Cancer/Radiothérapie 21 (2017) 89–98

Disponible en ligne sur
ScienceDirect
www.sciencedirect.com

Elsevier Masson France
EM|consulte
www.em-consulte.com

Original Article

Thoracic irradiation in 3 weeks for limited-stage small cell lung cancer: Is twice a day fractionation really needed?

Radiothérapie thoracique de 3 semaines pour le traitement des cancers bronchiques à petites cellules de stade limité : le traitement biquotidien est-il vraiment nécessaire ?

G.A. Turgeon[a], L. Souhami[a], N. Kopek[a], V. Hirsh[b], L. Ofiara[c], S.L. Faria[a,*]

[a] *Department of Oncology, Division of Radiation Oncology, McGill University Health Centre, 1001 Decarie Boulevard, H4A 3J1 Montreal, Quebec, Canada*
[b] *Department of Oncology, Division of Medical Oncology, McGill University Health Centre, 1001 Decarie Boulevard, H4A 3J1 Montreal, Quebec, Canada*
[c] *Division of Respiratory Medicine, McGill University Health Centre, 1001 Decarie Boulevard, H4A 3J1 Montreal, Quebec, Canada*

ARTICLE INFO

Article history:
Received 14 July 2016
Received in revised form 7 September 2016
Accepted 11 September 2016

Keywords:
Hypofractionation
Concomitant chemoradiation
Prophylactic cranial irradiation
Tumor cell rapid doubling time

ABSTRACT

Purpose. – Many Canadian institutions treat limited-disease small cell lung cancer with 40 Gy in 15 fractions delivered once-a-day in 3 weeks concomitantly with chemotherapy. This regimen is convenient and seems to be effective. Here, we report and compare with a literature review the outcomes of patients with limited-stage small cell lung cancer treated in our institution with this hypofractionated regimen.
Patients and methods. – From January 2004 to December 2012, patients with limited-stage small cell lung cancer treated curatively with platinum-based chemotherapy and concurrent thoracic radiotherapy at a dose of 40 Gy in 16 fractions once-a-day were eligible for this review.
Results. – Sixty-eight patients fit the analysis criteria, including ten patients with small pleural effusion. The median age was 66 years old. After a median follow-up of 77 months for those alive, the median survival was 28 months. At 3 and 5 years respectively, the locoregional control rates were 67 and 64%, while the overall survival rates were 40 and 35%. Prophylaxis cranial irradiation was delivered to 68% of the patients. Grade 2 and 3 acute esophagitis occurred in respectively 49 and 9% of the patients. There was no grade 4 radiation-induced toxicity. All patients, except for one, completed their thoracic irradiation course without interruption.
Conclusion. – Once-a-day hypofractionated radiation with concurrent chemotherapy followed by prophylactic cranial irradiation is a practical regimen. Based on our experience and the published literature, it appears to be similarly effective as regimens using twice-daily fractionation in 3 weeks, or once-daily in 6 to 7 weeks with higher radiotherapy doses. Further prospective comparisons of hypofractionation with the current recommendations are needed.

Mots clés :
Hypofractionnement
Chimiothérapie concomitante
Irradiation panencéphalique prophylaxique
Dédoublement cellulaire rapide

RÉSUMÉ

Objectifs de l'étude. – Plusieurs institutions canadiennes prennent en charge les cancers bronchiques à petites cellules de stade limité par une chimioradiothérapie concomitante, délivrant 40 Gy en 15 fractions quotidiennes pendant trois semaines. Cette radiothérapie hypofractionnée est pratique et semble efficace. Nous présentons ici notre expérience institutionnelle ainsi qu'une revue de la littérature de patients atteints de cancer bronchique à petites cellules de stade limité traité avec cet hypofractionnement.
Patients et méthodes. – De janvier 2004 à décembre 2012, tous les patients atteints d'un cancer bronchique à petites cellules de stade limité et ayant été pris en charge à visée curative par une chimiothérapie à base de sels de platine et une radiothérapie thoracique délivrant 40 Gy en 16 fractions étaient éligibles à cette étude.

* Corresponding author.
E-mail address: sergio.faria@muhc.mcgill.ca (S.L. Faria).

http://dx.doi.org/10.1016/j.canrad.2016.09.015
1278-3218/

Résultats. – Soixante-six patients étaient éligibles, dont dix avec un épanchement pleural léger au moment du diagnostic. Après un suivi médian de 77 mois chez les survivants, la survie médiane était de 28 mois. À 3 et 5 ans, les taux de contrôle locorégionaux étaient respectivement de 67 et 64 %, tandis que ceux de survie globale étaient de 40 et 35 %. Soixante-huit pour cent des patients ont reçu une irradiation panencéphalique prophylaxique. Une œsophagite aiguë de grade 2 et 3 a été diagnostiquée chez respectivement 49 et 9 % des patients. Aucune toxicité radio-induite de grade 4 n'a été rapportée. Tous les patients, à l'exception d'un seul, ont complété leur radiothérapie thoracique sans interruption.
Conclusion. – La radiothérapie thoracique quotidienne hypofractionnée concomitante avec une chimiothérapie et suivie d'une irradiation panencéphalique prophylaxique est un traitement pratique utilisé couramment au Canada. Appuyé par la littérature et notre expérience institutionnelle, ce fractionnement semble avoir une efficacité similaire au bifractionnement en trois semaines ou à la radiothérapie classique de haute dose. Une comparaison prospective de ce traitement hypofractionné avec ceux actuellement recommandés est nécessaire.

1. Introduction

Limited-stage small cell lung cancer is a relatively uncommon disease. The incidence of small cell lung cancer as a whole has decreased to less than 14% of all lung cancers compared to 20% a few years ago, with limited-stage small cell lung cancer accounting for only 20 to 25% of patients diagnosed with small-cell lung cancer [1–3]. Contrary to non-small cell lung cancer, where new-targeted agents have become available, the systemic treatment of small-cell lung cancer has remained essentially unchanged for many years. Limited-stage small cell lung cancer has been treated for the last decades with platinum-based chemotherapy and concurrent thoracic radiotherapy, followed by prophylactic cranial irradiation [4–6]. Limited-stage small cell lung cancer is initially very responsive to both chemotherapy and radiotherapy, but the disease tends to recur yielding a median overall survival of 15 to 38 months [7–30]. In the absence of more effective systemic agents, advances in the treatment of limited-stage small cell lung cancer have come from radiotherapy including twice-a-day fractionation, higher total doses, shorter treatment duration with higher daily dose, early integration of concurrent thoracic irradiation with systemic chemotherapy, and prophylactic cranial irradiation.

Since the publication of the randomized National Cancer Institute of Canada (NCIC) study using a 3-week radiotherapy regimen of 40 Gy delivered in 15 once-daily fractions for the thoracic irradiation [7], hypofractionated schedule has been widely used in Canada.

The Intergroup 0096 study, shortly after, showed that 45 Gy delivered in 3 weeks, but with twice-daily fractions, was superior to the same dose given in 25 once-daily fractions [10]. This twice-daily regimen has since, been internationally used. The median and 3-year overall survival in the Canadian trial (21 months and 30%, respectively) did not differ much from those obtained by the Intergroup trial (23 months and 33%). Moreover, the rate of esophageal acute toxicity grade 3 or more of 15% in the NCIC study compares favourably with the rate of 33% observed in the Intergroup study using twice-daily fractionation [10]. Although these two studies were conducted more than 15 years ago, their results are still among the best results published to date. The salient feature of both trials is that these outcomes were obtained using dose schedules of short duration (3 weeks) rather than protracted courses of conventionally fractionated radiotherapy to higher doses given in 6 to 7 weeks [9,12,13,16,19,23,31,32].

Since 2004, all new cases of limited-stage small cell lung cancer at our institution have received the thoracic radiotherapy in 3 weeks, once-a-day hypofractionated schedule, with concurrent platinum-based chemotherapy followed by prophylactic cranial irradiation. Internationally, however, this hypofractionated regimen is less common and this fact has raised the question of a need for management change at our institution. The aim of the present paper is to report the outcomes of limited-stage small cell lung cancer patients treated with a once-a-day hypofractionated radiotherapy schedule in our hospital and to review the literature on this topic.

2. Patients and methods

2.1. Patients

In our institution, we have given the dose of 40 Gy in 16 fractions instead of 15 as used in the NCIC trial. All patients with histologically proven limited-stage small cell lung cancer and treated curatively at our institution by concurrent chemoradiotherapy using the hypofractionated thoracic radiotherapy regimen of 40 Gy delivered in 16 daily fractions were eligible for this retrospective review. Limited-stage small cell lung cancer was defined as tumor confined to the ipsilateral hemithorax and regional lymph nodes (including supraclavicular nodes) that could be safely encompassed in the curative radiotherapy field. Patients were considered for prophylactic cranial irradiation if there was no progression of the tumor at the end of the last cycle of chemotherapy. Patients with limited small pleural effusion treated curatively were included in this analysis. This review was approved by the ethics committee of our institution.

2.2. Clinical staging

Pre-treatment assessment and staging included complete history, full physical examination, routine laboratory studies, and computerized tomography (CT) of the chest, abdomen and brain for all patients. The staging was often completed by either a positron emission tomography (PET/CT) or a bone scan. All patients had a pathologically proven diagnosis prior the start of treatment.

2.3. Treatment

2.3.1. Chemotherapy

The majority of patients (52 cases) received cisplatin (80 mg/m^2 intravenous, day 1) and etoposide (100 mg/m^2, day 1–3) in 21 day cycles. In 11 patients, carboplatin replaced cisplatin, and in five patients irinotecan (175 mg/m^2 intravenous, day 1) replaced etoposide (choice of the treating physician). Patients were planned to receive four to six cycles of chemotherapy.

2.3.2. Thoracic radiation therapy

Thoracic irradiation usually started with cycle 3 or 4 of chemotherapy (Table 1). Radiotherapy was delivered 5 days a week, for a total of 40 Gy in 16 fractions of 2.5 Gy once daily. All patients were treated with three-dimensional planning using three fields