

Multidisciplinary Team Management of Patients with Hepatocellular Carcinoma

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Abstract

Purpose of Review The purposes of the current review are to (1) define multidisciplinary care and a proposed composition for a multidisciplinary team and (2) summarize process and outcome measures associated with multidisciplinary care for patients with hepatocellular carcinoma (HCC).

Recent Findings There has been a shift from multidisciplinary tumor boards to multidisciplinary clinics, which facilitates greater provider discussion and interaction over patients' treatment course. Although most studies examining the effect of multidisciplinary care for the management of a newly diagnosed patient with HCC rely on surrogate measures of quality cancer care, recent studies have demonstrated significant improvement of stage-stratified survival. **Summary** HCC is a complex and heterogeneous disease due to the concomitant presence of underlying liver disease and cancer. Given the variety of available treatment options and data showing improved outcomes, it should be considered best practice for HCC patients to be managed by a multidisciplinary team.

Keywords Hepatocellular carcinoma · Cancer care · Multidisciplinary care

Introduction

Hepatocellular carcinoma (HCC) is the third leading cause of cancer deaths worldwide and the leading cause of death in patients with cirrhosis [1]. Currently, HCC is the fastest-growing etiology of cancer-related deaths in the USA with rapidly increasing incidence and mortality [2].

Patients with HCC are a heterogeneous cohort due to varying severity of their underlying chronic liver disease and differences in tumor burden. The treatment algorithm for these patients encompasses physicians from several fields including hepatology, surgery, interventional radiology, radiation oncology, medical oncology, and palliative care. In an attempt to coordinate this multimodal care, multidisciplinary teams (MDT) have been established to promote interdisciplinary collaboration and improve outcome measures of patients with HCC.

The aims of this review are to (1) define multidisciplinary care, (2) describe the composition of a MDT, and (3) examine outcome measures associated with the formation of a MDT in the care of HCC patients.

Multidisciplinary Team Defined

The care of a newly diagnosed cancer patient is complex and depends on coordination between multiple providers including specialist physicians, primary care physicians, patients, and other support services. This coordination permits the exchange of technical information and improves communication between all those involved in providing care to the patient. The complexity of cancer care is more pronounced in the treatment of HCC compared to other solid organ tumors. For a newly diagnosed patient with HCC, entering into the healthcare system through multiple potential ports of entry secondary to the

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multitude of available treatment options adds to the complexity of care for the HCC patient (Fig. 1). Historically, HCC patients were often discussed in tumor board conferences, where the “port of entry” physician presented patients to consultants from various specialties to formulate a treatment plan at the time of initial consultation [3, 4].

Over time and with the support of the National Cancer Institute through the formation of cancer networks, there has been a paradigm shift away from tumor boards and towards creation of MDTs [5–7]. The multidisciplinary team approach to cancer care confers a more proactive and interactive structure involving providers from a broad range of medical specialties. This differs in a subtle but important way from the tumor board conference format. In a tumor board conference, the treating physician gathers information from specialists to formulate a treatment plan and implements the plan in a “silo” without continuous collaborative consultation along the patient’s disease course. On the other hand, the MDT approach provides the team framework, which enables the treating physician to continuously converse with a broad array of the treating physicians and alter the patient’s treatment during the disease course [8]. In addition, the MDT approach facilitates increased patient involvement in the decision-making process so that patients comprehend the

underlying cancer diagnosis and the available treatment options in a patient-centric manner.

The importance of the paradigm shift from a tumor board to a MDT approach in formulating treatment plans in HCC cannot be overstated. The MDT format enhances fluidity in decision-making among physicians and combines all physicians and ancillary support services under one team leading to fewer treatment delays and smoother transitions in care [9]. These advantages particular to MDT are critical for the treatment of HCC patients given the heterogeneity in patients and the multitude of available treatment options. For example, a patient who initially undergoes a curative treatment (surgical resection or orthotopic liver transplantation) and subsequently develops a local recurrence within the liver may be eligible for locoregional or systemic treatment options. Depending on the characteristics of the recurrence such as venous invasion or presence of metastatic disease and the patient’s performance status, potential treatment options will differ and the fluidity of a MDT approach eases transitions from one treatment modality to another. Similarly, a patient with tumor burden beyond Milan Criteria may be downstaged with locoregional therapy, such as transarterial chemoembolization (TACE), and therefore considered for liver transplantation. However, these

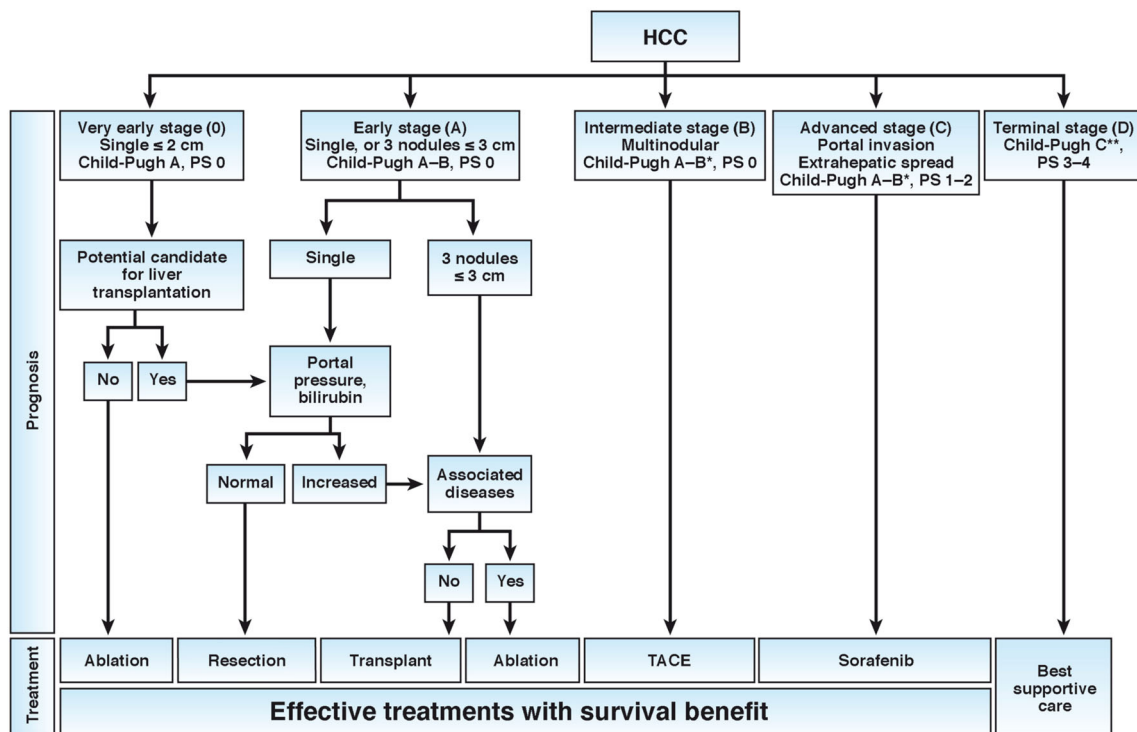


Fig. 1 Staging and treatment of hepatocellular carcinoma according to the Barcelona Clinic Liver Cancer system. Reprint from Gastroenterology, Volume 150, Issue 4, Jordi Bruix, Maria Reig, Morris Sherman, “Evidence-Based Diagnosis, Staging, and Treatment of Patients with Hepatocellular Carcinoma”, April 2016, with permission from Elsevier. *, Child-Pugh classification is not sensitive to accurately

identify patients with advanced liver failure that would deserve liver transplant consideration; **, patients with end stage cirrhosis due to heavily impaired liver function (Child-Pugh C or earlier stages with predictors of poor prognosis, high MELD score) should be considered for liver transplantation. In them, HCC may become a contraindication if exceeding the enlistment criteria. PS, Performance status

transitions may be missed if providers are operating on their own, outside of a MDT setting.

Unfortunately, the MDT approach in HCC has not been widely implemented. A recent study in the Veterans Administration setting demonstrated that either a surgeon or oncologist saw only 31% of newly diagnosed HCC patients, and only 34% of them received treatment [10•]. Similar findings in a study utilizing the Surveillance Epidemiology and End Results (SEER)-Medicare database demonstrated that 22% of HCC patients saw a single medical provider, and only 39% saw 3 or more providers [11]. Both of these studies imply that most patients with HCC were not seen in the MDT care setting but rather were evaluated by a single provider, and their treatment was predicated by the specialty of this one provider.

Composition of an HCC MDT

The success of a HCC MDT is determined by the composition and size of the team [12, 13]. An effective HCC MDT requires a basic composition to adequately discuss the heterogeneous treatment options available to a patient with HCC. Specifically, an effective MDT requires at least one provider from the following specialties: hepatology, surgery, interventional radiology, and medical oncology. Addition of providers from radiation oncology and palliative care can be beneficial depending on local expertise. As for team size, a large team is usually necessary for the treatment of HCC, albeit larger teams are more difficult to coordinate. Notably, in various cancer types, large teams have been associated with worse team performance and poor patient outcomes [14]. Thus, a careful balance between proper team composition and reasonable team size is necessary to ensure harmonious team dynamic and optimal patient outcomes.

Ancillary support is also crucial to the long-term success of the HCC MDT. The ideal team composition would also include a physician extender who will administer and coordinate the program and navigate patient care. A recent study highlighted the importance of a nurse coordinator as a portal of entry into the HCC MDT system [15•]. A nurse coordinator should be responsible for maintenance of patient records and for navigating patients during assessments, treatments, and follow-up visits. Additional ancillary support needed for a successful HCC MDT may include nutritionists, social workers, and psychologists.

In addition to team composition and size, a third component of a HCC MDT that must be established is whether an “actual” or “virtual” setting is appropriate. Actual MDTs have providers that see patients in the same setting and time period, thereby allowing for interactive and collaborative treatment decisions in a real-time fashion. Virtual MDTs have no conjoined clinic time or place and merge a tumor board type

conference with a sequence of separate, disjointed clinic visits with multiple providers over a short period of time. Both settings rely on the nurse coordinator to maintain careful coordination of patient care and facilitation of communication through formally structured medical records. As a MDT is formed and seen an increase in patient referrals, there is usually a shift from a “virtual” to an “actual” MDT as revenue streams justify both physician time and space in a single clinic.

UT Southwestern Medical Center Model of Multidisciplinary HCC Care

Prior to establishment of the UT Southwestern (UTSW) HCC MDT in 2008, care for newly diagnosed and established HCC patients was fragmented and largely driven by the portal of entry site into the healthcare system [16•]. Treatment decisions were largely made in isolation and were biased towards the initial provider’s specialty. Following the establishment of the UTSW HCC MDT, all newly diagnosed or referred patients have been triaged by a single dedicated nurse coordinator who ensures all patient records and images are collected and entered into the electronic medical record in preparation for the initial clinic consultation (Fig. 2). During the initial clinic consultation visit, a patient is evaluated first by the medical and surgical co-directors of the HCC MDT clinic. Then, patients, during the same clinic visit, are appropriately scheduled with providers from transplant hepatology, surgical oncology, interventional radiology, and/or medical oncology. Patients who require evaluation by two providers (e.g., transplant hepatology and interventional radiology for bridging therapy with TACE while awaiting liver transplantation) are

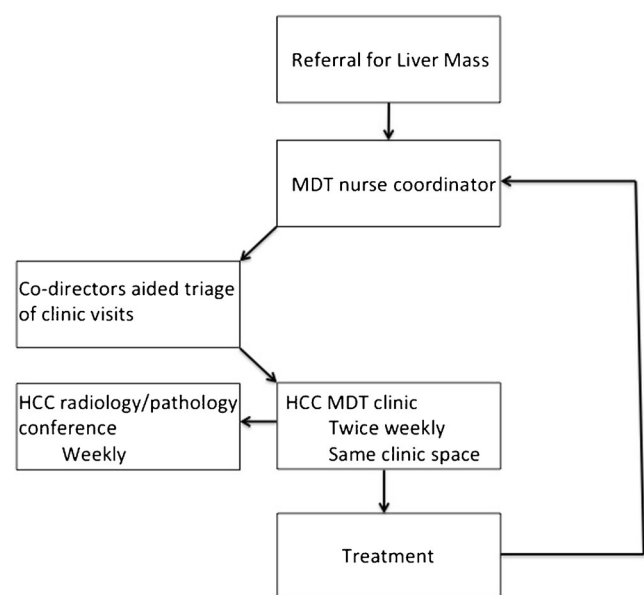


Fig. 2 UT Southwestern Medical Center Liver Tumor Clinic workflow

scheduled with both providers during the same clinic visit. These providers are gathered in the same clinical space allowing for ease of collaborative decision-making. Additional ancillary services from social workers, dieticians, and palliative care are provided within the clinic on an as-needed basis.

In conjunction with the HCC MDT clinic, a weekly HCC radiology/pathology conference is held to discuss imaging and pathology findings of patients with newly detected liver lesions or those with possible changes in their treatment plans. The nurse coordinator schedules patient follow-up visits, records treatment plans from tumor board, and enters patient data into the electronic medical records. The recommendations from the weekly conference are incorporated in to the medical record to allow follow-up communications with referring physicians. In addition to the clinical aspect of the MDT, dedicated HCC research coordinators within the clinic setting screen patients for entry into available clinical trials.

Outcome Measures Following the Establishment of a HCC Multidisciplinary Team

The delivery of HCC cancer care following diagnosis is a complex process with multiple points along the cancer continuum where process failures can occur in the absence of a HCC MDT program. Delays in referrals to treating physicians following HCC diagnosis of nearly 3 months have been seen in the absence of a speciality HCC clinic [17]. In addition, both delays in treatment and treatment underuse are also seen in the absence of a HCC MDT clinic [18, 19].

In spite of the overwhelming consensus regarding the utility of multidisciplinary cancer care and MDT formation, very little documented evidence demonstrates a benefit in clinical outcomes or even surrogates of clinical outcomes. Most studies on multidisciplinary care, tumor board conference, or MTD fail to demonstrate an improvement in overall survival rates, and instead, focus on surrogates of improved clinical outcomes including changes related to clinical care recommendations, consensual team decision-making, good teamwork, and increased adherence to clinical practice guidelines.

Gashin et al. described their experience with respect to adherence of treatment decisions recommended by a HCC multidisciplinary tumor conference [20]. In their study, 137 patients were enrolled and generated 419 tumor board discussions over the course of a 2-year period. The recommendations made by the tumor board were not followed in 145 discussions (35%) of 90 individual patients. Among those discussions, approximately half were not followed due to physician-related reasons including the treating physician preferring an alternative treatment or deeming a patient to be ineligible for the MDT-recommended treatment. After the first tumor board conference discussion, patients who received the

recommended treatment were more likely to be alive at 1 year and more likely to receive curative therapies including surgical resection or liver transplantation. Similar to other studies, it is difficult to ascertain whether the authors classified their MDT correctly. It may have been more appropriate to broadly reclassify the MDT as a tumor board conference, as by the authors' own conclusions, the majority of physician-related decisions for not following recommendations were due to the absence of the treating physician at the initial decision-making conference. This study highlights the potential drawback of team mechanics when all members of the team are not involved on a regular basis or when the team does not have an egalitarian decision-making process.

Zhang et al. examined the impact of establishing a multidisciplinary liver tumor clinic on changing treatment decisions implemented by outside physicians prior to referral [21]. Seventy of the 168 patients (42%) referred to the multidisciplinary clinic with a formal management plan had a change in the original plan following discussion in the clinic. Unfortunately, less than 30% of the patient cohort had a diagnosis of HCC, and there were no changes in outcome measured. Surprisingly, only 51% of patients returned for follow-up visits with only 89% receiving some form of treatment. The lack of follow-up and treatment argues that the described clinic was more responsible for "second opinion" visits and not actual treatment visits, and it is therefore difficult to draw firm conclusions about the validity of their findings.

Chang et al. published the first study, which demonstrated that the formation of a HCC MDT was associated with improved outcome measures and not surrogates of survival [22]. In their study, the authors examined the change in survival following the establishment of a HCC MDT in a VA setting and compared data from an administrative database from the same setting in the 3-year period prior to the formation of the HCC MDT. There was a significant improvement in overall survival in HCC patients presenting with advanced stage patients following the establishment of the HCC MDT. This difference in survival was partly attributed to an increase in curative (19 vs 6%) and palliative (45 vs 31%) treatment received following the establishment of the clinic. Importantly, the authors also found that the number of HCC referrals nearly doubled, and the percentage of early stage HCC tumors increased dramatically (14 to 75%) following the establishment of the HCC MDT.

A recent study by our group at UTSW also demonstrated that the establishment of a HCC MDT is associated with improved clinical outcomes [16•]. We compared 105 patients diagnosed in the year following the establishment of the HCC MDT with 250 patients diagnosed in the four previous years. Similar to the previous study, patients diagnosed in the later time period had less advanced disease (BCLC A stage, 44 vs 26%) and were more likely to undergo curative treatments (21 vs 10%). The time to treatment following HCC diagnosis was also dramatically reduced following

establishment of a HCC MDT (2.3 vs 5.3 months). The improvements in rate of treatment and as well as a reduction in treatment delays correlated with improved overall median survival in BCLC B (12.5 vs 9.0 months), BCLC C (9.7 vs 3.1 months), and BCLC D (4.4 vs 1.6 months) staged patients. Similar to the study by Chang et al., there was no difference in survival in early stage or BCLC A patients, as this cohort was more likely to be referred in a timely fashion for curative resection or orthotopic liver transplantation.

Both of these studies demonstrated an improvement in overall survival and, interestingly, increased numbers of referred early staged HCC patients. In the study by our group, there was no difference in rates of surveillance (abdominal US or alpha-fetoprotein) in the early vs later time periods to help explain the increase in diagnosis of early stage tumors. However, we anticipated that with greater institutional awareness of HCC following the establishment of a MDT, patients were being referred at an earlier time point due to the ease of collaborative care. Notably, the increase in referrals for both early and late HCC staged patients increased the inflow of patients with non-HCC benign liver lesions to our clinic. Nevertheless, the increase was trivial as less than 9% of patients seen in the clinic had non-HCC benign etiologies.

Conclusions

Providing quality care in the newly diagnosed patient with HCC has become more difficult secondary to the plethora of treatment options offered by a multitude of different providers. Over time, the decision-making process to determine which treatment best serves a newly diagnosed HCC patient has evolved from tumor board discussions to the formation of MDTs. Recently, outcome data has demonstrated the utility of HCC MDT in the face of a multitude of treatment options and a large number of providing physicians. Further research is needed to determine the financial impact of these teams and whether the use of valuable resources can justify the benefits. In light of current data showing improved outcomes, it should be standard of care for HCC patients to be managed in a multidisciplinary format.

Compliance with Ethical Standards

Conflict of Interest Caitlin A. Hester and Ali A. Mokdad each declare no potential conflicts of interest.

Adam C. Yopp reports grants from Peregrine and Novartis outside the submitted work.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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