Cancer Epidemiology 50 (2017) 107–112

Contents lists available at ScienceDirect

Cancer Epidemiology

journal homepage: www.elsevier.com/locate/canep

Clinical epidemiology of tracheal invasion from thyroid cancer in Japanese population: Functional outcomes and effect of aging

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ARTICLE INFO

Keywords:
Thyroid cancer
Trachea
Invasion
Age
Sex
Descriptive epidemiology
Nationwide study
Reconstruction
Tracheostomy
Functional outcome

ABSTRACT

Background: Although tracheal invasion from thyroid cancer is life-threatening, the epidemiology of its development remains unclear. This study aimed to determine the epidemiology (prevalence, incidence, and risk factors) and functional outcomes of tracheal invasion from thyroid cancer among Japanese patients who were eligible for full-layer tracheal resection.

Methods: Patients with thyroid cancer and with or without tracheal invasion were identified based on procedure codes using a large inpatient database that is maintained by a data vendor. The prevalence and incidence were estimated for each age and sex using Japanese volume of thyroidectomies and Japanese population data. We also explored whether a tumor-related tracheal defect was successfully reconstructed after full-layer tracheal resection.

Results: Among the 8482 patients with thyroid cancer, the overall prevalence of tracheal invasion was 0.4–0.7%. The overall incidence of thyroid cancer was 12.0/100,000 persons, and the incidence of tracheal invasion was estimated to be 0.05–0.09/100,000 persons. The age distributions were noticeably different between thyroid cancer cases with and without tracheal invasion. The highest incidence was observed at ages of 70–79 years for thyroid cancer with tracheal invasion and 60–69 years for thyroid cancer without invasion. Approximately one-half of patients experienced long-term use of a tracheal tube and/or multiple operations for tracheal reconstruction.

Conclusion: The peak incidence of tracheal invasion from thyroid cancer was observed at ages of > 70 years. In addition, conventional surgical management appears to be limited in its ability to reconstruct tracheal defects.

1. Introduction

Invasion of the trachea from thyroid cancer is rare but is the main cause of death during the clinical course of thyroid cancer [1,2]. In addition, surgical management reduces patients' quality of life in severe cases, because it causes tracheal wall defects after full-layer tracheal resection. Nevertheless, tracheal reconstruction continues to be challenging, despite advances in reconstructive strategies, because postoperative restenosis often occurs due to scarring, chronic infection, and granulation tissue growth [3]. Given the rarity of severe tracheal invasion, the risk factors for its development and its clinical features remain unclear.

Aggressive carcinogenesis because of tracheal invasion could be associated with many patient characteristics. For example, previous studies have revealed that the prognosis of thyroid cancer is related to the acronyms AMES (age, distant metastasis, extent, size) and MACIS (metastasis, age, complete resection, invasion size) [4–6]. Furthermore, recent epidemiological studies have confirmed that age is an important prognostic factor for thyroid cancer [7,8]. Moreover, a previous single-center study revealed that higher age was a possibly specific characteristic of tracheal invasion [9]. However, no population-based cohort analysis has investigated the clinical characteristics of tracheal invasion from thyroid cancer.

Surgical management for tracheal invasion from thyroid cancer is mainly divided to two approaches: full-layer tracheal wall resection with or without laryngectomy and surface resection [10–13]. Full-layer tracheal resection makes it possible to resect the malignancy with negative margins but increases morbidity because of tracheal defects after reconstruction failure [13]. However, there is no epidemiological data of functional outcomes for tracheal invasion eligible for full-layer resection from large numbers of facilities.

The present study used a large inpatient database of Japanese cases that were eligible for full-layer tracheal resection and aimed (1) to evaluate the epidemiology (prevalence, incidence, and risk factors) of

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http://dx.doi.org/10.1016/j.canep.2017.08.011
Received 25 May 2017; Received in revised form 17 August 2017; Accepted 19 August 2017
Available online 31 August 2017
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severe tracheal invasion from thyroid cancer and (2) to describe the clinical characteristics of these severe tracheal invasion cases, based on whether the trachea is successfully reconstructed. We aimed to clarify the risk factors for tracheal invasion from thyroid cancer, as well as the efficacy and limitations of conventional tracheal reconstruction.

2. Methods

2.1. Data source

This study evaluated data from the Diagnosis Procedure Combination inpatient database in Japan, which is maintained by Medical Data Vision Co. Ltd. (Tokyo, Japan). This database covers 270 facilities that represent approximately 17% of all Japanese institutions, and includes approximately 15.6 million patients who were treated between April 1, 2008 and June 30, 2016. This database contains the patients' demographic information (age and sex), diagnostic information (disease code and date of diagnosis), procedure information (surgery and date), and prescription information (drug name and prescription date) [14–16]. The diseases and diagnoses are identified using codes from the 10th revision of the International Classification of Diseases. The study's protocol was approved by the ethical committee of Kyoto University Hospital. The requirement for informed consent was not applicable, because we performed a secondary analysis of an anonymous patient database.

2.2. Study cohort

We extracted data from patients with thyroid cancer who underwent thyroidectomy between April 1, 2008 and June 30, 2016. These patients were identified using the procedure code for thyroidectomy for malignant tumors (procedure code number: K469). We excluded patients with a major diagnostic code for primary tracheal, esophageal, hypopharyngeal, and laryngeal cancers, because these patients are eligible for total thyroidectomy with laryngectomy despite the absence of a thyroid malignancy. Based on the procedure codes ("the specific case definition"), we identified eligible patients who underwent full-layer tracheal resection and reconstruction (K398, K399, and K403) after thyroidectomy. However, some patients may undergo tracheostomy to manage tracheal invasion without tracheal reconstruction [17]. Therefore, in combination with the specific case definition, we identified patients who underwent tracheostomy on the day of the thyroidectomy and were eligible to receive a tracheostomy tube during a > 30-day period ("the sensitive case definition"). We excluded patients with anaplastic thyroid cancer from the sensitive case definition, because these patients may undergo tracheostomy as a palliative treatment [18,19]. We also excluded patients with other refractory diseases who were eligible for long-term tracheostomy placement (e.g., bilateral recurrent nerve paralysis) [20,21].

2.3. Prevalence analysis and incidence estimation

The Japanese prevalence of tracheal invasion among all thyroid cancer cases was calculated according to sex and age ranges for the specific and sensitive case definitions. Based on the prevalence, we also estimated the incidences based on the specific or sensitive case definitions of tracheal invasion (Y*i*) during the 2014 fiscal year using the following equation:

$$Yi = Ni \times Xi.$$

In this equation, N*i* is the prevalence of the sensitive or specific definitions stratified according to sex and age, and X*i* is the incidence of thyroid cancer stratified according to sex and age, which was based on publicly available information from the Japanese Ministry of Health, Labour, and Welfare (National Database of Health Insurance Claims and Specific Health Checkups of Japan) [22]. This database supplies data regarding all Japanese surgery case volumes stratified according to age and sex, and the incidence of thyroid cancer was estimated to be 15,278 during the 2014 fiscal year. This incidence has a high specificity for thyroid cancer, because it was estimated using the number of surgeries for thyroid cancer. We subsequently calculated the incidences of thyroid cancer according to the sensitive and specific case definitions of tracheal invasion using the following equation:

$$yi = (Yi/Pi) \times 100{,}000.$$

In this equation, P*i* is the Japanese population stratified according to sex and age during the 2014 fiscal year, as estimated by the Japanese government [23].

2.4. Clinical course of tracheal invasion cases

We also evaluated the clinical course for tracheal invasion from thyroid cancer. The procedure codes for the sensitive definition cases were used to identify cases with successful reconstruction, which was defined as removal of the tracheostomy tube.

3. Results

Among the approximately 15.6 million inpatient admissions that were recorded in the database during the study period, we identified 8509 patients who underwent thyroidectomy for a malignant thyroid tumor. Twenty-seven patients fulfilled the exclusion criteria because they had esophageal cancer (n = 11), laryngeal cancer (n = 11), hypopharyngeal cancer (n = 3), or tracheal cancer (n = 2). Among the 8482 eligible patients, the specific case definition identified 34 patients (0.4%) with tracheal invasion from thyroid cancer and the sensitive case definition identified 62 patients (0.7%) with tracheal invasion from thyroid cancer. Among patients with histopathological information, 96.2% of the thyroid cancers were the papillary type. Cases with tracheal invasion had larger tumor size, more frequent lymph node metastasis, more frequent distant metastasis, and longer hospitalization, compared to the overall group of cases (Table 1).

3.1. Prevalence of tracheal invasion according to age and sex

Tables 1 and 2 show the age- and sex-specific prevalence of tracheal invasion from thyroid cancer. The overall prevalence based on the specific case definition were 0.6% and 0.3% among male and female patients, respectively. Based on the sensitive case definition, the prevalence was 1.1% among male patients and 0.6% among female patients. The prevalence of tracheal invasion was generally higher among male patients, compared to female patients, for both case definitions (Table 2). However, the prevalence of thyroid cancer was higher among female patients, compared to male patients (Table 1). This finding was consistent with the finding of a previous study, which revealed that the prevalence of tracheal invasion from thyroid cancer was higher among male patients [9]. The prevalence of tracheal invasion based on the sensitive case definition increased with age among both male and female patients (Table 2).

3.2. Estimated incidences of tracheal invasion according to age and sex

The estimated incidence of tracheal invasion in Japan was 61 cases using the specific definition, based on a prevalence of 0.4% and the number of patients with thyroid cancer (n = 15,278) (Table 3). Using the sensitive definition, we estimated an incidence of 112 cases with invasive disease (15,278 cases with thyroid cancer, prevalence of 0.7%) [22]. The total Japanese population was 127,023,000 in 2014 [23]. Thus, the overall incidence of thyroid cancer was 12.0/100,000 persons, and the incidences of tracheal invasion were 0.05/100,000

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