Short Communication

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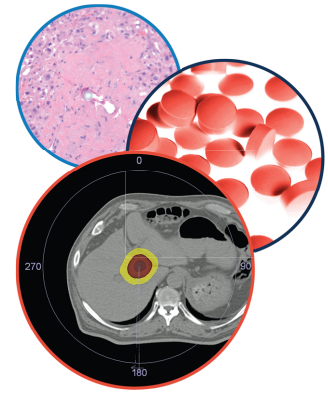

Hepatic Oncology

Treatment journey of patients with hepatocellular carcinoma using real-world data in British Columbia, Canada

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Aim: This study examined treatment patterns, survival outcomes and healthcare costs related to hepatocellular carcinoma (HCC) in British Columbia. **Methods:** The study utilized data from two physician databases (HCC and MOTION) and the provincial British Columbia transplant database. **Results:** The analysis revealed diverse treatment approaches and identified the varying treatment journeys of patients. Liver transplant and systemic therapies demonstrated improved survival rates. However, there was a scarcity of Canadian-specific cost data. **Conclusion:** The research emphasizes the complexities of managing HCC and underscores the need for personalized treatment strategies to enhance patient outcomes. These findings contribute valuable insights into HCC management and provide a foundation for future studies and interventions aimed at optimizing care and resource allocation.

Tweetable abstract: This study examined HCC treatment patterns, survival, and healthcare costs in British Columbia. Data revealed diverse treatment modalities and etiologies. Liver transplant and systemic therapies were associated with improved survival. #HCC #TreatmentPatterns #Survival #Costs

Plain language summary: This study looked at how people diagnosed with liver cancer in British Columbia were treated, how long they lived and how much treatment cost. Treatment records were reviewed, and depending on the extent of the disease, treatments could include surgery, treatments directed at the liver and/or anti-cancer therapy. The average survival time varied from 21–33 months, with an average cost per patient of $94,000. This helps us understand the patient journey and future studies would include current treatment options.

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Keywords: Canada • cost • HCC • hepatocellular carcinoma • resource utilization • survival • treatment patterns

Hepatocellular carcinoma (HCC) is the most common form of primary liver cancer in adults [1]. Early HCC can be treated with surgery (i.e., resection or liver transplant) and/or ablation (i.e., radiofrequency ablation, microwave ablation or ethanol ablation) [2]. If ineligible for resection or ablation, locoregional therapies (LRT) include bland embolization, transarterial chemoembolization (TACE) with lipiodol or drug-eluting beads, transarterial radioembolization (TARE or yttrrium-90 [Y90]) and stereotactic body radiation therapy) [3]. Patients who are refractory to or ineligible for LRT can receive systemic therapies, which in some cases may provide response permitting localized therapy [4]. In advanced HCC, the 2008 SHARP clinical trial established sorafenib as the standard of care [5,6], however, in 2018 the REFLECT trial found that lenvatinib was non-inferior to sorafenib [7,8]. More recently, combination therapy with immunotherapy has an established role in the first line treatment

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of Child-Pugh score (CPS) A advanced HCC, such as atezolizumab with bevacizumab, and durvalumab with tremelimumab [9–11].

Based on Canadian studies of patients treated with systemic therapy, the median overall survival (mOS) with first-line tyrosine kinase inhibitors (generally sorafenib) ranges from 9 to 12 months [12,13] with 2-year and 5-year survival rates of 17.9 and 3.9%, respectively, and a mOS of 2.7 months without treatment [13]. A study of HCC patients in Manitoba had a 1- and 5-year OS of 41 and 14%, respectively [14].

However, Canadian-specific studies analyzing healthcare resource utilization and costs are limited with only a single study that calculated the mean (95% CI) 5-year net costs of HCC care as $77,509 ($60,410–$94,607) in 2010 USD [15].

Understanding the treatment journey is important, in addition to survival and costs. Systemic therapy treatment options have changed significantly in the last 5 years, and there is a need to understand treatment patterns, prior to and after systemic therapy. The main objective of our study was to understand the treatment patterns of HCC patients from diagnosis through various treatment modalities that can include any combination of LRTs and systemic therapies in the province of British Columbia, Canada, in the era of limited systemic therapy options. Secondary study objectives included survival outcomes, healthcare resource utilization and costs directly related to HCC across the entire treatment trajectory. This study was exploratory, with no formal hypothesis being tested.

Methods

Data sources

This was a retrospective, real-world study using data from three data sources: British Columbia Cancer (BC Cancer), 'HCC database' mostly reflecting disease factors and systemic therapy, with limited LRT data; Vancouver General Hospital (VGH), 'MOTION database' including LRT, diagnostic imaging and interventional radiology and surgical therapy information; and British Columbia Transplant, the provincial agency responsible for the oversight of all transplants performed in British Columbia that provided liver transplant information for the patients in both databases. No surveillance information was available, and therefore not included in our analysis.

British Columbia, Canada has publicly funded healthcare, serving the population of 5 million [16]. BC Cancer operates six regional cancer centers in the province, providing care including systemic therapy, radiation therapy and supportive care. Using BC Cancer pharmacy records, which dispenses publicly-funded anti-cancer therapy for the province, the HCC database included patients aged 18 years or older, who were diagnosed with HCC and were dispensed at least one cycle of systemic therapy (i.e., sorafenib) from a BC Cancer pharmacy between January 2008 and December 2016. This was supplemented by a retrospective chart review to collect patient demographics, cancer and treatment information.

MOTION included all patients diagnosed with HCC who presented at Multidisciplinary Liver Tumor Rounds between 2004 and 2017, a requirement for LRT, and received any LRTs afterward. Personal health information for all patients in both the MOTION and HCC databases were then sent to BC Transplant to identify patients who received a transplant. MOTION, HCC and BC Transplant data were linked initially by patient identifiers, then patients were assigned a unique study number and personal health information was removed. The patients found in both the MOTION and HCC databases were named the 'Common cohort,' and the majority of the 'COMMON' patients received LRTs first and then went on to receive systemic therapy after; however, there were some instances of overlap where patients received both simultaneously.

Research Ethics Board applications for MOTION (H19-03084) and HCC (H17-01147) were amended to allow their data to be used as a part of this study. Research Ethics Board approval for this study was obtained from both the BC Cancer Agency (H21-00394) and the Sunnybrook Research Institute (3564).

Data analysis

Diagnosis date was based on the first date of diagnosis (radiologic or histologic) listed, and if incongruent between MOTION and HCC databases, the MOTION date was used. Dates of LTR treatments, and start and stop dates of systemic therapies were used to determine treatment patterns. HCC patients were excluded if they had missing, unverifiable, or invalid start or stop dates (i.e., stop date prior to start date) for their systemic therapy. MOTION patients were excluded if the database noted them as having received sorafenib, chemotherapy or palliation as their first treatment and they received no subsequent LRTs. This was an important exclusion criterion as patients in the MOTION database could not be confirmed as having received sorafenib or chemotherapy, only that they were recommended to receive those treatments during Multidisciplinary Liver Tumor Rounds.

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Costing

Costs were calculated for each patient. Systemic treatment costs were provided by BC Cancer Pharmacy department. Medical oncology visit costs were available through the British Columbia Medical Services Plan [17]. Visits to medical oncologists were assumed to be every 90 days after the initial medical oncology visit until the start of systemic treatment, then every 28 days while on systemic treatment. LRT costs were based on departmental expenditures (Liu D, Pers. Comm.) and costs of liver transplant care were provided by the regional health authority (Nickel J, Pers. Comm.). Costs were provided in 2021 Canadian dollars and analyzed using descriptive statistics.

Statistical analysis

Baseline characteristics were summarized by number and percentage for categorical variables and by mean (standard deviation) for continuous variables. To protect patient privacy, small cells were defined as values <5 and not reported. Clinical outcome of interest was OS and was calculated using the Kaplan-Meier estimate. OS was defined from either the time of diagnosis or from start of treatment to death, censoring on either end of study or date of last follow-up. Some patients in the MOTION database were not confirmed to have passed away and were given a lost to follow-up date of 31 July 2017. These patients were censored on this date. While the start of treatment for the MOTION and Common groups was defined as the date of receipt of their first LRT, the start of treatment for the HCC group was defined as the date of first systemic therapy. Duration of treatment was defined from start of treatment to the end of treatment (i.e., first LRT to last LRT or first dose of systemic to last dose of systemic treatment).

Bias

There are some biases present in this study. First, there is a sampling bias since all of the patients in this study were only collected from one regional cancer area in Vancouver. Patients that received cancer treatment in other cities or local centers would not be represented. However, Vancouver is the largest city in British Columbia and BC Cancer and VGH have the two largest cancer programs in the province. Second, the time that these data were collected may not reflect current practices, but it is still important to quantify previous treatment practices as it provides a reference point to which newer treatment regimens can be compared. Unfortunately, due to the nature of the data collection for the two datasets (MOTION and HCC), there is no way to minimize the biases inherent to each dataset. However, there is discussion to create a newer, longitudinal dataset that would address these concerns.

Results

Baseline characteristics

Overall, there were 417 patients in the HCC database and 413 patients in the MOTION database. A total of 63 patients were in both databases (referred to as the 'Common' group). Table 1 provides the baseline characteristics of these three groups. The median age at diagnosis was 64, 62 and 62 years for HCC, MOTION and the Common groups respectively, while the proportion of patients who were female was 17.5, 18.2 and 15.9%. The majority of patients in all three groups presented with CPS A disease, however, the MOTION dataset had a slightly higher proportion of CPS B patients (14.8%). Although the Barcelona Clinic Liver Cancer (BCLC) staging information is missing for the majority of the patients in our study, for HCC and Common patients that did have BCLC staging information, BCLC A was the most common. Almost all the patients in the HCC and Common groups died before the end of the study, whereas nearly 40% of patients in the MOTION dataset were still alive at the end of the study period. HBV, HCV and alcohol were the most common etiologies; however, HCV was most common among the MOTION patients, and HBV among the Common patients. Over 60% of patients in all three groups had evidence of cirrhosis.

Time to event

Table 2 presents the various time to event analyses conducted for the three groups. The mean follow-up time from diagnosis to death or end of follow-up was 31.5, 30.1 and 34.6 months for the HCC, Motion and Common patients, respectively. The mean follow-up time from the start of first treatment to death or end of follow-up was 15.3 months (from first systemic therapy) for HCC patients, and 27.2 months (from first LRT) for the Motion patients and 32.6 months (from first treatment, systemic or LRT) for the Common patients. In the HCC cohort, this reflected some patients being monitored for a period prior to initiation of systemic therapy.

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Table 1. Baseline characteristics.

	HCC patients (n = 417), n (%)	MOTION patients, (n = 413), n (%)	Common patients (n = 63), n (%)
Age (years):			
– Mean (SD)	64.0 (10.5)	63.0 (8.8)	63.2 (10.9)
– Median (Q1–Q3)	64 (58–72)	62 (57–69)	62 (57–71)
– Missing data (%)	0.0%	4.1%	0.0%
– Min–Max	13–87	30–90	30–83
Gender:			
– Male	344 (82.5%)	338 (81.8%)	53 (84.1%)
– Female	73 (17.5%)	75 (18.2%)	10 (15.9%)
CPS:			
– Mean (SD)	6.0 (0.6)	5.7 (0.9)	5.3 (0.6)
– Median (Q1–Q3)	6 (6–6)	5 (5–6)	5 (5–5)
– Missing data (%)	14.4%	1.9%	0.0%
– Min–Max	5–9	5–11	5–7
CPS category:			
– Missing	60 (14.4%)	8 (1.9%)	0 (0.0%)
– CPS A	308 (73.9%)	343 (83.1%)	58 (92.1%)
– CPS B	49 (11.8%)	61 (14.8%)	5 (7.9%)
– CPS C	0 (0.0%)	1 (0.2%)	0 (0.0%)
Missing	274 (65.7%)	413 (100.0%)	22 (34.9%)
BCLC stage:			
– 0	7 (1.7%)	0 (0.0%)	1 (1.6%)
– A	52 (12.5%)	0 (0.0%)	20 (31.7%)
– B	34 (8.2%)	0 (0.0%)	11 (17.5%)
– C	49 (11.8%)	0 (0.0%)	9 (14.3%)
– D	1 (0.2%)	0 (0.0%)	0 (0.0%)
Diagnosis year:			
– 2000–2011	225 (54.0%)	124 (30.0%)	16 (25.4%)
– 2012	31 (7.4%)	50 (12.1%)	7 (11.1%)
– 2013	45 (10.8%)	35 (8.5%)	9 (14.3%)
– 2014	37 (8.9%)	67 (16.2%)	10 (15.9%)
– 2015	37 (8.9%)	71 (17.2%)	17 (27.0%)
– 2016	24 (5.8%)	53 (12.8%)	3 (4.8%)
– 2017	18 (4.3%)	13 (3.1%)	1 (1.6%)
Status at study end:			
– Alive	19 (4.6%)	156 (37.8%)	0 (0.0%)
– Dead	398 (95.4%)	235 (56.9%)	63 (100.0%)
– Lost to follow-up	0 (0.0%)	22 (5.3%)	0 (0.0%)
Disease etiology[†]:			
– HBV	121 (29.0%)	113 (27.4%)	29 (46.0%)
– HCV	153 (36.7%)	226 (54.7%)	24 (38.1%)
– No prior viral hepatitis	153 (36.7%)	79 (19.1%)	12 (19.0%)
– EtOH	118 (28.3%)	71 (17.2%)	12 (19.0%)
– NASH	10 (2.4%)	14 (3.4%)	3 (4.8%)
– Cirrhosis	262 (62.8%)	314 (76.0%)	41 (65.1%)
– Other	19 (4.6%)	44 (10.7%)	2 (3.2%)

[†]Totals are greater than 100% as patients may have had multiple etiologies.
BCLC: Barcelona Clinic Liver Cancer; CPS: Child-Pugh score; EtOH: Ethanol; HCC: Hepatocellular carcinoma; NASH: Non-alcoholic steatohepatitis; SD: Standard deviation.

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Table 2. Time to event analyses.

	HCC patients (n = 417)	MOTION patients (n = 413)	Common patients (n = 63)
Diagnosis to first treatment‡ (months):			
– Mean (SD)	17.1 (27.3)	3.4 (3.4)	4.7 (4.2)
– Median (Q1–Q3)	6 (2–20)	3 (2–4)	4 (2–5)
– Missing data (%)	2.9%	3.1%	12.7%
– Min–Max	0–279	0–37	0–23
Diagnosis to death (months):			
– Mean (SD)	31.5 (33.1)	30.1 (27.5)	34.6 (26.2)
– Median (Q1–Q3)	21 (9–44)	21 (11–39)	28 (18–48)
– Missing data (%)	0.2%	0.0%	0.0%
– Min–Max	1–301	2–202	4–167
First treatment to death‡ (months):			
– Mean (SD)	15.3 (19.2)	27.2 (27.8)	32.6 (27.3)
– Median (Q1–Q3)	9 (4–19)	18 (8–36)	26 (16–38)
– Missing data (%)	0.2%	0.2%	0.0%
– Min–Max	0–162	0–202	3–162
First LRT to transplant (months):			
– Mean (SD)	N/A	28.4 (22.6)	1–5†
– Median (Q1–Q3)	N/A	21 (10–44)	1–5†
– No transplant (%)	N/A	93.0%	1–5†
– Min–Max	N/A	0–88	1–5†
Transplant to first systemic (months):			
– Mean (SD)	23.8 (12.2)	N/A	N/A
– Median (Q1–Q3)	22 (12–35)	N/A	N/A
– No transplant (%)	97.8%	N/A	N/A
– Min–Max	10–42	N/A	N/A

†Cells are suppressed because of a small number of patients (i.e., <5).
‡First treatment - start of treatment was defined as receipt of first systemic therapy for the HCC patients, date of first LRT for the MOTION patients and either first treatment (systemic or LRT) for the common patients.
HCC: Hepatocellular carcinoma; LRT: Locoregional therapies; SD: Standard deviation.

Liver transplants were received by 10, 29 and <5 ,patients in the HCC, MOTION and Common groups, respectively. All 29 MOTION patients in received their transplant after starting LRTs, with a mean time of 28.4 months after their first LRT. Nine of the 10 HCC patients received their transplant before starting systemic therapy (i.e., at time of recurrence) with a mean time of 23.8 months before starting systemic therapy.

Treatment patterns

Figure 1 illustrates the sequence of first line (1L) to second line (2L) liver directed treatment patterns for MOTION patients. The majority (55.9%) of patients received a chemoembolization as first LRT, namely the drug-eluting bead transarterial chemoembolization (DEB-TACE) at 41.6% and TACE using lipiodol (Lipiodol TACE) at 14.3%. The third most frequent LRT was transarterial radioembolization with the radioisotope yttrrium-90 (Y90) at 12.8%. The y-axis in the figure indicates that DEB-TACE continued to be the most frequent procedure in 2L, as well as in subsequent lines (data not shown). However, radiofrequency ablation was the second most frequent procedure for 2L LRTs. Last, MOTION patients received a mean of 2.7 LRTs over 14.7 months (i.e., from first LRT to last LRT).

Similarly, Figure 2 illustrates 1L to 2L treatment patterns for the Common patients. DEB-TACE was the most frequent LRT in 1L (34.9%) followed by Y90 (20.6%). In 2L, DEB-TACE and radiofrequency ablation were the top two LRTs given to the Common patients. On average, the Common patients received 3.2 LRTs over 15.9 months (i.e., from first LRT to last LRT). Liver transplant information could not be numerically shared (e.g., <5) due to small cell suppression.

Nearly everybody (99%) received sorafenib in 1L among both the HCC and Common patients, however, a very small number of patients received Nivolumab in 1L. The vast majority of patients in both groups did not go on

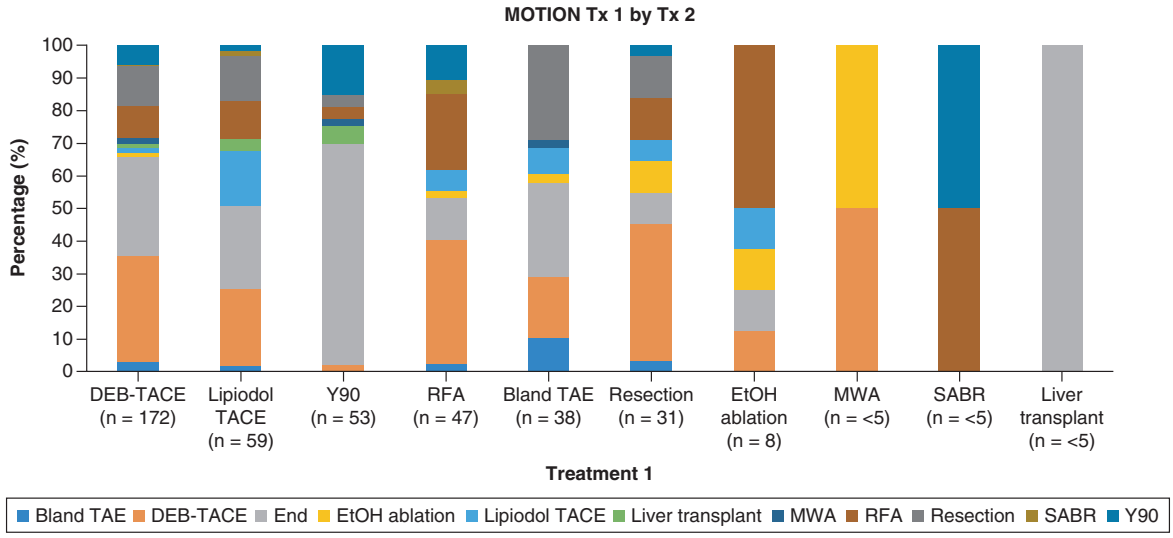

Figure 1. Locoregional therapy sequencing from treatment 1 to treatment 2 for MOTION patients.
DEB-TACE: Drug-eluting bead transarterial chemoembolization; End: No further treatment; EtOH: Ethanol; MWA: Microwave ablation; RFA: Radiofrequency ablation; SABR: Stereotactic ablative radiotherapy; T: Treatment; TACE: Transarterial chemoembolization; TAE: Transarterial embolization; Y90: Yttrrium-90.

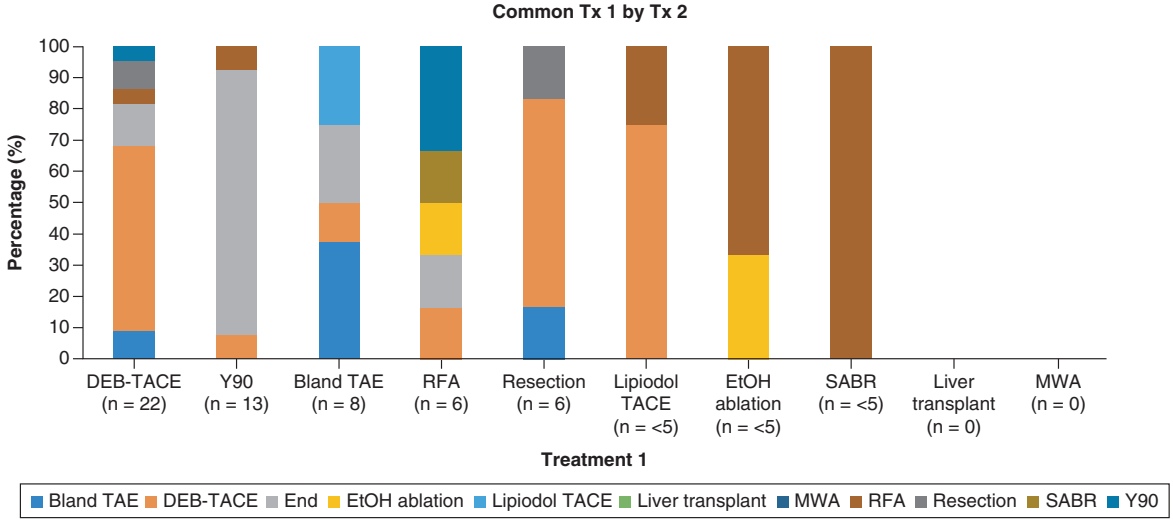

Figure 2. Locoregional therapy sequencing from treatment 1 to treatment 2 for common patients.
DEB-TACE: Drug-eluting bead transarterial chemoembolization; End: No further treatment; EtOH: Ethanol; MWA: Microwave ablation; RFA: Radiofrequency ablation; SABR: Stereotactic ablative radiotherapy; T: Treatment; TACE: Transarterial chemoembolization; TAE: transarterial embolization; Y90: Yttrrium-90.

to receive a 2L systemic treatment. Both the HCC and Common groups were on systemic therapy for an average of 5.5 months. For the Common group who received both LRTs and systemic therapy, 80.9% received LRTs prior to starting systemic therapy, 11.1% received LRTs while also on systemic therapy, and 7.9% received LRTs after completing systemic therapy.

Survival outcomes

Figure 3 illustrates the overall survival of the three groups from diagnosis until death (all-cause mortality). The mOS from diagnosis was 21 months (95% CI: 17–23 months; IQR: 10–45 months), 33 months (95% CI: 27–38 months; IQR: 16–89 months) and 28 months (95% CI: 23–33 months; IQR: 18–48 months) for the HCC, MOTION and Common groups, respectively.

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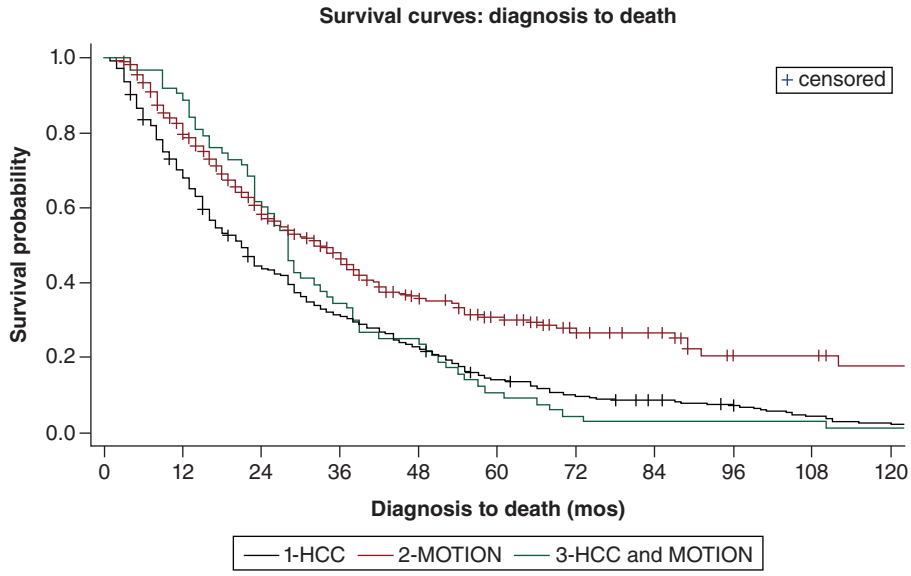

Figure 3. Overall survival from diagnosis.
HCC: Hepatocellular carcinoma.

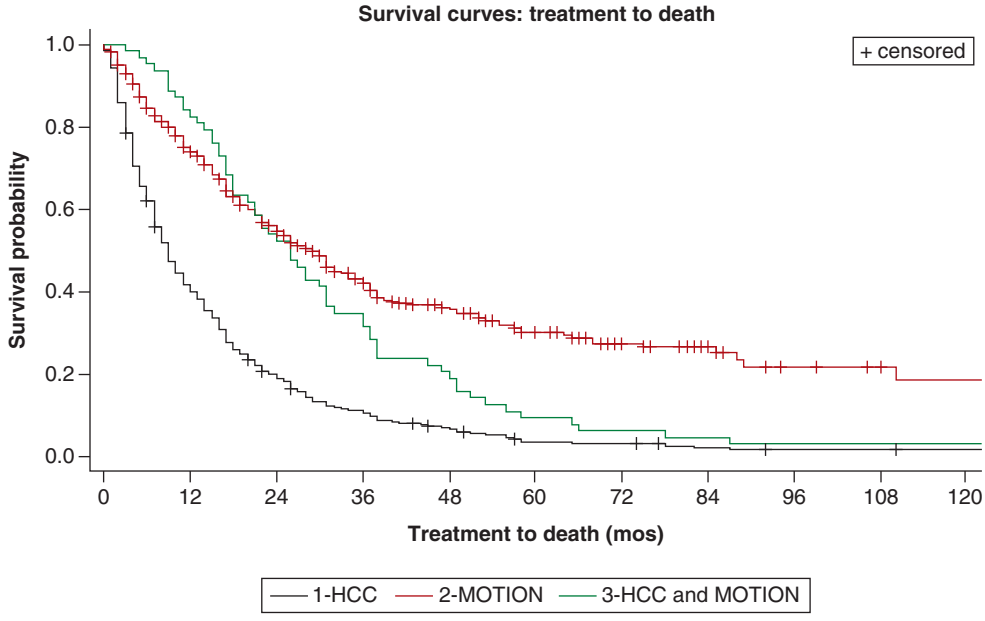

Figure 4. Overall survival from start of treatment.
HCC: Hepatocellular carcinoma.

Figure 4 provides the overall survival from the start of treatment until death for the three groups. The mOS was 9 months (95% CI: 8–10 months; IQR: 4–20 months), 29 months (95% CI: 24–33 months; IQR: 12–88 months) and 26 months (95% CI: 20–31 months; IQR: 16–38 months) for the HCC, MOTION and Common groups, respectively. The MOTION and Common patient groups had small differences in their mOS when comparing survival from diagnosis versus start of treatment. However, the HCC group had a larger difference in their mOS (21 months from diagnosis vs 9 months from start of systemic therapy), which occurred as systemic therapy was generally indicated for more advanced disease and following local therapies, resulting in HCC patients having a larger gap between diagnosis and start of treatment with a mean time of 17.1 months compared with 3.4 and 4.7 months for MOTION and Common patients, respectively.

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Table 3. 1-year, 5-year and 10-year survival rates.

Patient groups	1-year survival	5-year survival	10-year survival
From diagnosis			
Hepatocellular carcinoma	68%	14%	3%
MOTION	80%	31%	18%
Common	89%	11%	3%
From treatment initiation			
Hepatocellular carcinoma	40%	4%	2%
MOTION	74%	30%	19%
Common	83%	10%	3%

Table 3 provides the 1-year, 5-year and 10-year survival rates from diagnosis and start of treatment for the HCC, MOTION and Common groups. Survival rate from diagnosis was longer for MOTION group (80% at 1 year and 31% at 5 years), which was expected as patients generally did not progress to require systemic therapy, whereas for HCC it was 68% at 1 year and 14% at 5 years, and for the Common group it was 89% at 1 year and 11% at 5 years. Similarly, the HCC also group had the lowest survival rates from the start of treatment, with a survival rate of 40% at 1 year and 4% at 5 years, reflecting the advanced disease requiring systemic therapy at treatment start. The MOTION group had a 10-year survival rate of 19% from first LRT, compared with 2% and 3% for HCC and Common groups respectively, reflecting the disease state for those progressing to need systemic therapy.

Costing

Cost analyses included treatment, medical oncology visits and transplant costs (in 2021 Canadian dollars). The mean cost per patient for the entire HCC treatment journey for the common patient group was $94,419 ± $56,844. The mean cost per patient per year was $51,649, with a mean duration of treatment, from first treatment to last treatment, of 21.9 months. The cost driver was the LRTs in which the mean cost per patient was $60,382 ± $38,841 and the mean cost per patient per year was $45,535. The mean cost of systemic therapy was $31,534 ± $37,198 and the mean cost per patient per year was $67,800. The higher systemic cost reflects the shorter median time on treatment (5.5 months) compared with time on LRT (14.7 months).

Discussion

This study sought to understand the treatment patterns and survival trajectories of patients with HCC, in an era with limited systemic therapies (mostly sorafenib) that was generally relegated to the treatment of the most advanced disease with preserved CPS based on the evidence and funding for treatment. On their own, the HCC and MOTION datasets provided incomplete disease treatment pathways, but we were able to determine the complete treatment pathway for the 63 Common patients found in both datasets. This cohort consisted of mostly men, with a mean age of 63 years, with preserved liver function based on Child-Pugh Score A. 81% of patients presented with viral hepatitis etiology and 20% with alcohol as an etiology, and two-thirds with evidence of cirrhosis. The majority of this cohort did not survive to the end of the study period, with 11% survival rate at 5 years and 3% at 10 years. We acknowledge that the Common subgroup may present a selection bias, however, they demonstrate the closest to a complete treatment pathway of all the datasets available in this study.

The findings in our study are aligned with existing published literature of studies using individual patient data, especially in the Canadian context. For advanced HCC patients, 9 months was the mOS from the start of systemic treatment in our cohort, which is in line with Canadian cohorts reporting a mOS of 9.2 months [12] and 9.4 months [13]. Similarly, the 5-year survival rate from diagnosis for the Common patients (11%) in our study was comparable to two other studies [14,18], but interestingly, our 1-year survival rate (89%) was higher than both studies [14,18].

Many international organizations and researchers have also tried to determine the survival of HCC patients using administrative data. Two studies in the UK used population data to estimate a 1-year survival rate between 40 and 47% and a 5-year survival rate between 15% and 18% [19,20]. A 2017 French study using administrative data determined that the mOS from diagnosis was 9.4 months, which is lower than the 28 months found in our study [21]. However, their 5-year survival rate of 9.6% is comparable to the 5-year survival rate in our study [21]. An Australian study using a publicly available cancer registry estimated a mOS of 20.8 months from diagnosis

and a 1-year survival rate of 62% from diagnosis, both of which are lower than that found in our study [22]. The differences in survival between our study and these studies can be attributed to different cohort creation criteria (i.e., more advanced patients with Child-Pugh B and C scores), more recent cohort of HCC patients, or different study methodologies. Since liver transplants have been shown to improve survival rates, it's important to understand the criteria used for selecting candidates for liver transplant, and at this center's transplant program, it recently changed from the Milan criteria to the total tumor volume criteria <145 cm^3 and alpha fetoprotein <1000. Also, the median model for end-stage liver disease (MELD) score is calculated for the program annually and the HCC patients are given MELD exceptions points which is equivalent to 3 points above the most recent median MELD score.

Our costing analysis has also found similar results as some studies conducted in Canada. One study using administrative databases found that the 5-year net cost of HCC in Ontario was US$77,509 in 2010 [15]. When converted to 2010 CAD and then inflated to 2021 CAD, the cost becomes $97,868 CAD [23,24]. Our mean cost per patient calculation of $94,419 CAD included costs directly related to HCC treatment such as LRT costs, systemic therapy costs and transplant costs, whereas, Thein and colleagues costed by phases of care (including emergency room visits, hospitalizations, and complex continuing care), however utilization of systemic therapies was limited [15].

To our knowledge, this combination of datasets is the first such effort to gain an understanding of the entire treatment journey. A major strength of this study is the size of the HCC and MOTION cohorts and the ability to combine the datasets, providing a more fulsome picture of the patient journey with HCC treatments.

The limitations in our study relate to therapeutic era, representativeness, treatments and costs. First, our study duration includes a period when sorafenib was the only systemic therapy in the first line advanced disease setting. Subsequently, lenvatinib and more recently immunotherapies have emerged as alternative first line therapies, providing more first line treatment options, opening the possibility of treatment sequencing, and there is new data supporting earlier use of systemic therapy. These can be evaluated in subsequent studies. Second, in terms of representativeness, the data reflects patients treated at a quaternary site for LRT and a provincial cancer program for systemic therapy, and therefore may not be applicable to other centers in Canada or globally. Additionally, we had very limited BCLC staging information, as the MOTION database did not collect BCLC staging and the majority of patients in the HCC database also had missing BCLC information. Third, the majority of patients in the HCC database received LRT treatment prior to systemic therapy, however, given the limited availability of specific data such as treatment dates, these LRTs were not included as part of the analyses, and we could not verify LRTs done outside the quaternary site or treatments received outside the date ranges of data capture. Similarly, many patients in the MOTION dataset had a recommendation from MLRT to consider systemic therapy, however receipt of systemic therapy could not be confirmed with HCC data, it is possible that patients may have been ineligible for systemic treatment at the time of medical oncology assessment. Finally, only costs associated with specific treatments (LRT, systemic therapy and liver transplant) and medical oncology visits were used to calculate the cost per HCC patient. Costs such as hospitalizations, emergency room visits, diagnostic and laboratory tests, nursing, pharmacy and allied health costs, and other physician visits should be considered in a more comprehensive costing analysis.

Conclusion

This was a collaborative effort to understand the HCC patient treatment journey and cost analysis across treatment modalities. However, given the limited generalizability of the results future studies should include a wider range of populations, assess more contemporary systemic treatments, the expanded use of LRT and sequencing of multimodality treatments, and ensure data capture of more relevant disease factors.

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Competing interests disclosure

The authors have no competing interests or relevant affiliations with any organization or entity with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Writing disclosure

No funded writing assistance was utilized in the production of this manuscript.

Ethical conduct of research

Research Ethics Board applications for MOTION (H19-03084) and HCC (H17-01147) were amended to allow their data to be used as a part of this study. Research Ethics Board approval for this study was obtained from both the BC Cancer Agency (H21-00394) and the Sunnybrook Research Institute (3564). As this data involved retrospective data, no informed consent form was required.

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Summary points

- Hepatocellular carcinoma (HCC) is a primary liver cancer, often treated via surgery, locoregional therapies and systemic treatments.
- Sorafenib was the standard for advanced HCC, but recent trials have introduced alternatives like lenvatinib and immunotherapies.
- There are limited Canadian studies on HCC healthcare utilization and costs. This study used data from BC Cancer, Vancouver General Hospital and BC Transplant.
- The objective of this study was to describe HCC patient treatment pathways, survival outcomes, healthcare resource utilization and costs in British Columbia, Canada.
- The study cohort included mostly males, with a median age of 63 years, and underlying liver disease of HBV, HCV and alcohol-related cirrhosis present.
- In the Common cohort, most patients were treated with LRTs (e.g., DEB-TACE) followed by systemic therapy (mainly sorafenib).
- Median overall survival from diagnosis was 21 months for the HCC cohort, 33 months for the MOTION cohort and 28 months for the Common cohort. Five and 10-year survival was 11 and 3% respectively for the Common cohort.
- The average cost per Common patient for their treatment journey was $94,419 ± $56,844, driven by LRTs ($60,382 ± $38,841) and systemic therapy ($31,534 ± $37,198).
- Study limitations included representativeness and incomplete data on treatments and costs. Future studies should address these gaps as well as including current HCC treatments.

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