A Review of Management of Hepatocellular Carcinoma

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ABSTRACT : Hepatocellular carcinoma represents about 90% of primary liver cancers and constitutes a major global health problem. HCC can be cured with surgical removal of the tumor, especially when the tumour is small and liver function is preserved. A liver tumour is usually treated by removing the area of the organ in which it is found. However, partial hepatectomy raises the risk of another HCC developing in the residual liver, which occurs in around half of the cases. Liver transplantation is often the most effective treatment for HCC when resection is unlikely to be successful due to the risk of liver failure or cancer recurrence. The requirement to protect native liver function during surgery is avoided with a liver transplant, which dramatically reduces the risk of cancer recurrence. The recurrence rate for HCC following transplantation is 10–20%, which is significantly lower than the resection rate. Other therapeutic approaches, such as percutaneous ablation, transarterial chemoembolization (TACE), radioembolization, external radiation, systemic molecular targeted therapy, or immunotherapy, may be appropriate for a select group of patients with small, favourably located tumors. In patients with more advanced HCC, effective treatment is also available. TACE, in which a chemotherapeutic cocktail is injected directly into the tumour and its blood supply is cut off, causes tumour death and is effective at controlling even larger tumors. TACE can also be used to keep tumours from growing while patients with smaller tumours are on the liver transplant waiting list. Radioembolization is a treatment that involves injecting radiation-emitting beads into the tumour as an alternative to TACE. Microspheres are injected into the portal vein to block off blood flow to the tumour during portal vein embolization. Without a doubt, systemic HCC therapies have reached their prime. Angiogenesis and immune evasion are two common features of cancers. The atezolizumab + bevacizumab regimen is a pioneer in the era of immunological combination therapy and the first to be shown to be more efficient than sorafenib in the first-line treatment of advanced HCC, which is regarded as a milestone and an encouraging breakthrough in the treatment of advanced HCC. Despite the fact that HCC is a fatal condition, early screening and diagnosis offer the best opportunity for a long life. Due to the intricacy of the condition, patients are frequently best treated in facilities with experience in managing HCC, where a multidisciplinary approach can be applied. A condition that was once believed to be fatal only a few decades ago has improved in terms of survival and prognosis thanks to improvements in HCC prevention, early recognition, and therapy.

KEY WORDS: HCC Management, BCLC, Intervention Radiology

INTRODUCTION

Hepatocellular carcinoma surveillance, diagnosis, and management have all improved significantly over the last decade.[1] Despite declining disease incidence rates, disease-specific mortality rates remain high[2], and early identification is critical for better outcomes.[3,4] Hepatocellular carcinoma surveillance is a great way to detect the disease early on.[5] The most often utilized surveillance tests are liver ultrasonography and serum fetoprotein. However, their accuracy in detecting early-stage hepatocellular carcinoma isn't great,[6] and new monitoring tests for the disease have been proposed, with promising preliminary results.[7-9] Improved imaging techniques have made non-invasive diagnosis of hepatocellular carcinoma extremely accurate and reliable, eliminating the need for a liver biopsy for histological confirmation. Biopsies can still be done on occasion to confirm hepatocellular carcinoma in tumours that don't have any obvious radiologic characteristics. Given the inherent risk of tissue biopsy of liver tumours, liquid biopsies may soon become a viable alternative for non-invasive tumour biology assessment.[10,11] Hepatocellular carcinoma treatment has improved dramatically in recent years, with systemic treatment making the most gain. The only systemic medication that has been shown to be clinically efficacious for treating advanced HCC for more than a decade is sorafenib. The fast development of molecular targeted treatments, however, over the past three years has significantly altered the landscape of modern HCC therapy options. This review

article seeks to give a comprehensive and evidence-based evaluation of the most recent improvements in hepatocellular carcinoma surveillance, diagnosis, and treatment.

EPIDEMIOLOGY

HCC is now the fifth-most common cancer in the world and the third cause of cancer-related mortality as estimated by the World Health Organization (**globacan.iarc.fr**). It is estimated that in 2012, there were 782,000 cases worldwide, of which 83% were diagnosed in less developed regions of the world. The annual incidence rates in eastern Asia and Sub-Saharan Africa exceed 15 per 100,000 inhabitants, whereas figures are intermediate (between 5 and 15 per 100,000) in the Mediterranean Basin, Southern Europe, and North America and very low (below 5 per 100,000) in Northern Europe.[12] Vaccination against hepatitis B virus (HBV) has resulted in a decrease in HCC incidence in countries where this virus was highly prevalent.[13] These data suggest that the geographical heterogeneity is primarily related to differences in the exposure rate to risk factors and time of acquisition, rather than genetic predisposition.

DIAGNOSIS AND SURVIELLANCE

Cirrhosis is present in more than 80% of people diagnosed with HCC. 3 As a result, any cause of chronic liver injury and, eventually, cirrhosis should be considered a risk factor for HCC. HBV, hepatitis C virus (HCV), alcohol, and nonalcoholic fatty liver disease (NAFLD) are the most common causes of cirrhosis, but less common disorders such hereditary hemochromatosis, primary biliary cholangitis (PBC), and Wilson's disease have also been linked to the development of HCC. The number of patients developing HCC on the background of NALFD may rise as the obesity pandemic progresses.[14]

Patients at high risk who are screened for HCC receive a diagnosis at an earlier stage than those who are not screened, hence surveillance is critical. Patients with an early diagnosis have more therapy options and a better prognosis as a result. Biannual screening was found to reduce HCC mortality by 37% in a randomised controlled experiment.[15]

On CT and MRI, typical HCC lesions display increased arterialization as well as decreased presence of contrast agents compared with the surrounding liver during portal vein and/or equilibrium phase imaging.[16] The 2010 AASLD recommendations propose that US be used for surveillance every six months.[17] CT or MRI, on the other hand, is chosen in individuals for whom US is insufficient due to technical reasons or because the patient is on the orthotopic liver transplantation (OLT) waiting list.[18] A retrospective review of the different imaging modalities ability to detect HCC revealed that CT and MRI had higher sensitivity than US, especially for tiny tumors.[19] (US, CT, and MRI overall sensitivities were 46 percent, 65 percent, and 72 percent, respectively.)

Although serum alpha-fetoprotein (AFP) levels are frequently increased in patients with HCC, one study found that its sensitivity and specificity are 41 percent to 65 percent and 80 percent to 94 percent, respectively.[20] Serum values more than 500µ/L in high-risk patients are generally considered diagnostic for HCC.[21] Negative results, on the other hand, do not rule out HCC. AFP levels can also be increased in the absence of cancer in patients with chronic liver illness (particularly when inflammation is present), in pregnancy, tumors of gonadal origin, and a variety of other malignancies. Due to the limitations of serum AFP measurements, various alternative HCC serum indicators have been evaluated, either alone or in combination with AFP.

A variety of additional biomarkers have been studied for surveillance in addition to AFP. These include the Lens culinaris lectin-binding subfraction of the AFP, or AFP-L3 %, which measures a subfraction of AFP that has been shown to be more specific, though generally less sensitive,[22] than the AFP, and des gamma carboxy prothrombin (DCP), also known as protein induced by vitamin K absence/antagonist-II, a variant of prothrombin that is also produced at high levels by a proportion of HCC [23-26]

In the United States, these biomarkers have been approved by the Food and Drug Administration (FDA) for risk stratification, but not for HCC surveillance.In the past few years, a diagnostic model has been proposed that incorporates the levels of each of the three biomarkers, AFP, AFP-L3%, and DCP, along with patient sex and age, into the Gender, Age, AFP-L3%, AFP, and DCP (GALAD) model.[27] GALAD has shown promise in phase II (case-control) biomarker investigations, but larger cohort studies will require phase III and IV research to assess its performance.Novel cancer biomarker assays, such as those for cancer-specific DNA mutations, differentially methylated DNA regions, microRNAs, long noncoding RNAs, native and posttranslationally modified proteins, and biochemical metabolites, are also being developed. Recent findings reveal that the expression of numerous biomolecules in exosomes generated by tumor cells differs from those released by normal cells.[28]

A mass found incidentally or through screening in the setting of a patient with known HBV-associated cirrhosis or cirrhosis of another etiology is likely to be HCC. Nodules less than 1 cm are frequently not HCC; they should be followed with an ultrasound

every three to six months until stability is established or they disappear, and if there has been no growth over a period of up to 2 years, the patient can revert to routine surveillance.

CT or MRI should be used to examine lesions greater than 1 cm in diameter. If the morphology is consistent with HCC, no additional investigation is necessary; however, if the characteristics are not consistent with HCC, a second study or a biopsy can be conducted. In almost 90% of instances, however, the diagnosis of HCC is made without a biopsy. If the biopsy for HCC is negative, patients should be imaged every 3 to 6 months until the nodule disappears, enlarges, or develops definite HCC features. A second biopsy is required if the lesion enlarges but remains atypical for HCC. It's crucial to understand that biopsies aren't fully risk-free.[29]

STAGING

Important factors affecting survival include the severity of underlying liver disease, the size of the tumour, its extension into nearby structures, and the occurrence of metastases. The Tumor, Node, Metastasis (TNM), the Okuda, the Barcelona Clinic Liver Cancer (BCLC), and the prognostic staging system for HCC (CLIP score) are the four most often used systems for staging and prognosis of HCC . There is no consensus as to which staging system is best in predicting the survival of patients with HCC.[30] The consensus statement of the American Hepato-Pancreato-Biliary Association, updated in 2010, recommends the BCLC plan for patients with advanced HCC who are not candidates for surgery and the TNM system to predict outcomes after resection or liver transplantation.[31] The Barcelona Clinic Liver Cancer (BCLC) staging system, which offers five distinct stages of hepatocellular carcinoma with varying prognoses and recommendations for treatment, considers both tumor-related characteristics and the severity of liver disease.[32,81]

- Very early stage (BCLC 0)

This is defined as a solitary HCC ≤2 cm without vascular invasion or extrahepatic spread in a patient with preserved liver function and no cancer-related symptoms.

- Early stage (BCLC-A)

This is defined as solitary HCC irrespective of size or as a multifocal HCC up to 3 nodules (none of them >3 cm), without macrovascular invasion, extrahepatic spread or cancer-related symptoms (Performance status, PS-0).

- Intermediate stage (BCLC-B)

This is defined as multifocal HCC (exceeding BCLC-A criteria) with preserved liver function, no cancer-related symptoms (PS 0) and no vascular invasion or extrahepatic spread. The 2022 BCLC version stratifies the BCLC-B stage into 3 groups of patients according to tumour burden and liver function.

- Advanced stage (BCLC-C)

This stage includes patients presenting with vascular invasion or extrahepatic spread who are still relatively fit, as reflected by a PS ≤2 at staging work-up, and who have preserved liver function.

- End-stage (BCLC-D)

Patients with major cancer-related symptoms (PS >2) and/or impaired liver function without the option of LT due to HCC burden or non–HCC–related factors present poor short-term survival and belong to the BCLC stage D.

TREATMENT

Over the past ten years, there have been tremendous developments in technology and patient selection, which have improved HCC treatment. Curative and noncurative therapies are two categories of therapeutic options. Surgical resection, orthotopic LT, and ablative methods like thermal ablation are examples of curative therapy. Each of these approaches offers the chance of long-term response and improved sur-vival. Noncurative therapies, which attempt to pro-long survival by slowing tumor progression, include transarterial chemoembolization (TACE), transarterial radioembolization (TARE), stereotactic body ra-diation therapy (SBRT), and systemic chemotherapy.

Resection

For eligible patients with early stage hepatocellular carcinoma, surgical excision is a possibly curative therapeutic option. Cirrhosis and the accompanying degree of underlying liver failure and portal hypertension are central determinants of resectability, in addition to tumour features such as size, location, and number. The lack of a uniformly applied definition of resectability is a limitation to interpreting reported outcomes. Patients with one to three unilobar lesions, no radiographic evidence of macrovascular invasion or extrahepatic metastases, and minimal or no portal hypertension in the absence of synthetic dysfunction are generally candidates for resection.[34-42] The randomized trials to date have included patients undergoing open resection, and have generally shown slightly

higher complication rates for resection than for radiofrequency ablation. Laparoscopic resection for hepatocellular carcinoma offers similar survival to open resection, with a reduced length of stay and a reduced perioperative complication rate based on propensity score matched analyses.[43-46]

Liver transplant

Among patients with unresectable disease, the most viable surgical option is often liver transplantation, frequently in conjunction with adjuvant therapy such as TACE or percutaneous ablation.[47,48] However, not every patient is a candidate for a liver transplant, and careful assessment is required to wisely spend the limited resources available. In 1996, Mazzaferro and colleagues published a landmark prospective study involving less than 50 patients who were transplanted for HCC under predefined criteria (single HCC ≤5 cm or 3 HCC ≤3 cm each), known as the Milan criteria, and showed a 4-year survival of 75%.[49] This established deceased-donor liver transplantation as a viable option for the treatment of HCC. Subsequent experiences of OLT for HCC inside the Milan criteria confirmed a survival rate exceeding 70% at 5 years, with recurrence in less than 15%.[50] These outcomes are also similar to expected survival rates for patients undergoing transplantation for cirrhosis without HCC.[51]

Several studies have investigated the effect of expanding the Milan criteria, primarily by liberalizing the restrictions on tumor size. The University of California, San Francisco criteria, which include a single nodule of 6.5 cm or greater or 2 to 3 nodules of 4.5 cm or greater and a total diameter of 8 cm or greater, have been studied retrospectively and prospectively and have shown survival and recurrence rates equal to those of persons transplanted using the Milan criteria.[52] Nevertheless, national and international guidelines still indicate OLT for HCC inside Milan criteria while awaiting further data to support expansion of the criteria.[50]

Recently, attention has been drawn to the adoption of a down-staging strategy in which patients with HCC who do not meet the criteria for transplantation are treated with locoregional therapy (ie, TACE and/or ablation therapy) to decrease the tumor burden to the point of meeting transplantation criteria.[53-55] The data are conflicting. Some experts suggest offering OLT to patients who achieve effective down-staging, while others favor OLT as a rescue treatment in patients who do not achieve an effective response.[56,57] Yao and colleagues published a downstaging protocol using TACE and/or RFA and have shown survival rates of 96.2% at 1 year and 92.1% at 4 years among patients who received transplants.[53]

The downstaging approach is also controversial. Some specialists worry that expanding the pool of prospective transplant candidates may result in longer wait lists, higher dropout rates, and higher wait-list mortality since they think big or multifocal tumours retain the same risk of recurrence despite successful downstaging.[52]

A major disadvantage of OLT is the long waiting time for donor organs. Under the current United Network for Organ Sharing policy, patients with HCC within the Milan criteria receive Model for End-Stage Liver Disease scores that begin at 22 and increase in a stepwise fashion (equivalent to an additional 10% increase in candidate mortality) every 3 months after the results of repeat imaging with either CT or MRI have confirmed that criteria are still met.[58] As a result, patients with HCC in some areas of the country may wait more than 2 years before being offered a liver graft. Living donor liver transplant (LDLT) is an alternative option; however, there is a donor risk of death of approximately 0.3% and of life-threatening complications of approximately 2%. For this reason, LDLT should be restricted to centers of excellence.[18] Data are still forthcoming as to whether LDLT offers the same survival as deceased donor liver transplant in patients with HCC.

Ablation

When a tumour is less than 3 cm in diameter, ablation is highly effective, but once the tumour is more than 3 cm, its effectiveness falls. Many treatment modalities are available for the local ablation of hepatocellular carcinoma with generally similar outcomes. Radiofrequency ablation and microwave ablation are the most commonly used ablation treatments. There were 76 patients for radiofrequency ablation and 76 patients for microwave ablation in a recent multicenter, single-blinded, phase II randomised controlled trial. Each patient had a maximum of three lesions of hepatocellular carcinoma that measured up to 4 cm each. The study showed an association between microwave ablation and higher rates of local tumor control (relative ratio 1.6, 95% confidence interval 0.7 to 3.9). Although the procedure time was shorter with microwave ablation, another randomised trial of 93 patients with hepatocellular carcinoma getting microwave ablation or radiofrequency ablation found no difference in treatment-related morbidity, overall survival, or disease free survival.[59-63]

Percutaneous ethanol ablation induces tumour cell death via intracellular dehydration and activation of coagulation cascades. Local tumour control is less effective than other forms of local ablation. As a result, it is now only used infrequently.[64] However, because it is relatively inexpensive to perform, percutaneous ethanol ablation is still utilised for the ablation of tumours near to major artery

or the bile duct to avoid thermal harm, and it is still employed in countries with little medical resources. 1 Cryoablation is an alternate ablation procedure that uses ice balls to create a distinct ablative boundary and avoids damage to peritumoral tissues. As a result, it's an effective local ablative method for tumours close to the bile ducts or main veins, with a lesser risk of vascular thrombosis.[65]

Transarterial Chemoembolization

Among patients with large multifocal HCC or those whose tumour characteristics are not appropriate for surgical or ablative therapy, TACE is recommended as a first-line, noncurative treatment for BCLC stage B multinodular asymptomatic tumours without vascular invasion or extra-hepatic spread.[66] Because the majority of the blood supply of HCC comes through the hepatic artery rather than the portal vein, strategies to cut off the tumor's blood supply or administer cytotoxic chemotherapy directly to the tumour have been developed. TACE caused substantial tumour necrosis in more than half of the patients, according to a systematic review, and the reported rate of objective response varied between 16 and 60 percent, according to standard World Health Organization criteria.[67]

TACE includes injecting a chemotherapeutic drug mixed with embolic material into the tumor's feeding arteries with precision in order to potentially increase intratumoral drug levels compared with intravenous therapy, with occlusion of the blood vessel causing infarction and necrosis.[67]

Although the selection of chemotherapeutic drugs is not standardised, many agents, including doxorubicin, cisplatin, mitomycin, and epirubicin, have been employed. In several institutions, the use of embolic, drug-eluting microspheres has almost completely supplanted conventional TACE. In a recent multicenter, phase 2, prospective, randomized, clinical trial, doxorubicin-eluting beads demonstrated a trend toward higher treatment response rates and increased tumor necrosis compared with conventional TACE.[67]

Estimating survival and recurrence rates is difficult due to the wide range of study designs, patient characteristics, and particular TACE procedures employed in the body of literature on TACE. The improvement in survival in treated patients may range from 20% to 60% at 2 years.[68] Nevertheless, it is evident that the significance of the improvement relative to the outcome if untreated depends in great part on the patient's baseline characteristics with regard to tumour stage, liver function, and general health state. Absolute contraindications to TACE include main portal vein thrombosis, severe encephalopathy, biliary obstruction, and Child-Pugh C cirrhosis. TACE causes some degree of ischemic hepatic damage, which has the potential to lead to hepatic decompensation, with a rate of up to 20% in one series.[69] However, the most common adverse effect of TACE is postembolization syndrome, which occurs in 60% to 80% of patients. There is varied degrees of pain in the right upper quadrant, nausea, moderate ileus, exhaustion, fever, and transient elevations in the levels of aspartate aminotransferase, alanine aminotransferase, and bilirubin. Symptoms are usually self-limited, lasting 3 to 4 days; full recovery is typical within 7 to 10 days.

Transarterial Radioembolization

TARE is another form of locoregional treatment for various stages of hepatocellular carcinoma.[70] TARE delivers radioactive microspheres loaded with β emitting yttrium 90 isotope into the tumor, leading to local tumor destruction. TARE can be performed as an outpatient procedure not requiring overnight observation, which is typically necessary for TACE. Patients do, however, need a planning or mapping angiography, 99mTc-MAA scans (technetium 99mTc macroaggregated albumin), as well as a yttrium 90 dose, to assess the lung shunt fraction, typically a few weeks before the treatment. However, two single center studies have shown the safety of same day TARE without a planning angiogram.[71,72]

For patients awaiting liver transplants, TARE can be utilized as a bridge therapy to halt the progression of early-stage hepatocellular carcinoma. Radiation segmentectomy with a target dose of greater than 190 Gy has been shown to provide excellent tumor control and survival outcomes comparable to treatments with curative intent for early stage hepatocellular carcinoma.[73] TARE can also provide radiation lobectomy to achieve remnant liver hypertrophy while providing tumor control before lobectomy or tri-segmentectomy in patients with hepatocellular carcinoma but an inadequate predicted volume of future liver remnant, which can lead to safe resection and favorable postoperative outcomes.[74,75]

Stereotactic body radiation therapy

SBRT is yet another successful hepatocellular cancer therapy strategy. It uses external beam radiation therapy, which is highly conformal and delivers large doses to the tumour over a limited number of fractions. Multiple studies have shown that SBRT is as effective as local ablation for early stage hepatocellular carcinoma and has similar efficacy to TACE for intermediate stage disease.[76-79] A small, open label, phase II randomized controlled trial showed that SBRT in combination with TACE was superior

to sorafenib in improving the survival of patients with advanced stage disease.[80] While SBRT is not currently considered as a first line treatment option for hepatocellular carcinoma, it could be a promising alternative treatment, especially when primary treatment modalities are not feasible.

2022 Update of BCLC Treatment Algorithm of HCC and role of Interventional Radiologists (IRs) at each stage.[81]

In accordance with the idea of stage migration, resection should be considered first and TACE second if it is not possible for any reason. TARE is only recommended in single HCCs under 8 cm despite being thought to be equally effective as TACE.

In BCLC A, resection is favored in > 2cm HCC because of higher recurrence rate after ablation. Although it is not specifically advised for large tumours, radiation lobectomy by TARE can be taken into account in the event of a small future liver remnant. The 2022 BCLC update advises against resection in non-LT candidates with multifocal tumours in favour of ablation for HCCs under 3 cm and TACE in all other cases. Ablation, TACE, or TARE can be used for bridging in LT candidates who have waiting time more than six months.

According to tumour burden and liver function, the BCLC-B patients are divided into three groups in the 2022 BCLC version. Patients who meet the "Extended Liver Transplant Criteria" (often based on size and/or AFP) recommended by each institution/country fall under the first grouping and are candidates for LT. Patients without LT options who have well-defined nodules and retained portal flow that enable for targeted access to feeding tumour arteries make up the second class. They are (the only) TACE candidates. Patients with substantial, widespread, and infiltrative bilobar liver involvement make up the third group. These individuals, who in essence do not profit from TACE, are advised to have systemic treatment. However, since no threshold is given, it is still up to the clinician to categorise patients into this third class. Notably, patients with mild fluid retention (even on imaging) who require diuretic medication or have a bilirubin level > 2 mg are not good candidates for TACE. The role of TACE in BCLC B is generally relatively constrained, while TARE is not even addressed.

Finally, due to negative phase III trials, the 2022 update does not acknowledge the importance of IRs in BCLC C patients, which is at odds with both real-world practise and the most recent outcomes of TARE in advanced HCC.

Systemic Therapy

Guidelines on the management of hepatocellular carcinoma were published on March 1, 2022, by the American Gastroenterological Association.[82]

- **First-line treatment for HCC in patients with preserved liver function.**

Atezolizumab+bevacizumab is recommended above sorafenib for HCC patients with intact liver function who are ineligible for locoregional treatment (LRT) or resection or who have metastatic disease.

Lenvatinib or sorafenib is recommended above no systemic therapy for HCC patients who have maintained liver function and are not candidates for LRT or resection or who have metastatic disease and are not candidates for atezolizumab+bevacizumab.

- **Second-line therapy for people whose disease has progressed or who are resistant to first-line systemic therapy.**

Cabozantinib, pembrolizumab, or regorafenib is advised above no systemic therapy for HCC patients who have maintained liver function and are not suitable for LRT or resection or who have metastatic disease and have seen disease progression on sorafenib.

Ramucirumab is recommended over no systemic therapy for HCC patients with maintained liver function, alpha-fetoprotein levels >400 ng/mL, who are ineligible for LRT or resection, who have metastatic disease and disease progression on sorafenib.

- **Systemic therapy for HCC in patients with poor liver function.**

For HCC patients who have poor liver function not eligible for LRT or resection or who have metastatic disease, the AGA suggests against routine use of sorafenib.

- **Systemic therapy for HCC as adjuvant therapy.**

  For HCC patients undergoing curative surgical resection or curative local ablation, the AGA suggests against adjuvant sorafenib therapy.

For HCC patients undergoing TACE (transarterial chemoembolization) LRT, the AGA suggests against adjuvant sorafenib therapy or adjuvant bevacizumab therapy.

Multidisciplinary approach

The management of HCC encompasses multiple disciplines that includes hepatologists, diagnostic radiologists, pathologists, transplant surgeons, surgical oncologists, interventional radioliogists, medical oncologists, radiation oncologists, nurses, and palliative care professionals. A recent study found that developing a truly multidisciplinary clinic for HCC patients with a

specialised tumour board evaluation improved survival.[83] Patients with HCC should be seen at these clinics whenever possible, and if this is not possible, a referral to a centre with a real multidisciplinary clinic should be considered.

Conclusion

Despite the fact that HCC is a deadly disease, the best chance for a long life is to screen and diagnose it early. Hepatology societies differ in their preferred methods of surveillance, but, in general, US with or without AFP every 6 months is adequate for most patients. There are a variety of therapeutic methods available, and additional approaches are being researched. Patients are frequently best served in centres with experience in HCC management, where a multidisciplinary approach can be used, due to the disease's complexity. Advances in HCC prevention, early identification, and therapy have improved survival and prognosis for a disease that was formerly thought to be fatal only a few decades ago.

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