Effect of proximity to specialty care on outcomes for biliary cancers: a population-based retrospective cohort study

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Abstract

Background: The management of biliary cancers is complex and requires a multidisciplinary approach. Because it is unknown how access to specialty care affects resource use and survival in patients with biliary cancer, we conducted a population-based study to understand the needs of these patients and the relation of geography to care delivery and clinical outcomes for biliary cancer in Alberta.

Methods: All patients with biliary cancer diagnosed in Alberta from Sept. 1, 2001, to Dec. 31, 2015 were included in this population-based retrospective cohort study. Data were extracted from administrative databases and the 2011 Canadian census. Driving time and types of medical services were tracked throughout the patients' clinical course. We categorized proximity to specialty care according to driving time to the nearest specialist. The primary outcome was overall survival. We conducted Cox proportional hazard regression to evaluate the effects of driving time on overall survival and multivariate logistic regression to evaluate the effect of driving time on treatment types and stage at diagnosis.

Results: We identified 1610 patients with biliary cancer; they accounted for 117 381 medical encounters. Patients living 120 minutes or more from the nearest hepatobiliary surgeon and from the nearest cancer centre had significantly decreased survival (hazard ratio [and 95% confidence interval (CI)] 1.27 [1.17–1.37]) and 1.27 [1.14–1.41], respectively). Location of residence was not associated with advanced stage or probability of undergoing surgery or a biliary drainage procedure. Patients who lived 120 minutes or more from a cancer centre were less likely than those who lived less than 120 minutes away to receive chemotherapy (odds ratio 0.51, 95% CI 0.29–0.88). Subgroup analysis showed that the effect of travel time was especially pronounced among those who received only best supportive care and those who had biliary drains.

Interpretation: Geography and accessibility to specialty care affected survival in patients with biliary cancer. Further study is required to understand how patients with biliary drains and those receiving best supportive care are affected by proximity to specialty care. This will aid in the identification of strategies to provide improved care for this subgroup who are particularly affected by geography.

B iliary cancers are rare tumours that are generally associated with a poor prognosis. Surgery is the only potential cure, although only a minority of tumours are candidates for resection.[1] Moreover, surgery is technically difficult and is associated with very high morbidity and mortality rates.[2,3] In patients with advanced disease and adequate performance status, palliative chemotherapy is advantageous.[4] However, the disease is often complicated by jaundice and sometimes sepsis, precluding chemotherapy. The mainstay of palliation consists of achieving stable biliary drainage, which generally necessitates repeated instrumentation of the biliary tract over the disease course.[5–7] In all, the management of biliary cancers is complex and requires the coordination of multiple specialties.

For the optimal management of biliary cancers, it is important that a patient have sufficient planned and emergent access to appropriate facilities and specialists including hepatobiliary surgeons, oncologists and interventional radiologists. Continuity of care is important to ensure management plans are followed. For patients living far from major population centres, these features of care are difficult to deliver. Our objective was to understand what disparities of care exist as a function of driving time to tertiary and quaternary care facilities in Alberta and how these disparities affect survival. Few data are available that provide a comprehensive picture of the needs of patients with biliary cancer, from diagnosis to death.

Given the need for highly expert care, we postulated that patients who lived more remotely would have worse survival.

Methods

Study population and data sources

The province of Alberta consists of an area of 660 000 km² with a population of 4 million. About 20% of the population lives in rural areas. In this population-based retrospective cohort study, we included all cases of biliary cancer diagnosed in Alberta from Sept. 1, 2001, to Dec. 31, 2015. This included intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, gallbladder cancer and ampullary cancer, all of adenocarcinoma histologic type.

Data were extracted from the Alberta Cancer Registry, physician billing claims, hospital discharge abstracts, ambulatory care records, the provincial population registry and the 2011 Canadian census. The Alberta Cancer Registry records patient demographic characteristics, treatments, diagnosis date, last date of follow-up, vital statistics and tumour characteristics including tumour type and American Joint Committee on Cancer stage. It has received gold-level certification status from the North American Association of Central Cancer Registries, which has standardized cancer registry data since 2014 (https://www.naaccr.org/certified-registries/). We used physician claims data to track medical encounters. Hospital discharge abstracts describe up to 25 diagnoses coded with the *International Statistical Classification of Diseases and Related Health Problems, 10th revision* (ICD-10) and up to 20 procedures described by Canadian Classification of Health Interventions codes. Data were linked by provincial health number. We calculated the Charlson Comorbidity Index score for each patient within a year of diagnosis using validated algorithms.[8] We derived neighbourhood socioeconomic status including average income and proportion with a postsecondary education from census data. The administrative data sets and ICD codes were previously validated.[8–10]

We used patient postal code to calculate driving time to the nearest facility with a hepatopancreatobiliary surgeon and to the nearest cancer centre (Table 1). We calculated travel times for each medical visit based on patient and medical facility postal codes. All driving times were calculated with the use of Google Maps application programming interfaces,[11] based on driving times at noon on a weekday. Previous publications did not provide a standard on how to categorize driving time. Our driving time categories (≤ 30 min, 31–60 min, 61–120 min, 121–180 min and > 180 min) were based on our own estimates of meaningful proximity intervals.

Outcomes

The primary outcome was overall survival, beginning from the date of tissue diagnosis or the first biliary intervention, whichever was first. Secondary outcomes included the proportion of patients with delayed diagnosis and treatments delivered.

Statistical analysis

We performed statistical analysis using SAS version 9.4 (SAS Institute) and data visualization using Tableau version 10.3 (Tableau Software). We used descriptive statistics to characterize the study cohort. We compared continuous data using the t test and used the χ^2 test for comparison of categorical variables. We conducted Cox proportional hazard regression to evaluate the effects of driving time on overall survival. Based on previously published studies,[12–14] we included key risk factors in the models, including age, sex, neighbourhood socioeconomic status, resection, chemotherapy, tumour type (intrahepatic cholangiocarcinoma, extrahepatic cholangiocarcinoma, gallbladder cancer or ampullary cancer), presence of stage IV disease, year of diagnosis (from 2001 to 2015) and Charlson Comorbidity Index for the entire cohort and subgroups. We conducted multivariate logistic regression to evaluate the effect of driving time on treatment types (adjusted for age, sex, Charlson Comorbidity Index score, stage, tumour type, year of diagnosis and socioeconomic status) and on stage at diagnosis (adjusted for age, sex, Charlson Comorbidity Index score, tumour type, year and socioeconomic status). A 2-sided p value ≤ 0.05 was considered statistically significant.

In tracking medical visits, we considered 3 intervals during each patient's disease trajectory. The prediagnosis interval included the 3 months before the date of diagnosis, the postdiagnosis interval was 24 months from the date of diagnosis, and the end-of-life interval included the final 8 weeks of life. For patients whose lifespan (after diagnosis) was 8 weeks or less, only activity in the final interval could be described.

Ethics approval

This study was approved by the Health Research Ethics Board of Alberta Cancer Committee.

Results

Incidence and geographic distribution of biliary cancers

During the study period, 1717 cases of biliary cancer were diagnosed. Among these, 107 patients (6.2%) had invalid provincial health numbers (nonresidents of Alberta) or no follow-up after diagnosis or primary treatment and were excluded, leaving 1610 patients for analysis (396 with extrahepatic cholangiocarcinoma, 386 with intrahepatic cholangiocarcinoma, 531 with gallbladder cancer and 243 with ampullary cancer; the remaining 54 patients had tumours that could not be classified because they were "not otherwise specified" or were at overlapping sites). The geographic case distribution throughout the province is depicted in Figure 1. Patient characteristics are summarized in Table 2 and Supplementary Table S1, Appendix 1 (available at www.cmajopen.ca/content/7/1/E131/suppl/DC1). Of the 1610 patients, 114 (7.1%) lived at least 120 minutes' driving time from the nearest cancer centre, and 245 (15.2%) had to drive 120 minutes or more to the nearest hepatopancreatobiliary surgeon. In all, 975 patients (60.6%) received best supportive care, 262 (16.3%) received

Table 1: Cancer centres, centres with hepatopancreatobiliary surgeons and centres with general surgeons in Alberta

Institution type	Institution	City/town
Cancer centre	Cross Cancer Institute	Edmonton
	Tom Baker Cancer Centre	Calgary
	Central Alberta Cancer Centre	Red Deer
	Jack Ady Cancer Centre	Lethbridge
	Grande Prairie Cancer Centre	Grande Prairie
	Margery E. Yuill Cancer Centre	Medicine Hat
Centre with hepatopancreatobiliary surgeons	University of Alberta Hospital	Edmonton
	Foothills Medical Centre	Calgary
	Red Deer Regional Hospital	Red Deer
Centre with general surgeons	Foothills Medical Centre	Calgary
	University of Alberta Hospital	Edmonton
	Peter Lougheed Centre	Calgary
	Red Deer Regional Hospital	Red Deer
	Royal Alexandra Hospital	Edmonton
	Sturgeon Community Hospital	St. Albert
	Chinook Regional Hospital	Lethbridge
	Rockyview General Hospital	Calgary
	Queen Elizabeth II Hospital	Grand Prairie
	Misericordia Community Hospital	Edmonton
	Grey Nuns Community Hospital	Edmonton
	Medicine Hat Regional Hospital	Medicine Hat
	Stollery Children's Hospital	Edmonton
	Fort Saskatchewan Community Hospital	Fort Saskatchewan
	St. Mary's Hospital	Camrose
	South Health Campus	Calgary
	Northern Lights Regional Health Centre	Fort McMurray
	Hinton General Hospital	Hinton
	Cold Lake Hospital	Cold Lake
	Drumheller Health Centre	Drumheller
	Canmore General Hospital	Canmore
	Crowsnest Pass Health Centre	Crowsnest Pass
	Strathcona Community Hospital	Sherwood Park
	Wetaskiwin Hospital and Care Centre	Wetaskiwin
	Alberta Children's Hospital	Calgary
	St. Therese – St. Paul Healthcare Centre	St. Paul

chemotherapy alone, 262 (16.3%) received surgery alone, and 103 (6.4%) received surgery and chemotherapy.

Survival as a function of residence

The median length of follow-up among the 1299 patients (80.7%) followed until death was 6.8 months (interquartile range [IQR] 2.5–16.8 mo). The median length of follow-up for the remaining 311 patients was 49.9 months (IQR 23.1–92.9 mo). As expected, median survival was best among patients who underwent resection (35.6 mo, 95% confidence interval [CI] 26.2–49.6 mo), followed by patients who had palliative chemotherapy (12.0 mo, 95% CI 10.6–13.4 mo); it was worst among patients who received best supportive care (4.6 mo, 95% CI 4.1–5.1 mo). Survival for ampullary cancer (24.5 mo, 95% CI 18.9–27.2 mo) was considerably better than that for intrahepatic cholangiocarcinoma (5.7 mo, 95% CI 4.7–7.0 mo), extrahepatic cholangiocarcinoma (10.2 mo, 95% CI 9.1–12.5 mo) and gallbladder cancer (8.0 mo, 95% CI 6.7–9.6 mo).
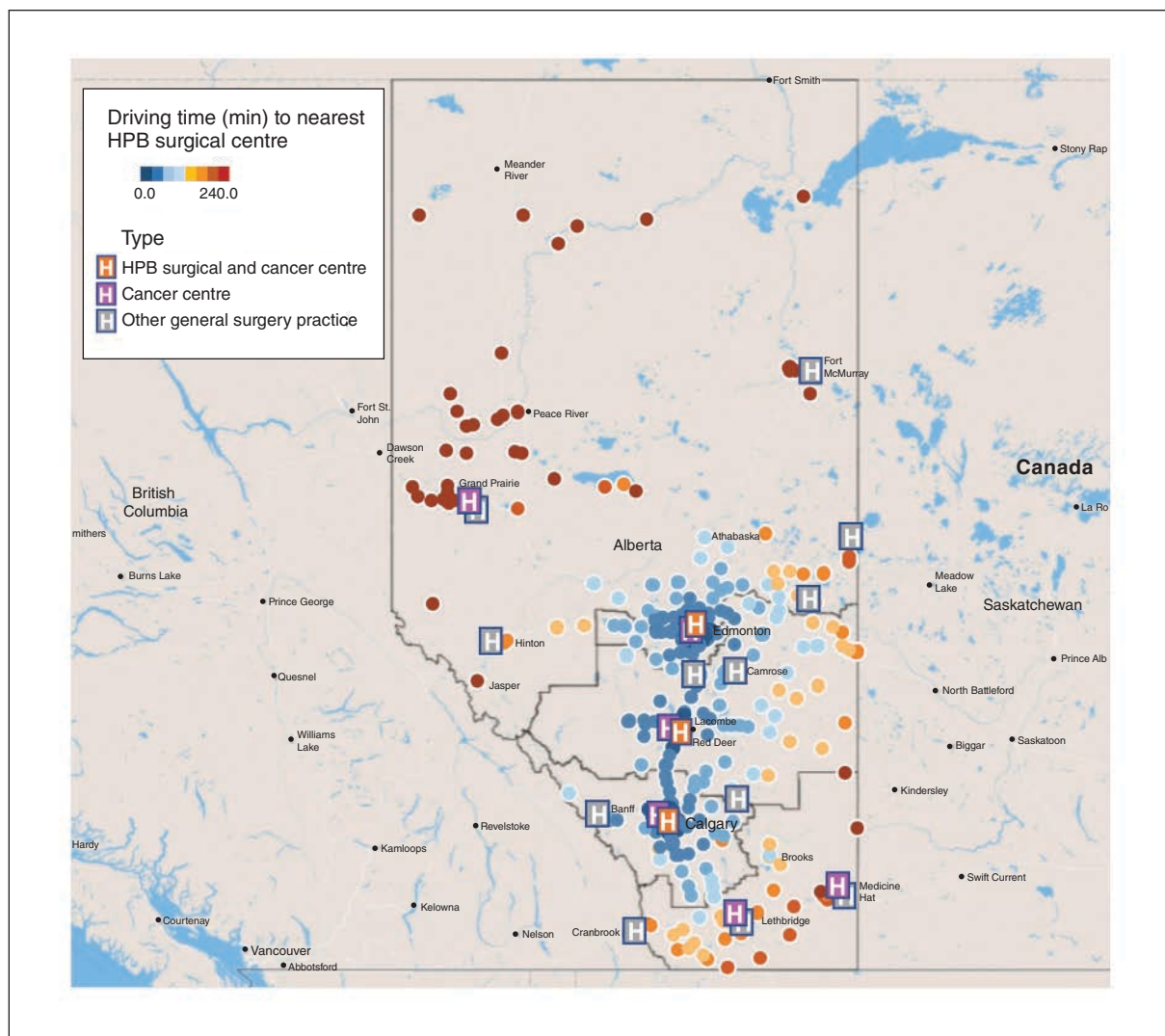
Figure 1: Geographic distribution of cases of biliary cancers in the province of Alberta between 2001 and 2015. Main population centres, cancer centres and sites where hepatopancreatobiliary (HPB) surgeons exist are marked.

Without adjustment for other factors, overall survival was not significantly different according to driving time to the nearest hepatopancreatobiliary surgeon, cancer centre or interventional radiologist (Table 2 and Supplementary Table S1, Appendix 1). However, longer driving time to the nearest hepatopancreatobiliary surgeon and to the nearest cancer centre were significantly associated with decreased survival ($p < 0.001$ and $p = 0.001$, respectively), after adjustment for age, sex, comorbidities, income and education levels, treatment (surgery or chemotherapy), stage and tumour type. Although driving time was significant as a continuous variable, the association was particularly pronounced for driving time of 120 minutes or more: living at least 120 minutes from the nearest hepatopancreatobiliary surgeon was associated with decreased survival (hazard ratio [HR] 1.27, 95% CI 1.17–1.37) (Table 3), as was living 120 minutes or more from the nearest cancer centre (HR 1.27, 95% CI 1.14–1.41) (Supplementary Table S1, Appendix 1). In the multivariate model, survival outcomes were better in cancers diagnosed from 2010

onward (HR 0.84, 95% CI 0.79–0.89) (Table 3), and the number of biliary drains was also a significant factor associated with survival (HR 0.97, 95% CI 0.95–0.98) (Table 3).

Further analyses focused on outcomes as a function of driving time to the nearest hepatopancreatobiliary surgeon (≥ 120 min v. < 120 min), since that had the greatest impact on survival. Subgroup analysis showed that the effect on survival of driving time to the nearest hepatopancreatobiliary surgeon was pronounced for older patients, those with a lower Charlson Comorbidity Index score, those who received best supportive care and those who had biliary drainage (Figure 2). In the tumour type subgroups, the effect of driving time was greatest for ampullary cancer, followed by intrahepatic cholangiocarcinoma.

Disease stage and treatment as a function of residence

Treatment strategies changed during the study period. The proportion of patients with extrahepatic cholangiocarcinoma,

Table 2: Patient characteristics as a function of driving time to the nearest hepatopancreatobiliary surgical centre

	Driving time, min; no. (%) of patients*						
Variable	≤ 30 n = 974	31–60 n = 237	61–120 n = 154	121–180 n = 128	> 180 n = 117	Total n = 1610	p value
Sex							
Female	524 (53.8)	115 (48.5)	73 (47.4)	67 (52.3)	61 (52.1)	840 (52.2)	0.4
Male	450 (46.2)	122 (51.5)	81 (52.6)	61 (47.7)	56 (47.9)	770 (47.8)	
Age, yr, mean ± SD	67.6 ± 13.0	65.4 ± 12.8	67.5 ± 11.5	67.7 ± 12.7	64.8 ± 13.5	67.1 ± 12.9	0.05
Charlson Comorbidity Index score							
≤ 2	391 (40.1)	95 (40.1)	64 (41.6)	46 (35.9)	52 (44.4)	648 (40.2)	0.9
3–4	251 (25.8)	59 (24.9)	37 (24.0)	36 (28.1)	24 (20.5)	407 (25.3)	
≥ 5	332 (34.1)	83 (35.0)	53 (34.4)	46 (35.9)	41 (35.0)	555 (34.5)	
Tumour type							
Intrahepatic cholangiocarcinoma	241 (24.7)	57 (24.0)	35 (22.7)	22 (17.2)	31 (26.5)	386 (24.0)	0.3
Extrahepatic cholangiocarcinoma	332 (34.1)	76 (32.1)	53 (34.4)	43 (33.6)	27 (23.1)	396 (24.6)	
Gallbladder cancer	232 (23.8)	56 (23.6)	42 (27.3)	36 (28.1)	30 (25.6)	531 (33.0)	
Ampullary cancer	132 (13.6)	40 (16.9)	22 (14.3)	24 (18.8)	25 (21.4)	243 (15.1)	
Other/overlapping	37 (3.8)	8 (3.4)	2 (1.3)	3 (2.3)	4 (3.4)	54 (3.4)	
Stage							
I–III	590 (60.6)	137 (57.8)	93 (60.4)	86 (67.2)	72 (61.5)	978 (60.7)	0.5
IV	384 (39.4)	100 (42.2)	61 (39.6)	42 (32.8)	45 (38.5)	632 (39.2)	
Treatment							
Surgery	156 (16.0)	37 (15.6)	29 (18.8)	22 (17.2)	26 (22.2)	270 (16.8)	0.08
Chemotherapy	169 (17.4)	48 (20.2)	14 (9.1)	13 (10.2)	18 (15.4)	262 (16.3)	
Chemotherapy + surgery	56 (5.7)	20 (8.4)	9 (5.8)	9 (7.0)	9 (7.7)	103 (6.4)	
Best supportive care	593 (60.9)	132 (55.7)	102 (66.2)	84 (65.6)	64 (54.7)	975 (60.6)	
No. of biliary drains							
0	450 (46.2)	105 (44.3)	75 (48.7)	48 (37.5)	49 (41.9)	727 (45.2)	0.3
1	230 (23.6)	56 (23.6)	36 (23.4)	31 (24.2)	34 (29.1)	387 (24.0)	
≥ 2	294 (30.2)	76 (32.1)	43 (27.9)	49 (38.3)	34 (29.1)	496 (30.8)	
Year of diagnosis							
Before 2010	493 (50.6)	99 (41.8)	92 (59.7)	62 (48.4)	63 (53.8)	809 (50.2)	0.01
2010 onward	481 (49.4)	138 (58.2)	62 (40.3)	66 (51.6)	54 (46.2)	801 (49.8)	
Overall survival length, mo, mean ± SD							
Intrahepatic cholangiocarcinoma	12.7 ± 19.4	10.7 ± 18.9	11.1 ± 12.2	11.6 ± 17.4	10.3 ± 13.4	12.0 ± 18.2	0.7
Extrahepatic cholangiocarcinoma	23.0 ± 33.3	20.4 ± 29.8	22.7 ± 38.6	21.0 ± 30.2	20.6 ± 31.8	22.2 ± 32.9	
Gallbladder cancer	25.6 ± 41.6	18.6 ± 33.3	22.2 ± 31.6	14.0 ± 22.8	26.5 ± 45.4	23.3 ± 38.6	
Ampullary cancer	35.5 ± 36.3	33.5 ± 39.3	40.0 ± 47.4	44.9 ± 53.3	22.2 ± 22.5	35.1 ± 38.8	
Neighbourhood education level (no. [%] with high school or above)							
< 75	386 (39.6)	82 (34.6)	53 (34.4)	52 (40.6)	51 (43.6)	624 (38.8)	0.2
75–85	261 (26.8)	78 (32.9)	49 (31.8)	40 (31.2)	40 (34.2)	468 (29.1)	
> 85	327 (33.6)	77 (32.5)	52 (33.8)	36 (28.1)	26 (22.2)	518 (32.2)	
Neighbourhood income level (average annual income, $)							
< 35 000	341 (35.0)	69 (29.1)	49 (31.8)	51 (39.8)	48 (41.0)	558 (34.7)	0.2
35 000–50 000	360 (37.0)	98 (41.4)	57 (37.0)	49 (38.3)	46 (39.3)	610 (37.9)	
> 50 000	273 (28.0)	70 (29.5)	48 (31.2)	28 (21.9)	23 (19.7)	442 (27.4)	
Average annual incidence per 100 000 (95% CI)							
Intrahepatic cholangiocarcinoma	0.58 (0.30–0.89)	0.14 (0–0.30)	0.09 (0–0.18)	0.05 (0–0.11)	0.07 (0–0.18)	0.93 (0.56–1.30)	
Extrahepatic cholangiocarcinoma	0.58 (0.30–0.89)	0.14 (0–0.30)	0.1 (0–0.24)	0.09 (0–0.24)	0.08 (0–0.18)	1.27 (0.84–1.70)	
Gallbladder cancer	0.79 (0.45–1.12)	0.17 (0.02–0.35)	0.14 (0–0.30)	0.1 (0–0.24)	0.07 (0–0.18)	0.98 (0.61–1.35)	
Ampullary cancer	0.32 (0.09–0.51)	0.09 (0–0.24)	0.05 (0–0.11)	0.06 (0–0.18)	0.06 (0–0.18)	0.58 (0.29–0.87)	

Note: CI = confidence interval, SD = standard deviation.
*Except where noted otherwise.

Table 3: Univariate and multivariate analyses of factors associated with overall survival in patients with biliary cancer, including driving time to the nearest hepatopancreatobiliary surgical centre as a covariate

	HR* (95% CI)	
Risk factor	Univariate analysis	Multivariate analysis
Sex (male v. female)	1.03 (0.97–1.08)	1.1 (1.04–1.17)
Age (per 1-yr increase)	1.01 (1.01–1.02)	1.01 (1.01–1.01)
Chemotherapy (yes v. no)	0.75 (0.70–0.80)	0.65 (0.60–0.70)
Surgery (yes v. no)	0.34 (0.31–0.36)	0.40 (0.37–0.44)
Tumour type		
Ampullary cancer (reference)	1.0	1.0
Intrahepatic cholangiocarcinoma	2.61 (2.38–2.87)	2.06 (1.86–2.28)
Extrahepatic cholangiocarcinoma	1.67 (1.52–1.84)	1.71 (1.55–1.89)
Gallbladder cancer	1.72 (1.57–1.88)	1.45 (1.32–1.59)
No. of biliary drains (per 1-drain increase)	1.0 (0.99–1.02)	0.97 (0.95–0.98)
Stage IV (v. stages I–III)	3.32 (3.13–3.53)	2.47 (2.30–2.66)
Charlson Comorbidity Index score (per 1-point increase)	1.1 (1.09–1.11)	1.09 (1.08–1.10)
Diagnosis in 2010 onward (v. before 2010)	1.02 (0.96–1.07)	0.84 (0.79–0.89)
Driving time to nearest hepatopancreatobiliary surgeon ≥ 120 min (v. < 120 min)	1.06 (0.99–1.15)	1.27 (1.17–1.37)
Neighbourhood education level (% with high school or above)		
< 75 (reference)	1.0	1.0
75–85	0.92 (0.87–0.99)	0.93 (0.86–1.00)
> 85	0.97 (0.91–1.04)	0.96 (0.88–1.05)
Neighbourhood income level (average annual income, $)		
< 35 000 (reference)	1.0	1.0
35 000–50 000	0.96 (0.90–1.03)	1.03 (0.96–1.10)
> 50 000	1.02 (0.95–1.09)	1.09 (0.99–1.19)

Note: HR = hazard ratio.
*Represents the ratio of the death rates between the compared 2 groups of the independent variable (if the variable is binary) or the logarithm of the change in death rate per unit change of the independent variable (if the variable is continuous).

gallbladder cancer and ampullary cancer who had surgery remained stable, whereas the proportion of patients with intrahepatic cholangiocarcinoma who underwent resection increased, from 18.8% before 2010 to 36.6% from 2010 onward (p = 0.001). Chemotherapy was administered to more patients from 2010 onward than before 2010 for extrahepatic cholangiocarcinoma (39.7% v. 16.0%, p < 0.001), gallbladder cancer (35.7% v. 13.2%, p < 0.001) and ampullary cancer (18.4% v. 8.0%, p = 0.002) but not intrahepatic cholangiocarcinoma (25.0% v. 24.8%, p = 0.4).

We evaluated secondary outcomes as a function of driving time to tertiary and quaternary care centres (Table 4 and Supplementary Table S3, Appendix 1). The proportion of patients with stage IV disease (a surrogate for delayed diagnosis) was not affected by driving time (odds ratio [OR] 0.86,

95% CI 0.63–1.19). Proximity to specialty care did affect treatments delivered: patients living 120 minutes or more from the nearest cancer centre were less likely than those living less than 120 minutes away to receive chemotherapy (OR 0.51, 95% CI 0.29–0.88). The likelihood of having surgery and receiving only best supportive care were unrelated to residence.

Because survival could be affected by timely access to gastroenterology or interventional radiology if a complication such as biliary sepsis occurred, we tracked the number of biliary drainage procedures. A total of 2027 drains were inserted in 861 patients. There was no difference in the average number of biliary drainage procedures per person between patients who lived less than 120 minutes away and those who lived 120 or more minutes away (1.3 v. 1.2 drains per person,
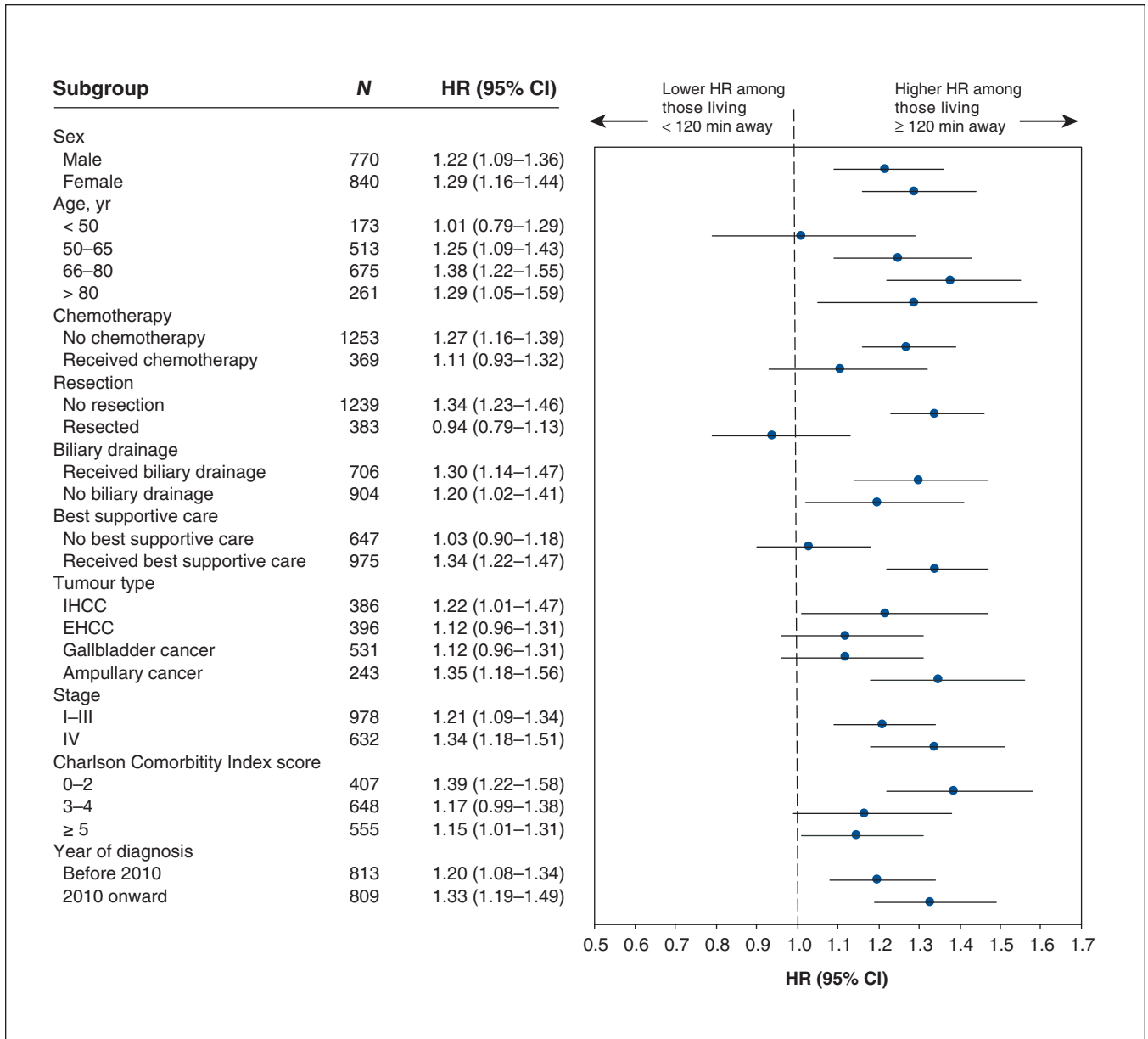
Subgroup	N	HR (95% CI)
Sex		
Male	770	1.22 (1.09–1.36)
Female	840	1.29 (1.16–1.44)
Age, yr		
< 50	173	1.01 (0.79–1.29)
50–65	513	1.25 (1.09–1.43)
66–80	675	1.38 (1.22–1.55)
> 80	261	1.29 (1.05–1.59)
Chemotherapy		
No chemotherapy	1253	1.27 (1.16–1.39)
Received chemotherapy	369	1.11 (0.93–1.32)
Resection		
No resection	1239	1.34 (1.23–1.46)
Resected	383	0.94 (0.79–1.13)
Biliary drainage		
Received biliary drainage	706	1.30 (1.14–1.47)
No biliary drainage	904	1.20 (1.02–1.41)
Best supportive care		
No best supportive care	647	1.03 (0.90–1.18)
Received best supportive care	975	1.34 (1.22–1.47)
Tumour type		
IHCC	386	1.22 (1.01–1.47)
EHCC	396	1.12 (0.96–1.31)
Gallbladder cancer	531	1.12 (0.96–1.31)
Ampullary cancer	243	1.35 (1.18–1.56)
Stage		
I–III	978	1.21 (1.09–1.34)
IV	632	1.34 (1.18–1.51)
Charlson Comorbitity Index score		
0–2	407	1.39 (1.22–1.58)
3–4	648	1.17 (0.99–1.38)
≥ 5	555	1.15 (1.01–1.31)
Year of diagnosis		
Before 2010	813	1.20 (1.08–1.34)
2010 onward	809	1.33 (1.19–1.49)

Figure 2: Forest plot depicting the effect of driving time to the nearest hepatopancreatobiliary surgical centre on survival in various subgroups. A hazard ratio (HR) less than 1.0 indicates increased survival. Note: CI = confidence interval, EHCC = extrahepatic cholangiocarcinoma, IHCC = intrahepatic cholangiocarcinoma.

$p = 0.6$) or in the proportion who had 2 or more drainage procedures (56.0% v. 55.8%, $p = 0.7$). Unexpectedly, in the final 8 weeks of life, the probability of having a biliary drainage procedure was slightly higher among patients who lived 120 minutes or more (v. < 120 min) away (19.8% v. 15.7%, $p = 0.08$, adjusted for age, sex, stage, tumour type, comorbidities, income and education level).

Physician visits and patterns of care as a function of residence

The 1610 patients had 117 381 physician encounters. The highest concentration of visits occurred in the final 8 weeks of life (Supplementary Figure S1, A, Appendix 1). The number of visits to physicians was not significantly different during any of the time intervals between patients who lived less than 120 minutes from the nearest hepatopancreatobiliary surgeon and those who lived 120 or more minutes away. However, in the period following diagnosis, there was a higher frequency of emergency department visits among patients who lived 120 minutes or more from the nearest hepatopancreatobiliary surgeon than among those who lived less than 120 minutes away (0.86 v. 0.15 visits/person per 4 wk, $p < 0.001$). This was particularly prominent among patients treated with chemotherapy and those who received best supportive care (Supplementary Figure S1, B, Appendix 1).

Table 4: Multivariate analysis of association between driving time to the nearest hepatopancreatobiliary surgical centre and secondary outcomes (stage IV disease, chemotherapy, surgery and biliary drainage)

Risk factor	Outcome; OR (95% CI)			
	Stage IV disease	Chemotherapy	Surgery	Biliary drainage*
Sex (male v. female)	0.76 (0.61–0.96)	1.19 (0.91–1.55)	1.16 (0.88–1.52)	0.81 (0.62–1.05)
Age (per 1-yr increase)	0.99 (0.99–1.01)	0.95 (0.94–0.96)	0.98 (0.97–0.99)	1.02 (1.01–1.03)
Tumour type				
Ampullary cancer (reference)	1.0	1.0	1.0	1.0
Intrahepatic cholangiocarcinoma	0.23 (0.14–0.36)	2.22 (1.45–3.40)	0.99 (0.674–1.44)	0.35 (0.24–0.52)
Extrahepatic cholangiocarcinoma	3.28 (2.47–4.36)	2.47 (1.71–3.56)	1.14 (0.76–1.71)	0.91 (0.64–1.30)
Gallbladder cancer	1.01 (0.76–1.34)	2.51 (1.73–3.62)	3.26 (2.32–4.57)	0.16 (0.11–0.23)
Stage IV (v. stages I–III)	–	1.11 (0.84–1.48)	0.04 (0.03–0.07)	0.86 (0.65–1.15)
Charlson Comorbidity Index score (per 1-point increase)	1.09 (1.05–1.13)	0.96 (0.92–1.01)	1.0 (0.95–1.05)	0.89 (0.85–0.93)
Diagnosis in 2010 onward (v. before 2010)	1.68 (1.34–2.11)	2.66 (2.03–3.49)	1.66 (1.26–2.18)	1.13 (0.87–1.45)
Driving time to nearest hepatopancreatobiliary surgeon ≥ 120 min (v. < 120 min)	0.86 (0.63–1.19)	0.75 (0.52–1.09)	1.07 (0.97–1.19)	0.84 (0.60–1.20)
Neighbourhood education level (% with high school or above)				
< 75 (reference)	1.0	1.0	1.0	1.0
75–85	1.17 (0.83–1.65)	1.28 (0.90–1.82)	1.01 (0.75–1.36)	0.80 (0.57–1.14)
> 85	1.10 (0.72–1.68)	1.32 (0.86–2.05)	1.06 (0.73–1.52)	0.82 (0.55–1.22)
Neighbourhood income level (average annual income, $)				
< 35 000 (reference)	1.0	1.0	1.0	1.0
35 000–50 000	0.87 (0.61–1.23)	0.89 (0.62–1.28)	1.10 (0.81–1.49)	1.12 (0.80–1.57)
> 50 000	0.80 (0.54–1.19)	0.92 (0.62–1.38)	1.13 (0.81–1.60)	1.31 (0.85–2.01)
Model diagnostics	n = 1610	n = 1610	n = 1610	n = 975
	C-statistic = 0.736	C-statistic = 0.754	C-statistic = 0.809	C-statistic = 0.714

Note: CI = confidence interval, OR = odds ratio.
*Modelling likelihood of biliary drainage among patients who received best supportive care.

Interpretation

In this comprehensive exploration of the association of proximity to specialty care and survival, treatment and use of health care services among patients with biliary cancer, our population-based, detailed data set provides insight on patient experiences and the effects of accessibility to care, with patients living far from hepatopancreatobiliary surgical centres and cancer centres generally having worse survival. Given the complexity of managing patients with biliary malignant disease, this is not surprising. Unexpected was the subgroup most affected: the deleterious effects of living remotely were particularly pronounced among patients who required biliary drainage and received best supportive care. This subgroup is particularly susceptible to biliary sepsis, which can lead to precipitous clinical deterioration in the absence of timely management.

The effects of proximity to specialist care are complex and are influenced by the health care system, socioeconomic factors and the disease process. In the United States, some studies have shown that patients travelling to high-volume cancer centres had improved survival compared to those who chose closer, lower-volume care facilities.[12–15] In those studies, where there was variable access owing to differences in health care insurance, improved survival may have been subject to "travel"[16] or "referral"[17] bias. That is, patients travelling farther to seek care were more capable of receiving complex treatments. In contrast, a United Kingdom study showed worse survival among patients with cancer who had greater travel burden.[18] Patients who underwent surgery for extrahepatic cholangiocarcinoma at one high-volume US institution had worse outcomes when they travelled large distances.[19] Our data, derived from a publicly funded health care system, would be expected to remove the effects of health insurance disparities on treatment choices,[20,21] but although the effects of socioeconomic factors (education and income levels)[22,23] may be smoothed out, they are not completely eliminated.

The trend toward centralization of surgical management of patients with cancer who require advanced and sophisticated

treatments[24,25] appears most apparent for those who need continuous management of complications of malignant disease, such as those with biliary cancer. Similarly, delivering chemotherapy to these patients requires a high level of expertise and support to manage complications. Centralization challenges the delivery of timely and appropriate care for rural patients.

Limitations

First, biliary cancers are rare, and therefore the study population was small despite the fact that the study was longitudinal and population-based. Second, Alberta has a relatively low population:area ratio relative to other provinces in Canada, and therefore the absolute number of patients who live remotely is small. The effects that we observed may be exacerbated in larger provinces, where the distances to advanced care centres are greater. Third, the findings stem from a constituency with universal health care, so the effects of geography may differ in constituencies with variability in health care insurance. Fourth, given the retrospective nature of the study and data availability, we were not able to address all the potential factors that affect survival. In interpreting our findings, one should also consider limits in the validity of administrative data. Fifth, previous publications did not provide any a priori information on the effects of driving time. We acknowledge that different categorizations may lead to different results. For this reason, we analyzed driving time as a continuous variable in the model. The results showed that every 1-minute increment of driving time was associated with worse survival. Thus, the driving time categories we selected would not change the conclusion and served as a meaningful way of conveying the results. Finally, we did not explore the effects of ethnicity on the studied outcomes because data are not reliably available. For example, Indigenous Peoples may be disproportionately affected by health care disparities.

Conclusion

In this cohort, geography and accessibility to specialty care affected survival in patients with biliary cancer. Further study is required to understand how patients with biliary drains who receive best supportive care are affected by proximity to specialty care. This will aid in the identification of strategies to provide improved care for this subgroup who are particularly affected.

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