

Rising Incidence and Improved Survival of Anal Squamous Cell Carcinoma in Norway, 1987-2016

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Abstract

The purpose was to provide population-based data of incidence and survival of anal squamous cell carcinoma. All 1548 primary anal cancers in 1987 through 2016 were identified in the Cancer Registry of Norway. Incidence rates increased in men and women, and net survival improved, in the period. Five-year net survival was 76% after curative and 18% after palliative radiotherapy.

Background: Anal squamous cell carcinoma (ASCC) is a rare, human papilloma virus-associated cancer. The purpose was to investigate the population-based incidence rates, age and gender distribution, and survival of ASCC. **Materials and Methods:** All primary ASCC in 1987 to 2016 were identified in the Cancer Registry of Norway (N = 1548), with information on age, gender, stage, county of residence, radiotherapy, and survival. **Results:** Median age was 66 years; 71% were females. World age-standardized incidence rates increased (1987-2016) from 0.79 (95% confidence interval [CI], 0.69-0.90) to 1.10 (95% CI, 1.00-1.22) per 100,000 person-years in females and, from 0.34 (95% CI, 0.28-0.42) to 0.47 (95% CI, 0.40-0.54) in males. Estimated annual percentage change was 1.7 (95% CI, 0.9-2.6) for females and 1.3 (95% CI, -0.1 to 2.7) for males. Incidence rates increased with age; the relative risk was higher in major cities. Five-year net survival increased from 63.4% to 72.7% (1987-2016), but for age ≥ 70 years remained $\sim 57\%$. Net survival was dependant on stage, age, and gender. Five-year net survival (1997-2016) was 76.4% after curative radiotherapy, and 18.0% after palliative radiotherapy. **Conclusion:** ASCC incidence rates increased from 1987 to 2016, and survival improved for patients < 70 years. Five-year net survival was 76% after curative radiotherapy in Norway.

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Keywords: Anal cancer, Cancer registry, Epidemiology, Radiotherapy, Human papilloma virus

Introduction

Anal cancer, or anal squamous cell carcinoma (ASCC) of the anal canal or the perianal region is a rare disease worldwide, but the incidence is increasing in high-income countries.¹ ASCC is strongly associated with human papilloma virus (HPV) infection.²⁻⁵ Other risk factors include immunosuppression, in particular, infection with human immunodeficiency virus (HIV), or solid organ transplant recipients.⁶ In addition, risk is increased by lifestyle factors

such as smoking or a high lifetime number of sexual partners.⁴ High-grade anal intraepithelial neoplasia (AIN) has been shown to progress to invasive anal cancer in HIV-positive or immunocompromised patients.⁷

Although a few small anal cancers may be treated surgically, most patients with anal cancer are treated with chemoradiotherapy (CRT) with curative intent. The radiotherapy (RT) is delivered with several treatment fields to high RT doses, most often with concomitant chemotherapy.^{8,9} Intensity-modulated RT enables delivery of high RT doses to tumor, simultaneous treatment to target volumes with different dose levels, and lower normal tissue dose.¹⁰ If complete tumor remission is not achieved, patients are considered for salvage surgery.^{8,11} Large, randomized trials have shown 5-year overall survival of 70% to 75% and 3-year progression-free survival of 73% to 74%.^{12,13} A national population-based retrospective study of all patients treated with RT in Norway,¹⁴ and a large series of patients treated in the Nordic countries¹⁵ have provided “real world data” of treatment of unselected patients in everyday practice with comparable treatment outcomes. A high rate of late effects and impaired quality of life was reported in survivors of anal cancer.^{16,17}

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Table 1 ASCC in Norway, 1987 to 2016, by Gender, Age Group, and Disease Stage at Diagnosis

	1987-1996		1997-2006		2007-2016		Total	
	Cases	%	Cases	%	Cases	%	Cases	%
No. ASCC	382	100	497	100	669	100	1548	100
Gender								
Females	276	72.3	349	70.2	474	70.9	1099	71.0
Males	106	27.8	148	29.8	195	29.2	449	29.0
Age group, y								
0-49	55	14.4	73	14.7	84	12.6	212	13.7
50-69	174	45.6	214	43.1	343	51.3	731	47.2
70+	153	40.1	210	42.3	242	36.2	605	39.1
Stage								
Localized	174	45.6	168	33.8	193	28.9	535	34.6
Regional	103	27.0	159	32.0	210	31.4	472	30.5
Distant	15	3.9	37	7.4	52	7.8	104	6.7
Missing	90	23.6	133	26.8	214	32.0	437	28.2

Abbreviation: ASCC = Anal squamous cell carcinoma.

ASCC incidence has increased in several countries.^{1,3,18-25} In the United States (US), the observed increased incidence was higher than for other HPV-related cancers.^{3,26} The increased incidence has only been demonstrated for squamous cell carcinoma, not for adenocarcinoma in the anal canal.²¹ However, an increased risk of AIN has been reported,^{21,22,26} probably related to risk factors and associated with an increased incidence of ASCC. In addition, a higher incidence of AIN and anal cancer in males has been reported in areas with a high rate of high-risk populations such as San Francisco (US) compared with nearby areas and national data.²⁷

Because ASCC is a relatively rare cancer, incidence rates of anal cancer are often reported together with colorectal cancer, although this is a total different disease entity. The incidence, demographics, and survival of patients with ASCC in Norway have not been previously described in detail. The aims of the present study were to analyze the overall incidence rates of ASCC, the age and gender distribution, the relationship with factors such as place of residence and treatment given, and the survival of patients with anal cancer in Norway, and to analyze the time trends of incidence and survival during the last 30 years.

Materials and Methods

The Cancer Registry of Norway (CRN) has registered all cases of cancer nationwide since 1953. Patients are identified through a unique national personal identification number.²⁸ For health care professionals, the reporting of cancer cases is mandatory, and the CRN receives notification on single patients with cancer from several independent sources, including pathology reports, clinical reports, details of radiotherapy, and death certificates. Therefore, CRN data on cancers in Norway has a high degree of completeness (98.8%) and high quality.²⁸

Patients

The present study included all new cases of histologically verified invasive squamous cell carcinoma of the anal canal in the Norwegian

population between January 1, 1987, and December 31, 2016. All new cases of malignant solid tumors located in the anal canal were identified, in addition to squamous cell carcinoma in the rectum, and cancer in the anal canal with simultaneous perianal extension. Although perianal tumors located close to the anal margin (< 5 cm) are usually treated as anal cancer, anal margin cancers (without anal canal involvement) were not identified as they were registered as skin tumors at the CRN.

A total of 1721 cases of anal canal cancer were identified, of which 1548 were squamous cell carcinomas (or poorly differentiated carcinomas) and were included in the analyses. Adenocarcinomas (N = 151), melanomas (N = 14), neuroendocrine carcinomas (N = 4), and sarcomas (N = 4) in the anal canal were excluded from the analyses.

Information on date of birth, gender, municipality of residence, date of diagnosis, disease stage at diagnosis, radiotherapy, surgery, and survival data were retrieved from the CRN. Patients were categorized by age at diagnosis into age groups (< 50, 50-69, and ≥ 70 years of age). Stage of disease at diagnosis was categorized as localized (T1-2N0M0), with regional spread (T3-4 and/or N1-3, M0), distant metastases (M1), or unknown, according to CRN definitions. Quality assurance of the data disclosed that patients with pathologic lymph nodes in the external iliac regions had been coded as distant metastases; these were recoded in the CRN as node-positive (regional spread). Because CRT is the primary treatment of ASCC, and most achieve complete remission of the tumor, disease stage is not based on pathologic assessment (pTNM) of a surgical specimen, but is a clinical (cTNM) stage based on clinical and radiologic examinations. To evaluate if the incidence of ASCC was higher in the major cities, the patients' municipality at diagnosis was used to create 2 groups. One group consisted of the largest cities (Oslo, Bergen, Trondheim, and Stavanger municipalities), whereas the other group consisted of all other municipalities. Information on HPV infection was not available in the CRN, as it has not been routinely recommended to perform on ASCC biopsies until recent years.

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Table 2 Anal Squamous Cell Carcinoma in Norway, 1987-2016: Number of New Cases, Age-specific and World-standardized Incidence Rates per 100,000 Person-years, by Calendar Period and Gender

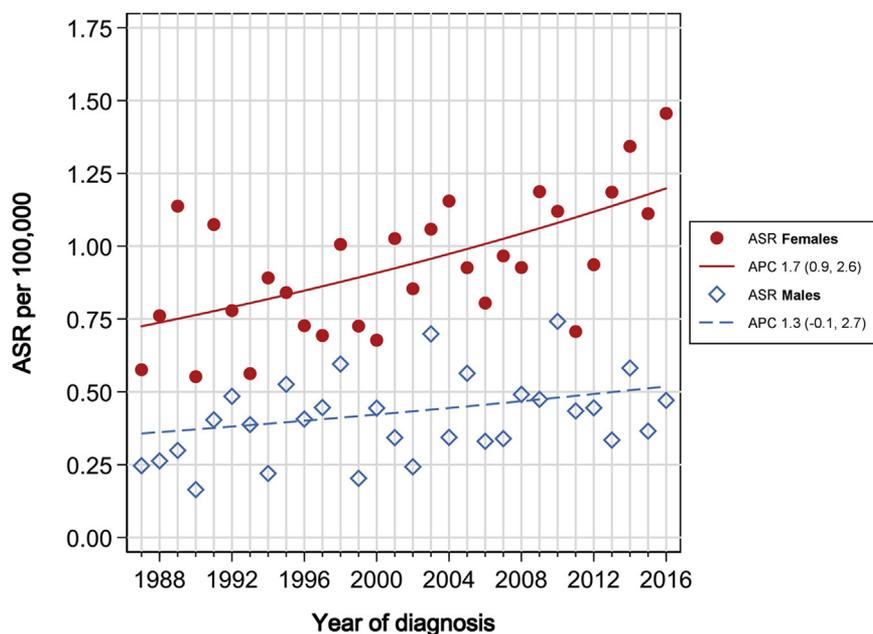
Period	Age	Females			Males			Total		
		Cases	Rate	95% CI	Cases	Rate	95% CI	Cases	Rate	95% CI
1987-1996	0-49	32	0.22	0.15-0.31	23	0.15	0.10-0.22	55	0.18	0.14-0.24
	50-69	134	3.29	2.76-3.90	40	1.03	0.74-1.40	174	2.19	1.87-2.54
	70+	110	3.71	3.05-4.47	43	2.22	1.61-2.99	153	3.12	2.65-3.66
	All	276	0.79	0.69-0.90	106	0.34	0.28-0.42	382	0.57	0.51-0.64
1997-2006	0-49	48	0.32	0.23-0.42	25	0.16	0.10-0.23	73	0.24	0.19-0.30
	50-69	147	3.15	2.66-3.70	67	1.44	1.12-1.83	214	2.30	2.00-2.63
	70+	154	5.00	4.25-5.86	56	2.75	2.08-3.57	210	4.11	3.57-4.70
	All	349	0.89	0.79-1.00	148	0.42	0.35-0.50	497	0.67	0.60-0.73
2007-2016	0-49	71	0.44	0.35-0.56	13	0.08	0.04-0.13	84	0.25	0.20-0.32
	50-69	229	4.00	3.50-4.56	114	1.95	1.61-2.34	343	2.97	2.66-3.30
	70+	174	5.65	4.84-6.56	68	3.05	2.37-3.87	242	4.56	4.00-5.17
	All	474	1.10	1.00-1.22	195	0.47	0.40-0.54	669	0.79	0.73-0.85

Abbreviation: CI = Confidence interval.

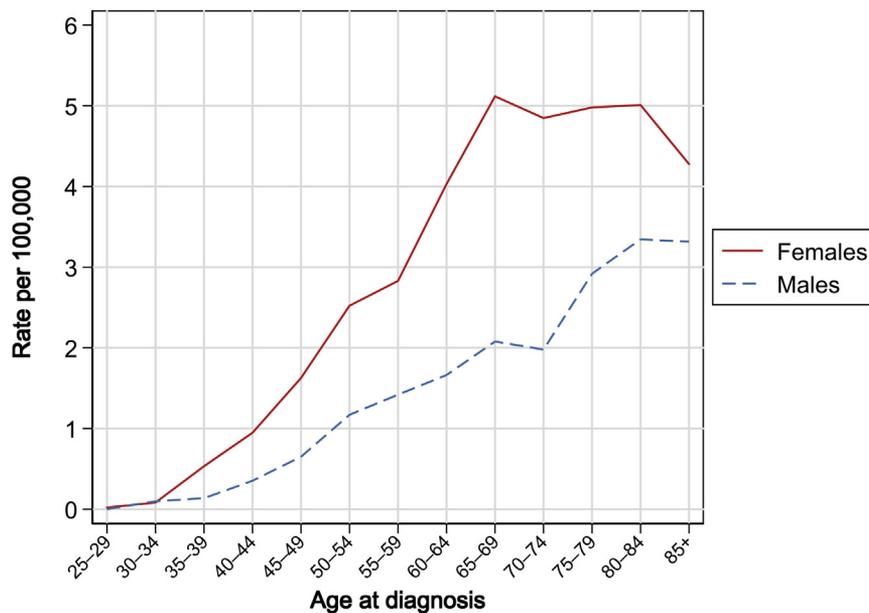
National complete data on RT was available from 1997 to 2016. Data on RT were received from each RT center and linked with the corresponding cancer case, and included date of RT, region irradiated, treatment intention, and RT dose.²⁹ Of all patients with ASCC (N = 1166) diagnosed in 1997 to 2016, RT was not delivered to 157 (13.5%), 6 were excluded owing to inconsistent data, and 28 were excluded owing to start of RT more than 6 months after the date of diagnosis. The remaining 975 patients received RT and were classified as having a first RT course of either curative or palliative intent. The first RT course

was defined as treatment (target dose registrations) with gaps of maximum 7 days within the first 6 months after diagnosis. Treatment intention was registered as curative in 86.9%, palliative in 5.7%, and unknown for 7.4% of the patients who underwent RT. For those 7.4% with unknown treatment intent, intention was allocated based on dose received; curative if maximum target dose in the first series was 50 Gy or more (N = 57) or palliative if the dose was less than 50 Gy (N = 15). The resulting distribution of treatment intent was 92.7% (N = 904) curative and 7.3% (N = 71) palliative.

Figure 1 World ASRs of Anal Squamous Cell Carcinoma With APC by Gender, in Norway, 1987 to 2016



Abbreviations: APC = Annual percentage change; ASR = Age-standardized incidence rate.

Figure 2 Incidence Rates of Anal Squamous Cell Carcinoma in Norway, 1987 to 2016, by Age and Gender

Patients diagnosed with ASCC (N = 1548) were followed from date of diagnosis to earliest of date of death (N = 858), emigration (N = 5), or end of follow-up December 31, 2016, with a median follow-up time of 4.2 years. A sub-analysis stratified by treatment intention of RT was performed on 975 patients with ASCC diagnosed in 1997 to 2016, with a median follow-up time of 3.9 years.

Statistics

Descriptive statistics are reported using proportions and median with quartiles (Q1, Q3).

World age-standardized incidence rates (ASR)³⁰ with 95% confidence intervals (CIs)³¹ were calculated using the Stata program, *distrate*.³² We also estimated incidence rates by age. Annual percentage change (APC) in incidence was estimated by a linear regression on the logarithm of ASR using the standard joinpoint model of the NCI Joinpoint Regression Program (version 4.5.0.1) applying the standard errors³¹ from the Stata program, *distrate*.³² To compare incidence between the most rural areas and other areas, a Poisson regression was applied to estimate incidence rate ratios (IRR) controlling for factors gender and age at diagnosis (0-4, 5-9, ..., 80-84, 85+).

To measure cancer survival adjusting for other causes of death, 5-year net survival was estimated in a relative survival setting, using the non-parametric Pohar Perme estimator³³ implemented in the Stata program, *strs*.³⁴ To supplement these estimates of 5-year net survival, annual change in excess mortality (excess hazard ratios [EHR]) adjusted for the factors age and stage was estimated applying a flexible parametric relative survival model using the Stata program *stpm2*. Both net survival and excess mortality analysis used national life tables stratified by gender, calendar year, and single year of age. Survival time was calculated from the date of diagnosis.

Stage was missing for 28.2% for all years combined, and by period for 23.6% (1987-1996), 26.8% (1997-2006), and 32.0% (2007-2016). A relatively high fraction of missing stage was expected, because disease stage for ASCC is based on cTNM reported from clinicians. To address the problem of missing data on stage, univariate multiple imputation was applied assuming data were missing at random. Stage was imputed³⁵ using an augmented multinomial logistic regression model including the Nelson-Aalen cumulative hazard estimate and the event indicator in addition to gender and year of diagnosis as categorical variables and age at diagnosis as a continuous variable. We created $m = 60$ datasets, choosing m based on assessment of Fraction of Missing Information and applying the rule of thumb that m should be at least equal to the percentage of incomplete cases.³⁶ All analyses including stage were conducted on the imputed datasets combining the results using Rubin's rules. The distribution of stage and estimates were similar using imputed and observed data. The multiple imputation estimates are reported for all analyses including stage.

All analyses, except the joinpoint regression, were performed using the statistical software package Stata 15.1.

Results

Incidence, 1987 to 2016

Of the 1548 patients with squamous cell carcinoma in the anal canal, 1099 (71.0%) occurred in women and 449 (29.0%) in men (Table 1). The gender distribution remained constant throughout 1987 to 2016. The median age at diagnosis was 66.0 years (Q1, 55.8 years; Q3, 75.9 years), and did not differ significantly between men (65.4 years) and women (66.4 years). At diagnosis, 34.6% had localized disease, 30.5% had regional disease, and 6.7% had distant metastases, whereas stage was not registered in 28.2% of patients.

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Table 3 ASCC in Norway, 1987-2016: 5-year Net Survival With 95% CI by Calendar Period, Gender, Age, and Stage

Period	Groups	Females		Males		Total	
		Net Survival, %	95% CI	Net Survival, %	95% CI	Net Survival, %	95% CI
1987-1996	0-49 y	78.9	59.8-89.6	53.0	30.9-70.9	68.0	53.7-78.8
	50-69 y	72.1	62.9-79.4	53.8	35.9-68.8	67.9	59.7-74.8
	70+ y	58.8	45.0-70.3	50.7	27.0-70.3	56.6	44.7-66.8
	Localized	80.5	68.8-88.1	67.2	49.0-80.2	76.2	66.6-83.3
	Regional	57.8	45.0-68.7	21.9	5.9-44.2	50.3	39.1-60.5
	Distant	23.9	5.7-48.8	0.0	NA ^a	20.1	4.7-43.1
	All	67.6	60.3-73.9	52.4	40.0-63.4	63.4	57.1-69.0
1997-2006	0-49 y	81.8	67.2-90.3	80.9	58.6-91.9	81.5	70.2-88.8
	50-69 y	74.6	66.1-81.2	59.5	45.9-70.7	69.9	62.7-75.9
	70+ y	63.1	51.4-72.6	42.4	24.7-59.1	57.6	47.8-66.2
	Localized	88.8	76.6-94.9	77.3	58.9-88.2	85.2	75.7-91.2
	Regional	64.5	54.1-73.1	45.8	29.5-60.6	59.4	50.6-67.2
	Distant	18.6	5.6-37.6	8.1	0.5-30.1	15.2	5.4-29.7
	All	70.5	64.1-76.0	56.7	46.6-65.6	66.4	61.0-71.2
2007-2016	0-49 y	74.7	57.6-85.6	>100	NA ^a	78.9	63.8-88.3
	50-69 y	85.5	78.3-90.5	75.8	64.2-84.0	82.3	76.4-86.8
	70+ y	52.4	38.2-64.7	65.8	41.2-82.0	56.7	44.6-67.0
	Localized	82.9	68.4-91.1	91.8	59.1-98.6	85.9	74.2-92.5
	Regional	72.1	59.5-81.4	64.5	47.3-77.4	70.2	60.3-78.1
	Distant	38.4	21.4-55.2	22.0	1.4-58.4	35.0	19.8-50.7
	All	71.9	64.8-77.8	74.2	63.4-82.3	72.7	67.0-77.6

Abbreviations: CI = Confidence interval.
^aCI not estimable.

The ASRs were higher for women than for men, and increased throughout the time (Table 2). For women, the ASR increased from 0.79 (95% CI, 0.69-0.90) per 100,000 person-years in 1987 to 1996 to 1.10 (95% CI, 1.00-1.22) in 2007 to 2016. For men, the ASR increased correspondingly from 0.34 (95% CI, 0.28-0.42) to 0.47 (95% CI, 0.40-0.54). The observed increase in ASR occurred in all age groups. The increase in ASR is depicted in Figure 1. The join-point regressions had zero join-points, and the estimated APCs for 1987 to 2016 were 1.7 (95% CI, 0.9-2.6) for women and 1.3 (95% CI, -0.1 to 2.7) for men.

Incidence rates increased with increasing age (Figure 2) for both men and women, up to 70 to 80 years. The relative risk of ASCC was higher for persons living in a major city than in the other municipalities in Norway. For the period of 1987 to 2016, the incidence rate ratio (IRR) of living in a major city was 1.24 (95% CI, 1.10-1.39).

Survival

The median survival time in years was 8.5 years (95% CI, 7.2-9.5 years); for women, 9.2 years (95% CI, 8.1-10.6 years) and for men, 5.8 years (95% CI, 4.3-7.5 years). The 5-year net survival increased in the time period, from 63.4% (95% CI, 57.1%-69.0%) in 1987 to 1996 to 72.7% (95% CI, 67.0%-77.6%) in 2007 to 2016 (Table 3). The improvement was present for both men and women. The improved survival was mainly observed for patients < 70 years; the 5-year net survival of patients ≥ 70 years was approximately 57% throughout the time periods. Survival improved over the time

periods for localized, regional, and metastatic disease. The model-based estimate of annual excess hazard ratio was 0.97 (95% CI, 0.96-0.98) adjusting for gender, stage, and age at diagnosis.

Net survival in the latest time period (2007-2016) varied with disease stage at diagnosis, age, and gender (Figure 3). Worse survival was observed in patients with distant metastases, patients ≥ 70 years of age, or in men.

Of patients with anal cancer (n = 975) where complete national RT data were available in the CRN (1997-2016), the intention of initial RT (first treatment series) was curative for 904 (92.7%) and palliative for 71 (7.3%) of patients. The median age was 64.4 years (Q1, 54.5 years; Q3, 74.1 years) and 77.5 years (Q1, 68.1 years; Q3, 84.1 years), for the curative and palliative intention groups, respectively. The distribution of stage was localized (44.7%), regional (47.6%), and distant (7.7%) for the group with curative intention of RT; and localized (16.1%), regional (45.2%), and distant (38.8%) for the group with palliative intention of RT. Median survival was 10.2 years (Q1, 8.9 years; Q3, 11.3 years) and 0.9 years (Q1, 0.6 years; Q3, 2.0 years), and the 5-year net survival was 76.4% (95% CI, 72.1%-80.1%) and 18.0% (95% CI, 6.9%-33.4%) for the curative and palliative intention groups, respectively (Figure 4).

Discussion

The incidence rates of ASCC have increased significantly during the past 30 years in Norway. The observed increased incidence occurred in all age groups and in both men and women. In the same time period, net survival increased significantly. Survival was better

Figure 3 Net Survival of Anal Squamous Cell Carcinoma in Norway, 2007 to 2016, by Stage, Age, and Gender

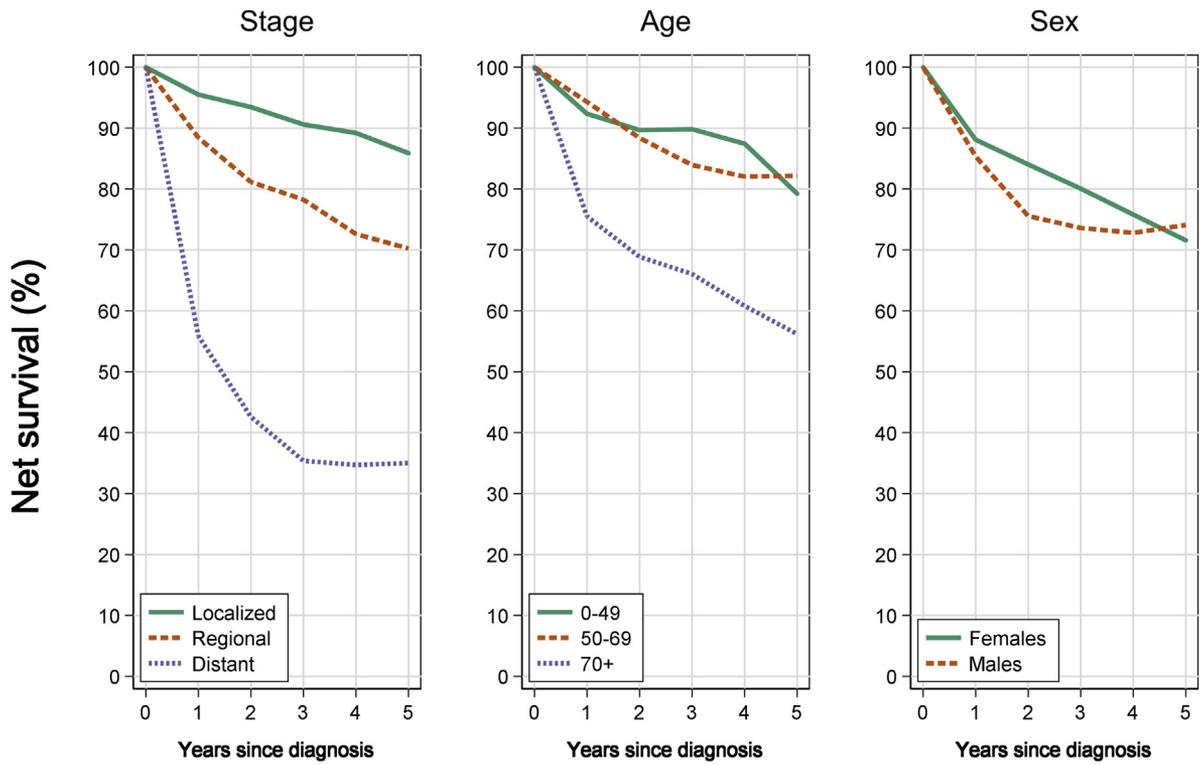
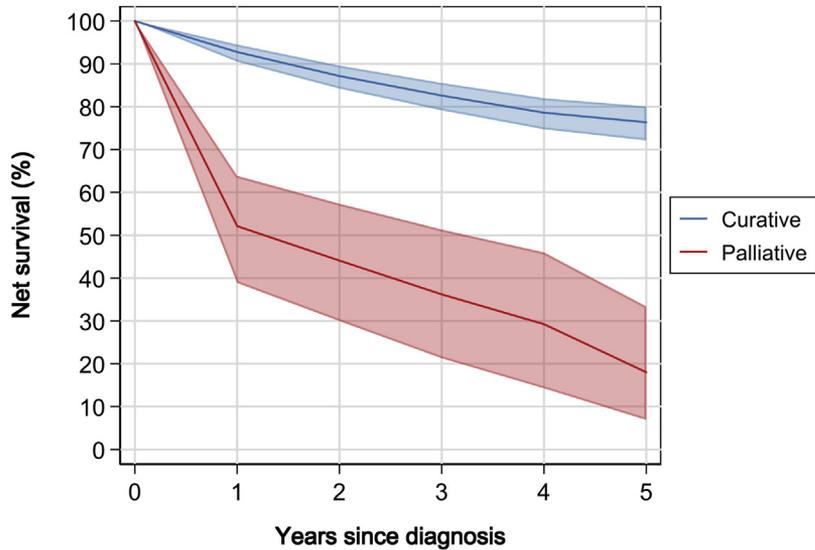


Figure 4 Net Survival With 95% Confidence Intervals for Patients With Anal Squamous Cell Carcinoma by Treatment Intention of Initial Radiotherapy (1997-2016)



Number at risk:

	0	1	2	3	4	5
Curative	904	759	649	549	470	409
Palliative	71	33	25	19	12	7

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for women, patients < 70 years, and for patients with localized or regional disease.

This observed increased incidence has been demonstrated in several countries in Europe, the US, and Australia.^{1,3,19-25} The estimated APCs were 1.7 for women and 1.3 for men, which is higher than the average APC of 1.2 for all cancers combined in Norway in the same time period (unpublished). The increased incidence in anal cancer has been shown to be limited to ASCC, and has not been observed for adenocarcinoma of the anal canal.^{1,18,20-22} Furthermore, an increase in AIN has been observed during later years.^{21,22} This is in line with the finding of increased incidence of other HPV-induced cancers, in particular cancer of the oropharynx.^{3,37} The increase in HPV-related head and neck cancers in Norway has been even larger than for anal cancer, with an average percentage change of 4.6 and 4.0 for men and women, respectively.³⁸ Both major morphological types of cervical cancer, squamous cell carcinoma (SCC) and adenocarcinoma, are causally related to persistent infection with high-risk HPV; however, screening is only effective for detecting SCC. Although the incidence of cervical SCC has decreased, the incidence of cervical adenocarcinoma has increased by 1.5% each year, which is slightly less than the observed increase in anal cancer.³⁹ For head and neck cancer, vulvar cancer, or anal cancer, early prevention through screening is not available. Vaccination for HPV has been implemented for young women in Norway, and is expected to have an impact on the incidence of all HPV-related cancers, including ASCC.³⁷

The majority of patients with ASCC are HPV-positive.⁴⁰⁻⁴² It has been shown that 80% to 85% of ASCC are HPV-16-positive, and an additional few are HPV-18-positive.⁴⁰ Recent studies have shown that HPV is a strong prognostic predictor for treatment outcome. Patients with p16-positive tumors and tumor-infiltrating lymphocytes had particularly good outcomes, suggesting that modulating the host response to tumor may improve treatment outcomes.^{42,43} Patients with HPV-16-negative or p16-negative tumors have significantly worse local recurrence rates and overall survival.^{40,42,44-46} For these patients, there is a need to investigate and develop better treatment strategies. Gene expression analysis in HPV-positive tumors revealed that patients could be divided into 2 distinct prognostic groups based on integration of HPV-16, which influenced gene expression, particularly E2F-regulated genes.⁴⁷ Also, miR-15b was induced by E2F modulated gene response,⁴⁸ and the expression of desmosomal proteins was associated with cancer-specific survival.⁴⁹ Validation of these findings and exploring targets for immune therapy may lead to further improvements in stratified treatment for anal cancer.

Interestingly, the risk of ASCC was higher in persons living in urban areas (major cities in this study) than in persons living outside the larger cities. This is in line with high incidence rates reported from some larger cities such as San Francisco (US) compared with neighboring regions.²⁷ This may be associated with a higher rate of persons with high-risk factors residing in larger cities than in more rural areas.

There is an increased risk of anal cancer after previous HPV-associated malignancy, and after treatment for anal cancer, there is an increased risk of a second HPV-related cancer.^{15,50,51} This increased risk is probably caused by common risk factors, including the risk caused by persistent HPV infection.

Although the CRN has very high data quality, disease stage was missing for a number of patients. This is mainly because disease stage in anal cancer is based on clinical and radiologic examination, and therefore registry data depend on accurate clinician reports. In contrast, for diseases like colorectal cancer, registration of disease stage is mostly based on pathology reports from surgical specimens. To address this issue, multiple imputations were used for all analyses involving stage. A strength in the CRN is the high-quality detailed reports received of all RT delivered for all patients with cancer, which enabled survival analyses based on given RT.

The 5-year net survival increased during these 30 years from 63.4% to 72.7%. Improved survival has also been observed in other countries.^{18,19,23,25} These population-based results of real-world data, and the 5-year survival of patients who received curative CRT of 76.4% seem to be comparable with survival results obtained in clinical trials, and demonstrate the previously known dependency on disease stage.^{12,52} During these 30 years, improvements in imaging have resulted in better staging, RT techniques have evolved with more precise radiation dose delivery and less risk of side effects,¹⁰ and clinical trials have investigated the optimal chemotherapy regimens in combination with RT.^{12,13} There was no information on HPV status in the CRN; however, if the increased incidence of ASCC is mainly associated with HPV-positive cancer with better prognosis, this may be a contributing factor to the improved survival over time.

Worse net survival was observed in elderly (≥ 70 years) patients with ASCC, in line with some,⁵³ but not all,⁵⁴ previous studies. Elderly patients with poor functional status or comorbidities are probably more likely to receive less intensive therapy with reduced RT doses, smaller radiation fields, omitting chemotherapy, or not receiving salvage surgery. Frail elderly may be treated with an adapted CRT regimen.⁵⁵

Conclusion

The incidence of ASCC has increased in the past 30 years in Norway. In the same time period, survival has improved, in particular for patients < 70 years. Further research of stratified treatment in relation to HPV status and the role of immunotherapy are warranted, as are optimal treatment strategies for elderly patients with ASCC.

Clinical Practice Points

- ASCC is a rare, HPV-associated cancer, with increasing incidence in several countries, and relatively good survival rates.
- This population-based study investigated all cases of ASCC over the past 30 years in the Cancer Registry of Norway, and provides real-world data on incidence and survival over time and survival according to age, gender, disease stage, and treatment.
- The study confirmed increased incidence rates across all ages, gender, and stage. In addition, increased ASCC risk was observed in major cities.
- The study demonstrated increased net survival over time, but only for patients < 70 years of age. Net survival was dependant on stage, age, and gender.
- After curative RT, 5-year net survival was 76% in recent years in this population-based study.

Disclosure

The authors have stated that they have no conflicts of interest.

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