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Palliative RT in rectal cancer

Efficacy of palliative radiation therapy for symptomatic rectal cancer

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ABSTRACT

99 patients with symptomatic locally advanced rectal cancer who were treated with palliative radiation alone were reviewed. Dose-fractionation ranged from 18 to 54 Gy. Response rate ranged from 62.5 to 86.7%, with a median response duration ranging 4.2–5.4 months. Median survival was 6.9 months. Using a BED cut-off of $39Gy_{10,}$ no dose–response relationship was found.

Locally advanced rectal cancer is frequently associated with significant morbidity [1]. Up to 25% of patients have distant metastases at presentation [2]. In patients who are treated with curative intent, up to 15% eventually develop a pelvic recurrence [3–7].

Studies on the efficacy of radiation therapy alone for the palliation of symptoms arising from locally advanced rectal tumours are mostly based on patients who were treated in the 1970s through to the early 1990s using old techniques such as field-based planning without conformal shielding, and often used cobalt sources which is rare in modern times [8].

We report the outcome of 99 patients with locally advanced or metastatic rectal cancer who were treated with palliative radiation therapy alone using modern 3D conformal radiation therapy.

Methods and materials

Patients with symptomatic locally advanced or recurrent rectal cancer who were treated with palliative radiation therapy alone at The National Cancer Institute of Singapore Radiation Therapy Centers, Singapore (The National University Hospital and Tan Tock Seng Hospital) were retrospectively reviewed. Eligibility criteria included patients who had symptomatic, biopsy proven rectal cancer and treated with palliative radiation therapy alone. Patients required at least one index symptom such as pain, bleeding, or obstruction. All patients received external beam RT only. Patients who received concurrent chemotherapy were excluded. Factors reviewed included patient demographics (age, gender, performance status), tumour details (stage, size, histology), and RT parameters (field size, whether computed tomography [CT] planned/not planned, total dose, dose fractionation regimens, field arrangements). All treatment planning was done by computerised tomography. Gross tumour volume (GTV) encompassed the rectal tumour with or without the involved regional lymph nodes. Planning target volume included the GTV with a margin of 1–2 cm. 6 or 10 MV photons were employed using a linear accelerator. Conformal shielding was applied using a multi-leaf collimator.

Patients were reviewed 1-month post-treatment. For patients with bleeding as the index symptom, a response was scored if haematochezia resolved and haemoglobin was maintained with no further transfusions required. For patients with pain as the index symptom, a response to RT was scored when they had decreased pain or decreased analgesia (or the same degree of pain but decreased analgesia). For patients with obstruction as the index symptom, a response was scored if constipation was improved or resolved, or if there was a decrease in the usage of laxatives.

All patients were reviewed on a weekly basis while on radiation therapy to detect any acute toxicities. Late toxicities were recorded at post-treatment visits. The Common Toxicity Criteria version 3.0 was used.

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Duration of response was defined as the time from initial response to radiation therapy until disease progression or death. The duration of symptom relief and survival time from RT was determined for each patient. The ratio between this duration of symptom relief and survival multiplied by 100 was designated "percent net symptom relief". This represented the percentage of the remaining patient's life after RT that was spent with relief of the index symptom, without need for further treatment. Survival time after treatment was also recorded. Statistical analyses were performed using STATA version 11.0 (StataCorp 2009. Stata Statistical Software: Release 11. College Station, TX: StataCorp LP).

Study end points included symptom response (including response rates, duration of response), median survival, and treatment toxicity. To investigate for a dose–response relationship, patients were grouped according to radiation therapy doses. The biologically effective dose (BED) was calculated using a tumour α/β ratio of 10. The median BED was $39Gy_{10}$; this corresponded to a dose fractionation regimen of 30 Gy in 10 fractions. Patients were divided into two subgroups using the median BED. Patients in the higher BED subgroup were compared to those in the lower BED group using the Fisher's exact test. The Kaplan–Meier method was used to draw the time to event curve. Cox proportional hazard regression was used to analyse the relationship between variables and outcomes. A p-value of less than 0.05 (two-sided) was considered to indicate statistical significance.

Results

A total of 99 patients were reviewed. As some patients had two or more symptoms, the total number of index symptoms included for analysis was 120. Median age was 74 years (range 32–97 years). The median follow-up duration was 6.9 months.

67 patients presented with bleeding alone, 13 patients with pain alone, and 1 patient with obstruction alone as the index symptom. 18 patients had a combination of these symptoms. All patients received RT alone without chemotherapy as the primary palliative treatment modality. Dose-fractionation regimen ranged from 18 Gy in 6 fractions to 54 Gy in 30 fractions. The most prevalent fractionation scheme was 30 Gy in 10 fractions delivered at 3 Gy per fraction, 5 fractions per week.

Relief from bleeding

83 patients presented with bleeding (with or without pain or obstruction). 86.7% of these patients (72/83) responded to radiation therapy. The median duration of response among those who responded to radiation therapy was 5.4 months (range 0–29.4 months). The mean percent net relief was 91.4%. This meant that for patients with bleeding who responded to radiation therapy, the bleeding did not recur for 91.4% of their remaining lifespan and no further treatment was required. 7 patients did not benefit from treatment, while 1 patient defaulted on treatment.

Relief from pain

29 patients presented with pain (with or without bleeding or obstruction). 79.3% of these patients (23/29) responded to radiation therapy. The median duration of response among those who responded to radiation therapy was 4.5 months (range 0–12 months). The mean percent net relief was 84.8%. 4 patients did not benefit from radiation therapy.

Relief from obstruction

8 patients presented with obstruction (with or without bleeding or pain). 62.5% of these patients (5/8) responded to radiation therapy. The median duration of response among those who responded to radiation therapy was 4.2 months (range 0–12 months). The mean percent net relief was 80.3%. 1 patient did not respond to radiation therapy. 1 patient underwent surgery for obstruction and another patient underwent surgery for creation of a colostomy.

Overall, the median survival of patients treated palliatively for advanced or recurrent rectal cancer was 6.9 months (range 0–33 months). Actuarial 12-month survival was 30.6%. The Kaplan–Meier survival curve for all patients is shown in Fig. 1.

To investigate for the presence of a dose–response relationship, patients were divided into 2 subgroups: one receiving a BED of $39Gy_{10}$ (high BED group) or greater and one receiving a BED of less than $39Gy_{10}$ (low BED group). No dose–response relationship was identified (Table 1).

Univariate and multivariate Cox regression was used to identify any prognostic factors (such as patient's age, radiation dose,

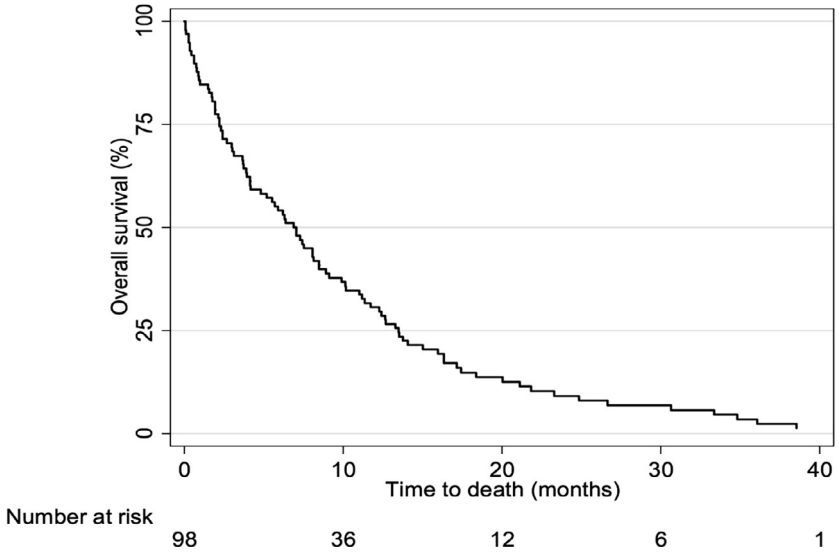

Fig. 1. Kaplan–Meier survival curve for all patients ($n = 99$).