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Travel distance does not affect overall survival in patients with appendiceal adenocarcinoma undergoing cytoreductive surgery and hyperthermic intraperitoneal chemotherapy

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ABSTRACT

Introduction: Cytoreductive surgery and hyperthermic intraperitoneal chemotherapy (CRS-HIPEC) is a potentially curative approach for appendiceal cancer (AC) with peritoneal dissemination and is most often employed at tertiary referral centers. Regionalization may provide geographic barriers to care for vulnerable patients. The aim of this study was to examine the effect of travel distance on oncologic outcomes of patients with AC treated with CRS-HIPEC.

Methods: The National Cancer Database (NCDB) was reviewed from 2006 through 2020 for patients with AC who underwent CRS-HIPEC. The primary comparison variable was distance (< 50 miles vs ≥ 50 miles from the CRS-HIPEC facility). Demographic and tumor characteristics were analyzed. Primary outcome was overall survival (OS). Secondary outcomes were 30-day and 90-day mortality, readmission, and length of stay (LOS).

Results: During the study period, 1703 patients met inclusion criteria, with 1000 patients travelling < 50 miles for CRS-HIPEC (59 %) and 703 travelling ≥ 50 miles (41 %). Patients who traveled ≥ 50 miles were more likely to be non-Hispanic White ($p < 0.001$), have annual income less than $74,062, be treated at an academic center and live in the South-Atlantic region of the United States. There was no significant difference in OS between groups (Figure 1). There were no significant differences in 30-day postoperative survival, 90-day survival, or 30-day readmission. Post-operative LOS was 8.0 versus 9.0 days ($p < 0.001$).

Conclusions: Travel distance ≥ 50 miles was not significantly associated with decreased OS or increased post-operative mortality, suggesting that regionalization of care does not worsen oncologic outcomes for patients with AC undergoing CRS-HIPEC.

Introduction

Appendiceal neoplasms are rare and account for less than 1 % of all malignancies.[1] The spectrum of clinical presentation of appendiceal neoplasms with pseudomyxoma peritonei (PMP), especially those of mucinous histology, can range from incidental findings of peritoneal mucin at the time of appendectomy for appendicitis, to malignant bowel obstruction due to advanced peritoneal disease.[2] Appendiceal cancer (AC) in the form of invasive epithelial adenocarcinoma, has propensity for both lymphatic and peritoneal spread of disease. The definitive treatment of AC with PMP varies based on the individual presentation and histology, though cytoreductive surgery and heated intraperitoneal chemotherapy (CRS-HIPEC) has become the standard of care for patients that are able to undergo a major abdominal operation in whom a complete cytoreduction can be achieved.[1,3] CRS-HIPEC is potentially curative in AMNs that involve metastases to the peritoneal surface. However, due to the requirement of surgeon expertise and established multidisciplinary programs in the management of peritoneal surface malignancies, CRS-HIPEC is most often employed only at tertiary referral centers in the United States (US).[4]

Regionalization of cancer care has become increasingly common.[5] Advantages include lower 30-day mortality for multiple complex oncologic procedures such as pancreatectomy, gastrectomy and rectal resections and improved 5-year survival for these conditions.[6,7] However, regionalization often results in increased travel distance for patients to receive definitive cancer care[8,9] and thus, may present a

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Table 1
Patient Demographics.

	Overall (N = 1703) N (%)	< 50 miles (N = 1000) N (%)	≥ 50 miles (N = 703) N (%)	p-value
Mean Age	58	58	59	0.400
Sex				0.200
Female	903 (53.0)	544 (54.0)	359 (51.0)	
Male	800 (47.0)	456 (46.0)	344 (49.0)	
Race				< **0.001**
American Indian	3 (0.2)	1 (0.1)	2 (0.3)	
Asian	56 (3.3)	45 (4.6)	11 (1.6)	
Black	116 (6.9)	76 (7.7)	40 (5.8)	
Other	36 (2.1)	29 (2.9)	7 (1.0)	
White	1467 (87.0)	833 (83.0)	634 (91.0)	
Unknown	25 (1.5)	16 (1.6)	9 (1.3)	
Ethnicity				**0.018**
Hispanic	94 (5.7)	66 (6.8)	28 (4.1)	
Non-Hispanic	1560 (94.0)	902 (93.0)	658 (96.0)	
Unknown	49 (2.9)	32 (3.2)	17 (2.4)	
Charlson-Deyo Score				0.800
0	1412 (83.0)	827 (83.0)	585 (83.0)	
1	230 (14.0)	140 (14.0)	90 (13.0)	
2	44 (2.6)	24 (2.4)	20 (2.8)	
≥ 3	17 (1.0)	9 (0.9)	8 (1.1)	
Urban/Rural				< **0.001**
Metro	1256 (87.0)	913 (95.0)	343 (73.0)	
Rural	24 (1.7)	7 (0.7)	17 (3.6)	
Urban	156 (11.0)	46 (4.8)	110 (23.0)	
Unknown	267 (16.0)	34 (3.4)	233 (33.0)	
Median Annual Income, 2020 Census				< **0.001**
< $46277	188 (11.0)	82 (8.3)	106 (15.0)	
$46277 - $57856	325 (19.0)	144 (15.0)	181 (26.0)	
$57856 - $74062	392 (23.0)	229 (23.0)	163 (24.0)	
> $74062	769 (46.0)	532 (54.0)	237 (34.0)	
Unknown	29 (1.7)	13 (1.3)	16 (2.3)	
Median Annual Income, Grouped				
Lower 3 quartiles (≤ $74062	905 (54)	455 (46)	450 (66)	< **0.001**
Highest quartile (> $74062)	769 (46)	532 (54)	237 (34)	
Year of Diagnosis				< **0.001**
2006-2010	382 (22.4)	186 (18.6)	196 (27.9)	
2011-2015	563 (33.1)	326 (32.6)	237 (33.7)	
2016-2020	758 (44.5)	488 (48.8)	270 (38.4)	
Insurance Status				< **0.001**
Medicaid	68 (4.1)	62 (6.3)	6 (0.9)	
Medicare	478 (28.0)	264 (27.0)	214 (31.0)	
Uninsured	25 (1.5)	18 (1.8)	7 (1.0)	
Other gov't	41 (2.4)	15 (1.5)	26 (3.7)	
Private	1067 (64.0)	624 (63.0)	443 (64.0)	
Unknown	24 (1.4)	17 (1.7)	7 (1.0)	
Facility Type				< **0.001**
Academic/Research Program	1193 (70.0)	600 (60.0)	593 (84)	
Community Cancer Program	24 (1.4)	20 (2.0)	4 (0.6)	
Comprehensive Community Cancer Program	300 (18.0)	224 (22.0)	76 (11.0)	
Integrated Network Cancer Program	186 (11.0)	156 (16.0)	30 (4.3)	
Facility Location				< **0.001**
East North Central	295 (17)	207 (21)	88 (13)	
East South Central	48 (2.8)	28 (2.8)	20 (2.8)	
Middle Atlantic	216 (13.0)	166 (17.0)	50 (7.1)	
Mountain	51 (3.0)	29 (2.9)	22 (3.1)	
New England	100 (5.9)	76 (7.6)	24 (3.4)	
Pacific	263 (15.0)	153 (15.0)	110 (16.0)	
South Atlantic	505 (30.0)	218 (22.0)	287 (41.0)	
West North Central	123 (7.2)	74 (7.4)	49 (7.0)	
West South Central	102 (6.0)	49 (4.9)	53 (7.5)	
Non-High School Diploma				0.13
< 5.0 %	470 (28.0)	296 (30.0)	174 (25.0)	
5.0-9.0 %	564 (34.0)	331 (33.0)	233 (34.0)	
9.1-15.2 %	400 (24.0)	224 (23.0)	176 (25.0)	
15.3 %+	248 (15.0)	138 (14.0)	110 (16.0)	
Unknown	21 (1.2)	11 (1.1)	10 (0.6)	

barrier to care for patients living in rural areas, or far from tertiary centers and compromise their ability to receive definitive care for uncommon diagnoses.[10–12] There exists concern that delayed presentation to care due to this potential barrier to receipt of care may also translate to worse oncologic outcomes.[13] A travel distance greater than 50 miles has been identified as a meaningful benchmark for exploring oncologic outcomes in patients living regionally or distantly from complex cancer care.[13–15] Recent institutional data suggests that regionalization may be

Table 2
Tumor Characteristics.

	Overall N = 1703 N (%)	< 50 miles N = 1000 N (%)	≥ 50 miles N = 703 N (%)	p-value
Grade				0.200
Well differentiated	543 (32.0)	300 (30.0)	243 (35.0)	
Mod differentiated	347 (20.0)	204 (20.0)	143 (20.0)	
Poorly differentiated	108 (6.3)	64 (6.4)	44 (6.3)	
Undifferentiated	22 (1.3)	17 (1.7)	5 (0.7)	
Unknown	683 (40.0)	415(42.0)	268 (38.0)	
T stage				0.077
pT0	11 (0.6)	5 (0.5)	6 (0.9)	
pT1	32 (1.9)	18 (1.8)	14 (2.0)	
pT2	19 (1.1)	10 (1.0)	9 (1.3)	
pT3	98 (5.8)	62 (6.2)	36 (5.1)	
pT4	244 (14.0)	120 (12.0)	124 (18.0)	
pT4A	381 (22)	232 (23.0)	149 (21.0)	
pT4B	245 (14.0)	144 (14.0)	101 (14.0)	
pTX	147 (8.6)	76 (7.6)	71 (10.0)	
Unknown	526 (31.0)	333 (33.0)	193 (27.0)	
TNM Stage				0.200
Stage 0	1 (< 0.1)	1 (0.1)	0 (0.0)	
Stage 1	27 (1.6)	19 (1.9)	8 (1.1)	
Stage 2	225 (13.0)	141 (14.0)	84 (12.0)	
Stage 3	49 (2.9)	33 (3.3)	16 (2.3)	
Stage 4	1271 (75.0)	727 (73.0)	544 (77.0)	
Unknown	130 (7.6)	79 (7.9)	51 (7.2)	
Mucinous Histology				**0.006**
No	241 (14.0)	161 (16.0)	80 (11.0)	
Yes	1462 (86.0)	839 (84.0)	623 (89.0)	
Liver Metastases				0.500
No	562 (33.0)	326 (33.0)	236 (34.0)	
Yes	84 (4.9)	52 (5.2)	32 (4.6)	
Unknown	1057 (62.0)	622 (62.0)	435 (62.0)	

Table 3
Patient Post-Surgical Outcomes.

	Overall (N = 1703) N (%)	< 50 miles (N = 1000) N (%)	≥ 50 miles (N = 703) N (%)	p-value
30-Day Mortality				0.052
No	1507 (99.0)	878 (99.0)	629 (98.0)	
Yes	15 (1.0)	5 (0.6)	10 (1.6)	
Unknown	181	117	64	
90-Day Mortality				0.120
No	1475 (97.0)	861 (98.0)	614 (97.0)	
Yes	41 (2.7)	19 (2.2)	22 (3.5)	
Unknown	187	120	67	
Readmitted within 30 days				0.300
No	1557 (94.0)	905 (93.0)	652 (94.0)	
Yes	105 (6.3)	67 (6.9)	38 (5.5)	
Unknown	41	28	13	
Length of Stay (Days, Median, IQR)	9 (6-14)	8 (6-14)	**9 (7-15)**	**< 0.001**
Unknown	350	190	160	

[1]n (%); Median (IQR)

safe for CRS-HIPEC procedures, though this inquiry has not yet been examined in AC in a national dataset.[15]

The aim of this study is to examine the relationship between travel distance and oncologic outcomes for patients with appendiceal cancer who undergo CRS-HIPEC in the United States. We hypothesize that a travel distance of greater than or equal to 50 miles from the treating center is not correlated with survival outcomes.

Methods

Data source

This study was approved by the Institutional Review Board (IRB) at the University of New Mexico (IRB Study #23–238) and considered exempt. A review of the National Cancer Database (NCDB) was performed from 2004 through 2020. The NCDB is a nationwide database that collects oncologic outcome data from over 1500 centers and represents a collaborative project between the American Cancer Society and the Commission on Cancer of the American College of Surgeons, capturing data on approximately 70 % of all new cancer diagnoses in the US.

Patient selection

Patients 18 years or older with AC were identified by the International Classification of Diseases for Oncology, 3rd Edition (ICD-O-3) topographical code C18.1. All patients diagnosed with histology codes 8140, 8144, 8210, 8255, 8261, 8263, 8323, 8440, 8441, 8470,

Table 4
Multivariable Cox Regression.

	N	HR[a]	95 % CI[a]	p-value
Age	1350	1.02	1.00-1.03	**0.017**
Sex				
Female	723	—	—	
Male	627	1.61	1.32-1.97	< **0.001**
Race and Ethnicity				
Non-Hispanic White	1132	—	—	
Hispanic	72	0.61	0.34-1.10	0.100
Non-Hispanic Black	86	1.43	0.98-2.09	0.062
Others	60	0.63	0.34-1.16	0.140
Travel Distance				
< 50 miles	779	—	—	
≥ 50 miles	571	1.03	0.81-1.31	0.820
Charlson-Deyo Score				
0	1124	—	—	
1	176	0.89	0.66-1.19	0.420
2	36	1.46	0.85-2.53	0.170
≥ 3	14	0.72	0.23-2.29	0.580
Median Annual Income (2020 US Census)				
< $46277	149	—	—	
$46277 - $57856	265	0.96	0.67-1.37	0.810
$57856 − 74062	316	1.09	0.77-1.55	0.610
> $ 74062	620	0.74	0.53-1.04	0.086
Median Annual Income, Grouped				
> $74062	620	—	—	
< $74062	730	1.39	1.12-1.73	**0.003**
Urban vs Rural				
Metro	993	—	—	
Rural	16	0.72	0.26-1.97	0.520
unknown/missing	220	0.81	0.59-1.11	0.190
Urban	121	1.27	0.90-1.78	0.170
Insurance Status				
Medicaid	56	—	—	
Medicare	382	1.10	0.57-2.09	0.780
Not insured	20	0.54	0.15-1.96	0.350
Other government	34	0.89	0.39-2.01	0.780
Private or managed care	858	0.86	0.47-1.56	0.620
Facility Type				
Academic/Research Program	955	—	—	
Community Cancer Program	19	1.00	0.41-2.49	> 0.99
Comprehensive Community Cancer Program	226	1.22	0.94-1.59	0.140
Integrated Network Cancer Program	150	0.94	0.66-1.35	0.750
TNM Stage				
Stage 1	20	—	—	
Stage 2	201	1.37	0.32-5.78	0.670
Stage 3	39	2.26	0.49-10.4	0.290
Stage 4	1090	4.56	1.12-18.5	**0.034**
Grade				
Well differentiated	462	—	—	
Mod differentiated	296	1.45	1.10-1.91	**0.009**
Poorly differentiated	93	2.88	2.05-4.04	< **0.001**
Undifferentiated	22	1.83	0.88-3.78	0.100
Unknown/missing	477	1.50	1.15-1.95	**0.003**
Mucinous Histology				
No	185	—	—	
Yes	1165	0.47	0.36-0.62	< **0.001**

[a] HR = Hazard Ratio, CI = Confidence Interval

8480, 8481, 8574 diagnosed between 2006 and 2020 were included. Low grade appendiceal tumors and in-situ histology were excluded. Patients undergoing CRS-HIPEC procedures were identified using the "Systemic Surgery Sequence" variable indicating intraoperative chemotherapy was given, a previously published methodology and one validated by the NCDB.[16]

Patient variables

Information collected included patient demographics, Charlson–Deyo comorbidity index, residence location (metro, rural, urban, unknown), socioeconomic status (according to median income quartiles in 2020), year of diagnosis, insurance status, facility type, facility geographic location, and percentage with high school degree (based zip code of residence). Travel distance is a pre-calculated variable in the NCDB, defined as the "crow fly" distance in miles between the center of the patient's zip code of residence and the center of the zip code of the treating facility. Patients were stratified by distance < 50 miles versus ≥ 50 miles traveled for treatment. Tumor characteristics included tumor grade, T stage, N stage, pathologic AJCC staging (6th and 7th editions), mucinous status, and presence of liver metastases. The primary outcome was overall survival (OS). Postoperative outcomes data included 30- and 90-day mortality, length of hospital stay following surgical resection, and 30-day unplanned hospital readmission rates.

Statistical analysis

Standard descriptive statistics were used to summarize the patients' demographic, geographic, and clinicopathologic characteristics. Categorical variables were summarized using frequencies and percentages. Pearson's Chi-squared tests and Fisher's exact tests were performed to compare categorical variables between groups. Continuous variables were summarized using median and interquartile range (IQR). Wilcoxon rank-sum tests were used to compare continuous variables between groups. Kaplan-Meier method was used to estimate survival probability over time, and the log-rank test was conducted to compare the difference in overall survival between the two geographic groups. We performed univariable and multivariable Cox proportional hazard regression models to examine the effects of demographic, geographic, and clinicopathologic factors on overall survival. Hazard ratios and 95 % confidence intervals were calculated to measure the associations between potential prognostic factors and the overall survival outcome.

Results

Study population and demographics

During the study period, 1703 patients with histologically confirmed AC who underwent CRS-HIPEC were identified and included for analysis. Patient characteristics are displayed in Table 1. Most patients (N = 1000, 58.7 %) traveled < 50 miles to the treating hospital compared to ≥ 50 miles (N = 703, 41.3 %). The distribution of age and sex in both travel groups were similar. Non-Hispanic White patients were the most common racial and ethnic group in the cohort. Charlson-Deyo comorbidity score of 0 comprised 83 % of the group examined. Patients who traveled ≥ 50 miles were more likely to be non-Hispanic White, live in rural or non-metropolitan areas (26.6 vs. 5.5 % in < 50-mile group; p < 0.001) and be in the first quartile for median income (< $46,277 per year). Additionally, patients in the further travel group were less likely to have Medicaid insurance, more likely to be treated at an academic center and reside in the south Atlantic region of the United States.

Tumor characteristics are displayed in Table 2. There were no significant differences in tumor grade, T stage, nodal status, overall cancer stage, or prevalence of liver metastases between the two travel groups. There was a statistically though likely not clinically significant difference in incidence of mucinous histology (89 % in the further travel group, 84 % in the < 50 miles group; p = 0.006). Postoperative outcomes were not significantly different between the travel groups, with equivalent 30-day and 90-day postoperative mortality, and 30-day hospital readmission rates (Table 3). Travel distance ≥ 50 miles was associated with a statistically significant increase in hospital LOS (mean 9 days vs. 8 days in < 50 miles cohort; p < 0.001).

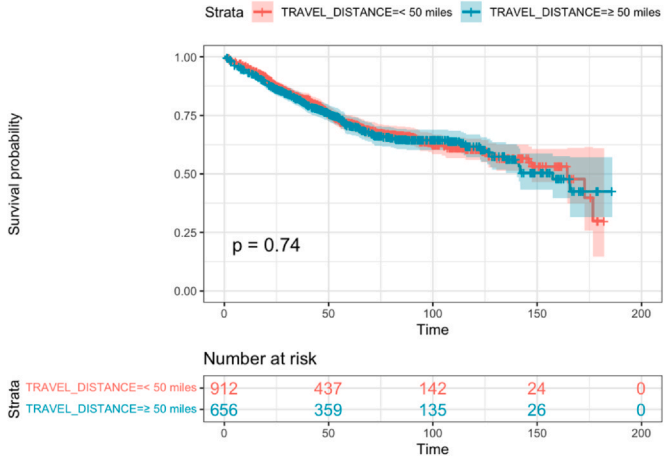

Fig. 1. Kaplan-Meier Overall Survival, Compared by Patient Travel Distance.

Cox proportional hazard regression

Univariable Cox regression (Supplemental Table 1) demonstrated worse survival was related to advanced age (HR 1.03, 95 % CI 1.02–1.04), male sex (HR 1.65, 95 % CI 1.38–1.99), non-Hispanic Black race (HR 1.43, 95 % CI 1.03–2.00), urban residence (HR 1.64, 95 % CI 1.23–2.17), Medicare insurance (HR 1.82, 95 % CI 1.01–3.28), comprehensive community cancer programs (HR 1.35, 95 % CI 1.08–1.69), stage IV disease (HR 4.84, 95 % CI 1.21–19.4), moderately differentiated (HR 1.50 95 % CI 1.17–1.93) and poorly differentiated histology (HR 4.68, 95 % CI 3.52 – 6.24). Mucinous histology was protective (HR 0.41, 95 % CI 0.33–0.52).

On multivariable Cox regression (Table 4), increased age was an independent prognostic factor of worsened OS (HR 1.02, 95 % CI 1.00–1.03; p = 0.017). Additionally, male sex was also found to be an independent predictor of worsened OS (HR 1.61, 95 % CI 1.32–1.97; p < 0.001) as well as stage IV status (HR 4.56, 95 % CI 1.12–18.5), moderately differentiated (HR 1.45, 95 % CI 1.10–1.91) and poorly differentiated histology (HR 2.88, 95 % CI 2.05–4.04). Mucinous histology again was protective (HR 0.47, 95 % CI 0.36–0.62). Race, ethnicity, Charlson-Deyo score, median income quartile, rural residence, insurance status, and facility type were not found to be significant prognostic factors of OS. However, having an income in the lower three quartiles in aggregate resulted in a HR of 1.39 as compared to patients in the top quartile of income (95 % CI 1.12–1.73). Travel distance ≥ 50 miles was not found to be prognostic of worsened OS (HR 1.03; CI 0.81–1.31; p = 0.82).

Stage IV cohort only

Due to the finding that 19 % of the overall cohort was designated as stage I-III in the NCDB, a dedicated analysis of stage IV patients was performed (n = 1271). This is to assure the survival outcomes and travel analysis pertained to only those patients with peritoneal disease, which is the standard indication for CRS-HIPEC. There were no major differences in patient demographics in the stage IV only cohort versus the overall cohort, or between travel groups (Supplementary Table 2). There were higher rates of poorly differentiated histology (11.0 % vs. 6.3 %) and liver metastases (17.0 % vs 4.9 %) compared to the overall cohort and slightly lower rates of mucinous histology (89 % vs. 86 %, Supplementary Table 3). A new finding of higher rates of hospital readmission within 30 days was noted in the < 50 miles group in the stage IV cohort (7.6 % vs. 4.7 %; p = 0.039). Univariable and multivariable regression analyses demonstrated similar findings as the overall cohort (Supplementary Tables 4 and 5).

Overall survival

Fig. 1 demonstrates the Kaplan-Meier curve overall survival comparison between the two travel groups (p = 0.74). There was no significant difference in OS between the travel groups up to 180 months. When performed in the stage IV cohort only, there were also no differences found between travel group OS (p = 0.77, Supplementary Figure 1).

Discussion

This study suggests that travel distance of ≥ 50 miles is oncologically safe for patients with AC undergoing CRS-HIPEC. Greater travel distance does not lead to a decrease in overall survival or increase in 30-day, or 90-day postoperative mortality. In addition, unplanned readmission rates following CRS-HIPEC did not significantly differ between patients who traveled < 50 miles versus those who traveled further for their care. However, length of stay following CRS-HIPEC was greater for patients who traveled ≥ 50 miles for care.

The incidence of appendiceal mucinous neoplasms is increasing in the U.S., especially in younger patients and those presenting with distance disease.[1] In this current study, our findings regarding OS are comparable to previously published literature, with multivariable analysis demonstrating worse OS in AC patients who are male and have non-mucinous histology. Although increased age showed a HR of 1.02 which demonstrated statistical significance, we do not feel that it represents clinical significance due to the small overall effect seen. In a previous SEER database study, Mo et al. also found similar risk factors for worsened survival.[17] Additionally, they found improved survival in patients diagnosed and treated between 1994–2014 compared to the 1973–1993 time period. Rozich et al. also identified female sex as a protective factor for mortality in patients undergoing CRS-HIPEC for appendiceal cancer in a NCDB study.[18]

The relationship between increased travel distance for complex cancer care and oncologic outcomes remains controversial. In laryngeal squamous cell cancer, a NCDB review demonstrated that patients who traveled ≥ 50-mile distance for their care had a greater likelihood of presenting with advanced, T4 stage disease.[19] However, these patients also were more likely to undergo total laryngectomy and had improved survival. These patients were also more likely to be male, Caucasian, live in a rural location, and receive their treatment at an academic/NCI-designated cancer center.[19] A Canadian study of rectal cancer patients in British Columbia suggested a possible association between increased distance and worse cancer-specific outcomes.[20] Interestingly, this association was independent of rural versus urban location of the patients' home address. Rural location alone was not an independent risk factor for lack of access but distance > 100 km was a risk factor for worse cancer-specific survival. Other studies in rectal cancer patients have suggested that rural patients are less likely to receive chemotherapy or radiation therapy and may even have increased risk of death.[21–23] In pancreatic cancer, overall survival was worse in patients who traveled more than 12.5 miles for their care [8]. However, distance traveled was not a negative factor for patients treated at high volume non-academic or academic centers suggesting a protective effect for high volume centers.[8]

Studies have identified several commonalities to patients residing in rural zip codes. Patients in large rural towns with cancer travel a mean of 51 min to receive specialized oncologic care.[24] Patients who live in smaller or isolated towns travel 59 min for this care. Historically, rural patients have a lower rate of employer-covered insurance than urban patients (51 % versus 57 %) under the age of 65.[25] Also, 1.6 million rural households do not have automobiles.[26] All of these factors may suggest that patients who live in rural addresses or need to travel longer distances for tertiary cancer care may be at risk for worse oncologic outcomes than urban patients or patients who reside closer to care. In this current study, no association between travel distance or rurality

was found in regards to OS, however when comparing the lower three income quartiles in aggregate compared to the highest quartile, there was a significant difference in predicting OS (HR 1.39; p = 0.003). The independent effect of income and financial toxicity on cancer survival is an important area of study going forward.

Complex oncologic care is increasingly being regionalized as recommended by multiple medical societies, patient advocacy groups and payer sources.[27–29] The Leapfrog Group has recommended that cancer operations be performed at tertiary referral centers that are high volume in order to optimize cancer specific outcomes and minimize morbidity and mortality from complex operations.[27,28,30] CRS-HIPEC is no exception due to the infrastructure costs and both technical and oncologic expertise required to provide quality care for patients with peritoneal surface malignancies.[31] This results in fewer centers performing complex cancer care. Regionalization of cancer care has demonstrated improved survival for various complex cancers.[32] Ho et al. demonstrated that OS from six different cancer operations (colon resection, rectal resection, pulmonary lobectomy, pneumonectomy, esophagectomy, and pancreatoduodenectomy) in Florida, New Jersey and New York improved from the time period of 1997–2000 compared to 1988–1991 and 1992–1996, a persistent volume-outcome effect.[32] This improvement in oncologic outcomes occurs even in the face of fragmented care, which is defined as modalities of cancer treatment being delivered at different facilities.[33] However, concerns regarding accessibility to care exist under this model of regionalization.[34,35]

Providing complex surgical care such as CRS-HIPEC at selected centers may increase travel distance and time for patients and this may pose a barrier to access to care.[24] Whether this increased required travel distance results in delay in care or barriers to accessibility remains unclear. Cancer centers have used several different strategies to mitigate potential harm from increased travel distances. Mujumdar et al. published on several strategies used in the care of gynecologic cancers.[37] The authors identified financial resources, lodging, clinical outreach, and telehealth as part of a multipronged strategy to reduce barriers to access.[37] In pancreatic cancer, care at high volume centers has been identified as protective for oncologic outcomes in patients who face increased travel distances.[38] While not yet standardized, many regional centers are developing various models of post-discharge follow-up, however it has not yet been confirmed that the incorporation of telehealth guarantees equitable access for all patients at this time.[39]

Postoperative mortality was not affected by travel distance in this study. The increased hospital LOS seen in patients with travel distance of ≥ 50 miles in CRS-HIPEC may be a result of concern for expedient follow-up in the event of postoperative complications. This could possibly be explained by the surgeon wanting to observe patients for another day in the hospital if they reside far from the index surgical center, versus logistical issues for the patient getting home the day they were medically ready for discharge.

CRS-HIPEC being performed in patients staged as I-III in NCDB was an interesting finding which merits attention. It is possible this is due to documentation and/or coding error. Nomenclature of peritoneal surface disease and pseudomyxoma peritonei has historically been convoluted and often difficult to interpret. It is also possible that this finding represents a cohort of patients who underwent “prophylactic” HIPEC, perhaps in the setting of perforated appendicitis, with the interest of decreasing risk of metachronous peritoneal metastases. Finally, the incorporation of stage I-III patients could be due to confusion about indication of CRS-HIPEC and was simply not indicated. However, in a dedicated analysis of stage IV patients only, the same findings regarding survival and comparison of travel distance were found as in the overall cohort.

This study includes a few notable limitations. First, there likely exists a selection bias for patients receiving CRS-HIPEC at a tertiary referral center with less comorbidities or more resources to receive multidisciplinary care at a distant facility.[36] Second, potential protective factors for rural patients should be identified and analyzed to further understand their role in CRS-HIPEC procedures. The NCDB does not contain the Peritoneal Carcinomatosis Index (PCI) which scores the burden of peritoneal disease prior to cytoreduction and the completeness of cytoreduction score (CCR). These data would provide more information on the extent of disease in each travel group as a potentially confounding factor for survival. Third, the NCDB does not have information on 30-day postoperative quality outcomes such as anastomotic leak, thromboembolic events, or deep space infections which would comparison between specific complication rates between travel distance cohorts. Finally, it is possible that patients who face greater travel distances may have been managed nonoperatively i.e. with systemic chemotherapy or palliative measures only, and are not captured in the current study. Barriers to care due to geographic distance may have resulted in patients developing more advanced disease prior to evaluation at a high-volume center thus precluding operability.

In conclusion, this study adds to a growing body of evidence suggesting that regionalization of surgical management of AC with CRS-HIPEC does not appear to compromise oncologic outcomes. The effect of travel on peritoneal disease-free survival specifically and fragmentation of multimodal care are future areas of investigation in AC pts who undergo CRS-HIPEC.

Author contributions

Study conception and design: Sadjadi, Luo, Fahy, Popek, Baste, Rai, Greenbaum. Collection, analysis and interpretation of data: Sadjadi, Luo, Fahy, Rai, McKean, Greenbaum. Writing and revising the manuscript: Sadjadi, Luo, Greenbaum. All authors critically read, revised and approved the final manuscript.

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Ethics Statement

None needed.

Editor Conflict of Interest

Given their role as Editorial Board Member in Peritoneal Surface Malignancies, Dr. Alissa Greenbaum had no involvement in the peer review of this article and has no access to information regarding its peer review.

Declaration of Competing Interest Statement

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.soi.2024.100068.

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