American International Journal of Multidisciplinary Scientific Research; Vol. 6, No. 1; 2020
ISSN 2638-1249 E-ISSN 2638-1273
Published by Centre for Research on Islamic Banking & Finance and Business, USA

Epidemiological and Morphological Characteristics of Urothelial Bladder Cancer in a Bulgarian and a French Sample of Patients

Milena Gulinac
Medical Faculty
Department of General and Clinical Pathology
Medical University-Plovdiv, Bulgaria
E-mail: mgulinac@hotmail.com

Dorian Dikov
Grand Hospital de l'Este Francilien, Jossigny, France
Medical Faculty, Department of General and Clinical Pathology
Medical University-Plovdiv, Bulgaria

Ts. Velikova
Medical Faculty
Department of Clinical Immunology
University Hospital Lozenetz-Sofia, Bulgaria

Abstract
Bladder carcinoma (BC) is one of the most common malignancies of the urinary system in developed countries, and it is also characterized by a high number of recurrences and progression rates despite multimodal treatment. BC is a biological and clinically heterogeneous tumor with a great propensity of divergent differentiation. Around the world, bladder cancer is responsible for 549.000 new cases и 200.000 deaths each year. In Bulgaria, bladder carcinoma is the 18th most common neoplasia. Our results on 105 proven bladder carcinoma cases confirmed that this tumor arises at 70 years at average (60-90 years), it affects men predominantly and there was no difference regarding the nationality of patients. In conclusion, it remains a diagnostic challenge.

Keywords: Bladder Cancer, Urothelial Carcinoma, Urinary Tract.

I. Introduction
Urothelial bladder cancer is a common disease that takes the 9th rank in worldwide cancer incidence (Ploeg et al., 2009). The incidence of bladder cancer is three times greater in males than in females (Hartge et al., 1990). These differences in gender prevalence explained largely by differences in exposure to certain risk factors. In the developed country, the major risk factor is smoking (Aydin et al., 2017; Battista Di Pierro et al., 2012; Gilbert et al., 2004). In Western countries, smoking is responsible for around 50% of urothelial bladder cancer in males and 35% in females (Ploeg et al., 2009). On the other hand, in countries where the infection caused by Schistosoma haematobium is endemic, like Egypt, primary squamous cell carcinoma of the bladder is the dominant histological type. The third most important risk factor for bladder cancer development is occupational exposure, as chronic exposure to arsenic.

Carcinoma of the bladder is a 7th most common malignant disease in men and 17th in women. The majority of bladder cancer is composed of urothelial carcinoma (90%), where the remaining less common types include primary bladder's adenocarcinoma, squamous cell carcinoma, and neuroendocrine carcinomas (small cell carcinoma) (Carneiro et al., 2015).

Urothelial carcinoma of the bladder is usually admixed with other morphologically recognizable differentiations (Beltran et al., 2017). In recent years, the spectrum of microscopic forms of urothelial carcinoma has been expanded to include several histological variants. Most of them are described in the World Health Organization (WHO2016) book (Moch et al., 2016). The recognition of histological variants in urothelial neoplasia is essential for a pathologist and oncologist because different

Copyright © CC-BY-NC 2020, CRIBFB | *AIJMSR*

histology subtypes of urothelial cancer of the bladder may be associated with different clinical outcomes and have a different therapeutic approach.

2. Materials and Methods

We examined 105 cases of urothelial carcinoma from tissue database of University Hospital "St. George "Plovdiv, Bulgaria and Grand Hospital de l'Este Francilien, Jossigny, France, and reviewed the period from 2016 to 2020. All analyzed patients in this study have been diagnosed with invasive or non-invasive high-grade (HG) and low-grade (LG) urothelial carcinomas of the bladder.

Histological analysis of the tissues was performed using automatic tissue processor „DIAPATH EN ISO 9001:2000" and 4-5 μm formalin-fixed paraffin-embedded tissue sections underwent routine staining with hematoxylin-eosin (HE) and hematoxylin-eosin-safran (HES) to determine the presence of individual histological features.

Statistical analysis was performed with the software package for statistical analysis (SPSS®, 92 IBM 2009, version 19) using descriptive statistics and dispersion analysis (ANOVA). We considered the results for significant if $p<0.05$.

3. Results

The analyzed 105 patients in our study were diagnosed with proven urothelial carcinoma. Still, we must clarify that we included a few cases of urothelial carcinoma of renal pelvis and ureter. The patients only with urothelial carcinoma of bladder were 95.2%. Nevertheless, all analyzed patients were characterized and separated by two features: 1) by localization and 2) by age and gender.

The most common site of urothelial carcinoma was in the bladder, presented by 100 (95.2%) cases. Second by frequency urothelial carcinoma was in the distal part of the ureter, observed in 3(2.9%) cases. The least of the urothelial carcinoma included in our study were 3(1.9%) cases in the renal pelvis. These results are presented in Table 1.

Table 1. Number and percentage of patients with urothelial carcinoma according to its location

	Bladder	Renal pelvis	Ureter	Total
Number of patients	100	2	3	105
Percentages of patients	95.2	1.9	2.9	100

Although we analyzed our result according to the average age, the mean age of our patients was 70±10.98 years, as the youngest patient was 42 years old, while the oldest was 93 years old. Because of that heterogeneity of the age, we separated all patients in our study into six decades, as it is shown in Figure 2. The majority of our patients fit in the 60-89 years of age.

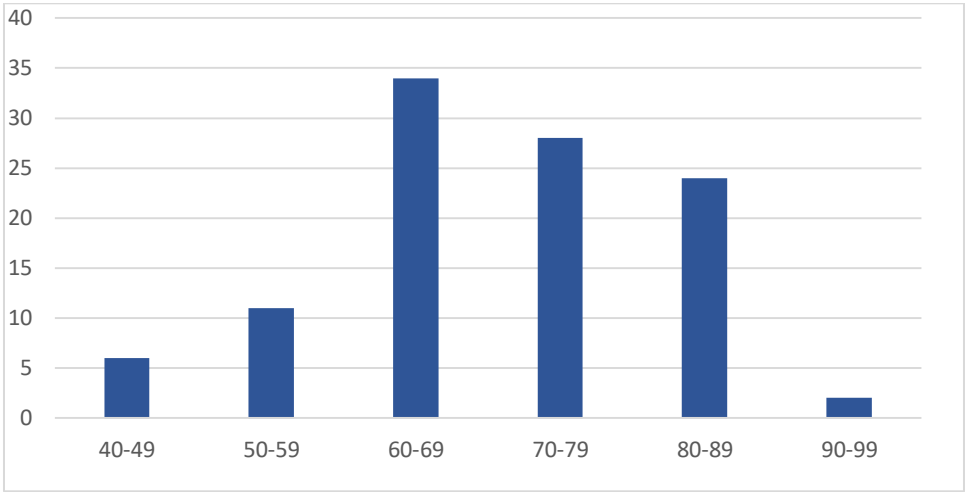

Figure 2. The number and % of patients with urothelial carcinoma according to age divided into decades

In regards to the age and nationality of our patients with urothelial carcinoma of the bladder, we did not find a significant difference between them. The median age of the patients from Bulgaria was 70.14 ±11.16 years, and from France was 69.62 ±10.09 years, p=0.873. This is graphically presented in Figure 3

Copyright © CC-BY-NC 2020, CRIBFB | *AIJMSR*

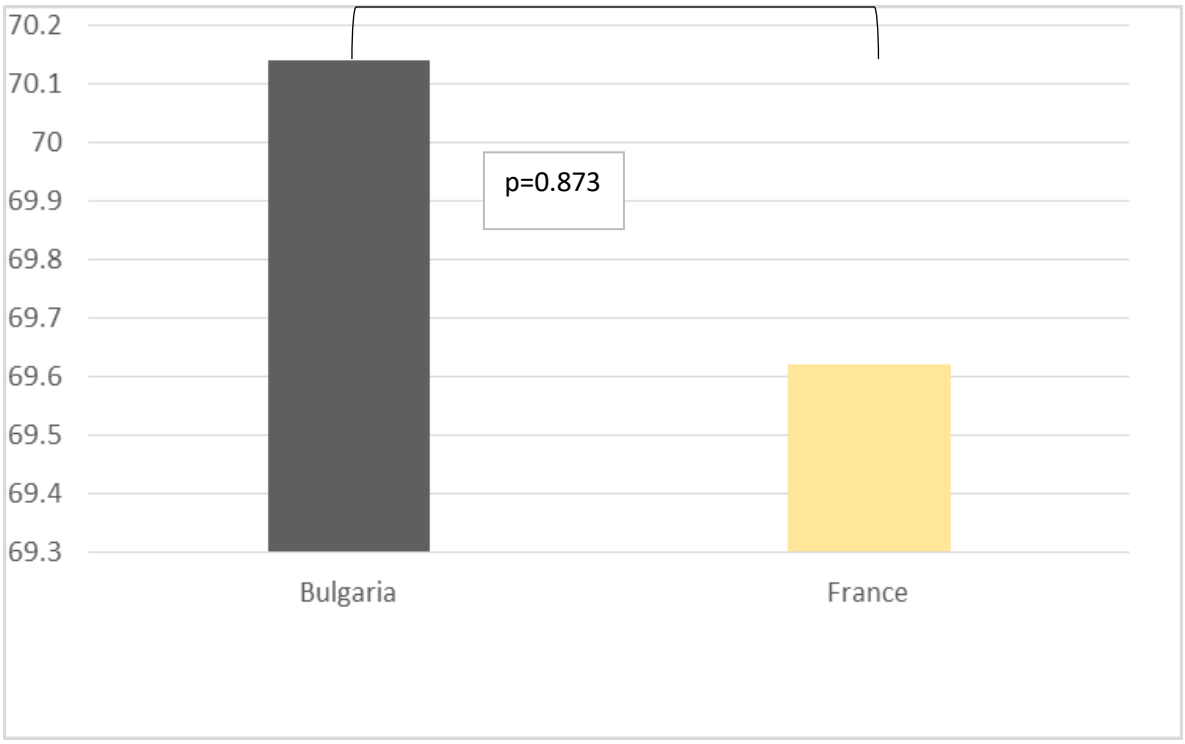

Figure 3. Differences in the average age of patients according to the nationality

We have obtained the following results according to the gender of the patients form cohort comprised of 105 patients with urothelial carcinoma: 72.4% (76/105) were males, and 27.6% (29/105) were females. The data are graphically presented in Figue 4.

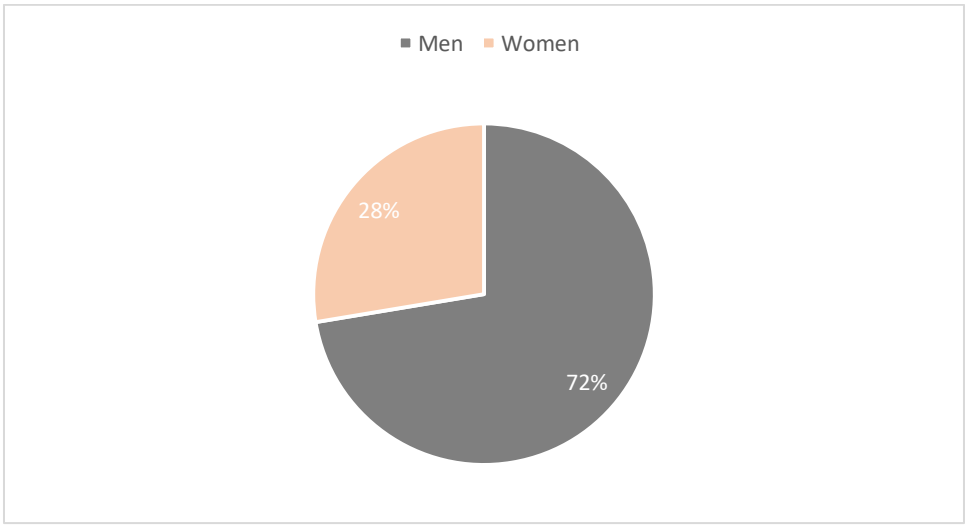

Figure 4. Distribution of patients according to the gender

Copyright © CC-BY-NC 2020, CRIBFB | *AIJMSR*

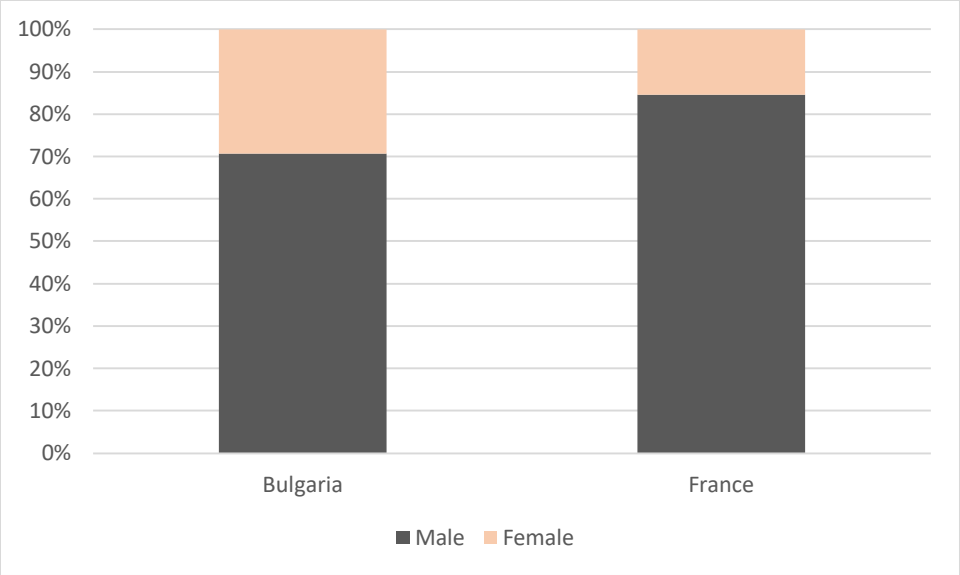

Figure 5. Distribution of the patients according to their nationality

Figures 4 and 5 show the distribution of urothelial carcinoma of bladder by gender, in Bulgarian and French samples of patients with a significant difference between male and female, for both countries. In essence, 65/92 (70.7%) for Bulgarian patients and 11/13 (84.6%) for France were males, and 27/92 (29.3%) in Bulgaria and 2/13 (15.4%) in France were females. Descriptive statistical methods showed no significant differences in patient's samples for both countries, p=0.292.

4. Discussion

Bladder carcinoma still presents a diagnostic challenge, and it remains the 7th most common malignant disease and the 2nd most common neoplasia of the excretory system right after prostatic carcinoma. It is also characterized by a high tendency for recurrence, necessitating expensive life-long clinical surveillance with repeated surgical interventions. Even in highly developed countries where standards of medical care and treatment are high, outcomes remain unchanged from 20 years ago. Urothelial carcinoma of the bladder is a significant public health problem in South Europe (especially in Greece, Spain, and Italy) and the most common cause for the lethal outcome of malignancies in males, and in Lebanon - in females (Bray et al., 2018).

This study demonstrated that the urothelial carcinoma of the bladder is a high-risk tumor. Moreover, among men, this is the most commonly diagnosed malignancy in Bulgaria and France, which is in correspondence with the data from other studies. According to literature, Bulgaria is the only country where males had a significant increase in both incidence and mortality (Wong et al. ,2018). In our study, we also established the ratio between man and women was 3.2:1, and the average age of the patients with urothelial carcinoma of the bladder is 70.14 years on average, which is similar to the results of almost all published studies (Horstmann et al., 2008; Gandomani et al., 2017).

5. Conclusion

This study demonstrated that bladder carcinoma is not a "simple" pathology but a common and aggressive malignant disease. It remains a diagnostic challenge. As we described in the interdiction, many factors affect its epidemiology. Still, most of them might be controlled with all common forces for one purpose only – reduces its incidence and mortality.

Conflict of interests

The authors state no conflict of interest.

References

Aydin, A. M., Woldu, S. L., Hutchinson, R. C., Boegemann, M., Bagrodia, A., Lotan, Y., ... & Krabbe, L. M. (2017). Spotlight on atezolizumab and its potential in the treatment of advanced urothelial bladder cancer. *Onco Targets and therapy*, *10*, 1487.

Beltran LA. Cheng I, Raspollini MR, Marques RC, Scarpelli M, Gasparrini S, Montironi R. (2017). Variants of Bladder Cancer: The Pathologist's Point of View. *European Urology Supplements, 16*(12), 210–222.

Copyright © CC-BY-NC 2020, CRIBFB | *AIJMSR*

Battista Di Pierro, G., Gulia, C., Cristini, C., Fraietta, G., Marini, L., Grande, P., ... & Piergentili, R. (2012). Bladder cancer: a simple model becomes complex. *Current genomics*, *13*(5), 395-415.

Bray, F., Ferlay, J., Soerjomataram, I., Siegel, R. L., Torre, L. A., & Jemal, A. (2018). Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, *68*(6), 394-424.

Carneiro, B. A., Meeks, J. J., Kuzel, T. M., Scaranti, M., Abdulkadir, S. A., & Giles, F. J. (2015). Emerging therapeutic targets in bladder cancer. *Cancer Treatment Reviews*, *41*(2), 170-178.

Gandomani, H. S., Tarazoj, A. A., Siri, F. H., Karimi Rozveh, A., Hosseini, S., Borujeni, N. N., ... & Salehiniya, H. (2017). Essentials of bladder cancer worldwide: incidence, mortality rate and risk factors. *Biomedical Research and Therapy*, *4*(9), 1638-55.

Gilbert, D. G., McClernon, F. J., Rabinovich, N. E., Sugai, C., Plath, L. C., Asgaard, G., ... & Botros, N. (2004). Effects of quitting smoking on EEG activation and attention last for more than 31 days and are more severe with stress, dependence, DRD2 A1 allele, and depressive traits. *Nicotine & Tobacco Research*, *6*(2), 249-267.

Hartge, P., Harvey, E. B., Linehan, W. M., Silverman, D. T., Sullivan, J. W., Hoover, R. N., & Fraumeni, J. F. (1990). Unexplained excess risk of bladder cancer in men. *JNCI: Journal of the National Cancer Institute*, *82*(20), 1636-1640.

Horstmann, M., Witthuhn, R., Falk, M., & Stenzl, A. (2008). Gender-specific differences in bladder cancer: a retrospective analysis. *Gender medicine*, *5*(4), 385-394.

Moch, H., Cubilla, A. L., Humphrey, P. A., Reuter, V. E., & Ulbright, T. M. (2016). The 2016 WHO classification of tumours of the urinary system and male genital organs—part A: renal, penile, and testicular tumours. *European urology*, *70*(1), 93-105.

Ploeg, M., Aben, K. K., & Kiemeney, L. A. (2009). The present and future burden of urinary bladder cancer in the world. *World journal of urology*, *27*(3), 289-293.

Wong, M. C., Fung, F. D., Leung, C., Cheung, W. W., Goggins, W. B., & Ng, C. F. (2018). The global epidemiology of bladder cancer: a joinpoint regression analysis of its incidence and mortality trends and projection. *Scientific reports*, *8*(1), 1-12.

Copyrights

Copyright for this article is retained by the author(s), with first publication rights granted to the journal. This is an open-access article distributed under the terms and conditions of the Creative Commons Attribution license (http://creativecommons.org/licenses/by/4.0/).

Copyright © CC-BY-NC 2020, CRIBFB | *AIJMSR*