

Chapter 5

Cancer of the Anus

Margaret M. Madeleine and Laura M. Newcomer

INTRODUCTION

Anal cancer includes tumors of the anus, anal canal, and anorectum. The anal canal extends from the rectum to the perianal skin and it is lined by a mucous membrane that covers the interior anal sphincter (1, 2). It is a rare disease, with an annual age-adjusted incidence rate of 1.5 per 100,000 people in the U.S. (3). Approximately 4,660 new cases and 660 deaths from anal cancer are expected in the U.S. annually (4). Although both sexes have seen an increase in incidence in recent years, this rise has been more pronounced in men.

Oncogenic human papillomavirus (HPV) types, the same HPV types found to cause cervical cancer, have been detected in the majority of anal tumors (5). Epidemiologic studies suggest that in addition to infection with HPV, smoking is a major risk factor for anal cancer in men and women; also, men who have sex with men are at a particularly increased risk of anal cancer (6-8).

Small tumors of the anal margin not including the anal sphincter are usually treated by wide local incision; however, tumors of the anal canal that involve the anal sphincter or that are too large for excision are treated by radiation or combination chemotherapy and radiation (9). In this report we use U.S. SEER registry data to explore the

impact of demographic and tumor characteristics on anal cancer survival.

MATERIALS AND METHODS

Between 1988 and 2001, 6,411 patients with primary invasive anal cancer were diagnosed in the SEER catchment area. The following cases were excluded from the analysis: patients for whom anal cancer was not the first primary cancer, cases identified through autopsy or death certificate only, those with unknown race, cases without active follow-up or alive with no survival time, patients less than 20 years old, cases without microscopic confirmation, and tumors identified as in situ lesions, sarcomas, or carcinoids. After these exclusions, 4,296 adult cases remained for analysis (Table 5.1).

This relative survival analysis focused on demographic descriptors of the patients and tumor characteristics. The demographics of interest included age at diagnosis (20-49, 50-64, 65+), sex, race (white, black), and geographic location. Key tumor characteristics, specifically histology, grade, size, site, and stage, are described in detail below.

Anal cancer histology was identified by using ICD-O-2/ICD-O-3 histology codes as follows: squamous cell cancer

Table 5.1 Cancer of the Anus: Number of Cases and Exclusions by Reason, 12 SEER Areas, 1988-2001.

Number Selected/Remaining	Number Excluded	Reason for Exclusion/selection
6,411	0	Select 1988-2001 diagnosis (Los Angeles for 1992-2001 only)
5,243	1,168	Select first primary only
5,232	11	Exclude death certificate only or at autopsy
5,162	70	Exclude unknown race
5,148	14	Exclude alive with no survival time and children (Ages 0-19)
4,329	819	Exclude in situ cancers
4,302	27	Exclude no or unknown microscopic confirmation
4,296	6	Exclude sarcomas

(coded as 8010-8089), cloacogenic or basaloid tumors (8123-8124), adenocarcinomas (8140-8263 and 8480-8481), melanomas (8720), and other for the remainder of the histologic types. Due to a small number of cases, melanoma of the anus was combined with other for black patients.

The amount of microscopically determined cell differentiation at diagnosis is described as grade 1 or well-differentiated tumors, grade 2 or moderately well-differentiated tumors, grade 3 or poorly differentiated tumors, and grade 4 or undifferentiated or anaplastic tumors. Information on grade was available for 69% of the tumors.

Tumor size is based on the length in the greatest dimension and was categorized as ≤ 2 cm, 2-5 cm, and >5 cm. When the site of the anal cancer was specified, it was described as occurring in the anal canal, as an overlapping lesion of the rectum, anus, and anal canal, or as in the cloacogenic zone. Cancers of the perianal skin are classified with skin cancers and are not included in this analysis.

The stage of disease is compiled from information on the size the tumor, extent of invasion, and lymph node involvement according to guidelines of the American Joint Committee on Cancer and the International Union Against Cancer, 5th edition (1, 2). Localized stage is defined as an invasive neoplasm confined entirely to the anal site. Regional stage is defined as a neoplasm that

has extended either beyond the anal site or into regional lymph nodes. Distant stage is defined as a neoplasm that has spread to parts of the body remote from the primary tumor. Unstaged cancers lack sufficient information to assign stage. Staging for localized, regional, and distant was available for 87% of the anal cancer tumors.

RESULTS

Demographic characteristics: Effect of age, gender, race, and geographic location

Table 5.2 shows the distribution of cases by race, sex and age, and the specific 5-year relative survival rates by these characteristics. The overall relative survival for men with anal cancer was 58% compared with 69% for women. Among women, the percent surviving decreased with increasing age: 76% for women 20-49 years old, 72% for women 50-64 years old, and 64% for women over 64 years old. In contrast, the worst prognosis for men was for the youngest age group, with better prognosis for middle-aged men. It should be noted that the case distribution among black men is younger, with 49% of black males falling in the 20-49 age group, compared to 28% of white males.

Relative survival was also markedly different by race, with 66% of white patients surviving at 5 years post di-

Table 5.2: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Age (20+) and Sex, 12 SEER Areas, 1988-2001.

Race/Age Group (Years)	Sex								
	Total			Male			Female		
	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
All Races	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
20-49	1,031	24.0	63.8	569	31.2	54.0	462	18.7	75.7
50-64	1,294	30.1	67.6	617	33.8	63.3	677	27.4	71.5
65+	1,971	45.9	61.7	638	35.0	56.2	1,333	53.9	64.1
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
20-49	800	22.0	66.7	418	28.1	56.4	382	17.8	78.0
50-64	1,090	30.0	68.8	515	34.7	65.7	575	26.7	71.5
65+	1,746	48.0	63.2	553	37.2	57.8	1,193	55.5	65.5
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
20-49	183	38.9	52.6	122	49.2	46.3	61	27.4	65.3
50-64	156	33.1	57.8	77	31.0	49.3	79	35.4	65.2
65+	132	28.0	44.0	49	19.8	43.1	83	37.2	43.7

Table 5.3: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Histology and Sex, Ages 20+, 12 SEER Areas, 1988-2001.

Race/Histology (ICD-O code)	Sex								
	Total			Male			Female		
	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
All Races	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
Squamous Cell (8010-8089)	2,594	60.4	67.0	1,129	61.9	60.3	1,465	59.3	72.3
Cloacogenic or Basaloid (8123-8124)	771	17.9	70.2	229	12.6	62.4	542	21.9	73.2
Adenocarcinoma (8140-8263,8480-8481)	757	17.6	53.4	387	21.2	52.9	370	15.0	54.2
Melanoma (8720)	75	1.7	26.9	23	1.3	~	52	2.1	22.0
Other	99	2.3	37.3	56	3.1	29.3	43	1.7	45.9
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
Squamous Cell (8010-8089)	2,226	61.2	68.1	946	63.7	62.1	1,280	59.5	72.6
Cloacogenic or Basaloid (8123-8124)	689	18.9	71.5	199	13.4	64.4	490	22.8	74.2
Adenocarcinoma (8140-8263,8480-8481)	580	16.0	55.6	280	18.8	54.9	300	14.0	56.4
Melanoma (8720)	64	1.8	27.4	19	1.3	~	45	2.1	20.2
Other	77	2.1	40.9	42	2.8	32.5	35	1.6	48.7
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
Squamous Cell (8010-8089)	296	62.8	57.3	155	62.5	50.3	141	63.2	65.2
Cloacogenic or Basaloid (8123-8124)	57	12.1	53.8	24	9.7	~	33	14.8	57.7
Adenocarcinoma (8140-8263,8480-8481)	104	22.1	40.8	60	24.2	43.4	44	19.7	35.5
Other	14	2.9	~	9	3.6	~	5	2.2	~

~Statistic not displayed due to less than 25 cases.

agnosis compared to 53% for black patients. Black patients had worse survival than white patients in every age group; markedly worse survival was reported for black men and women in the oldest age group.

Geographic differences as represented by the 12 contributing tumor registries were not assessable due to small numbers of patients by registry.

Tumor characteristics: effect of primary site, histology, size, stage, and differentiation

Tumors of the anus, anal canal, cloacogenic zone, and overlapping lesions of the rectum and anus are reported separately. The distribution of cases by site of diagnosis was 38.8% anus, 29.5% anal canal, 7.8% cloacogenic zone, and 23.9% overlapping lesions. Overall, 5-year relative

survival did not differ substantially by site, ranging from a high of 68% for anal canal tumors to a low of 56% for overlapping lesions.

The largest proportion of invasive anal cancer cases had squamous cell histology (60.4%), followed by cloacogenic (or basaloid) tumors (17.9%), adenocarcinomas (17.6%), melanomas (1.7%), and other histologies (2.3%). The distribution of histologic types varies with sex, with more adenocarcinomas among males and more cloacogenic cancers among females. The 5-year relative survival by histology was 67% for squamous cell cancers, 70% for cloacogenic cancers, 53% for adenocarcinomas, 27% for melanoma, and 37% for other histologies. Survival rates were higher for females than for males especially for squamous cell carcinomas and cloacogenic carcinomas (Table 5.3).

Figure 5.1: Cancer of the Anus: 5-Year Relative Survival Rate (%) by Tumor Size and Subsite, Ages 20+, 12 SEER Areas, 1988-2001

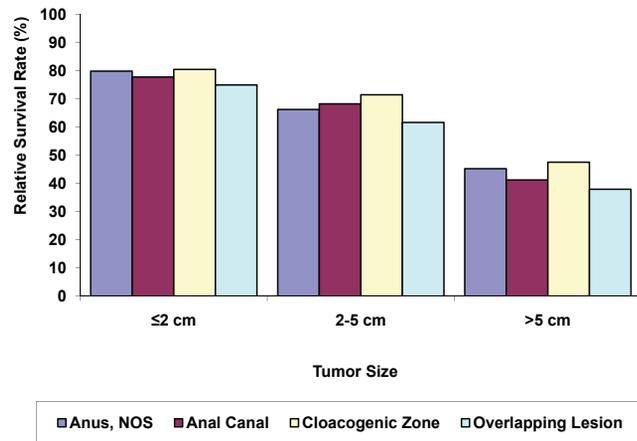


Figure 5.2: Cancer of the Anus: 5-Year Relative Survival Rate (%) by Grade and Sex, Ages 20+, 12 SEER Areas, 1988-2001

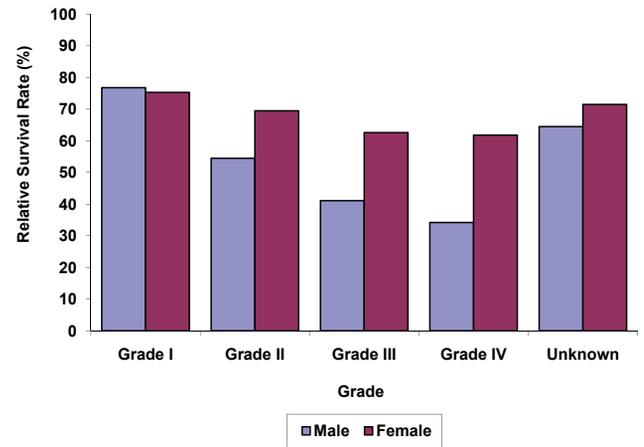


Figure 5.3: Cancer of the Anus: 5-Year Relative Survival (%) by Grade and Race, Ages 20+, 12 SEER Areas, 1988-2001

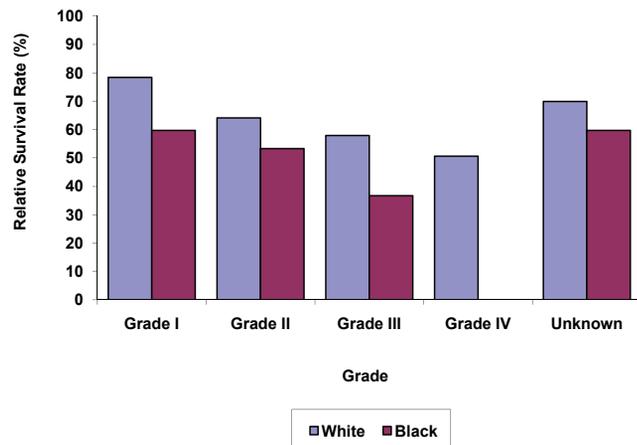
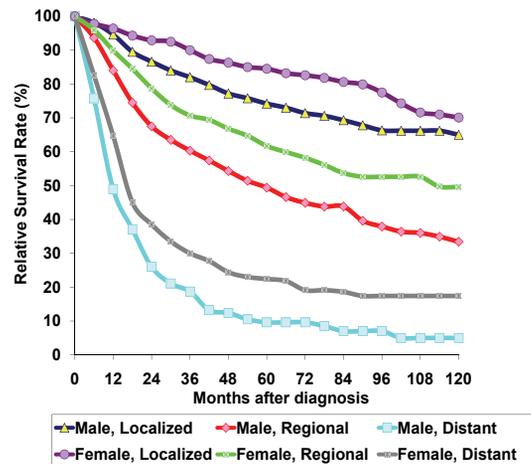


Figure 5.4: Cancer of the Anus: Relative Survival Rate (%) by Sex and Stage, Ages 20+, 12 SEER Areas, 1988-2001



For anus, NOS, the relative survival rate at 5 years post diagnosis decreased with increasing size: 80% for ≤ 2 cm, 66% for 2-5 cm, and 45% for >5 cm for all races and both genders. Figure 5.1 shows relative survival by site and size of tumor, with less than 50% survival for tumors larger than 5 cm for each site.

The amount of cell differentiation or grade of disease at diagnosis was unknown for 31% of the tumors, but tumors with unknown grade had a relatively high survival rate (69%). For tumors with a known grade, the 5-year relative survival ranged from 77% for well-differentiated grade I lesions, 62% for moderately differentiated grade II lesions

to a low of 55% for poorly differentiated, undifferentiated or anaplastic grade III and IV lesions. Men had slightly better prognosis for well-differentiated tumors only, and women had better prognosis for the other grades especially for grade III/IV (Figure 5.2, Table 5.4).

The 5-year relative survival by grade also differed strongly by race, with consistently lower survival for every grade of tumors for black as compared to white patients (Figure 5.3). There were fewer than 25 black patients with grade IV tumors and therefore, the survival rate was not calculated for this group.

Table 5.4: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Grade and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Race/Grade	Sex								
	Total			Male			Female		
	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
Total	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
Well differentiated (I)	459	10.7	76.5	257	14.1	76.8	202	8.2	75.3
Moderately differentiated (2)	1,355	31.5	62.4	634	34.8	54.5	721	29.2	69.5
Poorly/undifferentiated (3/4)	1,159	27.0	55.1	396	21.7	40.7	763	30.9	62.5
Unknown	1,323	30.8	68.7	537	29.4	64.5	786	31.8	71.5
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
Well differentiated (I)	388	10.7	78.4	217	14.6	77.3	171	8.0	78.8
Moderately differentiated (2)	1,124	30.9	64.1	506	34.1	56.8	618	28.7	70.1
Poorly/undifferentiated (3/4)	998	27.4	57.4	326	21.9	45.4	672	31.3	63.2
Unknown	1,126	31.0	69.9	437	29.4	65.8	689	32.0	72.5
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
Well differentiated (I)	48	10.2	59.7	31	12.5	62.5	17	7.6	~
Moderately differentiated (2)	171	36.3	53.3	93	37.5	45.6	78	35.0	62.0
Poorly/undifferentiated (3/4)	115	24.4	37.7	52	21.0	20.2	63	28.3	51.8
Unknown	137	29.1	59.7	72	29.0	60.8	65	29.1	58.7

~Statistic not displayed due to less than 25 cases.

Stage of disease was the most important single predictor of survival. Overall, local disease had an 80% 5-year relative survival rate, regional disease had 57% survival rate, and distant disease had only a 17% survival rate. About 13% of the tumors were unstaged, and their survival rate was 55% (Table 5.5).

Stage was an important prognostic factor for men and women of all races, with women having better survival at every stage of disease (Figure 5.4). Among patients with distant disease, 5-year relative survival was only 10% for men compared to 22% for women. Stage and sex together predict outcome at 5 years that is similar to the outcome at 10 years post-diagnosis (data not shown).

DISCUSSION

The major prognostic factors are stage, sex (females have better prognosis at every stage of disease), and race. Blacks have worse prognosis than whites overall, and black men have the worst prognosis at all tumor stages. There were

also differences in prognosis predicted by two components of stage: tumor size and differentiation. Primary tumors 2 centimeters or less in size have a better prognosis than larger tumors, and well-differentiated tumors are more favorable than poorly differentiated tumors.

The worse prognosis for men less than 50 years old was seen consistently across races, stage of disease, anal cancer sites, grades, and tumor size. It may be that this worse survival is due to the toll of HIV/AIDS on young men. Although anal cancer is not an AIDS-defining illness, there is an increased risk for anal dysplasia and cancer among men who have sex with men that is increased more strongly among HIV positive men who have sex with men (10). This increased risk has led to higher cytologic surveillance of this group, which may have affected the survival trends for anal cancer.

Table 5.5: Cancer of the Anus: Number and Distribution of Cases and 5-Year Relative Survival Rates (%) by Race, Historic Stage and Sex, Ages 20+, 12 SEER Areas, 1988-2001

Race/Historic Stage	Sex								
	Total			Male			Female		
	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent	Cases	Percent	Relative Survival 5-Year Percent
All Races	4,296	100.0	64.0	1,824	100.0	57.9	2,472	100.0	68.5
Localized	2,031	47.3	79.9	899	49.3	74.2	1,132	45.8	84.5
Regional	1,342	31.2	56.6	550	30.2	49.4	792	32.0	61.7
Distant	384	8.9	16.8	173	9.5	9.6	211	8.5	22.4
Unstaged	539	12.5	54.7	202	11.1	47.6	337	13.6	58.7
White	3,636	100.0	65.7	1,486	100.0	60.2	2,150	100.0	69.5
Localized	1,735	47.7	81.3	748	50.3	75.6	987	45.9	85.6
Regional	1,130	31.1	58.4	436	29.3	51.7	694	32.3	62.8
Distant	296	8.1	17.4	128	8.6	9.5	168	7.8	23.0
Unstaged	475	13.1	54.7	174	11.7	50.1	301	14.0	57.1
Black	471	100.0	52.5	248	100.0	47.0	223	100.0	58.5
Localized	198	42.0	66.9	108	43.5	63.3	90	40.4	70.3
Regional	150	31.8	51.9	81	32.7	46.7	69	30.9	58.3
Distant	73	15.5	17.2	37	14.9	11.9	36	16.1	21.9
Unstaged	50	10.6	45.1	22	8.9	~	28	12.6	66.9

~Statistic not displayed due to less than 25 cases.

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