Effect of geographic distance from a cancer centre on choice of systemic therapy in metastatic colorectal cancer

Introduction: Due to limited data in the literature, we initiated a study with the objective of determining if geographic distance from patient residence to a treatment facility is a predictor of systemic therapy utilization or clinical trial enrolment.

Methods: Consecutive patients with metastatic colorectal cancer (mCRC) assessed by a medical oncologist at the Juravinski Cancer Centre (JCC), Hamilton, Ontario, during 2006 were selected. Patients with pathology other than adenocarcinoma and those with complete surgical resection of metastases were excluded. Distance and time to the JCC were calculated using online mapping software.

Results: 249 patients were included. Median travel time and distance to the JCC were 22.0 minutes and 18.6 kilometers (km), respectively. Distance and time were highly correlated ($p<0.0001$). Distance was not a statistically significant ($p=0.89$) predictor of number of treatment regimens; however, 32% of patients <50 km from the JCC received $\geq 3$ lines of treatment compared with 25% of patients $\geq 50$ km away. Overall, 38% of patients had discussed a clinical trial with their oncologist and 18% went on to enrol. Although distance did not attain statistical significance as a predictor of trial discussion (odds ratio [OR]=0.97, 95% CI=0.87–1.08, $p=0.60$), it approached significance as a predictor of enrolment, (OR=0.88, 95% CI=0.76–1.01, $p=0.071$).

Interpretation: Patients with mCRC residing greater distances from the JCC received fewer systemic regimens and were less likely to discuss or enter a clinical trial, but this finding did not attain statistical significance.

Key words: Metastatic, colorectal cancer, systemic therapy, geography

INTRODUCTION

The distance patients with cancer must travel from their residence to a treatment facility influences the decision-making process when choosing treatment. Breast cancer patients who live further away from a treatment facility are more likely to choose mastectomy instead of breast-conserving surgery, which is usually followed by several weeks of daily radiation therapy.1 Women are also less likely to receive radiotherapy once they have undergone a mastectomy or breast-conserving surgery if they have further distances to travel.2,3 Concern about travel has been described as a contributing factor to decreased accrual in breast cancer treatment trials,4 while longer distance from a patient’s residence to a cancer centre has also been shown to be associated with improved survival of patients on clinical trials.5

Not only must patients consider the time and distance required to get to a treatment facility, but many rely on someone else to provide transportation, such as a family member or volunteer driver.6 Repeating a long journey for daily radiation therapy or for an “experimental” therapy might be difficult for some patients, particularly those with deteriorating or poor health. Some patients, however, may choose to travel the extra distance for specialized oncology services available only at select or higher-volume centres.7 Data on the impact of patient travel on systemic therapy use, which may be more broadly available at the community level in some regions including our own, has been conflicting.8,9 As a result, we conducted a retrospective review to explore whether travel time and distance from patient residence to a cancer centre is associated with utilization of systemic therapy and clinical trial enrolment for patients with metastatic colorectal cancer (mCRC). This population was selected due to the large number of patients with mCRC.
of treatment options available. It was hypothesized that patients living further away would be likely to receive a smaller number of regimens. During the time of this review, cetuximab was unavailable at the Juravinski Cancer Centre (JCC) due to funding issues. Patients who were eligible for cetuximab treatment could be referred to a centre located approximately 100 km away (Roswell Park Cancer Institute, Buffalo, New York) for therapy. Thus, it was possible to explore potential associations between cetuximab treatment and distance.

**Methods**

Consecutive patients with Stage IV colorectal cancer seen by a medical oncologist at the JCC in Hamilton, Ontario on at least one occasion from January 1 to December 31, 2006 were eligible for enrolment in the study. Patients with Stage I–III colorectal cancer, squamous cell carcinoma, gastrointestinal stromal tumours, neuroendocrine tumours and those undergoing resection of liver or lung metastases for curative intent were excluded.

The JCC is located in the Hamilton Niagara Haldimand Brant Local Health Integration Network, with a total population of approximately 1.4 million people (Figure 1). This cancer centre receives on average 6000 new referrals — with over 220,000 patient visits — per year, and is the only comprehensive regional cancer centre within 6600 km² of the network.¹²

Demographic, staging, treatment and outcome information was obtained retrospectively from the institutional patient information system. An online, publicly available calculator (http://maps.google.ca) was used to estimate the travel distance and time by car from a patient’s residence to the JCC. Travel time and distance from patient residence to the Roswell Park Cancer Institute were determined by the same method. The Charlson score was calculated to reflect the burden of comorbid disease;¹³ however, since all patients had metastatic cancer, malignant solid tumour was excluded from this calculation.¹⁴ Approval from the local Research Ethics Board was obtained before proceeding with this study.

Descriptive statistics were used to summarize patient characteristics. The relationship between time in minutes and distance to the JCC in kilometers was evaluated using the Spearman rank correlation coefficient. Analysis was conducted using the distance to JCC variable, as there existed a near-perfect correlation between time and distance.

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(p=0.986) and distance was not subject to external factors such as traffic volume, driving speed or weather conditions. Distance to the JCC was evaluated as a predictor of outcomes such as systemic therapy use, clinical trial discussion and clinical trial enrolment using logistic regression analysis. As distance was highly skewed, a square-root transformation was performed to approximate normality, with visual inspection and quantile-quantile (Q-Q) plots to check the normality assumption. Three patients were outliers in terms of distance to the JCC, living 120, 300 and 451 km away, while all other patients lived ≤94 km away. These patients all stayed with relatives living nearby while undergoing treatment. For analysis of continuous outcomes, to better approximate normality and reduce the outlier effect, these distances were set to 96, 98 and 100 km, respectively. A second analysis was conducted by categorizing distance to the cancer centre into 4 strata selected a priori — <25 km, 25–<50 km, 50–<75 km and ≥75 km — and using a Cochran-Armitage test for trend. Logistic regression was also used to evaluate whether distance from patient residence to Roswell Park was a predictor of the patient receiving cetuximab treatment. All tests were 2-sided and a p-value of ≤0.05 was considered statistically significant.

**RESULTS**

**Summary statistics**

Two hundred and forty-nine consecutive patients with Stage IV colorectal cancer seen by a medical oncologist at the JCC in 2006 were eligible for inclusion. Baseline characteristics, such as age (p=0.52), gender (p=0.76), stage at diagnosis (p=0.82), primary site (p=0.49), Eastern Cooperative Oncology Group Performance Scale (p=0.51) and Charlson score (p=0.89), were not statistically significantly associated with distance (Table 1). The median distance to the JCC was 18.6 km and time was 22 minutes, with a maximum of 451 km and 285 minutes, respectively. Over half (55.8%) of all patients lived within 25 km of the cancer centre.

**Systemic therapy**

Distance to the JCC was not a statistically significant predictor of use of number of regimens (p=0.55), use of surgery (p=0.88) or radiotherapy (p=0.26). However, 45/139 (32.4%), 13/46 (28.3%), 12/50 (24.0%) and 3/14 (21.4%) patients living <25 km, 25–<50 km, 50–<75 km and ≥75 km away, respectively, received ≥3 regimens (test for trend p-value=0.19; Figure 2).

**Clinical trials**

The option of enrolling in a clinical trial was discussed with 94 (37.8%) patients during treatment for metastatic disease. The odds ratio (OR) for distance to the JCC was 0.97 (95% CI=0.87–1.08, p=0.60). The proportions of patients having a clinical trial discussion with their oncologist were 38.9%, 37.0%, 38.0% and 28.6% by distance group, respectively (p=0.59). Forty-five (18.1%) patients eventually enrolled in a clinical trial. The OR for distance as a predictor of clinical trial enrolment was 0.88.
(95% CI=0.76-1.01, p=0.072). Based on the pre-defined groups of distance to the JCC, 20.9%, 15.2%, 16.0% and 7.1%, respectively, enrolled in a clinical trial (p=0.17).

Of the 94 patients who discussed a clinical trial, 47.9% eventually enrolled. The OR for distance to the JCC as a predictor of clinical trial enrolment including only those patients for whom a clinical trial was discussed was 0.84 (95% CI=0.70–1.01, p=0.059). Based on the categorized groups of distance from the JCC, 57.5%, 41.2%, 42.1% and 25.0%, respectively, enrolled (p=0.18).

**Cetuximab use**
The median distance and time to Roswell Park were 109.0 km and 80 minutes, respectively. Distance to Roswell Park was not a statistically significant (p=0.55) predictor of treatment with cetuximab (OR=0.97, 95% CI=0.88–1.07). The median (inter-quartile range) distance to Roswell Park for those (n=36) who received cetuximab was 110 (101–125) km, compared to 109 (99–126) km for those who did not receive the drug (n=213).

**INTERPRETATION**
This study examined the effect of geographic distance on choice of systemic therapy and clinical trial decisions for patients with a diagnosis of mCRC by a medical oncologist at a major referral cancer centre in Ontario during a 1-year period. The results failed to demonstrate a statistically significant difference in number of treatment regimens, utilization of surgery or radiation, clinical trial decision making or cetuximab use at Roswell Park based on travel distance. While not statistically significant, a trend was observed that did seem to indicate that patients who lived farther away from the cancer centre were approached less often for clinical trials, enrolled into clinical trials less often (overall and even after being approached) and received at least 3 lines of systemic therapies less frequently.

Previous studies have demonstrated varying results of the effect of distance on cancer treatment. A study of lung and colorectal cancer patients showed that travel distance decreased the likelihood of radiotherapy use among the latter but did not play a role with respect to chemotherapy. An older American study demonstrated no statistical effect of distance on use of radiotherapy or chemotherapy for lung cancer patients not undergoing surgical resection. A more recent study in England of patients with any stage of prostate, lung, colorectal, breast or ovarian cancer showed that only rectal and lung cancer patients with the greatest travel times to the hospital had a reduced chance of receiv-
ing chemotherapy compared with those living closer.\textsuperscript{10} This association was seen despite controlling for several factors known to influence treatment, such as age, sex and tumour stage. A subset of this study focusing on lung cancer patients demonstrated that travel time amplified the effects of socioeconomic deprivation, such that patients living in the most distant and deprived areas were less likely to receive treatment.\textsuperscript{11} Therefore, travel time and distance do influence treatment decisions in some groups. In our study, statistical significance was not observed, perhaps due to confounding factors present in the local population, such as patient willingness to travel to receive specialized care, family/driver support systems, race/ethnicity, income or education level. It is possible that a real trend between distance and treatment exists; however, the sample size was too small to detect the difference. Although the total sample size was 249 patients for this study, very few (14) actually lived ≥75 km away from the JCC, which could reduce the available statistical power. It may be that any difference is small and clinically unimportant for the vast majority of patients who live relatively close to the cancer centre, although it could be argued that any difference in treatment patterns due to distance is of interest.

With respect to clinical trial participation, our study revealed that 38\% of patients had discussed a clinical trial with their oncologist and 18\% went on to enrol. Patients living ≥50 km from the JCC were less likely to have a discussion or participate in a clinical trial than patients who lived closer to the cancer centre. Although distance did not attain statistical significance as a predictor of trial discussion, it approached significance as a predictor of enrolment, and enrolment given that a clinical trial was discussed. These findings agree with a previous study of patients with gynecologic cancers referred for consideration of a Phase I clinical trial. Patients were more likely to be enrolled in a study as travel time from their residence to the treatment centre decreased.\textsuperscript{15}

Many studies estimate travel distance or time from the centroid (geographic centre) of patient’s zip/postal code to treatment facility. We used a patient’s actual street address, except in a small number of cases where the patient only had a postal box or rural route listed as the main address; then, the centroid of the postal code was utilized. Although distance and time were highly correlated, we chose the former as a potential predictor of systemic treatment. We did not collect data on patients’ actual travel times in comparison to those estimated by the geographic information system (GIS). Despite some evidence that GIS estimates of car travel times may be superior to reported travel times because the latter contain errors and can reflect unusual circumstances,\textsuperscript{16} we elected to avoid this bias entirely by using distance as the determinant of geographic access.

A limitation of this study is that the population consisted of Stage IV colorectal patients only, and therefore these results cannot be applied to patients with other stages of disease or other malignancies. Furthermore, the generalizability of these results to other geographic areas may be difficult due to variations in patient populations, access to treatment centres, and different treating physicians. Survival estimates for each of the distance categories could not be compared because survival information for patients who are not under the continued care of their medical oncologist might not be reliably ascertained for all patients, particularly for those who live further away from the cancer centre.

Slightly more than half of the patients in this study lived within 25 km of the cancer centre. In areas where patients must travel much further for care, geographic access would play a larger role in systemic treatment delivery and represents an area of future research. In our study, patients with mCRC living further from the JCC received fewer systemic regimens and were less likely to discuss or enter a clinical trial, although this did not reach statistical significance. It is important to note that this finding does not imply a decrease in quality of care for patients, provided patients are fully aware of their treatment options and capable of making informed decisions. Ultimately, oncologists should be aware that travel distance may play a role in the systemic therapy plan for their patients with metastatic disease, particularly in decisions around clinical trial accrual.

**Disclosure**

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