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Original Article

Experience of Definitive Chemoradiation for Oesophageal Cancer Within a Large Regional Cancer Treatment Centre: Improving Outcomes and Tolerability

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Abstract

Aims: To review delivery of definitive chemoradiation (dCRT) for patients with oesophageal cancer within a large regional cancer centre. To assess toxicity, tolerability and outcomes and compare with published data.
Materials and methods: A retrospective review of patients undergoing dCRT between November 2009 and November 2014 was carried out. Data were collected regarding treatment completion, radiotherapy plans, toxicity, failure and death. Kaplan–Meier survival curves with a Log-rank test for significance were used for survival analysis.
Results: In total, 179 patients were analysed. The median age at diagnosis was 70 years. Forty-four (24.6%) patients had T1 or T2 tumours, 113 (63.1%) T3 and 18 (10.1%) T4; 117 (65.4%) patients were node positive on initial staging. One hundred and forty patients were treated before 2012 with CRT and two adjuvant cycles of cisplatin and capecitabine. Of these, only 50% completed both adjuvant cycles of chemotherapy. Thirty-nine patients were treated after 2012 with neoadjuvant cisplatin and capecitabine followed by CRT. Of these, 92% completed all planned chemotherapy. Ninety-five per cent of patients completed radiotherapy without interruption, but only 46% completed concurrent capecitabine. The mean planning target volume (PTV) length was 13 cm (range 6.9–22.2 cm) and 27 (15%) patients had a PTV length greater than 16 cm. After a median follow-up of 19.6 months (range 3.0–71.9), 83 patients (46%) had relapsed, with 43 (24%) patients having isolated locoregional recurrence. The median overall survival was 26 months (95% confidence interval 20.2–31.8) with a 5 year overall survival rate of 19.7% (95% confidence interval 10.4–31.2).
Conclusions: Our series shows comparable survival rates with published data despite an unselected population. The transition to neoadjuvant chemotherapy before CRT has improved tolerability and increased rates of completion of treatment. The locoregional failure rate remains significant and strategies for improving this, such as changing the chemotherapy back bone and radiation dose escalation, are eagerly awaited within the SCOPE-2 study.

Key words: Chemoradiation; oesophagus; outcomes; toxicity

Introduction

Oesophageal cancer is the 13th most common cancer in the UK, with 57% of cases diagnosed in people over 70 years of age. Five year overall survival has only marginally improved over the last 40 years and in 2010–2011 was 15.5% for all stages of disease [1].

Surgery remains the mainstay of curative treatment and in 2012–2014, 23% of patients underwent surgical resection [2]. This relatively low proportion is a reflection of late presentation of disease, advancing age at diagnosis and medical inoperability due to comorbidity. In patients with non-metastatic disease, definitive chemoradiation (dCRT) is an alternative to perioperative chemotherapy and surgery. In the UK, localised resectable squamous cell carcinoma has been increasingly treated by dCRT, whereas for adenocarcinoma, dCRT has been reserved for those unfit for surgical resection or due to the extent of locoregional disease.

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There have been few large prospective case series published looking at dCRT. One large case series (266 patients) of experience in southeast Wales was published in 2011. This found a median overall survival of 20.6 months and a 5 year survival rate of 19.5% in patients treated with dCRT [3]. The review crossed a time period when treatment changed from infusional 5-fluorouracil chemotherapy to oral capecitabine and the introduction of single-phase radiotherapy using a three or four beam approach.

Subsequently, the UK multicentre SCOPE-1 trial published in 2013 standardised dCRT protocols and introduced radiotherapy planning guidelines. It also switched treatment sequence from adjuvant cycles of chemotherapy to neoadjuvant. The trial closed early to recruitment as criteria for futility were met and no benefit was seen from the addition of cetuximab to standard treatment. However, there was a reported median overall survival of 25.4 months in those receiving standard treatment [4]. These outcomes exceeded some previously reported phase III trials of neoadjuvant chemotherapy and surgery.

More recently, a retrospective review of 235 patients treated with dCRT or radiotherapy alone in Glasgow reported a median overall survival in patients receiving dCRT (190 patients) of 37 months compared with 25 months for those receiving radiotherapy alone ($P = 0.01$). They commented that the improvement in overall survival compared with previously published series may be a reflection of improved patient selection as a result of modern staging and advances in radiotherapy techniques [5].

Since the introduction of a specialist upper gastrointestinal cancer multidisciplinary team in Greater Manchester in 2009, selected patients with localised disease considered not suitable for surgery have been offered dCRT at the Christie Cancer Centre. Here we report the results from our series of 179 patients treated in this way.

Materials and Methods

A retrospective analysis of all patients treated with dCRT (defined as 50 Gy/25 fractions with concurrent cisplatin and 5-fluorouracil) between November 2009 and November 2014 was conducted. Patients were identified from a prospectively maintained database. A total of 200 patients received treatment during this time. Twenty-one patients were excluded from the analysis as they were either staged as M1a disease initially (TNM 6 classification including upper third primary with cervical lymph nodes or lower third primary with coeliac nodes) [6], were receiving treatment for postoperative recurrence or received a weekly carboplatin and paclitaxel-based chemotherapy regimen.

All cases were discussed and the treatment plan agreed in a specialist upper gastrointestinal cancer multidisciplinary meeting. All patients underwent endoscopy and biopsy to provide histological confirmation. Where possible, patients were staged with positron emission tomography–computed tomography scan (PET–CT). Endoscopic ultrasound (EUS) formed part of the standard staging. Where EUS was not possible, radiological staging was accepted. Staging laparoscopy was recommended in patients with lower third or gastro-oesophageal junction (GOJ) tumours. There was no upper limit to the length of primary tumour and any involved node(s) identified. dCRT was offered where radiotherapy planning constraints could subsequently be met. Where planning constraints could not be met, patients went on to receive lower dose palliative radiotherapy or palliative chemotherapy and were excluded from this analysis. Most patients had formal assessment of renal function with nuclear medicine EDTA glomerular filtration rate (GFR). There was no routine access to a specialist dietician in the cancer centre, although most patients were linked in to their community dietician. The local policy was to arrange a feeding gastrostomy (favoured method as a radiologically inserted gastrostomy) if the patient had an O'Rourke dysphagia score [7] of 3 or greater (blending food and pureed diet) or had ongoing dysphagia with more than 10% weight loss from their baseline.

Initially between 2009 and 2012, treatment consisted of two cycles of cisplatin 75 mg/m^2 3 weekly and capecitabine 625 mg/m^2 BD for 5 weeks concurrent with radiotherapy. This was followed by two cycles of adjuvant chemotherapy with cisplatin 75 mg/m^2 and capecitabine 625 mg/m^2 for 21 days. Some patients in this time period received neoadjuvant chemotherapy with the addition of epirubicin while on the surgical management pathway, but were later deemed unsuitable for surgery. After the introduction of the SCOPE-1 protocol and subsequent publication, local protocols changed to giving two neoadjuvant cycles of chemotherapy followed by the concurrent CRT [4].

Patients were scanned supine with either arms above the head and immobilised on a lung board for middle or lower third patients or with arms by their side and immobilised with a five-point thermoplastic shell for upper third patients or where nodal disease was proximal to aortic arch. A three-dimensional scan was acquired with slice thickness of 5 mm before 2012 and then changed to a 3 mm interval thereafter. Intravenous contrast was used at the time of scanning and images were loaded on to the Pinnacle treatment planning system (Philips Healthcare™). Gross tumour volume (GTV) was defined using information from the staging PET scan, endoscopic information from EUS and the planning computed tomography scan. The clinical target volume was defined to include a 2 cm length of oesophagus superiorly and inferiorly up to GOJ and expanding this volume by 5 mm radially. Where disease extended inferiorly beyond the GOJ, a total of 2 cm from the GTV was contoured along the line of the cardia and lesser curve of stomach including the gastro-hepatic space. A final expansion of 1 cm in all directions was used to construct the planning target volume (PTV).

The prescribed radiotherapy dose to the isocentre was 50 Gy in 25 daily fractions over 5 weeks. Up until 2011 this was delivered with a standard forward planned four-field beam arrangement in a single phase. From 2011 onwards, seven equidistant beams were employed using inverse planning and single segments per beam. Intensity-modulated radiotherapy was allowed where organ at risk doses were high to keep within departmental tolerances,

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