et al., (2015)*** (294 vs. 270 min, P<0.25).

No significant difference was found in the operating time between the two groups consistent with ***Wang et al., (2015)*** (133 vs. 170 min, P=0.073), ***Hu et al., (2011)*** (180 vs. 170 min, P>0.05) and ***Zhang et al., (2015)*** (120vs 150 min, P>0.05).

Hasegawa et al., (2015) and ***Spampinato et al., (2015)*** have confirmed the trend of significant reduction in operative time related to increasing experience, both in minor and major resections.

Regarding blood loss in our study, *The mean blood loss* in open group was 390 ±193.7ml while the laparoscopic group mean blood loss was 386 ±371.1ml with no statistically significant difference relations between the 2 groups, (P= 0.671). Ten cases (20%) only needed intraoperative blood transfusion in laparoscopic group compared with 10 cases (20%) in open group. 15 cases (30%) showed no need for plasma transfusion in laparoscopic group compared with only 13cases (26%) in open group.

In our study, There were no significant differences in intraoperative blood loss and blood transfusion as well as other studies done by ***Komatsu et al., (2016)*** (median 80 vs. 100 ml; p= 0.094) (2.6 vs. 5.2 %; p = 0.556), and ***Hu et al., (2011)*** (520 vs. 480 g), while another study ***Bhojani et al., (2012)*** which reported intra- and postoperative transfusions separately did not find a significant difference between the groups ***(Bhojani et al., 2012).***

In our work, there were 5cases converted from laparoscopic to open technique with percentage of 10% of group A, which is in line with data found in literature, in particular at the beginning of our experience. The main causes of conversion were excessive intraoperative bleeding in two cases and the inability to view the lesion and failure of its localization by laparoscopic intraoperative ultrasound probe in the other 3 cases. The reported conversion rate is in the range of 0%- 20%, varying mostly according to the indication for LLR ***(Edwin et al., 2011).*** In patients with cirrhosis reported conversion rates ranged from 7% to 19.4% **(Twaji et al., 2014).**

The conversion rate is also related to the complexity of the surgical procedure and accumulated experience. However, with surgical expertise the conversion rate can be reduced to < 5% in high-volume expert centers **(Hasegawa et al., 2015).**

Concerning our study, Among Group A, 49 patients (98%) had non-anatomical wedge resection while the remaining 1 patient had anatomical resection in form of segmentectomy in one patient (2%). Among group B, 49 patients (98%) had non-anatomical wedge resection while the remaining 1 patient had anatomical resection in form of segmentectomy in one patient (2%).

In patients with HCC, achieving laparoscopic anatomic resection with adequate resection margins is

difficult. Anatomical resection of the liver may be preferred for HCC for systematic removal of a segment confined by tumor-bearing portal tributaries **(Kim et al., 2017).**

However, non-anatomical resection is selected because of the patient's background, impairment of liver function and tumor factors **(Kim et al., 2017).**

As regarding the mean hospital stay in our study, the mean hospital stay in open group was 5.9±.88 days ranging from 3-7 days, while the laparoscopic group was 3.74±.85 days ranging from 2-5 days with highly statistically positive correlation difference between 2 groups (P< 0.001). Also the drain was removed in the laparoscopic group earlier showing highly statistical difference between two groups (P< 0.001).

Most studies have consistently demonstrated a significantly lower hospital stay as compared to the open approach **(Rao et al., 2012).**

As stated in the study done by ***Lee et al., (2015)*** which showed in their study high significance in shorter hospital stay in laparoscopic group (5d vs. 7d, P<0.001). Similar studies shared the same result with him and successively with our result as ***Zhang et al., (2015)*** (5d vs. 8 d P<0.001), ***Wang et al., (2015)*** (5d vs. 10 d, P<0.001). ***Bell et al., (2015)*** (3d vs. 7d, P<0.002), ***Leong et al., (2015)*** (7.5dvs 11.4d, P<0.015), ***Luo et al., (2015)*** and (10 d vs. 12 d, P<0.015) ***Kim et al., (2014)*** (12d vs. 17d, P<0.44) ***Hu et al., (2015)*** (13d vs. 20 d, P<0.01).

Better integrity of the abdominal wall may be attributable to early discharge from hospital and to reduction of pain at the surgical site. Rapid recovery from surgery and an earlier discharge from the hospital provide further evidence for the safety and feasibility of LLR **(Kim et al., 2011).**

The drain was removed in the laparoscopic group earlier than open group 2.9±0.97 vs. 4.31±1.1 days, showing highly statistical difference between two groups (P< 0.001). The use of prophylactic abdominal drainage in liver resection is a controversial. Traditionally, prophylactic drainage has been advocated for the prevention of postoperative fluid collections and the detection and drainage of bile leak. By contrast, since the late 1990s, most Western series have advised against the routine placement of drains in elective liver surgery due to negative effects of routine abdominal drainage on the incidence of postoperative infection and development of ascites.

In ***Ishizawa*** and others study, they tried to identify the clinical factors that predict failure of the "no drain" policy after laparoscopic hepatectomy (LH) in 342 consecutive patients. They concluded that prophylactic drainage during liver resection should be considered in the presence of uncontrollable bile leak, concern for postoperative bleeding risk and those in whom intraoperative blood loss is >400 ml. Otherwise, a "no drain" policy is safe and would enhance the advantages of minimally invasive liver surgery **(Ishizawa et al., 2014).**

In our study, regarding postoperative complications, postoperative ascites which was the most frequent complication in 35 (70%) cases in the open group and in 23 (46%) cases in laparoscopic group showing highly significant difference between two groups as it occurred much more frequent in open group.

Preservation of collateral circulation in the abdomen, avoiding long incisions and reducing the damage to muscle and round ligament, which may contain important collateral vessels along with other mechanisms that could be part of this phenomenon are the smaller mobilization and manipulation of the liver parenchyma, which reduces the trauma the reduced section of lymph vessels, and minor demand for intraoperative fluids **(Siniscalchi et al., 2014).** Due to these reasons, a reduced incidence of postoperative ascites in resected patients by laparoscopic approach has been reported **(Kanazawa et al., 2014).**

The reduced incidence of postoperative complications laparoscopic liver resection for HCC compared to conventional approach has been clearly reported in the literature both by single center experience **(Kanazawa et al., 2013; Cheung et al., 2013)** and by meta-analysis **(Yin et al., 2013; Xiong et al., 2012).**

Discussing the study done by ***Belli et al*** which showed that a significantly decreased postoperative morbidity rate in the laparoscopic group ***(Belli at al., 2009).***

The study done by ***Truant et al.*** showed lower rates of post-operative ascites and liver failure in the LLR group as well ***(Truant et al., 2011).***

Comparative studies as done ***Mizuguchi et al., (2011)*** showed significant decrease in the complication rate in patients undergoing LLR. A meta-analysis published by ***Mirnezami et al., (2011)*** showed a significant decrease in the incidence of liver specific complications with LLR compared with OLR.

Although laparoscopic liver resection for HCC theoretically carries the risk of seeding at the port site, reports of port-site metastasis of HCC are extremely rare. In our present study, we report a case of port-site metastasis of HCC of female patient 67 yrs. old presented with 2cm nodule in the left subcostal abdominal wall where the 10mm laparoscopic port had been inserted 10 months after performing LLR for a 3cm HCC in segment III in left lobe of the liver mostly due to contamination of the port wound during extraction of the resected tumor. After Triphasic CT was done, local excision of the nodule was performed. A scar derived from port insertion was found on the peritoneum. Histological examination of the excised

nodule confirmed moderately differentiated HCC, which was consistent with recurrence of the laparoscopically resected HCC.

There is first known published report of port-site recurrence or related peritoneal seeding in LLR for HCC was in 2011, Chen and Yen reported one case of subcutaneous seeding of HCC appearing over the surgical wound 12 months after LLR (Chen and Yen, 2011).

Liver resection gives information about the pathology of the resected tumors. A major concern regarding LLR for malignant lesions is difficulty assessing resection margins, due to the lack of tactile sensation and distance perception in laparoscopic resection (Soubrane et al., 2014). However, our study showed that there was no difference in resection margins in both series. We are able to make up for the lack of palpation in LLR and hence achieve the intended margins laparoscopically, with pre-operative surgical planning using a variety of imaging techniques and the use of intra-operative ultrasonography to demarcate surgical margins.

The best evidence available to date indicates that surgical margins in LLR are as good as in conventional procedures. Recent Comparative studies and meta-analysis as done by **(Yin et al., 2013; Twaji et al., 2015; Rao et al., 2012)** have indicated that patients operated with LLR have no increased risk of positive surgical margins.

An important reason for adequate margins relies on patient selection and surgical planning for laparoscopic cases. Surgery should be extensively planned to include peripheral tumors located away from vascular structures and far from the transection plane **(Gobardhan et al., 2014).**

Follow-up was done after one month by measuring the value of the Alpha feto-protein. Then, every 3 months for 12 months. Whenever AFP re-elevated, further imaging studies such as Triphasic CT scan was performed.

In our study, local recurrence was found to be more frequent after LLR than OLR with no significant difference (p 0.391). In LLR Group, local recurrence at the site of the treated tumor occurred in 2 patients (4%). In OLR Group, it had occurred in only one patient (2%) who was treated by TACE.

Also in our study, during follow up period, de novo lesions were found in 5 patients in LLR group (10 %) and 7 patients in OLR group (14%) and all of them were treated by TACE.

In the laparoscopic group, the 1-year survival was (98 %), while in the open group was (96%). (P=1.00).

In a study done by ***Kim et al.*** (2014) conducted on 58 patients (29 patients in LLR group and 29 patients in OLR group) showed The 1- year survivals were 100%, in LLR, and 96.5% in OLR (p = 0.267) while The 1-year disease-free survivals were 81.7% in LLR and 78.6 % in OLR, respectively (p = 0.929) **(Kim et al., 2014).**

Several factors contributed to reduce mortality after hepatectomy from 5% to almost 0%. Among these factors, better knowledge of both liver anatomy and physiology, including of liver regeneration and preoperative volume modulation, better morphological assessment, advances in parenchymal transection with the selective use of vascular control and sophisticated perioperative management have all contributed to reduce the risks associated with liver resection **(Dokmak et al., 2013).**

Limitations of our study were the total number of patients was not a large number in both groups (50 patients in laroscopic group and 50 in the open group) and the relatively short median follow-up of 12 months. Also, all patients in our study underwent minor resection or even thermal ablation and all tumors were mainly located in the peripheral portion, so the results of this study have to apply to the selected patients but not to general HCC.

Conclusion

- Laparoscopic approach in management of HCC is a safe and feasible treatment option.
- Laparoscopic approach for HCC has superior short term- comparable oncological outcomes to open liver resection and was shown not to increase the tumor recurrence risk or adversely affect oncologic outcomes.
- Lap. Approach should be performed for carefully selected patients and by an expert surgical team.
- Converting to a new surgical method does not mean that the old surgical method was a failure. With advances in surgical techniques and instruments, laparoscopic liver resection has been performed more frequently, even for tumors in difficult anatomical locations.

Recommendations

- Laparoscopy should be routinely considered in selected patients in centers experienced in liver surgery and in advanced laparoscopy.
- This study could serve as useful background research for future randomized controlled trials on lap. Approach for HCC with well-compensated liver cirrhosis.
- Further well-designed, large scale, comparative studies and randomized controlled clinical trials should be continued in this field.
- Longer follow-up periods are needed to make more definite conclusions about the comparative

survival probability of the two groups (laparoscopic and open).

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