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Published in:
European Journal of Surgical Oncology

DOI:
10.1016/j.ejso.2017.02.017

Available online at www.sciencedirect.com

ScienceDirect

EJSO 43 (2017) 1494–1502

EJSO the Journal of Cancer Surgery

www.ejso.com

Variation in head and neck cancer care in the Netherlands A retrospective cohort evaluation of incidence, treatment and outcome

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Accepted 23 February 2017
Available online 8 March 2017

Abstract

Background: To explore variation in numbers and treatment between hospitals that treat head and neck cancer (HNC) in the Netherlands.
Material and methods: Patient, tumor and treatment characteristics were collected from the Netherlands Cancer Registry, while histopathological features were obtained by linkage to the national pathology record register PALGA. Inter-hospital variation in volume, stage, treatment, pathologically confirmed loco-regional recurrence and overall survival rate was evaluated by tumor site.
Results: In total, 2094 newly diagnosed patients were included, ranging from 65 to 417 patients in participating hospitals treating HNC in 2008. Oral cavity cancer was mainly treated by surgery only, ranging from 46 to 82% per hospital, while the proportion of surgery with (chemo)radiotherapy ranged from 18 to 40%. Increasing age, male sex, and high stage were associated with a higher hazard of dying. In

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http://dx.doi.org/10.1016/j.ejso.2017.02.017

oropharynx cancer, the use of (chemo)radiotherapy varied from 31 to 82% between hospitals. We found an indication that higher volume was associated with a lower overall hazard of dying for the total group, but not by subsite. Low numbers, e.g. for salivary gland, nasopharynx, nasal cavity and paranasal sinus, did not permit all desired analyses.
Conclusion: This study revealed significant interhospital variation in numbers and treatment of especially oropharyngeal and oral cavity cancer. This study is limited because we had to rely on data recorded in the past for a different purpose. To understand whether this variation is unwanted, future research should be based on prospectively collected data, including detailed information on recurrences, additional case-mix information and cause of death.

Keywords: Head and neck cancer; Outcome; Survival; Epidemiology; Treatment; Quality of care

Introduction

Head and neck cancer (HNC) consists of a heterogeneous group of cancers. The individual types are characterized by their low incidences, but as group they take the 7th and 9th place in men and women, respectively, in the Netherlands.[1]

Because of the many vital functions in the head and neck, the delicate balance between optimal oncological and functional outcome characterizes treatment choices for of HNC. Centralization of care was shown to improve outcome in HNC and other high-complex types of cancer treatment.[2–9]

Since the foundation of the Dutch Head and Neck Society (DHNS) in 1984, over 90% of HNC patients are treated in specialized head and neck cancer centers (HNCC) in the Netherlands.[10] Several HNCCs collaborate with regional hospitals (Preferred Partner clinics (PPC)). In the Netherlands, possibly related to this centralization, survival rates are good for HNC compared to other European countries.[11,12]

Despite the presence of national guidelines, differences in treatment patterns have been described for the American[13] and British[14] setting. To discover the extent of variation between hospitals treating HNC in the Netherlands, we studied variation in patient and tumor characteristics, type of treatment, volume, recurrences and overall survival for HNC patients within the participating hospitals.

Patients and methods

Data sources

All patients diagnosed with primary invasive HNC in 2008 identified in the Netherlands Cancer Registry (NCR) and known in one of the participating hospitals were included. Patients with carcinoma in situ, skin cancer, sarcomas or hematological malignancies of the head and neck area were excluded.

The NCR is population-based and cancer cases are identified from pathology records received from the nationwide pathology network PALGA, as well as from the hospital discharge registry. The completeness of the NCR was estimated to equal at least 95%.[15] Following notification, trained tumor registration clerks abstract a minimum data set, including patient, tumor and treatment characteristics from hospital records.

To evaluate recurrences within 5 year from diagnosis, the dataset of the NCR was linked to PALGA data by a trusted third party. PALGA data included all conclusions from pathology reports, containing information on tissue site, procedure for tissue retrieval, histopathological diagnosis and date of specimen retrieval.

Participating hospitals (HNCC N = 7 and PPC N = 3) consented to anonymous analyses of their data; an independent employee at the NCR performed anonymization. Because of the retrospective character of the study, ethical approval was not required, as was advised by the institutional review board.

Definitions

Patients were classified based on ICD-O-3[16] code: oral cavity cancer (C02, C03, C04, C05.0, C05.8, C05.9, C06), oropharyngeal cancer (C01.9, C05.1, C05.2, C09, C10 (except C10.1)), laryngeal cancer (C10.1, C32), hypopharyngeal cancer (C12, C13) and cancer at other subsites [salivary gland, nasopharynx, para-nasal sinus or nasal cavity] (C07, C08, C11, C30, C31, C14).

In case patients were known in more than one HNCC, the center in which patients were treated was chosen as coding center. Second opinions without treatment were not included in the numbers per center. Volume was included in accordance with the previous report by Halm et al.[17]

Pathological TNM (6th edition[18]) was used and complemented with the clinical classification if pathological stage was unavailable.

Treatment was classified into 4 groups: surgery only, surgery plus (chemo-)radiotherapy (C)RT, (C)RT or other/palliative therapy. Patients with distant metastases at diagnosis (M+) or untreated patients were excluded from analyses on treatment and survival.

All recurrences reported are pathologically verified recurrences, since the pathology databank was our only

source with information on recurrences; thus clinical recurrences could not be included.

Statistical analysis

Univariate testing was done by Chi-square, Kruskal–Wallis or Fisher's Exact test. Recurrence and survival analyses using the Kaplan–Meier method. Multivariate survival analyses including sex, age, stage and hospital volume was performed using the Cox regression analysis.

P-values <0.05 were considered statistically significant.

Statistical programs used were SPSS (version 22.0, IBM Chicago, IL) and STATA data analysis and statistical software (version 10.0, StataCorp LP, TX, 1996).

Results

In total 2094 patients, were included in this study. The number of newly diagnosed patients in 2008 ranged from 129 to 417 in HNCC and from 65 to 86 in PPC. There was variation in site distribution and in sex between hospitals (Table 1). In all subsites, men were more affected than women.

Oral cavity cancer

There were 602 patients with oral cavity squamous cell cancer. Hospital volume ranged from 23 to 119.

Most patients had stage I disease (36%), followed by stage IVM0 (27%), stage II (18%), stage III (12%) and stage IVM1 (6%). The stage distribution was not different between hospitals ($p = 0.639$). After exclusion of M+/untreated patients 565 patients were analyzed. Surgery only was treatment of first choice, ranging from 46% to 80% between hospitals ($P < 0.001$) (Table 2). The proportion of surgery with adjuvant (C)RT, which was almost exclusively postoperative radiotherapy (PORT), ranged from 18% to 40%. The use of PORT differed significantly between the hospitals ($p < 0.001$), but appeared independent from hospital volume ($p = 0.162$).

The pathology proven loco-regional recurrence rate after 5 years was 29% (162 recurrences). There was no significant difference in recurrence rates between the hospitals ($p = 0.779$).

The overall 5-year survival was 60% (227 events) and was significantly associated with stage ($p < 0.001$): stage I 78% (45 events), stage II 71% (30 events), stage III 52% (32 events) and stage IV M0 36% (113 events) [Fig. 1a].

In multivariate cox regression analysis: higher age, male sex and higher stage were negatively associated with overall survival (Table 3).

Oropharyngeal cancer

In total 453 patients were diagnosed with oropharyngeal cancer. The number of newly diagnosed patients ranged from 13 to 91 in participating hospitals. Most patients were diagnosed with stage IV (55%). The stage distribution did not differ between hospitals ($p = 0.647$). For patients without distant metastases and undergoing treatment ($n = 406$; 90%) organ-sparing treatment was performed in most cases (73%), ranging from 31 to 85% ($p = 0.002$). Primary surgery was given in up to 36% (range 15–36%) of the patients in HNCCs (Table 2). Use of primary radiotherapy varied from 7% to 58% between HNCCs and the use of primary chemoradiation ranged from 20% to 55%.

The 5-year pathology proven loco-regional recurrence rate was 26% (107 recurrences). There was no statistically significant difference in recurrence rate between the hospitals ($p = 0.901$).

Five-year overall survival was 52% (196 events) and did not statistically differ by stage (I: 59% (21 events), II: 56% (28 events), III 53%, (36 events) and IVM0 47% (110 events); $p = 0.310$) [Fig. 1b].

In multivariate Cox regressions analysis stage IV (HR 1.60 (95%CI 1.02–2.49) and higher age (HR 1.04 for each year (95%CI 1.02–1.05) were associated with a lower overall survival (Table 3).

Laryngeal cancer

In total 585 patients were identified with laryngeal cancer. Hospital volume ranged from 10 to 133 newly diagnosed patients per year.

Stage distribution varied significantly between the hospitals; stage I ranged from 30 to 41% and stage IV from 18% to 33% ($p = 0.012$).

The proportion of stage I patients was higher in PPCs compared to HNCCs (36% vs. 26%, $p = 0.003$). Stage II, III and IV did not significantly vary between PPCs and HNCCs ($p = 0.804$, 0.096 and 0.084 respectively).

After exclusion of M+/untreated patients, 566 patients were left for additional analyses.

Most patients with laryngeal cancer were treated by an organ preserving treatment (55%–94%, $p = 0.004$) (Table 2).

After 5 years, pathology proven loco-regional recurrences were found in 20% of the patients (114 events). The recurrence rate did not vary between hospitals ($p = 0.779$). The 5-year overall survival of laryngeal cancer equaled 66% (194 events) (stage I: 80% (39 events), stage II 74% (39 events), stage III 58% (38 events), stage IVM0 40% (74 events) ($p < 0.001$) [Fig. 1c].

Multivariate Cox regression analysis showed significantly increased hazard rates of dying for higher stage (stage III: HR 3.20 (95%CI 2.12–4.85) & stage IV disease: HR 5.74 (95%CI 3.96–8.33), increasing age (HR 1.07 95%CI 1.05–1.08) and (borderline significant) female gender (HR 1.42 95%CI 1.00–2.01). Hospital volume was not associated with overall survival (Table 3).

Table 1
Patient and tumor characteristics by hospital.

	HNCC1	HNCC2	HNCC3	HNCC4	HNCC5	HNCC6	HNCC7	PPC1	PPC2	PPC3	Total	P-value
Age (median (min–max))	62 (19–94)	63 (14–94)	62 (13–93)	63 (10–92)	63 (10–97)	64 (15–91)	63 (36–93)	62 (29–88)	60 (31–91)	64 (15–87)	63 (10–97)	P = 0.893 (Kruskal wallis)
Sex (N (%))												
Male	162 (65)	220 (68)	177 (67)	204 (64)	310 (74)	136 (78)	96 (74)	58 (67)	46 (70)	41 (63)	1450 (69)	0.010 (Chi-square)
Female	88 (35)	102 (32)	86 (33)	117 (36)	107 (26)	39 (22)	33 (26)	28 (33)	20 (30)	24 (37)	644 (31)	
Stage (N (%))												
I	76 (30)	79 (25)	64 (24)	82 (26)	99 (24)	38 (22)	37 (29)	28 (33)	25 (38)	23 (35)	551 (26)	0.065 (Chi-square)
II	42 (17)	71 (22)	43 (16)	79 (25)	75 (18)	21 (12)	25 (19)	19 (22)	9 (14)	15 (23)	399 (19)	
III	33 (13)	44 (14)	41 (16)	44 (14)	69 (17)	30 (17)	24 (19)	10 (12)	10 (15)	4 (6)	309 (15)	
IV M0	85 (34)	101 (31)	92 (35)	100 (31)	130 (31)	76 (43)	38 (29)	24 (28)	20 (30)	18 (27)	684 (33)	
IV M1	9 (4)	9 (3)	14 (5)	12 (4)	35 (8)	8 (5)	3 (2)	2 (2)	2 (3)	4 (6)	98 (5)	
Missing	5 (2)	18 (6)	9 (3)	4 (1)	9 (2)	2 (1)	2 (2)	3 (4)	0 (0)	1 (2)	53 (3)	
Site (N (%))												
Oral cavity	80 (32)	94 (29)	61 (23)	119 (37)	100 (24)	40 (23)	29 (22)	23 (27)	20 (30)	36 (55)	602 (29)	<0.001 (Chi-square)
Oropharynx	45 (18)	64 (20)	83 (32)	57 (18)	91 (22)	33 (13)	33 (26)	19 (22)	13 (20)	15 (23)	453 (22)	
Larynx	72 (29)	92 (29)	55 (21)	83 (26)	133 (32)	63 (36)	40 (31)	19 (22)	18 (27)	10 (15)	585 (28)	
Hypopharynx	15 (6)	25 (8)	25 (10)	21 (7)	43 (10)	19 (11)	12 (9)	6 (7)	8 (12)	1 (2)	175 (7)	
Other	38 (15)	47 (15)	39 (15)	41 (13)	50 (12)	20 (11)	15 (12)	19 (22)	7 (11)	3 (5)	279 (13)	
Total (N)	250	322	263	321	417	175	129	86	66	65		

Abbreviations: HNCC – head neck cancer center, PPC – preferred partner clinic.

Hypopharyngeal and other types of HNC

Hypopharyngeal cancer (n = 175, hospital range 1–43) was mostly diagnosed staged IV disease (>70%). The stage distribution did not differ between hospitals.

After exclusion of primary metastasized or untreated patients 149 patients were included in the treatment and survival analyses.

The majority of the patients were treated with organ preserving treatment regimens [mean 80%, hospital range 58%–100% (p = 0.149)] (Table 2).

The pathology proven recurrence rate was 25%. This did not statistically differ between the hospitals (p = 0.257).

Five-year overall survival was 39% with the worst survival (32%) for stage IV patients (p = 0.08). Due to low number of events, multivariate analysis could not be performed.

Hundred patients (hospital range 1–18) with salivary gland cancer were represented in this study cohort. For nasal cavity and para-nasal sinus cancer, the number of patients was 114 (hospital range 1–25). For nasopharyngeal cancer, there were 63 patients ranging from 0 to 14 per hospital. These low numbers did not allow further analysis.

Discussion

This study describes HNC patients' characteristics and outcome from 7 HNCCs and 3 PPCs in 2008 in the Netherlands. The number of HNC patients equaled 2094 and ranged from 65 to 417 per center.

Variation in treatment is one of the primary findings in this study and has been described in the literature before. In previous American[13] and British[14] studies, differences in treatment regimens were described, despite the presence of national guidelines, mainly due to health care organization. However, these studies are not representative for the Dutch setting because there are fundamental differences in health care organization between these countries and the Netherlands (e.g. insurance for every inhabitant and only cancer care in non-private hospitals). Our study is the first to show significant variation in treatment in a country with centralized head and neck cancer care.

In oral cavity cancer, the use of PORT differed. This difference could probably be explained by unmeasured pathological characteristics, such as the presence of close or involved resection margins, extracapsular lymph node extension, or perineural growth: all indicating adjuvant treatment according to the guideline.[13,19] Therefore, we cannot draw further conclusions about the source of this difference.

In oropharynx cancer patients there was a wide variation in the primary use of (C)RT. Because the updated version of the national guideline, with chemoradiation as standard treatment for advanced stages instead of radiotherapy alone, was published in 2010, early adoption of the guideline in 2008 by some centers could be an explanation for

Table 2
Treatment variation by tumor site and hospital.

	HNCC1	HNCC2	HNCC3	HNCC4	HNCC5	HNCC6	HNCC7	PPC1	PPC2	PPC3	Total	P-value
	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	N (%)	
Oral cavity cancer patients												
Surgery only	35 (46.1%)	52 (58.4%)	34 (60.7%)	69 (62.2%)	43 (48.3%)	21 (53.8%)	15 (53.6%)	18 (81.8%)	12 (60.0%)	23 (65.7%)	322 (57.0%)	<0.001 (Fisher Exact)
Surgery with (C)RT	25 (32.9%)	29 (32.6%)	12 (21.5%)	38 (34.2%)	36 (40.4%)	7 (17.9%)	7 (25.0%)	4 (18.2%)	6 (30.0%)	12 (34.3%)	176 (31.2%)	
(C)RT	15 (19.5%)	8 (8.9%)	10 (17.9%)	4 (3.6%)	10 (11.2%)	10 (25.7%)	6 (21.4%)	0	2 (10.0%)	0	65 (11.5%)	
Other therapy	1 (1.3%)	0	0	0	0	1 (2.6%)	0	0	0	0	2 (0.4%)	
Total	76	89	56	111	89	39	28	22	20	35	565	
Oropharynx cancer patients												
Surgery with or without (C)RT	13 (31.7%)	12 (20.3%)	27 (35.5%)	8 (14.8%)	16 (21.1%)	6 (20.0%)	11 (35.5%)	9 (69.2%)	2 (18.2%)	4 (30.8%)	108 (26.7%)	0.004 (Fisher Exact)
(C)RT	28 (68.3%)	47 (79.7%)	49 (64.5%)	46 (85.2%)	60 (78.9%)	24 (80.0%)	20 (64.5%)	4 (30.8%)	9 (81.8%)	9 (69.2%)	296 (73.3%)	
CRT	10 (24.4%)	12 (20.0%)	29 (38.2%)	19 (35.2%)	19 (35.2%)	9 (30.0%)	7 (22.6%)	3 (21.4%)	6 (54.5%)	6 (46.2%)	120 (29.6%)	
RT	18 (43.9%)	35 (58.3%)	20 (26.3%)	27 (50.0%)	41 (53.9%)	15 (50.0%)	13 (41.9%)	1 (7.1%)	3 (27.3%)	3 (23.1%)	176 (43.3%)	
Total	41	59	76	54	76	30	31	13	11	13	404	
Larynx cancer patients												
Surgery with or without (C)RT	28 (40.1%)	19 (20.9%)	15 (28.8%)	26 (32.6%)	29 (22.8%)	16 (27.2%)	17 (42.5%)	4 (21.1%)	1 (5.6%)	1 (10.0%)	156 (27.6%)	0.004 (Fisher Exact)
(C)RT	42 (60.0%)	71 (78.0%)	37 (71.1%)	54 (67.6%)	98 (77.1%)	43 (72.9%)	22 (55.0%)	15 (79.0%)	17 (94.4%)	9 (90.0%)	408 (72.1%)	
Other therapy	0	1 (1.1%)	0	0	0	0	1 (2.5%)	0	0	0	2 (0.3%)	
Total	70	91	52	80	127	59	40	19	18	10	566	
Hypopharynx cancer patients												
Surgery with or without (C)RT	1 (8.3%)	2 (9.5%)	4 (20.0%)	6 (31.6%)	10 (29.4%)	1 (6.3%)	5 (41.7%)	0 (0.0%)	1 (12.5%)	0 (0.0%)	30 (20.1%)	0.149 (Fisher Exact)
(C)RT	11 (91.7%)	19 (90.5%)	16 (80.0%)	13 (68.4%)	24 (70.6%)	15 (93.8%)	7 (58.3%)	6 (100.0%)	7 (87.5%)	1 (100.0%)	119 (79.9%)	
Total	12	21	20	19	34	16	12	6	8	1	149	

Abbreviations: HNCC – head neck cancer center, PPC – preferred partner clinic, (C)RT – (chemo)radiotherapy, RT – radiotherapy.

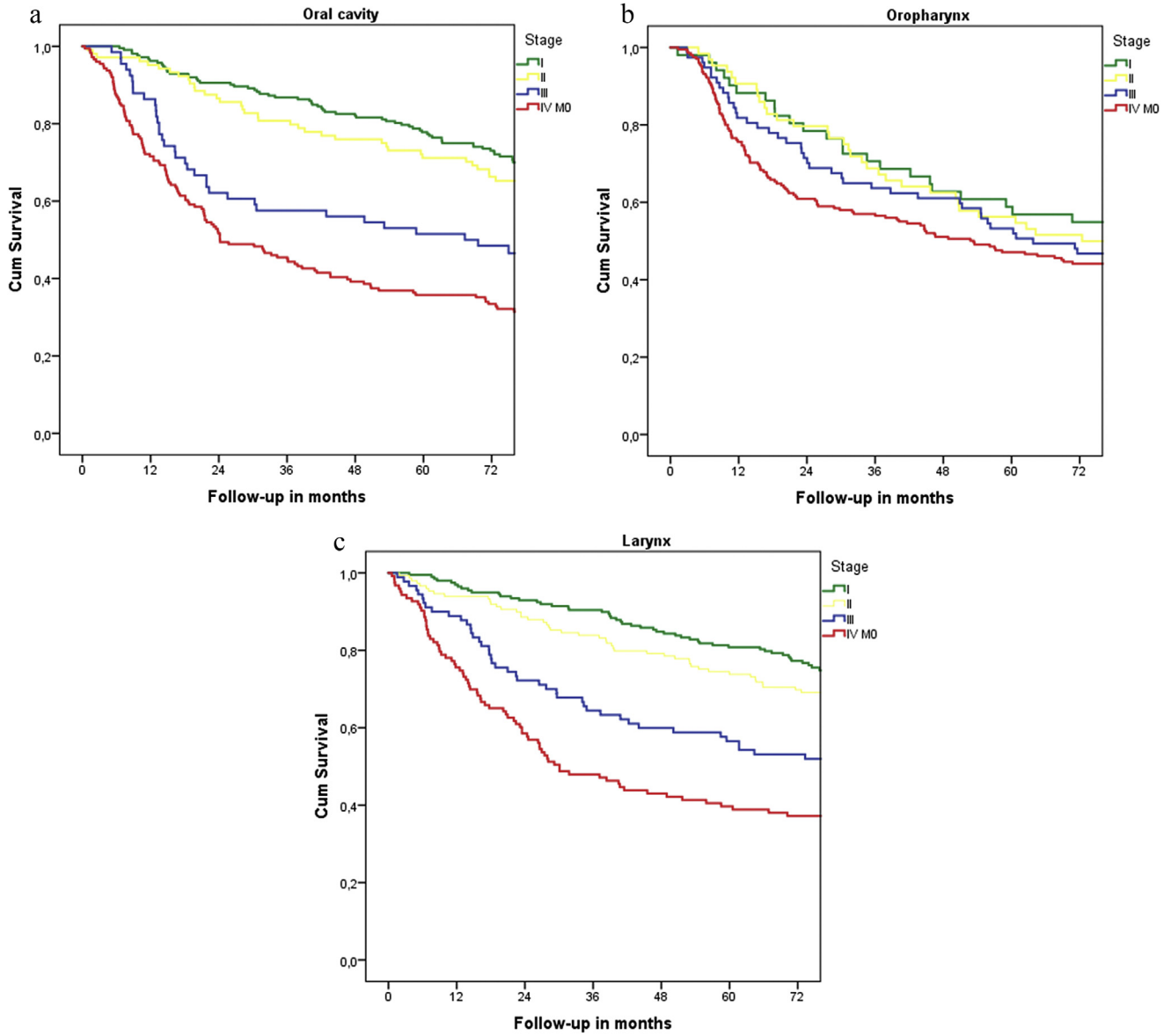

Figure 1. a. Kaplan Meier curve of overall survival in oral cavity cancer patients by stage. b. Kaplan Meier curve of overall survival in oropharynx cancer patients by stage. c. Kaplan Meier curve of overall survival in larynx cancer patients by stage.

this observed variation. For national uniformity in treatment, continuously updated guidelines and rapid adherence are essential.

For laryngeal cancer, the differences in treatment between hospitals were less clear, probably because the treatment guidelines can be applied more straightforward in an organ setting with more clearly defined anatomical boundaries as compared with other head and neck sites. An ongoing debate on treatment of laryngeal cancer is how to treat T4 laryngeal carcinomas. Unfortunately, our series contained insufficient number of T4 laryngeal cancer patients per center to evaluate differences. However, there is a recent publication of Timmermans et al.[20] that showed there is a declining tendency in primary laryngectomy for laryngeal cancer in the Netherlands over the past 20 years. However, this analysis was not split for different centers, so whether there is hospital based variation in treatment of T4 laryngeal cancer remain a topic of future research.

Another interesting observation in the laryngeal cancer group was the higher hazard of dying for female patients (HR: 1.42 (95%CI: 1.00–2.01), while for most cancer types, the survival is better for women compared to for men.[21] This can be explained by the fact that women more often have supraglottic cancer, associated with higher stage, as shown in another study from the Netherlands.[22]

The exclusion of untreated or metastasized patients from treatment analyses may introduce bias because differences in techniques used to evaluate distant metastasis may differ between hospitals, as well as the decision to treat or not to

Table 3
Multivariate analyses for 5-year overall survival.

	Oral cavity			Oropharynx			Larynx			Total		
	HR	95%CI	P	HR	95%CI	p	HR	95%CI	p	HR	95%CI	P
Male	Ref.			Ref.			Ref.			Ref.		
Female	0.71	0.55–0.92	0.009	0.84	0.62–1.13	0.245	1.42	1.00–2.01	0.049	0.89	0.77–1.03	0.108
Age (per year)	1.04	1.03–1.06	<0.001	1.04	1.02–1.05	<0.001	1.07	1.05–1.08	<0.001	1.04	1.04–1.05	<0.001
Stage I	Ref.			Ref.			Ref.			Ref.		
Stage II	1.18	0.79–1.77	0.409	1.20	0.71–2.02	0.501	1.50	1.01–2.23	0.046	1.37	1.10–1.72	<0.001
Stage III	2.40	1.59–3.63	<0.001	1.40	0.84–2.32	0.205	3.20	2.12–4.85	<0.001	2.33	1.87–2.92	<0.001
Stage IV	3.69	2.70–5.02	<0.001	1.60	1.02–2.49	0.042	5.74	3.96–8.33	<0.001	3.56	2.97–4.28	<0.001
Hospital volume per 25	0.96	0.92–1.00	0.075	0.97	0.93–1.02	0.193	0.98	0.94–1.03	0.461	0.98	0.95–1.00	0.034
HNCC	Ref.			Ref			Ref.			Ref		
PPC	0.99	0.60–1.64	0.970	1.11	0.63–1.98	0.714	1.20	0.68–2.13	0.538	0.99	0.75–1.31	0.950

HR – hazard ratio, Ref. – reference, HNCC – head and neck cancer center, PPC – preferred partner clinic.

treat curatively. However, a fairly good consensus on when to treat curatively was shown in the Netherlands.[23]

A second important finding of our study is the variation in site distribution per hospital. Quite a large difference in site distribution is found, which might be explained by historically defined referral patterns. Another explanation could be the variation in composition of the population in the adherence area of the HNCC. A clear example of that is the distribution of Asian immigrants across the Netherlands and the clustering of nasopharyngeal cancer in accordance with that distribution.

Our survey revealed low numbers of salivary gland, nasopharynx, nasal cavity and paranasal sinus cancer, rarely exceeding twenty cases per center. These low numbers did not permit any robust data analysis, and will never be sufficient to evaluate variation. To obtain sufficient numbers, centralization may be advocated. However, other considerations should be taken into account: salivary gland cancers are part of a larger cohort of benign salivary gland tumors also providing surgical expertise. Another example is chemoradiation for nasopharynx, which demands experience and specific expertise from the radiation oncologist, as well as experience and specific expertise of the supporting personnel with toxicity and complications related to the treatment. More or less similar considerations play a role for paranasal sinus cancer with the need of functional endoscopic and neuro-surgical expertise. Assuming that increasing volume contributes to improved quality of care, further centralization of these rare HNC might contribute to better outcomes.

We found a significantly lower hazard of dying with increasing hospital volume, after correction for age, gender and stage (HR 0.98 per 25 patients, $p = 0.034$). However, volume was no longer statistically significant in analyses restricted by subsite. This is probably the result of the lower number of patients by subsite in combination with the low effect for volume.

Our findings are in line with a report on head and neck surgery[24] showing, that the hazard of dying was lower in high-volume hospitals (HR per 25 patients 0.976 (95%CI 0.955–0.997) in multivariate analysis). A recent meta-analysis, including five large (n = 805–19,326) studies showed a similar volume-survival relationship in 49,403 HNC patients (HR 0.886 (95%CI, 0.820–0.956).[25] However, volume cutoffs of the original studies were used, causing heterogeneity in numbers classified as high or low volume. It was argued that differences in definitions of volume only change the amplitude and not the relationship of the effect.[26]

This study was mainly limited by the fact that data were recorded in the past, and not specifically for this goal. Specific characteristics necessary for case-mix adjustments, like performance status, comorbidity, smoking, alcohol drinking and HPV status, are lacking.

Another limitation of this study was the missing pathology data; available information was mainly free unstandardized text, complicating complete and uniform extraction of data. Despite insufficient information to score perineural growth, extracapsular spread or resection margins, pathologically proven recurrences could be scored. Several studies showed that the use of standardized pathology reports improves the quality of the reports.[27,28] Furthermore, the list of important pathology items for HNC grows rapidly PALGA is currently working on a national protocol for synoptic reporting in HNC. The use of only pathology proven recurrences definitely leads to an underestimation of the recurrence rate, and may contribute to differences in tumor recurrence rates between hospitals, since centers may utilize different techniques to prove a recurrence. Therefore recurrence-free survival should be interpreted with caution. Some precaution should also be made in the interpretation of survival, since only overall survival data was available for this cohort. Ideally disease specific survival is the outcome parameter of choice.

The Dutch national prospective audit will provide additional detailed information on case-mix, recurrences (both clinical and pathological) and cause of death in the future.

Summarizing, our study revealed significant variation in treatment of head and neck carcinomas and low numbers of salivary gland, nasopharyngeal and paranasal cancer per

hospital. To understand whether this variation is unwanted or not, we need more detailed information on large number of cases to accommodate robust analysis. Even though HNC care is already at a high level of centralization in the Netherlands, there may still be opportunities for improvement.

Funding

This study was financially supported by the Dutch Cancer Society (grant number: 2013-6480).

Role of funding source

Personnel costs, data acquisition and quality control costs.

The funding source was not involved in data interpretation or manuscript preparation

Acknowledgements

This study was supported by the Dutch Head and Neck Cooperative Group (study number: NWHHT 2014-02). The authors thank the registration team of the Netherlands Comprehensive Cancer Organization (IKNL) for the collection of data for the Netherlands Cancer Registry (NCR) as well as the participating Head and Neck Cancer Centers (HNCC) and their Preferred Partner Clinics (PPC) for approval to use these data.

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