The next generation of hepatocellular cancer experts: what do they think?

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It is generally accepted that most cancers are best managed by a multidisciplinary team (MDT) of healthcare professionals, each bringing their own area of specialist skill to the care of the patient. Hepatocellular carcinoma (HCC), the second commonest cause of cancer-related deaths globally, is an excellent example of this. Only a minority of patients has potentially curable disease, with cure dependent on surgery or ablation. Most patients have advanced disease on presentation or progress to advanced disease, when the only evidence-based life-prolonging interventions require an oncologist. The vast majority of HCC patients worldwide have underlying cirrhosis/chronic liver disease and one of the key determinants of potential treatment strategies is the liver’s underlying function; hence, the input of a hepatologist is essential. At our institution, we have instituted a weekly MDT clinic for our HCC patients. The clinic is attended by a medical oncologist, surgeon and hepatologist as well as a trainee in each discipline. All our patients are discussed as a team and seen by one or more of the relevant specialist teams on the day, as necessary. In addition to the patient benefits, we believe this is also a good way for trainees to learn about the MDT management of HCC. However, what do the trainees think? In this article, our specialist trainees in medical oncology, hepatology and surgery consider what the next generation of trainees needs to deliver excellent HCC care, and what they anticipate will be the major challenges and breakthroughs during their future careers.

The trainee hepatologist

The roles of hepatologist include ensuring chronic liver disease patients undergo appropriate surveillance, in other words, ensuring the underlying liver disease, as well as any potential complications, are optimally managed and diagnosing any HCC as soon as possible. When HCC does develop and one first looks at the Barcelona Clinic Liver Cancer (BCLC) treatment algorithm [1], life appears relatively straightforward; patients fall neatly into a category based on the radiological characteristics of their tumor and then they filter down to the appropriate treatment options based on their liver function. However, a significant number of our ‘real-life’ patients challenge this simplistic model. The resectability of their tumor is debated by differing radiological and surgical opinion, their synthetic function fluctuates or their performance status is such that simply relying on their laboratory parameters to deny curative therapy is not met with consensus agreement. The challenge of modern multidisciplinary HCC care is to identify the marginal cases where a more aggressive approach is justified while still relying on the cross-specialty expertise from experienced colleagues to prevent futile treatment.
Learning the skills to negotiate these complex cases and reach an agreed multidisciplinary consensus is the challenge of providing excellent care. The training requirements to effectively engage in this type of process as a hepatologist require a blended skill-set, a solid evidence-based knowledge of the field, a close working relationship with local transplant centers, the clinical experience gained from managing a wide range of complex marginal cases and the teamwork and leadership attributes that allow effective cross-specialty engagement.

An obvious major challenge to the treatment of HCC is the late diagnosis of many tumors, often resulting in patients presenting with advanced multifocal disease where treatment options are limited. Unfortunately, many patients who pass through our specialist HCC clinic have had no regular screening despite a longstanding diagnosis of cirrhosis. Even in specialist liver centers, there are few examples of exemplary screening programs. There is a clear deficit in the execution of HCC screening in most countries and a concerted effort, accompanied with financial and infrastructure support, is urgently needed. A more comprehensive national screening program should be adopted that exploits IT technologies and permits a catch-all system, which automatically enrolls and recalls all at-risk patients.

Looking into the future, an accurate and less costly screening modality would be hugely welcomed. Discriminatory metabolic profiles have been described in urinary 1H nuclear magnetic resonance spectroscopy studies with diagnostic sensitivities outperforming serum alpha-fetoprotein [2]. Clearly, these technologies are in their development stages, but the novel approach of being able to exploit a bedside urinary biomarker to indicate the development of early HCC is hugely exciting.

The trainee surgeon

Despite all the advances in our knowledge of HCC and surgical techniques, HCC treatment still represents a challenge for surgeons. Surgery by resection or transplantation, along with ablation for small single HCCs, represents the only current potential curative treatment for HCC [3]. However, only a minority of patients with HCC is suitable for surgery, since management depends on tumor-related factors, hepatic function, liver remnant and patient’s fitness. Furthermore, recurrence rates remain significantly high, in the absence of transplantation. Different treatment and management modalities can also be combined, potentially leading to improved treatment outcomes [3,4].

An MDT approach is essential to coordinate, personalize and improve the management of HCC patients [5]. Clearly, hepatopancreato-biliary (HPB) surgeons need to possess the knowledge, skills and clinical experience to perform surgery in these complex patients. However, apart from surgical expertise, a strong understanding of pathology, oncology, liver function, diagnostic and interventional radiology is essential for surgeons to deliver excellent HCC care in close collaboration with hepatologists, oncologists and radiologists. HPB surgery is a complex subspecialty that requires long and dedicated subspecialty training. It has been demonstrated that high-volume HPB centers achieve better surgical outcomes and offer better training opportunities. Training should focus not only on achieving necessary operative competency, but also remain within a multidisciplinary environment to ensure interspecialty liaison. Last but not least, research is an integral part of modern medicine. It may seem difficult to coordinate the need for intense and continuous clinical practice, research and residency length, especially in HPB surgical training, which already requires additional years of dedicated training on top of the standard general surgical training. However, research should be an integral part of HPB surgical training to form expert surgeons who are also good doctors and can contribute to teaching and scientific progress [6].

Medicine and surgery are fields in continuous and rapid evolution driven by developments in technology. In the future, as has happened for laparoscopic surgery, technical developments will help in overcoming the present limitations of delivering robotic surgery in the field of liver surgery [7]. Surgery will continue to have a significant role in the treatment of HCC, but indications may change and surgery may become part of a combined treatment approach where novel oncological agents and interventional radiology may have a greater role in curative strategies. Hopefully, improved understanding of tumoral and host factors and molecular biology will help in identifying the best treatment strategy for HCC [8]. Surgeons need to be ready to evolve along with these innovations and developments.
The trainee medical oncologist

Training in medical oncology in the UK involves, over a 48-month period, learning about the management of different cancer types through specialist rotations. Currently, HCC is not seen as an ‘essential’ training need within the UK medical oncology curriculum, and treatment of HCC is focused in centers with access to HPB physicians and surgeons, interventional radiology and oncologists. Concentrating patients into a small number of centers facilitates the development of better surgical techniques, better drugs and better treatments delivered by an interventional radiology approach. It also delivers high standard training, with easy access to participation in discussions and structured consultations, good educational supervision, research and clinical trials and participation in the development of standards for safe administration of treatment. However, this model is also a stumbling block for training. A large proportion of ‘The Next Generation’ may never have been exposed to HCC in their training. I strongly feel, the modern curriculum may never have been exposed to HCC in their own rotation does not have ready access to.

From an oncologist’s point of view, one of the most frustrating parts of being involved in HCC management is the general lack of biopsy material. HCC is one of very few cancers diagnosed on the basis of imaging characteristics alone [1]. While this saves the patient from the potential small risk of tumor seeding or hemorrhage from biopsy, it does may delay the development of novel agents for advanced or inoperable disease. Treatment with sorafenib, the current standard of care in unresectable HCC, extends life by between 2.1 and 2.8 months [1]. However, there are reports in the literature of ‘super-responders,’ patients deriving longer than 18 months of benefit from treatment. Without biopsies and biomarker-driven research, we struggle to identify what ‘signatures’ of potential response are out there, how to identify patients for whom treatment will yield only toxicity and compromised quality of life without clinical benefit or how to identify novel targets in a timely manner.

Nonetheless, this is an exciting time to be practicing in the HCC arena. There is an increasing recognition for the need to obtain histology, at least in the context of trials of advanced HCC, to improve our understanding of the molecular pathogenesis of the disease. The use of radiological evaluation, alone or in combination with different drugs, is a promising new approach. The concept of ‘down staging’ is also exciting, using treatments typically associated with palliative stage disease to open up the possibility of transarterial chemoembolisation or radio- or micro-wave ablation (TACE or RFA/MWA), and even resection. Working in a center with high recruitment to clinical trials is thrilling, and I hope that much of what we are doing now will become ‘gold standard’ in the years to come.

References


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