The Influence of Gender on Incidence and Outcome of Patients with Bladder Cancer in Harlem

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Although African Americans have a lower incidence of bladder cancer, overall survival is worse compared with American whites. This phenomenon has been attributed to the higher incidence of advanced disease at diagnosis and poor follow-up. Fifty-nine cases of bladder cancer were identified through the Tumor Registry at Harlem Hospital and reviewed retrospectively. Complete data were obtained for 42 patients. The primary independent variables of interest were primary care utilization, comorbid conditions, social variables, and gender. The outcome variables of interest were stage of disease at presentation and death. The median age at diagnosis in this group was 73 years compared with 68 for bladder cancer patients in the United States. There was no statistically significant correlation between primary care utilization or severity of comorbidities, and clinical stage at presentation. Similarly, these variables did not influence the occurrence of death as an outcome. For women, the mean age at diagnosis was 74.2 years compared with 67.3 in men (P=.112). The ratio of male-to-female cases in this group was 1.3 to 1 compared with 2.7 to 1 for the general US population. Women had lower odds of being diagnosed with superficial disease (OR=0.24, 95% CI, 0.06-0.94) and a higher incidence of a cancer-specific death (OR=2.7, 95% CI).

The poor outcome and high incidence of bladder cancer cases among women in Harlem is intriguing. Overall, primary care utilization, comorbidities, and other social factors did not seem to influence stage or death as an outcome. The significantly elevated prevalence of smoking among women in this community, increased age at diagnosis, and possible environmental influences may play a role. (*J Natl Med Assoc.* 1999;91:144-148.)

Key words: bladder cancer ◆ gender differences

Bladder cancer is an important malignancy of the genitourinary tract, second only to prostate cancer in occurrence among genitourinary malignancies. Bladder cancer ranks as the fourth most common cause of cancer deaths in men after lung, prostate, and colorectal cancer.[1] Currently, bladder cancer accounts for 4.5% of all new malignant neoplasms and 1.9% of cancer deaths in the United States. According to recent estimates, 52,000 new cases of bladder cancer were diagnosed in the United States, and almost 10,000 deaths were attributed to this malignancy.[2]

Bladder cancer typically affects Americans with a male-to-female ratio of 2.7 to 1. In addition to gender differences, there are also racial variations in incidence and outcome. The incidence among white patients is 37% greater than that of African Americans. However, only 50% of blacks have potentially curable

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localized disease at diagnosis compared with 72% for whites. There has been a 51% increase in incidence over the past 35 years. The impact of this increased incidence rate has been greatly tempered through earlier detection and improved treatment, resulting in a 33% reduction in mortality.[3]

Bladder cancer survival is influenced primarily by stage of disease at presentation, initial treatment, and degree of follow-up. Overall and stage-specific survival has improved by more than 45% during the past 35 years. However, racial differences in outcome exist. The relative overall five-year survival rates for whites versus blacks is 81% versus 58%. By stage, the survival in blacks versus whites is 88% versus 74% for localized disease, 44% versus 30% for regional disease, and 9% versus 8% for distant disease. Although racial differences in outcome exist, no gender differences in patients with bladder cancer have been reported.

This article describes the differences in stage of disease at initial presentation and outcome (ie, death) in patients diagnosed with bladder cancer in an indigent population. Based on clinical experience in Harlem, patients in this community have a higher incidence of presenting with advanced bladder cancer because of clinical and social reasons, including gender and utilization of primary care.

MATERIALS AND METHODS

Harlem Hospital is a municipal community hospital, serving the impoverished neighborhood of Central Harlem. Approximately 90% of Harlem residents are African American. More than two-thirds of Harlem residents live at or below the poverty line. Fifty-nine cases of bladder cancer initially diagnosed at Harlem Hospital over a 10-year period (January 1, 1984-December 31, 1993) were identified through the Harlem Hospital Tumor Registry. Cases were excluded for inaccurate tumor site, incomplete charts, and cases diagnosed initially at other institutions. Complete data were obtained on 42 patients. This represents approximately 26% of incident cases in central Harlem. The medical records were reviewed and abstracted onto data collection forms, condensing 21 different variables, including sociodemographic data.

The outcome variables of interest included clinical stage of disease at initial presentation and the occurrence of a death. Independent predictor variables examined included alcohol use, tobacco use, marital status, and occupation. Tobacco use was defined as heavy if consumption exceeded one pack per day. Tumor grade, histology, comorbidities, access and utilization of primary care, location of primary care (hospital clinic, community clinic, VA) also were examined. The utilization of primary care was arbitrarily defined as a medical clinic visit occurring in two consecutive years or two visits in one year for a chronic condition. Visits to the emergency department using the same criteria were included since many indigent patients use emergency services as their source of primary care.

Comorbid conditions were recorded and quantified using the Charlson Index.[4] The Charlson Index is a method used to quantify comorbidities by assigning weights between 0 and 6 for various comorbidities. These weights are based on one-year mortality rates of common conditions in hospitalized patients. The assigned weights increase with increasing disease severity. Treatment options pursued and short-term crude mortality also were recorded.

After abstraction of the charts, the data were cleaned and subsequently analyzed using the SPSS statistical software package, version 5.0. Descriptive and analytic statistics were generated. All data were stratified by tumor grade, age, and gender. Relationships between categorical variables were assessed using the chi-square test. Odds ratios (OR) with 95% confidence interval (CI) were calculated to assess relative risks.

RESULTS

The mean and median age at diagnosis in this cohort were 70.3 and 73, respectively (range: 40-92 years). The mean age for men was 67.3 while the mean age for women was 74.2 (P=.112). Approximately one-third of the patients diagnosed were >80 years. Of the 42 patients, 57.1% were men and 42.9% were women (ratio: 1.33 to 1). Of those patients, 88.1% were African American, 11.9% were Latinos, and none were white. The mean age for African Americans was 71.7 while the mean age for Latinos was 59.4. Heavy tobacco use was documented in 35.7% of the patients (ie, more than one pack per day), while 54.8% were not (9.5% had no documentation of smoking history). Sixteen of the 18 women were smokers (88.8%) 3 of whom were heavy tobacco users (18.6%). In contrast, 22 of 24 men were smokers (91.7%), 12 of whom (54.5%) were heavy tobacco users. Only 16.7% of the patients, were married.

Table 1 shows the distribution of patients according to clinical stage and gender. Only 40.5% of the

Table 1. Distribution by Clinical Stage and Gender

Stage	No. (%)	No. Males	No. Females
Superficial (Ta/T1)	17 (40.5)	13	4
Invasive (T2/T3)	13 (31.0)	5	8
Metastatic (N+M+)	12 (28.6)	6	6
Total	42 (100)	24	18

Table 2. Histology

Cell Type	No. (%)
Transitional-cell carcinoma	33 (78.6)
Squamous-cell carcinoma	3 (7.1)
Adenocarcinoma	5 (11.9)
Unknown	1 (2.4)
Total	42 (100)

patients had superficial disease at the time of initial presentation. Tables 2 and 3 show histology and tumor grade (transitional-cell carcinoma only). Interestingly, 11.9% of the patients had adenocarcinoma. Of the 37 African-American patients, four had adenocarcinoma (12.2%), while two of the five Latino patients had adenocarcinoma. The unadjusted crude mortality in this group was 43.6%. Table 4 shows mortality by cause of death and gender. Of the fatalities, 58.8% were cancer specific. Five patients with superficial disease died, two of whom died of bladder cancer.

At least 83.3% of the patients reported utilization of primary care. Of the 35 patients who utilized primary care, 7 (16.7%) used the emergency room as their sole source. There were no gender differences in primary care utilization. Twenty of 24 men compared with 15 of 18 women reported primary care utilization (83.3% in both cases). There was no significant correlation between primary care utilization and stage of disease at presentation. The incidence of diagnosis with superficial disease in primary care utilizers was 87% higher than nonutilizers. However, the 95% CI was wide (0.32-11.0) due to the small sample size and relatively large proportion of utilizers compared with nonutilizers. Similarly, there was no difference in risk of death between utilizers and nonutilizers.

The most common comorbidity was diabetes mellitus, which occurred in 21.4% of the patients. Five of the six patients with renal disease died while only two of the nine diabetic patients died. Table 5 shows the distribution of patients by Charlson Index. There was no correlation between severity of comorbidities (as Charlson Index did not predict death as an outcome). The remaining predictor variables did not significantly correlate with stage presentation or death. The incidence of diagnosis with superficial disease was significantly higher in men compared with women (OR=4.13, 95% CI, 1.05-16.3). The two outcome variables of interest, stage and death, strongly correlated with each other. The incidence of death was significantly less in patients presenting with superficial disease compared with advanced disease (OR=0.2, 95% CI, 0.05-0.76). Of the 19 deaths, the odds ratio of women dying of bladder cancer was 2.7 (95% CI, 0.33-21.8).

DISCUSSION

Bladder cancer is a malignancy of the older population (median age at presentation is 68). Racial differences in bladder cancer expression have been documented by a variety of authors. Typically, bladder cancer affects more whites than African Americans. However, African Americans are usually diagnosed with the disease at an advanced stage. Hence, mortality rates for African Americans are high in comparison to whites.

Hankey and Myers[5] used SEER data (Surveillance, Epidemiology, and End Results program) to confirm that five-year survival rates among African Americans were significantly lower compared with whites. This is related to a higher incidence of disease at initial presentation in African-American patients. Studies by Mayer and McWhorter[6] suggested that initial diagnosis of bladder cancer at more advanced stages in African Americans may be a result of advancing age, lack of access to medical care, and other factors including initial therapy and degree of follow-up.

In this study, we attempted to explain the factors (other than tumor characteristics) associated with stage at presentation and death in patients with bladder cancer in an indigent area. Since delays in seeking health care play a role in the poor outcome among African Americans, primary care utilization should enhance the likelihood of being diagnosed at an earlier stage. Although there was a suggestion that primary care utilization may enhance the odds of being diagnosed with superficial disease, this was not borne out (ie, not statistically significant). The utilization of primary care did not have a significant impact

Table 3. Tumor Grade

Grade	No. (%)
Grade 1	9 (21.4)
Grade 2	9 (21.4)
Grade 3	12 (28.6)
Unknown	6 (14.3)
N/A*	6 (14.3)
Total	42 (100)

*Grading not performed routinely on patients with squamous-cell carcinoma and adenocarcinoma.

Table 4. Cause of Death by Gender

Deaths	No. (%)	No. Males	No. Females
Bladder cancer	14 (63.7)	5	9
Unrelated	5 (22.7)	3	2
Unknown	3 (13.6)	1	2
Total	22 (100)	9	13

Table 5. Charlson Index

Score	No. (%)
0	14 (33.3)
1	19 (45.2)
2	7 (16.7)
6	2 (4.8)
Total	42 (100)

on the stage presentation of these cases since most cases (83.3%) had documented care. This proportion is typical for noncancer Harlem residents in this age group (written communication, 1996). We also believed that chronic comorbid conditions requiring continuous care (proxy for medical care utilization) would similarly enhance the likelihood of an early diagnosis. No significant correlation was found between disease stage and the presence or quantity of comorbid conditions. In terms of stage and death as outcome variables, there was no predictive value of any other independent variable (ie, occupation and alcohol and tobacco use) other than gender.

The data suggest that gender differences in bladder cancer expression in Harlem is of clinical interest since it supports our clinical suspicions. The mean age at diagnosis for men was 67.3 (not statistically different from other US men with bladder cancer), while the mean age for women was 74.1. The ratio of women to men with bladder cancer in Harlem is significantly higher. Bladder cancer typically affects US men and women in a 2.7 to 1 ratio. The male-to-female ratio at Harlem Hospital was 1.3 to 1. This ratio, however, is consistent with other African Americans with bladder cancer in the United States.[7] The poor outcome of female patients evokes great concern. The odds of being diagnosed with potentially curable superficial bladder cancer was lower in women compared with men (OR= 0.24, 95% CI, 0.06-0.94). The odds of a woman dying of a bladder cancer-related death was 2.7 times that of men. Although differences in outcome (ie, stage at diagnosis and death) may be accounted for by age, differences in tobacco use among African-American women in Harlem may account for these gender differences.

Urinary bladder cancer has long been associated with specific etiologic factors, and our knowledge of these factors has increased during this century. The most important risk factor is cigarette smoking.[8] Cigarette smokers have four times the normal incidence of bladder cancer compared with nonsmokers.[9] The prevalence of smoking among African Americans in the United States is 32.5% for men and 21.2% for women.[10] Unpublished data from Harlem reveal a significantly higher prevalence of smoking in this community compared with African Americans in the general population. In central Harlem, the prevalence of smoking is 46.9% for men and 41.6% for women (written communication, 1996).

Histologic findings in this cohort also were interesting. In larger studies, 70% to 80% of bladder cancer tumors are superficial at initial diagnosis.[8] However, in this sample, the proportion of patients with superficial disease was 40.5%. This proportion is low when compared with other African Americans.[7] Since patients with invasive or metastatic disease have a higher incidence of a cancer-related death, these patients typically require more aggressive treatment. Due to other adverse social conditions, quality of life therefore may be greatly affected compared with the general population.

The other interesting histologic finding is the proportion of patients with adenocarcinoma. Adenocarcinoma typically accounts for <1%-2% of all bladder malignancies. In this group, adenocarcinoma accounted for 11.9% in the patients. Given the indigence of this community, these findings bring to question the possible influence of synergistic environmental expo-

sures on bladder carcinogenesis. Poverty-stricken communities are often the target of environmental injustices. The synergism of tobacco exposure and environmental exposures could possibly explain variations in cell type; however, this is merely speculative.

CONCLUSION

The suggestion of a poor outcome of women in this group of patients with bladder cancer is consistent with our clinical observations. Women appeared more likely to have extensive disease and were subsequently more likely to die of a bladder cancer specific-death. No other variables could predict the stage presentation or the likelihood of death in patients with bladder cancer. The influence of gender on bladder cancer expression is currently inexplicable. There are no prior epidemiologic studies to date documenting this increased female-to-male ratio among African Americans with bladder cancer. The poor outcome among African-American women with bladder cancer also has yet to be described. The most significant explanatory risk factor in this cohort is the increased prevalence of smoking among women in this community. An investigation of the synergistic risk factors that may account for the altered male-to-female characteristics of bladder cancer might best be performed in a case-control fashion. A larger study is necessary to re-examine the risk factors in order to achieve statistical significance.

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