Treatment Approaches to Primary Tracheal Cancer

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KEYWORDS

• Tracheal cancer • Treatment • Radiotherapy • Chemotherapy • Combined modality

KEY POINTS

- A patient identified with tracheal cancer benefits most from evaluation by an experienced center.
- There should be an extensive effort to assess the possibility of a complete surgical resection as the most efficient treatment option for cure.
- Localized, nonoperable disease may still be controlled by combined modality using chemotherapy and concurrent radiation.

INTRODUCTION

Primary tracheal cancer represents a rare disease with a potentially curative therapeutic option, if localized. Standard of care with a curative intention should include complete surgical resection. Disease with locoregional extension that is not amenable to complete surgical resection requires combined therapy approaches in order to preserve the chance for long-term disease control. A specific therapeutic approach for locally advanced adenoid cystic carcinoma with a propensity for submucosal and perineural extension beyond the visible borders of the tumor is discussed separately. For palliative treatment of more extensive disease, systemic therapy has been used similar to treatment for lung or head and neck cancer.

To give patients access to potentially curative treatment, a diligent diagnostic workup, preferably in a center with expertise for tracheal tumors, is essential. Honings and colleagues[1] have recently suggested that in centers with experience, more than half of patients may be candidates for surgical resection, whereas in population-based studies, this treatment is applied to less than 25% of patients. Once the diagnosis has been established, treatment approaches should be discussed by a multidisciplinary board.

Surgery

Surgery has long been viewed as the primary curative treatment modality for malignant tracheal tumors. About 40% of these cancers are squamous cell cancers, with adenoid cystic tumors making up a similar proportion and other tumor types being rare.[2] Patients with squamous cancer typically present at a later age (60–70 years), are men (~90%), have a history of smoking, and have friable irregular endotracheal lesions. Adenoid cystic carcinomas occur in a broad age distribution (average ~45 years), have equal male/female distribution, and have more smooth endotracheal lesions.[1] Adenoid cystic carcinomas are discussed specifically later in this article.

The goal of surgical resection of a tracheal squamous carcinoma is an R0 resection. This goal can be achieved in about two-thirds of resections in

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larger centers (Table 1). Most R1,2 resected patients have undergone adjuvant radiotherapy (RT). In one of the largest studies with a detailed analysis, a positive resection margin did not translate to worse survival (many received RT).[3]

The long-term survival rates in this group of patients seem to be reasonable (5-year survival of around 40% to 50%, 10-year survival of 20%–40%, see Table 1). The impact of nodal involvement, which is found in about 25% of surgical patients, is unclear, with larger studies showing either no difference or a nonsignificant trend to worse survival.[3,4]

A review of this experience points out several aspects of tracheal squamous carcinoma at the world's largest tracheal centers: (1) even at these centers, resection is performed in only a few patients per year, (2) many patients are able to undergo resection, (3) achieving a complete resection is difficult, (4) the operative mortality is low, and (5) 5-year and 10-year survival is reasonable. It is questionable whether lower-volume centers can achieve the same results.

RT

Indications for radiation include locoregional disease that is not amenable for complete surgical resection (contraindications to surgery include >50% of tracheal length involved by tumor, extensive locoregional tumor extension, poor patient performance status, and multiple positive nodal stations or distant metastasis, although a palliative resection may sometimes still be indicated in patients with adenoid cystic carcinoma).

In addition, sometimes, adjuvant RT is given after tumor resection with macroscopic or microscopic residual tumor and even after complete resection. Webb and colleagues[6] suggested adjuvant postoperative RT for most patients. The prognosis is better for patients who have adenoid cystic carcinoma than squamous cell carcinoma. The mean dose of adjuvant RT was 55 Gy; in some cases, adjuvant combined chemoradiation therapy was given. In patients presenting with distant metastases, chemotherapy has been used and was usually combined with local therapy, such as RT.

Radiation may be applied as an alternative to surgery in patients who do not qualify for surgery.

There are only scarce data on modern combined therapy approaches using high-precision radiation techniques such as image-guided RT (IGRT) and intensity-modulated RT (IMRT) or volumetric intensity-modulated arc therapy (VMAT) in combination with platinum-based chemotherapy, as has been established for locally advanced non–small cell lung cancer, which has resulted in long-term control of around 20%. Xie and colleagues[7] performed a matched-pair analysis of patients from the SEER (Surveillance Epidemiology and End Results) database with resectable and advanced tracheal malignancies, comparing patients who were treated with or without RT. Most patients had undergone a subtotal resection in both matched groups (only 5% in either arm underwent an R0 resection). Furthermore, there were no differences in age, gender, race, histology, disease extent (trachea only, trachea plus nodes, trachea plus regional organ extension). The investigators reported a significant overall survival benefit in the radiation group. Because most of the patients had squamous cell histology, this group was further analyzed, Overall survival was significantly better in patients undergoing surgery with RT versus surgery alone (5-year survival of 58% vs 7%; and a median survival of 91 months vs 12 months, respectively, but this study included few R0 resected patients). Among patients with squamous cell carcinoma treated without surgery, the survival was also better with radiation versus other (nonsurgical) treatments (4-year survival 41% vs 9%, with a median survival of 33 months vs 5 months, respectively). Although the retrospective nature of this analysis bears limitations, radiation in this setting apparently conveys a treatment advantage with acceptable toxicity.

For definitive therapy for tracheal cancer, a dose of 70 Gy in daily fractions of 1.8 to 2.0 Gy delivered

Table 1
Results of surgery for tracheal squamous carcinoma

Study	N	% of All Patients Seen	% Positive Nodes	% Positive Surgical Margin	% Operative Mortality	% 5-y Overall Survival	% 10-y Overall Survival
Regnard et al,[4] 1996	98	—	31	26	14	47	36
Gaissert et al,[3] 2004	90	66	27	40	4	39	18
Honings et al,[1] 2009	59	—	37	10	—	46	27
Grillo & Mathisen,[5] 1990	44	63	23	31	7	—	—