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Socioeconomic and gender disparities in anal cancer diagnosis and treatment

Karel-Bart Celie, B.A. [a, 1], Christopher Jackson, B.S. [a, 1], Surbhi Agrawal, B.A. [a, 1], Chetan Dodhia, M.D. [b], Carlos Guzman, M.D. [b], Theodor Kaufman, M.D. [b], Nicholas Hellenthal, M.D. [b], Daphne Monie, PhD. [a, *], Jose Monzon, M.D. [b], Luis Oceguera, M.D. [b]

[a] Columbia-Bassett Medical School Program, Bassett Healthcare Network, Cooperstown, NY, United States
[b] Department of Surgery, Bassett Healthcare Network, Cooperstown, NY, United States

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ABSTRACT

Background and objectives: We investigated whether receipt of radiation in patients with anal carcinoma is related to income level and other demographic factors.
Methods: The SEER database (1988–2011) was queried and linked to the Area Health Resources File (AHRF). We used logistic regression and Kaplan-Meier analyses to correlate receipt of radiation and overall and cancer-specific survival with tumor stage, age, gender, and income.
Results: Of 28,028 patients with anal cancer, 14,783 (53%) received radiation. Patients in the lowest quartile for median household income were significantly more likely to present at higher stages, were 1.87 times more likely to receive radiation (95% CI 1.74–2.00, $p < 0.001$), and 1.27 times more likely to die of anal cancer (95% CI 1.18–1.33, $p < 0.001$) than those in the highest income quartile. Within most stages, however, the wealthiest patients were more likely to receive radiation therapy than the poorest patients. Additionally, we found that women presented at higher stages ($p < 0.001$), were 2.67 times more likely to receive radiation (95% CI 2.55–2.81, $p < 0.001$), and were 1.25 times more likely to die of anal cancer than men (95% CI 1.17–1.32, $p < 0.001$).
Conclusions: Women and poorer patients present with more advanced stages of anal cancer, more commonly receive radiation, and are more likely to die of anal cancer than men and wealthier patients, respectively.

1. Introduction

According to the American Cancer Society, there are about 8000 new cases of anal cancer and 1000 deaths due to anal cancer in the United States each year. If caught early, treatment results in high cure rates with a five-year survival rate over 65% [1]. However, later stage disease, especially involving spread to nodes or distant metastases have lower survival rates. Although metastasis occurs in only 10–20% of anal cancer cases, the most common sites of distant metastases are lungs and liver, which are difficult to treat and result in high mortality [2]. Therefore, early diagnosis and treatment of anal cancer is critical for favorable prognosis.

Anal cancer typically presents with rectal bleeding, pain, or the sensation of a lump, and is confirmed by biopsy. Anal Pap smears, that detect Human Papillomavirus (HPV) infection, are sometimes used to screen for anal cancer in certain high-risk populations, such as men who have sex with men and Human Immunodeficiency Virus-positive men. Although HPV is estimated to be responsible for approximately 90% of anal carcinomas, the use of anal Pap testing to screen for anal cancer is surprisingly low. [3], [4].

Tumor stage at the time of diagnosis governs the treatment plan and prognosis of the patient. Anal cancer staging is based on the American Joint Committee on Cancer (AJCC) TNM staging system which involves determination of the local extent of the tumor (T), the status of nodal metastasis (N0 for node negative versus N+), and degree of tumor metastasis outside of the pelvis (M0 for no

* Corresponding author. Columbia-Bassett Medical School Program, One Atwell Road, Cooperstown, NY 13326, United States.
E-mail address: daphne.monie@bassett.org (D. Monie).
[1] Note: co-first authors of this article.

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metastases versus M+). Carcinoma *in situ* (Tis) is a designation for tumors that have not penetrated beyond the mucosal layer. T1 tumors are 2 cm or less across, T2 tumors are greater than 2 cm but 5 cm or less across, and T3 tumors are greater than 5 cm across. Tumors that have invaded adjacent organs are classified as T4.

Anal cancer is treated with radiation as part of the Nigro protocol [5–8]. The Nigro protocol is a regimen recommended by the National Comprehensive Cancer Network (NCCN) for anal carcinoma and is based on the findings described by Nigro et al., in 1974 [9]. For stage Tis-T1N0 anal margin lesions, local excision is recommended with possible radiation therapy and/or chemotherapy if inadequate margins are achieved [10]. Recommended treatment for stages T1-2N0, T3-T4N0, or any N+ stage consists of concomitant 5-fluorouracil (5-FU) and mitomycin-C (or mitomycin-C and capecitabine) plus radiotherapy [10]. For metastatic anal cancer, cisplatin-based chemotherapy plus radiotherapy is recommended [10]. Radiation therapy is therefore recommended as the primary treatment for all patients with T2N0 or larger tumors and patients who have node positive or metastatic disease. Radiation is also recommended as subsequent treatment in patients with positive margins after resection and in late stage metastatic disease as palliative therapy.

Previous studies have elucidated disparities in diagnosis and treatment of cancers such as breast, prostate, lung, and cervical cancer based upon socioeconomic status [11–14]. One survey of 28,237 patients demonstrated that patients without insurance were more likely to be diagnosed with late stage colorectal, melanoma, breast, and prostate cancer than patients with insurance [15]. The annual burden on the U.S. healthcare system for the care of anal cancer patients in 2014 was estimated to be $13 million [16]. The most recent estimate of the average lifetime cost for a patient above the age of 66 who is diagnosed with anal cancer in the U.S. is $50,150, and the higher the stage at the time of diagnosis, the higher the cost [16]. The average monthly cost for stage IV anal cancer was three times higher than the monthly cost of care for patients with stage I-III disease [16].

Given that radiation therapy is a crucial component of anal cancer treatment and that receipt of radiation could be impacted by the patients' ability to pay for healthcare, we sought to examine the relationship between socioeconomic status and receipt of radiation therapy in patients with anal cancer. Taking previous studies on healthcare disparities in cancer treatment into account, we hypothesized that wealthier patients with anal cancer would have better access to healthcare and therefore have higher rates of radiation therapy when compared to anal cancer patients from lower income households.

2. Materials and methods

2.1. Subjects and databases

This was a cross-sectional, observational study using the Surveillance, Epidemiology, and End Results (SEER) database (1973–2011) as the source for the data regarding disease and demographics. This database is a publicly-available cancer registry maintained by the National Cancer Institute that includes approximately 26% of the United States population representing Connecticut, Iowa, rural Georgia, Alaska, New Mexico, Greater California, Utah, Hawaii, Kentucky, New Jersey and Louisiana as well as the metropolitan areas of Detroit, San Francisco-Oakland, Seattle, Metropolitan Atlanta, Los Angeles and San Jose-Monterey. Records before 1988 were excluded as the SEER registry did not collect detailed lymph node data from 1973 to 1987. We linked the SEER data to the Area Health Resources File (AHRF) based upon patients' state and county codes to ascertain poverty level and median household income.

2.2. Inclusion and exclusion criteria

We included patients who were diagnosed with anal carcinoma (ICD-9 of 154.2, 154.3, and 154.8) from 1988 to 2011. We excluded patients whose staging could not be determined, and whose tumors were not histologically classified as adenocarcinoma or squamous cell carcinoma. For each patient, data on age, stage, gender, receipt of radiation therapy, cause of death, and time to death from date of diagnosis were abstracted. Age was classified as <50 years, 50–59 years, 60–69 years, 70–79 years, and 80 years or older. Data on tumor stage was stratified into Tis-T1N0M0, T2N0M0, T3-T4N0M0, N+, and M+ based on the AJCC TNM staging system. Tis-T1N0M0 was further broken down into TisN0M0 and T1N0M0 and N+ and M+ were grouped together in some analyses. We used state-county Federal Information Processing Standards (FIPS) codes to link SEER county data to the AHRF for the purpose of analyzing socioeconomic status. We utilized median household income in 2011 as our socioeconomic metric. We divided this variable into quartiles or halves for final analysis. The wealthiest quartile had a median household income of $68,650-$110,200, the second quartile had $54,910-$68,590, the third quartile had $50,460-$54,890, and the poorest quartile had $21,860-$50,370 per year.

2.3. Statistical analysis

Receipt of radiation as it related to stage, socioeconomic status, and gender were the primary outcome measures. Logistic regression analysis was used to determine the likelihood of undergoing radiation treatment based upon age group, gender, TNM stage, and median household income. Chi-squared analysis was used to ascertain differences in radiation treatment as related to tumor stage for gender and patients' median household income. Kaplan-Meier analyses and Cox proportional hazard modeling were used to evaluate overall and cancer-specific survival by percentage of patients below the poverty level and by gender. All statistical analyses were performed using STATA® statistical software version 10.0 (College Station, TX) and all testing was 2-sided.

Table 1
Patient characteristics and receipt of radiation therapy by demographic.

Demographic	Total (%)	Radiation (%)	OR (95% CI)	p-value
Age group				
<50	8677 (31)	3250 (37)	Reference 1.0	
50–59	6924 (25)	4057 (59)	2.36 (2.22–2.52)	<0.001
60–69	5335 (19)	3421 (64)	2.98 (2.78–3.20)	<0.001
70–79	4165 (15)	2561 (61)	2.67 (2.47–2.88)	<0.001
80+	2927 (10)	1494 (51)	1.74 (1.60–1.89)	<0.001
Gender				
Male	13,575 (48)	5475 (40)	Reference 1.0	
Female	14,453 (52)	9308 (64)	2.67 (2.55–2.81)	<0.001
Median Household Income				
Wealthiest quartile	6079 (22)	2735 (45)	Reference 1.0	
2	7658 (27)	4124 (54)	1.42 (1.33–1.53)	<0.001
3	7208 (26)	3643 (51)	1.25 (1.17–1.34)	<0.001
Poorest quartile	7083 (25)	4281 (60)	1.87 (1.74–2.00)	<0.001
Total	28,028	14,783 (53)		
TNM Stage				
Tis-T1N0M0	10,837 (51)	2404 (22)	Reference 1.0	
T2N0M0	5389 (25)	4430 (82)	16.2 (14.9–17.6)	<0.001
T3-T4N0M0	2752 (13)	2282 (83)	17.0 (15.3–19.0)	<0.001
N+	1097 (5)	803 (73)	9.58 (8.32–11.0)	<0.001
M+	1342 (6)	821 (61)	5.52 (4.91–6.22)	<0.001
Total	21,417	10,740 (50)		