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ORIGINAL ARTICLE

Association Between Travel Distance, Hospital Volume, and Outcomes Following Resection of Cholangiocarcinoma

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Abstract

Background The objective of the current study was to characterize the association between travel distance/hospital volume relative to outcomes following resection of cholangiocarcinoma.

Methods Patients were identified using the 2004–2015 National Cancer Database and stratified into quartiles according to travel distance/hospital volume. Multivariable regression models were utilized to examine the impact of travel distance and hospital volume on quality-of-care metrics and overall survival.

Results Among 5125 patients, the majority of patients had T1/2 ($N = 2006$, 41.1%) and N0 disease ($N = 2498$, 50.9%). Median hospital quartile surgical volumes in cases/year were low volume (LV) 6, intermediate low volume (ILV) 7, intermediate high volume (IHV) 12, and high volume (HV) 24 cases/year. Median travel distance quartiles in miles were short travel (ST) 2.7, intermediate short travel (IST) 7.9, intermediate long travel (ILT) 18.9, and long travel (LT) 84.7. Longer travel distances were associated with better overall survival, as every 10 miles was associated with a 2% decrease in mortality ($p = 0.02$). Differences in quality-of-care metrics were largely mediated through travel distance.

Conclusions Travel distance and hospital volume were associated with certain quality-of-care metrics among patients with cholangiocarcinoma. After controlling for hospital volume and travel distance simultaneously, only travel distance was associated with decreased risk of mortality.

Keywords Travel distance · Hospital volume

Introduction

Cholangiocarcinoma is a rare epithelial cell malignancy that arises from various locations within the biliary tree and is often categorized as intrahepatic, perihilar, and distal.[1] Surgical treatment—including resection and transplantation—is the only curative option for cholangiocarcinoma.[2,3] The majority of patients present with advanced and unresectable disease and 5-year survival even after curative-intent resection or transplantation is low.[3] Achievement of optimal patient outcomes requires involvement of a multi-disciplinary team including surgical, medical, and radiation oncologists, as well as interventional radiologists and advanced gastroenterology services.[4]

Previous studies have demonstrated an association between hospital and surgeon volume with outcomes among patients undergoing complex abdominal surgeries such as pancreaticoduodenectomy and liver resection.[5–12] In particular, high-volume hospitals/surgeons generally have lower morbidity, mortality, length of stay, and hospital costs compared with low-volume hospitals/surgeons.[5–12] Many patients, however, may need to travel long distances to receive care from high-volume hospitals/surgeons. In turn, travel distance may confer excess mortality risk among patients undergoing major abdominal surgeries.[13] Some data have suggested that increased travel distance may be associated with reduced overall survival, while other studies have demonstrated that, despite an increased travel burden, patients treated at high-volume centers have improved perioperative outcomes, short-term mortality, and overall survival.[14] For example, a recent study of patients undergoing cystectomy for invasive

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bladder cancer noted that the association between longer travel distance and improved overall survival was mainly mediated by hospital volume.[15] As such, whether the benefits of undergoing surgery at a high-volume hospital outweigh the disadvantages of longer travel distance remain poorly defined.

The impact of travel distance and hospital volume among patients undergoing resection for cholangiocarcinoma has not been examined. Therefore, the objective of the current study was to characterize the association between travel distance and hospital volume relative to short- and long-term outcomes following resection of cholangiocarcinoma.

Methods

Data Source

The National Cancer Database (NCDB) is a quality improvement initiative jointly administrated by the American College of Surgeons Commission on Cancer and the American Cancer Society. The available participant user file (PUF) contains data from 2004 to 2015 on patients who received at least a portion of their care at a site accredited by the Commission on Cancer. These programs represent 30% of US hospitals and approximately 70% of patients with newly diagnosed cancer.[16] The NCDB includes data on sociodemographic information, Charlson-Deyo comorbidity score, cancer diagnosis, disease stage, treatment details, and survival. Specific to surgical patients, the NCDB captures a wide array of surgical procedures, as well as information on length of stay, readmission to the index hospital, death within 30 and 90 days of surgery, and long-term survival.[17] For purposes of the current analysis, patients were included in the analytic cohort who had a histologic diagnosis of cholangiocarcinoma (histology = 8160) with primary site of liver or bile duct (Fig. 1). Patients with metastatic disease were excluded.

Analytic Variables

Data were obtained on age, race, Charlson-Deyo comorbidity score, insurance status, patient area of residence (metropolitan vs. urban vs. rural), median income (median household income in each area of residence), education level (number of adults in the area of residence who did not graduate from high school), cT stage, cN stage, pT stage, pN stage, and adjuvant chemotherapy. The exposures of interest were travel distance and hospital volume among patients undergoing resection of cholangiocarcinoma. All patients with cholangiocarcinoma diagnosed (histology = 8160) between 2004 and 2015 at the reporting Commission on Cancer (CoC) facility were included. The complete cohort of patients with cholangiocarcinoma was used to calculate hospital volume. Annual hospital surgical volume for cholangiocarcinoma was calculated and assigned to each individual patient as a continuous variable, as described previously.[15] Travel distance was defined as "great circle" distance in miles between the patient's residence and the hospital, calculated using zip codes and the Haversine formula in the NCDB.[17] Quartiles for travel distance and hospital volume were determined.

The primary outcome of this study was overall survival. Overall survival was calculated as the time from the date of diagnosis to the date of last follow-up or death from any cause. Secondary outcomes included receipt of preoperative and postoperative chemotherapy, lymph node yield ≥ 6 lymph nodes, surgical delay greater than 3 months, and positive surgical margin. Surgical delay was considered to be surgery occurring greater than 90 days from the date of diagnosis.

The primary independent variables were travel distance and hospital volume considered as continuous and categorical

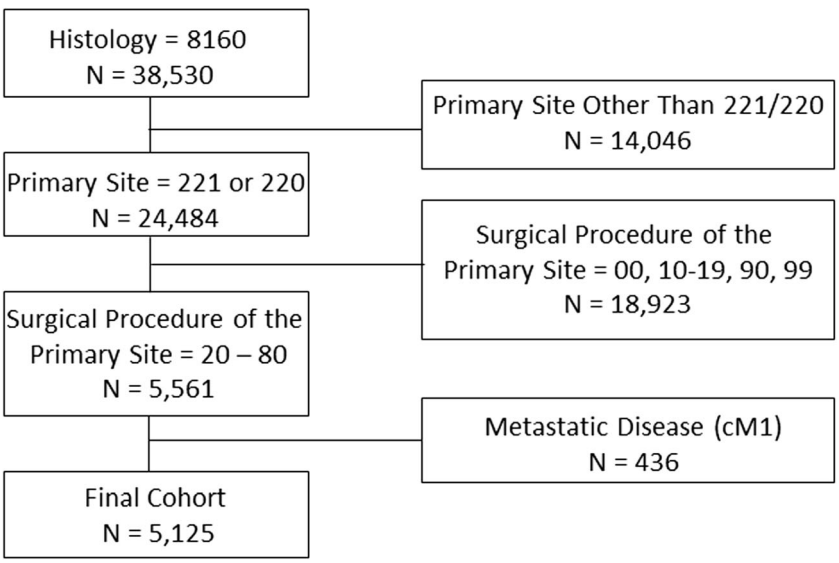

Fig. 1 STROBE compliant diagram demonstrating inclusion and exclusion criteria

data (i.e., quartiles). Travel distance was divided into first quartile/short travel (ST), second quartile/intermediate short travel (IST), third quartile/intermediate long travel (ILT), and fourth quartile/long travel (LT). Hospital volume was divided into first quartile/low volume (LV), second quartile/intermediate low volume (ILV), third quartile/intermediate high volume (IHV), and fourth quartile/high volume (HV).

Statistical Analysis

Descriptive statistics were calculated for the overall cohort and for each quartile of travel distance and reported as frequencies and proportions for categorical variables and medians and interquartile ranges (IQRs) for continuous variables. Associations between travel distance quartiles with demographics and clinical variables were compared using chi-square tests and Kruskal-Wallis one-way analysis of variance for categorical and continuous variables, respectively. Where appropriate, Fisher's exact tests were used. To assess the association between travel distance and hospital volume relative to secondary outcomes, multivariable logistic regression models were constructed and evaluated. Additionally, multivariable Cox proportional-hazard models were utilized to assess the association between travel distance and hospital volume relative to overall survival controlling for relevant covariates.

Survival analyses were performed using three different multivariable models to assess possible associations of hospital volume, travel distance, and outcomes. The first and second models evaluated the independent effect of travel distance alone and hospital volume alone; in contrast, the third multivariable model assessed the impact of travel distance combined with hospital volume. This analytic approach has been used in previous studies to examine the relative contributions of travel distance and hospital volume on overall survival for other surgical procedures.[10,15,18] Statistical significance was assessed at $p = 0.05$. All analyses were performed using SAS v9.4 (Cary, North Carolina).

Results

Study Cohort

A total of 5125 patients with a histologic diagnosis of cholangiocarcinoma with the primary site of liver or bile duct met final inclusion/exclusion criteria. Hospital volume, travel distance, patient demographic, and clinical characteristics are summarized in Table 1. Median (IQR) age was 66 (58–73); the majority of patients was male ($N = 2799$, 54.6%) and Caucasian ($N = 4402$, 85.9%). Most patients had a Charlson-Deyo Score of 0 ($N = 3626$, 70.8%). Insurance status was largely Medicare ($N = 2438$, 49.1%) or private insurance ($N = 2062$, 41.5%). The vast majority of patients lived in metropolitan areas ($N = 4116$, 83.5%) and most patients had an income ≥ $48 k ($N = 3170$, 62.9%) per year. The majority of patients with available preoperative staging data were clinical stage T1 or 2 ($N = 2006$, 41.1%) and had clinical N0 disease ($N = 2498$, 50.9%). A minority of patients received preoperative chemotherapy ($N = 1780$, 35.5%). Additionally, the median number of lymph nodes retrieved was 0 (IQR 0–1) and only a small minority of patients has six or more lymph nodes resected ($N = 132$, 2.6%).

Among all hospitals, median (IQR) hospital cholangiocarcinoma surgical volume and travel distance were nine[4–22] cases per year and 19.9 (7.9–60.2) miles, respectively. Hospital quartile median surgical volumes were first quartile/LV 6 cases/year, second quartile/ILV 7 cases/year, third quartile/IHV 12 cases/year, and fourth quartile/HV 24 cases/year. Travel distance median quartiles were first quartile/ST 2.7 miles, second quartile/IT 7.9 miles, third quartile/ILT 18.9 miles, and fourth quartile/LT 84.7 miles. There was an increase in hospital volume with increasing travel distance (Table 1 and Fig 2; $p = 0.006$).

Impact of Hospital Volume and Travel Distance on Quality-Of-Care Indicators and Overall Survival

Multivariable logistic regression models assessing the association between hospital volume, travel distance, and quality-of-care indicators are summarized in Tables 2 and 3. When only hospital volume or travel distance was included in the model, both variables were associated with higher odds of certain quality-of-care indicators. Specifically, patients treated at ILV (OR 0.61, 95% CI 0.48, 0.78), IHV (OR 0.72, 95% CI 0.57–0.91), and HV (OR 0.63, 95% CI 0.51–0.79) hospitals were less likely to have a surgical delay compared with LV hospitals (all $p < 0.001$; Table 2). Travel distance also had an effect on quality-of-care metrics (Table 3). In particular, patients who underwent resection at IST (OR 0.80, 95% CI 0.65–0.99), ILT (OR 0.58, 95% CI 0.46–0.72), or LT (OR 0.33, 95% CI 0.26–0.43) (all $p < 0.05$) hospitals were less likely to have undergone preoperative therapy vs. patients at ST hospitals. However, these patients were more likely to have undergone postoperative chemotherapy (IST OR 1.24, 95% CI 1.06–1.52; ILT OR 1.74, 95% CI 1.39–2.17; LT OR 3.00, 95% CI 2.32–3.88, all $p < 0.05$). Additionally, patients in the longest travel distance quartile (LT) were more likely to have had a surgical delay greater than 3 months (OR 1.78, 95% CI 1.41–2.25), but were less likely to have a positive surgical margin (OR 0.68, 95% CI 0.54–0.86) vs. patients at ST hospitals. Of note, in the model that contained both hospital volume and travel distance as covariates, differences in quality-of-care metrics were largely mediated through travel distance rather than by hospital volume (Table 4).

Table 1 Hospital volume, travel distance, patient demographics, and clinical characteristics of overall cohort stratified by travel distance

Variables	Overall ($N = 5125$)	First quartile (ST) ($N = 1337$)	Second quartile (IST) ($N = 1270$)	Third quartile (ILT) ($N = 1256$)	Fourth quartile (LT) ($N = 1262$)	*P* value
Travel distance, miles, median (IQR)	19.9 (7.9–60.2)	2.7 (1.7–3.9)	7.9 (6.4–10.0)	18.9 (15.5–26.2)	84.7 (54.2–152.8)	–
Hospital volume per case, median (IQR)	9 (4–22)	6 (3–11)	7 (4–15)	12 (5–25)	24 (8–42)	*< 0.001*
Age (median (IQR))	66 (58–73)	66 (58–73)	67 (58–74)	66 (57–73)	65 (57–72)	*0.003*
Sex—male	2799 (54.6%)	723 (54.1%)	670 (52.8%)	701 (55.8%)	705 (55.9%)	*0.025*
Race						*< 0.001*
White	4402 (85.9%)	1061 (79.4%)	1073 (84.5%)	1124 (89.5%)	1144 (90.6%)	
Black	340 (6.6%)	143 (10.7%)	79 (6.2%)	60 (4.8%)	58 (4.6%)	
Other	383 (7.5%)	133 (9.9%)	118 (9.3%)	72 (5.7%)	60 (4.8%)	
Charlson-Deyo Score						*< 0.001*
0	3626 (70.8%)	960 (71.8%)	876 (69.0%)	871 (69.3%)	919 (72.8%)	
1	1065 (20.8%)	271 (20.3%)	295 (23.2%)	265 (21.1%)	234 (18.5%)	
≥2	434 (8.5%)	75 (5.6%)	62 (4.9%)	82 (6.5%)	62 (4.9%)	
Insurance status						0.080
Private	2062 (41.5%)	520 (39.7%)	551 (44.2%)	506 (41.0%)	485 (41.3%)	
Medicare	2438 (49.1%)	647 (49.4%)	591 (47.4%)	605 (49.0%)	595 (50.6%)	
Medicaid and other government	338 (6.8%)	107 (8.2%)	71 (5.7%)	95 (7.7%)	65 (5.5%)	
Not insured	128 (2.6%)	37 (2.8%)	33 (2.6%)	28 (2.3%)	30 (2.6%)	
Residence area						*< 0.001*[a]
Metropolitan	4116 (83.5%)	1210 (98.3%)	1186 (95.6%)	954 (78.1%)	766 (62.1%)	
Urban	720 (14.6%)	21 (1.7%)	53 (4.3%)	249 (20.4%)	397 (32.2%)	
Rural	92 (1.9%)	0 (0.0%)	2 (0.2%)	19 (1.6%)	71 (5.8%)	
Median income[b]						*< 0.001*
< $38,000	747 (14.8%)	242 (19.2%)	85 (6.7%)	151 (12%)	269 (21.3%)	
$38,000–$47,0000	1125 (22.3%)	243 (19.3%)	190 (15%)	285 (22.7%)	407 (32.3%)	
$48,000–$62,999	1360 (27.0%)	309 (24.5%)	376 (29.6%)	341 (27.2%)	334 (26.5%)	
≥63,000	1810 (35.9%)	465 (36.9%)	618 (48.7%)	477 (38%)	250 (19.8%)	
Education level[c]						*< 0.001*
≥21%	781 (15.5%)	283 (22.5%)	155 (12.2%)	158 (12.6%)	185 (14.7%)	
13–20%	1200 (23.8%)	261 (20.7%)	238 (18.8%)	320 (25.5%)	381 (30.2%)	
7–12.9%	1658 (32.9%)	330 (26.2%)	438 (34.5%)	483 (38.5%)	407 (32.3%)	
< 7%	1407 (27.9%)	385 (30.6%)	438 (34.5%)	295 (23.5%)	289 (22.9%)	
cT stage						0.213
cT0	12 (0.25%)	3 (0.3%)	1 (0.1%)	5 (0.4%)	3 (0.2%)	
cT1	1181 (24.2%)	321 (27.4%)	269 (24.3%)	281 (25.6%)	310 (28.8%)	
cT2	825 (16.9%)	105 (8.9%)	97(8.7%)	103 (9.3%)	90 (8.3%)	
cT3	627 (12.8%)	140 (11.9%)	158 (14.3%)	160 (14.5%)	169 (15.7%)	
cT4	148 (3.0%)	43 (3.6%)	38 (3.4%)	32 (2.9%)	35 (3.2%)	
cTX	2086 (42.7%)	559 (47.7%)	542 (49.0%)	516 (47.0%)	469 (43.5%)	
cN stage						0.106
cN0	2498 (50.9%)	647 (50.6%)	631 (51.7%)	635 (52.5%)	585 (48.7%)	
≥cN1	423 (8.6%)	90 (7.0%)	110 (9.1%)	110 (9.1%)	113 (9.4%)	
cNx	1987 (40.4%)	541 (42.3%)	479 (39.2%)	464 (38.3%)	503 (41.8%)	
pT stage						0.401
pT0	20 (0.4%)	3 (0.2%)	4 (0.3%)	8 (0.3%)	5 (0.5%)	
pT1	1129 (22.7%)	281 (26.0%)	276 (27.2%)	270 (27.1%)	302 (29.9%)	
pT2	1546 (31.2%)	281 (26.0%)	276 (27.2%)	270 (27.1%)	302 (29.9%)	

Table 1 (continued)

Variables	Overall ($N = 5125$)	First quartile (ST) ($N = 1337$)	Second quartile (IST) ($N = 1270$)	Third quartile (ILT) ($N = 1256$)	Fourth quartile (LT) ($N = 1262$)	*P* value
pT3	1424 (28.7%)	364 (33.8%)	344 (33.9%)	358 (35.9%)	358 (35.4%)	
pT4	272 (5.4%)	73 (6.7%)	77 (7.6%)	68 (6.8%)	54 (5.3%)	
pTx	563 (11.3%)	165 (15.3%)	135(13.3%)	134 (13.4%)	129 (12.7%)	
pN stage						*0.007*
pN0	1831 (37.6%)	443 (35.4%)	448 (36.9%)	499 (37.7%)	491 (40.6%)	
≥pN1	1068 (21.9%)	245(19.6%)	281 (23.1%)	262 (22.0%)	267 (22.1%)	
pNx	1974 (40.5%)	561 (44.9%)	484 (39.9%)	479 (40.2%)	450 (37.2%)	
Preoperative chemo	1780 (35.5%)	359 (27.4%)	310 (25.0%)	245 (20.0%)	163 (13.1%)	*< 0.001*
LNY (median (IQR))	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	0 (0–1)	*0.002*
LNY ≥ 6	132 (2.6%)	33 (3.7%)	25 (2.8%)	31 (3.5%)	41 (4.5%)	0.329
PSM	1290 (25.1%)	359 (26.8%)	336 (26.4%)	347 (27.6%)	248 (19.6%)	*< 0.001*
Postoperative chemo	3228 (64.5%)	947 (72.5%)	929 (47.9%)	979 (79.9%)	1073 (86.8%)	*< 0.001*
Surgical delay (> 3 months)	1132 (22.0%)	260 (19.4%)	246(19.3%)	269 (21.4%)	357 (28.2%)	*< 0.001*
Radiation	1280 (24.9%)	259 (29.9%)	284 (27.5%)	368 (26.4%)	369 (20.1%)	*< 0.001*

Values in italics are statistically significant ($p < 0.05$)

IQR interquartile range, LNY lymph node yield, PSM positive surgical margin, ST short travel, IST intermediate short travel, ILT intermediate long travel, LT long travel, cT clinical T stage, cN clinical N stage, pT pathological T stage, pN pathological N stage

[a] Indicates Fischer exact test

[b] Median household income in patient's area of residence

[c] Number of adults in patient's area of residence who did not graduate from high school

When only travel distance or hospital volume was included in the model (Table 5), only the fourth quartile of travel distance was associated with improved overall survival (OR 0.87, 95% CI 0.77–0.98). In particular, when assessed as a continuous measure, longer travel distances were associated with better overall survival, as every 10 miles distance traveled was associated with a 2% decrease in mortality ($p = 0.02$).

Discussion

Some patients may choose to travel longer distances to seek care at major centers that have a higher surgical volume. In addition, as regionalization of care increases, more patients may be forced to travel longer distances to obtain specialized surgical care. Traveling longer distances to obtain care may,

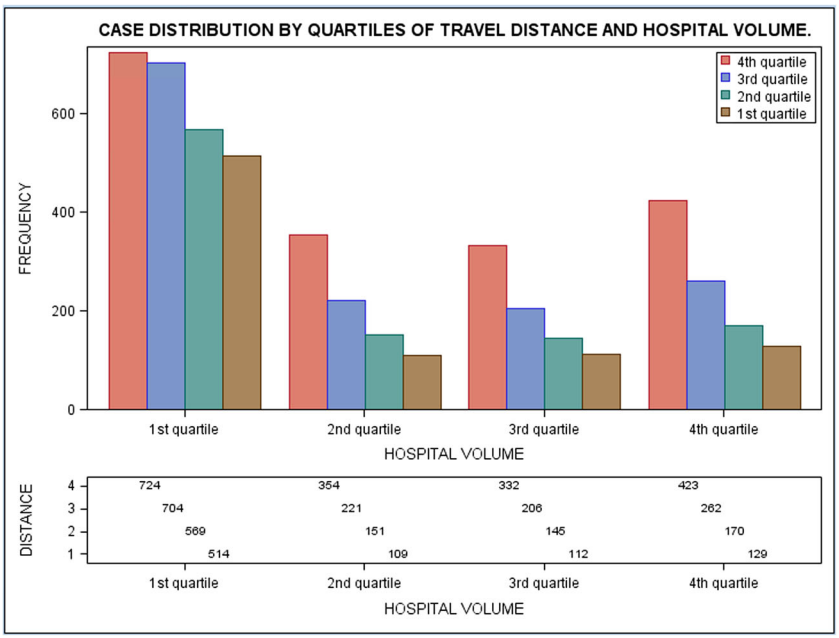

Fig. 2 Case distribution by quartiles of travel distance and hospital volume

Table 2 Multivariable logistic regression for receipt of neoadjuvant chemotherapy and adjuvant chemotherapy, surgical delay, and positive surgical margin including hospital volume in comparison to low volume

Variable	Hospital volume—continuous (number of case)		Hospital volume—categorical					
			ILV		IHV		HV	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Preoperative chemo	*0.99 (0.98–0.99)*	*0.004*	0.91 (0.72–1.14)	0.39	0.99 (0.79–1.23)	0.93	0.89 (0.73–1.10)	0.29
Postoperative chemo	*1.07 (1.03–1.12)*	*0.004*	1.10 (0.88–1.38)	0.39	1.01 (0.81–1.26)	0.93	1.12 (0.91–1.38)	0.29
Surgical delay	*0.99 (0.99–0.99)*	*0.003*	*0.61 (0.48–0.78)*	*<0.001*	*0.72 (0.57–0.91)*	*0.006*	*0.63 (0.51–0.79)*	*<0.001*
Positive margins	1.00 (0.99–1.01)	0.39	*1.45 (1.18–1.77)*	*<0.001*	1.21 (0.98–1.49)	0.07	1.12 (0.92–1.36)	0.28

Analysis adjusted for age, sex, race, Charlson-Deyo score, insurance status, patient residence area (metropolitan vs. urban vs. rural), median income, education level, cT stage, and cN stage. The values in italics are statistically significant (*p*-values less than 0.05)

OR odds ratio, CI confidence interval, ILV intermediate low volume, IHV intermediate low volume, HV high volume

however, present additional economic and social burdens to patients. Therefore, understanding the potential impact of travel distance on patient outcomes may have important implications. To this point, cholangiocarcinoma is a relatively rare disease that often requires expert care by multi-disciplinary teams at centers of excellence. Patients with cholangiocarcinoma may, therefore, be particularly affected by the need or desire to travel in order to seek appropriate expert care. As such, in the current study, we examined the association between travel distance, hospital volume, and outcomes among patients undergoing resection of cholangiocarcinoma. Hospital volume and travel distance were each associated with several quality-of-care metrics. For example, hospital volume was associated with decreased risk of surgical delay, while increasing travel distance was associated with decreased mortality, decreased receipt of preoperative therapy, yet increased surgical delay. Of note, when evaluating hospital volume and travel distance concurrently in the same statistical model, only increasing travel distance was associated with improved overall survival.

Both increasing travel distance and increasing hospital volume were associated with certain quality-of-care metrics. Quality measures can help quantify health care processes, outcomes, and organizational structure and/or systems that are associated with the ability to provide high-quality health care. The National Comprehensive Cancer Network (NCCN) has established a number of quality metrics including obtaining negative surgical margins, adequate lymph node assessment, and delivery of adjuvant therapy.[19] Previous work from our own group demonstrated that less than half of patients with biliary tract cancers received systemic chemotherapy in adherence with NCCN guidelines.[20] While a subset of patients had contraindications or refused chemotherapy, other factors such as insurance status and ethnicity were associated with adherence. The current study expanded on this previous work; in that, it specifically examined the impact of travel distance on cancer quality-of-care metrics. We noted that increasing hospital volume and increasing travel distance were both associated with better cancer quality-of-care metrics including margin status. Interestingly, while increasing travel distance was correlated with a lower odds of preoperative chemotherapy, LT was associated an increased likelihood of postoperative chemotherapy. The reasons for these findings are undoubtedly

Table 3 Multivariable logistic regression for receipt of neoadjuvant chemotherapy and adjuvant chemotherapy, surgical delay, and positive surgical margin including travel distance in comparison to short travel

Variable	Travel distance—continuous (10-mile)		Travel distance—categorical					
			IST		ILT		LT	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Preoperative chemo	*0.99 (0.97–0.99)*	*0.001*	*0.80 (0.65–0.99)*	*0.044*	*0.58 (0.46–0.72)*	*< 0.001*	*0.33 (0.26–0.43)*	*< 0.001*
Postoperative chemo	*1.02 (1.01–1.03)*	*0.002*	*1.24 (1.06–1.52)*	*0.044*	*1.74 (1.39–2.17)*	*< 0.001*	*3.00 (2.32–3.88)*	*< 0.001*
Surgical delay	1.00 (1.00–1.00)	0.09	1.06 (0.84–1.33)	0.63	1.19 (0.94–1.50)	0.14	*1.78 (1.41–2.25)*	*< 0.001*
Positive margin	*0.99 (0.98–0.99)*	*0.001*	1.03 (0.84–1.26)	0.78	1.11 (0.90–1.37)	0.32	*0.68 (0.54–0.86)*	*0.001*

Analysis adjusted for age, sex, race, Charlson-Deyo score, insurance status, patient residence area (metropolitan vs. urban vs. rural), median income, education level, cT stage, and cN stage. Values in italics are statistically significant (*p*-value less than 0.05)

OR odds ratio, CI confidence interval, IST intermediate short travel, ILT intermediate long travel, LT long travel

Table 4 Multivariable logistic regression for receipt of neoadjuvant chemotherapy and adjuvant chemotherapy, surgical delay, and positive surgical margin including travel distance and hospital volume

Variable	Travel distance—continuous (10-mile)		Travel distance—categorical					
			IST		ILT		LT	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Preoperative chemo	*0.99 (0.97–0.99)*	*0.001*	*0.81 (0.66–0.99)*	*0.042*	*0.57 (0.46–0.72)*	*< 0.001*	*0.33 (0.25–0.43)*	*< 0.001*
Postoperative chemo	*1.02 (1.01–1.03)*	*0.002*	*1.24 (1.01–1.53)*	*0.042*	*1.75 (1.40–2.19)*	*< 0.001*	*3.03 (2.34–3.94)*	*< 0.001*
Surgical delay	*1.00 (1.00–1.00)*	*0.005*	1.07 (0.85–1.35)	0.57	*1.27 (1.01–1.61)*	*0.041*	*2.00 (1.58–2.53)*	*< 0.001*
Positive margins	*0.99 (0.99–0.99)*	*0.005*	1.02 (0.83–1.25)	0.85	1.07 (0.87–1.32)	0.52	*0.64 (0.51–0.81)*	*< 0.001*
Variable	Hospital volume—continuous (number of case)		Hospital volume—categorical					
			ILV		IHV		HV	
	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*	OR (95% CI)	*P*
Preoperative chemo	*0.99 (0.98–0.99)*	*0.001*	1.01 (0.81–1.28)	0.91	1.10 (0.88–1.38)	0.40	1.03 (0.84–1.28)	0.76
Postoperative chemo	*1.01 (1.01–1.01)*	*< 0.001*	0.99 (0.78–1.24)	0.91	0.91 (0.73–1.14)	0.40	0.97 (0.78–1.20)	0.77
Surgical delay	*0.99 (0.99–0.99)*	*0.001*	*0.57 (0.44–0.72)*	*< 0.001*	*0.67 (0.53–1.85)*	*0.001*	*0.57 (0.46–0.72)*	*< 0.001*
Positive margins	1.00 (0.98–1.01)	0.22	*1.51 (1.22–1.85)*	*< 0.001*	*1.26 (1.02–1.56)*	*< 0.001*	1.18 (0.97–1.44)	0.11

Analysis adjusted for age, sex, race, Charlson-Deyo score, insurance status, patient residence area (metropolitan vs. urban vs. rural), median income, education level, cT stage, and cN stage. Values in italics are statistically significant (*p*-value less than 0.05)

OR odds ratio, CI confidence interval, ST short travel, IST intermediate short travel, ILT intermediate long travel, LT long travel, LV low volume, ILV intermediate low volume, IHV intermediate low volume, HV high volume

multifactorial and may be related to the fact that patients traveling long distances for surgery were less likely to want preoperative chemotherapy prior to an operation. In addition, a subset of patients may have been seen initially at small center and were started on chemotherapy for what was deemed to be unresectable disease; some of these patients may have

Table 5 Multivariable Cox proportional-hazard regression for overall survival

A								
Variable	Hospital volume—continuous (number of case)		Hospital volume—categorical					
			ILV		IHV		HV	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Mortality	1.00 (0.98–1.02)	0.69	1.07 (0.96–1.20)	0.20	0.93 (0.83–1.04)	0.21	1.03 (0.93–1.15)	0.50
B								
Variable	Travel distance—continuous (10-mile)		Travel distance—categorical					
			IST		ILT		LT	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Mortality	*0.98 (0.97–0.99)*	*0.024*	0.99 (0.88–1.10)	0.85	1.02 (0.89–1.12)	0.98	*0.87 (0.77–0.98)*	*0.028*
C								
Variable	Travel distance—continuous (10-mile)		Travel distance—categorical					
			IST		ILT		LT	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Mortality	*0.99 (0.97–0.99)*	*0.021*	0.99 (0.88–1.10)	0.85	0.97 (0.89–1.11)	0.96	*0.86 (0.76–0.98)*	*0.022*
Variable	Hospital volume—continuous (number of case)		Hospital volume—categorical					
			ILV		IHV		HV	
	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*	HR (95% CI)	*P*
Mortality	0.99 (0.98–1.03)	0.54	1.09 (0.97–1.22)	0.12	0.94 (0.84–1.06)	0.33	1.05 (0.95–1.17)	0.31

A. Including hospital volume in comparison to low volume. B. Including travel distance in comparison to short travel. C. Including hospital volume and travel distance

Analysis adjusted for age, sex, race, Charlson-Deyo score, insurance status, patient residence area (metropolitan vs. urban vs. rural), median income, education level, cT stage, and cN stage. Values in italics are statistically significant (*p*-value less than 0.05)

HR odds ratio, CI confidence interval, ST short travel, IST intermediate short travel, ILT intermediate long travel, LT long travel, LV low volume, ILV intermediate low volume, IHV intermediate low volume, HV high volume

subsequently been evaluated at a larger, more experienced center and considered resectable. Xia et al. had noted that, after controlling both travel distance and hospital volume, increasing hospital volume was associated with increased receipt of neoadjuvant chemotherapy.[15] However, in a separate study, Reardon et al. reported that increased travel distance was negatively associated with receipt of neoadjuvant chemotherapy.[21] Collectively, the data suggest that travel distance can impact certain treatment-related factors among patients receiving surgical care for cholangiocarcinoma.

The association and interaction of travel distance and hospital volume on patient long-term survival has been more controversial. Xia et al. reported on patients undergoing cystectomy for invasive bladder cancer and noted that increased travel distance was associated with improved overall survival.[15] However, the effect of longer travel distance on improved overall survival was mediated by hospital volume and the authors concluded that the benefits of undergoing surgery at a high-volume hospital outweighed the disadvantages of longer travel distance.[15] In a separate study that examined patients undergoing pancreaticoduodenectomy for pancreatic adenocarcinoma, Lidsky et al. reported that patients with the combination of long travel/high volume had higher stage disease, but a lower incidence of positive margins, higher rate of lymphadenectomy, as well as shorter hospitalization and lower 30-day mortality.[14] Jindal et al. reported improved survival among patients with a longer travel distance after pancreatectomy and attributed this primarily to higher hospital volume.[18] In the current study, we similarly noted that patients with cholangiocarcinoma in the LT quartile had a modest—yet significant—better long-term survival compared with patients in the ST quartile. Interestingly, our findings that increased travel distance was associated with improved overall survival among patients with cholangiocarcinoma was at odds with data published by O'Connor et al.[22] In this study, O'Connor et al. reported that there was an association between increased travel distance and worse overall survival, but these data were hard to interpret as only the third quartile of travel distance was associated worse overall survival on multivariable analysis.[22] In addition, Birkmeyer et al. reported on the potential impact of regionalization policies on travel burden using Medicare claims data and US road network data.[23] In this study, the authors noted that many patients traveled past a high-volume center to undergo surgery at a low-volume hospital. The data suggested that some patients endured increased travel burden without necessarily benefiting from being seen at a high-volume hospital.[23]

Several limitations should be considered when interpreting data from the current study. The NCDB included patients who received a portion of their care at a cancer program accredited by the Commission on Cancer, which included 30% of US hospitals and captures approximately 70% of patients with a new diagnosis of cancer. While the database allowed for a large cohort size, the data may not represent the entire US population. For example, there is a lower proportion of people of Hispanic ethnicity and of older patients in the NCDB compared with the general US population.[16] In addition, while Veterans Affairs and Department of Defense facilities contribute to the NCDB, data from these facilities are not included in the PUF. Additionally, some health-associated patient factors including weight, body mass index, smoking status, or performance status are not currently captured by the NCDB.[16] Because differentiating the specific anatomic sub-type of cholangiocarcinoma can be challenging using the NCDB, the current study examined cholangiocarcinoma as a single disease entity. As such, future studies will need to examine whether travel distance impacts intrahepatic, hilar, or distal cholangiocarcinoma differently.

In conclusion, travel distance and hospital volume were associated with certain quality-of-care metrics among patients with cholangiocarcinoma. After controlling for hospital volume and travel distance simultaneously, only travel distance was associated with decreased risk of mortality. Additionally, increasing travel distance was associated with decreased receipt of preoperative chemotherapy and increased receipt of postoperative chemotherapy. Increased hospital volume was also associated with decreased risk of surgical delay, while increased travel distance was associated with decreased risk of a positive surgical margin. While patients who traveled a longer distance to receive care had improved quality-of-care metrics, this translated into only a modest improvement in overall survival that did not appear to be mediated by hospital volume. Therefore, there seems to be an interplay between both travel distance and hospital volume relative to quality-of-care metrics, short-term outcomes, and long-term prognosis. Future studies will need to further assess the impact of travel distance relative to the actual place to which patients are traveling to receive care with a particular emphasis on hospital characteristics beyond case volume.

Author Contribution EWB, RM, JMH, AP, KM, MED, JC, AE, and TMP conceived of and designed this work. RM and EWB performed the data analysis. EWB drafted the manuscript. EWB, RM, JMH, AP, KM, MED, JC, AE, and TMP critically revised the manuscript, provided approval of the final version, and agree to be accountable for all aspects of the work.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

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