Is hepatocellular carcinoma preventable?

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Hepatocellular carcinoma (HCC) represents the fifth most common cancer in the world, and is responsible for up to one million deaths annually worldwide.[1,2] In Saudi Arabia, liver cancer ranked second in males, and seventh in females. The overall Age-Standardized Ratio (ASR) was 4.2/100,000. The ASR was 6/100,000 for males and 2.4/100,000 for females. The mean age at diagnosis was 65 years in males and 59 years in females.[3]

Recognizing the importance of this disease in Saudi Arabia and in the Middle East, the Saudi Medical Journal has kindly accepted my initiative to invite international experts to write 4 review articles that address the most recent advances in the diagnosis and management of hepatocellular carcinoma (HCC), and will be of major benefit to those involved in the medical care of patients with HCC.[4-7]

The 5-year survival rate for untreated symptomatic HCC is <5%,[8] whereas the 5-year survival rate in patients with cirrhosis who have a small (<2cm) HCC lesion and undergo liver transplantation is 80%; therefore, detection of small HCCs is highly critical to patient outcome.[9] Hepatocellular carcinoma remains a highly malignant tumor, with average survival rates after the onset of symptoms of less than one year.[10] Survival of patients with HCC is related directly to the number, size, and extent of liver lesions at diagnosis. Despite the debate on the efficiency and cost-effectiveness of screening or surveillance programs,[11] routine surveillance showed greater rate of early detection of smaller and lesser – stage tumors compared with those of clinically symptomatic tumors.[12] Since the people at risk are well identified, early detection of HCC is possible. The well-established clinical practice in the follow up of patients with chronic liver diseases with non-invasive and low cost methods of screening, via monitoring of α-fetoprotein levels and regular hepatic ultrasonography is now an acceptable routine standard of care for cirrhotic patients. There are promising novel circulating biomarkers for early detection of HCC, however, they are not validated for clinical practice.[13]

Imaging plays a major and central role in the diagnosis of HCC. Most HCC's are hypervascular and readily identified by contrast enhancement during magnetic resonance imaging (MRI) and computed tomography (CT). Most of the studies comparing dynamic MRI and dynamic triple phase CT scan have shown a slightly better performance with MRI compared with CT, and therefore, it should be the preferred modality for imaging in HCC.[14] Advances in molecular imaging should enhance the development of new diagnostic and targeted therapeutic methods.[15]

In the treatment of HCC, surgical management strategies including liver resection and transplantation play a central role. Liver transplantation remains the only curative option for the majority of early stage cases, as the vast majority arises in cirrhotic livers,[16] while surgical therapy also offers potentially curative treatment for HCC, only 10-20% of patients will be candidates for this modality.[17] Mazzaferro et al[18] showed that by restricting transplantation to patients with a single tumor of less than 5 cm in diameter, or 3 tumors of less than 3 cm, and without macrovascular or lymphatic invasion, overall survival figures of 75% at 4 years could be achieved, with only 8% tumor recurrence.[18] Liver transplantation should be the first option, and liver resection considered only in those not transplant eligible and who have well-preserved hepatic function. The limiting factor is shortage of donor organs, which has resulted in long waiting times for transplantation and increased the proportion of patients who will be removed from the waiting list due to tumor progression.[19] This shortage of donor organs is being further addressed by the use of split liver grafts, living donor transplantation and giving additional priority to patients with HCC.[20] The demand for donor organs and strict selection criteria mean this is not a realistic option for the majority.[21] Non-surgical management of HCC with radiofrequency thermal ablation (RFA) and percutaneous ethanol injection have been the 2 most common percutaneous tumor ablation modalities for the treatment of focal HCC.[22] Advanced (stage) non-surgical HCC requires combined therapeutic modalities of local, chemoembolization, or systemic therapies.

The treatment of HCC is usually difficult specially if diagnosed in an advanced stage, thus, future strategies

for HCC management should be directed towards development and evaluation of effective preventive measures in order to reduce HCC-related morbidity and mortality.

Hepatitis B and C viruses are the most common risk factors, therefore, a) the establishment of strict infection control measures to prevent new cases of Hepatitis B and C infections, b) wider distribution of Hepatitis B vaccination programs in high risk areas, c) development of Hepatitis C vaccine candidate and, d) the initiation of antiviral treatment to prevent progression of chronic hepatitis B and C to cirrhosis would be the best practice towards HCC prevention. In addition, primary prevention of other causes of chronic liver diseases such as non-alcoholic steatohepatitis and alcoholic liver disease should be addressed.

Indeed, HCC would be considered an ultimately preventable disease.

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References

1. Rustgi VK. Epidemiology of hepatocellular carcinoma. ***Gastroenterol Clin North Am*** 1987; 16: 545-551.
2. Fung J, March W. The quandary over liver transplantation for hepatocellular carcinoma: The greater sin? ***Liver Transpl*** 2002; 8: 775-777.
3. National Cancer Registry. Cancer Incidence Report, 2002: Saudi Arabia. Kingdom of Saudi Arabia: Ministry of Health; 2007.
4. Camaggi V, Piscaglia F, Bolondi L. Recent advances in the imaging of HCC: from Ultrasound to PET scan. ***Saudi Med J*** (In Press)
5. Hasegawa K, Kokudo N, Makuuchi M. Surgical Managements of Hepatocellular Carcinoma: Liver resection and liver transplantation. ***Saudi Med J*** (In Press)
6. Shiina S, Tateishi R, Yoshida H, Fumihiko K, Omata M. Local Ablation Therapy for Hepatocellular Carcinoma: From ethanol injection to radio frequency ablation. ***Saudi Med J*** (In Press).
7. Ng K, Poon R. Current treatment strategy for hepatocellular carcinoma. ***Saudi Med J*** (In Press)
8. El-Serag HB, Mason AC. Rising incidence of hepatocellular carcinoma in the United States. ***N Engl J Med*** 1999; 340: 745-750.
9. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. ***N Engl J Med*** 1996; 334: 693-699.
10. El-Serag HB, Mason C, Key C. Trends in survival of patients with hepatocellular carcinoma between 1977 and 1996 in the United States. ***Hepatology*** 2001; 33: 62-65.
11. Gebo KA, Chander G, Jenckes MW, Ghanem KG, Herlong HF, Torbenson MS, et al. Screening tests for hepatocellular carcinoma in patients with chronic hepatitis C: A systematic review. ***Hepatology*** 2002; 36 Suppl 1: S84-S92.
12. Bruix J, Llovet JM. Hepatocellular carcinoma: Is surveillance cost effective? ***Gut*** 2001; 48: 149-150.
13. Marrero J, Lok A. Newer Markers for Hepatocellular Carcinoma. ***Gastroenterology*** 2004; 127: S113-S119.
14. Noguchi Y, Murakami T, Kim T, Hori M, Osuga K, Kawata S, et al. Detection of Hepatocellular carcinoma: A comparison of dynamic MR imaging with dynamic double arterial phase helical CT. ***AJR Am J Roentgenol*** 2003; 180: 455-460.
15. Gharib H, Thomasson D, Li K. Molecular Imaging of Hepatocellular Carcinoma. ***Gastroenterology*** 2004; 127: S153-S158.
16. Freeman RB. Liver Allocation for HCC: A moving target. ***Liver Transpl*** 2004; 10: 49-51.
17. Cha CH, Ruo L, Fong Y, Jarnagin WR, Shia J, Blumgart LH, et al. Resection of hepatocellular carcinoma in patients otherwise eligible for transplantation. ***Ann Surg*** 2003; 238: 315-321.
18. Mazzaferro V, Regalia E, Doci R, Andreola S, Pulvirenti A, Bozzetti F, et al. Liver transplantation for the treatment of small hepatocellular carcinomas in patients with cirrhosis. ***N Engl Med*** 1996; 334: 693-699.
19. Llovet JM, Fuster J, Bruix J. Intention-to-treat analysis of surgical treatment for early hepatocellular carcinoma: Resection versus transplantation. ***Hepatology*** 1999; 30: 1434-1440.
20. Sharma P, Balan V, Hernandez JL, Harper AM, Edwards EB, Rodriguez-Luna H, et al. Liver transplantation for hepatocellular carcinoma: The MELD impact. ***Liver Transpl*** 2004; 10: 36-41.
21. Perry JF, Poustchi H, George J, Farrell GC, McCaughan GW, Strasser SI. Current approaches to the diagnosis and management of hepatocellular carcinoma. ***Clin Exp Med*** 2005; 5: 1-13.
22. Lopez L, Marrero J. Hepatocellular Carcinoma. ***Curr Opin Gastroenterol*** 2004; 20: 248-253.