Bladder cancer in Africa

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Accurate epidemiological data about the incidence and mortality of bladder cancer are unavailable for most African countries. Transitional cell carcinoma (TCC) of the bladder is probably less common in rural African regions than in industrialized countries, due to lower levels of exposure to carcinogenic chemicals. In areas with endemic schistosomiasis (bilharzia) caused by parasitic schistosomes (blood flukes), most bladder cancer cases are comprised of squamous cell carcinoma (SCC). However, with increased urbanization, industrialization, and cigarette smoking in many African countries, there is an increasing incidence of TCC relative to SCC of the bladder.

SCC of the bladder presents in patients who are on average 10 to 20 years younger than those with TCC. In Egypt and other North African countries, SCC is more common in men (the male to female ratio ranges from 3:1 to 5:1), probably because boys and men performing agricultural work are more exposed to schistosomiasis-infested water. In some sub-Saharan countries, SCC of the bladder is equally common in men and women, probably due to equal schistosomiasis exposure of girls and boys, and because women obtain household water and perform most agricultural tasks.

Although SCC of the bladder often presents at a locally advanced stage, the tumors are usually well differentiated, with a relatively low incidence of lymphatic and hematogenous metastases. Patients with localized SCC are ideal candidates for cystectomy and orthotopic neobladder construction, because they are relatively young and healthy, and there is no risk of urethral recurrence, unlike with TCC. Unfortunately, many patients in Africa still present with advanced and inoperable bladder cancer, and many do not have access to healthcare facilities that can provide a cure and a good quality of life by means of radical cystectomy and neobladder construction.

Key Words: bladder, transitional cell, squamous cell, carcinoma, schistosomiasis, Africa

Introduction

The aim of this paper is to review the literature on bladder cancer in Africa, focusing on how bladder cancer seen in Africa differs from that seen in the rest of the world. Whereas much medical literature from Europe and North America deals with bladder cancer, relatively few reports about bladder cancer in Africa have been published. This paper attempts to include most of the available reports on the epidemiology, pathology, etiology, and treatment results of bladder cancer in Africa.

Incidence

Bladder cancer is almost never found incidentally at autopsy, making it unlikely that differences in incidence rates among different gender, race, and age groups are due to underdiagnosis in certain groups. Different incidence rates among different countries may, however, be due to underdiagnosis (patients not presenting to hospital), or to underreporting of

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diagnosed cases, or unreliable population statistics.

In the United States, in a 1995 report, almost all bladder tumors were transitional cell carcinoma (TCC; 93.6% of cases). The remaining cases were squamous cell carcinoma (SCC; 2.1%), adenocarcinoma (1.4%), or sarcoma or other histological types (3%).[1] In addition, bladder TCC incidence rates were considerably lower among black (African-American) patients compared to white (Caucasian) patients. The yearly incidence rates of bladder TCC per 100000 were 30.3 for white males, 14.2 for black males, 7.1 for white females, and 4.3 for black females. However, SCC was more common among black patients, especially females; the rates of SCC were 1.4% among white males, 3.3% among white females, 5.3% among black males, and 10.4% among black females.[1]

Incidence data for bladder cancer in Africa show large variations between countries, suggesting that the incidence rates may not be reliable, due to incomplete reporting of diagnosed cases and/or incorrect population statistics. The frequency of bladder cancer as a percentage of all malignancies, and the age-standardized incidence rates (ASR) of bladder cancer differ by as much as 10-fold between some African countries, Table 1.

In countries such as Malawi and Zambia where schistosomiasis (bilharzia) — which is caused by parasitic schistosomes (blood flukes) — is endemic, bladder cancer has been reported to be the leading type of malignant disease. In schistosome-free countries such as the United States, England, and Germany, bladder carcinoma is reported to rank from the 5th to the 7th most common cancer in men and from the 7th to the 14th most common cancer in women.[2]

In Egypt, during 1970 to 1974, bladder cancer accounted for 30.8% of the total cancer incidence. It was the most common cancer in Egyptian males and second only to breast cancer in females. In 1980, bladder cancer accounted for 27.6% of all cancers in Egypt — 38.5% of cancers in males and 11.3% in females.[3] Currently, bladder cancer accounts for 16.2% of male cancers in Egypt; it is the most common cancer in men and the 4th most common in women, and it occurs in 10.1% of the total population.[4]

Studies from Nigeria reported that bladder cancer represented 2.7% to 6.4% of all cancers, and its prevalence was estimated as 6.7 per 100000 cancer cases.[5-7]

Age

In 1995 it was reported that in the USA the median age of patients with bladder cancer was 69 years for males and 71 for females with TCC, and 71.5 years for males and 72 for females with SCC. As a proportion of all urinary bladder cancers, the prevalence of SCC steadily increased among both males and females along with advancing age, reaching 2.1% among males and 4.4% among females in the 85+ age group.[1]

In schistosome-free countries, the peak incidence of bladder cancer is in the seventh or eighth decade of life reaching a maximum between age 65 to 75 years, and only 12% of bladder cancer cases occur in people younger than 50 years old. In countries with endemic schistosomiasis, the peak age of incidence of bilharzial-related bladder cancer is between 40 and 49 years.[2]

The mean patient age at presentation in African countries with a high incidence of SCC of the bladder due to endemic schistosomiasis has been variously reported as 43 to 49.4 years in Egypt, 47 years in Sudan, 49 years in Nigeria, and 50 years in South Africa.[5-9,10-12] In other countries and population groups with a predominance of TCC of the bladder, the mean age at presentation has been reported as 57 years in Kenya and 73 years in South Africa.[10,13,14]

TABLE 1. **Frequency and age-standardized incidence rates of bladder cancer in some African countries***

Country	% of cancers that are bladder, cancer: in males	Bladder cancer ASR/100000 males	% of cancers that are bladder, cancer: in females	Bladder cancer ASR/100000 females	Male:Female ratio
Algeria	11.7	10.8	2.4	2.3	4.7:1
The Gambia	1.4	1.2	0.6	0.5	2.4:1
Mali	10.1	11.3	4.2	5.8	2:1
Uganda	0.8	2.9	0.4	1.2	2.4:1
Zimbabwe	2.5	8.3	2.7	8.3	1:1

*based on data from the International Agency for Research on Cancer (IARC)
ASR = age-standardized incidence rates

Male to female ratio

In the United States, in 1995, the male to female ratio for bladder cancer was reported to be 2.8:1 for bladder TCC and 1.2:1 for bladder SCC.[1] A 1999 report found that the male to female ratio of bladder cancer in countries with endemic schistosomiasis varied from 4:1 to almost 6:1, compared to 3:1 in countries without endemic schistosomiasis. One possible explanation is that in rural areas with endemic schistosomiasis, the main route for infection is through contact with infected water during agricultural activities that are normally performed by men.[2]

Different male to female prevalence of SCC and TCC of bladder are found in Northern African countries (such as Egypt and Sudan) compared to sub-Saharan countries such as Nigeria, Kenya, Zimbabwe, and South Africa.

In African countries with endemic schistosomiasis and a predominance of SCC of the bladder, the reported male to female ratio of bladder cancer has varied from 3:1 to 5.6:1 (Egypt), 2.5:1 to 5:1 (Nigeria) to as high as 12:1 (Sudan).[5-9,11] In Kenya, with a predominance of TCC of the bladder, the male to female ratio of bladder cancer was 4:1.[13,14] In Zimbabwe the male to female ratio for SCC of the bladder was 1:1 and in South Africa the ratio for TCC of the bladder was 2:1, whereas for SCC of the bladder it was 1:1.[10,15]

The fact that the male to female ratio for SCC of the bladder in Southern African countries such as Zimbabwe and South Africa is 1:1 versus a ratio of 3:1 and higher for Northern African countries such as Egypt is possibly due to sociocultural differences, equal exposure to schistosomiasis infestation at a young age by boys and girls in Northern Africa, and the fact that women in rural sub-Saharan areas usually obtain household drinking water and perform agricultural tasks.[10]

Histological type, grade and stage

A study from Egypt in the mid1990s reported SCC in 53% of bladder cancer patients, TCC in 23% of these patients, and adenocarcinoma in 13% of these patients; 90% of the patients had schistosomiasis.[16] A more recent study of bladder cancer patients from Egypt reported TCC in 59% of patients, SCC in 28% of patients, and adenocarcinoma and sarcomatoid carcinoma in 13% of patients.[12]

In a study of 1095 Egyptian patients with bladder cancer treated by radical cystectomy during 1967 to 1978, schistosome eggs were present in 82.4% of the bladders. SCC was more frequent in egg-positive cases and TCC was more frequent in egg-negative cases. Grade 1 carcinomas predominated in the egg-positive group and grade 3 predominated in the egg-negative group. The tumors were locally advanced in most patients, with a limited tendency to lymphatic and hematogenous spread.[8]

In another large series of 1026 patients with invasive bladder cancer treated during 1969 to 1990 in Mansoura, Egypt, SCC was present in 59%, TCC in 22% and adenocarcinoma in 11% of cases. Bilharzial eggs were seen in 85% of the specimens. SCC was mostly well differentiated, and most TCC was moderately differentiated: SCC was grade 1 in 50%, grade 2 in 33%, and grade 3 in 17% of cases; whereas TCC was grade 1 in 14%, grade 2 in 53%, and grade 3 in 33% of cases. The most common pathological stage was pT3. A total of 80% of SCC, 58% of TCC, 73% of adenocarcinoma, and 85% of mixed/unclassified tumors were pT3. The correlation between clinical and pathological staging was good in 67% of cases; understaging occurred in 20% of cases and overstaging occurred in 13% of cases. Regional lymph nodes were involved in 18% of pT3a and 42% of pT3b tumors.[11]

A study from Sudan reported that SCC constituted 27% of all bladder tumors; 31% of the patients had a previous history of urinary bilharziasis; 60% of patients had locally advanced (T3 N0 M0) tumors at presentation; and the 5-year survival rate after radical cystectomy was 75%.[9] Another report from Sudan found carcinoma of the bladder in 10% of patients presenting with hematuria, and of these, 50% had SCC of the bladder in association with urinary bilharziasis.[17]

Studies from Nigeria have reported that SCC constituted 39% to 53% of bladder cancers, with TCC in 26%, mixed tumors in 16%, and adenocarcinoma in 5% of cases.[5-7] In Nigerian patients presenting with hematuria, the cause was bladder carcinoma in 31% of cases.[18]

A changing trend was observed in Nigeria during 1979 to 1989. Whereas earlier reports indicated a preponderance of SCC, there has been a rise in the frequency of TCC relative to SCC. However, among patients aged 50 years and younger, SCC was more frequent (45.5% of bladder cancer cases) than TCC (18% of cases). Increasing urbanization and industrialization may be factors leading to the increasing incidence of TCC of the bladder.[19]

A study from Tanzania reported that SCC represented 72% of bladder cancers and of these, 46% had *schistosoma haematobium* (*S. haematobium)* infestation.[20]

A study from Kenya during 1977 to 1984 reported TCC in over half (53%) of bladder tumors (which constituted only 0.75% of all reported cancers), while anaplastic cancer occurred in 17% of cases, and SCC occurred in the minority of cases (13%), mostly from schistosoma-endemic areas.[13] A more recent study from Kenya also reported TCC in the majority (67%) of bladder tumors, with advanced disease in 60% of cases.[14]

In one report from Zambia in the 1970s, SCC was the most common form of bladder cancer; patients almost always presented at a late stage.[21] In another study from Zambia from the same period, bladder cancer was the third most common malignancy. The bladder tumors were well-differentiated; SCC accounted for 75% of cases, and 65% of cases had concomitant schistosomiasis.[22] In a later study from Zambia, it was reported that bladder cancer, predominantly SCC, was the commonest urological tumor (51%), and in nearly 32% of cases, bilharzial ova were demonstrated histopathologically.[23]

A study from Zimbabwe during 1963 to 1977 found that 71% of bladder cancer cases were SCC.[24] Another study from Zimbabwe during 1984 to 1987 reported that SCC comprised 69% of bladder cancers and 31% were TCC.[15]

One study reported that in Mozambique, which has a high prevalence of bilharziasis, the incidence of SCC of the bladder is the highest in the world, with a yearly frequency of 24 cases per 100000 of the male, and 19 cases per 100000 of the female population. Bladder cancer was the second most common malignancy in men (after primary liver cancer) and the third most common malignancy in women (after liver and cervix cancer).[25]

Researchers from South Africa reported that in a histology study of bladder tumors from Natal (a region with endemic schistosomiasis) during 1971 to 1982, TCC was found in 62% of cases, SCC in 56% of cases, and adenocarcinoma or undifferentiated cancer in 10% of cases. Among black patients with bladder tumors, 61% had SCC, and among Asians (Indians), 29% had SCC. The prevalence of schistosomiasis was higher in blacks (44%) than in Indians (23%), and schistosomal infection was most commonly associated with SCC (61%).[26]

In a 1980 to 1990 study from the same region, the distribution of histological types of bladder cancer differed between races. Among white patients TCC constituted 95%, SCC 2%, and undifferentiated/mixed histology cancers 3% of cases; in black Africans TCC occurred in 30%, SCC in 53%, and undifferentiated/mixed tumors in 17% of cases; whereas among Asians (Indians), TCC occurred in 75%, SCC in 18% and undifferentiated/mixed histology in 7% of cases. In Caucasians, TCC was early stage (T1 or T2) in 76% of cases; whereas in Africans, SCC was advanced disease in 90% of cases, and 27% of cases were regarded as inoperable due to local fixation or distant metastases.[10]

A 1975 study from South Africa reported that the Western Cape region (which is non-endemic for bilharzia) had a low percentage of SCC bladder cancer compared with other parts of Africa. TCC constituted 79%, SCC 6%, TCC with squamous metaplasia 5%, undifferentiated cancer 6%, and adenocarcinoma 2% of bladder cancer cases.[27] In a more recent study from the same area reporting on 112 cystectomy cases, 83% were TCC, 9% SCC, 5% adenocarcinoma, and 3% sarcoma. The low frequency of SCC is similar to that seen in the United States and Europe, and underlines the importance of bilharziasis in the etiology of SCC.[28]

Etiology

In a recent study, researchers estimated that 75% of men in Egypt with bladder cancer were smokers, in contrast to studies from Western countries reporting that about 50% of men with bladder cancer are smokers. Urinary schistosomiasis was estimated to account for 16% of bladder cancer cases in Egypt; thus, for men, tobacco smoking was a far greater risk factor than schistosomiasis.[29,30] This was not the case for Egyptian women, who had low rates of smoking. The study authors estimated that combined exposure to tobacco smoking and a high-risk occupation or schistosomiasis led to an approximately 10-fold higher risk of bladder cancer.[29]

A study from Zimbabwe during 1963 to 1977 found that schistosomiasis was associated with a significantly increased risk of bladder cancer in both genders. The proportion of bladder cancer attributable to schistosomiasis was estimated to be 28%. Tobacco smoking in men had no effect on the risk of SCC. For TCC or adenocarcinomas, there was a nonsignificant increased risk of 2.0 for men in the highest smoking categories.[24]

Schistosomiasis may lead to malignancy through local tissue damage, mechanical irritation, bilharzial toxins, or secondary bacterial infection. Exposure to carcinogenic N-nitroso compounds is probably the most important mechanism. Inflammatory cells such as macrophages and neutrophils are important sources of endogenous oxygen radicals, which are implicated in the formation of carcinogenic N-nitrosamines. Hydroxyl radicals released from inflammatory cells induce genotoxic effects, such as mutations, sister chromatid

exchanges, and DNA strand breaks. Inflammatory cells participate in the activation of procarcinogens, such as aromatic amines and polycyclic aromatic hydrocarbons, to their ultimate carcinogenic metabolites.[2]

Nitrate-reducing bacteria in the urine of *S. haematobium*-infected patients can mediate nitrosation reactions between secondary amines and nitrate, producing high concentrations of N-nitrosamines that act like carcinogenic alkylating agents. Host cell DNA damage due to alkylating agents, together with inefficiency in the capacity of relevant enzymes to repair this damaged DNA, may lead to SCC.[2,31] Schistosomiasis may cause liver involvement and dysfunction, which disturbs tryptophan metabolism, leading to the excretion of carcinogenic metabolites. In addition, vitamin A deficiency may be responsible for squamous metaplasia in the bladder, predisposing to SCC.[3] N-nitroso compounds and N-nitrosodimethylamine in the urine of *S. haematobium*-infected patients might have a role not only in the initiation of the carcinogenic process, but also in its progression.[32]

More than 90% of bilharzia-related bladder carcinoma (BBC) cases at presentation are advanced-stage tumors. The frequency of p53 nuclear overexpression in BBC is lower than that reported for conventional TCC. Nevertheless, tumors with p53 alterations have a greater propensity to progress. The prominent number of cases displaying an mdm2-positive phenotype suggests that this may be an early incident in BBC and should be regarded as a potential oncogenic phenomenon. The association of an aggressive clinical course with the coexpression of both p53 and mdm2 products might be viewed as a cooperative effect that develops in tumor progression.[33]

A 9p gene, possibly CDKN2, may contribute to the development of the majority of schistosomiasis-associated bladder tumors, but genes on 9q play a much less important role.[34] The frequency of human papillomavirus (HPV) was reported to vary from 23% to 46% in bladder cancers in Egypt, but HPV was not detected in bladder cancers from South Africa, indicating that it does not play a role in schistosoma-associated bladder carcinoma there.[35]

The fact that in Egypt over the past three decades the incidence of bladder cancer has decreased from 30.8% to 10.1% of total cancers may be due to a decreased prevalence of schistosomiasis as a result of eradication of the snails that host the parasites, decreased contamination of water sources through improved sanitation, decreased population exposure to infested water, or better treatment of acquired bilharzia. The relative increase of TCC versus SCC of the bladder in Egypt may be partly due to schistosomiasis control, but appears to be largely due to increased cigarette smoking and industrialization. The apparent decrease of bladder cancer as a percentage of all other cancers in Egypt is more difficult to explain, but may be due to increasing rates of lung cancer (due to smoking) and prostate cancer (diagnosed with prostate specific antigen).

Early detection

A study conducted to detect early bladder carcinoma by selective cytologic screening in a rural Egyptian population infested with *S. haematobium* targeted a high-risk group, i.e., farmers aged 20 years and older. Bladder carcinoma was detected in 11 patients among the 4769 individuals screened in the high-risk group, which translated into 2.3 cases per 1000 high-risk individuals. No tumors were detected in the 3975 individuals in the low-risk group. The primary tumors included 5 SCC, 4 TCC and 1 undifferentiated carcinoma; 7 of the tumors were in early stages. The authors concluded that selective cytologic screening in the high-risk group in Egypt is feasible and effective for the early detection of bladder carcinoma associated with schistosomiasis.[36]

The use of urine cytology in the diagnosis of SCC was studied in a schistosomiasis-endemic area of Kenya. The prevalence of inflammation (39%), hyperkeratosis (30%), metaplasia (33%), and frank atypia (0.4%) was higher than in previously studied, non-endemic populations. Overall, *S. haematobium* infection was strongly associated with increased risk for cytologic abnormality. The data suggested an age-dependent progression of cellular abnormalities in the urinary epithelium that is associated with chronic *S. haematobium* infection, which becomes independent of concurrent infection intensity as subjects grow older.[37]

A study from Egypt reported that the BTA stat and BTA TRAK tests were extremely sensitive (99% and 94%, respectively) in both SCC and TCC, but specificity was only 15% in patients with bilharziasis, i.e., false positive results for cancer were observed in 85% of patients with active bilharziasis.[38] A significant elevation of urinary cytokeratin 19 (CYFRA21-1) was found in 82.3% of bladder cancer patients and 11.4% of patients with bilharzia.[39,40] The authors concluded that urinary CYFRA 21-1 and BTA stat are valuable non-invasive urinary markers for the detection of bladder cancer, with a high sensitivity compared to urine cytology.[41]

Prevention

Educational and marketing campaigns about effective and convenient treatments for schistosomiasis, aimed to increase awareness in the general public and the medical community have contributed dramatically to the primary prevention of bladder cancer in Egypt.[42] Primary prevention could be possible if the schistosomiasis parasite is eliminated. Chemoprevention using retinoids or cyclooxygenase 2 (COX-2) inhibitors is a possible alternative.[43]

Treatment of superficial TCC

A study from South Africa was one of the first to report on the use of intravesical Bacillus Calmette-Guerin (BCG) immunotherapy in patients with recurrent superficial TCC of the bladder. Among 13 patients who received BCG prophylactically to reduce recurrence, 70% were in remission after 2 years, and of the 14 patients who received BCG therapeutically for in situ carcinoma, 69% responded favorably. Most patients (78%) experienced irritable bladder symptoms, but only one patient discontinued treatment. A statistically significant reduction in the number of recurrences was experienced by the patients who received BCG prophylactically.[44]

Intravesical therapy for superficial TCC of the bladder was studied by a group in Egypt who prospectively randomized 156 patients with superficial (Ta and T1) TCC to treatment with 150 mg BCG weekly alternating with 50 mg epirubicin for 6 weeks, and maintenance with monthly doses of BCG alternating with epirubicin for 1 year (Group 1). Group 2 patients were treated with the same protocol, but in a reversed order, with epirubicin being used initially. At a mean follow-up of 42.8 months, the cancer recurrence rate was 18% and the progression rate was 12%. Side effects occurred in 26% of the patients and were most often mild cystitis. The two groups were comparable in terms of cancer recurrence and progression rates. The side effects were less frequent than in historical controls treated with BCG alone. The authors concluded that it does not make any difference whether treatment is started with epirubicin or BCG.[45]

In a more recent study by the same authors, 84 patients in Egypt with T1 TCC were prospectively randomized, following an initial 6-week course of sequential BCG and epirubicin. Group 1 received 3-week courses of 120 mg BCG at 3, 6, 12, 18 and 24 months, while Group 2 received monthly BCG at the same dose for 1 year. At a mean follow-up of 31months, the recurrence rates of the two groups (24% and 18%, respectively) and the progression rates (6% and 4%, respectively) were comparable. Toxic side effects were more frequent in Group 1 than in Group 2 (50% versus 20%, respectively). The authors concluded that monthly BCG maintenance is as effective and is less toxic than multiple 3-week courses in recurrence prophylaxis of T1 bladder TCC.[46]

In another study from Egypt, 66 patients with superficial TCC were treated at Cairo University with either Nd:YAG laser therapy (16 patients) or transurethral resection (TUR) of the bladder (50 patients) and followed for a mean of 5.5 years. Local tumor recurrence at the site of the original tumor occurred in 39% of patients and remote recurrence occurred in 33% of patients. The total recurrence rate was 59%. Tumor progression to invasive cancer occurred in 11% of patients, while 4.5% of patients died of disease-related causes. The authors concluded that superficial TCC is a serious condition that merits close, long-term follow-up.[47]

Treatment of invasive bladder cancer

In a large series of 1,026 patients with invasive bladder cancer treated during 1969 to 1990 in Mansoura, Egypt, SCC was present in 59%, TCC in 22%, and adenocarcinoma in 11% of the patients. At a median follow-up of 4 years after cystectomy, postoperative mortality was 4%. The 5-year overall survival rate was 48%-50% for patients with SCC, 47% for those with TCC, 46% for those with adenocarcinoma, and 36% for those with mixed/unclassified tumors. Only tumor stage and grade and lymph node status had a significant impact on survival.[11]

A study from Sudan reported that SCC constituted 27% of all bladder tumors. A total of 60% of patients had locally advanced (T3 N0 M0) tumors at presentation, and the 5-year survival rate after radical cystectomy was 75%.[9]

Researchers from South Africa reported on 100 consecutive patients with infiltrating TCC who underwent cystectomy during 1978 to 1989. Radiotherapy was given preoperatively in 39% of cases and postoperatively in 15% of cases, and systemic chemotherapy was used postoperatively in 12% of cases. The tumors were pathological grade 1 in 5%, grade 2 in 21% and grade 3 in 53% of cases, and the pathological stage was T0 in 10%, T1 in 17%, T2 in 12%, T3 in 43%, and T4 in 15% of cases. At a mean follow-up of 40.8 months, the overall 5-year survival was approximately 70%.[48]

Another study from South Africa reported on 112 patients who underwent radical cystectomy and Bricker diversion for bladder cancer during 1978 to

1989 in a university teaching hospital. The overall perioperative mortality was 11%, but perioperative mortality was 3% for surgeon A who performed 30 surgeries and assisted in 2, 8% for surgeon B who performed 26 surgeries and assisted in 4, and 26% in a group of 12 surgeons (E-P) who performed 29 surgeries and assisted in 46. The mean operation times were 206 minutes for surgeon A, 265 minutes for surgeon B and 285 minutes for surgeons E-P. Perioperative mortality and major early complications were greater in patients older than 71 years old versus those younger than 60 years old. Perioperative mortality was also lower in patients with T0-1 tumors than in those with T2-4 tumors. The authors concluded that perioperative mortality was higher in the following patient groups: those operated on by surgeons with limited experience, those older than 71 years old, those who had not received preoperative radiotherapy, and those with locally advanced tumors.[28]

A further study from South Africa reported on 63 patients (73% male) who underwent radical cystectomy during 1988 to 1994. The patients' mean age was 61 years (range, 33-77years). A total of 14% of the patients had clinical stage T1 disease and 24% had pathological stage T1 disease; the corresponding numbers for prevalence of clinical and pathological stage T2 disease were 24% and 6%, respectively; for stage T3 disease 46% and 45%, respectively; and for stage T4 disease 16% and 25%, respectively. Node metastases occurred in 0% of pT1-2 tumors, 29% of pT3 tumors, and 38% of pT4 tumors. The operative mortality was 2%, and the overall survival rate was 33% at a median follow-up of 42 months. The estimated 5-year survival rates were 91% for pT1, 75% for pT2, 31% for pT3, and 29% for pT4 disease. The authors concluded that cystectomy is the standard against which other treatments for bladder cancer must be measured.[49]

Investigators from Nigeria recently reported on 58 patients with bladder carcinoma treated from 2000 to 2005. Cystectomy was performed in 30 patients (25 male and 5 female) who had a mean age of 50 years; 28 patients with metastases were excluded from analysis. Surgery consisted of construction of an orthotopic ileal neobladder in 15 cases (50%), a continent cutaneous reservoir in 11 cases (37%) and non-continent drainage in 4 cases (13%). A 40% survival was achieved with follow-up ranging from 6 to 60 months.[50]

A recent study from Cairo reported on 27 patients selected for laparoscopic cystectomy. The procedure was aborted in seven patients and was completed laparoscopically in 20 patients (16 male, 4 female). The mean operative time was 8 hours and the mean blood loss was 680 ml. Postoperative complications occurred in five patients (25%), and four patients (20%) died in the postoperative period.[51]

Radiotherapy

A study from South Africa reported on 46 patients who underwent salvage cystectomy during 1981 to 1992 for persistent or recurrent carcinoma after radical irradiation for bladder carcinoma. The overall 5-year survival rate was 43%. There were three deaths (a mortality rate of 7%) and 12 nonfatal major complications due to prior irradiation or surgery — an overall rate of fatal and nonfatal 5-year complication of 33%. The authors concluded that salvage cystectomy is indicated for selected patients with persistent or recurrent disease after radical irradiation for bladder cancer, but that the expectation of a survival rate similar to that found in patients treated with immediate cystectomy may not be justified.[52]

In a prospective study of neoadjuvant radiotherapy in Egypt from 1996 to 2000, 104 patients with infiltrating bladder cancer were treated with a total preoperative dose of 45 Gy given over 3 weeks (1.5 Gy/fraction, 2 fractions/day, 5 days/week). Three weeks later, this was followed by radical cystectomy with pelvic node dissection. Only 56 of the 104 patients completed the treatment program. At a median follow-up of 26 months, disease-free survival was 64%, with 50% of failures due to pelvic cancer recurrence. The authors found no increased operative difficulty or increased postoperative morbidity related to irradiation.[53]

Bladder conservation

A bladder conserving approach has been used in some African centers. A study from South Africa reported on the use of neoadjuvant chemotherapy (cisplatin, methotrexate, and vinblastine) and radical irradiation in 18 patients with T3 or T4 bladder cancer. After chemotherapy, a complete response was obtained in four patients (22%) and a partial response in eight patients (44%). After irradiation, a complete response was obtained in 12 patients (67%). The 3-year continuously disease-free survival rate (with preserved bladders) was 44%, and the overall 3-year survival rate was 61%. The authors concluded that the local control rate was unsatisfactory.[54]

In a study from Egypt, 27 patients (24 males, 3 females; mean age 58 years) with invasive nonmetastatic bladder cancer for whom radical

surgery was not suitable were treated with three cycles of chemotherapy (carboplatin, methotrexate, and vinblastine) and radiotherapy (65 Gy) in two phases. The authors concluded that DNA ploidy status seems to be a useful prognostic factor when bladder sparing therapy is applied.[55]

Mortality

The management of bladder cancer is mainly surgery, and 5-year survival rates after radical cystectomy have increased from 35% in the 1970s to around 50% in the 1990s. The addition of adjuvant and neoadjuvant radiotherapy and chemotherapy to surgery since 1976 significantly improved both disease-free and overall survival rates.[43]

In 1995 it was reported that in the USA males had higher 5-year bladder cancer survival rates than females, while African-American women had the lowest survival rates. The survival rates were 84% in white males, 71% in black males, 76% in white females, and 51% in black females. One reason for the lower survival rates among black patients may be presentation with more advanced stages of disease. TCC at first diagnosis was localized in 76% of white males, 74% of white females, 66% of black males, and 56% of black females. Factors that may lead to a more advanced stage at diagnosis in black Americans, particularly women, include possible underreporting of superficial cancers, delayed diagnosis, and/or more frequent occurrence of more aggressive variants of TCC in African-Americans. A contributing factor to the lower survival rates may be differences in therapy. In a study that looked at treatment from 1978 to 1985, black American males were more likely than whites to go untreated after diagnosis, suggesting that differences in initial therapy may have contributed to the survival differential.[1]

From 1979 to 1985, bladder cancer mortality among North African migrants of both sexes[56] and among migrant males from West Africa[57] living in France was higher than the rate among the native population. Among people of European origin living in Southern Africa for over 30 years, bladder cancer rates were higher than normally seen in white populations elsewhere.[58] These findings indicate that environmental factors may be more important than ethnicity in determining bladder cancer mortality.

Summary

Bladder cancer in parts of Africa with endemic schistosomiasis (bilharzia) is different from that seen in North America and Europe. There is a predominance of SCC rather than TCC of the bladder. The patients with SCC are on average 10 to 20 years younger than those with TCC of the bladder. The male to female ratio for bladder cancer is high in areas where more men than women are exposed to schistosomiasis or are smokers, and the ratio is equal where bilharzia exposure is equal between men and women. In many parts of Africa, the population is unaware that bilharzia is transmitted via snail-infested water sources, and they regard hematuria almost as a normal rite of passage into adulthood. Consequently, SCC of the bladder usually presents at a locally advanced stage and is often inoperable.[59] However, SCC of the bladder is usually well differentiated, with a low incidence of lymph node and distant metastases, possibly due to capillary and lymphatic fibrosis resulting from chronic schistosomal infection. There is a changing pattern in Africa from SCC to TCC of the bladder, probably due to decreased schistosomiasis infestation and increased cigarette smoking and industrialization. □

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