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The Prevalence of Psychosocial Barriers and Their Impact on Receipt of HCC Care in US Veterans: Role of Tumor Board Model of Care

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1. Abstract

1.1. Background & Aims: Psychosocial barriers, including low socioeconomic status, homelessness, alcohol and substance abuse, and psychiatric disorders are prevalent in US veterans. Our study aims to identify the prevalence of psychosocial barriers in veterans diagnosed with HCC, and their impact on receipt of cancer care.

1.2. Methods: A retrospective cohort study was performed of all veterans diagnosed with HCC from January 2007 through December 2016 (n=149), whose tumor care was coordinated through our multi-disciplinary tumor board. Outcomes included receipt of any HCC-specific therapy and overall survival.

1.3. Results: Substance abuse was reported in 124/149 patients. Psychiatric illness was documented in 55/149 patients, 23/149 patients had incomes below the poverty threshold, and 7/149 were homeless. Average distance traveled for care was 128.7 miles (s.d. 172.7 miles), with 50/149 and 33/149 veterans utilizing travel and lodging assistance, respectively.

Seventy-one of 149 patients had HCC exceeding T2 stage at diagnosis. Curative treatment was offered to 78/149 patients, with 127/149 receiving any HCC-specific care. Median survival from diagnosis was 727 days (95% CI 488-966 days). Factors that decreased the likelihood of receipt of curative HCC therapy included >T2 stage and diagnosis of depression, whereas provision for lodging was associated with increased likelihood of receiving HCC-care. Predictors of receiving curative therapy included absence of substance abuse, tumor within T2 stage, and CTP class A cirrhosis.

1.4. Conclusion: Psychosocial barriers were common in our veteran cohort. Individualizing care, and coordination of travel and lodging, assisted in enabling high rates of receipt of HCC-specific therapy and improving patient survival.

2. Introduction

Hepatocellular carcinoma (HCC) remains a major global health problem and is the third leading cause of cancer-related mortality worldwide [1]. Management of HCC is complex; as it largely occurs in the background of chronic liver disease, its management must simultaneously address challenges related to the patient's tumor burden, as well as their underlying liver dysfunction and performance status [2]. HCC is universally fatal without treatment, with a 5-year survival less than 10% [2]. If detected early, however, it is potentially curable, with treatments such as hepatic resection, ablation and/or liver transplantation, which are associated with 5-year survival rates as high as 70% [2]. Further, HCC-specific palliative treatments, in-

cluding intra-arterial therapies, such as trans-arterial chemoembolization (TACE) and radioembolization, and systemic chemotherapy, have also been shown to prolong survival in patients with advanced HCC (2). Therefore, a key driver of patient survival is receipt of HCC-specific therapy.

There is rising incidence and mortality related to HCC in the US veteran population, largely attributed to acquisition of chronic HCV infection decades prior [3]. There is also a high prevalence of psychosocial barriers in this population, such as low socioeconomic status, homelessness, alcohol and substance abuse, and psychiatric disorders which can negatively influence receipt of medical treatment, including cancer care [4-5]. Given the complexity of managing HCC, as well as the plethora of potential treatment options available, it is widely accepted that a multidisciplinary team approach (the multidisciplinary tumor board or MDTB) provides optimal care to patients with HCC [2, 6]. The aim of the present study was to identify in a population of US veterans diagnosed with HCC the prevalence of psychosocial barriers to care and assess, in the context of an MDTB, their impact on receipt of HCC-specific care in this cohort.

3. Methods

In June 2007, we organized a joint institutional MDTB for patients with primary liver tumors receiving care at the Wm Middleton Memorial Veteran's Affairs Hospital. As we have described elsewhere, individual cases with their corresponding imaging studies were reviewed at a weekly conference attended by transplant hepatologists, medical oncologists, hepatobiliary and transplant surgeons, pathologists, diagnostic and interventional radiologists and nurse coordinators [6]. The gamut of potential therapies offered includes surgical resection, liver transplantation, thermal ablation, intra-arterial therapies such as chemo- and/or radioembolization, systemic chemotherapy, stereotactic radiation and best supportive care. Decisions regarding the appropriate treatment modality were made based on patient factors, review of their cross-sectional imaging studies and/or histopathology, in context of their underlying liver dysfunction. The tumor board discussion was summarized in meeting minutes as well as tumor board encounters recorded in each patient's medical chart. Although patients with benign tumors are presented at MDTB, only patients with a diagnosis of HCC were included in this study.

A database analysis of all veteran patients with HCC managed through our MDTB, since its inception up to December 31, 2016, with follow up until December 31, 2018 was performed. Data for analysis included demographics, laboratory parameters at time of diagnosis and treatment, imaging findings, histopathology and/or surgical pathology, treatment rendered and follow-up information. The outcomes measured in this study include receipt of any therapy and patient survival.

4. Statistical Analysis

Discrete variables were analyzed with Chi square statistics or Fishers Exact test and continuous variables with Students t test. Multivariable analyses were carried out with logistic regression. Variables with a $P<0.05$ were considered statistically significant. Analyses were carried out with SPSS v24.0

5. Results

From January 2007 through December 2016, a total of 149 veteran patients with HCC were managed through our MDTB. Baseline demographic data as well as Model for End-Stage Liver Disease (MELD) score and Child-Turcotte-Pugh (CPT) class, and baseline HCC characteristics of the cohort are shown (Tables 1 and 2).

Table 1: Baseline demographic data.

Variable	Study Cohort (N=149)
Age (years) at presentation (mean ± s. d.)	63.6 ± 7.48
Sex (M:F)	148:01:00
Race	
Caucasian	131
African American	8
Hawaiian	2
Native American	2
Other	5
Etiology of Chronic Liver Disease	
Alcohol-associated liver disease (ALD)	26
Chronic hepatitis C viral (HCV) infection (HCV)	36
ALD and HCV	57
Non-alcohol-related fatty liver disease (NAFLD)	23
Other	7

Table 2: Baseline clinical and HCC data.

Variable	Study Cohort (N=149)
Total bilirubin at presentation (mg/dl) (mean ± s.d.)	1.6 ± 2.7
MELD score at presentation (mean ± s.d)	10.9 ± 5.4
CPT Class at presentation	
Class A	111
Class B	29
Class C	8
Serum AFP (ng/mL) [Median and range]	13.6 (1.3 to 110,955)
Number of patients within T2 Tumor Stage at Diagnosis	78

5.1. Psychosocial Barriers to Care

There was a high prevalence of psychosocial barriers in our study cohort, including alcohol or substance use disorder, mental illness diagnosis, and low socioeconomic status (Table 3). The mean distance traveled to our facility for HCC-specific care was nearly 129 miles, with 50 patients in the cohort utilizing travel assistance and 33 patients utilizing lodging assistance provided.

Table 3: Baseline psychosocial data of study cohort.

Psychosocial Variable	Study Cohort N=149 (%)
Alcohol Use Disorder	98 (66)
Polysubstance Use Disorder	26 (17)
Other Mental health diagnoses	
Any	55 (37)
Post-traumatic stress disorder (PTSD)	13 (9)
Anxiety	15 (10)
Major depressive disorder (MDD)	32 (21)
Other	10 (7)
> 1 μενταλ ηεαλτη διαγνοσισ	23 (15)
Homelessness	7 (5)
Income below poverty threshold	23 (15)
Private health insurance coverage	44 (30)
% Service connection (mean, s.d.)	22.4 (35.1)
Medicare Eligibility	73 (49)
Distance traveled to receive HCC care (Miles) (mean, s.d.)	128.07 (127.7)
Travel assistance utilization	50 (34)
Lodging assistance utilization	33 (22)

5.2. HCC Treatments

There was a high rate of receipt of treatment in our study cohort with 127 patients of 149 being the recipient of at least one HCC-specific therapy. Care was individualized and coordinated through our institutional MDTB, with a variety of treatment modalities, both curative and palliative, utilized (Table 4).

Curative treatment, which includes Liver Transplantation (LT), ablation or resection, was able to be offered to 78 of the 149 patients in our cohort who were within T2 stage. Of these 78 patients who were potential candidates for LT as a curative treatment for HCC, 31 were not deemed suitable transplant candidates. Amongst this subgroup of 31 patients who were not listed for LT, psychosocial barriers precluded listing in 7 patients due to active substance abuse, homelessness in 1 patient, and severe mental illness in 3 patients.

In a univariate analysis, factors that decreased the likelihood of receipt of curative HCC therapy included >T2 stage at diagnosis and a diagnosis of depression, whereas provision for lodging was associated with increased likelihood of receiving HCC-specific care (Table 5). Other factors that influenced receipt of *any* treatment including patient's MELD score, total bilirubin, and serum alpha-fetoprotein. In a multivariable analysis, predictors of receiving curative therapy included absence of substance abuse, within T2 stage of tumor and CTP class A cirrhosis (Table 5). The presence of psychosocial barriers apart from substance use did not predict a lower chance of receiving curative HCC therapy (including homelessness, distance traveled to center, mental health disorder and low income).

Median survival of our study cohort was 727 days from diagnosis, with 95% confidence interval 488-966 days. Survival from HCC diagnosis in study cohort was 72% at 1 year, 50% at 2 years, 39% at 3 years and 36% at 5 years. Death occurred in 71 of 149 patients, with HCC accounting for the cause of death in 52 of these patients, complications of end-stage liver disease in 13 patients, and other causes for the remainder of patients.

Table 4: HCC Treatment data.

Treatment Modality	Study Cohort N=149 (%)
Any Treatment	127 (85)
Curative Treatment (includes ablation, liver transplantation and/or resection)	78 (52)
Thermal Ablation (with or without subsequent LT)	65 (44)
Trans-arterial chemoembolization (TACE)	56 (38)
Radioembolization	24 (16)
Hepatic resection	11 (7)
Liver Transplantation	21 (14)
Systemic chemotherapy	5 (3)
Other (SBRT, Cryoablation)	5 (3)
Palliative/Best supportive care	22 (15)

Table 5: Univariable and multivariable analyses of receipt of HCC treatment

Curative HCC treatment offered	Hazard Ratio	95% CI	P Value
>T2 stage at diagnosis	0.02	0.01-0.06	0.0001
diagnosis of depression	0.29	0.09-0.94	0.05
provision for lodging	3.59	1.50-8.61	0.003
Any HCC treatment offered	Mean diff	95% CI	P Value
MELD score	-2.08	-3.85 to -0.31	0.02
total bilirubin	-0.84	-1.72 to 0.03	0.059
Serum AFP	-5868	-9581 to -2154	0.004
Multivariable analysis (predictors of curative therapy)	Hazard Ratio	95% CI	P Value
Absence of substance abuse	7.14	1.39-37	0.02
T2 stage of tumor or less	10.1	2.53-40	0.001
CTP class A cirrhosis	9.41	2.44-36.3	0.001

6. Discussion

Increases in prevalence and mortality related to cirrhosis and HCC have been reported among the US veteran population [3]. This is in large part attributable to the burden of chronic hepatitis C (HCV) infection in this population. As mirrored in the US population in general, we may be at a turning point regarding the gradual increase in prevalence in HCC [8]. The prevalence of cirrhosis and viral-related HCC related to HCV infection will decline with availability of effective antiviral therapy, Alcoholic Liver Disease (ALD) remains a main etiological factor for development of cirrhosis and HCC. Non-alcoholic fatty liver disease (NAFLD) is becoming a more prevalent cause for development of cirrhosis, indication for liver transplantation, and development of HCC, and indeed may lead to HCC even in the absence of cirrhosis [9].

HCC remains a challenging clinical problem [2]. As the vast majority of cases arise in the background of cirrhosis, management of HCC must not only address the cancer stage at diagnosis, but also the patient's underlying liver dysfunction and performance status. Receipt of HCC-specific therapy is a key driver of patient outcome, with available curative therapies for those diagnosed with early stage disease. We and others have shown that multidisciplinary approach to coordinate, individualize and optimize care for these complex patients can improve the rate of treatment utilization, reduce treatment delays and improve patient survival [6, 9-10].

Patient psychosocial barriers, such as low socioeconomic status, homelessness, alcohol and substance abuse, and psychiatric disorders, are more prevalent among the veteran population and have the potential to negatively influence successful delivery of health care. One retrospective study of 100 Veterans at the Palo Alto VA treated for HCC from 2009 to 2014 showed a majority of the patients lived on a meager income, there was high prevalence of homelessness, substance abuse history was identified in 96% of their cohort and psychiatric illness in 65% patient [11]. Other studies have documented similar findings in the Veteran population, with alcohol and substance abuse as well as other uncontrolled co-morbidities as barriers to providing care, such as antiviral therapy for chronic HCV infection [12].

Herein, we present a large cohort of Veterans with HCC managed through our MDTB from 2007 to 2016, amongst whom chronic HCV infection and/or ALD were the main causes of cirrhosis. Our cohort had a high burden of alcohol and substance abuse disorders while other psychiatric illnesses were also common. Our cohort includes patients who were poor, and even some veterans who lacked a stable home. This profile of poverty and social deprivation among US veterans is matched in national data [13-15]. Using a tumor board model of nurse navigation and multidisciplinary care, we were able to provide travel and lodging assistance to 37% and 22% of patients, respectively, in order to facilitate their care.

Our data demonstrate that the impact of psychosocial barriers on our capacity to deliver care varies with the nature of the treatment under consideration: curative v. cancer control. For example, active substance abuse, homelessness and severe established mental illness were often considered insurmountable when the treatment in question was LT. Nevertheless, despite the high prevalence in our study group of barriers such as lack of transport while living a far from the VA medical center, or AUD, a curative treatment with either LT, tumor ablation or resection, could be offered to over half of our cohort. When non-curative therapies are included, the vast majority (85%) of patients received HCC-specific care, with good relative survival.

Our reported high receipt of HCC-specific care and patient survival is in contrast to previously reported low rates of HCC-specific care in in a national survey of management of 1,296 veteran patients, infected with HCV, who developed HCC during 1998-2006. In this population, HCC-specific treatment was provided to 34% [16]. However, our data are consistent with our previously published data of patients with HCC managed through an institutional multidisciplinary tumor board [6]. Indeed, as shown by a univariate analysis in our present

study, individualizing care to address modifiable patient barriers, such as providing provisions for lodging if needed, was associated with an increased likelihood of receiving HCC-specific care. On the other hand, advanced tumor stage (>T2) at diagnosis and a diagnosis of depression, which was the most common psychiatric diagnosis amongst our cohort, were both associated with decreased likelihood of receiving HCC-specific care. Clinical factors such as patients' MELD score, total bilirubin and serum AFP, a surrogate marker for tumor stage, all affected the likelihood of providing HCC-specific care. In a multivariate analysis, factors that predicted ability to receive curative therapy included absence of substance abuse, T2 stage of tumor and Child-Turcotte-Pugh (CTP) Class A cirrhosis. This is expected as patients with HCC within T2 stage (or Milan criteria), with compensated cirrhosis are most likely to receive curative therapies, such as resection, ablation or liver transplantation [2].

Our study demonstrates a high burden of psychosocial challenges in veterans with HCC. These accounted for a significant barrier to receipt of HCC-specific care.

Despite the presence of these patient barriers, high rates of HCC-specific treatment are attainable through individualization and coordination of patient care in the context of a multidisciplinary tumor board model with nurse navigation. Provision of targeted social support to ameliorate these modifiable factors improves patient outcomes.

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