

Hypopharynx

1. Introduction

1.1 General Information and Aetiology

The human pharynx is the part of the throat situated between the nasal cavity and the esophagus and can be divided into three parts: the nasopharynx at the top, the oropharynx in the middle and the hypopharynx at the bottom of the pharynx. The superior boundary of the hypopharynx is formed by the hyoid bone, while the inferior boundary is at the lower level of the cricoid cartilage. The hypopharynx itself can be divided into three sub-sites: the pyriform sinus, the postcricoid region and the posterior pharyngeal wall (Figure 1). The hypopharynx is richly supplied with lymphatics.

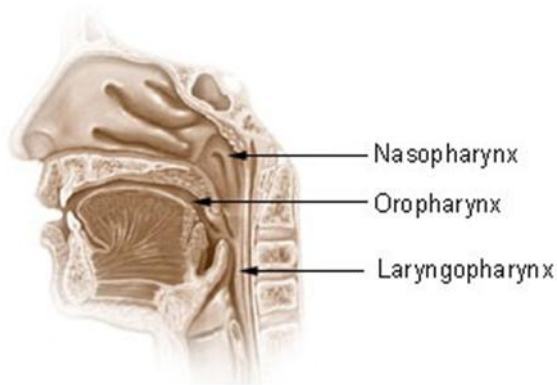


Figure 1. Hypopharynx (i.e. Laryngopharynx)

Hypopharyngeal cancer is most frequently diagnosed in men between 55 and 70 years old. However, women are becoming increasingly affected because of increased smoking behavior and are proportionally more represented in the age category above 75 years [1].

Next to alcohol and tobacco consumption, the development of hypopharyngeal cancer might be influenced by environmental exposure to certain substances (for example metals, wood fibre, coal mine dust, ceramic substances), exposure to radiotherapy of the head-and-neck region at young age, HPV-infection or Plummer-Vinson syndrome [1, 2].

Symptoms are rather vague and range from sore throat, hoarseness and referred headache to lymph node swelling in the neck, dysphagia and stridor. Therefore, hypopharyngeal cancer often presents at advanced stage at diagnosis.

1.2 Diagnosis and Treatment

A detailed history and physical examination needs to be performed in first instance, supplemented with a direct or indirect visualization of the tumour by endoscopy (laryngo-hypopharyngoscopy). In patients presenting with dysphagia, X-ray of the swallowing tract should routinely be performed. Imaging by CT and/or MRI is necessary for determining the tumor size and invasion depth. As for most head and neck cancer types, a careful search for second primary tumours of the upper aerodigestive tract is indicated [3]. Most of the hypopharyngeal cancers arise from the sinus pyriformis and 60-70% of the patients presents with a neck lymph node metastasis [2].

As for all cancers, histological confirmation of the disease is mandatory. In alignment with other head and neck regions, almost all hypopharyngeal cancers are squamous cell carcinoma (+/- 95%) [1].

Treatment of hypopharyngeal cancer is historically based on surgery followed by radiotherapy. This surgery is large and encompasses extirpation of pharynx +/- larynx accompanied by an "en bloc" removal of the neck lymph nodes. Plastic surgery is often needed to restore continuity of the digestive tract. As international randomized clinical trials on larynx preservation have shown no worse outcome for treatment by combinations of chemotherapy and radiotherapy (eventually followed by salvage surgery), this conservative approach is often preferred [3-5].

5-year relative survival rates for hypopharyngeal cancer are around 30% in Belgium, but can differ between sexes, age categories, stages and subsites [6].

2. Data Selection

All hypopharyngeal cancers diagnosed between 2004 and 2007 for patients with an official residence in the Flemish Region are selected, resulting in 451 cases (for detailed information on selected topography and morphology codes, see Appendix A). As described in Figure 2, 67 of them are excluded, resulting in 384 patients for whom results are presented in this chapter.

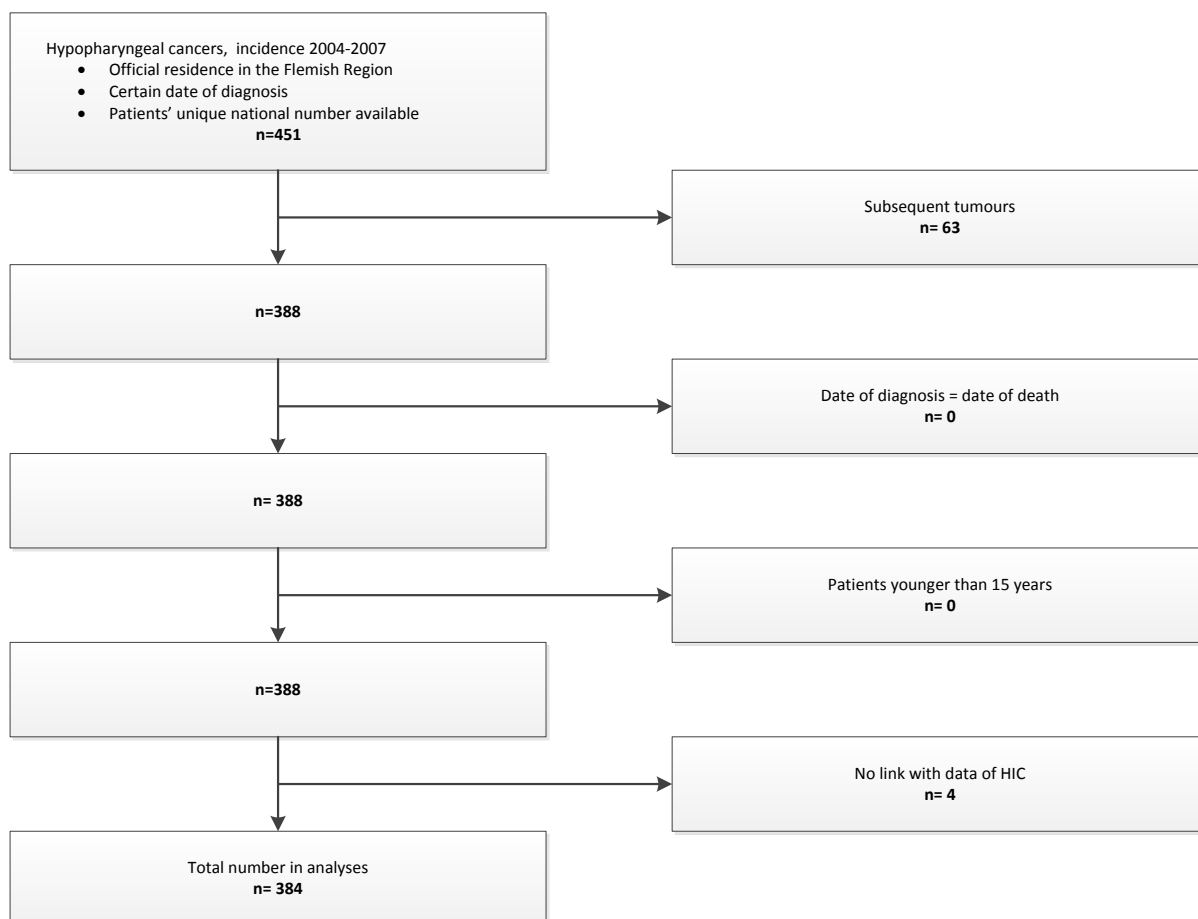


Figure 2. Selection of Hypopharyngeal Tumours (Flemish Region, 2004-2007)

3. Patient Characteristics

Males are much more often diagnosed with a hypopharyngeal tumour (male/female ratio: 7.88) during the incidence years 2004-2007. No clear trend in age-standardised rates can be observed over these incidence years (Table 1).

Table 1. Hypopharyngeal Cancer: Incidence (Flemish Region, 2004-2007)

Incidence year	Males		Females		Total	
	n	ESR	n	ESR	n	ESR
2004	92	2.81	12	0.34	104	1.56
2005	71	2.10	11	0.30	82	1.19
2006	83	2.43	7	0.20	90	1.28
2007	92	2.74	16	0.44	108	1.58
2004-2007	338	2.52	46	0.32	384	1.40

ESR: age-standardised rate, using the European Standard Population (n/100,000 person years)

The median age is 58 years for males and 57.5 years for females. Age at diagnosis ranges between 38 and 90 years. For further analyses, patients are divided into three age groups: 15-59 years, 60-69 years and 70+ years (Table 2).

Table 2. Hypopharyngeal Cancer: Age Distribution (Flemish Region, 2004-2007)

	Males	Females	Total
15-59 years	193	24	217
60-69 years	95	11	106
70+ years	50	11	61

4. Tumour Characteristics

Sublocalisation, morphology, differentiation grade and stage (clinical, pathological and combined stage) are described in Table 3. Almost all hypopharyngeal tumours with a defined localisation are located in the pyriform sinus, the other sublocalisations are rather rare. The majority of the tumours are moderately or poorly differentiated. Most patients are diagnosed with a stage IV tumour.

Table 3. Hypopharyngeal Cancer: Tumour Characteristics (Flemish Region, 2004-2007)

	N	% of total	% of known
Localisation			
Malignant neoplasm of pyriform sinus (C12.9)	239	62.2	89.8
Postcricoid region (C13.0)	4	1.0	1.5
Aryepiglottic fold, hypopharyngeal aspect (C13.1)	13	3.4	4.9
Posterior wall of hypopharynx (C13.2)	10	2.6	3.8
Overlapping lesion of hypopharynx (C13.8)	5	1.3	/
Hypopharynx, unspecified (C13.9)	113	29.4	/
Morphology			
Squamous cell carcinoma	379	98.7	/
Other specified carcinoma	5	1.3	/
Differentiation grade			
Well differentiated	28	7.3	8.4

Moderately differentiated	150	39.1	45.2
Poorly differentiated	145	37.8	43.7
Undifferentiated	9	2.3	2.7
Unknown	52	13.5	/
Clinical stage			
I	10	2.6	3.0
II	19	5.0	5.7
III	58	15.1	17.5
IV	245	63.8	73.8
Unknown	52	13.5	/
Pathological stage			
I	9	2.3	7.0
II	2	0.5	1.6
III	18	4.7	14.0
IV	100	26.0	77.5
Unknown	255	66.4	/
Combined stage			
I	14	3.6	4.0
II	17	4.4	4.8
III	58	15.1	16.4
IV	264	68.8	74.8
Unknown	31	8.1	/

Females are diagnosed with less severe stages than males, resulting in a higher proportion of stage I and II tumours (Figure 3). More males than females have tumours with an unknown stage. Patients in the oldest age group seem to have lower stages at diagnosis than the younger patients (Figure 4).

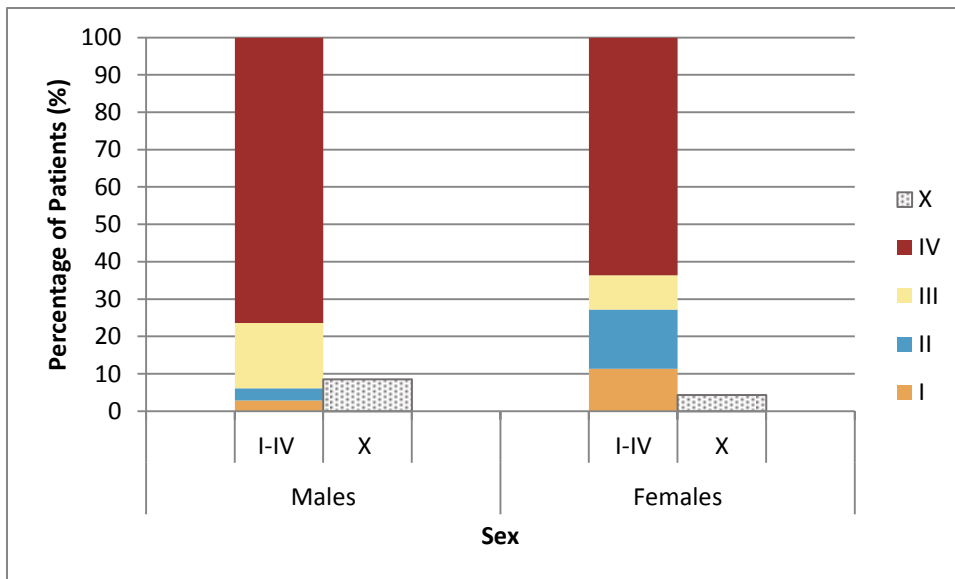


Figure 3. Hypopharyngeal Cancer: Stage Distribution by Sex (Flemish Region, 2004-2007)

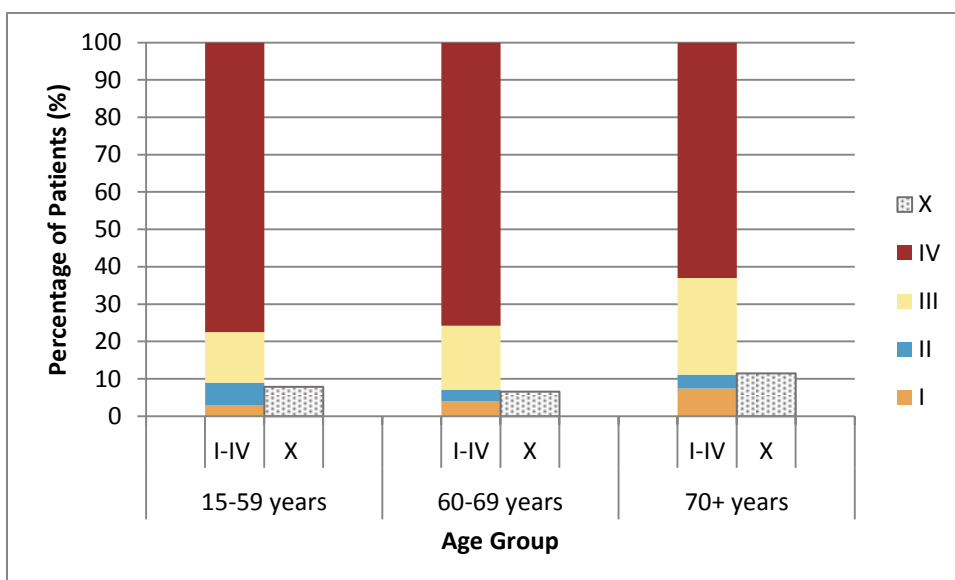


Figure 4. Hypopharyngeal Cancer: Stage Distribution by Age Group (Flemish Region, 2004-2007)

5. Diagnostic and Therapeutic Procedures

5.1 Diagnosis and Staging

An overview of the diagnostic and staging procedures for the hypopharyngeal cancer patients in the Flemish Region diagnosed between 2004 and 2007 is given in Table 4. Almost all cancers are confirmed by pathological examination (97.9%). For the majority of the patients, endoscopy is found to be charged (93.2%). While CT scanning is most often used in the staging procedure (97.7%), an X-

ray of the chest is also frequently performed (88.0%). Other imaging techniques such as PET-scanning are somewhat less frequently used but nevertheless seem to have a role in the diagnosis of hypopharyngeal cancer. Screening of the respiratory tract is not commonly used as a diagnostic technique (13.3%), although screening of the digestive tract is done for a large part of the patients (76.0%).

Table 4. Hypopharyngeal Cancer: Overview of Diagnostic and Staging Procedures (Flemish Region, 2004-2007)

Diagnostic Procedure (-3m<inc<+3m)	Total (N=384)		2004 (N=104)		2005 (N=82)		2006 (N=90)		2007 (N=108)	
	n	%	n	%	n	%	n	%	n	%
Tissue Examination	378	98.4	103	99.0	80	97.6	88	97.8	107	99.1
Histological Diagnosis	377	98.2	103	99.0	80	97.6	88	97.8	106	98.1
Cytology	80	20.8	17	16.3	20	24.4	20	22.2	23	21.3
Imaging	378	98.4	103	99.0	80	97.6	88	97.8	107	99.1
CT	375	97.7	101	97.1	79	96.3	88	97.8	107	99.1
MRI	133	34.6	38	36.5	25	30.5	24	26.7	46	42.6
Larynx/Pharynx X-ray	78	20.3	23	22.1	20	24.4	20	22.2	15	13.9
Ultrasound Neck	78	20.3	19	18.3	17	20.7	22	24.4	20	18.5
PET Scan	196	51.0	47	45.2	42	51.2	45	50.0	62	57.4
Chest X-ray	338	88.0	98	94.2	69	84.1	77	85.6	94	87.0
Ultrasound Abdomen	186	48.4	57	54.8	39	47.6	41	45.6	49	45.4
Screening for Second Primary Malignancies	297	77.3	84	80.8	56	68.3	71	78.9	86	79.6
Respiratory Tract	51	13.3	14	13.5	8	9.8	17	18.9	12	11.1
Digestive Tract	292	76.0	82	78.8	56	68.3	69	76.7	85	78.7
Other Procedures										
Lymph Node Biopsy	28	7.3	6	5.8	10	12.2	6	6.7	6	5.6

5.2 Multidisciplinary Oncological Consult

About 73% of all hypopharyngeal cancer patients are discussed at a multidisciplinary oncological consult (MOC) within 1 month before till three months after incidence date (Table 5). No clear trend can be observed over the incidence years.

Table 5. Hypopharyngeal Cancer: Frequency of Multidisciplinary Oncological Consult (Flemish Region, 2004-2007)

Incidence year	MOC	
	n	%
2004 (n=104)	77	74.0
2005 (n=82)	58	70.7
2006 (n=90)	62	68.9
2007 (n=108)	85	78.7
Total (n=384)	282	73.4

5.3 Therapeutic Procedures

Two different surgery types are taken into account for the treatment analyses: surgery for larger hypopharyngeal tumours (i.e. major surgery) and lymphadenectomies. Major surgeries always receive priority when performed within the studied timeframe. In contrast to other head and neck tumours, minor surgeries are not incorporated in the analyses of surgery because they are mostly used for diagnostic rather than therapeutic purposes. Therefore, it is possible that the number of patients treated with primary surgery is somewhat underestimated.

Within the timeframe of one month before until six months after the incidence date, about one-third of the patients (125 patients) undergo surgery as primary treatment. 62 patients received a major surgery within six months after diagnosis (Table 6). 58 of these patients treated with major surgery also received a lymphadenectomy within the timeframe. Additionally, 63 patients only received a lymphadenectomy.

Table 6. Hypopharyngeal Cancer: Overview of the Selected of Surgeries (Flemish Region, 2004-2007)

Type of Surgery	n	%
Major Surgery	62	49.6
Lymphadenectomy	63	50.4

For 9 patients, the surgical procedure is carried out soon after radiotherapy and therefore considered as salvage surgery. For the remaining 116 operated patients, the surgical procedure is considered to be the cornerstone of the treatment. Most of these are postoperatively irradiated either with or without concomitant chemotherapy (94.0%).

However, the majority of the patients are primarily treated with radiotherapy (57.6%). Irradiation is in about one-third of the cases performed alone and in two-third of the cases in combination with chemotherapy.

Based on the health insurance data, no oncologic treatment (surgery, radiotherapy or chemotherapy) was found within the studied timeframe for 6.8% of the patients.

Table 7. Hypopharyngeal Cancer: Overview of Treatment Schemes (Flemish Region, 2004-2007)

Treatment Scheme	n	%
Surgery	116	30.2
Adjuvant radiotherapy	53	13.8
Adjuvant chemoradiotherapy	51	13.3
No other therapy	7	1.8
Other therapy		
Surgery < chemotherapy	3	0.8
Chemotherapy < surgery < radiotherapy	1	0.3
Chemotherapy < surgery < chemoradiotherapy	1	0.3
Radiotherapy only	71	18.5
Concomitant chemoradiotherapy	159	41.4
Chemotherapy only	12	3.1
No primary treatment registered	26	6.8

6. Survival

6.1 Observed and Relative Survival

Survival is poor for patients diagnosed with a hypopharyngeal tumour (Table 8). About one-third of the patients dies in the first year after diagnosis. After five years of follow-up, relative survival has further decreased to 29.6%.

Table 8. Hypopharyngeal Cancer: Observed and Relative Survival (Flemish Region, 2004-2007)

N at risk	Observed Survival (%)					Relative Survival (%)				
	1 year	2 year	3 year	4 year	5 year	1 year	2 year	3 year	4 year	5 year
384	67.4	49.2	38.3	32.3	27.3	68.5	50.7	40.1	34.4	29.6

6.2 Relative Survival by Sex

Survival is very similar between males and females, both having a five-year relative survival around 30% (Table 9).

Table 9. Hypopharyngeal Cancer: Relative Survival by Sex (Flemish Region, 2004-2007)

	N at risk	%	Relative Survival (%)				
			1 year	2 year	3 year	4 year	5 year
Males	338	88.0	68.8	50.6	40.3	34.1	29.3
Females	46	12.0	66.1	51.3	38.3	36.3	32.0

6.3 Relative Survival by Age Group

No clear trend can be observed between the age of the patient at diagnosis and the prognosis. A somewhat better prognosis is seen for the middle age group.

Table 10. Hypopharyngeal Cancer: Relative Survival by Age Group (Flemish Region, 2004-2007)

	N at risk	%	Relative Survival (%)				
			1 year	2 year	3 year	4 year	5 year
15-59 years	217	56.5	69.5	47.5	37.5	33.0	27.5
60-69 years	106	27.6	67.9	55.2	44.2	37.9	34.4
70+ years	61	15.9	65.9	54.8	42.3	32.7	28.1

6.4 Relative Survival by Stage

Survival is not displayed for the lower stages because the number at risk is too low. Survival is much better for patients diagnosed with a stage III tumour (45.7%) than for patients diagnosed with a stage IV tumour (23.5%, all stage IV tumours together). It should however be noted that, in line with other head and neck cancers, some locally or regionally advanced diseases are also categorised as stage IV (stage IVA or IVB, more precisely). Shortly after diagnosis, survival of stage IVA is slightly better than survival of stage IVB, but this difference disappears later onwards (Figure 5). Hypopharyngeal tumours with distant metastases, categorised as Stage IVC, are rare in this study (only 31 patients in this selection of patients).

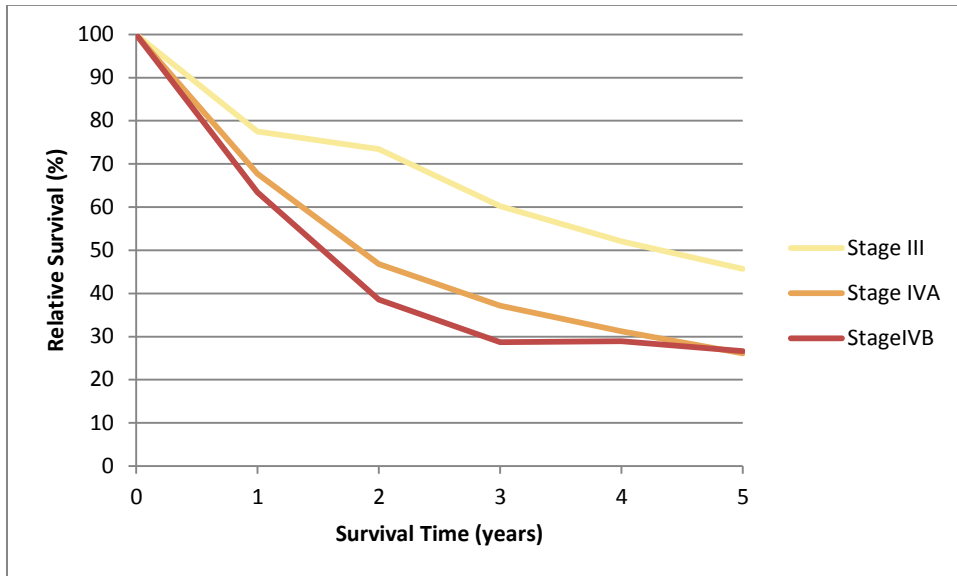


Figure 5. Hypopharyngeal Cancer: Relative Survival by Stage (Flemish Region, 2004-2007)

6.5 Relative Survival by Primary Treatment

Survival is similar for patients primarily treated with radiation or surgery. A small advantage for patients for which radiation is the cornerstone of the treatment is observed from two years after diagnosis till the end of the observation period.

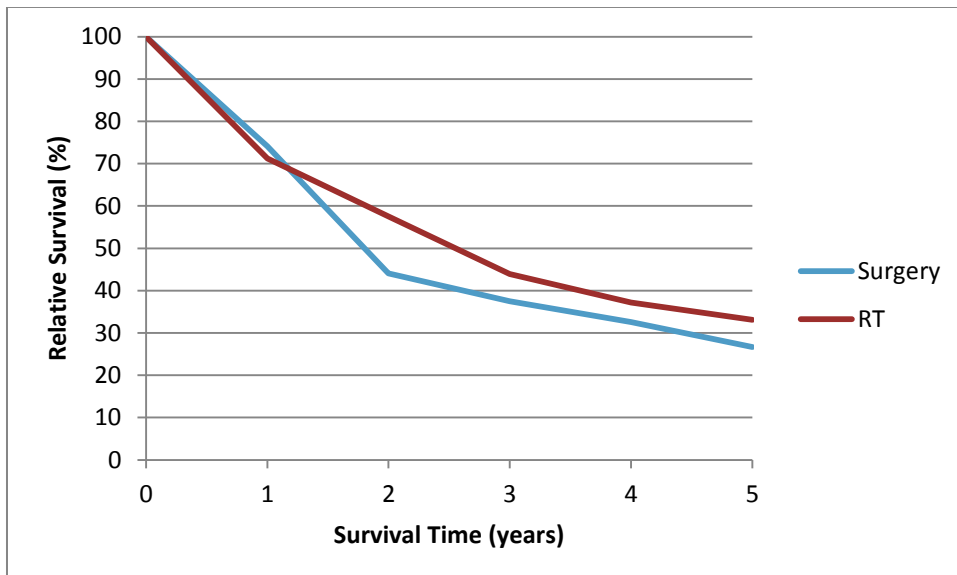


Figure 6. Hypopharyngeal Cancer: Relative Survival by Primary Treatment (Flemish Region, 2004-2007)

7. Analyses by Volume

During the period 2004-2007, Belgian patients with hypopharyngeal cancer are treated in 29 different Flemish hospitals. The mean number of patients (during the period 2004-2007) by hospital is 13.5 and the median number is 2, with a range between 1 and 56. The distribution of the number of patients (=volume) per hospital is displayed in Figure 7.

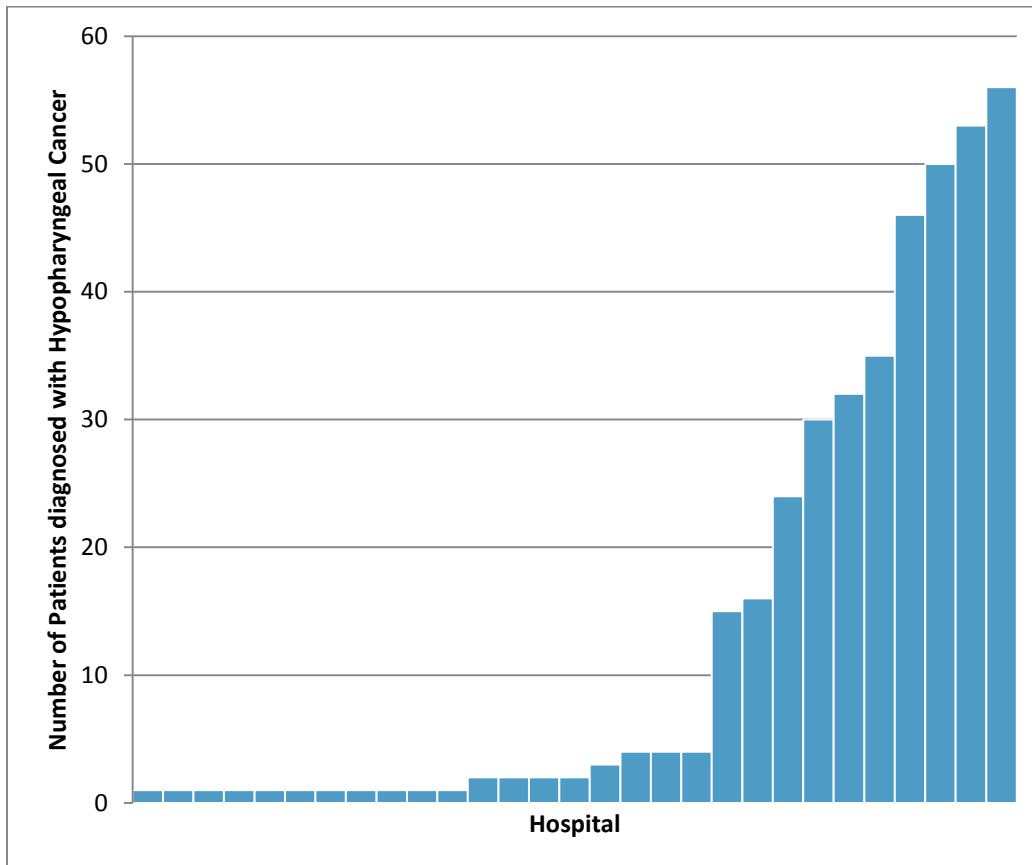


Figure 7. Hypopharyngeal Cancer: Distribution of Patients by Hospital (Flemish Hospitals, 2004-2007)

370 of the Flemish patients (96.4%) can be assigned to a hospital (see Methodology for the rules applied to assign a patient to one hospital). Considering hospitals having taken care of 40 or more patients diagnosed during the period 2004-2007 as high-volume hospitals, 189 patients are assigned to high-volume hospitals and 181 are assigned to low-volume hospitals.

Treatment schemes are similar for high-volume and low-volume hospitals (Figure 8). A frequently used treatment scheme is chemoradiotherapy (45.5% in high-volume hospitals and 40.3% in low-volume hospitals). The second most often used treatment is surgery (with or without (neo-) adjuvant treatment), with 32.8% of the patients in the high-volume hospitals and 29.8% in the low-volume hospitals. The third regularly used treatment is radiotherapy only (16.4% in high-volume hospitals

and 21.5% in low-volume hospitals). Chemotherapy only and no oncological treatment are uncommon.

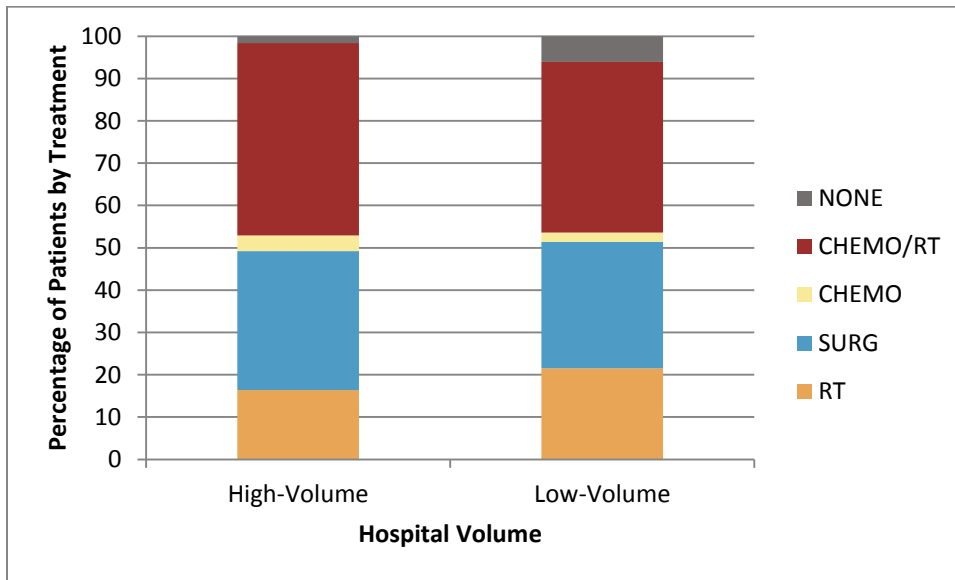


Figure 8. Hypopharyngeal Cancer: Primary Treatment by Hospital Volume (High-Volume versus Low-Volume Hospitals) (Flemish Region, 2004-2007)

8. References

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