# DIFFERENT MODALITIES IN MANAGEMENT OF HEPATOCELLULAR CARCINOMA

*By*

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**ABSTRACT**

**Background:**Historically, the diagnosis of HCC was almost always made when the disease was advanced, when patients were symptomatic and presented with a variable degree of liver function impairment **(1).**Today, many patients are diagnosed at an early stage when liver function is preserved and there are no cancer related symptoms. In addition, there are several active treatments available that will potentially have a positive impact on survival. However, to achieve the best outcomes requires the careful selection of candidates for each treatment option and the expert application of these treatments**(2).**

**Methods:**Thisprospectivestudy was conducted upon fifty patients with hepatocellular carcinoma treated from March 2008 to May 2010 with exclusion of patients with extra-hepatic metastasis in ***Zagazig University hospitals***, ***AL-Azhar University hospitals*** and ***International Medical Center (IMC)***.Our fifty patients were divided into two groups: ***Group A*** (Surgical Management) (30 patients 60%), Subdivided into (Subgroup 1)where Hepatic Resection was done in 15 patients (30%) and (Subgroup 2)whereLiving Donor Liver Transplantation was done in 15 patients (30%). and ***Group B*** (Non Surgical Management) (20 patients 40%), Subdivided into (Subgroup 3)where Radio Frequency Ablation (RFA) was done in 10 patients (20%) and (Subgroup 4)whereTrans-Arterial Chemo-Embolization (TACE) was done in 10 patients (20%).

**Results:**Regarding ***Liver Resection***; Right hepatectomy was done for 9 patients (60%) left hepatectomy for 2 patients (13.3%), atypical (localized) resection for 4 patients (26.6%). Regarding ***LDLT*** Right lobe graft was done in all 15 patients. The mean time stay in ICU was 7.4 (5-10 days). The hospitalization stay period was 20.7 (17-30 days). Regarding ***RFA***of the 10 treated patients, 20 HCC nodules were treated in 20 sessions. 2 patients were with a single session and 8 patients with two sessions. Regarding ***TACE***Seventeen sessions were done for these ten patients. 2 sessions were done in the hepatic artery proper for patients suffering from bilateral hepatic lesions, 10 sessions in the right hepatic artery and 5 sessions in the left hepatic artery for right sided & left sided hepatic tumors respectively. Seven patients had taken two sessions. While three patients received only one session.

**Conclusion:** Liver Resection still plays a key role in the treatment of patients with HCC and a good functional hepatic reserve, after accurate selection on the basis of strict criteria. Liver Transplantation is the only treatment left for many patients with end-stage liver disease which fulfill Milan Criteria.

**Keywords:***Hepato-Cellular Carcinoma, Liver Resection, Living Donar Liver Transplantation, Radio-Frequency Ablation and Trans-Arterial Chemo-Embolization.*

## INTRODUCTION

The importance of a precise knowledge of parenchymal structure, blood supply, lymphatic drainage, and variant anatomy on outcome is perhaps nowhere more apparent than in hepato-biliary surgery **(3).** With the development of hepatic surgery during the past few decades, a greater appreciation for the complex anatomy beyond the misleading minimal external markings has been realized **(4).** Major surgical complications are often avoidable and frequently the result of three tragic surgical errors. These errors are: 1) a failure to possess sufficient knowledge of normal anatomy and function, 2) a failure to recognize anatomic variants when they present, and 3) a failure to ask for help when uncertain or unsure. All but the last of these errors are remediable with study and effort. In regard to the last error, most surgeons learn humility through their failures and at the expense of their patients, while some never learn **(4).**

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**Risk factors and causes:**Both a linear dosage-effect relationship and a respective time exposure relationship can be observed: the higher the dosage and the longer the exposure, the greater is the

likelihood of carcinoma formation. The extent of risk correlates with (1) Aetiology, (2) Duration, and (3) Inflammatory activity of the liver disease. In 10-15% of patients, no risk factor could actually be determined in the development of HCC**(5).**

**Pathology:**HCC begins in the small diploid hepatocytes, which have a higher growth rate. Differentiation between RN and low-grade DN and then between high-grade DN and overt HCC is difficult. An increase in size correlates with malignancy. As these nodules grow in size, there is a loss of normal histological architecture and the portal supply is replaced by newly formed arterial vasculature **(6)**.

**Hepato-Cellular Carcinoma in Egypt:**Egypt has the largest epidemic of hepatitis C virus (HCV) in the world and well documented in the international medical scientific literature. The recently released Egyptian Demographic Health Survey [EDHS] tested a representative sample of the entire country for HCV antibody. The overall prevalence (percentage of people) positive for antibody to HCV was 14.7%.**(7)**.

**Investigations:**While non specific signs of inflammation may be present in liver cirrhosis, they are much more obvious in HCC. Conspicuous enzyme activities include a disproportionate increase in GGT, AP and LDH. This constellation is thought to be an important indicator of HCC. Hepatic synthesis capacity (albumin and cholinesterase) decreases progressively **(8).** Often the combination of imaging studies is superior to any one test alone in detecting liver pathology and the associated involved anatomy. **MRI** identifies certain intra-hepatic tumors better than CT scan, but does not outline anatomic borders as well as CT; however, due to unique aspects of MRI, it may give histologic differentiation of benign tumors, such as hemangiomas and FNH. **PET** scans are sensitive in picking up metastatic disease, but lack the resolution to define specific anatomy. Similarly, A**ngiography** is the gold standard to evaluate the intra-hepatic vasculature, but does not show the tissues through which the blood vessels flow. **US**is an excellent screening test for many patients; however, body habits, underlying hepatic disease, and overlying bowel gas can limit its use **(9).**

**Staging and Prognosis:**Staging is essential for the management of HCC, as the choice of therapy depends on the functional state of the liver and the extent of tumor growth. The functional status of the liver in a patient with cirrhosis is usually assessed by the Child-Pugh classification **(10).** The prognosis of solid tumors is generally related to tumor stage at presentation and thus tumor stage guides treatment decisions. However, in HCC patients the prediction of prognosis is more complex because the underlying liver function also affects prognosis. There is no worldwide consensus on the use of any given HCC staging system, and which is the preferred system remains controversial. Any staging system should classify patients into subgroups with significantly different outcomes, and at the same time should help to direct therapy **(11).**

**Surgical Management of HCC:A. Surgical Resection:**This is the treatment of choice for HCC in non-cirrhotic patients, who account for just 5% of the cases in Western countries, and for about 40% in Asia. These patients will tolerate major resections with low morbidity, but in cirrhosis candidates for resection have to be carefully selected to diminish the risk of postoperative liver failure with increased risk of death **(12).** After resection, tumor recurrence rate exceeds 70% at 5 years, including recurrence due to dissemination and de novotumors. The most powerful predictor of recurrence is the presence of micro-vascular invasion. This suggests that the majority of recurrences are due to dissemination from the primary tumor and not metachronous tumors developing in a liver with cirrhosis. Furthermore,

recurrence due to dissemination is more likely to appear during the first 3 years of follow-up **(13).** Complications of hepatic resection include; intra-operative haemorrhage, post-operative haemorrhage, subacute hepatic insufficiency (ascites, encephalopathy, jaundice, GI bleeding), bile leak, acute hepatic failure, sepsis, abscess, biliary stricture, arterio-venous fistula, hepatic artery pseudo-aneurysm or renal failure **(14).**

**B. Living donar Liver transplantation (LDLT):**Living donation has been advocated in the setting of HCC. The degree of liver dysfunction due to cirrhosis is assessed by the Child-Pugh point scoring system consisting of clinical and biochemical measurements.More recently Model for End-Stage Liver Disease (MELD) has replaced the Child Pugh score as a predictor of death within 3 months due to chronic liver disease. MELD is based on serum creatinine, bilirubin and INR **(15).**Evaluation of patients for liver transplantation involves a multidisciplinary approach by transplant hepatologists and surgeons, dieticians, psychologists, social workers, transplant coordinators and radiologists. A comprehensive medical assessment is essential to determine significant co-morbid conditions that may preclude transplantation, or negatively impact on the patient's peri-operative and/or postoperative course. Evaluation of the extent of liver disease, the presence of complications of cirrhosis, and the need of urgency for transplantation are important. Tumor characteristics including size, number of lesions, and anatomical location are the cornerstone to preoperative staging and strongly influence patient management **(16).** ***Milan Criteria*** for liver transplantation for HCC include; Single tumor <5 cm diameter, Up to 3 tumors <3 cm diameter, No vascular invasion and No extra hepatic disease. But ***UCSF*** Criteria include; Single tumor <6.5 cm diameter, No more than 3 tumors largest <4.5 cm and Total diameter <8 cm **(17).** While all four allografts have been successfully applied to select adult recipients, the right lobe allograft, accounting for greater than 60% of the donor's total liver mass, is the most commonly employed allograft for LDLT worldwide. Utilization of a right lobe allograft was initially described by **Habib**and **Tanaka** of Kyoto, who were attempting to harvest a left lobe for LDLT when anatomical considerations favored a right lobe hepatectomy**(18).** The transplantation procedure usually involves four stages:(1) Hepatectomy of the diseased native liver (2) Anhepatic stage, which is the time interval between liver removal and interruption of blood flow through the IVC, PV, and HA (3) Reperfusion stage when the donor liver is being revascularized in the recipient and (4) Biliary reconstruction stage **(19).** Postoperative complications are a major concern both in the donor and the recipient. Bile leak, bleeding, thrombosis, or infection may occur in either the recipient or the donor, or both. Rejection is an additional complication in the recipient. The LDLT procedure has been found to be safe both for the donor and the recipient **(20).**

**Non Surgical Management of HCC:A. Radio Frequency Ablation (RFA):**Radiofrequency thermal ablation (RFA) works by converting RF waves into heat. The alternating current passing down from an un-insulated electrode tip into the surrounding tissues generates changes in the direction of ions and creates ionic agitation and frictional heating. The tissue heating then drives extracellular and intracellular water out of the tissue, which results in the final destruction of the tissue as a result of coagulative necrosis **(21).** RFA has a specific role in dealing with multiple metastases. Patients who were considered unsuitable for surgery at initial presentation due to the presence of multiple or bilateral lesions, surgical resection could be achieved in one segment or lobe while the multiple small deposits in the remaining lobe or segments could be successfully ablated. So the resectability of

those patients was increased **(22).** Common causes of major morbidity following RFA are bile leaks, liver abscesses at the ablation sites, haemorrhage, heat damage to surrounding organs and fulminant liver dysfunction. Local control can be a problem and local recurrences are variable and often unacceptably high. Once these tumors recur, they are often more difficult to treat and are associated with a worse prognosis **(23)** .

**B. Trans-arterial Chemo-embolization (TACE):**The objectives of TACE are clear and consist of delivering high concentrations of chemotherapeutic agents directly to the tumor cells. In addition, the oily medium (lipiodol) enhances the antitumor effect of chemotherapy because it remains within HCC nodules for long periods of time, allowing prolonged contact time between cancer cells and the chemotherapeutic agents. Finally, particle embolization of the tumor-feeding arteries renders the tumor ischemic, which may also potentiate the effects of the chemotherapy by allowing the drugs to penetrate inside the cancer cells with greater ease. However,several recent studies have shown that tumorischaemia and hypoxia upregulate severalmolecular factors, such as the vascular endothelialgrowth factor (VEGF) and hypoxia induciblefactor-1 (HIF-1), thereby preventing cell apoptosisand stimulating tumor metabolism, growth andinvasion**(24).** Several variations of TACE protocols have been used to combat HCC; however, neither the optimal chemotherapeutic agent nor the best embolization method has yet been established. Non-occlusive and occlusive techniques have been described and single drug therapies or combinations of agents have been used. Several types of embolic agents have been utilised in conjunction with lipiodol for chemoembolization, including gelfoam powder and pledgets, polyvinyl alcohol, starch and glass microspheres. The most widely used single chemotherapeutic agent is doxorubicin and the combination of cisplatin, doxorubicin and mitomycin C is the most common drug combination infused **(25).** Chemoembolization can be hazardous with the potential for numerous procedural errors and complications such as liver failure, abscess or infarction, biloma, cholecystitis, and the effects of extra-hepatic embolization **(26).**

**Methods: Group A (surgical management) (30 patients 60%):Subgroup (1): Liver resection:**15 patients were managed by liver resection (30%), 9 of them done right hepatectomy (18%), 2 of them done left hepatectomy (4%) and 4 of them done non anatomical resection (8%).

**Follow up:Early postoperative (2-4 weeks):**Complete laboratory investigations were done including: CBC, LFT, KFT and Coagulation profile.

Clinical and radiological evaluation were done by abdominal US for detection of early postoperative complication. CT was done if the US is not conclusive.

**Long-term follow up:** Patients' data were collected at three months, six months, twelve months and eighteen months up to May 2010. Clinical follow up, Laboratory results CBC, LFT, KFT and bleeding profile, Radiological changes (US) and Level of alpha feto-protein.

**Subgroup (2): Living Donar Liver Transplantation (LDLT):**15patientswere managed byLDLT (30%) all of them with right lobe graft.

**Inclusion criteria for LDLT:** Patients with Child class C. Milan criteria: Single mass less than 5 cm or two to three masses less than 3 cm. After fulfillment of these investigations there is informed special consent for each of these patients; they had to sign it. Full explanation about the severity of the surgical technique to both patients was done. Also stress for the donor on the possible complications that may happen. Lastly the post operative period for the recipient including post operative ICU period, follow up

investigations and immuno-suppressive drugs which will continue for life.

**Follow up: A. Short term: For donor:**Patients were admitted to ICU for one to two days, then about another five days in word with daily:

CBC,LFT, KFT, Bleeding profile and Abdominal US.

After discharge the patient followed up for one month with weekly investigations as before.

**For recipient:**Patients were admitted to ICU for about one week with daily: CBC,LFT,KFT, RBS, Blood gasses, LDH,ammonia,bleeding profile, Chest X ray, Liver duplex,Abdominal US andImmuno-suppressive level.

Then patients admitted to isolation room for about another two weeks with daily:

CBC, LFT, KFT, RBS, Abdominal US, liver duplex chest X ray and CT were done as needed. The level of immuno-suppressive is also done every three days to adjust the dose and to change the regimen when needed.

**B. Long-term follow up:** It was done till May 2010. It collected data of the patients at three months, six months, twelve months & eighteen months including:

Clinical follow up, Laboratory results(CBC, LFT, KFT and bleeding profile), Radiological changes (US), Level of alpha feto-protein and Immune-suppressive level.

**Group B (non surgical management) (20 patients 40%):Subgroup (3): Radio Frequency Ablation (RFA):**10 patients were managed by RFA(20%). We assessed the efficacy of the RF ablation by using spiral CT within 2-5 weeks after the procedure and by using alpha fetoprotein assays within 10-15 days after the procedure. The presence of well defined, non-enhancing tissue on images obtained during both phases of contrast-enhanced CT was indicative of tissue necrosis. The maximum diameters of these non enhancing areas were equal to or larger than the maximum pretreatment diameters of the HCC nodules.A second RF procedure was planned for one patient who did not show complete response after the first procedure. Long term follow up studies included serum alpha fetoprotein assay and US every 3 months and spiral CT every 3 months in the 1st year and every 6 months thereafter up to 2 years.

**Subgroup (4): Trans-Arterial Chemo-Embolization (TACE):**10 patients were managed by TACE (20%). Non-contrast CT scan was done on the second day after the procedure to assess post-embolization lipiodol distribution. Follow-up ultrasonography and liver function assessment were done after three weeks. Pre- and post-contrast CT scan was done after 6 weeks to determine the residual lipiodol distribution, residual enhancement within the lesion to detect development of recent tumor nodule and to plan the next chemo-emobolization session.

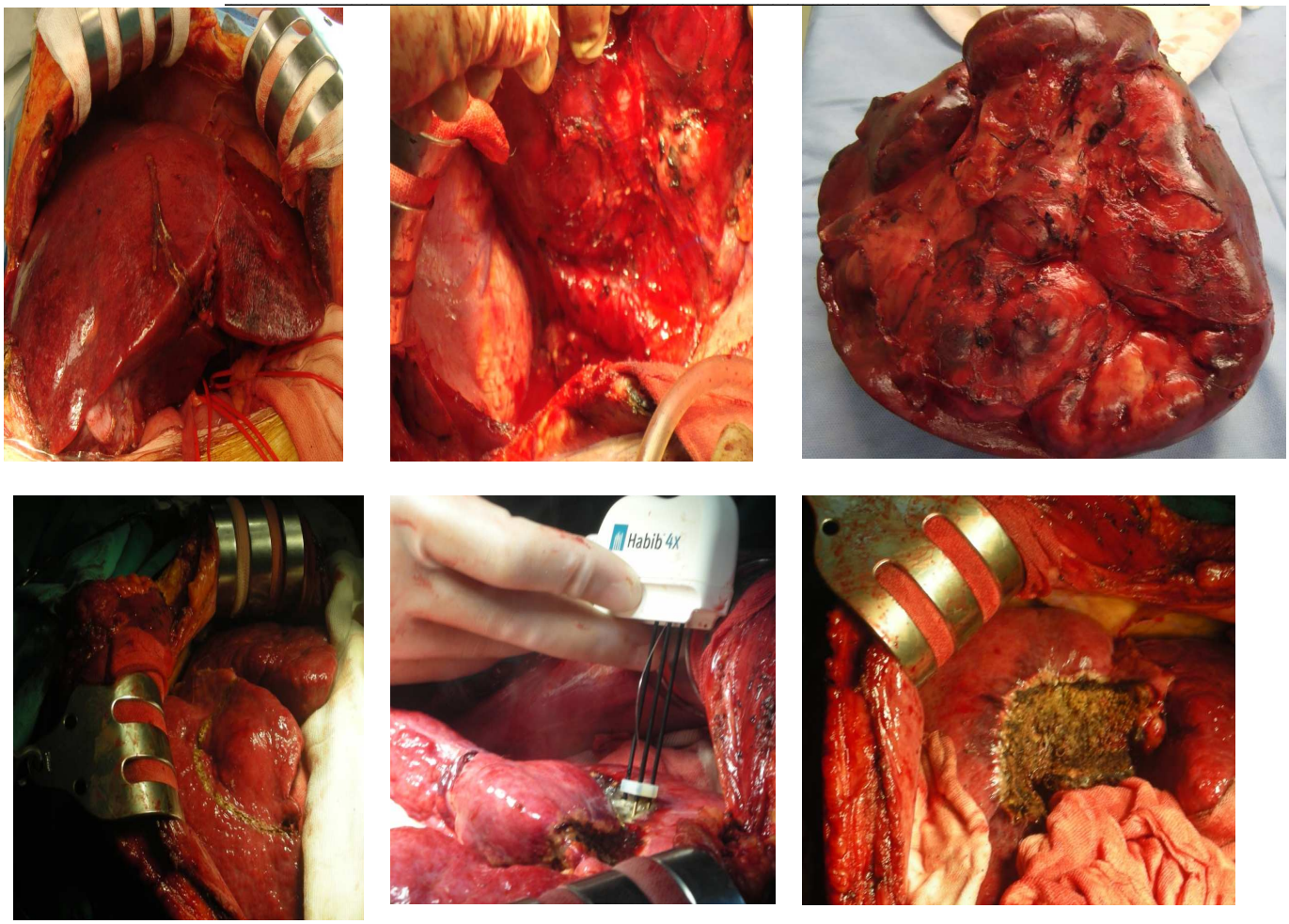
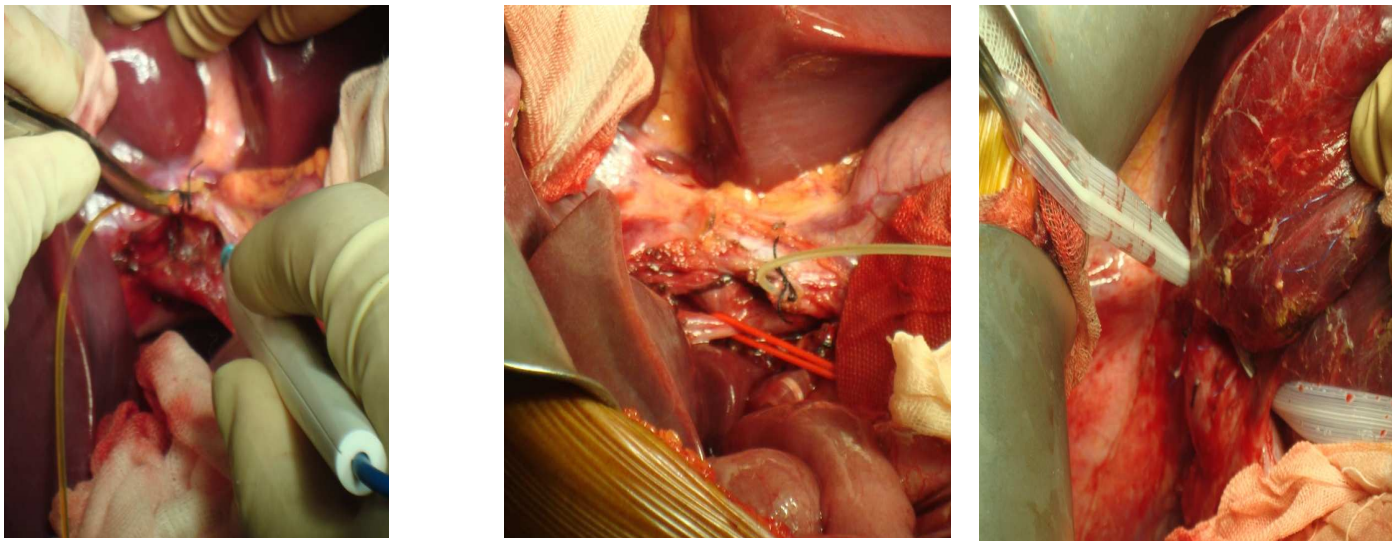



**Fig. (1)** Shows liver resection operation.



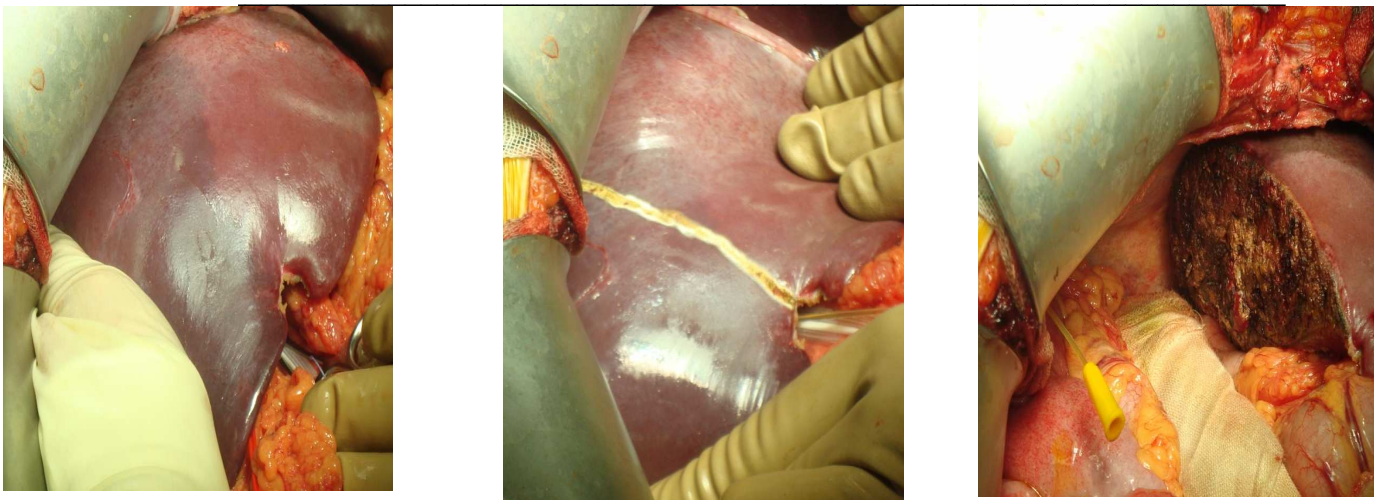


**Fig. (2)** Shows donor operation

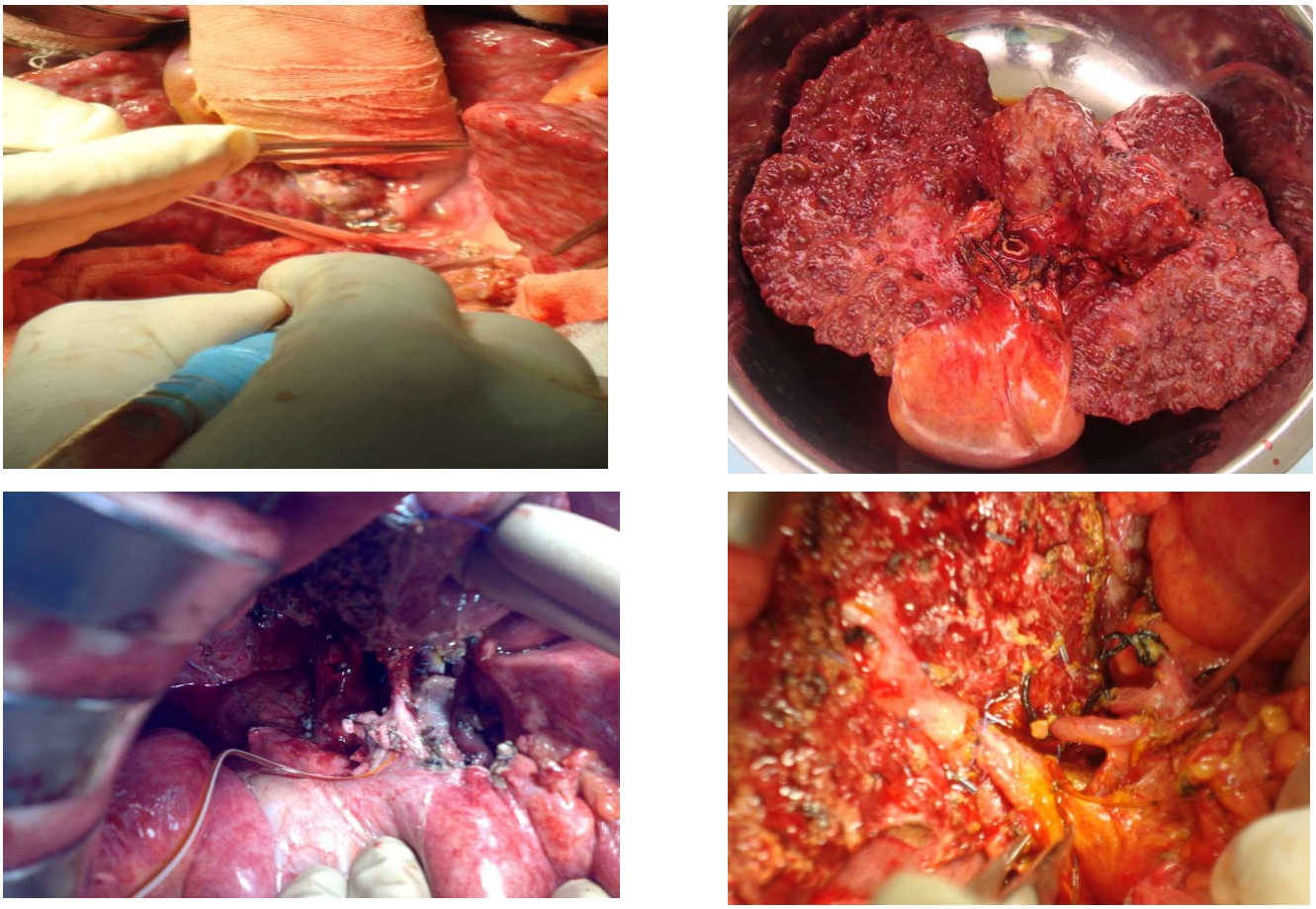


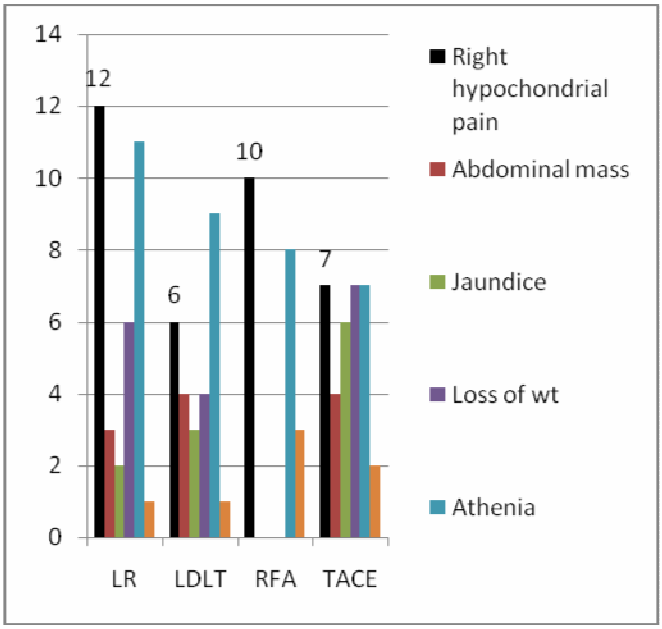
**Fig. (3)** Showsrecepient operation.

## Results: A. Clinical analysis:

Table (1) shows age and sex distribution of our patients.

| Variable | Surgical | | Non Surgical | | Total |
|---|---|---|---|---|---|
| | Subgroup (1) | Subgroup (2) | Subgroup (3) | Subgroup (4) | |
| **Age:** | | | | | |
| < 50 | 2 (4%) | 2 (4%) | 1 (2%) | 0 | 5 (10%) |
| 50-60 | 11 (22%) | 13 (26%) | 8 (16%) | 5 (10%) | 37 (74%) |
| >60 | 2 (4%) | 0 | 1 (2%) | 5 (10%) | 8 (16%) |
| **Sex:** | | | | | |
| Male | 11 (22%) | 13 (26%) | 9 (18%) | 9 (18%) | 42 (84%) |
| Female | 4 (8%) | 2 (4%) | 1 (2%) | 1 (2%) | 8 (16%) |

They were classified according to their ages into 3 groups, the first one included 8 patients above 60 year (16%), 37 patients between 50 and 60 years (74%) in the second group and 5 patients (10%) below 50 years in the last group. With a mean age of 55.84 years.




{Fig.(4) Shows different presentations in our 4 subgroups}.

**B. Laboratory investigations:**

Patients are classified according to child Pugh as shown in table (2).

| Class | No. of patients % | | | | X2 | p |
|---|---|---|---|---|---|---|
| | surgical | | Non Surgical | | | |
| | Subgroup (1) | Subgroup (2) | Subgroup (3) | Subgroup (4) | | |
| Class A | 15 | 0 | 0 | 0 | 36.12 | 0.001* |
| Class B | 0 | 0 | 10 | 10 | 36.11 | 0.001* |
| Class C | 0 | 15 | 0 | 0 | 50.0 | 0.001* |
| Total | 15 | 15 | 10 | 10 | | |

## C. Radiological investigations:

Preoperative abdominal ultrasound and tri-phasic CT revealed site and size of the tumor.

Table (3) shows tumor size and number of masses in our patients.

| Variabe | surgical | | Non Surgical | |
|---|---|---|---|---|
| | Subgroup (1) | Subgroup (2) | Subgroup (3) | Subgroup (4) |
| **Tumor size:** | | | | |
| 3cm | 5 (10%) | 7 (14%) | 2 (4%) | 0 |
| >3cm | 10 (20%) | 8 (16%) | 8 (16%) | 10 (20%) |
| **No of masses:** | | | | |
| Single | 10 (20%) | 11 (22%) | 2 (4%) | 1 (2%) |
| Multiple | 5 (10%) | 4 (8%) | 8 (16%) | 9 (18%) |
| **Site (lobe):** | | | | |
| Right | 11 | 11 | 5 | 4 |
| Left | 4 | 2 | 2 | 2 |
| Both | 0 | 2 | 3 | 4 |

**Group A (surgical management):Sub-Group (1): Liver resection (15 patients):Morbidity and mortality:**

Table (4) Complications of surgery in liver resection group.

| Variable | Number | % |
|---|---|---|
| **Surgical resection** | 15 | 100% |
| **A) Early complications:** | | |
| 1.Intra-operative bleeding. | 2 | 13.3% |
| 2.Acute LCF. | 2 | 13.3% |
| 3.Bile leak | 2 | 13.3% |
| 4.Intra-peritoneal collection. | 2 | 13.3% |
| 5. Wound infection. | 1 | 6.6% |
| 6. Pleural effusion. | 2 | 13.3% |
| **B) Late complications:** | | |
| 1. recurrence | 3 | 20% |
| 6 month | 1 | 6.6% |
| Within 2 years | 2 | 13.3% |
| 2. Liver cell failure | 2 | 13.3% |

Table (5) Factors affecting recurrence rate in liver resection group.

| Pathological variables | No | % | X2 | P |
|---|---|---|---|---|
| **1) Vascular invasion** | | | | |
| a. with (2) | 2 | 100% | 4.36 | 0.03* |
| b. without (13) | 1 | 7.6% | | |
| **2) Grade of differentiation** | | | | |
| a. Well differentiated (3) | 0 | | 3.28 | 0.19 Ns |
| b. Mod. differentiated (8) | 1 | 12.5% | | |
| c. undifferentiated (4) | 2 | 50% | | |
| **3) Active cirrhosis** | | | | |
| a. with (3) | 2 | 66.6% | 5.1 | 0.02* |
| b. without (12) | 1 | 8.3% | | |
| **5) Satellites** | | | | |

| | | | | |
|---|---|---|---|---|
| a. with (1) | 1 | 100% | 4.29 | 0.03* |
| b. without (14) | 2 | 14.2% | | |
| **6) Tumor size** | | | | |
| a. ≤ 3cm (5) | 0 | 0% | 0.47 | 0.49 Ns |
| b. >3cm (10) | 3 | 30% | | |
| **7) Hepatitis virus** | | | | |
| a. Positive B&C (2) | 1 | 50% | 0.04 | 0.81 Ns |
| b. Negative C (15) | 2 | 13.3% | | |
| **8) Type of surgery** | | | | |
| a. Right (9) | 3 | 33.3% | 2.5 | 0.28 Ns |
| b. Left (2) | 0 | 0% | | |
| c. Non anatomical (4) | 0 | 0% | | |
| **9) Blood transfusion** | | | | |
| a. without (4) | 0 | 0% | 0.19 | 0.66 Ns |
| b. with (11) | 3 | 27.2% | | |

Mortality: Six months and 18 months mortality was 13.3% and 26.6% respectively. The causes of death in this group were intra-operative bleeding in one patient, liver cell failure in three patients, and progression of the tumor with local & distant metastasis in two patients.

Sub-group (2): Living Donar Liver Transplantation (LDLT) (15 patients):Morbidity and Mortality:

1. Recipient:

Table (6) Complications of surgery (LDLT group) (recipient).

| Variable | Number | % |
|---|---|---|
| **Liver transplantation (recipient)** | | |
| **a) Early complications** | | |
| 1. Bleeding. | 1 | 6.6% |
| 2. Wound infection. | 2 | 13.3% |
| 3. Bile leak. | 2 | 13.3% |
| 4. Septicaemia. | 1 | 6.6% |
| 5. Pleural effusion. | 2 | 13.3% |
| **b) Late complications** | | |
| 1. Bile stricture. | 2 | 13.3% |
| 2. Recurrence. | 1 | 6.6% |
| 3. Liver cell failure. | 1 | 6.6% |

Mortality: **Six months and two years mortality was 13.3% and 26.6% respectively. The causes of death in this group were intra-operative bleeding in one patient, septicaemia in another patient, liver cell failure in one patient, and progression of the tumor with local & distant metastasis in one patient.**

**2. Donors:**

Table (7) Complications of surgery (LDLT group) (donar).

| Variable | Number | % |
|---|---|---|
| Wound infection. | 2 | 13.3% |
| Bile leak. | 1 | 6.6% |
| Biloma. | 1 | 6.6% |

**Mortality:**no mortality was present in our donors.

**Group B (non-surgical management): A. Sub-Group (3): Radio Frequancy Ablation (RFA) (10 patients):Morbidity and mortality:**Generally the patients tolerated the procedure well. No fatal or major complications related to this way of management.

Three (30%) of the 10 patients experienced mild to moderate abdominal pain during the RF procedure, this was treated medically. Other three patients (30%) complained from persistent fever for 24 hours. Ascitis was found in two patients (20%) diagnosed by follow up US. One patient (10%) was with haematoma which was managed conservatively.No late complications were observed. One patient (10%) died of unrelated cause (cardiac cause; heart failure).

**Sub-Group (4): Trans-Arterial Chemo-Embolization (TACE) (10 patients):Morbidity:**Post TACE syndrome in the form of persistent unrelieved pain, fever and vomiting for more than one week occurred in one patient. Other complications were; mild anaphylaxis, puncture site hematoma, fever and ascitis occurred in four patients with complete rapid relieve on the same or next day. **Mortality:**Six months, one year and 18 months mortality was 80%, 50% and 20% respectively. The causes of death in this group was liver cell failure in 2 patients, progression of the tumor with incomplete response to therapy in 3 patients and local & distant metastasis in 3 patients.

## DISCUSSION

Hepato-Cellular Carcinoma is especially difficult to treat because cancerous tumors typically arise in the setting of underlying liver disease or cirrhosis. As a result, actual destruction of the cancer may not be enough to cure the patient if damage to the underlying functioning liver is too significant. This may explain the relative failure of the traditional weapons against liver cancer. Surgical resection and liver transplantation are the only two treatment options that offer the possibility of a cure. However, only 10%–15% of patients with HCC are eligible for such treatments, either because of the advanced stage of the disease at the time of diagnosis, thereby limiting hepatic reserve, or because of the presence of co-morbid disease **(27).** The limitations of the traditional weapons against liver cancer (surgery, systemic chemotherapy, and radiation therapy), combined with the fact that liver cancer has a tendency to stay confined to the liver, have led to the hunt for new forms of therapy that share a common concept, namely that of loco-regional therapy. A role for loco-regional therapy can be further justified by the fact that patients with HCC usually die of liver failure as a result of local growth and resultant liver tissue destruction, but not as a result of extra-hepatic metastatic disease. Loco-regional therapies are now commonly used to treat un-resectable liver cancer **(28).**

Our study included 15 patients who underwent liver resection. Regarding their age; 2 patients were less than 50 years, eleven between 50 - 60 years and 2

patients were more than 60 years. Eleven of them were males and four were females. Regarding Liver Donar liver Transplantation (LDLT) our study included 15 patients; two patients were less than 50 years and 13 patients were between 50 and 60 years. Regarding sex; 13 patients were males and only two female patients were present. In radio frequency group there were 10 patients. One patient was under 50 years, 8 patients were between 50 and 60 years and one patient above 60 years. 9 patients were males and 1 patient was female. Ten patients was our number in Trans-Hepatic Chemo-Embolization (TACE group). Five patients were between 50 and 60 years and another five patients above 60 years. Nine patients were males and one was female.

Our fifty patients were classified according to Child Pugh score into 15 patients with Child A, 20 patients with Child B and lastly 15 patients with Child C. Hepatitis C infection was positive in our 50 patients but combined HBV& HCV infection was in 8 patients.

Mass size less than or equal to 3cm was found in 14 patients. 36 patients had mass size more than 3cm. 24 patients were with single masses and 26 patients with multiple masses. Regarding site of masses, 31 patients were with right lobe masses, 10 with left lobe masses and 9 patients were with bilateral masses.

Regarding biliary anastmosis in LDLT group, which is the most common complication in LDLT. We used duct to duct technique in biliary anastmosis in 7 patients and hepatico-jejunostomy in 3 patients, also we put stents in all our cases.Biliary anastmosis in **(29)** study was**;** Among the 310 patients reviewed, hepatico-jejunostomy was primarily performed in 87 patients (28%), and duct-to-duct anastomosis was performed in 223 patients (72%). A biliary anastomotic stent tube was placed in 266 patients (86%) at the time of transplantation in this series.

Complications following hepatectomy in cirrhotic patients are common. This is attributed to inadequate liver reserve, bleeding tendency and usually poor general condition. Complications may be early in the first 30 days post-operative or late after this period. The most important and common late complication of liver resection is recurrence. Regarding our results, recurrence was in 3 patients (12%), one patient developed recurrence after 6 months, 2 patients within two years. Recurrence incidence was 8%, 52.5% and 71% at 6 months, one year and 2 years respectively.**(30)**, after a median follow-up period of 34 months, 98 patients (51%) had recurrent cancer; initial tumor recurrence was confined to the liver in 86 patients (88%).

Regarding LDLT group early complications were one patient complicated with intra operative bleeding. Septicaemia was in one patient. Wound infection (seroma) was in 2 patients. Bile leak was in 2 patients in which both cases underwent re-exploration with hepatico-jejenostomy bile diversion after evacuation of the biloma. Lastly Pleural effusion was in 2 patients.**(31)** had encountered 50 complications in 222 right lobe grafts, mostly biliary.Four of the **donors in LDLT group** showed complications. Two of them complained from wound infection. Another two patients showed biliary leak. This was also with **Hwang et al., (2006),** as there was no donor mortality in this series.

## CONCLUSION

Unlike the incidence and death rate of most cancers that have stabilized or decreased during the past two decades, the incidence of HCC has been steadily increasing. HCC is usually diagnosed at a late stage, with many patients presenting with upper abdominal pain, weight loss, ascites, and other sequelae of portal hypertension.

***Liver Resection*** still plays a key role in the treatment of patients with HCC and a good functional hepatic reserve, after accurate selection on the basis of strict criteria. In these cases surgery achieves good survival rates with acceptable peri-operative

morbidity; in order to make surgery fully competitive with other treatments, the goal should be the achievement of zero mortality. Non-anatomic resection has no adverse effects on the oncologic outcomes of single and small (≤ 4 cm) HCC in patients with well preserved liver function (Child-Pugh class A).

***Liver Transplantation*** is the only treatment left for many patients with end-stage liver disease. The optimal candidates for transplantation are patients with a single HCC < 5 cm or with up to 3 nodules < 3 cm in diameter. In conclusion, there is really no doubt that liver transplantation offers better survival than liver resection in patients with early stage tumors, compensated cirrhosis, and hepatitis C. However, delay in access to liver transplantation may minimize the benefits of liver transplantation and make liver resection an equivalent or preferable option in regions where time to transplant exceeds 6months.

Treatment with ***Radio Frequency Ablation***, local ablation is safe and effective as palliative therapy for patients who cannot undergo resection, or as a bridge to transplantation.

***Trans-Arterial Chemo-Embolization*** should be used for multi-nodular (>3 nodules) HCC. TACE considered for patients with nonsurgical hepatocellular carcinoma that are also ineligible for percutaneous ablation, provided there is no extra-hepatic tumorspread. The main contraindication is the lack of portal blood flow.

As we have in Egypt a high incidence of HCV infection, which proved to have a direct relation with occurrence of HCC. So we recommend a surveillance program to provide a data-supported approach to the diagnosis, staging, treatment and management of HCC.

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