European Journal of Cancer 92 (2018) 69–76

Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.ejcancer.com

Original Research

Prognostic value of circulating biomarker score in advanced-stage head and neck squamous cell carcinoma

Marn Joon Park [a], Jong-Lyel Roh [a,*], Sung-Bae Kim [b], Seung-Ho Choi [a], Soon Yuhl Nam [a], Sang Yoon Kim [a]

[a] *Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea*
[b] *Department of Internal Medicine (Oncology), Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea*

Received 15 October 2017; received in revised form 15 December 2017; accepted 7 January 2018

KEYWORDS
Head and neck squamous cell carcinoma;
Advance stage;
Circulating biomarker;
Prognosis;
Survival

Abstract ***Background:*** Circulating biomarker (CB) is a convenient, emerging predictive tool for treatment response and outcomes in human cancers. Therefore, we examined the prognostic value of pre-treatment and early post-treatment CBs and their summated scores in patients with head and neck squamous cell carcinoma (HNSCC).
Methods: This study prospectively included 310 consecutive patients who underwent definitive treatment for previously untreated advanced-stage HNSCC between 2010 and 2015. The CB score was determined by complete blood counts (CBCs) and blood chemistry before and 2 months after the treatment, and the number of abnormal CB was counted from 0 to 10. Univariate and multivariate analyses with Cox proportional hazards models were used to find factors associated with disease-free survival (DFS) and overall survival (OS).
Results: Most CBC profiles were significantly changed at 2-months post-treatment compared with those at pre-treatment. Univariate analyses showed that hypoalbuminemia, leucocytosis, C-reactive protein, high CB scores ($\geq$6), age, performance status and comorbidity and tumour site were significantly associated with DFS and OS (all $P < 0.05$). Both pre- and post-treatment CB scores were independent factors predictive of DFS and OS outcomes in the multivariate analyses ($P < 0.05$). High CB scores at pre-treatment were associated with 7–10-fold increased risk of unfavourable DFS and OS outcomes, and those at 2-months post-treatment were associated with 2 to 4-fold increased risk of poor survival outcomes (all $P < 0.05$).

* *Corresponding author*: Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea. Fax: +82 2 489 2773.
E-mail address: rohjl@amc.seoul.kr (J.-L. Roh).

https://doi.org/10.1016/j.ejca.2018.01.069

Conclusions: CB scores at pre-treatment and early post-treatment are useful for predicting survival outcomes in patients with advanced-stage HNSCC.

1. Introduction

Circulating biomarker (CB) is a convenient, emerging predictive tool for treatment response, outcomes and survival in a variety of human cancers [1–3]. Circulating markers related to systemic inflammatory conditions are associated with unfavourable prognostic outcomes in human cancers [4–6]. Tumours grow, invade and spread, causing a systematic inflammatory response via the paraneoplastic secretion of various proinflammatory and proangiogenic cytokines and growth factors [7,8]. The increased CB levels related to inflammation, without clinical evidence of infection, might reflect tumour burden, predictive of persistent, residual, or recurrent lesions after treatment [9,10]. The clinical significance of blood markers has been reported in head and neck squamous cell carcinomas (HNSCCs) treated with chemoradiation therapy [7,11,12].

Serum markers of nutritional status in cancer patients have been associated with treatment outcomes in several cancer types [13,14]. Poor nutritional status in cancer patients affects their immune function for tumour surveillance of the host, resulting in decreased treatment compliance, increased treatment failure and adverse effects and high recurrence [15]. Decreased body mass index (BMI) and haemoglobin levels are also associated with poor treatment outcomes in cancer patients [16,17]. All the CBs can be easily measured with routine blood tests prior, during and after treatments, and further, the number of abnormal CBs in combination might be useful.

The clinical importance of CBs has been proposed in many cancer types but rarely in advanced-stage HNSCC related to relatively high tumour burdens, recurrence and mortality. The prospective examination of CBs before and after treatment for HNSCC might be required to validate their results in the clinical setting. Further, the summated scores of pre- and post-treatment values and their CB change might better predict the recurrence and survival of patients who undergo definitive treatments for HNSCC than individual CBs. Therefore, this study prospectively examined the prognostic value of CBs and their summated scores for predicting patient survival with definitive treatment for HNSCC.

2. Methods

2.1. Study population

We prospectively enrolled patients over the age of 18 years who were initially diagnosed with primary HNSCC at our tertiary referral hospital between September 2010 and August 2015. A total of 677 patients with HNSCC arising in the oral cavity, oropharynx, larynx or hypopharynx were initially enrolled. Patients with early-stage (I–II) HNSCC (n = 275), previous history of cancer treatment (n = 17), palliative treatment (n = 18), incomplete initial radiotherapy or chemoradiotherapy (n = 18), no initiation for any treatment modality (n = 22), or the absence of follow-up CB data or lost to follow-up (n = 17) were excluded. A total of 310 patients with definitive treatments for clinically advanced (III–IV) stage HNSCC were included in the final analyses. The patients underwent examination of circulating laboratory biomarkers (complete blood count [CBC], electrolyte battery, chemical battery and C-reactive protein [CRP]) at the time of initial diagnosis and regularly after treatments. Patients were staged according to the tumour-node-metastasis (TNM) staging system of the American Joint Committee on Cancer (AJCC 7th ed., 2010) [18]. This study was reviewed by our Institutional Review Board and written informed consent was obtained from each patient.

2.2. Treatments and follow-up

The study patients underwent definitive treatments of surgery and/or radiotherapy or chemoradiotherapy. The primary treatment modalities were determined by the multidisciplinary consensus of tumour boards consisting of head and neck surgeons, oncologists, radiologists, pathologists, and rehabilitation specialists. Surgery included a complete extirpation of the primary tumour with or without combined prophylactic or therapeutic neck dissection and reconstructive surgery, according to tumour location and staging. Definitive radiotherapy was performed by intensity-modulated radiotherapy of total 58–78 Gy, with a daily fraction of 1.8–2.0 Gy for 5 d each week, for 6–8 weeks. For patients who underwent definite chemoradiotherapy, combined chemotherapy was intravenously administered with 80–100 mg/m^2 of cisplatin on the first 22th, 34th day in addition to the intensity-modulated radiation. Patients with adverse pathological features underwent postoperative radiotherapy or chemoradiotherapy [18]. Response Evaluation Criteria in Solid Tumor (RECIST) was used to determine the therapeutic effect of each treatment modality at 2 months after completion of the definite therapy [19]. Salvage surgery was conducted in patients with residual