Cancer/Radiothérapie 20 (2016) 268–274

Disponible en ligne sur
ScienceDirect
www.sciencedirect.com

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

Original article

Treatment failure prediction for head-and-neck cancer radiation therapy

Outils de prédiction de l'échec du traitement pour les cancers de la tête et du cou traités par irradiation

H. Rocha [a,b,*], L. Khouri [c], M.C. Lopes [d], J. Dias [b,e], B. Ferreira [f]

[a] *School of Health Sciences, University of Minho, Braga, Portugal*
[b] *Institute for Systems Engineering and Computers (INESC), Coimbra, Portugal*
[c] *Radiation Therapy Department, Portuguese Institute of Oncology of Coimbra (IPOCFG, EPE), Coimbra, Portugal*
[d] *Medical Physics Department, Portuguese Institute of Oncology of Coimbra (IPOCFG, EPE), Coimbra, Portugal*
[e] *Faculty of Economics, University of Coimbra, Coimbra, Portugal*
[f] *School for Allied Health Technologies, Porto, Portugal*

ARTICLE INFO

Article history:
Received 10 September 2015
Received in revised form 3 December 2015
Accepted 24 February 2016

Keywords:
Head-and-neck cancer
Radiation therapy
Primary tumour volume
Prognosis

ABSTRACT

Purpose. – Treatment outcome prediction is an important emerging topic in oncologic care. To support radiation oncologists on their decisions, with individualized, tailored treatment regimens increasingly becoming the standard of care, accurate tools to predict tumour response to treatment are needed. The goal of this work is to identify the most determinant factor(s) for treatment response aiming to develop prediction models that robustly estimate tumour response to radiation therapy in patients with head-and-neck cancer.
Patients and methods. – A population-based cohort study was performed on 92 patients with head-and-neck cancer treated with radiation from 2007 until 2014 at the Portuguese Institute of Oncology of Coimbra (IPOCFG). Correlation analysis and multivariate binary logistic regression analysis were conducted in order to explore the predictive power of the considered predictors. Performance of the models is expressed as the area under the curve (AUC) of the receiver operating characteristics (ROC) curve. A nomogram to predict treatment failure was developed.
Results. – Significant prognostic factors for treatment failure, after multivariate regression, were older age, non-concomitant radiation therapy and larger primary tumour volume. A regression model with these predictors revealed an AUC of .78 for an independent data set.
Conclusion. – For patients with head-and-neck cancer treated with definitive radiation, we have developed a prediction nomogram based on models that presented good discriminative ability in making predictions of tumour response to treatment. The probability of treatment failure is higher for older patients with larger tumours treated with non-concomitant radiation.

Mots clés :
Cancer de la tête et du cou
Radiothérapie
Volume de la tumeur primaire
Pronostic

RÉSUMÉ

Objectif de l'étude. – La prévision des résultats du traitement est un sujet émergent et très important dans le domaine des soins oncologiques. Pour soutenir les oncologues radiothérapeutes sur leurs décisions, les régimes de traitement sur mesure deviennent, de plus en plus, la norme des soins. En ce sens, des outils précis pour prédire la réponse tumorale au traitement s'avèrent nécessaires. Ce travail se propose, donc, d'identifier le(s) facteur(s) le(s) plus pertinent(s) pour déterminer la réponse au traitement, visant à développer des modèles de prédiction qui puissent estimer, le plus efficacement possible, une réponse tumorale à la radiothérapie, chez les patients atteints du cancer de la tête et du cou.

* Corresponding author. INESC, Rua Antero de Quental No. 199, 3000 - 033 Coimbra, Portugal.
E-mail address: hrocha@mat.uc.pt (H. Rocha).

http://dx.doi.org/10.1016/j.canrad.2016.02.012
1278-3218/

Patientes et méthodes. – Une étude de cohorte basée sur la population a été réalisée sur 92 patients atteints d'un cancer de la tête et du cou traité par irradiation à partir de 2007 jusqu'en 2014, à l'institut portugais d'oncologie de Coimbra (IPOCFG). Une analyse de corrélation, ainsi qu'une analyse multifactorielle par régression logistique binaire ont été menées afin d'explorer le pouvoir prédictif des prédicteurs présentés. La performance des modèles est exprimée par la surface située sous la courbe (AUC) de la courbe des caractéristiques opérationnelles du récepteur (ROC). Il a été développé un nomogramme pour prédire l'échec du traitement.

Résultats. – Les facteurs pronostiques déterminants pour l'échec du traitement, après une régression multifactorielle, étaient un âge plus avancé, une radiothérapie non concomitante et un plus grand volume de tumeur primaire. Un modèle de régression avec ces prédicteurs a démontré une AUC de 0,78 pour un ensemble de données indépendantes.

Conclusion. – Pour les patients atteints d'un cancer de la tête et du cou traité par irradiation définitive, nous avons développé un nomogramme de prédiction basé sur des modèles qui ont présenté une bonne capacité discriminative à faire des prédictions de la réponse tumorale au traitement. La probabilité d'échec du traitement est plus élevée pour les patients plus âgés, atteints de plus grandes tumeurs et recevant des radiothérapies non concomitantes.

1. Introduction

Treatment outcomes prediction is an important emerging topic in oncologic care, with individualized tailored treatment regimens increasingly becoming the standard of care [1]. Outcomes in oncology treatments include the risks and benefits of cancer therapy in terms of side-effects, tumour response to treatment and follow-up outcomes such as local recurrences, evolution to metastatic disease, survival or a combination of these endpoints. Recently, online predicting tools have become available [2–4]. These aim to supplement clinical judgment by giving information to physicians and health professionals about possible outcomes. The involvement of the patients in the treatment decisions is becoming generalized and ultimately these tools will also be assessed by patients with all the associated pros and cons. These tools have been validated by peer review for a variety of tumour sites including lung, colorectal, head-and-neck, breast, ovarian, endometrial, gastric or prostate [5–13]. Although the prediction models were validated by peer review, they require validation for different populations and treatments. Moreover, the factors found relevant during the model development stage concern a given population and different factors may prove to be important for different populations. For instance, different drugs or different radiation therapy modalities may be used in different countries or even in different cancer institutes within the same country.

Radiation therapy is one of the main treatment modalities for cancer, along with surgery and chemotherapy, being used for around 60% of all patients. Radiation therapy is generally used as a locoregional treatment, irradiating tissues with proven or suspected disease with ionizing radiation. In many cases, radiation therapy alone, or combined with chemotherapy and/or surgery, is a successful treatment, curing patients or giving important symptom relief. However, even with state-of-the-art practice, the tumour is not eradicated in all patients treated with curative intent. Moreover, mild or severe complications may occur, having a large impact on patients' quality of life. Following radiation therapy of head-and-neck complex cases, due to the large number of organs at risk, radiation induced side-effects with significant impact on health-related quality of life include xerostomia or swallowing dysfunction [8].

Few prediction models for radiation therapy of head-and-neck cancers are available [7]; the existing ones are focused on subpopulations (e.g. larynx cases [8]), and many of the outcomes of interest have no prediction model yet. Furthermore, in radiation therapy, the abundance of new treatment options and the numerous patient parameters that nowadays can be assessed accurately have created new challenges. There is thus a growing need for the development of prediction models testing the increasingly amount of information that is becoming easily assessed.

In this study, we aim to identify the most determinant factor(s) for the specific outcome of tumour response to radiation therapy, then construct prediction models that robustly estimate head-and-neck tumour response to radiation therapy, integrating all the relevant information in a quantitative manner. To implement personalized radiation therapy, clinical decisions based on validated and quantified factors (predictors) will be crucial. We aim to contribute to a long-term objective that will consider the incorporation of the developed model in treatment planning systems for inverse treatment planning optimization.

2. Patients and methods

2.1. Patients

Population-based cohort included head-and-neck cancer patients receiving a radiation therapy at IPOCFG. Demographic and clinical characteristics of consecutively treated patients with head-and-neck cancer were recorded from May 2007 to June 2014 in RESPONSE, the electronic health information system used at IPOCFG to store patient response to radiation therapy [14]. Exclusion criteria were palliative and re-irradiated patients, patients with distant metastasis at presentation and postoperative patients. Patients receiving neoadjuvant or adjuvant chemotherapy as well as patients not receiving intensity-modulated radiation therapy (IMRT) were also excluded. Thus, a total of 92 patients were included in our cohort study (Table 1). The demographic and clinical characteristics assessed for this investigation included age at diagnosis, gender, tumour location, T-classification and N-classification of tumour–node–metastasis (TNM) system of the American Joint Committee on Cancer (AJCC), anaemia, radiation therapy concomitant or non-concomitant, primary tumour volume (the volume of the macroscopic volume of the tumour), overall treatment time and mean doses delivered to the total planning target volume and planning target volume of the primary tumour. Other dosimetric features were initially considered but to simplify the analysis only these metrics were included in this study.

Patient and clinical characteristics are shown in Table 1 for the entire study cohort and for two groups corresponding to patients with different tumour response to the initial treatment protocol. All patients were subjected to a standardized follow-up program prior to, during and at regular intervals after curative