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Editorial

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Comprehensive Review of Biomarkers, Clinical Considerations, and Treatment for Hepatocellular Carcinoma

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Abstract

Worldwide, Hepatocellular Carcinoma (HCC) is a factor in a number of cancer-related deaths. Curative procedures such surgical resection, liver transplantation, and local ablation can increase a patient's chance of survival in the early stages. However, the disease is only discovered at an advanced stage, and some treatments are only local and palliative care. To increase longevity and enhance the patient's quality of life, early identification of HCC and adequate treatment are essential. The Golgi 73 protein (GP73), Glypican-3 (GPC3), Osteopontin (OPN), microRNAs, and other molecular biomarkers have thus been the subject of extensive research due to their great sensitivity and dependability. Important carcinogenic processes, such as tumor angiogenesis and development, can be controlled by microRNAs.

Keywords: Biomarkers; Hepatocellular carcinoma; Treatment; Causes; Prognosis

Introduction

Hepatocytes are the source of Hepatocellular Carcinoma (HCC), the predominant form of liver cancer that accounts for more than 80% of cases. Incidence of HCC is higher in China at typical ages of diagnosis between 55 and 59 years, and in North America and Europe at 63 to 65 years. East and Southeast Asia, as well as East and Western Africa, have higher rates of HCC. According to GLOBOCAN's most recent estimates, there were 745,000 liver cancer fatalities and 782,000 new cases globally in 2012. In light of this, the World Health Organization (WHO) ranks HCC as the second most common cancer death cause. Environmental and genetic factors interact to cause the development of HCC [1]. Important risk factors for the development of HCC include liver cirrhosis, infection with the hepatitis B and C viruses, excessive alcohol intake, ingestion of aflatoxin B1, and Non-Alcoholic Steato-Hepatitis (NASH). The stage of the malignancy at diagnosis affects the life expectancy of HCC patients. Although a few months are anticipated in the advanced stages, a five-year survival rate is achievable with an early diagnosis and efficient therapy. Early diagnosis allows for restricted and successful treatment; nevertheless, when the disease is progressed and standard chemotherapy fails to produce the desired results, a bad prognosis is anticipated.

Curative therapies include surgical resection, liver transplantation, and local ablation can prolong patients' lives when HCC is still in an early stage. Therefore, to maximize survival and enhance the quality of life for HCC patients, early detection and appropriate therapy are essential. Sorafenib has been proven to increase patient survival when stage C (advanced stage) liver cancer is present, whether or not there is vascular invasion and retained liver function, according to the Barcelona Clinic Liver Cancer (BCLC) classification [2]. In the diagnosis of HCC by serum, Alpha-Fetoprotein (*AFP*) has been employed as a biomarker. Due to its limited specificity and sensibility, AFP is not a precise marker. A biomarker with improved diagnostic precision and high reliability is therefore required. In HCC, numerous tumor biomarkers have been discovered recently, including the Golgi 73 protein (*GP73*), Glypican-3 (*GPC3*), microRNAs, and others. Current genetic research can help with HCC diagnosis, prognosis, and treatment in addition to offering insights into future molecular cancer treatment procedures. The current review stands out in this context for highlighting recent developments in the causes, therapies, biomarkers, clinical features, and outcomes of hepatocellular carcinoma.

Causes and risk factor

The development of HCC is frequently linked to liver cirrhosis brought on by long-term liver conditions like chronic hepatitis, HBV or HCV infection, and autoimmune hepatitis. Aflatoxin exposure and ingestion, diabetes mellitus, smoking, and sporadic genetic diseases like alpha-1 antitrypsin deficiency, hemochromatosis, tyrosinemia, porphyria, and Wilson's disease are additional risk factors. Other risk factors include excessive alcohol consumption, NASH, non-alcoholic fatty liver disease (NAFLD), NASH, and NASH. Risk factors for the development of HCC include male gender, advanced age, obesity, and VHB co-infection. A significant population-based study with 11,801 male participants from Taiwan (followed up for 15 years) found that independent alcohol consumption (2.1%), HBV infection (55.7%), and HCV infection (153.3%) all contributed to an elevated risk for the development of HCC [3].

The study found a relationship between HBV and HCV infection and an elevated risk of developing HCC (1.7%), and that the risk increases by 4.2% when HBV infection and alcohol use are combined. When compared to an HCV infection alone, the presence of chronic HCV infection with excessive alcohol intake cans double the risk of HCC. In contrast to men, women are more likely to acquire liver lesions and cirrhosis from drinking alcohol due to the influence of hormones like estrogen. The liver is the organ in charge of metabolizing these hormones, and alcohol use increases the oxidative stress and inflammation brought on by high levels of female hormone steroids in the liver. Alcohol is converted in the liver to acetaldehyde, which is extremely toxic to hepatocytes and can lead to the development of adducts that can damage mitochondria and inactivate the glutathione peroxidase system. A deficiency in DNA synthesis and repair in liver cells, as well as the production of reactive oxygen species (ROS), which causes oxidative stress and increases pro-inflammatory signaling, are some of the harmful effects of alcohol and its toxic byproducts. NAFLD is another risk factor for the development of HCC, according to several researches. At the moment, metabolic illnesses like diabetes,

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obesity, and metabolic syndrome are a global public health issue. NAFLD is prevalent in 90% of obese adults and around 70% of people with diabetes mellitus [4].

Independent of co-infection with HBV or HCV and alcohol intake, diabetic people has an increased risk (2.5 times) of developing HCC. NAFLD can develop into NASH, cirrhosis, and HCC because to the inflammation brought on by the buildup of fat in the liver. According to a study done in Europe, smoking could be a risk factor for the emergence of hepato-carcinogenesis. Tobacco use was linked to liver illness and an elevated mortality risk from alcoholic beverages. Consumption and exposure to fungi-caused aflatoxins, in particular aflatoxin B1, which frequently contaminates stored grains like wheat and peanuts in resource-constrained settings, is another risk factor for hepato-carcinogenesis. When mycotoxins bind to the DNA of hepatocytes, they cause proto-oncogenes or tumor suppressor genes, specifically the *p53* gene, to mutate. This occurs in mitotically active cells, such as those in cirrhotic or chronic HBV-infected livers.

Discussion

There are numerous curative and/or palliative treatments available for HCC. The stage of the cancer, the specialists' level of experience, the resources at hand, the patient's age, and any coexisting conditions should all be considered while choosing the best course of action. The BCLC categorization divides patients into very early, early, moderate, advanced, and terminal stages by taking into account the pertinent HCC criteria [5]. For patients in the early stages, resection, ablation, and transplantation are thought to be possibly curative alternatives. Chemoembolization is recommended for people in the intermediate stage, whilst Sorafenib can be used to treat individuals in the advanced stage. Finally, palliative care is given to patients who are nearing the end of their lives in order to improve their quality of life. Early-stage HCC patients without cirrhosis should opt for surgical resection as their preferred treatment. Only when cirrhotic individuals have a single nodule, retained liver function, and no portal hypertension is surgical excision recommended. Patients who undergo resection have a five-year survival rate that ranges from 50% to 75%, but the recurrence rate (tumor formation and metastasis) can be as high as 50%. Therefore, for HCC coupled with vascular invasion or tumor metastases, surgical resection is not advised.

Ablation is a popular treatment that involves employing radiofrequency treatments to eradicate tumors that are less than 5 centimeters in diameter. For patients who cannot undergo resection or transplantation, ethanol and cryosurgery are options. Ischemia and necrosis in the tumor microcirculation are brought on by ablation [6]. There were no appreciable differences in survival or recurrence rates between surgical resection and radiofrequency ablation, according to studies of randomized controlled trials, though the ablation was linked to decreased rates of hospitalizations and treatment-related problems. Transplantation is the recommended treatment for HCC patients with cirrhosis due to the decreased recurrence rate and increased survival. However, patients who could demonstrate superior outcomes are given priority for the liver transplant due to the shortage of accessible organs. Living donor liver transplants have been used as a way to shorten the waiting period for transplants and lower the mortality rate due to the restricted availability of deceased donor liver. For patients with severe cirrhosis and HCC, transplantation from living donors provides an alternate course of treatment. Studies have revealed that the relapse rate for transplants from living donors is greater.

The current treatment of choice for advanced HCC patients with retained liver function is sorafenib, an oral multikinase inhibitor with anti-angiogenic and anti-proliferative effects. Studies in multicenter trials and meta-analysis have demonstrated the effectiveness of sorafenib in extending life expectancy and delaying the onset of disease development. However, typical side effects such increased incidence of hypertension, diarrhea, tiredness, and dermatologic toxicity were tolerable and serve as pathways in clinical practice. Sorafenib has a significant cost of treatment, and Brazilian Public Health does not supply this medication for its use. The HCC is genetically varied, which presents a problem in the search for new treatments. As a result, VEGF plays a role in a number of processes that lead to tumor growth, invasion, and metastasis. The discovery of novel targets as a result of experimental investigations could forecast liver carcinogenesis, define novel biomarkers, and outline effective therapeutic approaches to drastically lower the number of HCC-related mortality [7].

Modern analytical methods including Next Generation Sequencing (NGS), mass spectrometry, proteomics, and metabolomics can help identify new molecular biomarkers for the diagnosis of HCC and provide crucial information for medical oncology. These biomarkers are discovered by genomic platforms and other genetic analyses of blood, tissue, urine, faces, and saliva, and they may help in the creation of tailored treatments based on a patient's genetic makeup and exposure to environmental risk factors. Biomarkers can be employed for HCC clinical staging, prognosis, and diagnostic purposes. Recent research suggests that promising molecular biomarkers, such as *GPC3* (Glypican-3), *OPN* (Osteopontin), *GP73* (Protein Golgi 73), *VEGF* gene (Vascular Endothelial Growth Factor), *EGF* gene (Epidermal Growth Factor), *PDGF* gene (Growth Factors Derived from Platelets), *IGF* gene (Growth Factor Similar to Insulin), mTOR.

GPC3 is a member of the family of cell-surface proteoglycans that functions as a regulator of cell division and is anchored to the plasma membrane by a glycosyl-phosphatidylinositol link. This protein is overexpressed in HCC, indicating a poor prognosis for patients, and it can inhibit the function of Dipeptidyl-Peptidase-4 *(DPP4),* causing apoptosis in various cell types. Because of its sensitivity (77%) and specificity (96%) in detecting tiny dysplastic nodules (2 cm), studies point to the *GPC3* as a potential marker of cancer. Researchers are presently looking on novel *GPC3*-based treatment plans for HCC [8].

Conclusion

Due to its various molecular pathways, causative agents, and late identification, HCC actually presents one of the toughest hurdles in the clinical therapy of cancer. However, in recent years, contemporary techniques such as genomic sequencing have been widely used to research and identify the risk factors for the development of carcinogenesis, and this work has the potential to lead to the identification of new molecular biomarkers. The improvement can also be attributed to the development of novel medications, such as the multi-kinase inhibitor Sorafenib from multi-center clinical research, which has showed promise in treating some patients in advanced stages. However, avoiding HBV and HCV infections and lowering alcohol consumption rates continue to be the greatest ways to drastically lower the incidence and fatality rates associated with HCC.

In conclusion, cirrhosis, HBV and HCV infection, alcohol use, the existence of NAFLD or NASH, intake and exposure to fungal aflatoxins, tobacco use, and hereditary factors all contribute to the development of HCC. Depending on the stage of the disease, there are a number of curative and/or palliative treatments available, including chemoembolization, surgical resection, ablation, transplantation,

and sorafenib, an oral multi-kinase inhibitor with anti-angiogenic and anti-proliferative effects that is commonly used and producing positive results, including high cure rates and low relapse rates. All treatments, however, have the potential to have negative side effects that reduce the patients' quality of life.

References

1. Abreu RM, Ferreira CS, Nasser PD, Kikuchi LO, Carrilho FJ, et al. (2013) Hepatocellular Carcinoma: The final moments of life. J Cancer Ther 4:377-383.
2. Adam R, Karam V, Delvart V, O'Grady J, Mirza D, al. (2012) Evolution of indications and results of liver transplantation in Europe: A report from the European liver transplant registry. J Hepatol 57:675-588.
3. Ba MC, Long H, Tang YQ, Cui SZ (2012) GP73 expression and its significance in the diagnosis of hepatocellular carcinoma: A review. Int J Clin Exp Pathol 5:874-881.
4. Buitrago-Molina LE, Vogel A (2012). MTor as a potential target for the prevention and treatment of hepatocellular carcinoma. Curr Cancer Drug Targets 12:1045-1061.
5. Cervello M, McCubrey JA, Cusimano A, Lampiasi N, Azzolina A, (2012) Targeted therapy for hepatocellular carcinoma: Novel agents on the horizon. Oncotarget 3: 236.
6. Eagon P (2010) Alcoholic liver injury:Influence of gender and hormones. World J Gastroenterol 16:1377-1384.
7. Dargel C, Bassani-Sternberg M, Hasreiter J, Zani F, Bockmann JH, et al. (2015) T cells engineered to express a T-cell receptor specific for glypican-3 to recognize and kill hepatoma cells in vitro and in mice. Gastroenterology 149; 1042-1052.
8. Gramantieri L, Fornari F, Callegari E, Sabbioni S, Lanza G, et al. (2008) MicroRNA involvement in hepatocellular carcinoma. J Cellular Mole Med 12; 2189-2204.

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