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Primary lung cancer after treatment of head and neck cancer without lymph node metastasis: Is there a role for autofluorescence bronchoscopy?

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KEYWORDS
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Summary
Background: Head and neck cancer (HNC) is the 5th most common cancer worldwide. As good locoregional tumor control can be achieved with current treatment strategies, patients who develop second primary tumors from field cancerization have poorer prognosis.
Objectives: To determine if autofluorescence bronchoscopy (AF) played a role in the detection of second primary lung cancer (SPLC), and impact of SPLC on survival of patients with HNC and no cervical lymph node metastasis (N0).
Methods: Patients with HNC(N0) referred for symptoms and/or radiology suspicious for lung cancer were assessed with AF. Data on patient demographics, smoking, cancer characteristics, and outcome were prospectively collected.
Results: Fifty-one patients (44 males) with curatively treated HNC(N0) were evaluated. Median age was 70 years, all were current or former smokers of 35 pack years, and 25 had chronic obstructive lung disease. Over a median follow up of 60 months, 8 patients were diagnosed with synchronous and 26 with metachronous SPLC. Forty-two SPLC were found; 12 (29%) affected the tracheobronchial tree and 30 (71%) involved the lung parenchyma. Median time to metachronous SPLC was 22 months. Most of SPLC were surgically resectable. Five radiographically occult lung cancers detected by AF were successfully treated with endobronchial therapy. Lung cancer mortality was 24%. HNC patients who developed synchronous and metachronous SPLCs had significantly shorter survival (51 and 144 months) compared to those without (240 months) ($p = 0.0005$).

Abbreviations: HNC, head and neck cancer; SPLC, second primary lung cancer; AF, autofluorescence; CXR, chest radiograph; CT, computed tomography; TNM system, tumor, node and metastasis system; NSCLC, non-small cell lung cancer; PET, positron emission tomography.

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Conclusion: SPLC impacted negatively on the survival of patients with HNC. Close surveillance with AF and CT for SPLC combined with aggressive treatment of early stage lung cancer might be a strategy to improve outcome.

1. Introduction

Head and neck cancer (HNC) is the 5th most common cancer worldwide, and is the most common neoplasm in Asia [1]. In the Netherlands, the total incidence of squamous cell carcinoma of the head and neck is about 2300 patients per year of which, 650 will die from it [2]. In the last decade, owing to better locoregional tumor control achieved with surgery and radiotherapy, more patients are at risk for second primary tumors [3]. These tumors often appear at unfavourable sites such as the lungs, esophagus and previously treated head and neck areas. Data from the Netherlands mirror the reported risk of 2—3% per year for second primary tumor with the majority occurring in the first 2 years [4—6].

Long term exposure to carcinogens namely tobacco smoke and alcohol causes field cancerization which can harbor many mutated cells and give rise to second primary or field tumors [7]. Patients with curatively treated HNC are followed regularly to facilitate early detection of locoregional recurrence to allow salvage surgery [8], and for second primary tumors. Although prospective data have not demonstrated significant survival benefit following treatment of asymptomatic recurrences or second primary lung cancers (SPLCs) detected during close surveillance [6,9,10], others have indicated better outcome for patients diagnosed early with limited disease who still retain the option for future intervention [11,12].

Our objectives were to evaluate role of autofluorescence bronchoscopy (AF) in the surveillance of patients with HNC and no cervical lymph node metastases (N0) treated with curative intent as well as to compare the outcome of those detected with synchronous and metachronous SPLC by AF and computed tomography (CT).

2. Patients and methods

2.1. Post-treatment surveillance of HNC by otolaryngologist

Post-treatment surveillance of HNC followed the guidelines of Dutch Head and Neck Cooperative Group where the patient was seen every 2 months in the 1st year; every 3 months in the 2nd year; every 4 months in the 3rd year; twice in the 4th and 5th years; and once yearly thereafter. These visits included detailed history, physical examination, indirect laryngoscopy and chest radiograph (CXR). If patients presented with cervical metastases or radiological pulmonary nodules after primary treatment, diagnostic work-up that included panendoscopy, CT and/or magnetic resonance imaging (MRI) was performed to exclude local recurrence or second primary tumor in the head and neck, lungs and esophagus. All routine and extra visits by patients who developed recurrence, SPLC and treatment were documented.

2.2. Post-treatment surveillance of HNC by pulmonologist

Included were patients with curatively treated squamous cell HNC(N0) who were referred to the pulmonary department for radiological abnormality and/or symptoms suspicious of lung cancer between 1995 and 2005, and prospectively followed until December 2006. All patients underwent conventional white light bronchoscopy and AF (LIFE® Xilix, BC, Richmond, Canada) to evaluate the tracheobronchial tree while CT was performed to detect lung parenchymal pathology. Subjects with radiographic abnormalities suspicious of lung cancers had histological confirmation of the neoplasms followed by appropriate staging and treatment. If pre-neoplastic lesions were found in the tracheobronchial tree, AF was repeated every 6 months for the duration of the study.

Staging of HNC and lung cancer was in accordance with the TNM classification system, and management based on a multi-disciplinary approach after considering results of staging procedures and patient's overall health status. All patients gave informed consent for AF, and the study protocol was approved by the institutional review board.

2.3. Definitions

A lung malignancy was classified as second primary tumor when it differed in histology from HNC squamous cell carcinoma. For lung cancers that were of the same histology, the criteria by Warren and Gates [13] had to be fulfilled: (1) each neoplasm must be geographically separate and distinct with 2 cm of normal appearing mucosa in between and (2) the possibility of metastasis excluded. Synchronous lung cancers were defined as those diagnosed at the same time or within 6 months of HNC, and metachronous as lung cancers that developed greater than 6 months later.

2.4. Statistics

Patient demographics, comorbidity, smoking history, cancer characteristics, time interval to second primary lung cancer, mode of detection and outcome were prospectively collected and entered into a database. Values were expressed as median, range and percentages. Comparison between two groups was performed with Mann—Whitney *U*-test, and survival was estimated by the Kaplan—Meier method. Differences in estimates between groups were assessed using the log rank test. Univariate and multivariate regression analyses were performed to identify prognostic factors. A p-value of <0.05 was considered statistically significant.