Distance to the closest radiotherapy facility and survival after a diagnosis of rectal cancer in Queensland

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I n Australia, colorectal cancer (CRC) is the most commonly diagnosed invasive cancer, and CRC incidence rates are among the highest in the world.[1,2] Significant geographical variation in survival after CRC diagnosis has been reported across Australia, with lower survival estimates for people living outside major cities.[3-6] The reasons for these rural inequalities are complex and multifaceted.[4,7] Although cancer stage explains much of the variation in survival outcomes,[8] urban–rural differences in survival remain after adjusting for cancer stage.[4] Thus, additional factors, including access to treatment, may have an independent association with survival after CRC diagnosis.

Access to treatment services is strongly influenced by distance. Most patients with CRC require surgery, but adjuvant radiotherapy can be used before and after surgery to reduce recurrence and improve outcomes.[9,10] For patients with rectal cancer, in particular, preoperative radiotherapy reduces the risk of local recurrence by at least half and improves disease-free survival.[11,12]

International studies have shown that the likelihood of patients with rectal cancer receiving radiotherapy is inversely associated with travel time to a radiotherapy facility, even after accounting for demographic, pathological and socioeconomic factors known to influence treatment patterns.[13,14] Equivalent Australian data for the effect of distance from a radiotherapy facility on rectal cancer survival, after adjustment for stage, have not been reported.

We report here the association between survival outcomes (adjusted for spread of disease) and distance to the closest radiotherapy facility for people diagnosed with rectal cancer in Queensland.

Methods

Study cohort

All Qld residents aged 20–79 years who were diagnosed with invasive

Abstract

Objective: To determine whether an association exists between distance from radiotherapy facilities and survival outcomes of people diagnosed with rectal cancer.

Design and setting: Descriptive population-based study using data from the Queensland Cancer Registry.

Patients: All patients aged 20–79 years (*n* = 6848) diagnosed with invasive rectal cancer between 1 January 1996 and 31 December 2006.

Main outcome measure: Cause-specific survival.

Results: The 5-year cause-specific survival was 62% (95% CI, 61%–64%); it was strongly influenced by stage at diagnosis (American Joint Committee on Cancer, Stages I–IV), ranging from 86% (Stage I) to 9% (Stage IV). After adjusting for age, sex, and stage at diagnosis, patients who lived 100–199 km, 200–399 km and 400 km or more from a radiotherapy facility were 16%, 30%, and 25%, respectively, more likely to die from rectal cancer than patients living within 50 km of such a facility. On average, there was a 6% increase in mortality risk (95% CI, 3%–8%; *P* < 0.001) for each 100 km increment in distance from the nearest radiotherapy facility. Shared frailty models showed that this association persisted after adjusting for the correlation between individual cancer patients living in the same remoteness or area-level socioeconomic status categories.

Conclusions: While centralisation of cancer treatment services has merit, our study provides evidence of a shorter survival for people with rectal cancer who live relatively far from radiotherapy facilities. It remains a priority to develop and implement policy, cultural and clinical measures to reduce the burden faced by rural and remote patients with rectal cancer.

rectal cancer (International classification of diseases, 10th edition, Australian modification [ICD-10-AM] codes C19, C20, and C21.8) between 1 January 1996 and 31 December 2006 were eligible for the study. We restricted the analysis to this age group because rectal cancer is very rare among children and teenagers, and death certification is known to be less accurate in older individuals.[15] Incident cases were obtained from the Queensland Cancer Registry (QCR), a population-based registry covering the entire state of Qld, with notifications required by law.[16]

Survival data

Survival data for the study cohort were examined up to 31 December 2007, thus providing at least a 1-year follow-up for each patient. For patients with multiple primary rectal cancer sites, only the site at the most advanced stage (and its associated pathological variables) was considered for our study. Survival duration

was defined as time in years between diagnosis and date of death or 31 December 2007 (the study end point), whichever was earlier.

Geocoding of patients' addresses

Patients' addresses were geocoded into longitude and latitude coordinates using automatic geographical information system (GIS) software. Because of lack of precise address information, 133 patients (1.9%) were excluded. The street addresses could be accurately geocoded for 6723 (98.2%) of the 6848 rectal cancer records with viable address information. The remaining addresses were geocoded either to a street at the centre of the residential suburb at the time of diagnosis (110 records, 1.6%) or to the centre of the postal code area of residence (15, 0.2%).

Location of radiotherapy facilities in Queensland

From 1996 to 2000, radiotherapy was available at two public and two private

1 **Impact of travelling distance and travel time to the nearest radiotherapy facility on cause-specific survival estimates for patients diagnosed with rectal cancer in Queensland, 1996–2006***

Variable	No. (%) of patients	2-year survival (95% CI)	5-year survival (95% CI)	Crude hazard ratio (95% CI)	Adjusted hazard ratio (95% CI)
Sex					$\chi^2 = 1.84$; df = 1; $P = 0.175$‡
Women	2455 (35.8%)	77.8% (76%–79%)	65.2% (63%–67%)	1.00	1.00
Men	4393 (64.2%)	75.3% (74%–77%)	60.7% (59%–62%)	1.08 (0.99–1.19)	1.07 (0.97–1.17)
Age group					$\chi^2 = 88.19$; df = 3; $P < 0.001$‡
20–59 years	2361 (34.5%)	82.0% (80%–84%)	70.1% (68%–72%)	1.00	1.00
60–69 years	2285 (33.4%)	76.0% (74%–78%)	62.9% (61%–65%)	1.25 (1.12–1.40)	1.29 (1.16–1.44)
70–74 years	1169 (17.1%)	72.5% (70%–75%)	57.0% (54%–60%)	1.35 (1.19–1.54)	1.51 (1.32–1.71)
75–79 years	1033 (15.0%)	67.5% (64%–70%)	49.5% (46%–53%)	1.58 (1.38–1.80)	1.81 (1.59–2.07)
Stage at diagnosis					$\chi^2 = 1687.02$; df = 4; $P < 0.001$‡
I	1622 (23.7%)	93.5% (92%–95%)	86.4% (85%–88%)	1.00	1.00
II	1470 (21.5%)	87.5% (86%–89%)	71.8% (69%–74%)	3.11 (2.49–3.89)	3.04 (2.43–3.80)
III	1688 (24.6%)	76.3% (74%–78%)	55.2% (53%–58%)	7.17 (5.84–8.81)	7.27 (5.92–8.94)
IV	616 (9.0%)	26.2% (23%–30%)	9.3% (7%–13%)	34.26 (27.71–42.36)	35.14 (28.41–43.46)
Unknown	1452 (21.2%)	66.3% (64%–69%)	55.1% (52%–58%)	7.48 (6.07–9.22)	7.67 (6.22–9.45)
Distance by road from nearest radiotherapy facility					$\chi^2 = 23.65$; df = 4; $P < 0.001$‡
< 50 km	4252 (62.1%)	77.9% (77%–79%)	64.5% (63%–66%)	1.00	1.00
50–99 km	469 (6.8%)	74.3% (70%–78%)	60.9% (56%–65%)	1.14 (0.96–1.35)	1.03 (0.87–1.22)
100–199 km	675 (9.9%)	74.2% (71%–77%)	59.6% (55%–63%)	1.18 (1.02–1.36)	1.16 (1.00–1.34)
200–399 km	964 (14.1%)	73.0% (70%–76%)	58.0% (55%–61%)	1.29 (1.14–1.45)	1.30 (1.15–1.47)
≥ 400 km	488 (7.1%)	72.7% (68%–77%)	57.4% (52%–62%)	1.37 (1.17–1.60)	1.25 (1.07–1.47)
Travel time to nearest radiotherapy facility†					$\chi^2 = 20.43$; df = 4; $P < 0.001$‡
0–1 hour	4517 (66.0%)	77.5% (76%–79%)	64.3% (63%–66%)	1.00	1.00
1–2 hour	736 (10.7%)	75.6% (72%–79%)	59.4% (56%–63%)	1.16 (1.01–1.33)	1.07 (0.93–1.23)
2–4 hour	897 (13.1%)	72.2% (69%–75%)	58.3% (55%–62%)	1.26 (1.11–1.43)	1.28 (1.13–1.45)
4–6 hours	624 (9.1%)	74.6% (71%–78%)	58.6% (54%–63%)	1.27 (1.10–1.47)	1.24 (1.08–1.44)
≥ 6 hours	74 (1.1%)	65.7% (54%–75%)	55.1% (42%–66%)	1.51 (1.05–2.17)	1.22 (0.85–1.76)

* Using multivariable Cox proportional hazards regression models. † Calculated using a separate model, also containing sex, age group and stage at diagnosis.
‡ Joint χ^2 tests for model ◆

hospitals in or near the Qld state capital, Brisbane, situated in the southeast corner of the state, and at one public hospital in Townsville, about 1300 km north of Brisbane. From 2001, an additional private hospital, also in the southeast corner, provided radiotherapy, as did another large public facility in Brisbane from 2002. Address details for these radiotherapy facilities were geocoded into latitude and longitude coordinates.

Distances to radiotherapy facilities

As Euclidean (straight-line) measures may underestimate travel times,[17,18] we calculated actual road travel distances and times between a patient's address of usual residence and the address of the closest radiotherapy facility, using GIS applications and a street network database. These calculations were made on a year-specific basis to accommodate the increasing coverage of radiotherapy facilities over

time. The distances and travel times were collapsed into categories (Box 1).

Rectal cancer staging

As with most population-based cancer registries, information on cancer stage is not routinely collected by the QCR. However, rectal cancer is one of the most amenable to stage extraction from pathology reports, and pathology stage is a reliable substitution for colorectal cancer stage reported by clinicians.[19] Two clinical coders extracted details of tumour size, nodal involvement and presence of metastases (the tumour, node, metastasis [TNM] system) from pathology reports and other clinical information held by the QCR. Rectal cancer stage was assigned to each patient according to the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control evidence-based TNM system.[20] AJCC Stages I–IV were derived from TNM

values with Stage I cancers being the least advanced. To assess coding consistency, stage information for a sample of 5% of records ($n = 347$) was extracted by both clinical coders, with 98% agreement for TNM stage.

Statistical analysis

Cause-specific survival was used; that is, deaths attributed to rectal cancer were considered to be events, and deaths from other causes were censored. Statistical analyses were performed using Stata version 11 (StataCorp, College Station, Tex, USA).

The association between distance by road or travel time and cause-specific survival was assessed using Cox proportional hazards regression. Separate models were used for distance by road and travel time to radiotherapy facilities. Estimates were adjusted by age group, sex and stage at diagnosis. Two stratified estimation

2 Effect of distance to the nearest radiotherapy facility on survival after a diagnosis of rectal cancer in Queensland, using stratified and shared frailty models

Model	Hazard ratio (95% CI)
Stratified models	
Strata by stage, adjusted for sex and age group	$\chi^2 = 22.44$; df = 4; $P < 0.001$*
< 50 km	1.00
50–99 km	1.04 (0.87–1.23)
100–199 km	1.16 (1.00–1.34)
200–399 km	1.30 (1.15–1.46)
≥ 400 km	1.24 (1.06–1.45)
Strata by age group and sex; adjusted for stage	$\chi^2 = 24.18$; df = 4; $P < 0.001$*
< 50 km	1.00
50–99 km	1.03 (0.87–1.22)
100–199 km	1.16 (1.00–1.34)
200–399 km	1.30 (1.15–1.47)
≥ 400 km	1.26 (1.07–1.48)
Shared frailty models (adjusted for sex, stage and age group)	
Random effect = ARIA+	$\theta < 0.0001$ (SE < 0.0001; $\chi^2 < 0.0001$; $P = 0.500$)*
Road distance	$\chi^2 = 23.65$; df = 4; $P < 0.001$*
< 50 km	1.00
50–99 km	1.03 (0.87–1.22)
100–199 km	1.16 (1.00–1.34)
200–399 km	1.30 (1.15–1.47)
≥ 400 km	1.25 (1.07–1.47)
Random effect = IRSD	$\theta = 0.017$ (SE = 0.013; $\chi^2 = 15.31$; $P < 0.001$)*
Road distance	$\chi^2 = 11.54$; df = 4; $P = 0.021$*
< 50 km	1.00
50–99 km	0.93 (0.78–1.11)
100–199 km	1.06 (0.91–1.23)
200–399 km	1.21 (1.06–1.37)
≥ 400 km	1.13 (0.96–1.34)

ARIA+ = Accessibility/Remoteness Index of Australia. IRSD = Index of Relative Socio-economic Disadvantage. θ = measure of variance for random effect. * Joint χ^2 tests for model fit. ◆

models (by stage and age/sex) were used to assess the validity of the proportional hazards assumption and to compare these stratified estimates against the original model estimates. If the estimates are similar then the data are consistent with the proposition that the proportional hazards assumption has not been violated.

To assess the impact of the unknown stage information on the observed associations, we conducted three different sensitivity analyses using Cox survival models, assuming that (i) all patient records with unknown stage were Stage I; (ii) all records with unknown stage were Stage IV; and (iii) all records with unknown stage were distributed equally over the four cancer stages (I–IV).

Random effects Cox models (or shared frailty models) were also used to examine whether distance was an independent predictor of survival, after adjusting for age, sex and stage, and accounting for the correlation between individuals within the same geographical areas, as defined by remoteness (Accessibility/Remoteness Index of Australia [ARIA+])[21] or socioeconomic disadvantage (Index of Relative Socio-economic Disadvantage [IRSD]).[22] In these models, the area-level variable is included in the model as a random effect with unit mean and unknown variance; this measures the between-area variation. Larger variance estimates imply greater variability in "frailty" between areas with a greater correlation of survival times of cancer patients within the same geographical category.

Ethics approval

Ethics approval was obtained from the Behavioural and Social Sciences Ethical Review Committee, University of Queensland. Permission to access confidential data from the QCR was given by the Research Ethics and Governance Unit, Queensland Department of Health.

Results

There were a total of 6848 people in the study cohort; 4393 (64.2%) were men (Box 1). The mean age at diagnosis was 63 years (median, 65 years; range, 20–79 years) and the mean follow-up was 4 years (median, 3 years; range, 0–12 years). During the follow-up period, 2556 patients (37.3%) died; 2034 (79.6%) of these deaths were due to rectal cancer. The 5-year overall cause-specific survival was 62% (95% CI, 61%–64%).

After adjustment for the other variables in Box 1, including stage at diagnosis, there was no statistically significant evidence of a survival difference related to sex (Box 1). The risk of dying from rectal cancer increased significantly with age, with more advanced stage, and with increasing distance by road from the nearest radiotherapy facility (Box 1). Compared with patients with rectal cancer who lived within 50 km of a radiotherapy facility, those living 100–

199 km, 200–399 km and at least 400 km from a radiotherapy facility were 16%, 30% and 25% more likely to die from rectal cancer, respectively, after adjustment for stage, sex and age group at diagnosis (Box 1).

The magnitude and significance of these effects were similar when age was treated as a continuous variable (results not shown). A separate model with road distance as a continuous variable found a significant increasing linear association (hazard ratio [HR], 1.06; 95% CI, 1.03–1.08; $P < 0.001$) between the risk of dying and the distance (per 100 km) to the nearest radiotherapy facility, after adjusting for stage, age at diagnosis and sex (full results not shown).

Estimated travel times to the closest radiotherapy faculty were also significantly associated with risk of death from rectal cancer after controlling for stage, sex and age (Box 1). Patients with travel times of 2–4 hours, 4–6 hours and 6 hours or more from the nearest radiotherapy facility had a lower survival (22%–28% increased risk of death) compared with those living within an hour of a radiotherapy facility. There was a 5% increase in risk per hour of travel when road travel time was treated as a continuous variable (HR, 1.05; 95% CI, 1.02–1.07; $P < 0.001$). Almost identical results were observed when the survival analysis was repeated with stratification by stage, and then by age and sex (Box 2).

In the sensitivity analyses for unknown cancer stage, the significant association between distance to a radiotherapy facility and survival remained for each assumption made (see Statistical analysis). For example, the adjusted HRs for distances of 200–399 km compared with < 50 km ranged from 1.25 to 1.33 for the three assumptions, with all being statistically significant ($P < 0.001$). Similar results were seen when distance was treated as a continuous variable, and also for the associations between road travel time and survival (results not shown).

The significant association between distance to a radiotherapy facility and rectal cancer survival remained after accounting for the correlation between individual cancer patients living in the same remoteness cate-

gory (impact of distance: $\chi^2 = 23.65$; df = 4, $P < 0.001$) or area-level socioeconomic status category (impact of distance: $\chi^2 = 11.54$; df = 4, $P = 0.021$) (Box 2). There was no evidence of a significant correlation between survival times for patients within the same remoteness category; however, there was a significant correlation between cancer patients in the same area-level socioeconomic status category. Similar results were seen when models were run with travel times to radiotherapy facilities (results not shown).

Discussion

To our knowledge, this is the first time that the association between distance to treatment centres and survival for patients with rectal cancer has been reported in Australia. Among patients with rectal cancer diagnosed in Qld, we found that, after adjusting for age group, sex and stage at diagnosis, the risk of cause-specific mortality increased by 6% for each 100 km increment in distance from a hospital offering radiotherapy.

The current Australian Clinical Practice Guidelines for the management and treatment of colorectal cancer recommend adjuvant preoperative or postoperative radiotherapy for high-risk (T3/4 or N1) rectal cancer, and that any postoperative adjuvant therapy program for rectal cancer should include radiotherapy and chemotherapy.[23] Preoperative radiotherapy reduces the risk of local recurrence for patients with rectal cancer by at least half and improves disease-free survival.[11,12,24] Although radiotherapy services are considered to be integral to a multidisciplinary approach to treatment of patients with rectal cancer,[10] the increased distances rural patients need to travel to use these services are recognised as a barrier to optimum treatment, particularly when prolonged absence from home disrupts normal life and involves financial hardship.[25] International studies have shown that patients with rectal cancer who need to travel longer distances are less likely to receive radiotherapy[13,14] and, consistent with this, Scandinavian patients with rectal cancer treated at local hospitals lacking radiotherapy

units were found to receive radiotherapy less often and to have significantly increased rates of local recurrence.[9,26] In New South Wales, patients in rural and remote areas with rectal cancer are reported to have lower radiotherapy completion rates than their urban counterparts.[27]

Although our study did not examine the type of treatment that patients in our cohort actually received, the results show that increasing distance from centres offering radiotherapy has a direct association with survival outcomes for patients with rectal cancer, independent of disease spread. Given that for complex treatments, such as radiotherapy, some centralisation may be inevitable, it is imperative that health services find ways to improve access when distance is a barrier. This includes realistic financial reimbursement for travel and accommodation costs incurred, and adequate outreach services to increase use of radiotherapy services when a facility is not located nearby.[28]

About 21% of the rectal cancer records contained insufficient information to determine cancer stage. This is a higher proportion than we found for colon cancer cases (14%), and is slightly higher than reported in a NSW study[29] and in United States data (based on Surveillance, Epidemiology, and End Results [SEER] data).[30] A higher percentage of patients with unstaged rectal cancer (compared with patients with colon cancer) has been found in other studies.[31] The main limitation with coding colorectal cancer stage using pathology reports is the lack of information on distant metastasis.[32] The stage-specific survival estimates in our study suggest that a large proportion of rectal cancers with unknown stage are likely to be fairly advanced at diagnosis. Using the sensitivity analyses for unknown stage, we found that the association between lower survival and increasing distance and time to reach a radiotherapy facility remained, irrespective of the assumptions made about the true distribution of cancer stages. It is possible that the broad grouping of stage into four categories could have resulted in residual confounding; however, on repeating the analysis using separate T, N and M stage descriptors the results did not change.

The strengths of our study include the use of population-based cancer registry data and GIS-based estimates of travel time (and distance) derived, in most cases, from exact street addresses. The limitations include a lack of knowledge of the type of treatment received. Furthermore, distance and time calculations were based on the closest radiotherapy facility, not the actual facilities at which patients received treatment. We were not able to quantify the extent to which these differed; however, distance from these centres was independently associated with survival. Finally, in using cause-specific survival, inaccuracies in cause of death coding may underestimate the true mortality attributable to the cancer.

It is possible that the association between distance from a radiotherapy facility and survival after rectal cancer is a result of currently unmeasured factors, which could relate to the demographic and socioeconomic characteristics of individuals, other clinical attributes of the cancer, or characteristics of patients' area of residence.[33] This possibility is strengthened by our finding of a significant correlation between survival estimates within the same category of area-level socioeconomic status. Further research is currently underway to look at the multilevel contribution of individual factors and geographical location on survival outcomes for patients with colorectal cancer in Qld.

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