

Hepatocellular carcinoma from diagnosis to treatment: 15 years of challenges and modification of resection strategies

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Background

Hepatocellular carcinoma (HCC) is a dismal tumor with a high incidence, prevalence, and poor prognosis and survival. Management necessitates multidisciplinary clinics due to the wide heterogeneity in presentation, different therapeutic options, and variable biologic behavior, especially with a background of chronic liver disease.

Patients and methods

This study was conducted in a specialized hepatobiliarypancreatic (HBP) clinic in Assiut University Hospital and Sohag University Hospital. We studied different types of patients and tumor characteristics with evaluation of the surgical management applied to them. Further analysis was performed using univariate and multivariate statistics.

Results

From December 2000 till March 2014, 220 patients with HCC presented to our clinics; they were predominantly male (mean age 56 years), mostly with cirrhosis due to hepatitis C virus (71%), with Child–Pugh A (52%) or Child–Pugh B (32%), and with a single lesion. Transarterial chemoembolization was the most common treatment (32.4%), followed by ablation therapy (27%). A major section was treated palliatively due to delayed discovery and advanced stage of the disease (63%); resection was the standard in operable cases (25.4%). Nonanatomic resection was commonly performed in 58% of the cases; however, other techniques were also used such as anatomic resection (27%) and laparoscopic resection (15%); unfortunately, the transplantation program was not yet started to be added in treatment. The overall survival was 80% at 6 months, 55% at 1 year, and 20% at 2 years. Serum bilirubin, portal hypertension, the site of the tumor, and the type of treatment were significant independent prognostic factors for survival.

Conclusion

Early discovery by surveillance protocols is very essential for better outcome; early interference, whether by surgery or by ablation, is a good substitute in the absence of transplantation programs. Our main prognostic variables are the bilirubin level, portal hypertension, bilobar affection, and the application of specific curative or palliative treatment. Multidisciplinary clinics enhance better HCC management.

Keywords:

hepatocellular carcinoma, multidisciplinary, prognosis, survival

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Introduction

Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer [1]. Worldwide, liver cancer is the fifth and the seventh most common cancer in men and in women, respectively. Most of the burden lies in developing countries. The regions of high incidence include Eastern and South-Eastern Asia and Middle and Western Africa. It is the third most common cause of death from cancer. Its high fatality is reflected in the high (0.93) mortality-to-incidence ratio [2]. In Egypt, liver cancer is the fourth most common cancer and is the second cause of cancer mortality in both sexes [2]. Risk factors for HCC are many and include hepatitis B virus and hepatitis C virus (HCV), cirrhosis, aflatoxins, alcohol, smoking, and male sex [3]. These risk factors vary among

countries, but chronic infection with hepatitis B virus and HCV are the most important precursors for HCC development on a global scale, together accounting for over 80% of the liver cancer cases. Worldwide, HCV infection is one of the most serious health problems. HCV-related liver disease can progress over several decades in an insidious manner, with liver cirrhosis and HCC in the advanced forms of the disease. About one-quarter of the patients with HCV chronic infection are estimated to develop liver cirrhosis 15–25 years later. In patients

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with compensated liver cirrhosis related to HCV, 1.8–8.3% develop HCC each year [4]. In Egypt, HCV is the main risk factor for HCC, where 71% of the HCC cases are positive for anti-HCV antibodies [5]. As different treatment modalities of HCC may prolong survival in some cases, this will not reflect the prognostic values of some factors accurately.

The only proven potentially curative therapy for HCC remains surgical, either hepatic resection or liver transplantation (LT); patients with a single small HCC (<5 cm) or up to three lesions less than 3 cm should be referred as a candidates for these treatment modalities [6]. However, only 30% of the patients with HCC are eligible for surgery, mainly because of the multiplicity of the lesions that often occurs in a background of chronic liver disease [7–9]. Over the past 10 years, there has been considerable progress in the diagnosis and the surgical treatment of HCC. The tumors are more often identified at an early stage, in particular through the screening of high-risk patients [10–13]. Surgery is safer, with an acceptable overall mortality rate in cirrhotic patients (55%); also, good long-term survival, up to 45%, is achieved after adequate anatomical resections [14,15]. Partial resection is associated with a high incidence of tumor recurrence, mainly due to the presence of the chronic underlying liver disease, which is a preneoplastic state [16]. Therefore, because LT removes the tumor(s) and the preneoplastic underlying chronic liver disease, LT appears to be the treatment of choice for small HCCs [8]. However, to avoid tumor recurrence, LT indications for HCC are restrictive and the limited availability of grafts and the cost of the LT represent the main potential limiting factors for its development [17]. In the vast majority of the cases, HCC develops in the setting of cirrhosis, but 5–15% of the patients have no underlying chronic liver disease [18]. Usually, the etiology of HCC development is undetermined; however, HCC tumors in patients with a normal liver are often large (>10 cm) and diagnosed when tumors are symptomatic [19,20]. The only curative treatment is major hepatectomy, which is often well tolerated in the absence of underlying liver disease and the good regenerative capacity of the remnant liver. The long-term results of resection of HCC without chronic liver disease are much better than in patients with cirrhosis, with disease-free 5-year survival rates as high as 50% [21,22]. These favorable results observed in both fibrolamellar and nonfibrolamellar HCC variants suggest that the absence of an underlying liver disease is a major factor in short-term and long-term prognoses [9,21].

The role of hepatic resection in the treatment of multiple and bilobar HCCs is more controversial [23–26]; bilobar HCCs may represent advanced disease with intrahepatic metastasis from one lobe to the other or may represent multifocal HCCs. However, in some selected patients with good liver function, the presence of a small solitary lesion in the contralateral lobe should not contraindicate the resection of the main tumor, and in selected cases, major hepatic resection can be associated with wedge resection or local ablative therapy (if the lesion is not superficial) [27,28]. Therefore, when possible, anatomical resection should be the treatment of choice and considered as the reference surgical treatment when comparing it with other treatments. Moreover, when anatomical resection does not seem to be possible, either because of the tumor location and/or the degree of the liver function, other therapeutic options such as LT and/or percutaneous treatment are considered [29].

Nonsurgical therapy should be used only when surgical therapy is not possible for instance, percutaneous ethanol injection to produce necrosis of small HCC is best suited to peripheral lesions, less than 3 cm in diameter. Radiofrequency ablation (RFA) is a good alternative ablative therapy. Chemoembolization can produce tumor necrosis and has been shown to affect survival in highly selected patients with a good liver reserve; using lipiodol is effective for pain or bleeding from HCC. Systemic chemotherapy with standard agents has a poor response rate and should be offered only in the context of trials of novel agents [6]

Patients and methods

This retrospective study was conducted at Assiut University hospitals and Sohag University hospitals, Assiut and Sohag Governorate, Egypt. These are the largest referral tertiary-level centers all over the Upper-Egypt territory. The study was approved by local faculty ethical committee, with a written consent from each patient included in the study. It included a random sample of 220 patients encountered, studied, and treated with various treatment modalities, except transplantation, which was not feasible during that period. The protocol was approved by local faculty ethical committee.

Tumor characteristics, investigations, staging, treatment modalities, and follow-up data were analyzed with evaluation of treatment protocols and its modification with time after the introduction of new tactics, drugs, and surgical techniques and the resulting cumulative experience of the team.

Results

This retrospective study included a random sample of 220 HCC patients who attended Assiut and Sohag University hospitals between December 2000 and March 2014. Their age ranged between 29 and 72 years, with a median of 50.5 years, with male predominance, as the male-to-female ratio was 5.6 : 1 (Table 1).

Preoperative assessment of patients

Almost two-thirds of the patients (142 patients about 64.5%) had a smoking history. The viral hepatitis markers status was determined in 86 patients and was positive in 38% of them, with HCV being the most predominant type among them (80%). Most of the patients (84%) had some evidence of cirrhosis, by clinical, imaging, or laboratory tools, with a history of schistosomiasis in 113 (51.3%) patients. Routine follow-up of cirrhotic patients led to the discovery of HCC among 50.9% of our patients, whereas symptomatic presentation accounted for the rest of them, the most common presentation being abdominal pain (26.4%), followed by jaundice (13.6%); however, a minority of them presented with other symptoms such as fatigue or ascites (20 patients, 9.1%). A minority of the patients (9.7%) had a positive family history of HCC. Child-Pugh A [diagnosed in 115 (52.2%) patients] and Child-Pugh

B [in 73 (33.1%) patients] were more prevalent in our study than Child-Pugh C, which was encountered in only 32 (14.5%) patients.

Concerning the tumor characteristics (Table 2), a single lesion (52.8%), right-lobe predominance (65.5%), and size smaller than 3 cm were the predominant features. Most of our patients (67.2%) had increased alpha feto protein (AFP) tumor marker (cut-off titer value <400 ng/ml). Features of more advanced HCC involvement such as portal-vein thrombosis, significant abdominal lymphadenopathy, and distant metastases were evident in the minority of the cases (17.2, 7.2, and 1.4%, respectively).

Treatment strategy

According to the Barcelona clinic liver cancer guidelines, different lines of treatment were offered to the patients (Fig. 1), such as curative treatment

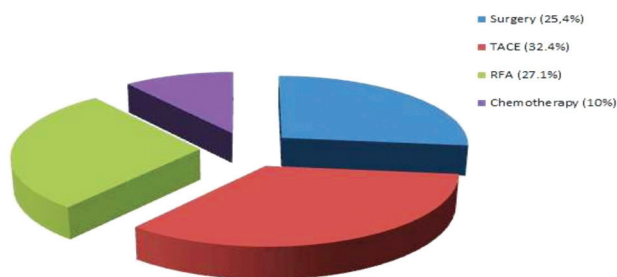
Table 1 Clinical characteristics of the patient sample studied

Characteristics	N (%)
Demographics	
Age (mean±SD) (years)	56.5±7.7
Sex	
Male	185 (84.1)
Female	35 (15.9)
Risk factors	
Smoking (number of patients assessed)	220
Yes (positive history)	142 (64.5)
Hepatitis (number of patients assessed)	86
Yes (positive patient)	67 (77.9)
Known hepatitis C	39 (58.2)
Known hepatitis B	11 (16.4)
Known hepatitis B and C	17 (25.3)
Diagnosed cirrhosis (positive)	184 (83.6)
Bilharziasis history (positive)	113 (51.4)
Clinical presentations	
Asymptomatic	112 (50.9)
Abdominal pain	58 (26.4)
Jaundice	30 (13.6)
Other (e.g. fatigue, ascites)	20 (9.1)
Child-Pugh class	
Class A	115 (52.2)
Class B	73 (33.1)
Class C	32 (14.5)

Table 2 Tumor and pathological characteristics of the patient sample studied

Characteristics	N (%)
Liver mass site	
Right lobe	106 (48.1)
Left lobe	48 (21.8)
Multiple	66 (30)
Number of lesions	
Single	96 (43.2)
Multiple	124 (56.3)
Tumor size (cm)	
≤5	78 (35.5)
>5	142 (64.5)
Residual liver	
Undetected pathology	36 (16.3)
Cirrhosis	124 (65.3)
Fibrosis	60 (27.2)
T stage	
I	3 (1.4)
II	5 (2.3)
III	109 (49.5)
IV	89 (40.5)
N stage	
0	184 (83.6)
I	22 (10)
M stages	
0	140 (63.6)
I	66 (30)
TNM staging system	
I	35 (15.9)
II	22 (10)
III	83 (37.7)
IV	80 (36.4)
Sites of metastasis	
Bone	10 (4.5)
Lung	22 (10)
Lymph nodes	48 (21.8)

Figure 1



Modes of treatment of the 220 patients. TACE, trans arterial chemo embolization.

including surgical resection in 56 (25.4%) patients, local curative radiofrequency ablation therapy in 18 (8.1%) patients, and palliative radiofrequency ablation therapy in 42 (19%) patients. Palliative treatment using transarterial chemoembolization (TACE) or sorafenib was applied to 32.4% and 10% of the patients, respectively. TACE was the most common line of treatment used (32.4%), followed by radiofrequency (27%) and surgery (25.4%).

Surgery for hepatocellular carcinoma

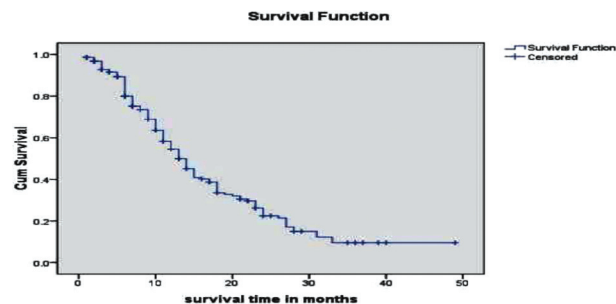
Non-anatomic open resection was the most common procedure used in 58% of the cases; however, other techniques such as anatomic resection (27%) and laparoscopic nonanatomic resection (15%) were also used; unfortunately, the transplantation program is yet to be added in the treatment. The overall survival was 80% at 6 months, 55% at 1 year, and 20% at 2 years.

The main aims of hepatic resection, especially in a cirrhotic liver, is to resect all of the malignant tissues with effective clearance, and to leave enough nontumorous liver parenchyma to prevent postoperative liver failure, especially in patients with poor liver function.

Several techniques were used to improve the outcome of liver resection and minimize intraoperative bleeding such as inflow occlusion of the portal triad with either the continuous Pringle maneuver, which can be applied safely to the normal liver under normothermic conditions for up to 60 min and under pathological (fatty or cirrhotic) conditions for up to 30 min [30], or intermittent inflow occlusion, which can also be repeated safely for up to 90 min in cirrhotic patients with good liver function [29].

Finger-fracture (digitoclasia) or clamp-crushing (kellyclasia) techniques were used for blunt transection when the liver parenchyma is crushed between the thumb and one

Figure 2



The Kaplan–Meier survival analysis of the 220 patients.

finger or with Kelly clamps so that vessels and bile ducts stand out for proper hemostasis by diathermy, metal clips, or suture ligatures. Unipolar and bipolar cauteries are used commonly for simultaneous hemostasis while transection is carried out [31]. Newer bipolar devices such as the LigaSure vessel sealing system has been used to seal off vessels up to 7 mm in diameter [32]; the liver tissue can be crushed between the blades of the device and then coagulation energy is applied to seal the vessels. A harmonic scalpel, an ultrasonically activated shear, was also used for resection. It causes protein denaturation and coagulation by high-frequency ultrasound vibration [33]. Vascular staplers were used for the division of hepatic veins and portal branches; moreover, it was also used for the transection of liver parenchyma after dividing the liver capsule by diathermy, followed by fracturing the liver tissue with a vascular clamp in a stepwise manner, and subsequently divided with endo-GIA vascular staplers [34].

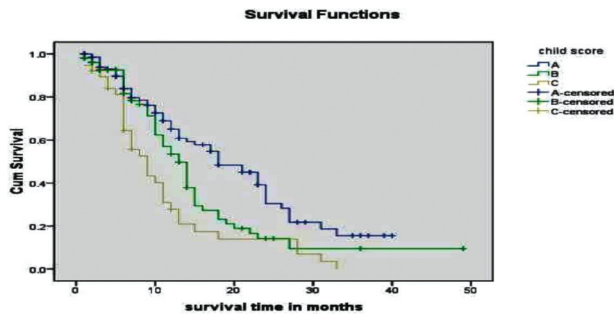
Intraoperative ultrasound is a very beneficial and essential tool during hepatectomy procedure [35], and its role was much emphasized in our work.

Laparoscopic resection of hepatic lesions was also used in some selected cases of accessible lesions [36,37], by the same surgical tools applied for open ones.

Postoperative data assessment

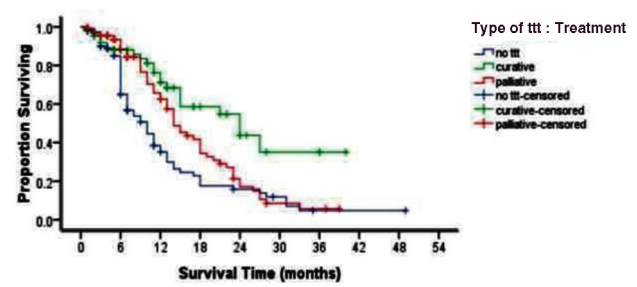
Data of our patients were analyzed using univariate analysis tools, and it revealed that survival was significantly better in Child-Pugh A patients than in Child-Pugh B and Child-Pugh C patients ($P < 0.001$) (Figs 2 and 3). Better performance states using the Eastern Cooperative Oncology Group (ECOG) 0–1 was associated with a significantly higher survival than presentation with lower performance states. It also found that patients with single tumors, located in the right lobe, with size less than and equal to 3 cm had a significantly higher

Figure 3



Survival analysis according to the Child–Pugh score.

Figure 4



Survival according to the type of treatment used.

Table 3 Multivariate analysis for the prognostic factors of hepatocellular carcinoma survival in the studied patients

	B	SE	Significance	HR	95% CI for HR	
					Lower	Upper
Bilirubin	0.538	0.188	0.004	1.71	1.18	2.47
Site of lesion			0.016			
Left vs. both	−0.332	0.31	0.285	1.39	0.76	2.56
Right vs. both)	−0.673	0.244	0.006	1.96	0.1.21	3.16
Treatment			0.002			
Symptomatic vs. curative	−0.863	0.262	0.001	2.37	1.42	3.96
Symptomatic vs. palliative	−0.446	0.196	0.023	1.56	1.06	2.29

B, regression coefficient; CI, confidence interval; HR, hazard ratio; SE, standard error of the coefficient.

survival than others. In contrast, patients with portal hypertension, ascites, portal-vein thrombosis, serum bilirubin greater than 2 mg/dl, serum albumin less than 3.5 g/dl, international normalized ratio greater than 1.7, and AFP greater than 400 ng/ml had significantly worse survivals than others. Specific treatment, either curative or palliative, increased survival significantly compared with patients receiving supportive or palliative symptomatic treatment only. Certainly, patients who received curative treatment showed a significantly higher survival (Fig. 4). All significant factors in the univariate analysis were further analyzed by a stepwise multivariate Cox proportional hazard. As a result, serum bilirubin, the site of the tumor, and the type of treatment were significant independent prognostic factors affecting survival (Table 3 and Photos 1–10).

Discussion

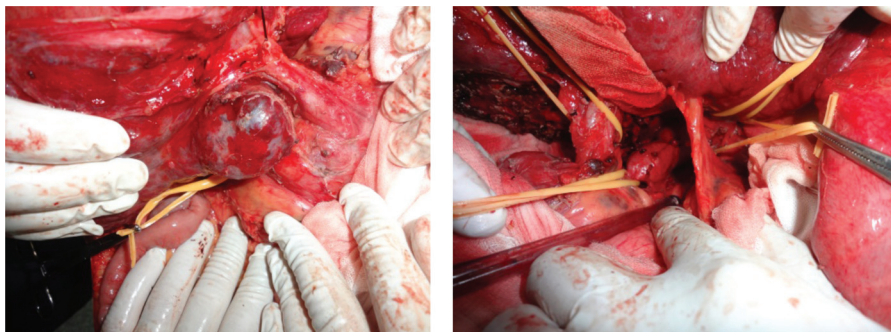
HCC is a major health problem in Egypt and it carries considerable concern for the health authority as many patients present with advanced disease beyond curative surgery or effective palliative local and regional therapies. Exceptionally, certain groups of patients with resectable disease and adequate liver reserve can benefit from resection or LT; otherwise, the treatment of HCC remains palliative with minimal survival benefit [38,39].

Presentations of HCC are variable, and misleading, with unexpected biologic behavior counteracted by multiple complex therapeutic options for management, with diverse responses documented in clinical practice; moreover, the presence of endemic chronic liver disease in our locality is evident in most of the patients [40,41], which necessitates the management of HCC in multidisciplinary clinics. In our study, we aimed to provide a clear view of the current situation of HCC in Egypt as sampled and represented by our specialized multidisciplinary clinic.

The Barcelona clinic liver cancer guideline represents the cornerstone for managing HCC in our center as it is the most accepted and widely used systems approved by many liver management societies [42]; moreover, it was included in the HCC guidelines published by the Egyptian Society of Liver Cancer [43].

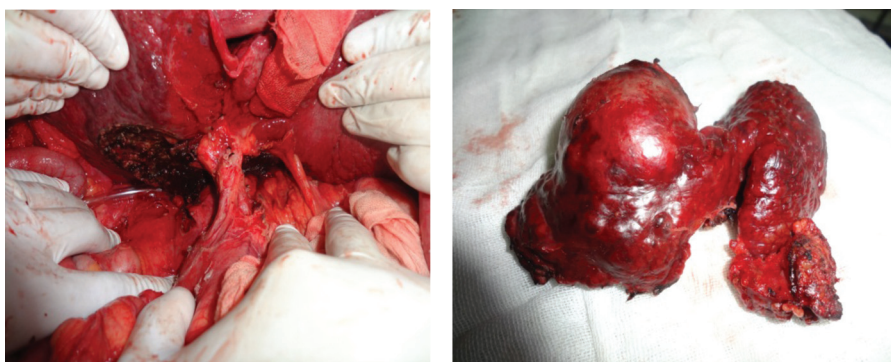
In our study, most of the patients (84%) developed HCC on top of liver cirrhosis that was mainly caused by HCV. Liver cirrhosis has been reported previously in many studies as the most predominant pathological lesion behind the development and the progression of HCC [44]. In a similar study, liver cirrhosis accounted for 96% of the HCC cases [45]. As for hepatitis seroprevalence among HCC cases, a recent worldwide systematic review documented a predominance of HBsAg among HCCs

Photo 1



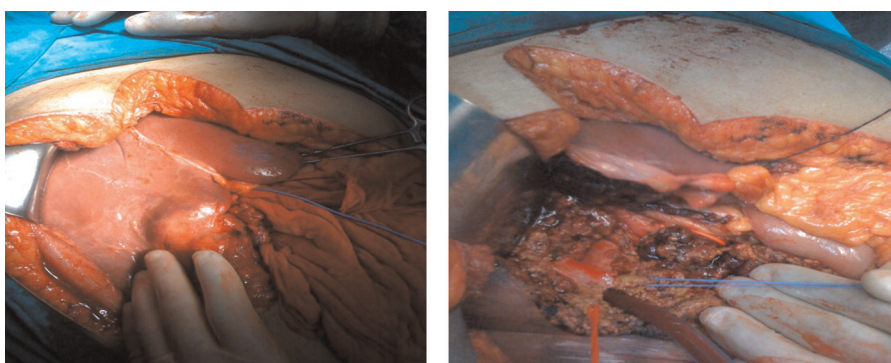
Caudate-lobe hepatocellular carcinoma.

Photo 2



Resection of caudate-lobe hepatocellular carcinoma.

Photo 3



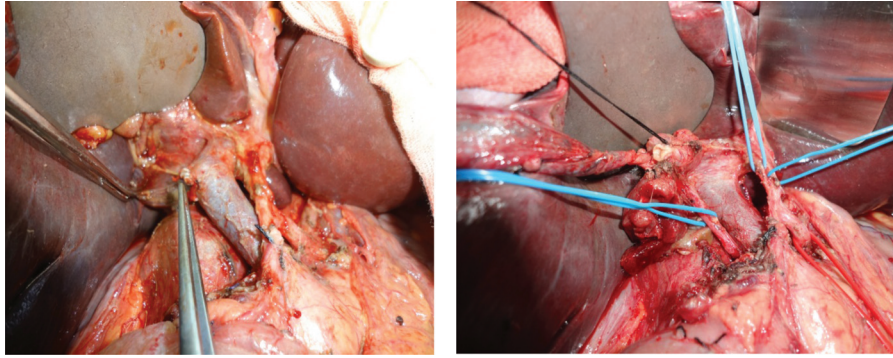
Hepatocellular carcinoma in the bed of the gall bladder (GB), which was resected.

from most Asian, African, and Latin-American countries, whereas anti-HCV predominated in Japan, Pakistan, Mongolia, and Egypt [46]. The highest prevalence of HCV in the world is reported in Egypt [47,48].

Although nearly half of the HCC patients (52.2%) had a compensated liver cirrhotic condition (Child-Pugh score A), curative treatment (surgery or radiofrequency therapy) was provided for only 33.5% of the HCC

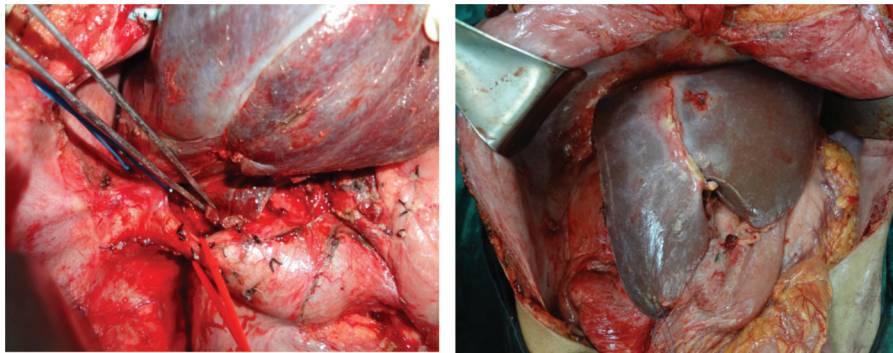
cases (25.4% for surgery and 8.1% for curative radiofrequency ablation), and 61.4% of cases received palliative therapy (19% for radiofrequency ablation, 32.4% for TACE therapy, and 10% for systemic chemotherapy treatment). In a recent study applied on a large western HCC cohort, 53.7% had compensated liver cirrhosis, and a potentially curative treatment was applied for only 24% of the patients [41]. These findings reflect the detection of

Photo 4



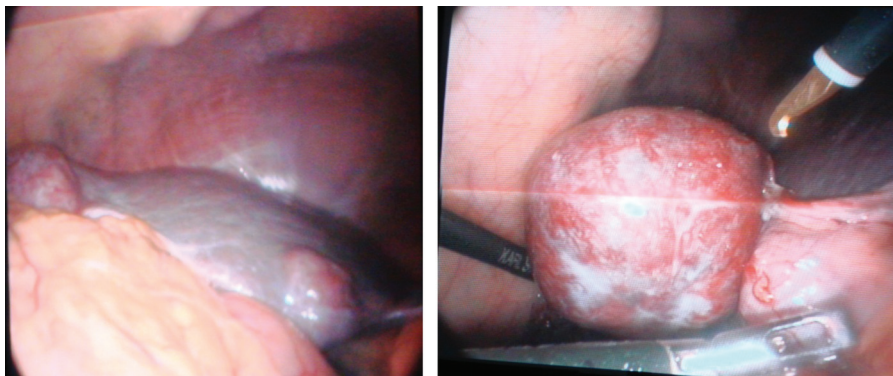
Central hepatocellular carcinoma in an otherwise healthy liver.

Photo 5



Right hepatectomy was performed.

Photo 6



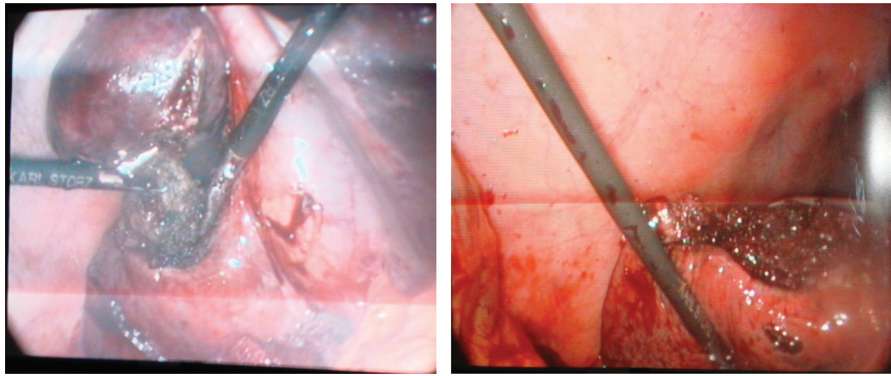
Laparoscopic resection of two focal lesion (hepatocellular carcinoma) in a mildly cirrhotic liver.

HCCs at advanced stages even with compensated liver cirrhosis, and documented that these findings are not so much related to distant metastases, but more related to locally advanced tumors and the consequences of cirrhosis [49].

Data of our patients, analyzed using univariate analysis tools, documented that low-burden disease (nonmetastatic disease), the absence of symptoms (ascites or fatigue),

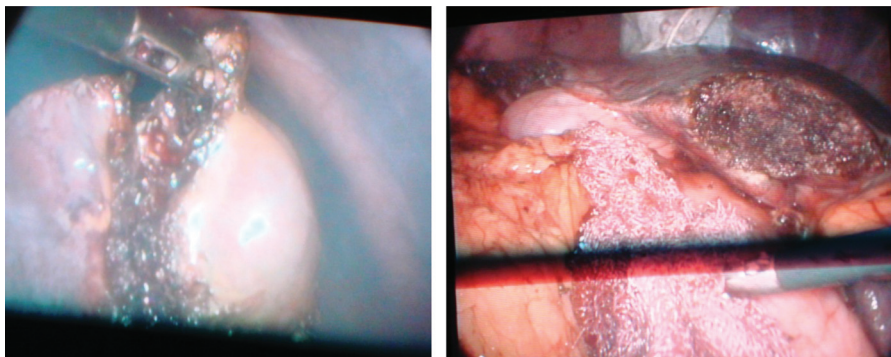
good liver reserve (Child–Pugh A), and female sex are significantly associated with an improved survival. Similar to our results, the absence of ascites was associated with an improved survival in the Italian group. However, in contrast, factors affecting survival in their study were international normalized ratio, bilirubin, portal hypertension, the performance status (not assessed in our study), and low albumin, reflecting a different disease biology [50]. In previous studies

Photo 7



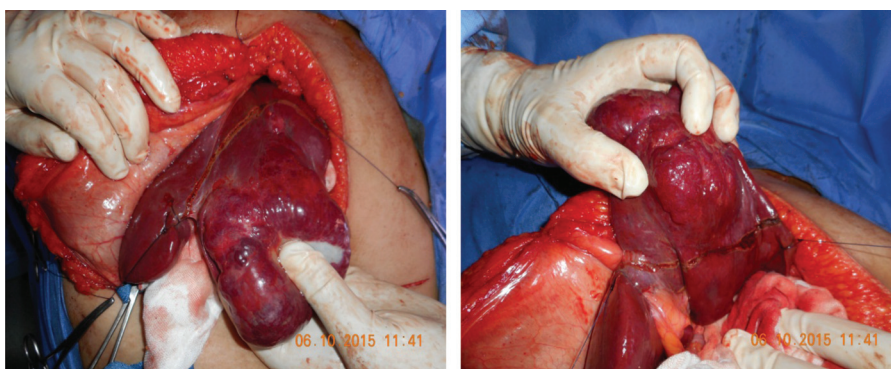
Laparoscopic resection of a segment-5 hepatocellular carcinoma lesion.

Photo 8



Laparoscopic resection of segment-6 hepatocellular carcinoma lesion.

Photo 9

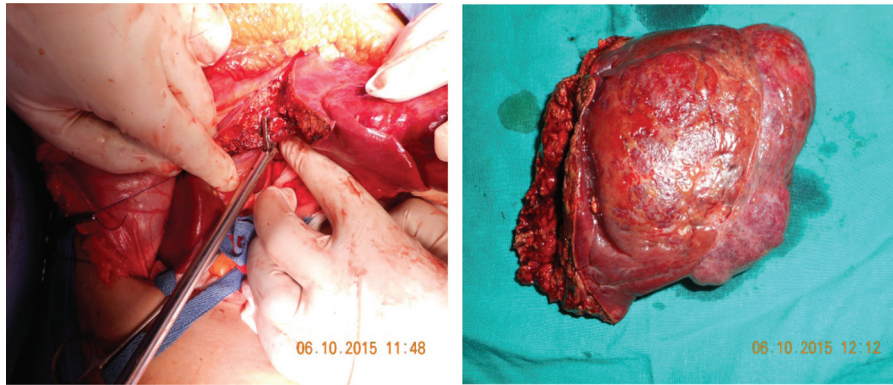


Large hepatocellular carcinoma in segment-4 during resection.

with a similar design, multivariate analyses showed many independent prognostic factors such as AFP, bilirubin, the performance status, and the disease stage being the most consistent between these trials. In agreement with Llovet *et al.* [13], the current study showed that extrahepatic spread was a predictor of poor survival as it is usually associated with a high burden of the disease and it precludes local treatments. Extrahepatic spread combined with the absence of

effective systemic treatments is responsible for the dismal outcome in such an advanced stage of the disease. Again, a higher Child-Pugh class and fatigue were independent factors of poor survival, mostly because they reflect the underlying poor liver reserve. Fatigue may also reflect a bad performance status (PS), consistent with Cabibbo *et al.* [50], who concluded that PS was an independent prognostic factor.

Photo 10



Resection of hepatocellular carcinoma.

Surgery was the main treatment strategy in early operable cases: through nonanatomic resection in 58%, anatomic resection in 27%, and laparoscopic nonanatomic resection in 15% of the cases. Our results are contradictory to several studies demonstrating that anatomical resections of small solitary HCC achieve a significantly better overall and disease-free survival than limited resections, without increasing the postoperative risk [29,51,52]. Therefore, when possible, anatomical resection should be the treatment of choice and considered as the reference surgical treatment when comparing it with other treatments. The main risk of limited resections is tumor recurrence by local metastasis and particularly by tumor cell seeding in adjacent or distal liver segments through the tumor portal venous territory [14,29,51]. Anatomical resections according to the architecture of the portal vein have the potential to remove undetected cancerous foci (portal-vein metastases and satellite nodules) disseminated from the primary gross tumor. In contrast, some authors found no difference in recurrence rates between the anatomic and the nonanatomic groups in either univariate or multivariate analysis, and the type of resection is not considered as a distinct risk factor for early (2 year) tumor recurrence in patients with solitary HCC and preserved liver function [53]. Hence, nonanatomical or wedge resection was a commonly used technique, especially for peripheral or superficial lesions, when the lesion crosses the boundary of multiple segments, or in situations where the preservation of liver substance is of paramount importance [30].

To perform liver resections safely and to minimize blood loss and the need for blood transfusions, different hepatic vascular occlusion techniques were used on the basis of the type of resection to be performed, the tumor size and location, and the preoperative liver function [54].

The commonly used type was inflow occlusion (Pringle maneuver) either continuous or intermittent [55]. However, intermittent occlusion was used more commonly, whereby clamping for 10 min and then unclamping for 3 min allows for a longer total occlusion time of up to 2 h in the normal liver, which can be useful for more prolonged complex liver resections [54], or 15 min of clamping and 5 min of unclamping can also be repeated safely for up to 90 min in cirrhotic patients with good liver function [29]. Sometimes, it involves inflow clamping for 15–20 min, followed by unclamping for 5 min (mode: 15/5 or 20/5), or 5-min clamping followed by 1-min unclamping (mode: 5/1) [30]; all techniques increase the warm ischemia time of the liver, allowing more time for major resection [29]. Ischemic preconditioning of the liver was adopted by some authors and refers to an endogenous self-protective mechanism by which a short period of ischemia followed by a brief period of reperfusion produces a state of protection against subsequent sustained ischemia-reperfusion injury [30,56].

Parenchymal dissection of the liver tissue was performed using the finger-fracture or the clamp-crushing technique in most of the cases, as these methods are practiced commonly in many centers around the world [30,52]; however, other techniques were used, such as unipolar or bipolar diathermy [31], and newer bipolar devices such as LigaSure sealing that has been used for liver transection with proven effectiveness [30,32], but it does not seem to work so well in cirrhotic livers compared with noncirrhotic livers [32]. A harmonic scalpel ultrasonic dissector was used effectively in many cases [33]; although it reduces the operative time and blood loss, when compared with clamp crushing, it was shown to have an increased incidence of biliary fistulae [33]. A recent randomized controlled trial comparing different transection methods in liver resection showed that the

clamp-crushing method remained the most efficient device in terms of the resection time, blood loss, and the blood transfusion frequency when compared with other methods and the dissecting sealer, and was also the least expensive [57]. In addition, there are other important factors to be considered when choosing a particular method, such as the operative time, the availability, the ease of use, the extent of hepatic injury affected, and the cost. The use of one tool over the other will also vary according to the type of resection, and different techniques can be more advantageous in one setting than another. It is important to be familiar with many strategies and be able to apply them in the most appropriate setting [54]. As these methods of transection involve quite a different set of skills, it is difficult to compare them, as it may well be a simple case of the surgeon's preference for one technique over another [30]; taking into consideration the preservation of as much liver parenchyma as possible is important because many patients will receive postoperative chemotherapy, and risks of liver failure are much higher [54].

Vascular stapler devices were commonly used for the division of hepatic veins and portal branches; moreover, it was used for the transection of the liver parenchyma [34]; although the technique appears attractive, the financial cost for the staplers is a serious drawback [30].

The role of intraoperative ultrasound was well emphasized in our work as it proved effective as an essential tool for hepatobiliary surgeons [30] to locate known liver lesions, to detect further liver lesions on-table, to guide the line of transection, and to mark important vascular patterns. It allows the accomplishment of anatomical resections such as segmentectomy, and it also allows better tumor clearance in nonanatomical resections [30,35].

Laparoscopic hepatectomy procedures evolved recently, but relatively slowly due to concerns about hemorrhage, air embolism, tumor seeding (port site and peritoneal), and oncological clearance [30]. Although successful laparoscopic major hepatectomy has been reported, most authors agree that laparoscopic liver resection should be offered to selected patients [36,58]: tumors located at segments II, III, IVb, V or VI, tumors of size 5 cm or less, lesions that are not close to major vascular trunks, and when there is no need for vascular or biliary reconstruction were considered as conditions favorable for laparoscopic resection [30]. It was associated with a shorter hospital stay, less analgesic requirement, and quicker resumption of oral intake, whereas

complications and conversion rates were acceptable [37]. Without doubt, laparoscopic liver resection is technically demanding and can be accomplished safely only by liver surgeons with experience in both laparoscopic and open hepatic surgery [30].

Although there were common prognostic factors shared between trials, there were still several other factors associated with bad outcome in HCC. This may reflect the aggressive biology of the disease that dependent on certain single factors. Hence, if we consider the aggressive biology of the disease, and the limited treatment options for HCC patients and the limited resources or access to effective treatment for most of Egyptian patients such as sorafenib or LT, we found that HCC is a fatal disease and constitutes a major national problem. Hence, we have to find other effective treatment modalities or try to stress the importance of screening programs that can enable diagnosis at an early stage with the opportunity for treatment with curative intent. However, the most valuable solution is to put more effort into a prevention program, whether through the prevention of infection by viral hepatitis or by treating it at early stages before causing cirrhosis, which is the main risk factor for HCC in Egypt.

Conclusion

HCC in Egypt is an aggressive disease and the overall survival in untreated HCC is very short. Many factors interact to produce this dismal survival. Our study reveals the different prognostic factors that affected the survival of our HCC patients. The main variables were the bilirubin level, portal hypertension, bilobar hepatic affection, and the application of specific treatment (either curative or palliative). We hope that these findings will ameliorate future early detection and management of HCC to gain a higher survival benefit. Till then, much effort should be put into the field of prevention and screening programs to get rid of the problem.

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Conflicts of interest

There are no conflicts of interest.

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