

Bladder Cancer in Young Patients: Management and Outcomes

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Abstract

Background and Objective: Bladder cancer frequently occurs between the ages of 50 years and 70 years and rarely occurs before the age of 40 years. It accounts for 1% - 4% of all cases of cancer. This study focuses on the clinical, etiological, histological, therapeutic, and evolutive profiles of patients with bladder cancer aged less than 45 years. **Materials and Methods:** This retrospective study was carried out over seven years (from January 2014 to December 2020) on 15 patients below 45 years of age who were being treated for bladder cancer. The diagnosis was made in all patients via cystoscopy and abdominal computerized tomography, while the nature, grade, and degree of infiltration were determined via endoscopic resection and pathology. **Results:** The mean age of the 15 patients in this study was 34.4 ± 5.19 years. In 86.6% of cases, the patients had macroscopic hematuria as the main presenting complaint. Twelve patients (80%) had bladder tumors that did not infiltrate the muscle. These patients were followed up clinically. In 86.6% of cases, there was a single tumor with a mean diameter of 2.53 cm. In four patients (26.6%), mitomycin was started early. The overall rates of tumor recurrence and progression were 26.6% and 20%, respectively. **Conclusion:** Bladder cancer also occurs in young people, with similar clinical and epidemiological profiles as exists in elderly patients. The prognosis of bladder cancer in young people depends on the treatment method chosen by the physician.

Keywords

Bladder Tumor, Young Patient, Histology, Evolution

1. Introduction

The bladder is a hollow pelvic organ that stores urine received from the kidneys through the urethra until micturition. This organ is lined by specialized transitional epithelial cells and smooth muscle that can relax to accommodate greater volumes of urine, as well as contract (under voluntary or reflex control) to expel urine down the urethra and out of the body. The bladder, like many other organs in the body, can be the site of malignant disease.

Bladder cancer is the 10th most common cancer in the world and its incidence is steadily rising worldwide, especially in developed nations [1]. An estimated 430,000 cases of this pathology were diagnosed in 2012 [2]. Bladder cancer is four times more common among men than among women and is the fourth most common malignancy in men. It is the sixth most incident and ninth most deadly neoplasm in men [3]. In Europe and the United States, bladder cancer accounts for approximately 5% - 10% of all malignancies in men [4]. Bladder cancer is mainly a disease of the elderly, with 90% of diagnoses made in those over 55, and 80% of diagnoses in those over 65 in the US [1]. It rarely occurs in people below the age of 40 years, with this age group accounting for just 1% - 4% of the cases [5].

The most common clinical presentation of this pathology is asymptomatic hematuria; however, patients could also have irritative voiding symptoms [6]. In patients with asymptomatic macroscopic hematuria and, in some cases, accompanying irritative voiding symptoms, clinicians should search for risk factors for bladder cancer, which include smoking (tobacco) and occupational exposure to carcinogenic chemicals [7]. Smoking has been reported to be the biggest risk factor for bladder cancer [8]. In patients with the characteristic clinical presentation and major risk factors, investigations such as cystoscopy, kidney function tests, and upper urinary tract imaging should be performed [6]. Computed tomography (CT) images of bladder tumors are presented in **Figure 1**.

Due to the paucity of available data on bladder cancer in young people, we decided to carry out this study that aimed to investigate the clinical, etiological, histological, therapeutic, and evolutive profiles of patients with bladder cancer aged less than 45 years.

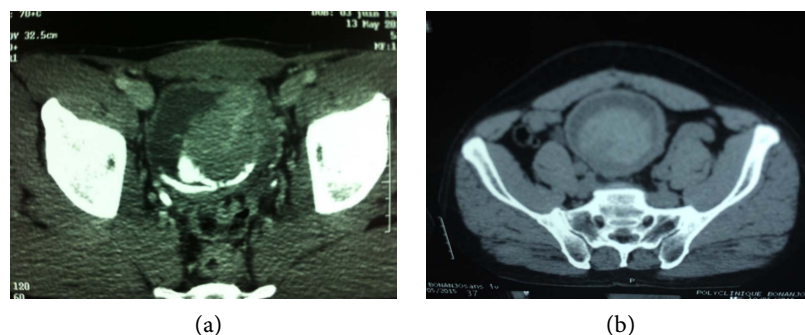


Figure 1. CT images of bladder tumors. (a) Muscle-invasive bladder tumor; (b) Nonmuscle-invasive bladder tumor.

2. Materials and Methods

This is a retrospective study that was carried out over six years, from January 2014 to December 2020, on 15 patients below 45 years of age who were being treated for bladder cancer. The diagnosis was made in all patients via cystoscopy and abdominal computerized tomography, while the nature, grade, and degree of infiltration were determined via endoscopic resection and pathology. Urinalysis was also performed for all the participants of this study.

We included all patients aged less than 45 years who were treated for bladder cancer within the study period at the *Centre medico-chirurgicale d'urologie* in Douala and had all the required information in their files. The data collected from the patients' files include age, sex, tobacco consumption (measured in pack-years), hemoglobin level, transfusion, the location of the tumors, the number of tumors in each patient, the macroscopic nature of the tumors, the histological nature of the tumors, the diameters of the tumors, and the presence or absence of signs and symptoms such as painful micturition, macroscopic hematuria, blood clots, irritative symptoms, and acute nephritic colic. Data on the presence of infection, the germ identified, the treatment administered, and the presence or absence of tumor recurrence were collected as well. We also collected data on the early use of mitomycin, an intravesical therapy that is given to reduce the rate of tumor recurrence for intermediate tumors and the rate of progression for high-risk tumors. In some of our patients, mitomycin was started early in the postoperative period, within two hours of the end of the surgical intervention. This drug was given at the highest possible dose (40 mg) in the first 24 hours after the operation. As required, the pH of the patients' urine was rendered alkaline before using this drug. While using this drug, we bore in mind its contraindications, including macroscopic hematuria and bladder perforation. Patients with tumors that did not infiltrate the muscle wall of the bladder underwent endoscopic resection of the tumor after which they were monitored via endoscopy every three months, while those with tumors that infiltrated the muscle wall of the bladder underwent surgical resection of the bladder, prostate gland (for men), and surrounding lymph nodes. We defined anemia as a hemoglobin level of less than 12 g/dL in women and less than 13 g/dL in men [9]. Biopsy and histology were performed for all patients initially, and one more time for those who experienced tumor recurrence. These histological assessments enabled us to identify the grades of the tumors. Tumors of grade pTaG1, pTaG2, pTaG3, pT1G1, pT1G2, and pT1G3 + CIS did not infiltrate the muscle wall of the bladder; as such, we referred to these tumors as non-muscle-invasive tumors in this study. On the other hand, those of grade pT2G1 and pT2G2 + CIS infiltrated the muscle wall of the bladder; so, we referred to them as muscle-invasive tumors in this study.

These data were entered into Microsoft excel 2007 and exported to Epi Info 7 for analysis. Continuous data were presented using the mean value and standard deviation for variables with normally distributed data and the median and in-

terquartile range for variables with skewed data distributions. Categorical data were presented as frequencies and percentages. This study was approved by the institutional review board of the Faculty of Medicine and Pharmaceutical Sciences of the University of Douala and the ethics committee of the *Centre medico-chirurgical d'urologie*, Douala, Cameroon. The requirement for informed consent was waived due to the retrospective study design.

3. Results

We recruited a total of 15 patients aged 27 - 43 years, with a mean age of 34.4 ± 5.19 years. Of these 15 patients, there were 5 (33.33%) females and 10 (66.67%) males. Three (20%) of the participants were active smokers with an average tobacco consumption of 11.33 pack-years. One patient was a passive smoker.

Thirteen (86.67%) patients had macroscopic hematuria and 6 (40%) patients had blood clots in their urine. Three (20%) patients had painful micturition, 4 (26.67%) had irritative symptoms, 1 (6.67%) had acute nephritic colic, and 2 (13.33%) had recurrent urinary tract infections, and the culprit pathogen in both cases was *E. coli*. The hemoglobin levels of the participants ranged from 7 g/dL to 15 g/dL, with a mean value of 11.88 ± 2.14 g/dL. Eight (53.33%) of our study participants were anemic. One (20%) woman and 7 (70%) men were anemic. However, the prevalence of anemia did not differ significantly between men and women ($P = 0.10$). Five (41.67%) out of 12 patients with tumors that did not infiltrate the muscle wall of the bladder were anemic, whereas all three patients with invasive tumors were anemic. However, the difference in the prevalence of anemia between the two groups was not statistically significant. Two patients (13.33%) required blood transfusion, with one patient needing two pints of blood and the other needing three.

Of the 15 patients in this study, thirteen had just one tumor while two had multiple tumors. The diameters of the tumors ranged from 1 cm to 4 cm, with a mean value of 2.53 ± 1.06 cm. The tumors were located at the left lateral surface of the bladder in two cases, at the trigone in two cases, at the left lateral surface in three cases, at the trigone in two cases, at the neck of the bladder in three cases, and at the left meatus, anterior surface, fundus, dome/left lateral surface (multiple tumors), trigone/right lateral surface (multiple tumors) in one case each. The tumors were pediculated in 13 cases and sessile in 2 cases. The clinical features of the study participants can be seen in **Table 1**.

Histological analyses were performed on the tumors after endoscopic resection of the tumors. All the participants of this study had urothelial carcinoma. According to histological analyses, the tumors were of the following histological grades: four tumors of grade pTaG2, three tumors of grade pT1G1, two tumors of grade pT2G1, two tumors of grade pTaG1, and one tumor of grades pT2G3 + CIS, pT1G2 + CIS, pTaG1, pT1G2, and pT1G2. In total, there were 12 patients with non-muscle-invasive tumors and three patients with muscle-invasive tumors. The three patients with invasive tumors were aged 32 years, 35 years, and

Table 1. Clinical features of the study participants.

Variable	Frequency (%)
Age (years)	
≤30	5 (33.33)
>30	10 (66.67)
Sex	
Female	5 (33.33)
Male	10 (66.67)
Smoking	
Yes	3 (20)
No	12 (80)
Clinical presentation	
Macroscopic hematuria	13 (86.67)
Painful micturition	3 (20)
Irritative symptoms	4 (26.67)
Acute nephritic colic	1 (6.67)
Recurrent UTIs	2 (13.33)
Anemia	
Yes	8 (53.33)
No	7 (46.67)

*UTI: urinary tract infection.

39 years, with a mean age of 35.33 ± 3.51 years. The mean age of patients with tumors that infiltrated the muscle wall of the bladder was 34.17 ± 5.64 years. There was no significant difference in the mean ages of patients with and without invasive tumors ($P = 0.74$). The invasive tumors had a mean diameter of 3.33 ± 0.58 cm while the non-invasive tumors had a mean diameter of 2.33 ± 1.07 . The difference between the mean diameters of the two types of tumors ($P = 0.15$). Tumor recurrence occurred in four cases, with a recurrence rate of 26.67%. Two of the tumors that recurred were of grade pT1G1, one was of grade pT1G2, and the other was of pT1G2 + CIS. In patients with tumors that recurred, the time-lapse from diagnosis to recurrence ranged from 6.27 months to 16.70 months, with an average time-lapse of 10.43 months. Two of the three initial grade pT1G1 tumors recurred, with one remaining at the same grade and the other progressing to grade pT1G2. One tumor that was initially at grade pT1G2 progressed to grade pTaG3 after relapsing. Lastly, the tumor that was initially at grade pT1G2 + CIS progressed to grade pT2G3 + CIS after relapsing. Hence, tumor progression occurred in three of the fifteen patients, which gives a tumor progression rate of 20%. It is worth noting that there was no case of a mus-

cle-invasive tumor among the four cases that recurred. Concerning the treatment of these patients, all patients were either monitored after endoscopic resection of the tumor or underwent cystectomy; three patients underwent radical cystectomy while eleven patients were monitored after endoscopic resection of the tumor. Early single instillation of intravesical chemotherapy with mitomycin (SIIC) was performed immediately after bladder resection in four participants. Of the four patients who experienced tumor recurrence, three of them received early SIIC while one underwent cystectomy. Radical cystectomy and construction of a Bricker bladder was performed in one patient with a grade pT1G3 + CIS tumor. This surgical technique was chosen despite the fact that the tumor did not infiltrate the bladder muscle because it had a diameter of up to 4 cm, it had recurred, it was an *in-situ* carcinoma (which is a risk factor for tumor progression), and the tumor had gone from grade 2 to grade 3. It is worth noting that none of the patients who underwent surgical treatment experienced tumor recurrence. The characteristics of the tumors are presented in **Table 2**.

The recurrence-free survival rates at one year, five years, and ten years were 80%, 73.33%, and 73.33%, respectively. Since no patient died in our study, the overall survival rate was 100%. The Kaplan-meier curve for the recurrence-free survival of our study participants is presented in **Figure 2**.

4. Discussion

This retrospective study aimed to explore the clinical, etiological, histological, therapeutic, and evolutive profiles of patients with bladder cancer aged less than 45 years. The mean age of our participants was 34.4 ± 5.19 years. This is higher than the 24 ± 2.86 years reported by Katafigiotis *et al.* in Greece [10] but lower than the 70.5 ± 11.4 years reported by Miñana *et al.* in Spain [11]. These discrepancies could be explained by the fact that Katafigiotis *et al.* carried out their study on patients below the age of 30 years and recruited only five participants, while Miñana *et al.* carried out a population-based study and included a total of 4285 cases of bladder cancer, which means their study sample was more representative of the actual population. Five (33.33%) of our study participants were

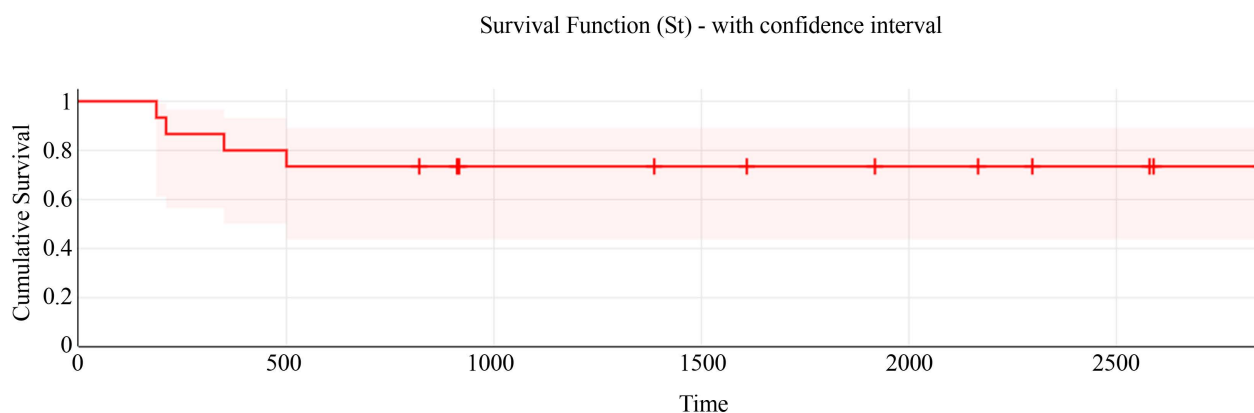


Figure 2. Recurrence-free survival of our study participants.

Table 2. Tumor characteristics.

Variable	Frequency (%)
Number of tumors	
Single tumor	13 (86.67)
Multiple tumors	2 (13.33)
Type of tumor	
Pedunculated	13 (86.67)
Sessile	2 (13.33)
Tumor grade	
pTaG2	4 (26.67)
pT1G1	3 (20)
pT2G1	2 (13.33)
pT2G3 + CIS	1 (6.67)
pT1G2 + CIS	1 (6.67)
pTaG1	1 (6.67)
pT1G2	1 (6.67)
pT1G2	1 (6.67)
Tumor diameter (cm)	
1	3 (20)
2	4 (26.67)
3	5 (33.33)
4	3 (20)
Tumor recurrence	
Yes	4 (26.67)
No	11 (73.33)
Management of tumors	
Monitoring	12 (80)
Radical cystectomy	3 (20)
SIIC	
Yes	4 (26.67)
No	11 (73.33)

*SIIC: single instillation of intravesical chemotherapy with mitomycin.

females while 10 (66.67%) were males. This is in line with many studies in the literature that report male predominance [2] [4] [11] [12]. However, this finding differs from those of Goonewardena *et al.* [13]. This is mainly because Goone-

wardena *et al.* focused primarily on women in their study.

Thirteen (86.67%) of our patients had macroscopic hematuria, which is in line with most other studies that report hematuria as the most common symptom of bladder cancer [1] [6] [11]. Four (26.67%) of our patients had irritative symptoms, 1 (6.67%) had acute nephritic colic, and 2 (13.33%) had recurrent urinary tract infections. This was in line with the findings of Kristine Burns Farling who reported that the clinical presentation of bladder cancer mimics those of urinary tract infections [14]. This could be because the tumors cause urine outflow obstruction, leading to stasis and ultimately to urinary tract infections. Eight (53.33%) of our study participants were anemic. This is in line with the findings of Bi *et al.* who reported a 52% prevalence of anemia in 2020 [15]. This can be explained by the fact that bladder cancer, like other types of cancer, has anemia as one of its main complications. In our study, 12 (80%) participants had non-invasive tumors. This is in line with the findings of Wang and McKenny, who reported that most tumors of the urinary bladder are non-invasive [16]. It is also similar to the 86.96% of non-muscle-invasive bladder cancer reported by Wang *et al.* [17] All the patients in our study had urothelial carcinoma. This 100% rate is similar to the 98.14% rate reported by Wang *et al.* in 2019 [17]. Four (26.67%) of the fifteen patients in our study experienced tumor recurrence after the initial endoscopic resection. Of these four patients, there was no patient with muscle-invasive tumor. This is contrary to the findings of Malcovicz *et al.* in 2007, who reported that up to 50% of cases of muscle-invasive tumor recur [18]. This discrepancy can be explained by the fact that all patients with muscle-invasive tumors in our study underwent radical cystectomy. As such, there was almost no possibility for the tumor to recur after radical surgical resection. The diameters of the tumors ranged from 1 cm to 4 cm, with a mean value of 2.53 ± 1.06 cm. The average diameter of the four tumors that recurred was 3 cm. This result is in line with the results of Zachos *et al.*, who reported that tumor size > 3 cm is associated with recurrence [19]. Tumor recurrence occurred in four cases, with a recurrence rate of 26.67%, which is different from the 39.1% recurrence rate reported by Chamie *et al.* in 2013. They also reported a progression rate of 33%, which is higher than the 20% we found in our study [20]. These differences can be explained by the fact that Chamie *et al.* carried out a community-based study in which they recruited 7410 participants, as opposed to ours which was a hospital-based retrospective study with just 15 participants. The rate of recurrence among patients with non-muscle-invasive tumors was 33.33%, which is similar to the 25% - 50% reported by Volpe *et al.* in 2010 [21]. All the patients included in our study survived. This differs from what was reported by Rezaianzadeh *et al.* in 2012, who reported that the overall survival rate at the end of 1, 3, 5, 10 years in patients with bladder cancer was 89.89%, 71.32%, 57.52%, and 24.59%, respectively [22]. Our 100% survival also deviates from the 82% and 71% one-year survival, 67% and 56% five-year survival, and 60% and 54% ten-year survival rates in men and women, respectively, reported by Shah *et al.* in 2008 [23]. This is because Razaianzadeh *et al.* carried out a prospective study

on 514 patients with bladder cancer from 2001 to 2009, while Shah *et al.* carried out a study that entailed collecting data from cancer registries in England and Wales.

The main limitation of our study was its small sample size, which is mainly due to the fact that patients in our setting are still skeptical about laparoscopic procedures. Hence, they tend to opt for open surgical procedures instead. We recommend that similar prospective studies with bigger study samples be carried out in the future to further investigate our findings.

5. Conclusion

Although bladder cancer is predominantly a disease of elderly patients, it can occur in young people too. This pathology affects predominantly males, has smoking as its main risk factor, and macroscopic hematuria as its principal symptom. In young people, non-muscle-infiltrating bladder tumors are more common than muscle-infiltrating ones. The prognosis of bladder cancer in young people depends on the tumor stage, with the more aggressive tumors having a worse prognosis.

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Conflicts of Interest

The authors have no conflicting interests to declare.

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