COMMUNICATION

The American College of Surgeons Commission on Cancer and the American Cancer Society

The National Cancer Data Base Report on Bladder Carcinoma

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BACKGROUND. Previous Commission on Cancer Data from the National Cancer Data Base (NCDB) have examined time trends in stage of disease, treatment patterns, and survival for selected cancers. The most current (1993) data relating to patients with bladder carcinoma are described here.

METHODS. Five calls for data have yielded a total of 3,700,000 cases for the years 1985 through 1993, including 447,679 cases for 1988 and 608,593 cases for 1993, from hospital cancer registries across the U.S. Data were received on 18,053 bladder carcinoma cases in 1988 and 22,606 cases in 1993.

RESULTS. Interesting trends are 1) younger patients (49 years of age and younger) present with earlier stages of disease than do older patients; 2) women are slightly more likely to be diagnosed with later stages (II, III, and IV) of bladder carcinoma than men; 3) African Americans are less likely to be diagnosed with Stage 0 or Stage I disease than either Hispanic or non-Hispanic whites; and 4) National Cancer Institute designated centers treat more patients with advanced disease than do other types of hospitals.

CONCLUSIONS. The NCDB data are important for analyzing what cancer treatments and outcomes are used and occurring in the country. The data suggest that African Americans are diagnosed at later stages of disease progression. The relative survival rates among African Americans are lower than among Hispanics or non-Hispanic whites. Also, the decreasing utility of adjuvant chemotherapy is being recognized.
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KEYWORDS bladder carcinoma, transitional cell carcinoma, treatment, surgery, radiotherapy, chemotherapy, transurethral resection, cystectomy, survival, National Cancer Data Base.

Bladder carcinoma is an important public health problem. It is the fifth most common human cancer, with current estimates suggesting that more than 52,900 new cases will be diagnosed in 1996.[1] More than 11,000 individuals die in the U.S. annually from bladder carcinoma. Bladder carcinoma is also a preventable disease. Well defined risk factors accounting for approximately 80% of all cases have been described? These factors include cigarette smoking, indus-

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trial carcinogen exposure, and chronic infection with schistosomiasis hematobium.[3] Other less well accepted risk factors for bladder carcinoma include past exposure to chemotherapeutic agents, pelvic irradiation, and human papilloma virus infection.[4–6] Changes in public health policy with regard to cigarette exposure coupled with a declining industrial work force may alter the epidemiology of bladder carcinoma. In addition, changes in health care delivery continue to unfold.

The National Cancer Data Base (NCDB), a joint project of the Commission on Cancer of the American College of Surgeons (ACOS) and the American Cancer Society, facilitates community, state, and national assessment of patient care by monitoring changes in the delivery of health care services to cancer patients and by following changing disease epidemiology. Data are currently being collected for a Patient Care Evaluation Study of bladder carcinoma. The current report details the most recent NCDB data on bladder carcinoma.

METHODS

Sources of the Data

Each year, the NCDB collects data for all forms of cancer from cancer registries throughout the country. The methods of the NCDB have been previously described.'

Five calls for data have been issued. Mailings were routinely sent to approximately 2,100 hospitals (1,340 ACoS-Approved Programs and 760 others), and all known central/state registries and software vendors/suppliers. Data were received on 18,053bladder carcinoma cases in 1988 and 22,606 cases in 1993. These data represent approximately 39% and 43% of all bladder carcinomas diagnosed in the U.S. in 1988and 1993, respectively. These cases were used for the basic patterns of care time trend analysis presented in this article. For relative survival analysis, cases reported with 5-year follow-up information for 1985,1986,1987,and 1988 were grouped together, accounting for 25,198 cases of bladder carcinoma. SPSS (for Windows, Release 6.1, SPSS, Inc., Advanced Statistics, Chicago, IL, 1994), a standard statistical software package, was used to analyze the data.

Data Definitions

Bladder carcinoma cases include those reported for ICD-0-2 C67.0 through C68.0, according to the International Classification of Diseases for Oncology.[8]

Of the reported 1993 bladder carcinoma patients, most (91%) had their carcinomas diagnosed and also received all or part of their treatment at reporting hospitals: 8% received all or part of their treatment at reporting hospitals but had their carcinomas diagnosed elsewhere; and 1% had their carcinomas diagnosed at reporting hospitals but were treated at another location.

TABLE 1
TNM Staging for Bladder Carcinoma

AJCC Stage	TNM Staging		
0	Ta-Tis	NO	MO
I	T1	NO	MO
II	T2-T3a	NO	MO
III	T3b-T4a	NO	MO
IV	T4b, any T	Any N	MO, M1

AICC American Joint Committee on Cancer; Ta: noninvasive papillary carcinoma; Ti: carcinoma in situ; T1: tumor invasion of subepithelial connective tissue; T2: tumor invasion of superficial muscle (inner half); T3a: tumor invasion of deep muscle (outer half); T3b: tumor invasion of perivesical fat, microscopically or macroscopically;T4a: tumor invasion of the prostate, uterus, or vagina; T4b tumor invasion of the pelvic or abdominal wall; NO: no regional lymph node metastasis; N1-N3: metastisis of one or more lymph nodes; MO no distant metastasis; M1: distant metastasis.

Treatment of all cases was analyzed by stage (anatomic extent of disease). Cases were staged using the American Joint Committee on Cancer (AJCC) staging system.[9] When possible, pathologic staging (pAJCC) was used, supplemented by clinical staging (cAJCC) when pathologic stage was not known. Stage groupings have been combined into summary categories to minimize the number of cases under analysis that did not have AJCC stage designation.

The TNM staging system is used by many investigators and predominates in the literature on bladder carcinoma. Table 1 summarizes the TNM staging system."

Treatment management strategies for bladder carcinoma include combinations of surgery, radiation, and chemotherapy. Surgery has been defined as any cancer-directed surgical procedure. Radiation includes beam radiation, radioactive implants, radioisotopes, or any combination thereof. Chemotherapy includes the use of single or multiple agents.

Surgical procedures have been defined in the following manner. Transurethral resection of the bladder (TUR) was identified as one procedure. The'heading of cystectomy included all procedures ranging from partial cystectomies (with or without lymph node dissection) to radical cystectomy. The category "other" combined surgery of regional sites and surgery not otherwise specified. The designation "none" was used when surgery was recorded as being noncancer directed.

Income level was inferred for each case based on the average family income of the zip code of the patient's residence.

RESULTS

Patient Characteristics

When patients diagnosed with bladder carcinoma in 1993were compared with those diagnosed in 1988, no

significant differences in age, sex, race/ethnicity, or income level were noted. Generally speaking, bladder carcinoma is a disease of older, non-Hispanic white men from a middle income level background. In **1993,** patients who were **60** years of age or older comprised **82.3%** of all reported cases. Approximately **73.5%** of reported diagnosed patients were male, **92.1%** of reported patients were non-Hispanic white, and **78.1%** of patients were from a middle income level.

The geographic distribution of cases remained the same between the two study years, with the exception of the Pacific states, in which the proportion of reported cases dropped from **20.3%** in **1988** to **14.1%** in **1993,** which was due to problems encountered in gathering data from institutions in California. In **1988, 91.7%** of patients were treated at teaching or community hospitals; by **1993,** this proportion had fallen to **84.4%.** Concomitant with the decrease in the proportion of patients treated at teaching or community hospitals was an increase from **5.8%** in **1988** to **13.5%** in **1993** in the frequency of patients with bladder carcinoma treated at nonapproved hospitals. The proportion of bladder carcinoma patients being treated at hospitals with large cancer patient case loads **(500** or more per year) remained constant between the **2** study years; in **1993, 73.2%** of reported bladder carcinoma patients were treated at these hospitals.

Disease Characteristics

The histology of bladder carcinoma remained unchanged between the study periods. Transitional cell carcinoma (TCC), which includes papillary and epidermoid carcinomas, was the most prevalent histologic type. TCC was reported in **93.4%** and **94%** of the cases in **1988** and **1993,** respectively.

The anatomic subsite of bladder tumors did not change appreciably between the two study years. The greatest proportion of tumor locations were not otherwise specified (NOS) in both years. The three most frequently reported subsites in **1993** were bladder NOS, the lateral wall, and overlapping lesions.

AJCC Stage Grouping

It is extremely important that all patients be properly staged to evaluate the effect upon therapy outcome. (Table **2)** shows the frequency distribution of all reported cases by stage at diagnosis in **1988** and **1993.** Elsewhere, because stage of disease and treatment modality are so closely associated, cases of unknown stage have been excluded from our analysis because reporting these results does not contribute to our understanding of changing patterns of treatment or outcome results.

In **1988, 36.8%** of reported bladder carcinoma patients were diagnosed with an unknown stage; this percentage dropped dramatically by **1993** when only **13.4%** of patients were reported with an unknown stage (Table **2).** Controlling for cases of unknown stage, analysis indicates a **5.8%** increase in the proportion of reported Stage 0 and Stage I cases and slightly more than a **1.6%** increase in the proportion of Stage II,III,and IV cases between **1988** and **1993,** suggesting improving documentation practice between the two study periods.

The relationship between stage and patient age indicates that the frequency of superficial disease (Stage 0) diminishes with advancing chronology. In **1993, 53.4%** of patients younger than age **40** were diagnosed with Stage 0 cancer, whereas only **32.8%** of patients **80** years of age and older presented with superficial disease. The elevated risk of invasive disease with advancing age was associated with increases in Stage II and Stage III disease. Only **8.5%** of patients younger than age **40** presented with Stage II bladder carcinomas, whereas **18.6%** of patients **80** years of age or older were diagnosed with Stage II disease. The pattern is similar for Stage III, increasing from **3.5%** among the youngest patients to **8.7%** in the oldest group of patients. The distribution of cases presenting with metastatic disease (Stage IV) did not appear to be related to age.

Although only one-third as many women as men developed bladder carcinoma, they were slightly more likely to be diagnosed with advanced stage disease (Stages II, III, and IV) than men **(33.1%** and 27.7%, respectively).

There was little difference in stage distribution between non-Hispanic whites and Hispanics with the exception of higher frequencies of Stage IV presentation among Hispanics. The most noticeable differences between ethnic groups existed between African Americans and non-Hispanic whites or Hispanics. Only **54.2%** of African Americans presented with superficial (Stage 0) or early (Stage I) disease, whereas **71.6%** of non-Hispanic whites and **70%** of Hispanics were diagnosed at these earlier stages. The likelihood of African Americans being diagnosed with invasive or metastatic bladder carcinoma was markedly higher than that of non-Hispanic whites, and slightly higher than Hispanics for metastatic disease. The small number of cases reported for the Asian American and Native American populations make comparative statements difficult.

The relationship between income level and stage at diagnosis indicated that increasing income favorably impacts on clinical stage. This is evident among patients diagnosed with either superficial or metastatic disease. Individuals from **a** low income back-

TABLE 2
Percentage of Bladder Carcinoma Cases by AJCC Stage at Diagnosis

Study year	AJCC stage 0	I	II	III	N	Unknown	capes
1988	13.3	28.6	8.3	6.7	6.2	36.8	18,171
1993	32.5	28.9	12.5	6.6	6.1	13.4	22,675

AJCC: American Joint Committee on Cancer.

ground were almost twice as likely as individuals from a high income background to be diagnosed with Stage IV bladder carcinoma (10.3% vs. 5.4%). This contrasts with the likelihood of diagnosis with superficial disease in which 39.6% of high income patients and 31.3% of low income patients presented with Stage 0 bladder carcinoma. Although the likelihood of patients in the medium income stratum presenting at any particular stage was between the low and high stratum, there was a tendency for them to be closer to those in the high stratus rather than the low.

National Cancer Institute (NCI)-designated centers tended to treat fewer early stage patients and more advanced stage patients when compared with other facilities. Of those patients treated at NCI-designated cancer centers, only 6.5% presented with Stage 0 disease whereas 21.1% were diagnosed with Stage IV bladder carcinoma. In contrast, 36.2% of reported patients, on average, were treated at other types of hospitals (teaching hospitals, community-comprehensive, community, other approved, and nonapproved) and presented with Stage 0 bladder cancer, whereas only 8.6% had been diagnosed with metastatic disease. NCI-designated centers also treated a higher proportion of patients with Stage III disease. These data suggest that resources available at NCI-designated centers are targeted toward the treatment of advanced stage disease. However, in spite of the fact that 67.2% of bladder carcinoma patients treated at NCI-designated centers had been diagnosed elsewhere, there is no evidence that proportionately more of these referred patients suffered from late or metastatic disease when compared with patients referred for treatment to other types of cancer treatment centers.

The percentages of patients who were diagnosed with Stage 0 or Stage I disease by histologic subtype are as follows: TCC, 73.3%; adenocarcinoma, 32.1%; squamous cell carcinoma (SCC), 13.8%; and others, 36.1%. These data suggest that nontransitional subtype patients are more likely to present with advanced disease than patients with TCC.

Treatment Management

Between the 2 study periods, the use of surgery without adjuvant treatment increased from 70.9% in 1988 to 79.6% in 1993. Surgery alone was the predominant treatment of choice across all age, sex, and ethnic categories. Treatment by surgery alone is sensitive to the stage of diagnosis. As stage at diagnosis increases, the reliance on surgical monotherapy decreases; 91.6% of patients with Stage 0 disease were treated with surgery alone whereas only 35.4% of patients with Stage IV disease received this type of treatment management (Table 3).

NCI-designated centers tended to use slightly less surgical monotherapy (73.5%) than other types of cancer treatment centers. This can be explained by the fact that late stage bladder carcinoma, which NCI centers tend to treat more of, is less likely to be treated by surgery alone than earlier stage disease.

Between the 2 study periods, the proportionate use of surgery with radiotherapy decreased slightly from 5.4% to 3.2%, in 1988 and 1993, respectively (Table 3). Adjuvant radiotherapy tended to be used with greater frequency in elderly patients, particularly those 80 years of age and older. Women were slightly more likely to receive a combination of surgery and radiation therapy than men. With respect to ethnic categories, African Americans were more than twice as likely to be treated with a combination of surgery and radiotherapy than were patients of non-Hispanic white or Hispanic backgrounds. Low income patients were more likely to receive adjunctive radiotherapy than either middle and high income patients. These demographic groups tended to be diagnosed with'more advanced stage disease and were thus more likely to be treated with a combination of surgery and radiation.

The treatment combination of surgery and radiation is linked to stage at diagnosis and, in contrast to treatment by surgery alone, was used with greater frequency as stage at diagnosis increased. Few patients who presented with superficial or early stage disease were treated with a combination of surgery and radiotherapy (Stage 0, 0.2%; Stage I, 1%). Patients with later stage (Stage II and III) and metastatic (Stage IV) disease were much more likely to receive adjuvant radiotherapy (9.6%, 9.9%, and 10.4%, respectively) (Table 3).

Between reporting periods, the use of surgery in

TABLE 3
Percentage of Bladder Carcinoma Cases by Treatment Management and AJCC Stage of Diagnosis[a]

	Treatment management						
Study Year	Surgery	Surgery& radiation	Surgery& chemotherapy	surgery radiation & chemotherapy	Other	None	Cases
1988	70.9	5.4	11.2	1.8	2.7	8	11,490
1993	81	3.3	6.9	2.1	1.8	4.9	19,636
AJCC stage[b]							
0	91.6	0.2	3.2	0	0.3	4.6	7366
I	88.6	1	5	0.2	0.5	4.8	6545
II	70.6	9.6	8.3	5.1	2.5	4	2844
III	58.2	9.9	15.6	7.6	4.1	4.6	1493
N	35.4	10.4	23.1	9.1	12.5	9.6	1388

AJCC: American Joint Committee on Cancer.
[a] Cases with unknown stage are excluded.
[b] 1993 data only.

combination with chemotherapy decreased from 11.2% in **1988** to **6.9%** in **1993.** Adjuvant chemotherapy tended to be used with slightly less frequency among older patients; this was particularly the case for individuals **80** years of age or older. Factors of sex, income, and ethnicity did not appear to be associated with differentialtreatment of chemotherapy in conjunction with surgical procedures. NCI-designated cancer centers tended to use adjuvant chemotherapy more frequently; **14.2%** of patients treated at these facilities received cytotoxic agents. In contrast, on average, other facilities combined surgery and chemotherapy treatment for **5.8%** of patients.

The use of surgery and chemotherapy together was also linked to the clinical stage at diagnosis. Few patients with early stage disease received chemotherapy in tandem with surgery (Stage 0, **3.2%;** Stage I, **5%).** Patients who presented with Stage II, III, or IV disease were likely to have received this treatment combination (8.3%, 15.6%, and 23.1%, respectively) (Table **3).**

The use of all three treatment modalities together was unchanged between **1988** and **1993,** and was comparably infrequent as a choice of treatment management. In **1993,** only **2%** of reported bladder carcinoma Patients were treated with a combination of all three modalities. Surgery with adjuvant radiation and chemotherapy was used with increasing likelihood as the clinical stage at diagnosis progressed. Among patients who presented with superficial or early stage disease, the use of a combination of all three treatment modalities was very infrequent. In later stages (StagesII, 111, IV), patients were more likely to receive surgery in combination with radiotherapy and chemotherapy.

Surgical Treatment

Bladder carcinoma is treated with a multidisciplinary approach, and has been discussed above. However, as the prior discussion made clear, surgery alone is the predominant treatment modality for bladder carcinoma. In **1993,** nearly **80%** of bladder carcinoma patients were treated with surgery alone. The two most frequently utilized surgical procedures performed for patients with bladder carcinoma were TUR and cystectomy. In **1993, 81.2%** of all patients treated by surgery alone underwent TUR and **12.1%** of surgical patients underwent a cystectomy.

The association of stage at diagnosis and disease histology clearly affect the choice of surgical procedure. Table **4** shows that in **1993** the frequency with which TUR was performed decreased for patients diagnosed with TCC as stage increased. Patients with TCC presenting with superficial disease and minimally invasive disease (Stages0 and I) were primarily treated by **TUR (94.4%and** 92.4%, respectively). TCC patients who presented with muscle invasive disease or metastatic disease (StagesIII and IV) were surgicallytreated with TUR only **(40.9%** and **44.7%,** respectively). The pattern of decreasing use of TUR for patients with more advanced stage disease also occurred in patients with adenocarcinoma and SCC.

In contrast, the use of cystectomy as the means of surgical treatment was rare for patients with TCC who had been diagnosed with either Stage 0 or Stage I disease. **A** cystectomy was more frequently used for patients with more advanced stages of adenocarcinoma, SCC, and TCC. Among patients diagnosed with Stage III disease, 80% of patients with adenocarcinoma, **62.2%** of patients with SCC, and **51.1%** of patients with TCC underwent a cystectomy (Table **4).**

TABLE 4
Percentage of Bladder Carcinoma Cases, Surgical Procedure by AJCC Stage and Histology[a]

Stage	Histology	TUR	Cystectomy	Other	None	Total	Cases
0	Adenocarcinoma	92.9			7.1	100	14
	SCC	75	25			100	12
	TCC	94.4	1.4	0.3	3.9	100	7163
	Other/unspecified	80.2	3.4	0.9	15.5	100	116
I	Adenocarcinoma	79.2	17		3.8	100	53
	SCC	53.1	34.4	3.1	9.4	100	32
	TCC	92.4	3.6	0.3	3.7	100	6330
	Otherlunspecified	72.7	12.7	1.8	12.7	100	55
II	Adenocarcinoma	52.9	41.2	2	3.9	100	51
	SCC	40.4	51.4	1.8	6.4	100	109
	TCC	63.8	31.4	0.6	4.3	100	2532
	Otherlunspecified	59.6	28.3	2	10.1	100	99
III	Adenocarcinoma	17.5	80	2.5		100	40
	SCC	3.2	62.1		5.8	100	103
	TCC	40.9	51.1	1.6	6	100	1225
	Otherlunspecified	38.2	49.4	3.4	9	100	89
IV	Adenocarcinoma	37	32.6	10.9	19.6	100	46
	SCC	42.7	41.5	1.2	14.6	100	a2
	TCC	44.7	35.9	4.8	14.6	100	1066
	Other/unspecified	36.3	22.1	2.7	38.9	100	113

AJCC: American Joint Committee on Cancer; TUR: transurethral resection of the bladder; SCC: squamous cell carcinoma; TCC transitional cell carcinoma.
[a] 1993 data only.

The type of surgical intervention varied among the types of cancer treatment centers. NCI-designated centers were almost half as likely to perform TUR but were more than two to three times as likely to perform cystectomies than other classifications of cancer treatment centers. NCI-designated centers also performed substantially more surgical procedures that were neither TUR nor cystectomy than any other type of cancer treatment center. Cystectomy and other non-TUR surgical procedures are typically reserved for late stage and metastatic bladder carcinoma. As reported earlier in this article, NCI-designated centers were more likely to treat patients diagnosed with late stage disease, many of whom had been referred for treatment from other medical institutions.

Survival

The relative survival rates for each stage of bladder carcinoma are presented in Figure 1. Survival rates were negatively impacted by advancing stage at diagnosis; for patients diagnosed with Stage 0, I, II, III, and IV disease, the 5-year relative survival rates were 90.2%, 86.6%, 65.1%, 47.9%, and 23.2%, respectively. Table 5 shows the 5-year relative survival rates broken down by sex, ethnicity, treatment modality, and the type of surgery performed. Regardless of the stage of diagnosis, survival rates for women were not as good as those for men. Similarly, survival rates among African Americans compared poorly with those of either non-Hispanic whites or Hispanics. Patients receiving radiation as part of a treatment modality had lower survival rates.

DISCUSSION

These data are in agreement with the well accepted epidemiology and history of bladder carcinoma. Most bladder carcinoma patients in the U.S. develop TCC. The majority of TCC patients (70–80%) present with superficial disease and are usually managed conservatively with TUR. In some cases, TCC can progress to muscle invasion or present de novo as invasive carcinomas. Once muscle invasion occurs, the 'threat to life increases. Consequently, more aggressive interventions (cystectomy, chemotherapy, and radiotherapy) are employed. Non-TCC are less common and often are associated with chronic inflammation.[3] Patients tend to present with more advanced stage and are less often managed by conservative means.

An increasing number of institutions have been participating in the NCDB data collection process in recent years and may account for some of the changes observed in this study. However, many of the demographic variables, such as sex, ethnicity, income, tumor location, and histology, remain largely unchanged over the two reporting periods. Conversely, the chang-

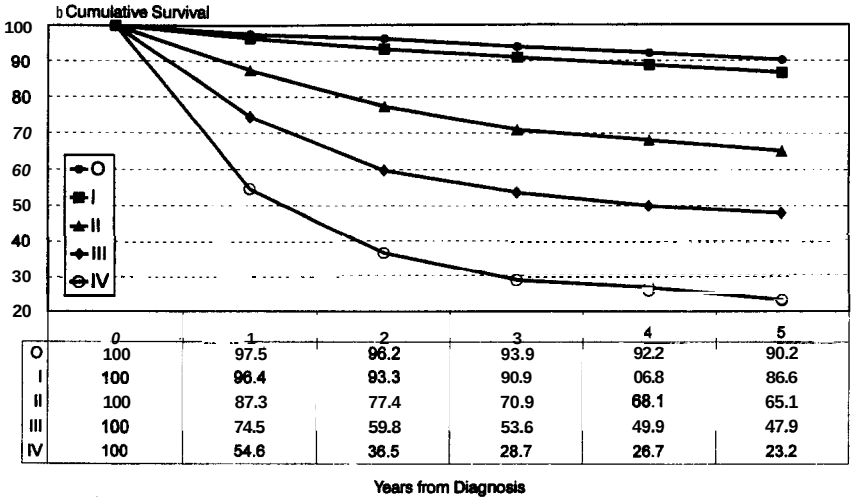

FIGURE 1. Five-year cumulative relative survival rates by *AJCC* stage at diagnosis.

TABLE
5-Year Relative Survival Rates (%), Bladder Carcinoma by AJCC Stage of Diagnosis and Selected Patient and Treatment Characteristics[a]

	AJCC stage					
	0	I	II	III	IV	Cases
Sex						
Male	94.7	87.8	68.3	48	26.8	18,525
Female	90.7	84.7	59.3	47.7	15.4	6672
Ethnicity[b]						
Non-Hispanic white	94.4	87.3	66.5	48.5	25.7	17,462
Hispanic	95.6	82.1	70.3	51.8	29.9	569
African American	81.4	79.4	48.9	42.6	18.3	964
Treatment						
surgery	94.9	89.1	71.3	54.7	34.5	17,698
Surgery & radiation	58	56.5	46.1	40.2	16.6	1791
Surgery & chemotherapy	91.3	89	70.4	54.8	24.4	2784
Surgery, radiation, chemotherapy	71.4	52.8	39.3	32.5	22	407
Other	68.7	45.3	38.8	23	9.9	742
None	92.2	78	67.5	34.7	7	1770
Surgery						
TUR	94.7	88.6	64.3	45.6	26.1	18,960
Cystectomy	80.5	79.1	72.2	54	28.1	3261
Other	94.3	90.3	70.1	47.5	22.4	852
None	87.5	67.1	50.5	29.3	9.7	1060

AJCC: American Joint Committee on Cancer; TUR: transurethral resection of the bladder.

[a] Cases diagnosed between 1985 and 1998. Survival data on treatment/surgery are presented only to provide a record of outcome experience when such treatments were used. Patients were not randomized into surgery/treatment groups, nor were they necessarily comparable with regard to all prognostic factors. Cases diagnosed between 1985 and 1988.

[b] Asian Americans and Native Americans are not included in this table because there were too few cases in each group to calculate meaningful results.

ing distribution of stage at diagnosis is likely related to improved reporting techniques in 1993.

Although the data reported here are consistent with established findings on bladder carcinoma, some Potentially important trends warrant discussion. An interesting trend is that individuals appeared to have been diagnosed with bladder carcinoma at a later age in 1993 than in 1988. This contrasts with other neoplasms, such as prostate carcinoma, in which the introduction of new diagnostic methods has shifted the

diagnosis trends to younger individuals." A hypothesized rationale for this shift may be related to diminishing smoking rates coupled with the high incidence of smoking cessation in bladder carcinoma patients prior to the time of diagnosis.[12,13] Further studies are necessary to formally test this hypothesis.

Regarding the influence of demographic features on stage, the most disturbing finding relates to the higher incidence of advanced stage disease among African Americans. Only 54.2% of African Americans presented with superficial disease compared with 71.6% of non-Hispanic whites. Several theories have been put forward to explain racial differences in disease presentation: access to care, cultural beliefs leading to symptom denial, and biologic differences.[14]

Stage procession in bladder carcinoma is generally not regarded as a definitive event. Most cases of superficial disease (AJCC Stage 0 or I) remain superficial and pose little threat to patient mortality.[15] Only 20–30% of superficial disease progresses to muscle invasion. In contrast, most cases of muscle invasive disease present de novo.[3] Therefore, it is unlikely that access to care or cultural differences entirely explain the findings presented in these data. African Americans, through differential exposure to uroepithelial carcinogens or preexisting genotypic differences in susceptibility, may possess an altered bladder carcinoma biology. Indirect evidence supports this view. Bums and Swanson have demonstrated that African Americans were more susceptible to cigarette smoke-induced bladder carcinoma than white Americans."Significant differences in the levels of glutathione transferase MU 1-1, a carcinogen metabolizing enzyme associated with bladder carcinoma, have been demonstrated to exist between ethnic groups." Data from individuals with lung carcinoma have also demonstrated ethnic differences in p53 tumor suppressor gene polymorphisms.[18] Mutations in p53 are associated with bladder carcinoma progression,[19] and it is conceivable that certain alleles are more prone to carcinogen-induced mutation.[18]

Another difference noted in these data relates to the proportion of African American patients who received no therapy (10.9%), compared with non-Hispanic white patients (5.4%). This difference may be related to differences in stage at diagnosis and access to care.

Surgical intervention is the major type of therapy used to treat patients with bladder carcinoma. As expected, TUR predominates over cystectomy (used principally for patients with TCC and early stage disease). TUR was performed proportionately less often at NCI-designated centers than other types of surgery. In contrast, cystectomy was performed primarily at NCI-designated centers for patients with invasive tumors.

Changes in the use of multimodal therapy have been noted. In particular, the use of adjuvant chemotherapy appears to be decreasing. The likely explanation for this phenomenon rests with the initial enthusiasm for methotrexate, vinblastine, doxorubicin, and cisplatin (M-VAC) combination therapy. Early reports suggested that durable complete remissions were attainable in 50% of patients who were diagnosed with metastatic disease." Recently however, diminished evidence of M-VAC efficacy along with increased evidence of treatment-related toxicity have tempered the enthusiasm for cytotoxic chemotherapy in patients with bladder carcinoma.[21,22] The toxicity of M-VAC likely explains the disproportionate use of chemotherapy in NCI-designated treatment centers as well as the less frequent use of these agents in elderly patients.

The data in Table 5 illustrate some important demographic risk factors associated with survival in patients with bladder carcinoma. Patients receiving radiotherapy generally did worse than nonradiated patients. The likely explanation for this finding relates to the use of radiotherapy in patients with poor performance status and bladder carcinomas associated with poor pathologic features (higher grade and tentacular pattern of muscle invasion).[23] In addition, women tend to fare worse, stage for stage, than men. The reasons for this finding are less clear and deserve further investigation.

The survival data in Figure 1 display the strong effect of stage at diagnosis on relative survival rates for bladder carcinoma. Patients diagnosed with Stage 0 disease have a 92.6% 5-year survival rate; Patients with Stage I disease also appear to have a low 5-year mortality rate. Although mortality may not be high, 40–60% of patients will experience at least 1 recurrent tumor? Recent data from Holmang et al., who report 20-year follow-up data, suggest that approximately 30% of patients with Stage I disease ultimately die from bladder carcinoma.[24] If these data are valid, more effort must be placed on defining biologic and life style risk factors related to disease progression.

Patients with muscle invasive disease (AJCC Stage II) have potentially curable disease with a 5-year survival rate of 64.5%. Surgery remains the most viable option for these patients. Although morbidity of surgery is diminishing with the increased use of continent urinary diversion, more effort should be made toward determining molecular risk factors for distant metastases. Detection of circulating tumor cells or other molecular alterations should be explored with the objective of eliminating unnecessary surgical intervention for patients expected to die with metastatic disease.

For patients with Stage IV disease, effective systemic therapy is required. Alternative cytotoxic agents, biologic response modifiers, or gene therapy strategies are necessary to improve prognosis.

CONCLUSIONS

This NCDB report demonstrates some important changes in the epidemiology of bladder carcinoma, most specifically a shift toward diagnosis of the disease in later age. Bladder carcinoma among African Americans may have a different disease phenotype, although differences in access to care may also explain these discrepancies. The early enthusiasm for cytotoxic chemotherapy appears to be waning, although effective systemic therapies are still needed. These findings provide fruitful avenues to guide further epidemiologic and basic research.

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