Clinical Oncology 27 (2015) 536–541

Contents lists available at ScienceDirect

Clinical Oncology

journal homepage: www.clinicaloncologyonline.net

Original Article

Acute and Late Bowel Toxicity in Radiotherapy Patients with Inflammatory Bowel Disease: A Systematic Review

D. Tromp *†, D.R.H. Christie ‡§

* Gold Coast University Hospital, Southport, Queensland, Australia
† Griffith University Gold Coast Campus, Southport, Queensland, Australia
‡ Genesis CancerCare Queensland, Tugun, Queensland, Australia
§ Bond University, Robina, Queensland, Australia

Received 5 February 2015; received in revised form 17 April 2015; accepted 4 May 2015

Abstract

Aims: Inflammatory bowel disease has traditionally been considered a relative contraindication for radiotherapy due to a perceived increased risk of disease exacerbation and bowel toxicity. The aim of this review was to evaluate the current literature regarding rates of radiotherapy-induced acute and late bowel toxicity in patients with inflammatory bowel disease and to compare these data with those of patients without the disease.
Materials and methods: An Ovid Medline search was conducted to identify original articles pertaining to the review question. Using the PRISMA convention a total of 442 articles screened, resulting 8 articles which were suitable for inclusion in the review.
Results: In general, the grading of toxicity was scored using either the Radiation Therapy Oncology Group or Common Terminology Criteria for Adverse Events scoring systems. It was found that acute bowel toxicity of $\geq$ grade 3 occurred in 20% of patients receiving external beam radiotherapy (EBRT) and in 7% of patients receiving brachytherapy. Late bowel toxicity $\geq$ grade 3 occurred in 15% of EBRT patients and in 5% of patients receiving brachytherapy. Brachytherapy was shown to have similar rates of toxicity and EBRT produced a moderate increase in both acute and late toxicity when compared with individuals without inflammatory bowel disease.
Conclusion: In view of these results, we suggest that brachytherapy should be considered as a suitable treatment option for treating pelvic malignancy in patients with inflammatory bowel disease, whereas EBRT should be used with caution.

Key words: Bowel toxicity; brachytherapy; inflammatory bowel disease; radiotherapy

Introduction

Ulcerative colitis and Crohn's disease are idiopathic inflammatory diseases involving the gastrointestinal tract. Collectively they are termed inflammatory bowel disease (IBD) and typically have a relapsing and remitting clinical course. Epidemiologically, the peak age of onset is between 15 and 30 years of age, affecting as many as 1.4 million people in the USA and 2.2 million in Europe [1]. Crohn's disease is characterised by transmural inflammation typically involving the terminal ileum and colon, but can affect any part of the gastrointestinal tract, producing skip lesions. Ulcerative colitis is characterised by mucosal inflammation, which always involves the rectum, with possible extension into the colon. The cause of IBD has not been precisely explained, but it is largely thought to result from a dysregulated mucosal immune response to environmental factors in susceptible patients [2]. IBD has historically been associated with increased risk of colorectal cancer, which has been thought to be associated with longstanding chronic inflammation [3], although recent data show that this risk is reducing, probably secondary to better control of intestinal inflammation [4]. In addition, an increased risk of extra-intestinal malignancies such as lung, skin, urinary bladder, liver-biliary cancer and leukaemia have been described and may have some relation to the use of thiopurines and monoclonal antibody therapies [5]. Despite increased rates of malignancy in IBD sufferers, there has been a historical reluctance to consider radiotherapy as part of the treatment for cancer in these patients. This is

Author for correspondence: D. Tromp, 37 Mitchell Ave, Molendinar, Queensland, 4214, Australia. Tel: +61-409-643-212.
E-mail address: dirktromp@gmail.com (D. Tromp).

http://dx.doi.org/10.1016/j.clon.2015.05.001
0936-6555/

probably due to the perceived risk of further aggravating the underlying mucosal inflammatory processes, and has therefore labelled IBD as a relative contraindication for radiotherapy. The aim of this review was to analyse the current literature to answer the question of whether radiotherapy causes increased rates of acute and late bowel toxicity in patients with IBD.

Materials and Methods

An Ovid Medline (1946 to February 2015) search was conducted to identify original study articles pertaining to the question of whether radiotherapy caused increased rates of gastrointestinal toxicity in patients with IBD. The search terms used were radiotherapy OR radiation therapy OR brachytherapy AND inflammatory bowel disease OR Crohn's disease OR ulcerative colitis AND toxicity. This produced 439 results, with a further three studies found by hand-searching. After initial screening, 12 studies were identified that were relevant to the review question. Four of the studies were excluded from the review: one article had a sample size of only two patients, one was a personal view article, one study was presented at a conference but the results were not published and the last article was a review that had only evaluated a small number of older case series. This process followed the PRISMA convention [6] and is summarised in Figure 1.

Results

Eight trials in total were included in the review. The demographics of each study are summarised in Table 1. The total number of individuals across the studies was 144, with ulcerative colitis sufferers making up around 60% of participants. There were significantly higher numbers of men across the studies, which was probably due to increased representation of prostate cancer among these groups. Five studies involved external beam radiotherapy (EBRT), with average radiation doses ranging from 40 to 54 Gy. The remaining three studies focused primarily on brachytherapy, with prescription radiation doses of 100–150 Gy.

The status of IBD at the time of radiotherapy was recorded in six of the studies, with between 0 and 43% of participants reporting the presence of active IBD symptoms. Interestingly, no studies recorded the rates or severity of bowel symptoms before radiotherapy.

In general, the rates of bowel toxicity for EBRT and brachytherapy were recorded using either the Radiation Therapy Oncology Group (RTOG) or the Common Terminology Criteria for Adverse Events (CTCAE) systems, with

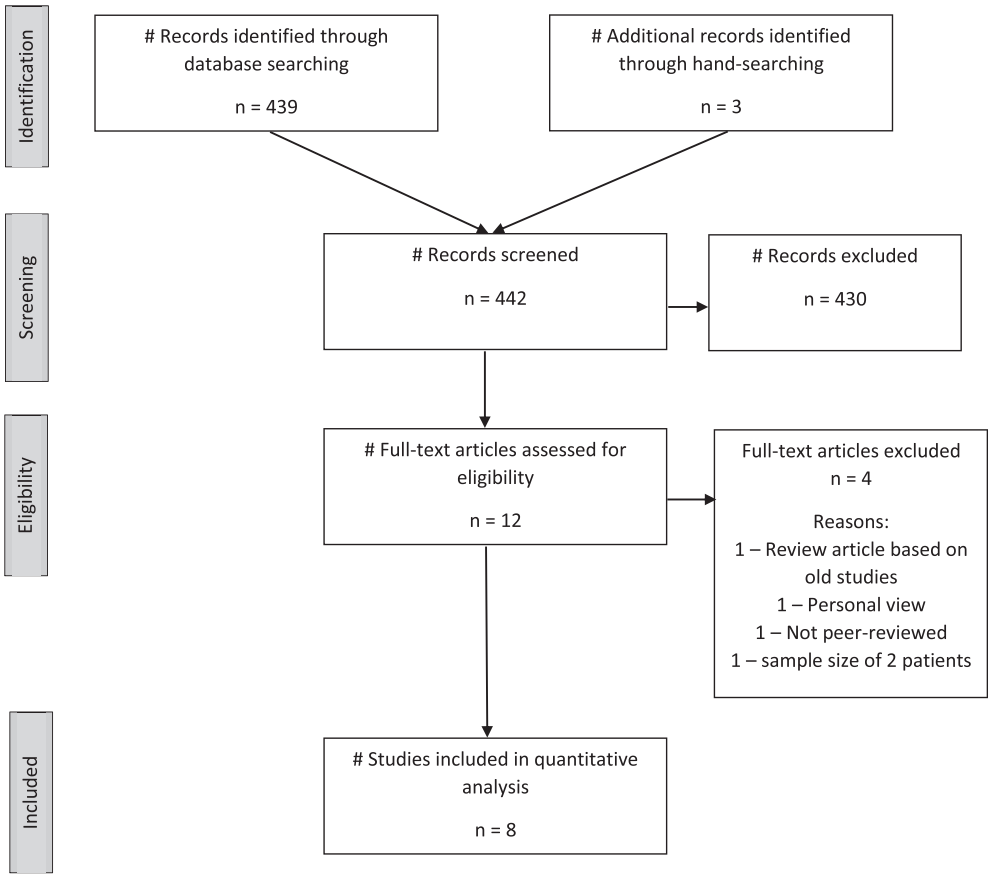

Fig 1. Flow diagram describing the data collection process following the PRISMA convention.