Anal Canal

1. Introduction

1.1 General Information and Aetiology

The anal canal is the terminal part of the large intestine and is situated between the rectum and the anus (Figure 1). At the anal verge, where the canal meets the outside skin of the anus, the squamous cells of the lower anal canal merge with the skin just outside the anus. The skin around the anal verge is also made up of squamous cells, but it also contains sweat glands and hair follicles.

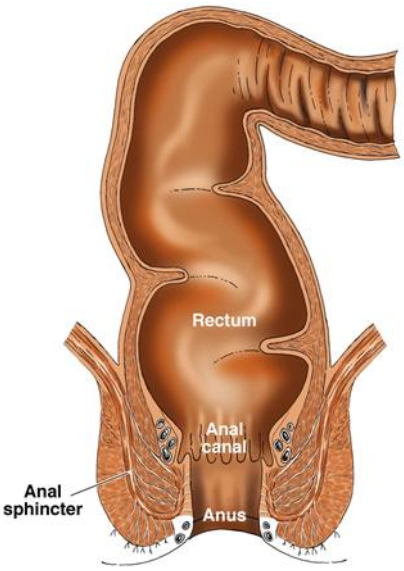

Figure 1. Anatomy of the Anus

In the Flemish Region, for the period 2004-2007, anal cancer accounts for only 1.3% of colorecto-anal tumours [1]. Squamous cell carcinomas (SCC) are the most frequent neoplasms at these sites [2] and represent around 80% of all anal cancers [1].

Human papilloma virus (HPV) infection, particularly when transmitted through anal intercourse, is pointed as the major risk factor in developing an anal SCC [3,4]. Having multiple sex partners, due to the increased risk of exposure to the HPV, is also a well-known risk factor. Tobacco smoking also plays a significant role in the anal-cancer development, independent of other risk factors such as

sexual activity. People infected with human immunodeficiency virus (HIV) have an at least 25 fold higher risk to develop anal cancer [5].

1.2 Diagnosis and Treatment

Digital rectal examination (DRE), anoscopy and palpation of inguinal lymph nodes with fine needle aspiration (FNA) of enlarged nodes are recommended. Inguinal and pararectal lymph nodes should be evaluated with computerised tomography (CT) or magnetic resonance imaging (MRI). It is recommended to search for lung metastases with chest X-ray or chest CT scan. A PET-CT scan should also be considered for staging or treatment planning [6-8].

The management of anal tumours changes considerably over the last three decades. Prior to this period, the standard treatment for cancer of the anal canal is abdominal-perineal resection (APR), which requires a permanent colostomy. The organ preservation concept gains ground following the finding of a high response rate from chemoradiation prior to APR by Nigro [9], and in the 1980s chemotherapy with fluorouracil (5-FU) plus and mitomycin combined with radiotherapy becomes the standard regimen, with APR only for unresponsive or recurrent cases (salvage surgery) [10]. In the following years two randomised trials show that chemoradiation with 5-FU and mitomycin is more effective than radiotherapy alone in controlling local disease [11].

Small, well differentiated tumors of the anal margin, not involving the anal sphincter and without lymph node metastases, may be treated with local excision. In cases with inadequate margins, re-excision or radio(chemo)therapy is performed.

In metastatic setting, cisplatinum-based chemotherapy is used. The necessary of radiotherapy depends on the location and symptoms of the metastasis.

2. Data Selection

All anal cancers diagnosed between 2004 and 2007 for patients with an official residence in the Flemish Region are selected, resulting in 168 cases (for detailed information on selected topography and morphology codes, see Appendix A). As described in Figure 2, nineteen of them are excluded resulting in 149 patients for which results are presented in this chapter.

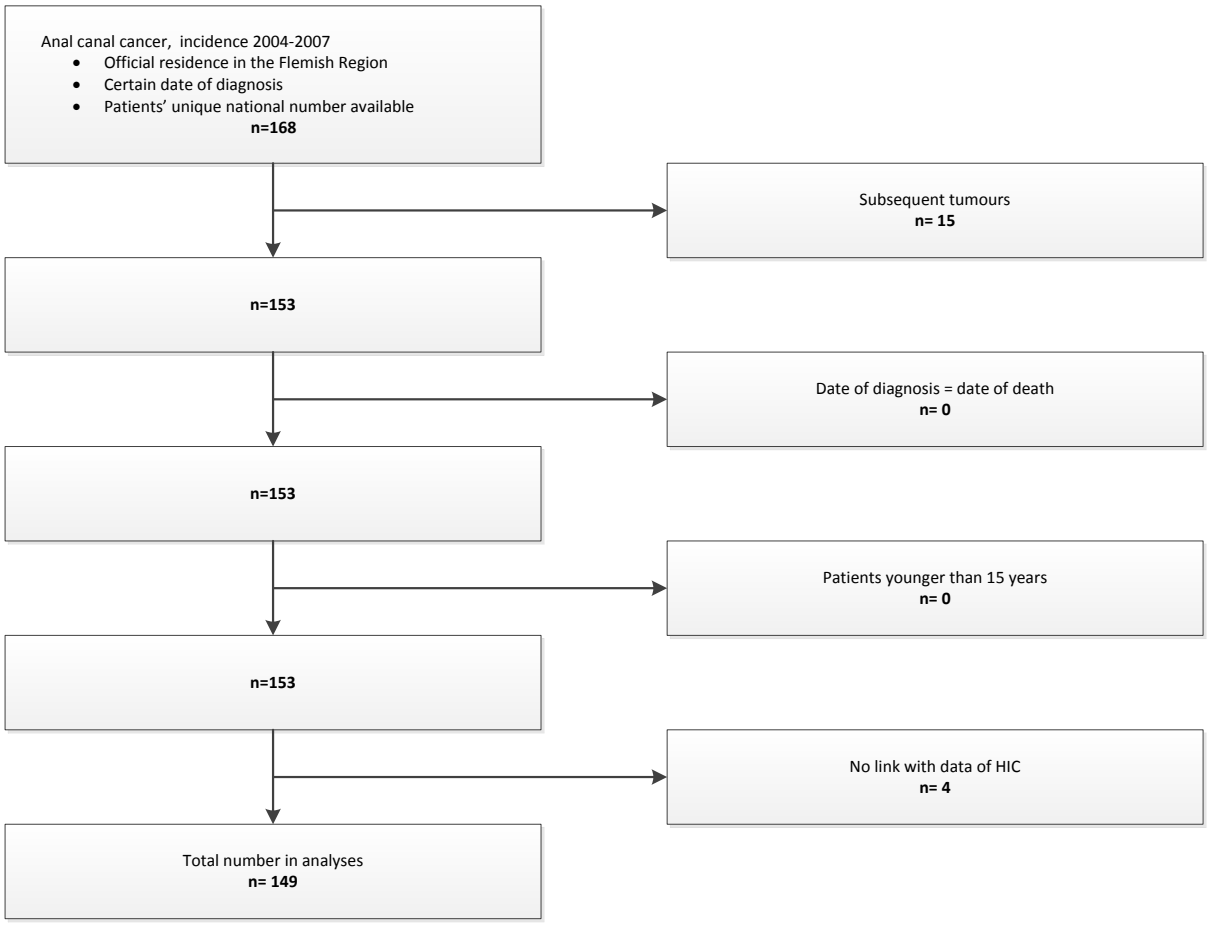

Figure 2. Selection of Anal Canal Tumours

3. Patient Characteristics

During the observed period, a larger number of females (n=91; 61.1%) in comparison with males (n=58; 38.9%) are diagnosed with an epithelial tumour of the anal canal, with a male/female ratio of 0.74 (Table 1). These numbers correspond to age standardised rates of 0.40/100,000 person years and 0.54/100,000 person years, for males and females respectively. No clear trend in incidence rates is observed over the years.

The median age at diagnosis is 63.5 years for males and 64.0 years for females. The minimum age is 34 years while the maximum age is 97 years. For further analysis, patients are divided into three age groups: 15-59 years, 60-74 years and 75+ years (Table 2).

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

	Males		Females		Total	
Incidence year	n	ESR	n	ESR	n	ESR
2004	13	0.38	18	0.46	31	0.42
2005	19	0.54	22	0.54	41	0.54
2006	12	0.32	23	0.57	35	0.44
2007	14	0.38	28	0.59	42	0.49
2004-2007	58	0.40	91	0.54	149	0.47

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

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

	Males	Females	Total
15-59 years	22	38	60
60-74 years	24	20	44
75+ years	12	33	45

4. Tumour Characteristics

Sublocalisation, morphology, differentiation grade and stage (clinical, pathological and combined stage) of the selected anal canal cancers are described in Table 3. Hundred and nine tumours (73.2%) cannot be staged because their localisation is coded as C21.0 (anus, unspecified) or C21.8 (overlapping lesion of rectum, anus and anal canal). These tumours are displayed as stage 'NA'. A larger proportion of tumours (n=98; 65.8%) are squamous cell carcinoma with an unspecified localisation. In 35.5% of the tumours, the differentiation grade is unknown. Most of the tumours for which staging is known are stage II-III (combined stage: n=27; 75%). Rarely, tumours are diagnosed with a stage IV (combined stage: n=2; 5.6%). For 10% of the stageable tumours, staging (i.e. combined staging) is unknown.

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

	N	% of total	% of known
Localisation			
Anus, unspecified (C21.0)	108	72.5	/
Anal canal (C21.1)	39	26.2	97.5
Cloacogenic zone (C21.2)	1	0.7	2.5
Overlapping lesion of rectum, anus and anal canal (C21.8)	1	0.7	/
Morphology			
Squamous cell carcinoma	134	89.9	/
Cloacogenic / basaloid transitional cell carcinoma	15	10.1	/
Differentiation Grade			
Well differentiated	27	18.1	28.7
Moderately differentiated	34	22.8	36.2
Poorly differentiated	33	22.1	35.1
Undifferentiated	2	1.3	/
Unknown	53	35.5	/
Clinical Stage			
I	3	7.5	10.3
II	14	35.0	48.3
III	10	25.0	34.5
IV	2	5.0	6.9
Unknown	11	27.5	/
Pathological Stage			
I	4	10.0	28.6
II	5	12.5	35.7
III	5	12.5	35.7
Unknown	26	65.0	/
Combined Stage			
I	7	17.5	19.4

II	15	37.5	41.7
III	12	30.0	33.3
IV	2	5.0	5.6
Unknown	4	10.0	/

Note: 109 cases (73.2%) have a localisation for which staging is not applicable (NA)

As 73.2% of patients are diagnosed with an anal cancer for which staging is not applicable, the number of remaining patients is too low to perform detailed analyses on the stage distribution by sex and by age category.

5. Diagnostic and Therapeutic Procedures

5.1 Diagnosis and Staging

An overview of the diagnostic and staging procedures that occur for the anal cancer patients diagnosed in the Flemish Region between 2004 and 2007 is given in Table 4. For the observed period, tissue examination is performed in the majority of patients (97.3%) and is mostly based on histological diagnosis (99.3%). Endoscopic examination is performed in 65.1% of patients. To evaluate the tumour extent, different imaging techniques are frequently used (94.0%), of which the majority are CT scanning (86.6%) and chest X-ray (76.5%). A PET scan is only performed in 31.5% of all patients.

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

Diagnostic Procedures (-3m<inc<+3m)	Total (N=149)		2004 (N=31)		2005 (N=41)		2006 (N=35)		2007 (N=42)	
	n	%	n	%	n	%	n	%	n	%
Tissue Examination	**145**	**97.3**	**29**	**93.5**	**40**	**97.6**	**35**	**100.0**	**41**	**97.6**
Histological Diagnosis	144	96.6	29	93.5	39	95.1	35	100.0	41	97.6
Cytology	9	6.0	4	12.9	2	4.9	0	0.0	3	7.1
Endoscopic examination	**97**	**65.1**	**19**	**61.3**	**27**	**65.9**	**24**	**68.6**	**27**	**64.3**
Anorectal Endosonography	39	26.2	7	22.6	13	31.7	10	28.6	9	21.4
Recto(sigmoido)scopy	70	47.0	15	48.4	21	51.2	15	42.9	19	45.2
Colonoscopy	43	28.9	11	35.5	11	26.8	10	28.6	11	26.2
Imaging	**140**	**94.0**	**28**	**90.3**	**38**	**92.7**	**35**	**100.0**	**39**	**92.9**
Ultrasound Transrectal/Pelvis/Abdomen	48	32.2	15	48.4	15	36.6	10	28.6	8	19.0
CT	129	86.6	24	77.4	36	87.8	32	91.4	37	88.1
MRI	62	41.6	12	38.7	14	34.1	18	51.4	18	42.9
PET Scan	47	31.5	5	16.1	16	39.0	13	37.1	13	31.0
Chest X-ray	114	76.5	26	83.9	33	80.5	27	77.1	28	66.7

5.2 Multidisciplinary Oncological Consult

For the observed period, 57% of anal canal cancer patients are discussed at a multidisciplinary oncological consult (MOC) within 1 month before till three months after incidence date (Table 5). The proportion of patients discussed at MOC fluctuates over the years and no trend can be observed.

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

	MOC	
Incidence Year	n	%
2004 (n=31)	17	54.8
2005 (n=41)	24	58.5
2006 (n=35)	22	62.9
2007 (n=42)	22	52.4
Total (n=149)	85	57.0

5.3 Therapeutic Procedures

Radiotherapy is the main treatment in the majority of patients (63.1%) and is always given in combination with chemotherapy (Table 6). From the patients receiving radiotherapy, 13 undergo salvage surgery.

For 20.1% of patients, surgery is the primary treatment. Two different surgery types are taken into account for the treatment analyses: major surgery (e.g. Miles surgery, Hartmann's procedure, proctocolectomy) and minor surgery (e.g. mucosal resection, anal fistula excision). Major surgeries always receive priority when performed within the studied timeframe. When no major surgery was performed within the timeframe, minor surgeries are taken into account. A major surgery was performed in 53.3% of the surgically treated patients (Table 7). In more than half of the patients, adjuvant chemo- and/or radiotherapy is given (56.7%).

A small percentage of patients (1.3%) receive chemotherapy only (for both these patients staging is not applicable).

For 15.4% of patients, no major treatment is found.

From the total number of patients, 5.4% undergo a lymphadenectomy.

Table 6. Anal Canal Cancer: Overview of Treatment Schemes (Flemish Region, 2004-2007)

Treatment Scheme	n	%
Radiotherapy	**94**	**63.1**
Chemoradiotherapy	94	63.1
Surgery	**30**	**20.1**
Alone	13	8.7
Surgery < Chemo and/or RT	17	11.4
Chemotherapy only	**2**	**1.3**
No primary treatment registered	**23**	**15.4**

Table 7. Anal Canal Cancer: Overview of the Selected Surgeries (Flemish Region, 2004-2007)

Type of Surgery	n	%
Major Surgery	16	53.3
Minor Surgery	14	46.7

6. Survival

6.1 Observed and Relative Survival

Relative survival for anal canal cancer patients is 71.1% at 5 years after incidence (Table 8).

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

	Observed Survival (%)					Relative Survival (%)				
N at risk	1 year	2 year	3 year	4 year	5 year	1 year	2 year	3 year	4 year	5 year
149	81.2	73.2	67.1	63.1	61.1	84.2	78.3	73.9	71.4	71.1

6.2 Relative Survival by Sex

5-year relative survival is slightly better for females (73.4%) than for males (67.3%) (Table 9).

Table 9. Anal Canal 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	58	38.9	80.4	77.5	72.5	69.1	67.3
Females	91	61.1	86.6	78.8	74.9	72.9	73.4

6.3 Relative Survival by Age Group

Five-year relative survival is at least 20% better in the youngest age group (15-59 years old), with a 5-year relative survival of 84.7% (Table 10). The other age categories have a more similar survival, with a 5-year relative survival of 61.3% and 59.4% for the age groups of '60-74 years old' and '75+ years old' respectively. This disparity between the youngest and the oldest age group enlarges throughout the follow-up time.

Table 10. Anal Canal 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	60	40.3	92.0	89.0	87.6	86.2	84.7
60-74 years	44	29.5	76.2	72.7	69.0	62.9	61.3
75+ years	45	30.2	81.2	67.7	56.8	56.4	59.4

6.4 Relative Survival by Sublocalisation

For patients with a known sublocalisation, the 5-year relative survival is 20% better (5-year relative survival: 85.8%) than for the patients with an unspecified sublocalisation (5-year relative survival: 65.9%). The number at risk for the sublocalisations 'cloacogenic zone' and 'overlapping lesion of rectum, anus and anal canal' is lower than 35. As a consequence, these sublocalisations are not represented in Figure 3.

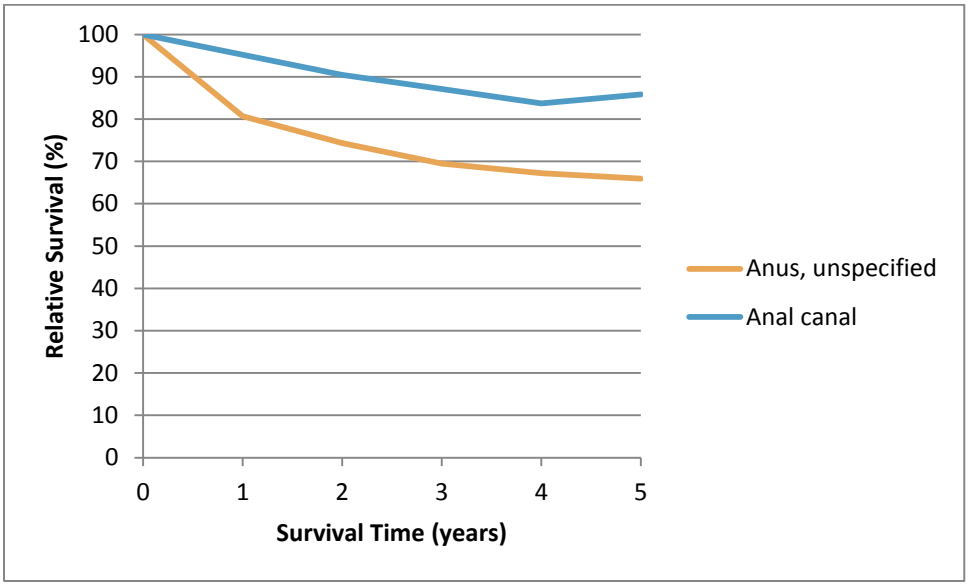

Figure 3. Anal Canal Cancer: Relative Survival by Sublocalisation (Flemish Region, 2004-2007)

7. Analyses by Volume

During the period 2004-2007, Belgian patients with anal canal cancer are treated in 36 different Flemish hospitals. The mean number of patients (during the period 2004-2007) by hospital is 3.8, with a range between 1 and 16. The distribution of the number of patients (=volume) per hospital is displayed in Figure 4.

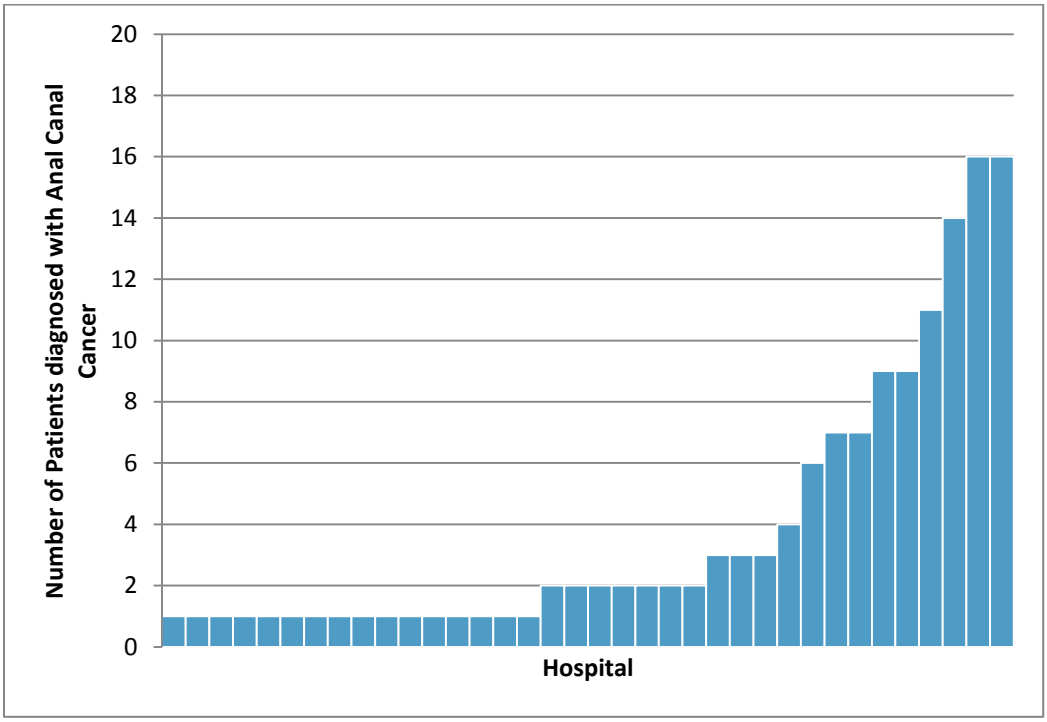

Figure 4. Anal Canal Cancer: Distribution of Patients by Hospital (Flemish Hospitals, 2004-2007)

Fourteen Flemish patients (9.4%) cannot be attributed to a centre. Because of the low number of patients diagnosed with a tumour of anal canal, who are treated in a large number of different hospitals, the maximum number of patients per hospital is very small. Therefore, no further analyses on the volume of the hospital are performed.

8. References

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