
HEPATOCELLULAR CARCINOMA

Editors: Shuyou Peng, Ghassan K. Abou-Alfa, Patrick Pessaux



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Hepatocellular carcinoma: a new century and a new optimism

It was not long ago that the incidence rate of hepatocellular carcinoma (HCC) approximated the mortality rate. Due to the causative relationship between chronic viral infection, chronic inflammation, hepatotoxins, and hepatocellular carcinoma, this cancer is responsible for nearly one million deaths yearly worldwide. The last years have seen tremendous progress in diagnosis and treatment of this common cancer. The current book edited by Professor Xiujun Cai comprehensively summarizes the current understanding of this disease within the context of patient treatment and outcome.

The broad impact of this cancer on the entire world is highlighted in Section 2: “*Current Status of HCC in Different Countries and Regions*”. It is not just a cancer ravishing Asia, its impact in the Middle East, Europe, and Americas is well presented. The world context of this disease is appropriately accompanied by a discussion of the evolution and current status of the languages used by clinicians and researchers to communicate. The language of “staging systems” and “clinical pathways of care” are presented in Chapters in Section 1. This is truly an intersection of the fields of hepatology, infectious disease, and oncology, where surgeons, interventional radiologists, radiation oncologists, and medical oncologists now stand. The common vocabulary of these fields as well as the scientific concepts encompassing cellular metabolism, cellular proliferation, infectious diseases, and homeostatic pathways are well articulated in this book.

Liver transplantation clearly would be an optimal therapy, treating simultaneously the cancer and the underlying cause of infection and inflammation in the diseased liver. The limited availability of organs for transplantation and the cost of maintaining transplantation programs have limited the use of this wonderful technology to only a small proportion of patients. In Asia, where cadaveric organs are particularly hard to come by, most procedures in liver transplantation involve grafts from living donors. In China, where a national policy limiting the number of offsprings has been in place, living-related transplantation means that two-thirds of a nuclear family will be undergoing surgery, posing another deterrent to transplantation.

Over the past decades, the greatest progress involves improvements in techniques of surgical resection that now allow for safe removal of cancers from livers using partial hepatectomy (Section 5). Such surgeries have clearly proven to be potentially curative. Needle based thermal ablations now allow for effective cancer killing, and particularly durable killing of small tumors (Section 6). These needle-based therapies afford safe treatments in patients with advanced cirrhosis by minimizing amount of liver parenchyma resected or damaged. For small tumors, ablation is also proving to be as potentially curative and equivalent cancer treatment as partial hepatectomy, with the advantage of less morbidity (1). Finally, minimally invasive liver resections now also allows less morbid surgery for patients, allowing rapid recovery and less ascitic leak and complications (Section 5) (Leung and Fong, p225) (Herman and Coelho, p222) (2). Overall, treatment using partial hepatectomy, thermal ablation, and minimally invasive resections including robotic surgery allow for increasingly less morbid therapies that extend life and provide potential cure.

Great progress is being made in the understanding of the pathogenesis of HCC, giving promise to better markers for early diagnosis (Song *et al.*, p193), and in time, better systemic therapies. Diagnosis is certainly improving rapidly. Due to increasingly sensitive markers, and increasingly higher resolution of scanning techniques, smaller and smaller tumors are being detected for effective killing by percutaneous ablative (Section 6) and transcutaneous radiation techniques (Section 7). Equally impressive is the rate of progress in treatment of liver inflammation and infection. Treatment of viral hepatitis can now cure hepatitis C (3), and eliminate viremia and inflammation from hepatitis B. Treatment of liver fluke and public education to decrease consumption of the raw fish leading to this parasitic infection should decrease another cause of liver cancer (4).

In summary, progress in public health and infectious disease is decreasing the incidence of HCC. Transplantation remains a most attractive therapy for those patients with HCC and moderate or advanced cirrhosis. Partial hepatectomy and ablative therapies provide for life prolonging and potential curative therapies for the majority of treatable patients. These are also now

being increasingly less invasive to optimize patient outcome. It is certainly a new day in the treatment of this disease. The world community of surgeons, oncologists, and scientists has combined forces to provide for “More Cures, Less Invasive”.

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Hepatocellular carcinoma (HCC), which accounts for more than 90% of all primary liver cancers, affects more than 800,000 individuals annually and stands as the second cause of cancer-related death, worldwide. Unique of this typically inflammatory tumor, is its development in the context of readily identifiable environmental risk factors, like viral hepatitis B and C, alcohol and obesity, which theoretically would allow this lethal cancer to be curbed by strategies of primary and secondary prevention. This notwithstanding, HCC is on the rise in many geographical regions, often reflecting epidemics of viral hepatitis associated to either risk behaviors or poor sanitation, whereas, due to a lack of awareness, most patients are still detected with an advanced cancer disease that effects delivery of potentially curative therapies. Fighting against liver cancer, therefore, relies on an integrated approach that spans from the pillar represented by the implementation of strategies of primary prevention to the development of user friendly, effective drug regimens for patients with advanced HCC. In the last decade, many efforts have met with little success in developing therapies tailored upon the genetic profile and molecular subclass of the tumor, not to speak about the many failures to identify performant biomarkers for predicting treatment response. While further research is deemed necessary for similar scientific breakthroughs to materialize, other unmet medical needs in HCC research have emerged that challenge the community of caregivers, one above all how to scale up patient access to early diagnosis, which stands as the only pragmatic approach to cure HCC and currently relies on hospital-based programs of screening with abdominal ultrasound. Though, in an era of shortened organ donations, a cure from HCC caused by hepatitis B or C can also be attained with non-transplant options like open and laparoscopic hepatic resection and percutaneous local ablation, owing to the possibility of preventing liver decompensation and tumor recurrence with interferon-free antiviral therapy. On the other hand, in the liver transplant setting, direct antiviral agents have gained popularity, having cancelled recurrent hepatitis C that was responsible in one patient every three for shortened graft and patient survival whereas in many patients it was an hurdle for re-transplantation ,too. As we move away from the ages when HCC was considered an inexorably fatal cancer, I am sure that the reading of this textbook will help appreciating the outstanding leaps forward that have been made by liver oncology with the contribution of all the authors listed here,

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