



A review of the Rapid Response Radiotherapy Program in patients with advanced cancer referred for palliative radiotherapy over two decades

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Abstract

Introduction The Rapid Response Radiotherapy Program (RRRP) is an outpatient radiotherapy clinic for palliative cancer patients where consultation, planning, and radiation treatment can take place in 1 day, allowing for rapid access to care. The objective of this study was to compare the patient population and overall survival of patients seen in the RRRP from 2014 to 2017 to that of patients seen in 1999.

Method Patient characteristics including sex, primary cancer site, sites of metastases, and Karnofsky Performance Status (KPS) were recorded at each clinic visit. Date of death (DOD) was retrieved from the Patient Care System (PCS) and Excelicare. To show overall survival from the first clinic visit, a Kaplan-Meier overall survival curve was generated in all patients from 2014 to 2017.

Results Five hundred ninety-six patients were included in the final analysis. Most patients were male ($n = 347$) with a primary cancer site of the lung ($n = 165$) and metastases to the bone ($n = 475$). Actuarial median overall survival was 15.3 months. In 1999, 395 patients were analyzed, in which a primary of the lung ($n = 143$) and metastases to the bone ($n = 277$) were the most prevalent. An additional 72 patients in this population had brain metastases. The actuarial median survival of the 1999 population was 4.5 months.

Conclusion The changing patient population in the RRRP has resulted in visible changes in survival. This may reflect differences in the proportion of patients with specific primaries and sites of metastases, as well as improvements in the availability of palliative radiation over the last two decades.

Keywords Palliative care · Radiotherapy · Survival outcome · Primary cancer site · Sites of metastases

Introduction

The Rapid Response Radiotherapy Program (RRRP) was first created in 1996 by the Toronto Sunnybrook Regional Cancer Centre (TSRCC) in response to the increasing need for timely access to palliative radiation for patients with terminal cancer diagnoses [1]. The high demand for palliative radiation resulted in significant wait times in Ontario, with the median wait time rising from 5 to 7 weeks between 1993 and 2002, which

was longer than the Canadian Association of Radiation Oncologists' suggested maximum period of 2 weeks [2, 3]. As such, the RRRP was designed as a specialized radiotherapy clinic for palliative patients where they could have a consultation with their radiation oncologist, complete radiation planning, and begin radiation treatment within a day when possible, relieving patients of the need to make multiple visits over several weeks.

Since its inception, the demographics of the RRRP have continued to evolve, reflecting changes in patterns of practice and referral [1, 4]. The RRRP offers radiation for a broad spectrum of patients with advanced cancer. Similar palliative radiotherapy clinics have been put in place over the years, resulting in overall improvements in the accessibility of palliative care. The primary objective of this study was to compare the patient population and overall survival of patients seen in

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RRRP from August 2014 to March 2017 to that of patients seen in the RRRP in 1999 [4].

Methods

Patient population

The present population consisted of all patients referred to the RRRP between August 18, 2014, and March 31, 2017. All patients included had a pathologic or radiological confirmation of a cancer diagnosis with metastases.

Data collection

Patient characteristics (e.g., sex, primary cancer site, sites of metastases, and Karnofsky Performance Status (KPS)) were collected by clinical research assistants from individual medical records at each clinic visit. The patients' date of death (DOD) and date of last contact were retrieved from the Patient Care System (PCS) and Excelicare on February 1, 2018.

Statistical analysis

A Kaplan-Meier (KM) curve was generated to show overall survival of patients from their first clinic date. Patients who did not have an available DOD were censored at their date of last contact. All analyses were conducted using Statistical Analysis Software (SAS version 9.4 for Windows) and R package (version 3.4.2).

Results

Patient demographics are summarized in Table 1. From August 18, 2014, to March 31, 2017, a total of 729 were seen in RRRP, of which only 596 had available demographic information and were included in the prospective database. These 596 patients were included in the final analysis. The median patient age was 72 years, with ages ranging between 22 and 96. The majority of patients were male ($n = 347$, 58%) with a primary cancer site of the lung ($n = 165$, 28%), prostate ($n = 131$, 22%), or gastrointestinal (GI) tract ($n = 104$, 17%). The bone ($n = 475$, 80%), lung ($n = 150$, 25%), and liver ($n = 135$, 23%) were the most common sites of metastases. KPS scores were available for 586 patients, with median KPS being 60 (range 20–100). Most patients had a KPS score between 50 and 70 ($n = 255$, 43%). Due to the fact that the RRRP operates largely as an outpatient clinic, most patients were new patients referred to RRRP from other hospitals ($n = 330$, 55%).

Table 1 Patient demographics

	Patients in 2014–2017	Patients in 1999 [4]
Age (year)		
<i>N</i>	596	395
Median (interquartiles)	71.8 (62.8, 80.4)	68*
Range	21.5, 95.9	31.0, 93.0
Sex		
Male	347 (58.00%)	198 (50%)
Female	249 (42.00%)	197 (50%)
KPS		
<i>N</i>	586	395
Median (interquartiles)	60 (50, 80)	60*
Range	20, 100	10, 100
Primary cancer site		
Lung	165 (27.68%)	143 (36%)
Prostate	131 (21.98%)	56 (14%)
GI	104 (17.45%)	42 (11%)
Breast	92 (15.44%)	80 (20%)
Urinary system	50 (8.39%)	NS
Gynecological	11 (1.85%)	NS
Skin	9 (1.51%)	NS
Other	34 (5.7%)	74 (21%)
Sites of metastases		
Bone	475 (79.70%)	277 (70%)
Lung	150 (25.17%)	NS
Liver	135 (22.65%)	NS
Lymph	125 (20.97%)	NS
Brain	75 (12.58%)	72 (18%)
Other	106 (17.79%)	NS
Vital status at the time of analysis		
Alive/lost to follow-up	424 (71.14%)	74
Dead	172 (28.86%)	321

NS not specified, KPS Karnofsky Performance Status, GI gastrointestinal

*Interquartiles for age and KPS were not reported in the 1999 population

Of the 596 patients, 172 had retrievable DODs. Four hundred twenty-four patients were either alive or lost to follow-up at the time of analysis. The censor rate for the Kaplan-Meier curve was 71%. Overall survival probabilities at month 3 to month 36 are summarized in Table 2. The range of survival was between 0.01 and 40.23 months. The actuarial median survival time from the first clinic visit was 15.3 months (95% confidence interval 12.5–21.4 months), as determined from the Kaplan-Meier overall survival curve where the two dotted lines represent the 95% confidence interval and the thick line represents the overall survival curve (Fig. 1).

In 1999, 483 patients were seen in the RRRP, of which 395 had available demographic information [4]. There was an equal proportion of males and females ($n = 198$ and 197 respectively), with median age being 68 years (range 31–93).

Table 2 Overall survival from first clinic visit

Time	Overall survival (95% CI)
Actuarial median survival (95% CI)—KM estimates	15.3 months (12.5–21.4)
Actual median survival (95% CI)	2.1 months (1.7–2.7)
3 months	76.8% (72.6–81.1%)
6 months	68.9% (64.0–73.7%)
12 months (1 year)	57.1% (51.4–62.8%)
24 months (2 years)	39.9% (32.8–47.0%)
36 months (3 years)	29.3% (19.5–39.1%)

KM Kaplan-Meier, CI confidence interval

Similar to the present study, the lung ($n = 143$, 36%) was the most common primary. The subsequent most common primaries included the breast ($n = 80$, 20%) and prostate ($n = 56$, 14%). In the 1999 patient population, 277 (70%) and 71 (18%) patients had bone and brain metastases respectively. The actuarial median survival was 4.5 months (range 0 and 23.7 months), where 321 patients had a confirmed DOD and 74 patients were alive at the time of analysis. Overall, the actuarial median survival in the present study (15.3 months) was much longer than that of the 1999 patient population (4.5 months).

Discussion

The patient population from 2014 to 2017 demonstrated a greater median survival when compared to the patient population from 1999 (15.3 months vs. 4.5 months), which may reflect changes in the proportions of certain primary cancer sites and sites of metastases. A significant

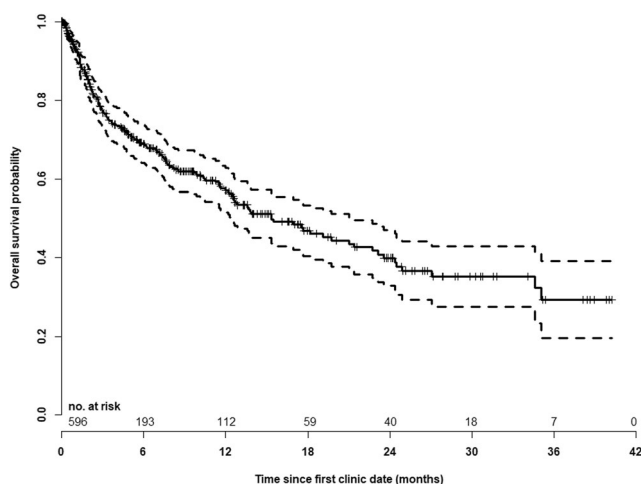


Fig. 1 Kaplan-Meier overall survival curve (thick line) in patients from 2014 to 2017 ($N = 596$) with the 95% confidence intervals (dotted lines)

correlation between survival and primary cancer site has been reported in the literature, with breast ($p = 0.002$) and colorectal ($p = 0.01$) primaries being correlated to longer survival in palliative cancer patients, whereas primaries such as the lung have been correlated to decreased survival length ($p < 0.0001$) [5]. While lung was the most common primary in both the 1999 population and the current patient population, the 1999 population had a greater proportion of patients with lung cancer (36% vs. 28%). As such, the present study may have had longer median survival due to the decreased proportion of lung cancer patients. Additionally, the present study had a greater proportion of patients with GI cancers (17% vs. 11%). Colorectal cancer has been shown to have favorable prognosis when compared to cancer of the lung, head and neck, or lymphoma, which may potentially provide rationale for the increased survival of the 2014–2017 patient population [5].

Sites of metastases have also been found to be correlated with survival, with a study by Wu et al. in stage IV breast cancer patients ($n = 7575$) finding metastases in the liver and brain to be significantly correlated to decreased survival ($p < 0.001$) when compared to bone or lung metastases [6]. Similar results have been reproduced in further studies, such as a survival analysis study by Gripp et al. which identified only brain metastases as significantly correlated to decreased survival ($p = 0.01$) [5]. An additional study by Chen et al. in metastatic breast cancer patients ($n = 4932$) found that patients with only bone metastases had greater longevity in comparison to other sites of metastases ($p < 0.001$) [7]. Improvements in survival from the 1999 population to the present population may reflect changes in patient characteristics concerning sites of metastases, where patients in the present study had a greater proportion of bone metastases (80% vs. 70%) and a slightly lower proportion of brain metastases (13% vs. 18%). The 1999 study of the RRRP patient population did not comment on the number of patients with liver metastases, which may have provided greater insight into these differences as metastatic lesions in the liver are correlated with decreased survival [4, 6]. Given the observed correlation between both primary cancer site and sites of metastases with overall survival, the consideration of these factors can have clinical usage in survival predictions and the determination of best treatment intent [5].

There has been a major decrease in the number of patients seen in the RRRP over successive years. From 1993 to 2003, 3290 patients were referred to the RRRP, averaging to about 548 patients per year [1]. Between August 18, 2014, and March 31, 2017, there were 729 patients referred to the RRRP, meaning approximately 243 patients were seen per year. This substantial decrease in patient referrals can largely be attributed to the increased number of palliative radiotherapy clinics now available in Ontario. For

example, the Princess Margaret Palliative Radiation Oncology Program based in Toronto and the Rapid Access Mets Program (RAMP) at the Juravinski Cancer Centre in Hamilton now provide rapid access to palliative radiation for a variety of symptoms related to advanced-stage cancer [8–10]. In Canada as a whole, there has been an increase in rapid access to radiation, such as the Tom Baker Cancer Centre in Alberta and the Cross Cancer Institute in Edmonton offering specialized palliative radiation clinics since 2002 and 2007 respectively [11, 12].

The majority of patients seen in the RRRP are treated for bone metastases, where the most common doses are 8 Gy in 1 fraction or 20 Gy in 5 fractions. The number of patients seen for painful bone metastases has been steadily increasing, with 70%, 77%, and 80% of patients having bone metastases in 1999, 2004, and 2014–2017 respectively [13].

The present analysis is limited by the number of patients with available DOD ($n = 172$), resulting in a high censor rate of 71%. The 1999 patient population had DOD available for the majority of patients ($n = 321$), providing substantially more accurate median survival than the present study. Additionally, liver metastases were not reported on in the 1999 patient population, thereby limiting comparisons.

Conclusion

Overall, the patient population in the RRRP has changed over the past 18 years, resulting in visible changes in survival outcome. The increase in patient survival from 4.5 months in the 1999 population to 15.3 months in the present population may reflect changes in the proportion of certain primaries and sites of metastases as well as improvements in the availability of palliative radiotherapy services over the last two decades.

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Compliance with ethical standards

Conflict of interest The authors declare that there are no conflicts of interest.

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