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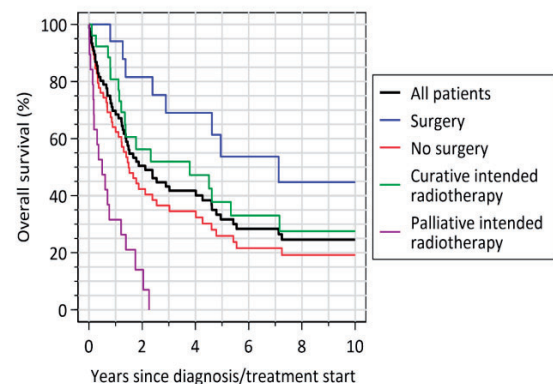
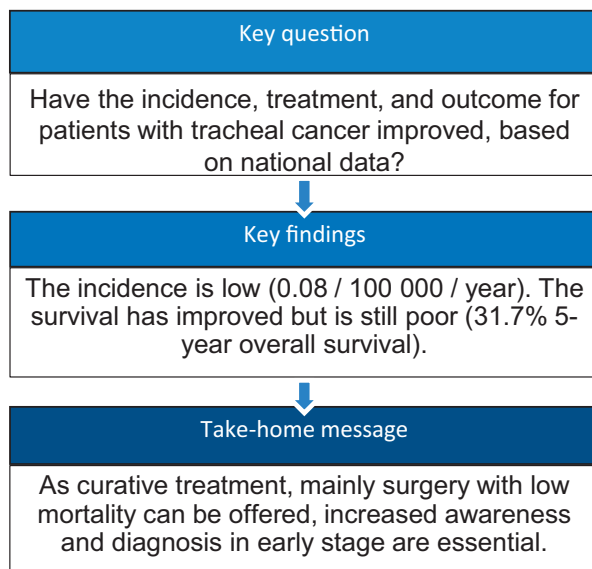
Tracheal cancer: a rare and deadly but potentially curable disease that also affects younger people

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| Number at risk | 0 | 2 | 4 | 6 | 8 | 10 |
|----------------------------|----|----|----|----|----|----|
| All 77 | 36 | 26 | 18 | 13 | 12 | |
| Surgery 16 | 12 | 9 | 7 | 5 | 4 | |
| No surgery 61 | 24 | 17 | 11 | 8 | 8 | |
| Curative radiotherapy 26 | 13 | 11 | 7 | 4 | 4 | |
| Palliative radiotherapy 19 | 2 | 0 | 0 | 0 | 0 | |

Abstract

OBJECTIVES: The incidence of tracheal cancer is low, few clinicians get much experience and the awareness may be low. Recent data on the treatment and outcome are limited. The aim of the present study was to present updated, national data on the incidence, characteristics, treatment and outcome for patients with tracheal cancer.

METHODS: All tracheal cancers registered at the Cancer Registry of Norway in 2000–2020 were extracted. The patient and tumour characteristics age, sex, stage, histology and treatment modality (surgery and radiotherapy) were examined. Overall, median and relative survival were estimated. Cox regression models were used to identify independent prognostic factors.

RESULTS: The 77 patients diagnosed with tracheal cancer equals a crude incidence rate and an age-standardized incidence rate of 0.075 and 0.046 per 100,000 per year respectively. The mean age was 63.8 years (range: 26–94). The numerical preponderance of men ($n = 41$) is not statistically significant. Eighteen patients (23.4%) were diagnosed in the localized stage. The 5-year overall survival was 31.7% [95%

confidence interval (CI): 21.0–42.9], and in those treated with surgical resection or curative radiotherapy, it was 53.7% (95% CI: 26.1–75.0) and 37.8% (95% CI: 18.8–56.7), respectively. Age, histological type and treatment modality were identified as independent prognostic factors.

CONCLUSIONS: Despite improved survival, the prognosis for patients with tracheal cancer is still poor. Few are diagnosed in the early stage and thus most are not eligible for curative treatment, mainly surgery. An increased awareness and diagnosis in the earlier stage is crucial.

Keywords: Trachea • Cancer • Surgery • Oncology • Survival • Epidemiology

ABBREVIATIONS

| | |
|-----|---------------------------------|
| AC | Adenocarcinoma |
| ACC | Adenoid cystic carcinoma |
| ASR | Age-standardized incidence rate |
| CI | Confidence interval |
| CRN | Cancer Registry of Norway |
| SCC | Squamous cell carcinoma |
| SD | Standard deviation |

INTRODUCTION

With a reported incidence of 0.1 per 100 000 per year, tracheal cancer is among the rarest malignancies [1–4]. The mean age at diagnosis ranges from 60.1 to 69.5 years, the range from the youngest to the oldest is 28–93 years and there has been a slight preponderance of men [1–8].

Untreated, the prognosis is poor. The 5-year survival for the entire group was 5.2% before 1980 [1], but recent publications have reported up to 27.1% [7]. When diagnosed at the early stage and surgery was possible, the prognosis was improved, and the 5-year survival among those operated ranged from 51.0% [3] to 84.5% [9]. From 8.3% [6] to 25.0% [10] have been operated and they tended to be younger and more often had adenoid cystic carcinoma (ACC). The main histological types have been squamous cell carcinoma (SCC) and ACC [6, 8, 11]. For those who do not undergo surgery, radiotherapy, medical treatment and endobronchial treatment should be considered [12]. National data on the use of and outcome after surgical and non-surgical treatment, especially radiotherapy, are scarce.

Due to the low incidence, data on tracheal cancer are not reported routinely neither nationally [13] nor globally [14], and no TNM staging has been established [6, 15]. Furthermore, little attention is seen with a limited number of scientific articles and scarcely described in the textbooks. The aim of this study was to provide updated data on the incidence, diagnostic, treatment and survival among all patients diagnosed with tracheal cancer in Norway in 2000–2020.

MATERIALS AND METHODS

Ethical statement

All analyses were performed at the Cancer Registry of Norway (CRN), which is statutory, and statistics were made available according to the Norwegian Health Register Act §19. Ethical approval was not required for the produced statistics.

Cancer Registry of Norway

Since 1952, it has been mandatory for all hospitals, pathology laboratories and general practitioners to report all diagnosed malignant diseases to the CRN. The unique, 11-digit personal identification number assigned to all citizens since 1964 enables the linking of the data. The CRN is updated regularly from the National Population Register on vital status (death or emigration) and from the Norwegian Patient Registry to ensure the completeness of cancer cases. The CRN also receives death certificates for all patients with a cancer diagnosis from the Cause of Death Registry. All data presented here is extracted from the national database at the CRN. The quality, comparability, completeness, validity and timeliness of the data in the CRN have been evaluated to be high [16], and the completeness of tracheal and lung cancers was estimated to be 99.2% in 2018–2022 [13]. Data on smoking, comorbidity, racial, marital and socioeconomic status were not available.

Diagnosis and treatment

For the present study, all patients reported with tracheal cancer (International Classification of Diseases, version 10 code C33) were extracted. Due to near-complete reporting from the pathology laboratories, the CRN has practically complete information regarding the surgery performed. In addition, complete information regarding radiotherapy intention, doses and fractions given are registered at the CRN and received directly from the radiotherapy units. For the small number ($n=8$) of patients who had unknown radiotherapy intention, intention was classified as *curative* if the total dose was over 60 Gy and otherwise *palliative*. Only treatments starting within 1 year of diagnosis were included. If a patient underwent several treatment modalities, the first occurrence was registered as the treatment. Details on tumour size and location, lymph node or metastases were not available, but the traditional staging (localized, regional, distant and unknown), as in the Surveillance, Epidemiology, and End Result program was available. No data on medical or endobronchial treatment were available.

Statistical analysis

Differences in the proportions between 2 groups were tested by Fisher's exact test, and differences in parameters as mean and standard deviation (SD) between 2 groups were tested by the *t*-test. The correlation between the proportion of the general population and the proportion of tracheal cancer cases in each of the 5 health regions as they were organized in 2000 was tested by one-way analysis of variance. The age-standardized incidence rate (ASR) was calculated by computing a weighted average of

age-specific incidence rates using 18 age groups and weights corresponding to the age distribution in the world population [17]. Differences between ASRs were also tested [18]. The time from diagnosis to start of treatment are presented as standard statistical measures such as proportions, mean, SD, median, ranges and 95% confidence interval (CI). Overall survival was estimated using the Kaplan–Meier approach. The Kaplan–Meier 95% CI corresponds to the 5th and 95th survival percentile. All-cause (overall) survival up to 10 years after diagnosis, median survival and relative survival [19, 20] were estimated for each patient characteristic and treatment group. Relative survival was estimated using the *stnet* command in Stata [21]. Follow-up time was defined as time from diagnosis to date of death or censoring, whichever occurred first. Complete vital information up until 31 December 2021 was available. Start of follow-up for treated patients was defined as time of treatment. When estimating survival for the entire patient group a time-dependent variable was used so that the treated patients were considered untreated from date of diagnosis to the date of treatment. A national population life table stratified by calendar year, sex and annual age was used to calculate expected survival. Relative survival was estimated using the Pohar Perme estimator, and here, the 95% CI was calculated using the delta method and a log–log transformation [20]. A multivariable Cox regression adjusting for age group, sex, histology type, stage and treatment type was performed to identify independent prognostic factors. Likelihood ratio tests were used to determine the statistical significance of the covariates to be included in the final model. A *P*-value of <0.05 was considered significant. The statistical program Stata 17.0 was used for all analyses (StataCorp. 2021. Statistical Software: Release 17: College Station, TX, USA).

RESULTS

Study population

From 1 January 2000 to 31 December 2020, 80 patients were registered with a primary tracheal cancer diagnosis at the CRN. After reviewing all patient notifications, 4 were identified as being other tumours (2 lung cancers, 1 thymoma, 1 granuloma) and were excluded. In the same period, 58 634 patients were registered with lung cancer, and of these, 25 had ACC as histology. These were reviewed and 1 was re-classified from lung to tracheal cancer. Thus, 77 patients were eligible for this study. The diagnosis was histologically confirmed in 75 patients (97.4%). No patients were lost to follow-up. All surgical resections were done with curative intent and have been performed by lateral thoracotomy, sternotomy or neck incision. None have been done by thoracoscopy or endobronchial procedure.

Incidence

A mean of 3.7 new patients were diagnosed per year. The crude incidence rate and the ASR were 0.075 and 0.046 per 100 000 per year, respectively. The ASR for women and men was 0.064 and 0.052, respectively (*P*=0.256). Forty-five patients (57.7%) were diagnosed in 2000–2010 (ASR=0.057), and 32 patients (41.6%) in 2011–2020 (ASR=0.035) (*P*=0.02). There was a correlation of 0.99 (*P*=0.002) between the proportion of tracheal

cancer patients and the proportion of the general population in the five health regions.

Age, sex and stage

The mean age was 63.8 (SD=13.7) years, and the range was 26–94 years. The mean age among men and women was 62.7 and 65.1 years, respectively (*P*=0.222). The age distribution revealed that the number under 50, 60 and 70 years was 8 (10.3%), 30 (38.5%) and 53 (67.9%), respectively. The distribution in stages was localized 18 (23.4%), regional 28 (36.4%), distant 12 (15.6%) and unknown 19 (24.7%).

Histology

The histological types were 33 patients (42.9%) with SCC, 22 (28.6%) with ACC and 7 patients (9.1%) with adenocarcinoma (AC) (Table 1). The mean age of those with ACC was 54.2 (SD=12.4) years, which was markedly lower than for those with AC and SCC (*P*<0.001 for both). In the 22 patients with ACC, 15 patients (68.2%) were women, while among the 33 patients with SCC, 10 patients (30.3%) were women (*P*=0.004).

Treatment

Forty-two patients (54.5%) were treated with curative intention; 26 patients (33.8%) with radiotherapy and 16 patients (20.8%) were resected (Table 1). Six of resected patients received radiotherapy which started 41–175 days postoperatively. Nineteen patients (24.7%) were given palliative radiotherapy. For 16 patients (20.8%), neither surgery nor radiotherapy was registered. The time from the date of diagnosis to surgery was ≤ 30 days for 10 patients (62.5%) and ≤ 90 days for 16 patients (100.0%), and the corresponding figures to start of curative radiotherapy were 5 patients (19.2%) and 24 patients (92.3%). The proportion of patients treated with surgery decreased as age increased, whereas the group not given surgery or radiotherapy increased with age (Fig. 1). The majority of those who received curative radiotherapy were in the age group 50–69 years.

Fifty-one patients (66.2%) were given radiotherapy, of whom 45 (88.2%) received this as primary treatment. The median (range) total dose given was 66 (15–70) Gy and 30 (8.5–96) Gy in the groups given curative and palliative radiation, respectively, and the corresponding median (range) number of fractions was 33 (3–37) and 10 (1–43), respectively. The mean age of those who received curative and palliative radiotherapy was 62.6 years (SD=10.9) and 68.0 years (SD=9.4) (*P*=0.060), respectively. Curative radiotherapy was given to 13 (36.1%) of the female patients and 13 (31.7%) of the male patients.

Surgery was performed in 16 (20.8%) patients (8 women) (Table 2). None of the 7 patients with AC, 4 of 33 (12.1%) patients with SCC and 10 (45.5%) patients with ACC were resected. Ten (62.5%) patients of those who underwent surgery had ACC, which is a significantly higher number than the other histology groups (*P*<0.001). Operative (30 days) mortality was zero and the first death occurred 293 days postoperatively. The mean age of those operated was 54.9 (SD=15.9) years, which was 11.3 years younger than those not resected (*P*=0.002).

Table 1: The number and proportion in the age groups by sex, histology, stage and treatment

| | N (%) | | | |
|---------------------------|------------|-------------|-----------|------------|
| | 0–49 years | 50–69 years | 70+ years | All |
| All | 8 (10.4) | 44 (57.1) | 25 (32.5) | 77 (100.0) |
| Sex | | | | |
| Women | 3 (37.5) | 21 (47.7) | 12 (48.0) | 36 (46.8) |
| Men | 5 (62.5) | 23 (52.3) | 13 (52.0) | 41 (53.2) |
| Histology | | | | |
| AC | 0 (0.0) | 4 (9.1) | 3 (12.0) | 7 (9.1) |
| SCC | 0 (0.0) | 18 (40.9) | 15 (60.0) | 33 (42.9) |
| ACC | 6 (75.0) | 15 (34.1) | 1 (4.0) | 22 (28.6) |
| Other | 2 (25.0) | 7 (15.9) | 6 (24.0) | 15 (19.5) |
| Stage | | | | |
| Localized | 4 (50.0) | 11 (25.0) | 3 (12.0) | 18 (23.4) |
| Regional | 3 (37.5) | 14 (31.8) | 11 (44.0) | 28 (36.4) |
| Distant | 0 (0.0) | 7 (15.9) | 5 (20.0) | 12 (15.6) |
| Unknown | 1 (12.5) | 12 (27.3) | 6 (24.0) | 19 (24.7) |
| Treatment | | | | |
| Operated | 5 (6.5) | 9 (11.7) | 2 (2.6) | 16 (20.8) |
| Not operated ^a | 3 (3.9) | 35 (45.5) | 23 (29.9) | 61 (79.2) |
| ACC not operated | 2 (2.6) | 9 (11.7) | 1 (1.3) | 12 (15.6) |
| ACC operated | 4 (5.2) | 6 (7.8) | 0 (0.0) | 10 (13.0) |
| Curative radiotherapy | 2 (2.6) | 18 (23.4) | 6 (7.8) | 26 (33.8) |
| Palliative radiotherapy | 0 (0.0) | 10 (13.0) | 9 (11.7) | 19 (24.7) |

^aImplies no surgical resection, but patients may have received radiotherapy, or no treatment registered.

AC: adenocarcinoma; ACC: adenoid cystic carcinoma; SCC: squamous cell carcinoma.

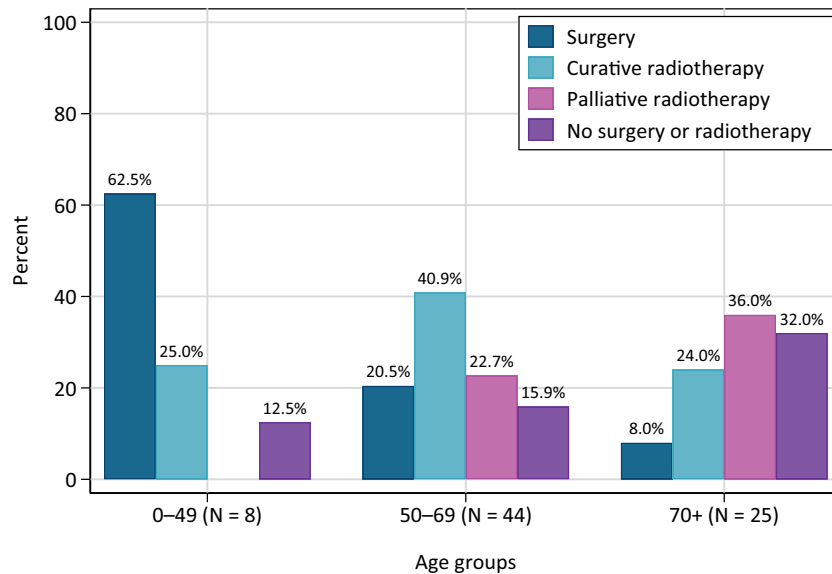


Figure 1: The proportions treated with the different modalities, by age group. The percentages are calculated with the number in each age group as denominator.

Survival

The 1-, 5- and 10-year overall survival for the whole group were 69.7%, 31.7% and 24.6%, respectively (Table 1 and Fig. 2). The corresponding data with relative survival are shown in Table 3. The 5-year overall survival for patients diagnosed in 2000–2010 and 2011–2020 was 26.7% (95% CI: 14.9–40.0) and 44.5% (95% CI: 25.9–61.6), respectively ($P = 0.52$). The tendency of higher median, 1-, 5- and 10-year survival in women compared to men (Table 3) did not reach statistically significance. The 5-year overall

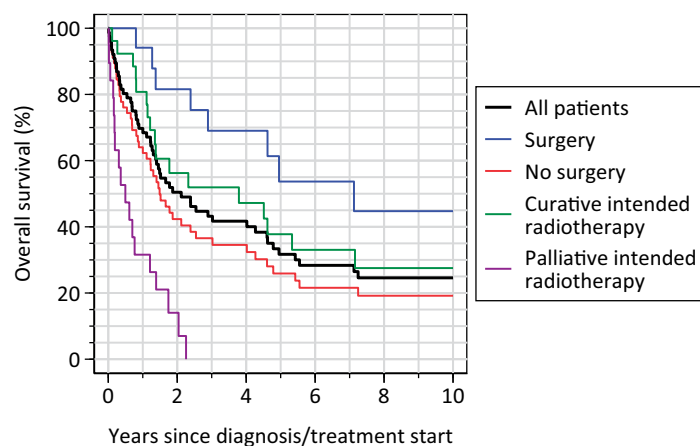
survival ranged from 18.2% in patients with SCC to 59.2% in patients with ACC. Univariable analysis shows that patients diagnosed with an ACC had a better survival compared to patients with SCC; however, after adjusting for the case mix, this difference was reduced (Table 4). Among patients who were resected, 53.7% were alive after 5 years, compared to 25.9% of patients who were not resected. In resected patients with ACC, 80.0% were alive after 5 years. In those treated with curative radiotherapy, 37.8% were alive after 5 years. In the group given palliative radiotherapy, the median survival was 6 months, 1-year overall

Table 2: Number and proportion of patients treated with different modalities by sex, histology and stage

| | Treatment, n (%) | | | | |
|-----------|------------------|-----------|--------------------|----------------------|---------------------------|
| | | Resected | Curative radiation | Palliative radiation | No treatment ^a |
| All | 77 (100.0) | 16 (20.8) | 26 (33.8) | 19 (24.7) | 16 (20.8) |
| Sex | | | | | |
| Women | 36 (46.8) | 8 (22.2) | 13 (36.1) | 7 (19.4) | 8 (22.2) |
| Men | 41 (53.2) | 8 (19.5) | 13 (31.7) | 12 (29.3) | 8 (19.5) |
| Histology | | | | | |
| AC | 7 (9.1) | 0 (0.0) | 2 (28.6) | 4 (57.1) | 1 (14.3) |
| SCC | 33 (42.9) | 4 (12.1) | 12 (36.4) | 12 (36.4) | 5 (15.2) |
| ACC | 22 (28.6) | 10 (45.5) | 7 (31.8) | 1 (4.5) | 4 (18.2) |
| Other | 15 (19.5) | 2 (13.3) | 5 (33.3) | 2 (13.3) | 6 (40.0) |
| Stage | | | | | |
| Localized | 18 (23.4) | 9 (50.0) | 4 (22.2) | 2 (11.1) | 3 (16.7) |
| Regional | 28 (36.4) | 6 (21.4) | 8 (28.6) | 8 (28.6) | 6 (21.4) |
| Distant | 12 (15.6) | 0 (0.0) | 2 (16.7) | 8 (66.7) | 2 (16.7) |
| Unknown | 19 (24.7) | 1 (5.3) | 12 (63.2) | 1 (5.3) | 5 (26.3) |

^aImplies no surgery or radiotherapy registered.

AC: adenocarcinoma; ACC: adenoid cystic carcinoma; SCC: squamous cell carcinoma.



| Number at risk | 0 | 2 | 4 | 6 | 8 | 10 |
|----------------------------|----|----|----|----|----|----|
| All 77 | 36 | 26 | 18 | 13 | 12 | |
| Surgery 16 | 12 | 9 | 7 | 5 | 4 | |
| No surgery 61 | 24 | 17 | 11 | 8 | 8 | |
| Curative radiotherapy 26 | 13 | 11 | 7 | 4 | 4 | |
| Palliative radiotherapy 19 | 2 | 0 | 0 | 0 | 0 | |

Figure 2: The overall survival as Kaplan-Meier estimates, stratified by treatment modality.

survival was 31.6% and none were alive after 3 years. From the multivariable survival analysis, age group, histology and treatment modality were identified to be independent prognostic factors (Table 4).

DISCUSSION

This study found a 5-year overall survival of 31.7% for the entire group of tracheal cancer patients, which is higher than previously reported [1, 4, 7]. The difference in 5-year overall survival of 26.7% and 44.5% in the first and last half period, respectively, did not reach statistical significance but may still be seen as a positive continuation of the improvement in survival seen in the last

decades [1, 4, 7]. The 5-year overall survival was 53.7% and 37.8% in those resected and those treated with curative radiotherapy, respectively. The proportion given surgical resection or curative radiation is highest in the youngest age group and the proportion given palliative radiotherapy or no therapy increases with increased age. Low age, ACC as histology and surgery as treatment came out as significant predictors for survival in the multi-variable analysis.

The incidence of 0.08 per 100 000 per year was slightly lower than what others have found [1-4]. This may be a reality, or an artefact due to distal tumours being miscoded as lung cancer. The age distribution with 38.5% of the patients being <60 years underscores the necessity of timely diagnosis and aggressive treatment. The high and significant correlation between the

Table 3: Survival data by sex, histology, stage and treatment

| | Median survival | Overall survival (%) (95% CI) | | | Relative survival (%) (95% CI) | | |
|-------------------------|--------------------|-------------------------------|------------------|------------------|--------------------------------|-------------------|-------------------|
| | Months (95% CI) | 1 year | 5 years | 10 years | 1 year | 5 years | 10 years |
| All | 25.8 (15.9–52.0) | 69.7 (58.1–78.7) | 31.7 (21.0–42.9) | 24.6 (14.8–35.6) | 71.4 (61.6–82.7) | 33.0 (22.0–49.6) | 27.2 (16.9–43.8) |
| Sex | | | | | | | |
| Women | 29.1 (15.9–67.5) | 74.3 (56.4–85.7) | 34.7 (18.6–51.5) | 26.5 (12.0–43.5) | 75.5 (62.0–91.8) | 36.0 (21.7–59.7) | 29.7 (16.0–55.1) |
| Men | 21.6 (10.8–52.0) | 65.9 (49.3–78.2) | 29.1 (15.7–43.9) | 22.9 (10.9–37.5) | 68.0 (54.8–84.4) | 30.6 (16.6–56.3) | 25.2 (12.5–50.7) |
| Histology | | | | | | | |
| AC | 25.8 (2.9–NA) | 71.4 (25.8–92.0) | 23.8 (1.0–63.8) | 23.8 (1.0–63.8) | 76.4 (48.4–120.7) | NA | |
| SCC | 10.8 (6.6–18.1) | 48.5 (30.8–64.1) | 18.2 (7.4–32.8) | 9.1 (2.3–21.7) | 50.9 (36.6–70.8) | 20.1 (9.2–43.6) | 11.3 (3.8–33.6) |
| ACC | 131.2 (36.8–150.0) | 100.0 (100.0–100.0) | 59.2 (34.2–77.3) | 51.8 (26.7–72.0) | 100.5 (100.5–100.5) | 60.6 (41.6–88.3) | 55.2 (35.3–86.5) |
| Other | 17.7 (5.3–60.3) | 71.4 (40.6–88.2) | 19.8 (3.4–46.0) | 19.8 (3.4–46.0) | 73.9 (52.7–103.6) | 22.0 (6.6–73.8) | 23.6 (7.0–79.1) |
| Stage | | | | | | | |
| Localized | 60.3 (22.7–150.0) | 100.0 (100.0–100.0) | 45.3 (21.0–66.9) | 30.2 (10.1–53.6) | 103.2 (103.2–103.2) | 47.7 (23.2–97.9) | 32.1 (12.5–82.5) |
| Regional | 16.7 (10.4–36.8) | 67.9 (47.3–81.8) | 25.0 (10.3–42.9) | 25.0 (10.3–42.9) | 69.3 (53.9–89.2) | 25.3 (12.4–51.9) | 25.9 (12.6–53.0) |
| Distant | 3.9 (1.6–10.8) | 16.7 (2.7–41.3) | 8.3 (0.5–31.1) | 8.3 (0.5–31.1) | 24.3 (10.0–59.2) | 12.9 (2.7–62.4) | 13.6 (2.8–65.6) |
| Unknown | 58.3 (12.2–131.2) | 77.8 (51.1–91.0) | 45.5 (20.5–67.5) | 30.3 (9.9–54.0) | 78.8 (61.1–101.6) | 47.6 (27.4–82.6) | 35.6 (16.4–77.1) |
| Treatment | | | | | | | |
| Not operated | 18.1 (12.2–31.0) | 64.0 (50.6–74.7) | 25.9 (15.0–38.3) | 19.2 (9.7–31.2) | 65.3 (54.1–78.9) | 26.3 (15.3–45.1) | 21.1 (11.2–39.9) |
| Operated | 86.8 (29.1–NA) | 94.1 (65.0–99.1) | 53.7 (26.1–75.0) | 44.7 (18.4–68.2) | 94.9 (83.6–107.7) | 58.4 (33.8–100.8) | 49.9 (26.0–95.9) |
| ACC not operated | 58.3 (18.5–134.1) | 100.0 (100.0–100.0) | 41.9 (13.3–68.8) | 41.9 (13.3–68.8) | 100.7 (100.7–100.7) | 44.0 (21.5–90.0) | 46.3 (22.7–94.6) |
| ACC operated | NA (16.7–NA) | 100.0 (100.0–100.0) | 80.0 (40.9–94.6) | 64.0 (22.6–87.5) | 100.3 (100.3–100.3) | 81.4 (59.8–110.9) | 66.1 (38.5–113.4) |
| Curative radiotherapy | 46.1 (14.8–87.1) | 80.8 (59.8–91.5) | 37.8 (18.8–56.7) | 27.5 (11.1–46.9) | 85.5 (72.4–101.1) | 40.3 (24.1–67.4) | 32.8 (16.8–63.9) |
| Palliative radiotherapy | 6.0 (2.0–14.7) | 31.6 (12.9–52.2) | 0.0 | 0.0 | 40.7 (24.2–68.7) | 0.0 | 0.0 |

AC: adenocarcinoma; ACC: adenoid cystic carcinoma; CI: confidence interval; NA: not applicable; SCC: squamous cell carcinoma.

proportion of tracheal cancer patients and the proportion of the population in the health regions gives no signs of geographically skewed distribution.

As found by others, none with AC in our study underwent surgery [9, 22]. The distribution of the histologic types in this study was in line with findings by others [1, 2, 6, 11]. The distribution of the histological types in tracheal and pulmonary cancer differs. SCC with 43.6% is the most frequent type in the trachea but accounts for 20.0% of lung cancers. ACC is the second most frequent tumour in trachea but is very uncommon in the lungs. AC accounts for 9.1% of tracheal cancers and 50.0% of the lung cancers [23].

No high-level evidence data on risk factors exist, but an increased proportion of tobacco smokers has been found in patients with tracheal cancer and the proportion of smokers was higher in those with AC and SCC compared to those with ACC [2, 9, 24, 25].

The present finding from the univariable analysis of the decreased risk of death in those with ACC has been found by others [26]. This significance, however, was not present in the multivariable analysis where age and treatment modality also were included in the predictors. Thus, the general assumption that ACC implies improved survival may, in the present population be explained by younger age and an increased chance of receiving curative treatment.

In the literature, there is variation in both the proportion resected [6, 10, 15] and the survival [3, 9], and this may be explained by differences in the admission and selection of the patients. The patients who underwent palliative radiotherapy experienced a very poor survival, whereas those given curative radiotherapy had markedly improved survival. Even though we have found no study to compare with, it may be concluded that radiotherapy deserves its place in the treatment of patients with tracheal cancer not eligible for

surgery. The operative mortality has been reduced [27], and the present study confirms that surgery can be offered as a safe procedure for patients diagnosed in the early stage.

The central airways—trachea and lungs—represent the extremes in cancer incidence. With a mean of 3.7 new cases of tracheal cancer per year, lung cancer is almost 1000 times more frequent [13].

Limitations

A limitation of our study is that it is retrospective. Also, data on smoking, other risk factors, marital status [28], medication and endobronchial treatment were not available. The lack of detailed data on tumour size and location, lymph node involvement and metastases is partly compensated by the registration of the traditional Surveillance, Epidemiology, and End Result staging. Despite these limitations, the study's population-based design and the use of national, comprehensive, high-quality data on diagnosis, treatment and survival provide results that are widely representative. We lack data on endobronchial treatment, which can reduce tumour size, and implant stent to improve respiration [12]. Endobronchial treatment is palliative, but it may be assumed that it also can prolong life. It should, in addition to surgery, medication and radiotherapy, be available in any combination for these patients.

Few clinicians get much experience, and it has been claimed that patients with tracheal cancer have been undertreated [4, 5] and that nihilism and ignorance [6], and limited knowledge [2], may have had a negative impact. Our data showed that the time from diagnosis to treatment was acceptable but could be shorter. The time used prior to diagnosis as presented by others [4, 5] indicates that this could also be reduced. Tracheal

Table 4: Univariable and multivariable analyses of survival (risk of death) by age group, sex, stage, histology and treatment

| | Univariable, hazard ratio (95% CI) | Multivariable, hazard ratio (95% CI) |
|---------------------------|------------------------------------|--------------------------------------|
| Age group (years) | | |
| 0–49 | 0.30 (0.07–1.26) | 0.38 (0.08–1.81) |
| 50–69 | Reference | Reference |
| 70+ | 3.39 (1.96–5.88) | 3.82 (1.97–7.40) |
| P-Value | <0.001 | <0.001 |
| Sex | | |
| Female | Reference | Reference |
| Male | 1.12 (0.66–1.88) | 1.20 (0.65–2.22) |
| P-Value | 0.68 | 0.5494 |
| Stage | | |
| Localized | 0.52 (0.26–1.07) | 0.65 (0.28–1.50) |
| Regional | Reference | Reference |
| Distant | 2.37 (1.12–5.01) | 1.58 (0.69–3.58) |
| Unknown | 0.73 (0.36–1.47) | 0.68 (0.30–1.55) |
| P-Value | 0.007 | 0.2441 |
| Histology | | |
| AC | 0.55 (0.19–1.56) | 0.30 (0.10–0.94) |
| SCC | Reference | Reference |
| ACC | 0.29 (0.15–0.57) | 0.85 (0.34–2.14) |
| Other | 0.65 (0.32–1.34) | 1.05 (0.46–2.38) |
| P-Value | 0.002 | 0.1270 |
| Treatment | | |
| No treatment ^a | 2.24 (0.85–5.89) | 1.89 (0.67–5.28) |
| Operated | Reference | Reference |
| Curative radiotherapy | 2.44 (1.02–5.82) | 1.52 (0.55–4.22) |
| Palliative radiotherapy | 12.30 (4.71–32.12) | 7.69 (2.53–23.41) |
| P-Value | <0.001 | <0.001 |

^aImplies no surgery or radiotherapy registered.

AC: adenocarcinoma; ACC: adenoid cystic carcinoma; CI: confidence interval; SCC: squamous cell carcinoma.

cancer is deadly but potentially curable and affects also younger age groups. No patient should experience delayed diagnosis or suboptimal treatment due to the ignorance caused by low incidence.

CONCLUSION

Even though survival has improved markedly, it is important to realize that 2 out of 3 patients are dead within 5 years of their diagnosis. Thus, tracheal cancer is one of the cancers with the poorest prognosis. Improvement in survival can be obtained by increased awareness, swift diagnostic process and increase in curative treatment.

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Roche, Janssen, Novartis, Takeda, Pfizer, BMS, Eli Lilly, Abbvie, Merck, Sanofi), and all honoraria has been donated to the hospital. The other authors declare no conflict of interest.

DATA AVAILABILITY

Data underlying this article can be requested from CRN through <https://helsedata.no>.

Author contributions

Yngvar Nilssen: Data curation; Formal analysis; Methodology; Writing—review & editing. **Steinar Solberg:** Conceptualization; Data curation; Formal analysis; Writing—original draft. **Odd Terje Brustugun:** Conceptualization; Methodology; Supervision; Writing—review & editing. **Bjørn Møller:** Conceptualization; Data curation; Funding acquisition; Resources; Supervision. **Arve Sundset:** Conceptualization; Data curation; Validation. **Sissel Gyrid Freim Wahl:** Conceptualization; Investigation; Methodology; Writing—review & editing. **Åslaug Helland:** Conceptualization; Funding acquisition; Supervision; Writing—review & editing.

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