Palliative radiotherapy

30 day mortality in adult palliative radiotherapy – A retrospective population based study of 14,972 treatment episodes

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Background: 30-day mortality (30DM) has been suggested as a clinical indicator of the avoidance of harm in palliative radiotherapy within the NHS, but no large-scale population-based studies exist. This large retrospective cohort study aims to investigate the factors that influence 30DM following palliative radiotherapy and consider its value as a clinical indicator.

Methods: All radiotherapy episodes delivered in a large UK cancer centre between January 2004 and April 2011 were analysed. Patterns of palliative radiotherapy, 30DM and the variables affecting 30DM were assessed. The impact of these variables was assessed using logistic regression.

Results: 14,972 palliative episodes were analysed. 6334 (42.3%) treatments were delivered to bone metastases, 2356 (15.7%) to the chest for lung cancer and 915 (5.7%) to the brain. Median treatment time was 1 day (IQR 1–7). Overall 30DM was 12.3%. Factors having a significant impact upon 30DM were sex, primary diagnosis, treatment site and fractionation schedule (p < 0.01).

Conclusion: This is the first large-scale description of 30-day mortality for unselected adult palliative radiotherapy treatments. The observed differences in early mortality by fractionation support the use of this measure in assessing clinical decision making in palliative radiotherapy and require further study in other centres and health care systems.

Keywords: Palliative radiotherapy; Clinical indicator; Fractionation

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Abstract

Half of all radiotherapy treatment episodes in England in 2012 were delivered with palliative intent (65,580 episodes) [1]. Palliative radiotherapy is widely used to relieve symptoms from either the primary tumour or sites of metastatic disease in advanced cancer. Clinical trials have demonstrated that hypofractionated treatment provides equivalent symptomatic benefit to longer courses, with limited toxicity [2]. The decision to fractionate treatment, with increased acute toxicity and treatment burden, is sometimes made when it is considered necessary to relieve symptoms or with the aim of durable disease control, although the evidence base for this approach is limited. The balance between symptomatic benefit and the opportunity costs associated with excessive interventions must, therefore, be carefully considered and studied.

Many factors may influence the decision to offer and to fractionate palliative radiotherapy. These include the performance status of the patient, anatomical site of disease, primary diagnosis, co-morbidity, age, access to a clinical oncology opinion, travelling time to the treatment centre, clinician specific factors (including financial incentives) and the estimated life expectancy of the patient [3]. However many of these factors are not prospectively recorded in national datasets.

Studies have shown that oncologists are poor at predicting survival of patients with advanced cancer with a tendency to be overly optimistic [4,5]. This may expose terminally ill patients to the burden of longer fractionated courses of radiotherapy [5,6]. Such overly aggressive cancer care at the end of life has a detrimental effect on quality of life and has previously been suggested as a quality of care issue [7,8]. Conversely, fear of over treatment amongst medical colleagues has also been cited as a possible factor reducing access to palliative radiotherapy [9].

The palliative intent of treatment in patients with symptoms of advanced cancer means it is inevitable that early mortality due to disease progression will occur in some patients. The NHS policy document, ‘Improving outcomes: A strategy for cancer’, proposed mortality within 30-days of treatment (a commonly used metric in other health interventions) as a clinical indicator to assess the...
avoidance of harm in palliative radiotherapy [10]. Early, US based, studies examining 30-day mortality (30DM) in palliative radiotherapy showed significant mortality in some groups [11,12], but no large population-based studies have been reported. These studies do not consider the relationship between fractionation and outcomes, focussing on access to treatment. Prognostic models for life expectancy amongst the general cancer population [13,14] and specifically death within 30 days of palliative radiotherapy [15] have recently been published. However these are not used in routine clinical practise.

Alongside the need to ensure avoidable harm is minimised, there is a need for global healthcare systems to justify treatments in terms of value for money. Excessive fractionation may be considered in both these contexts (hypofractionation being increasingly advocated in the USA) [16]. Measures which can aid the assessment of the appropriateness of treatment are, therefore, needed.

The use of 30DM as a clinical indicator for the avoidance of harm, through appropriate patient selection, in palliative radiotherapy has not previously been demonstrated. This study investigated the rate of 30DM following palliative radiotherapy in a single cancer centre serving a population of 2.8 million over a 7 year period and considered its value as a clinical indicator.

Methods

All radiotherapy episodes delivered in a large UK cancer centre (Leeds Cancer Centre), between January 2004 and April 2011, were identified using the electronic patient record system (Patient Pathway Manager (PPM)). PPM collates and prospectively integrates electronic information on all cancer patients treated within the centre; patient (date of birth and sex) and treatment information (date of treatment, planned fractionation, dose, intent of treatment and site of treatment) were extracted for this analysis.

These data were then linked to the cancer registrations held by the National Cancer Registration Service (Northern and Yorkshire) and diagnostic, death and socioeconomic status (SES) information was extracted for all linked records. SES was categorised on the basis of rank quintile of deprivation score (Index of Multiple Deprivation (IMD), ONS 2010 version) [17], for the Lower Super Output Area (population defined geographical region of approximately 1500 people [18]) the patient lived in at diagnosis.

Leeds Cancer Centre (LCC) is a university affiliated centre serving a population of 2.8 million. The number of clinical oncologists increased from 18 to 30 during the study period. All oncologists are site specialised to a maximum of three primary diagnostic groups and are trained in the use of palliative radiotherapy. LCC is resourced through a national NHS tariff system where the reimbursement of the centre reflects the complexity of treatment planning and separately the number of fractions with complexity of treatment delivery. LCC were early adopters of the evidence supporting hypofractionation within palliative radiotherapy. Throughout the study period treatment has been delivered within well-defined clinical protocols e.g., palliative radiotherapy for uncomplicated bone metastases is delivered as a single fraction unless there is clear justification for a fractionated high dose approach. Departmental clinical protocols and a robust electronic patient record allow the study cohort to be defined.

Definition of palliative intent

Treatment intent was identified as palliative by the treating clinician (centre policy) or if delivered in less than five fractions (exceptions to this were identified e.g., stereotactic body radiotherapy). The site treated was allocated as bone, brain, chest, soft tissue (e.g., treatment to the chest for oesophageal cancer), or unknown on the basis of the treatment site protocol (a free text field entered at the time of treatment), the diagnosis and intention of treatment.

In order to limit this investigation to adult palliative radiotherapy treatments, for solid organ tumours and to ensure data quality, a number of exclusions were made (Fig. 1). Radical treatments (24,516), episodes with incomplete data (540), treatments for benign diagnoses (37), non-melanomatous skin cancer (196) and haematological diagnoses (901) were excluded. Within the centre patients under the age of 25 are treated within the paediatric and young adolescent practice, 96 episodes delivered to this group were also excluded. Where multiple palliative treatments were delivered with the same start date, these were amalgamated into a single record (having been related to a single clinical decision). The fractionation allocated to this event was the largest of the concurrent treatments, this being the more significant clinical decision. 1534 episodes were amalgamated with another record in this way and considered as a single episode. Where overlapping treatment episodes were delivered with differing start dates it is not possible to know if these relate to a single clinical decision. For clarity these were considered separately.

The primary diagnosis was categorised into seven groups based on the most commonly occurring tumours. The major primary diagnoses were lung, breast, prostate, colorectal, bladder and oesophagus, with a separate category, ‘other’, consisting of all other cancer diagnoses and those patients with multiple, non-coincident diagnoses.

30-day mortality and survival

The proportion dying within 30-days from treatment start was assessed for all treatments within the cohort and by numbered courses in relation to fractionation delivered, primary diagnosis and site treated. The Chi-squared test was used to assess the impact of various factors upon early mortality. A logistic regression model was used to investigate the factors associated with death within 30-days of the start of palliative radiotherapy. The dependent variable, death within 30-days, was considered as a binary outcome. Covariates (explanatory variables) in the model included, age at start of radiotherapy, sex, socioeconomic status, site of the primary tumour, site of irradiation, fractionation pattern and year of treatment.

Survival was calculated from the start of each palliative radiotherapy episode to date of death or when censored (30th April 2012). The start date of treatment was used as it is closer to the clinical decision to treat than the end of treatment and provides a uniform time point across all fractionation regimens, aligning with NCEPOD systemic therapy methodology [19]. As individuals who underwent multiple sequential treatment episodes had, by definition, to survive all previous treatments and to ensure people could not enter survival analyses twice the univariate logistic regression model and illustrative Kaplan–Meier survival curves were produced based on first and second treatment episodes separately. Multivariate analysis considered only the first treatment episode. Univariate logistic regression was also carried out for all treatment episodes combined, this overall analysis is likely to be a closer reflection of the measure as applied in future, on a population level; including every clinical decision within the cohort. Statistical analyses were carried out using STATA IC 13.

Results

42,792 radiotherapy treatment episodes were identified. Within this a total of 18,275 palliative treatment episodes, delivered to 12,240 individuals, were identified. Of these, 3303 (18.1%) episodes