



Original Research

Incidence of and survival after glottic squamous cell carcinoma in Denmark from 1971 to 2011—A report from the Danish Head and Neck Cancer Group



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Abstract *Aim:* To describe the incidence, disease-specific mortality (DSM), and overall survival (OS) of patients with glottic squamous cell carcinomas (SCC) in Denmark from 1971–2011 in a national population-based cohort of consecutive patients.

Materials and methods: All patients diagnosed with glottic SCC stage I–IV between 1971 and 2011 in Denmark were included. Patients were identified from the Danish Head and Neck Cancer database, which has a coverage of approximately 100% of registered glottic cancer in Denmark. Information on vital status and cause of death were updated using patient charts and national registries.

Results: In total 5132 patients with glottic SCC were included. The yearly number of new cases increased from 107 in the 1970s to 139 in the 2000s. Overall, the incidence increased from 1.9 to 2.6 per 100,000, with a more prominent increase in men (3.5 to 4.7) compared with women (0.4 to 0.6). The 5-year DSM was 16% (15–17%) and the 5-year OS was 63% (61–64). The hazard rate of DSM adjusted for patient characteristics, tumour characteristics and waiting-time was significantly lower in the 2000s ($p < 0.01$), and the hazard rate of OS was significantly higher ($p < 0.01$) compared to the earlier decades. Longer waiting-time for treatment (>25 d) significantly increased DSM and reduced OS.

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Conclusion: Despite being highly avoidable with smoking cessation, the incidence of glottic SCC increased in Denmark from 1971–2011. The adjusted hazard rate of DSM and overall death after glottic SCC was significantly lower in the 2000s compared to previous decades. Waiting-time for treatment significantly influenced DSM and OS.
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1. Introduction

Laryngeal cancer is subdivided into three subsites: supraglottic, glottic, and subglottic tumours, of which subglottic tumours are negligible [1,2]. Glottic cancer originates from the true vocal cords and is histologically dominated by squamous cell carcinomas (SCC) [2]. Most glottic tumours are diagnosed in early stage and are lymph node negative, probably due to early voice alterations [3,4] and modest lymph drainage from the area [5]. This is in contrast to supraglottic tumours, which are more often diagnosed in advanced stage [2,6]. Studies concerning incidence, survival and mortality often consider laryngeal cancer as one entity [7,8]. However, the prognosis of supraglottic and glottic tumours is significantly different, favouring glottic tumours [9–11]. Thus, if possible, each subsite should be described separately.

The aim of this study was to describe the incidence, disease-specific mortality (DSM) and overall survival (OS) of patients with glottic SCC over a period of 41 years in a national population-based cohort of consecutive patients.

2. Materials and methods

Since 1971, the Danish Head and Neck Cancer Group (DAHANCA) has registered information about all patients diagnosed alive with a biopsy-proven SCC of the larynx in the national DAHANCA database. Patients were excluded from the database under the following criteria: treatment abroad or having a previous cancer expected to influence the treatment choice and outcome evaluation. Since 1968, all Danish residents have been assigned a unique personal registration code allowing for accurate linkage between registers. To ensure mutual full patient coverage, the DAHANCA database was regularly compared to the Danish Cancer Registry (DCR) [12]. The few cases (<1%) of laryngeal cancer registered in the DCR but not in the DAHANCA database were confirmed by national chart reviews before inclusion in the DAHANCA database.

For this analysis, patients diagnosed with a biopsy-proven glottic SCC stage I–IV were included. Patients with carcinoma *in situ* and transglottic tumours were excluded due to the pre-invasive nature and the uncertain origin [13], respectively. Regarding vital status, all patients were followed from the first contact with the

oncology centre until death or the day of assessment (February 15, 2015) by linkage to the Danish Civil Registration System, except for ten patients who were lost to follow-up (n = 4) or emigrated (n = 6). If not already known by the oncology centre, the cause of death was explored at the patient's general practitioner and secondly in the Cause of Death Registry supported by data from the Pathology Registry. New primary tumours (NPTs), excluding basocellular skin cancer, were identified in the DCR by January 1, 2014.

In case of conflicting or missing data, charts of patients diagnosed after 1992 were reviewed, whereas data on patients diagnosed before 1992 were considered adequate due to extensive updates (on most patients) in relation to previous clinical studies [5,14–18], except for vital status and cause of death. All tumours were classified or re-classified according to the Union for International Cancer Control (UICC) 1987 classification.

2.1. Treatment

Radiotherapy, reserving surgery for salvage, was the standard treatment for glottic cancer in Denmark throughout the period. The treatment strategy was homogeneous nationwide due to the collaboration of the DAHANCA group. Radiation fields were lateral and opposing beams using Cobalt-60 until the early 1980s and 4–6 MV thereafter. From 2005, Intensity-modulated radiotherapy (IMRT) was gradually put into use for larger tumours. The total dose administered increased over time and, from 1977, larger tumours received larger doses: 1971–1976 60 Gy, 1977–1985 62–64 Gy, 1986–2000 62–68 Gy, and 2000–2011 66–68 Gy. Five weekly fractions of 2 Gy were standard between 1971 and 2002, except for some patients receiving split-course treatment between 1979 and 1985 [19]. Six weekly fractions of 2 Gy became standard in 2003 [20]. For stage II–IV tumours, elective lymph node irradiation was recommended from 2001 and hypoxic modification with nimorazole from 2002.

2.2. Statistics

The incidence of glottic SCC per 100,000 person-years overall and in individual 10-year age groups (<40, 40–49, 50–59, 60–69, 70–79, 80–89, 90+) was calculated using the annual January 1st Danish population

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