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## Review

## Palliative radiotherapy for locally advanced non-metastatic head and neck cancer: A systematic review

Muhammad Shahid Iqbal<sup>a,\*</sup>, Charles Kelly<sup>a</sup>, Josef Kovarik<sup>a</sup>, Bojidar Goranov<sup>b</sup>, Ghazia Shaikh<sup>a</sup>, David Morgan<sup>c</sup>, Werner Dobrowsky<sup>a</sup>, Vinidh Paleri<sup>d</sup>

<sup>a</sup> Department of Clinical Oncology, Northern Centre for Cancer Care, The Newcastle upon Tyne Hospitals NHS Foundation Trust; <sup>b</sup> Department of Clinical Oncology, Derriford Hospital, Plymouth; <sup>c</sup> Department of Physics, Northern Centre for Cancer Care, The Newcastle upon Tyne Hospitals NHS Foundation Trust; and <sup>d</sup> The Royal Marsden NHS Foundation Trust, London, United Kingdom

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## ABSTRACT

**Objectives:** The objective of this systematic review was to identify and appraise the existing evidence of role of palliative radiotherapy for locally advanced non-metastatic head and neck cancer. **Methods:** A systematic search of the literature was conducted using Medline, Embase and Cochrane databases and relevant references were included. **Results:** Literature search revealed a wide variation in dose fractionation regimens. Reported outcomes showed high efficacy and low rate of significant side effects, except in studies utilising higher doses of radiotherapy where higher grade toxicities were seen. Reported median overall survival was in the range of 3.3–17 months, but most studies reported median survival of around 6 months. **Conclusions:** The choice of palliative radiotherapy varies significantly. This is in contrast to regimens of curative radiotherapy for locally advanced head and neck cancer, which are well standardised. Given the reported relatively short overall survival of this patient group, an ideal treatment should be of the shortest possible duration whilst ensuring effective palliation and minimal side effects. Future well designed trials are needed to evaluate quality of life and duration of side effects in addition to survival and severity of toxicities in this group of patients.

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Head and neck squamous cell carcinoma (HNSCC) is the fifth most common malignancy worldwide with an estimated global incidence of over half a million [1]. Fifty to seventy per cent of the patients present at advanced stage and a significant proportion of the patients are not candidates for curative therapy mainly because of advanced stage, co-morbidities, poor performance status or patient choice [2–4]. In this situation, the five-year survival even with aggressive treatment is less than 20%, with a median survival of about 6 months in studies with the largest number of patients [3–6]. In highly selected patient groups with a good response to initial treatment and with good tolerance to concomitant chemotherapy, the median survival can reach up to 12 months [2,7,8]. Best supportive care alone is associated with a median survival in the range of between 3 and 4 months [9].

Much of the clinical research into the management of HNSCC focuses on curative treatment. High quality data from large randomised trials and meta-analysis are available resulting in

formulation of consensus guidelines [10]. Radical radiotherapy or radio-chemotherapy of the head and neck cancer is a lengthy, highly toxic treatment with mortality rate up to 2% [11]. Therefore, shorter less intense regimens have been sought in patients where palliation is the main goal. However, little high level evidence is available about the outcomes of palliative radiotherapy in HNSCC.

Hypofractionated palliative radiotherapy is often used and evidence of effectiveness has come from retrospective institutional studies or small phase II trials [2,4,12–16]. These studies indicate that such treatment may be effective but assessments of quality of life vary considerably. Nonetheless, these studies indicate that palliative radiotherapy can improve speech, swallowing, breathing and pain [5,17–20].

We conducted a systematic review of the literature to identify the current evidence base to guide recommendations regarding optimal regimens of palliative radiotherapy of HNSCC.

## Methods

Published data for this review were identified by searching the PubMed-MedLine, EMBASE database and Cochrane library from

\* Corresponding author at: Department of Clinical Oncology, Northern Centre for Cancer Care, Freeman Hospital, Freeman Road, Newcastle upon Tyne NE7 7DN, United Kingdom.

E-mail address: shahid.iqbal@nhs.net (M. Shahid Iqbal).

1996 until present (date of search was 16th October 2016) with the following Medical Subject Heading (MeSH) terms: 'head and neck cancer', 'radiotherapy', 'palliation, and 'quality-of-life' using BOOLEAN search algorithms. The following key words were also used: 'palliative radiotherapy', 'palliative therapy', 'head-and-neck cancer', 'head and neck neoplasm', 'HNSCC'. A professional librarian conducted the systematic search and two authors (MSI and JK) went through the list to identify the suitable studies. All pertinent articles were retrieved and selected studies were considered for this review. One author (MSI) collected the literature data and another author (BG) checked it over for quality assurance. Two authors (MSI and VP) carried out quality assessment of the selected studies using NIH quality assessment tool for observational cohort and cross-sectional studies [32]. Any discrepancy between author's assessments was resolved by mutual discussion.

## Results

The literature search identified 197 papers, from which 24 were selected after meeting the inclusion criteria (Diagram 1). Out of 24 selected studies, none were randomised phase III studies, only four were phase II prospective trials and the remaining were a combination of prospective, retrospective institutional studies. Patient numbers in each study ranged from 15 to 505, with a median sample of 55.

The study end points and the study cohort were heterogenous and therefore we conducted a quality assessment procedure using a validated tool (Table 2). The most frequent deficiencies were noted in reporting of (a) sample size justification, power description, or variance and effect estimates (23 of 24 studies), (b) measurement and adjustment of potential confounding variables for impact on relationship between exposure and outcomes (21 of 24 studies) and (c) clearly defined, valid, reliable, and consistently implemented outcome measures (dependent variables) across all study participants (9 of 24 studies).

Palliative care outcome variables differed between studies thus limiting comparisons, but all studies showed that palliative radiotherapy was effective for the management of symptoms related to advanced head and neck cancer. From the available studies, reported median overall survival was in the range of 3.3–17 months, but most studies reported median survival of around 6 months.

Since the year 1996, the literature review revealed a significant variation in treatment worldwide and in the quality of studies conducted and therefore the standard of care cannot be ascertained on the basis of these data.

The findings of the literature search are summarised in Table 1 (in descending chronological order with respect to year of publishing). The quality assessment for the selected studies is summarised in Table 2.

## Discussion

There is no firm evidence base to recommend a specific palliative radiotherapy regimen. A wide range of palliative radiotherapy regimens have been utilised in the treatment of advanced HNSCC. This systematic review summarises the palliative radiotherapy schedules for head and neck cancers.

Patients with advanced head and neck cancer and good performance status may benefit from more intensive regimens as tumour response and control is dose dependent [12]. However, conventional fractionation with 6–7 weeks treatment may not be ideal because of short overall survival and a greater risk of significant side effects. The largest series report median survival in the range of 5–7 months [5,6]. Available data suggest that the response and palliative effect is dose related – Corry et al. with the Quad Shot regimen reported improvement in 44% of patients and this increased in the group who received the full 3 courses (63%) [14,20,21]. Porceddu et al. in a phase II study of 36 Gy in 6 fractions reported improvement in 62% of patients [16]. Agarwal et al. treated 110 patients with

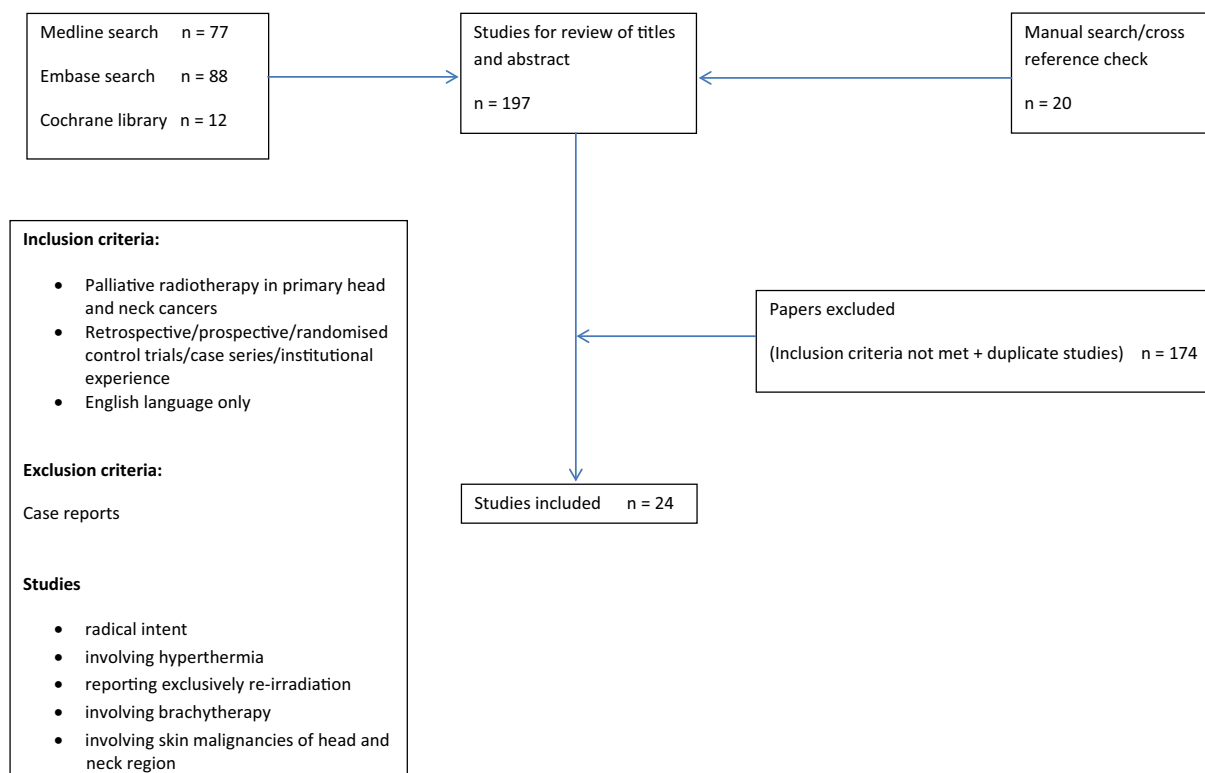


Diagram 1. The flow chart of systematic search.

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