

Editorial

Call to Action: Palliative Care for Hepatocellular Cancer

Manisha V* and Victor N

Department of Hepatology, Einstein Medical Center, USA

***Corresponding author:** Manisha Verma, Department of Hepatology, Einstein Medical Center, 5501 Old York Road, Klein 505, Philadelphia PA 19141, USA**Received:** July 08, 2016; **Accepted:** July 13, 2016;**Published:** July 14, 2016

Keywords

Hepato cellular cancer; Palliative care; Collaborative model

Editorial

Hepato Cellular Cancer (HCC) is currently the 2nd leading cause of cancer related death worldwide, 6th most common solid malignancy, accounts for 7% of all cancers, and is a major global health problem [1,2]. Patients with HCC, who are commonly diagnosed at advanced stages, suffer from several somatic ailments (muscle cramps, abdominal pain, and fatigue) and psychological distress (depression, anxiety) that significantly decreases their Quality of Life (QOL) [3]. Unfortunately, effective therapies for HCC are limited, life-changing, and expensive. Therefore, strategies to manage the projected increased burden of disease by improving QOL and disease acceptance must be an immediate focus of attention.

Palliative Care (PC) is an evolving subspecialty. Historically, PC was equated by clinicians with terminal or hospice care. The more contemporary view of PC is of patient and family support in the context of serious illness, integrating knowledge of the disease process with a strategy to manage and mitigate symptoms and stress associated with the illness [4]. Despite clear evidence that palliative care improves symptom burden and QOL in other terminal illnesses, referral of HCC patients to PC specialists is rare and delayed until the very end of life.

The overall purpose of this article is 1) to highlight the unmet palliative care needs of patients with Hepato Cellular Cancer, and 2) discuss the potential role of integrated palliative care services at an early stage to alleviate those needs. We will then propose development of an optimal model of PC within routine treatment of HCC which can improve the quality of life and patient satisfaction or experience.

Needs of HCC Population

The mere diagnosis of HCC is a serious illness which impacts the patient's life trajectory, requiring the need of comprehensive interventions addressing the wide variety of symptoms in this seriously ill population [5]. The most effective curative option for early stage HCC is liver transplantation, as it removes the cancer and the underlying scarred liver. However, only 20% of patients are optimal candidates for transplantation, as the majority of patients have Comorbid medical and/or psychological conditions, or advanced malignant disease which does not allow them to be on the transplant list [6]. Some patients are removed from the transplant

list due to tumor growth or progression of co-morbid conditions, making them no longer suitable candidates for LT. Research shows that only 10% of the patients removed from the transplant list due to disease progression received adequate palliative care services, in spite of suffering extreme pain and other symptoms. Of those removed from the list, 48% were consequently admitted to intensive care units, with a median survival of less than 2 months [7]. Of those who are listed for LT, most have a lengthy wait time to find the donor organ, and some patients die before surgery. During this wait time, patients suffer from extreme fatigue, anxiety, uncertainty about life and overwhelming experiences about their disease and its impact on family [8]. In addition, the overall survival is dismal with progressive deterioration in health related quality of life. Usually it's only the terminal stage HCC patients who get palliative care referral as a part of their routine care, and all other stages either do not get any referrals or get delayed referrals. A systematic review of Health Related Quality of Life (HRQOL) in patients with HCC found that patients with HCC generally have worse physical, emotional and functional HRQOL than the general population or those with chronic liver disease [9]. They also found that HRQOL correlates inversely with depression, and symptoms like pain, fatigue, and performance status.

Role of Palliative Care

The Institute of Medicine has highlighted addressing supportive care needs of patients with advanced illnesses as one of the national priorities [10]. According to an evidence report by the Agency for Healthcare Research and Quality, as a part of "Closing the quality gap: Revisiting the state of science" series, palliative care interventions are often missing in routine clinical practice. PC helps patients and their families identify their individual goals of care, and live well with the disease [11]. The main goal of PC is to ameliorate suffering and enhance the QOL for patients with serious illness and their families. PC helps to identify and address symptoms, and establish goals of care tailored to individual patients through enhanced communication about the disease process. According to the National Consensus Project-Clinical guidelines for PC, it is essential to offer PC starting from the time of diagnosis of serious illnesses like cancer [12]. PC should be ideally offered simultaneously as an adjunct to medical care at the point of care. This will help the interdisciplinary team understand the patient's goals of care, and emotional/ spiritual needs.

A randomized controlled trial in patients with newly diagnosed metastatic lung cancer was one of the first studies using an RCT design to test early PC intervention in advanced cancer. The intervention arm (receiving PC in addition to routine clinical care) showed better QOL, decreased depression and a 2.7 month survival benefit [13]. A cluster randomized control trial for advanced cancers (stage IV) tested the early PC intervention with clinics as the unit of randomization. It showed positive impacts on QOL, symptom control and satisfaction with care [14]. Another RCT testing a nurse led palliative care intervention, for patients with unresectable advanced cancers showed improved QOL, better symptom

Table 1: Ambulatory palliative care guidelines (adapted from Jacobsen et al.) [21].

1	Illness understanding/education: inquire about illness and prognostic understanding; offer clarification of treatment goals.
2	Symptom management: based on NCCN evidence based guidelines.
3	Distress Management: based on NCCN guidelines.
4	Decision making: assist with treatment decision-making, if needed.
5	Coping with life-threatening illness.
6	Referrals/Prescriptions: identify a care plan for future appointments, indicate referrals to other care providers, and account for the new medications prescribed.
7	Identify and address spiritual and social needs of patients (using within network resources)

NCCN: National Comprehensive Cancer Network.

management and reduced depression even at the last assessment just prior to death. But the intervention was very intense. It targeted only advanced unresectable cancers, involved additional visits than usual care (4 weekly sessions, with monthly follow ups), and seems to be unfeasible in routine practice [15]. A review article by Davis et al. highlights several success stories of outpatient PC for newly diagnosed metastatic cancer. However, none of those studies were conducted in an outpatient hepatology practice (which is the hub of HCC care), or for early stage HCC. Hence, there is not much evidence for feasibility or effectiveness of PC interventions for early stage cancers, especially HCC [16]. Apparently, HCC develops in patients with an underlying chronic liver disease which jeopardizes the QOL even before the cancer progresses, thereby indicating the urgency for PC interventions.

Walling and Wenger further point to the critical need of addressing advanced liver disease patient's palliative care needs, irrespective of the transplant status, through an integrated collaborative model i.e. offering palliative and clinical care together [17].

Proposed Collaborative Model of PC for HCC

Based on the needs of HCC patients, an integrated collaborative approach will be an ideal approach. The Hepatologists should lead these efforts in collaboration with a palliative care specialist (physician or nurse), with access to social work and chaplain service. The PC team should offer support, counseling, review the treatment plan, and initiate advanced care planning. Psycho-educational and supportive counseling through providing information about the liver disease and ways to manage the disease should be added. General guidelines for outpatient PC from the National Consensus Project for Quality Palliative care should be followed [18] (Table 1).

Referral to psychotherapy and chaplain services should be offered on as needed basis, and a continuous timely follow up must be included. The key for success of these kinds of programs would be the communication between the PC team and Hepatologists taking care of patients. If offered as a part of routine care within the same office, it is expected that the providers will have easy communication either through their shared EMR or through regular meetings/ case conferences.

The evaluation of the program can target measuring the QOL using available validated instruments for HCC like FACT-Hep (Functional Assessment of Cancer Therapy- Hepatobiliary Cancer) or CLDQ (Chronic Liver Disease Questionnaire). PROMIS (Patient Reported Outcomes Measurement Information System) instruments can also be utilized for evaluation purposes. PROMIS is an NIH supported system which has been developed over the

course of a decade, can be utilized for any chronic disease, and allows comparisons with the US general population [19,20]. Other potential outcomes include symptom burden, psychological distress, patient provider communication, patient satisfaction or experience, and health outcomes. Furthermore, other endpoints could include resource utilization, such as hospitalizations and re-hospitalizations, ER visits, unscheduled office visits, and survival.

In summary, HCC is a high need population which can be served by PC team to potentially improve their QOL and health outcomes. Further research is needed to develop and test healthcare delivery models to assess the feasibility, efficacy and effectiveness of PC interventions. Based on evidence from other similar diseases and oncology models, we can assume that addition of PC to routine care is definitely better than routine standard of care; so the comparisons should target finding the best possible model (e.g. in person PC service vs. using Telehealth vs. direct access to a PC clinic). The evidence generated could support the addition of PC service as a part of routine care to address the needs of HCC population.

References

1. International Agency for Research on Cancer. World cancer report 2014, Geneva, WHO. 2014.
2. Gish RG. Early detection of hepatocellular carcinoma through surveillance using biomarkers. *Gastroenterology and Hepatology*. 2014; 10: 121-123.
3. Bruix J, Sherman M. Management of hepatocellular carcinoma: an update: *Hepatology*. 2011; 53: 1020-1022.
4. Smith TJ, Temin S, Alesi ER, Abernethy AP, Balboni TA, Basch EM, et al. American Society of Clinical Oncology provisional clinical opinion: the integration of palliative care into standard oncology care. *Journal of Clinical Oncology*. 2012; 30: 880-887.
5. Potosek J, Curry M, Buss M, Chittenden E. Integration of Palliative Care in End-Stage Liver Disease and Liver Transplantation. *Journal of Palliative Medicine*. 2014; 17: 1271-1277.
6. Edwards BK, Brown ML, Wingo PA, Howe HL, Ward E, Ries LA, et al. Annual report to the nation on the status of cancer, 1975-2002, featuring population-based trends in cancer treatment. *Journal of the National Cancer Institute*. 2005; 97: 1407-1427.
7. Poonja Z, Brisebois A, Van ZS, Tandon VP, Meeberg G, Karvellas CJ. Patients with cirrhosis and denied liver transplants rarely receive adequate palliative care or appropriate management. *Clinical Gastroenterology and Hepatology*. 2014; 12: 692-698.
8. Gandhi S, Khubchandani S, Iyer R. Quality of life and Hepatocellular Carcinoma. *Journal of Gastrointestinal Oncology*. 2014; 5: 296.
9. Fan SY, Eiser C, Ho MC. Health-related quality of life in patients with hepatocellular carcinoma: a systematic review. *Clinical Gastroenterology and Hepatology*. 2010 ; 8: 559-564.
10. Dying in America: Improving Quality and Honoring Individual Preferences Near the End of Life. Institute of Medicine (IOM). Washington DC: The

- National Academies Press. 2015.
11. AHRQ. Series Overview: Closing the Quality Gap: Revisiting the State of Science. 2016.
 12. The National Consensus Project for Palliative Care. Clinical Practice Guidelines for Quality Palliative. 2013.
 13. Temel JS, Greer JA, Muzikansky A, Gallagher ER, Admane SJ, Jackson VA, et al. Early palliative care for patients with metastatic non-small-cell lung cancer. *New England Journal of Medicine*. 2010; 363: 733-742.
 14. Zimmermann C, Swami N, Krzyzanowska M, Hannon B, Leigh N, Oza A, et al. Early palliative care for patients with advanced cancer: a cluster-randomised controlled trial. *The Lancet*. 2014; 383: 1721-1730.
 15. Bakitas M, Lyons KD, Hegel MT, Balan S, Brokaw FC, Seville J, et al. Effects of a palliative care intervention on clinical outcomes in patients with advanced cancer: the Project ENABLE II randomized controlled trial. *Jama*. 2009; 302: 741-749.
 16. Davis MP, Temel JS, Balboni T, Glare P. A review of the trials which examine early integration of outpatient and home palliative care for patients with serious illnesses. *Annals of Palliative Medicine*. 2015; 4: 99-121.
 17. Walling M, Wenger NS. Palliative Care and End-Stage Liver Disease. *Clinical Gastroenterology and Hepatology*. 2014; 12: 699-700.
 18. Clinical Practice Guidelines for Quality Palliative Care 3rd edition. 2013.
 19. Cella D, Riley W, Stone A, Rothrock N, Reeve B, Yount S, et al. The Patient-Reported Outcomes Measurement Information System (PROMIS) developed and tested its first wave of adult self-reported health outcome item banks: 2005–2008. *Journal of Clinical Epidemiology*. 2010; 63: 1179-1194.
 20. Rothrock NE, Hays RD, Spritzer K, Yount SE, Riley W, Cella D. Relative to the general US population, chronic diseases are associated with poorer health-related quality of life as measured by the Patient-Reported Outcomes Measurement Information System (PROMIS). *Journal of Clinical Epidemiology*. 2010; 63: 1195-1204.
 21. Jacobsen J, Jackson V, Dahlin C, Greer J, Perez-Cruz P, Billings JA, et al. Components of early outpatient palliative care consultation in patients with metastatic nonsmall cell lung cancer. *Journal of Palliative Medicine*. 2011; 14: 459-464.