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### Palliative Care for People With Hepatocellular Carcinoma, and Specific Benefits for Older Adults

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#### **ABSTRACT**

Purpose: Hepatocellular carcinoma (HCC), the most common type of primary liver cancer, has a rapidly rising prevalence in the United States and a very poor overall rate of survival. This epidemic is driven by the cohort of aging Baby Boomers with hepatitis C viral infection and the increasing prevalence of cirrhosis as a result of nonalcoholic steatohepatitis. Because curative options are limited, the disease course creates, in patients and their families, distressing uncertainty around prognosis and treatment decisions. Older adults are disproportionately affected by HCC and have more comorbidities, adding to the complexity of the disease. This population would benefit from increased access to palliative care services, which can potentially complement the treatments throughout the disease trajectory. The purpose of this review was to use existing evidence to propose a new model of palliative care integration in patients with HCC. Thus, we focus on the HCC stage and the treatment algorithm, the ways that palliative care can offer support in this population at each stage, as well as elements that can enhance patient and family support throughout the entire disease trajectory, with an emphasis on the care of older adults with HCC.

Methods: This is a narrative review in which we identify evidence-based ways that palliative care can help younger and older adults with HCC and their families, at each stage of HCC and throughout the disease trajectory.

Findings: We propose ways to integrate HCC and palliative care based on the existing evidence in both fields. Palliative care offers support in symptom management, advanced care planning, and decision

making in ways that are specific to each stage of HCC. We also discuss the evidence that illustrates the palliative care needs of patients with HCC that span the entire course of illness, including coping with the stigmatization of liver disease, addressing informational needs at different stages, and discussing quality of life longitudinally.

Implications: Integrating palliative care into the treatment of patients with HCC has the potential to improve outcomes, although more research is needed to build this evidence base. (*Clin Ther.* 2018;**I**:**III**-**III**) Published by Elsevier HS Journals, Inc.

Key words: cirrhosis, geriatric oncology, hepatocellular carcinoma, palliative care, supportive oncology.

#### **INTRODUCTION**

Hepatocellular carcinoma (HCC) is a dreaded complication of liver disease that has a poor rate of overall survival. Patients undergo many different types of treatments throughout the course of the disease. The treatment algorithm can be complex, and patients face considerable uncertainty around treatment and prognosis. Because HCC occurs in the context of underlying liver disease, this population may experience the symptoms of both end-stage liver disease and cancer. Hepatologists play a central role in HCC management. Multidisciplinary HCC tumor

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boards are often led by hepatologists, with the involvement of many different types of specialists to address the different treatment modalities.<sup>6</sup> In addition to the medical complexity of HCC, a diagnosis of HCC is emotionally overwhelming for anyone, but in particular for older adults, who may face additional treatment and symptom challenges due to chronic conditions.<sup>7</sup>

Palliative care, specialized interdisciplinary care that focuses on quality of life while living with a serious illness, has the potential to offer additional support in patients with HCC and their families as they navigate life with the disease. However, little is known about the specific palliative care needs of these patients, and particularly older adults with multiple comorbidities. No HCC-specific models of palliative care delivery have been described, and patients with end-stage liver disease rarely receive palliative care, even at the end of life. 10-12 This narrative review focuses on the aspects of HCC that make it a uniquely complex and distressing illness, and the ways that existing evidence suggests that palliative care can provide support throughout the course of HCC. Specifically, we review the course of HCC by stage and propose specific ways that palliative care can be helpful at each stage of HCC, as well as longitudinally throughout the disease course. We then discuss some of the challenges of integrating palliative care into the HCC treatment landscape, and propose future research directions to address this gap in the healthcare literature.

#### **MATERIALS AND METHODS**

This is a narrative review to identify evidence-based ways in which palliative care can help people with HCC, and in particular older adults, at each stage of HCC and throughout the illness trajectory. PubMed was searched using a variety of keywords related to palliative care (including palliative care, palliative medicine and hospice) and hepatocellular carcinoma: (((("Palliative Care"[Mesh]) OR ((palliative) AND (care OR medicine))) OR hospice)) AND (("Carcinoma, Hepatocellular"[Mesh]) OR hepatocellular carcinoma). English-language articles were included, and no date restrictions were employed. Search results as well as the reference lists of identified articles were manually reviewed. Articles pertaining to the field of hospice and palliative medicine were included, and

those that focus exclusively on palliative treatments (and not the field of palliative care) were not.

#### **RESULTS**

The search string described above reveals 871 articles in pubmed. However the majority of the articles do not refer to the fields of palliative medicine or hospice, but rather palliative, or non-curative treatments of HCC. Thus we reviewed the results of the search manually and included relevant articles here.

# HCC: A Complex Disease With an Uncertain Course

HCC is the most common type of primary liver cancer and the second-leading cause of cancer-related mortality worldwide.<sup>2</sup> In the United States, ~30,000 adults are diagnosed with HCC each year, and 21,000 die.<sup>13</sup> The incidence is rising<sup>14</sup> in the setting of a hepatitis C viral epidemic.<sup>15,16</sup> Of note, relatively new, highly effective antiviral hepatitis C treatments are available, but their effect on the rising prevalence of HCC is not yet known.<sup>17</sup> The proportion of patients on the liver transplant waiting list due to malignancy tripled between 2005 and 2015.<sup>18</sup> In addition, an increasing proportion of those affected by HCC have nonalcoholic steatohepatitis, which is associated with the obesity epidemic and the metabolic syndrome.<sup>19</sup>

HCC affects older adults with chronic liver disease. The risk for HCC rises with age, with a >15-fold increase after 65 years of age among hepatitis C-infected patients.<sup>20</sup> The mean age of patients with HCC awaiting liver transplantation has risen in recent years, from 51.2 to 55.7 years, and the percentage of those waiting who are aged >60 years has more than doubled, from 19% to 42%.<sup>21</sup>

HCC develops in the context of chronic liver inflammation or infection, and in most cases, underlying cirrhosis.<sup>2</sup> Thus, because of concurrent liver disease, this cancer has an unpredictable disease course, and the treatment algorithm is uniquely and increasingly complex, with many potential new treatments on the horizon.<sup>22</sup> Treatment modalities include surgical resection, liver transplantation, interventional radiology procedures (embolization), chemotherapy,<sup>2</sup> and immunotherapy,<sup>23</sup> in addition to the management of the underlying chronic liver disease. Older adults often face multimorbidity,<sup>24</sup> requiring many medical visits; thus, the uniquely

2 Volume ■ Number ■

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