

## Multidisciplinary Clinic in the Management of Hepatocellular Carcinoma

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In this issue of *Annals of Surgical Oncology*, Yopp and colleagues from the University of Texas Southwestern Medical Center examine their experience in implementing a multidisciplinary clinic for the evaluation and treatment of patients with hepatocellular carcinoma (HCC). The authors are to be congratulated for their work that details the positive clinical impact of a multidisciplinary approach in treating patients with HCC.

HCC is the third leading cause of cancer related death worldwide.<sup>1</sup> The treatment of HCC is particularly complex as it frequently involves both liver-specific (cirrhosis, ascites, and portal hypertension) and tumor-specific (size, number, and portal vein thrombosis) issues. As such, the delivery of care to patients with HCC is well suited for a multidisciplinary clinic in which varied providers from surgery, medicine, radiology, and interventional radiology can see the patient simultaneously. Dedicated assessment of a multidisciplinary clinic's ability to improve outcomes has thus far been somewhat limited.<sup>2–4</sup> The earliest reports of multidisciplinary clinics in the care of cancer patients involved breast cancer in the early 1990s.<sup>5</sup> The potential benefits of multidisciplinary care can, however, span across many different diseases beyond breast cancer. In addition, the benefits of such clinics can also be broad and may include the potential for improved patient satisfaction, shorter time to initial treatment, and changes in management strategies.<sup>5–9</sup>

At Johns Hopkins Hospital, our Hepato-Pancreatico-Biliary group has established multidisciplinary clinics for both pancreas and liver. We reported that, in our own experience, treatment in either the pancreas or liver multidisciplinary clinic led to treatment recommendations being modified in up to 25–40 % of patients.<sup>10,11</sup> Alterations in patient care included changes in imaging interpretation, revisions in diagnosis after re-review of outside pathology, or different treatment recommendations based on physician experience.<sup>10,11</sup> We also reported a 62 % increase in clinical trial accrual in our liver multidisciplinary clinic, as well as a near doubling in registration in the National Familial Pancreas Tumor Registry though implementation of the pancreas multidisciplinary clinic.<sup>10,11</sup>

In the current study, Yopp et al. similarly reported a benefit of a multidisciplinary clinic for patients—specifically patients with HCC. In particular, Yopp et al. noted that most patients saw multiple providers and that the median time from diagnosis to treatment was shorter after the implementation of the HCC multidisciplinary clinic. In a recent US population-based study using the Surveillance, Epidemiology and End Results–linked Medicare database, we demonstrated that referral patterns for HCC patients varied considerably.<sup>12</sup> In fact, nearly 25 % of patients with newly diagnosed, potentially resectable HCC were never referred to a surgeon, and only 57 % actually underwent resection. Overall, less than half of HCC patients saw 3 or more specialists, and 22 % of patients saw only one provider. In fact, provider subspecialty and other institution-level factors significantly influenced HCC treatment selection, thus making it critical that patients see a variety of providers relevant to their diagnosis.<sup>13,14</sup> A multidisciplinary clinic approach similar to that of Yopp and colleagues addresses this issue by promoting patient care

decisions derived from the simultaneous collaboration of multiple specialists.

Minimizing the time from diagnosis to the initiation of treatment is an important benefit of any multidisciplinary clinic because it increases efficiency and improves patient satisfaction. Outside of a formal multidisciplinary setting, the time between confirmed HCC diagnosis and visits with multiple medical providers can be prolonged and can vary considerably among specialists.<sup>12</sup> In contrast, the simultaneous attendance of specialty physicians at a multidisciplinary clinic leads to rapid and definitive treatment decisions. In the current study, Yopp and colleagues make, however, another interesting and provocative assertion: that the implementation of a multidisciplinary clinic for the evaluation and treatment of patients with HCC is associated with improved overall survival. Whereas previous studies have largely reported on improvements in process measures, Yopp and colleagues concluded that the multidisciplinary clinic actually resulted in improvements in patient survival. Undoubtedly, changes in management due to multidisciplinary expert care delivered at such institutions as University of Texas Southwestern benefit patient outcomes. Ascribing a clear survival benefit to the implementation of the multidisciplinary clinic seems, however, to be potentially problematic according to the data provided. Although there was no difference in the degree of chronic liver dysfunction between the premultidisciplinary and postmultidisciplinary clinic cohorts, the multidisciplinary clinic cohort did have earlier-stage tumors, fewer symptoms (e.g., ascites and encephalopathy), and decreased evidence of metastases. As such, the cohorts were not comparable, and the different patient characteristics of the individuals seen in the multidisciplinary clinic may have confounded any survival analysis comparing the two groups. Our group and others have documented that multivariate analyses cannot completely account for large differences when comparing two groups with very disparate baseline characteristics and can in fact be misleading and lead to inappropriate causal inferences.<sup>15,16</sup> Notwithstanding this issue, among the 134 patients in the multidisciplinary clinic cohort in the multivariate survival analysis, 46 (34.3 %) patients were diagnosed and evaluated before the initiation of the clinic. These patients obviously survived long enough to be seen in the multidisciplinary clinic. Although the authors attempt to correct for this “lead-time” bias, these patients were probably still “clinically” selected on the basis of improved performance status and favorable underlying tumor biology. As such, the differences in the survival curves are probably due more to underlying tumor biology than to the implementation of the multidisciplinary clinic. Stratified analysis suggested no difference in survival among early-stage BCLC A patients, with the effect of the multidisciplinary clinic being relegated to patients with advanced

disease (BCLC B, C, and D). Although, again, it is difficult to define which element of the multidisciplinary clinic approach (faster time to treatment, stage migration from better staging, or increased utilization of available therapies) is most beneficial, the data suggest that the benefit of the clinic was most pronounced among advanced patients who required more complex management.

In conclusion, the authors are to be commended for their efforts. With increased awareness of HCC, as well as greater patient empowerment and self-education through Internet utilization, patients now are more likely to seek care at cancer centers with formal multidisciplinary approaches. In fact, in our own multidisciplinary clinics, approximately half of the patients were “self-referred.”<sup>11</sup> Therefore, it is readily apparent that patients perceive the multidisciplinary setting as superior to the more traditional care “serial” clinic model. In turn, patients are increasingly seeking opportunities to be seen in a comprehensive multidisciplinary clinical setting. Multidisciplinary clinics will remain an essential part of cancer management moving forward, particularly as more novel and effective treatment regimens become available in increasingly complex disease states. Analyses such as that of Yopp et al. enhance our understanding of the impact and importance of multidisciplinary clinics in caring for patients with cancer.

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