Vagina

1. Introduction

1.1 General Information and Aetiology

The vagina is part of internal female reproductive system. It is an elastic, muscular tube that connects the outside of the body to the cervix.

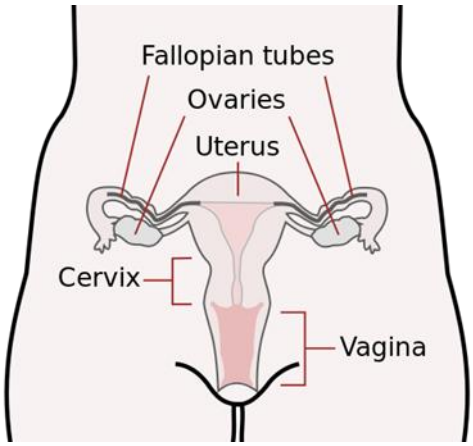

Figure 1. Location of the Vagina

In the Flemish Region, for the period 2004-2007, vaginal cancer accounts for about 2% of gynaecological tumours. Squamous cell carcinoma of the vagina are the most frequent neoplasms at these sites [1]. In the Flemish Region (2004-2007), squamous cell carcinoma represent 70% of vaginal cancers.

One of the major risk factor in developing an epithelial (pre-)malignant tumour of the vagina is Human Papilloma Virus (HPV) infection [1]. Prior pelvic radiation and in situ or invasive cervical cancer history also increase the risk of developing vaginal squamous cell cancer [2].

Tumours involving the vagina often consist of metastatic spread of cancer from a different origin, that can be gynaecological or not [2,3]. Tumours of the vagina involving other genital sites are classified as primary cancer of this other genital organ. For example, a tumour extending to the vulva, will be classified as primary vulvar cancer [2].

Most vaginal cancers are more frequent in post-menopausal or elderly women. Similarly to vulvar cancer, when the tumour occurs in younger patient, the tumour is assumed to be HPV-related. Lung, liver and bony skeleton are metastatic sites for vaginal tumours [2].
Prognosis of vaginal cancer is expected to be worse than for vulvar cancer. The overall 5-year relative survival for squamous cell carcinoma of the vagina ranges from 42% to 54% [1].

1.2 Diagnosis and Treatment

In order to confirm diagnosis with certainty, an histological confirmation by biopsy is needed [3]. Given the proximity and the possible extension of the tumour to the vulva [2], colposcopy will also be considered in analysis for the diagnostic workup. MRI and possibly PET-scan of the pelvis are performed to evaluate local extension of the lesion. CT-scan and preferably PET-scan of the abdomen/pelvis allow an evaluation of the regional extent of the tumour [3]. Chest X-ray is performed, particularly if nor PET-scan neither CT-scan have been performed, in order to assess possible metastasis to lung [3]. If there is suspicion for an invasion of the bladder of the rectum, structures close to the vagina, a cystoscopy and/or rectoscopy are indicated [3,4]. Abdominal or transvaginal echography may also permit to evaluate the state of adjacent organs [2,3].

Treatment tends to be as conservative as possible and has to be adapted to the general state of the person. Similarly to vulvar cancer, treatment for vaginal cancer can have an important psychological impact. Moreover, when considering surgery, the proximity of urethra, bladder and rectum should be taken into account seeing the risk of collateral damages to these structures [2,4].

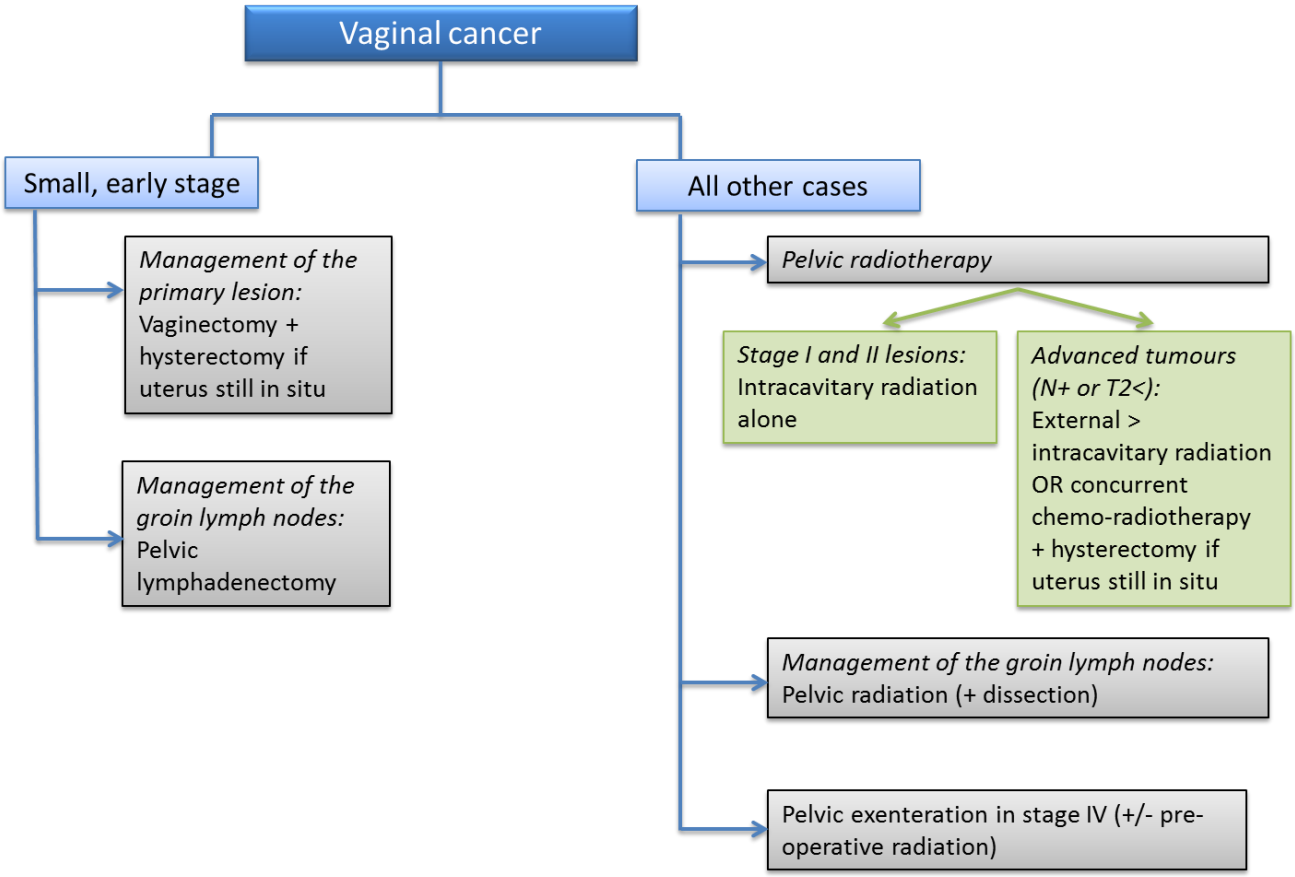

Figure 2. Treatment Schemes of Vaginal Cancer

Radiation therapy as sole or first treatment modality allows to achieve excellent outcome in invasive squamous cell carcinoma of the vagina [5].

Surgery seems to have been more frequently performed in the past than it is nowadays. Surgery is now considered to have a limited role, being only effective for small and early stage tumours. Moreover, damage or injury to bladder and rectum are factors to be taken into account when considering surgery [2]. If the uterus is still in situ, a radical hysterectomy is exerted.

Radiation therapy or concomitant chemoradiation are therefore preferred. Intracavitary radiation is selected in early stage and small lesions, while external radiation, with or without concomitant chemotherapy, is preferred for more advanced and larger lesions. Due to the complex lymphatic drainage of the vagina, every pelvic lymph node is potentially involved. Pelvis lymph node dissection and irradiation should be therefore always be considered [2].

Pelvic exenteration (after primary treatment) is performed in patient with stage IV tumours or if no complete remission is obtained within 2-3 months [2]. Chemotherapy (for advanced stage) –

5-fluorouracil and/or cisplatinum – in combination with radiotherapy allows to some extent a better control of the disease [2].

2. Data Selection

All vaginal cancers diagnosed between 2004 and 2007 for patients with an official residence in the Flemish Region are selected, resulting in 75 cases (for detailed information on selected topography and morphology codes, see Appendix A). As described in Figure 3, 10 of them are excluded resulting in 65 patients for which results are presented in this chapter.

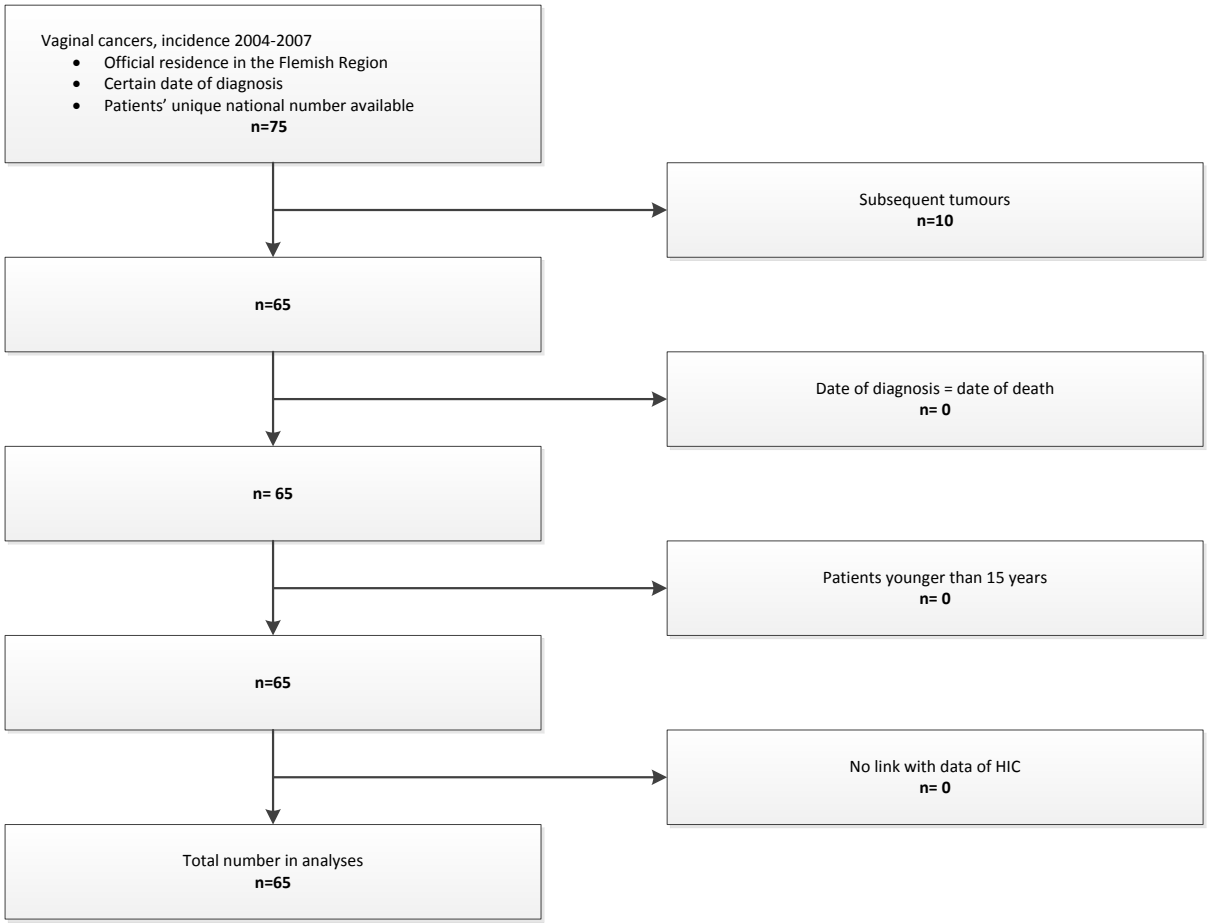

Figure 3. Selection of Vaginal Cancers (Flemish Region, 2004-2007)

3. Patient Characteristics

From 2004 to 2007, 65 women are diagnosed with vaginal cancer in the Flemish Region. No clear trend can be observed between the incidence years (Table 1).

The median age is 73 years, with a range from 31 years to 95 years. For further analyses, the patients are divided in three age categories: 15-59 years, 60-74 years and 75 years and older (Table 2).

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

	Females	
Incidence year	n	ESR
2004	16	0.33
2005	16	0.33
2006	12	0.21
2007	21	0.43
2004-2007	65	0.33

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

Table 2. Vaginal Cancer: Age distribution (Flemish Region, 2004-2007)

	Total
15-59 years	9
60-74 years	27
75+ years	29

4. Tumour Characteristics

Table 3 shows the sublocalisation, morphology, differentiation grade and stage (clinical, pathological and combined stage) of the selected tumours. Undifferentiated tumours are seldom (3.1%), but all other differentiation grades are regularly observed in this tumour selection. The majority of the tumours have an unknown stage (clinical stage: 55.4%, pathological stage: 80.0% and combined stage: 49.2%).

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

	N	% of total	% of known
Localisation			
Malignant neoplasm of vagina (C52.9)	65	100.0	/
Morphology			
Squamous cell carcinoma	65	100.0	/
Differentiation grade			
Well differentiated	13	20.0	25.0
Moderately differentiated	20	30.8	38.5
Poorly differentiated	17	26.2	32.7
Undifferentiated	2	3.1	3.8
Unknown	13	20.0	/
Clinical stage			
I	10	15.4	34.5
II	3	4.6	10.3
III	6	9.2	20.7
IV	10	15.4	34.5
Unknown	36	55.4	/
Pathological stage			
I	4	6.2	30.8
II	4	6.2	30.8
III	4	6.2	30.8
IV	1	1.5	7.6
Unknown	52	80.0	/
Combined stage			
I	8	12.3	24.2
II	5	7.7	15.2
III	9	13.8	27.3
IV	11	16.9	33.3
Unknown	32	49.2	/

Stage distribution seems to differ for the different age group. However, due to the low numbers of patients in all age groups, no reliable conclusions can be drawn (Figure 4).

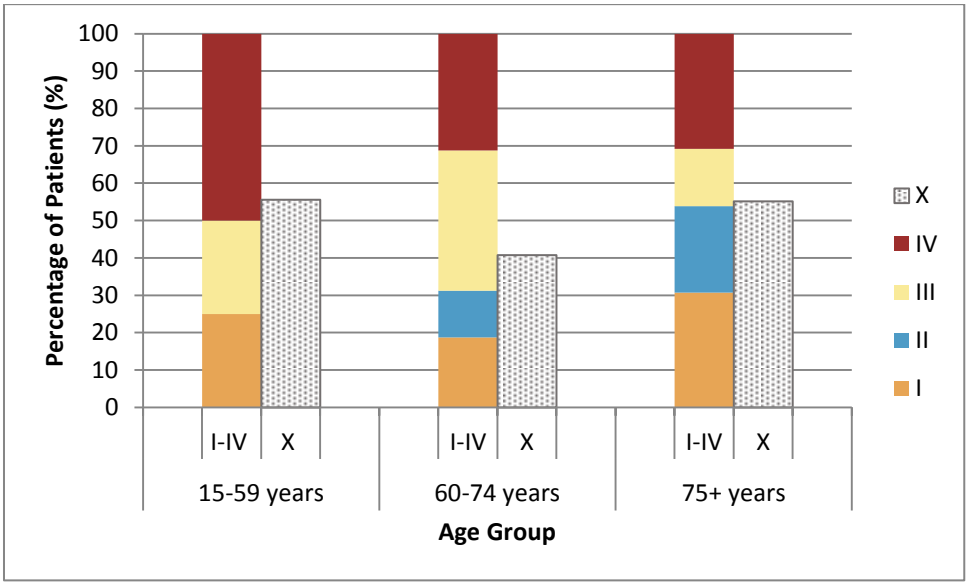

Figure 4. Vaginal Cancer: Stage Distribution by Age Group (Flemish Region, 2004-2007)

5. Diagnostic and Therapeutic Procedures

5.1 Diagnosis and Staging

An overview of the performed diagnostic and staging procedures can be found in Table 4. Almost all cancers are confirmed by pathological examination (96.9%). Pap smear and cytology are also charged as diagnostic procedures in about half of the patients, but their use largely fluctuates over the incidence years.

Imaging procedure are used in 95.4% of the patients. The most often used techniques are CT scanning (83.1%) and X-ray of the thorax (81.5%). MRI and PET scan are performed in more than one patient on three.

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

Diagnostic Procedure (-3m<inc<+3m)	Total (N=65)		2004 (N=16)		2005 (N=16)		2006 (N=12)		2007 (N=21)	
	n	%	n	%	n	%	n	%	n	%
Tissue Examination	**64**	**98.5**	**16**	**100.0**	**16**	**100.0**	**12**	**100.0**	**20**	**95.2**
Histological Diagnosis	63	96.9	16	100.0	15	93.8	12	100.0	20	95.2
Cytology	36	55.4	8	50.0	8	50.0	9	75.0	11	52.4
Smear	28	43.1	4	25.0	9	56.3	7	58.3	8	38.1
Imaging	**62**	**95.4**	**16**	**100.0**	**15**	**93.8**	**12**	**100.0**	**19**	**90.5**
Colposcopy	9	13.8	3	18.8	0	0.0	2	16.7	4	19.0
Pelvic Ultrasound	17	26.2	6	37.5	5	31.3	2	16.7	4	19
Vaginal Ultrasound	20	30.8	1	6.3	7	43.8	4	33.3	8	38.1
Cystoscopy	29	44.6	7	43.8	7	43.8	5	41.7	10	47.6
Rectoscopy	10	15.4	2	12.5	4	25.0	2	16.7	2	9.5
CT	54	83.1	15	93.8	14	87.5	9	75.0	16	76.2
Chest X-ray	53	81.5	15	93.8	14	87.5	10	83.3	14	66.7
MRI	22	33.8	6	37.5	5	31.3	3	25.0	8	38.1
PET Scan	24	36.9	5	31.3	4	25.0	5	41.7	10	47.6

5.2 Multidisciplinary Oncological Consult

About 65% of all vaginal cancer patients are discussed at a multidisciplinary oncological consult (MOC) within one month before till three months after the incidence date. The number of patients discussed at a MOC varies per year between 56.3% (2004) and 75.0% (2005) (Table 5).

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

	MOC	
Incidence year	n	%
2004 (n=16)	9	56.3
2005 (n=16)	12	75.0
2006 (n=12)	7	58.3
2007 (n=21)	14	66.7
Total (n=65)	42	64.6

5.3 Therapeutic Procedures

In line with the literature (see Introduction), radiotherapy is seen as the major treatment option. Therefore, chemotherapy and surgery are studied in relation to the date of the last radiotherapy session.

Nomenclature codes for surgery are grouped into major surgery (e.g., hysterectomy) or minor surgery (e.g., laser therapy). If a major surgery has taken place within the studied timeframe (see Appendix), this surgery is always selected irrespective of the date of the minor surgery. As a small surgery can also be done for diagnostic purposes, small surgeries are only taken into account when no radiotherapy is performed within the selected timeframe.

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

Type of Surgery	n	%
Major Surgery	26	92.9
Minor Surgery	2	7.1

Patients treated with radiotherapy as primary treatment represent 35.4% of all patients. Nine of them (13.8% of all patients) are also treated with chemotherapy.

Surgery as the primary treatment is found in 28 patients (43.1% of all patients). This is the only treatment for the majority of them (15 patients). Twelve patients are postoperatively treated with radiotherapy and chemotherapy. Adjuvant treatment with chemotherapy only is seen in one patient. Chemotherapy as the sole treatment is found in three patients.

Based on the health insurance data, no oncological treatment (radiotherapy, surgery or chemotherapy) is found in eleven patients (16.9%).

For ten patients, a lymphadenectomy has been charged. For the group of surgically treated patients, this is the case for 6 patients (21.4%). For the group of patients treated with radiotherapy, this is the case for 2 patients (8.7%). Finally, also one of the patients treated with chemotherapy and one of the patients without a primary oncological registered treatment are treated with a lymphadenectomy.

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

Treatment Scheme	n	%
Radiotherapy	**23**	**35.4**
Radiotherapy only	14	21.5
Chemoradiotherapy	9	13.8
Surgery	**28**	**43.1**
Surgery only	15	23.1
Surgery + radiotherapy + chemotherapy	12	18.5
Surgery + chemotherapy	1	1.5
Chemotherapy only	**3**	**4.6**
No primary treatment registered	**11**	**16.9**

6. Survival

6.1 Observed and Relative Survival

Survival is bad for patients diagnosed with a vaginal cancer with only slightly more than half of the patients surviving the first year (Table 8). Five years after diagnosis, relative survival has decreased to 34.7%. Due to an insufficient number of patients at risk, no further detailed analyses for survival are performed.

Table 8. Vaginal 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
65	55.4	36.9	33.8	32.3	30.8	57.7	39.5	36.8	35.7	34.7

7. Analyses by Volume

During the period 2004-2007, Belgian patients with vaginal cancer are treated in 29 different Flemish hospitals. The mean number of patients (during the period 2004-2007) by hospital is 2.1 and the median 2, with a range between 1 and 7. The distribution of the number of patients (=volume) per hospital is displayed in Figure 5.

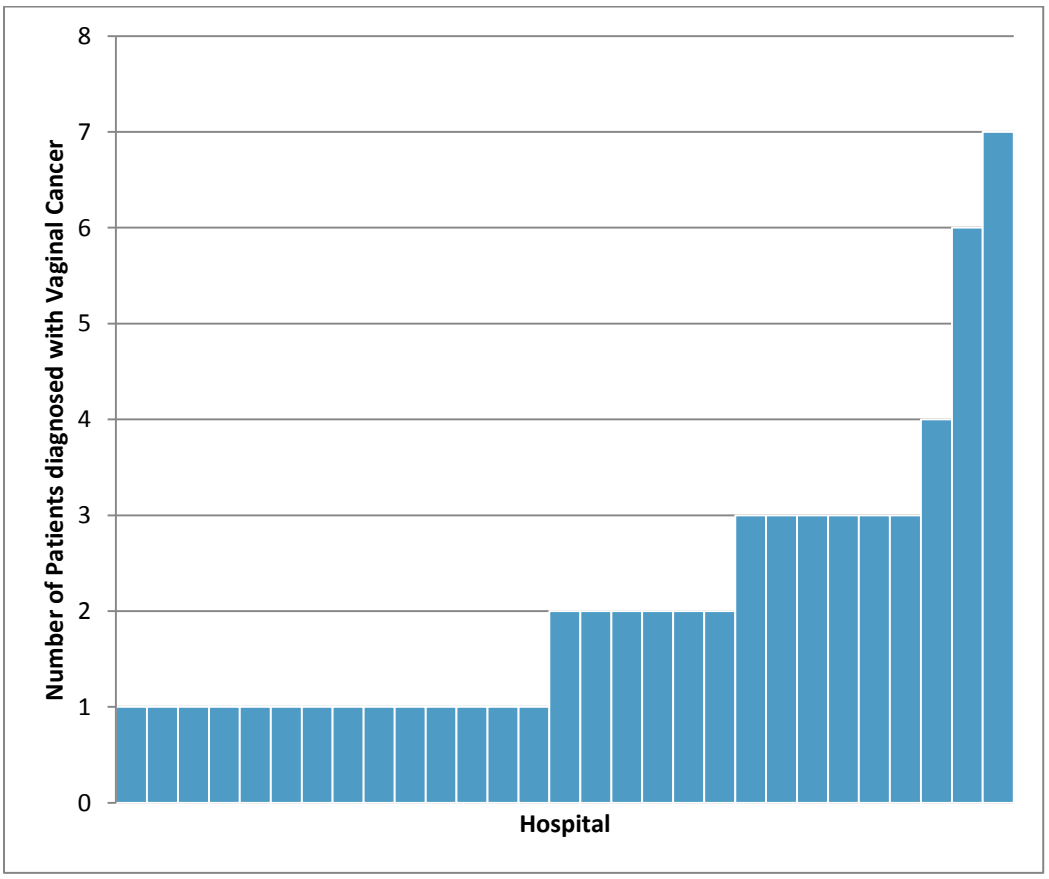

Figure 5. Vaginal Cancer: Distribution of Patients by Hospital (Flemish Hospitals, 2004-2007)

Six of the Flemish patients (9.2%) can't be attributed to a centre. Because of the low number of patients diagnosed with a tumour of vagina 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

1. Andersen ES, Paavonen J, Murnaghan M et al. Tumours of the vagina. In: Tavassoli F.A., Deville P. (eds.): World Health Organization Classification of Tumours, Pathology and Genetics of Tumours of the Breast and Female Genital Organs. IARC Press: Lyon 2003.
2. Benedet J, Hacker N, Ngan H et al. Staging classifications and clinical practice guidelines of gynaecologic cancers. Int J Gynaecol Obstet 2000; 70: 207-312.
3. Mazeron J-J, Gerbaulet A, Pötter R, Meertens H, Van Limbergen E. Primary Vaginal Cancer. In: Pötter R, Haeie-Meder C, Gerbaulet A (eds.). The GEC ESTRO Handbook of Brachytherapy. Leuven, ACCO, 2002.
4. Best Clinical Practice. Gynaecological Cancer Guidelines 2009. Obtained from: http://www.aci.health.nsw.gov.au. Accessed on October 1, 2013.
5. Frank S, Jhingran A, Levenback C et al. Definitive radiation therapy for squamous cell carcinoma of the vagina. Int J Radiation Oncology Biol Phys 2005; 62: 138-147.