

Bladder cancer in young adults: Disease and treatment characteristics of patients treated at a tertiary cancer center

Mahmoud Albakri, Ramiz Abu-Hijlih¹, Samer Salah², Akram Al-Ibraheem³, Fawzi Abuhijla¹, Hashem Abu Serhan⁴, Ala'a Farkouh, Zeinab Obeid, Mohammed Shahait⁵

Departments of Surgery, ¹Radiation Oncology, ²Medical Oncology and ³Nuclear Medicine, King Hussein Cancer Center, ⁴King Hussein Cancer Center, Amman, Jordan, ⁵Clemenceau Medical Center, Al Jaddaf, Dubai, United Arab Emirates

Abstract

Objectives: The incidence of bladder cancer in the Middle East is increasing. Nevertheless, data on the young population with urothelial carcinoma (UC) of the urinary bladder in this region is scarce. Therefore, we evaluated clinical and tumor characteristics, in addition to treatment details in patients younger than 45 years old.

Methodology: We reviewed all patients presenting with UC of the urinary bladder from July 2006 to December 2019. Clinical characteristics including demographics, stage at presentation, and treatment outcomes were extracted.

Results: Out of 1272 new cases of bladder cancer, a total of 112 (8.8%) patients were ≤ 45 years old. Seven patients (6%) had nonurothelial histology and were excluded from the study. The remaining 105 eligible patients with UC had a median age at presentation of 41 years (35–43). Ninety-three patients (88.6%) were males. Tumor stage at presentation: nonmuscle invasive disease (Ta-T1), locally advanced muscle-invasive bladder cancer (MIBC) (T2-3), and metastatic disease were 84.7%, 2.8%, and 12.5%, respectively. All patients with MIBC received neoadjuvant cisplatin-based chemotherapy. Radical cystectomy was performed in 8 (7.6%) cases; three patients with MIBC and five with high-volume non-MIBC. Neobladder reconstruction was done in six patients. A total of 13 patients with metastatic disease (93%) received palliative chemotherapy (gemcitabine/cisplatin), and one (7%) was a candidate for best supportive care only.

Conclusion: Bladder cancer is relatively rare in the young population, although the incidence at our region is higher than other reports in the literature. Most patients present with early disease. Early diagnosis and multidisciplinary approach are paramount for the management of these patients.

Keywords: Transitional cell carcinoma, urinary bladder neoplasms, urothelial carcinoma, young population

Address for correspondence: Dr. Mohammed Shahait, Clemenceau Medical Center, Al Jaddaf, Dubai, United Arab Emirates.

E-mail: mshahait@yahoo.com

Received: 06.06.2022, **Accepted:** 02.01.2023, **Published:** 17.03.2023.

INTRODUCTION

Urothelial carcinoma (UC) is the 10th most common cancer worldwide and the 6th leading cause of cancer in men.^[1] The 2020 Global Cancer Statistics of the

World Health Organization estimates an incidence of 45,000 new cases of UC per year with a total burden of over 1,720,000 cases.^[2]

This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

For reprints contact: WKHLRPMedknow_reprints@wolterskluwer.com

How to cite this article: Albakri M, Abu-Hijlih R, Salah S, Al-Ibraheem A, Abuhijla F, Serhan HA, *et al.* Bladder cancer in young adults: Disease and treatment characteristics of patients treated at a tertiary cancer center. *Urol Ann* 2023;15:207-10.


Access this article online	
Quick Response Code:	Website: www.urologyannals.com
	DOI: 10.4103/ua.ua_87_22

Table 1: A review of the literature encompassing all the articles that discuss bladder cancer in young patients

Author	Number of patients	Median follow-up (months)	Superficial bladder cancer (%)	Invasive bladder cancer	Recurrence rate (%)	Progression (%)
Gunlusoy <i>et al.</i> ^[4]	91	224	91.2	8.8	18.6	10.9
Yossepowitch and Dalbagni ^[5]	74	28.1	83.4	16.6	38.7	16
Erözenci <i>et al.</i> ^[6]	156	87	89.1	10.9	48.7	22.8
Huguet Pérez <i>et al.</i> ^[7]	30	66	67.6	23.3	32	0.1
Nomikos <i>et al.</i> ^[8]	31	38.52	90	10	32	
Sataa <i>et al.</i> ^[9]	158	41.7	85.4	14.5	18.4	3
Aboutaieb <i>et al.</i> ^[10]	26		42.4	57.6	19.2	
Blanchard <i>et al.</i> ^[11]	26		84.6	15.4	55	9
Na <i>et al.</i> ^[12]	≤40-42		88.1	11.9	7.1	2.4
	≥60-44		88.6	11.4	38.6	2.3

UC is frequently encountered in the elderly population with diagnosis occurring in patients over the age of 65 years.^[1] A minority of patients present at a young age with an age-standardized rate of 0.2/100,000 person-years.^[3] Several factors have been identified to increase the risk of developing UC including age, smoking, and exposure to carcinogenic chemicals. Nevertheless, advanced age remains the most recognized factor associated with the presence of UC.^[3]

A scarce number of studies in the literature have reported the clinical outcomes of UC in a young population; aged <40 years.^[4-12] Generally, younger patients tend to have well-differentiated slow-growing tumors.^[13] Moreover, patient-tailored treatment regimens vary among different age groups. Elderly patients with high frailty are at an increased propensity for treatment-related complications, which may render them ineligible for various therapeutic measures including surgical excision and certain chemotherapy regimens. Oncological outcomes and survival in the young remain inadequately reported and with conflicting data. As per a meta-analysis conducted by Shariat *et al.*, several studies emphasize slow progression, whereas others report similar outcomes to that of elder patients.^[14] Therefore, a standardized management plan in young patients has not been defined.

Finally, the incidence of bladder cancer in the Middle East is increasing. Data on the young population with UC of urinary bladder in the region are limited.^[15] Therefore, we evaluated clinical and tumor characteristics, in addition to management details in patients younger than 45 years old who were treated at a tertiary cancer center in the Middle East.

METHODOLOGY

Patients' characteristics

Data of newly diagnosed patients with bladder cancer presenting to our center from July 2009 to December 2019, were reviewed. We retrospectively abstracted data

of potentially eligible patients from the electronic medical records following the acquisition of an institutional review board approval. Data of interest included age, date of diagnosis, primary histology, stage at diagnosis, receipt of systematic treatment as neoadjuvant treatment or adjuvant treatment, radical cystectomy, and type of urine diversion.

All included patients had a histological diagnosis of bladder cancer reviewed at our institution by a dedicated genitourinary (GU) pathologist. Patients' management plans were based entirely on decisions from the GU multidisciplinary team consisting of urologists, radiation oncologists, pathologists, radiologists, and medical oncologists.

Statistical analysis

Descriptive statistics were utilized when appropriate to report means, median, standard deviations, and proportions. Overall survival was calculated from the date of diagnosis of metastatic disease until the last follow-up or death. All statistical analyses were performed using SPSS version 19 (SPSS Inc., Chicago, IL, USA).

RESULTS

Out of 1272 new cases of bladder cancer treated between 2009 and 2019, a total of 112 (8.8%) patients were ≤45 years old. Seven patients (6%) with nonurothelial histology were excluded from the study. The remaining 105 eligible patients with UC had a median age at presentation of 41 years (35–43). Of our cohort, 93 (88.6%) patients were males.

The majority of the patients (95; 84.7%) had nonmuscle-invasive disease (Ta-T1), 3 (2.8%) patients had locally advanced muscle-invasive bladder cancer (MIBC), and 14 (12.5%) had metastatic disease. Nine patients with non-MIBC received an immediate single intravesical instillation of mitomycin within 24 h of the first transurethral resection of bladder tumor. Out of 38 patients with non-MIBC who would have been candidates for

induction bacille Calmette-Guérin (BCG) therapy, only 25 (66%) received BCG. All patients receiving BCG had induction cycles of six instillations. Only 15 (60%) patients completed 3 years of maintenance.

Radical cystectomy was performed in 8 (7.6%) patients; three patients with MIBC and five with high-volume non-MIBC. Neobladder reconstruction was done in six patients. All patients with MIBC planned for radical cystectomy received neoadjuvant cisplatin-based chemotherapy.

A total of 13 patients with metastatic disease (93%) received palliative chemotherapy (gemcitabine/cisplatin, dose-dense methotrexate, vinblastine, adriamycin, and cisplatin), and one (7%) was a candidate of best supportive care only. During the follow-up of the cohort, seven patients required palliative radiation to control local recurrence ($n = 4$), bone pain ($n = 2$), or symptomatic brain metastasis.

DISCUSSION

In this study, we found that 8.8% of bladder cancer patients referred to our center were younger than 45 years. Our cohort majority consisted almost entirely of males and yielded a higher prevalence of non-MIBC. Only two-thirds of the patients who would have been candidates for BCG therapy received initial induction treatment, and 39% of those completed the 3 years of treatment. Neobladder reconstruction was the most commonly preferred urinary diversion among patients who underwent radical cystectomy.

Bladder cancer is characterized by male predominance. The European Society of Medical Oncology defines an age-standardized incidence rate of 17.7 for males and 3.5 for females.^[12] In line with our findings, where men comprised 88% of our cohort, studies on bladder cancer in young patients found that the majority of the cohort consisted of men. However, in a cohort with a lower mean age of 23 years, females made up a larger portion, comprising 36% in comparison with 64% of males, as reported by Stanton *et al.*^[16] Generally, the higher incidence of disease in men may be attributed to several factors such as high smoking rates among young men, occupational exposure to chemicals and fumes, and NAT1 gene polymorphism.^[12]

Several reports have shown that young patients with bladder cancer are more likely to be diagnosed with low-grade tumors at early nonmuscle-invasive stages.^[17] This is consistent with our findings, as 88.7% of our

patients presented with locally nonmuscle-invasive disease; corresponding to Ta and T1 tumor staging. Nomikos *et al.* noted that 90% of young patients (<40 years) had NMIBC, whereas 10% had muscle-invasive cancer.^[8] Gunlusoy *et al.* published similar findings in 2015, on a larger cohort of 91 patients aged 17–40 years, and found NMIBC in 91.2% of cases. In their study, the majority of patients presented with Grade 1, whereas only 5% and 13% had evidence of Grades 2 and 3 diseases, respectively. This is in contrast with elderly patients who routinely present with more advanced histology and stage. Gunlusoy *et al.* also noted that a higher percentage of patients with a mean diagnostic age of 70 years are likely to have MIBC (39.2%) [Table 1].^[4]

Of note, the clinical behavior of MIBC and high-grade disease in younger patients is similar to that of elderly patients. Yossepowitch and Dalbagni depicted that younger patients who ultimately underwent radical cystectomy had significantly lower disease-free survival, attributed larger to a higher rate of distant metastases than in the older group (41% vs. 24%). Nevertheless, the rate of local recurrence was similar.^[5]

All the patients with MIBC who were referred to radical cystectomy in our cohort received neoadjuvant chemotherapy, and none received adjuvant treatment. Contrary to our practice, Wen *et al.* have reported high utilization showed high utilization of adjuvant chemotherapy after radical cystectomy and underutilization of neoadjuvant chemotherapy in this subgroup of patients.^[18]

Future directions

Several methods may be utilized to aid in the early detection and prevention of bladder cancer, principally, the adoption of novel screening programs for high-risk patients.^[19] Moreover, there is an exigent need to validate the quality of life indicators and patient-reported outcomes for bladder cancer among the young. Furthermore, germline testing of patients with a positive family history of UC or risk factors may prove beneficial for the prediction of the nature of the disease. Whereby, germline testing allows for the identification of individualized treatment and risk factor prevention. Genome sequencing depicts molecular alterations which may prove responsible for the diversity in clinical staging at presentation compared to older patients. Potential therapeutic targets specific for the young age group may also be available following genomic sequencing. In addition, novel treatments such as immunotherapy can be considered, which may be a more appropriate approach for younger patients. As per Kohjimoto *et al.*, immunotherapy relies heavily on the

activation of cell-mediated immunity and thus proves less effective in older age groups who commonly show decreased immune status.^[20]

Limitations

Our study is a retrospective study and yields data from a single institution. Therefore, we cannot extrapolate our findings to reflect the actual burden of the disease in the region. Furthermore, there are several factors that were not captured in the database, such as the availability of intravesical treatment, patient-reported outcomes, smoking status, and occupational exposure. The median follow of the cohort is short due to the pattern of the referral to the institution; therefore, we opted not to report survival outcomes. Finally, the technique of cystectomy, urine diversion, and lymph node dissection template was based on surgeons' experience and preference.

CONCLUSION

Bladder cancer is relatively rare in the young population, although the incidence at our region is higher than other reports in the literature. Most patients present with early disease. Early diagnosis and multidisciplinary approach are paramount for the management of these patients.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W, *et al.*, editors. SEER Cancer Statistics Review, 1975-2008. Bethesda, MD: National Cancer Institute; 2011. Based on November 2010 SEER Data Submission, Posted to the SEER Web Site; 2011. Available from: https://seer.cancer.gov/csr/1975_2008/. [Last accessed on 2022 Feb 01].
- Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al.* Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021;71:209-49.
- Palumbo C, Pecoraro A, Rosiello G, Luzzago S, Deuker M, Stolzenbach F, *et al.* Bladder cancer incidence rates and trends in young adults aged 20-39 years. *Urol Oncol* 2020;38:934.e11-9.
- Gunlusoy B, Ceylan Y, Degirmenci T, Kozacioglu Z, Yonguc T, Bozkurt H, *et al.* Urothelial bladder cancer in young adults: Diagnosis, treatment and clinical behaviour. *Can Urol Assoc J* 2015;9:E727-30.
- Yossepowitch O, Dalbagni G. Transitional cell carcinoma of the bladder in young adults: Presentation, natural history and outcome. *J Urol* 2002;168:61-6.
- Erözenci A, Ataus S, Pekyalçin A, Kural A, Talat Z, Solok V. Transitional cell carcinoma of the bladder in patients under 40 years of age. *Int Urol Nephrol* 1994;26:179-82.
- Huguet Pérez J, Errando Smet C, Regalado Pareja R, Martínez de Hurtado J, Batista Miranda E, Chéchile Toniolo G, *et al.* Transitional cell carcinoma of the bladder: Behavior in young adults. *Arch Esp Urol* 1996;49:607-12.
- Nomikos M, Pappas A, Kopaka ME, Tzoulakis S, Volonakis I, Stavrakakis G, *et al.* Urothelial carcinoma of the urinary bladder in young adults: Presentation, clinical behavior and outcome. *Adv Urol* 2011;2011:480738.
- Sataa S, Dahmani Z, Cherif K, Chelly I, Kchir N, Horchani A. Transitional cell carcinoma of the bladder in young adults: Presentation, natural history, and outcome of 158 cases. *UroToday Int J* 2012;5:art 07. <http://dx.doi.org/10.3834/uij.1944-5784.2012.04.07>.
- Aboutaieb R, Dakir M, Sarrf I, el Moussaoui A, Bennani S, el Mrini M, *et al.* Bladder tumors in young patients. *Prog Urol* 1998;8:43-6.
- Blanchard JM, Graziana JP, Bonnal JL, Biserte J, Mauroy B. Bladder tumor in young patients: A series of 26 cases. Comparison with a review of the literature. *Prog Urol* 2003;13:227-33.
- Na SW, Yu SH, Kim KH, Hwang EC, Jung SI, Kwon DD, *et al.* The prognosis of patients less than 40 years with bladder cancer. *J Cancer Res Ther* 2014;10:710-4.
- de la Calle CM, Washington SL 3rd, Lonergan PE, Meng MV, Porten SP. Bladder cancer in patients younger than 40 years: Outcomes from the National Cancer Database. *World J Urol* 2021;39:1911-6.
- Shariat SF, Sfakianos JP, Droller MJ, Karakiewicz PI, Meryn S, Bochner BH. The effect of age and gender on bladder cancer: A critical review of the literature. *BJU Int* 2010;105:300-8.
- Hajjar RR, Atli T, Al-Mandhari Z, Oudrhiri M, Balducci L, Silbermann M. Prevalence of aging population in the Middle East and its implications on cancer incidence and care. *Ann Oncol* 2013;24 Suppl 7:vii11-24.
- Stanton ML, Xiao L, Czerniak BA, Guo CC. Urothelial tumors of the urinary bladder in young patients: A clinicopathologic study of 59 cases. *Arch Pathol Lab Med* 2013;137:1337-41.
- Bellmunt J, Orsola A, Leow JJ, Wiegel T, De Santis M, Horwich A, *et al.* Bladder cancer: ESMO practice guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2014;25 Suppl 3:iii40-8.
- Wen YC, Kuo JY, Chen KK, Lin AT, Chang YH, Hsu YS, *et al.* Urothelial carcinoma of the urinary bladder in young adults – Clinical experience at Taipei Veterans General Hospital. *J Chin Med Assoc* 2005;68:272-5.
- Shahait M, Bulbul M. Bladder cancer screening in Lebanese population: There is nothing more unequal than the equal treatment of unequal people. *Bladder Cancer* 2016;2:467-8.
- Kohjimoto Y, Iba A, Shintani Y, Inagaki T, Uekado Y, Hara I. Impact of patient age on outcome following bladder-preserving treatment for non-muscle-invasive bladder cancer. *World J Urol* 2010;28:425-30.