Original Article

DOI: 10.4274/uob.galenos.2023.2023.2.2

Bull Urooncol 2023;22(4):144-149

Smoking Status in Relation to Clinicopathological Characteristics, Oncological Outcome, and Presence of Second Primary Lung Cancer in Patients with Bladder Cancer: A Population-based Registry Study

Deniz Bolat[1], İlker Tinay[2], Güven Aslan[3], Serdar Özkök[4], Erdem Göker[5], Atila Akkoçlu[6]

[1]*University of Health Sciences Turkey, Izmir Faculty of Medicine, Tepecik Training and Research Hospital, Department of Urology, Izmir, Turkey*
[2]*Anadolu Medical Center, Clinic of Urology, Kocaeli, Turkey*
[3]*Dokuz Eylül University Faculty of Medicine, Department of Urology, İzmir, Turkey*
[4]*Ege University Faculty of Medicine, Department of Radiation Oncology, İzmir, Turkey*
[5]*Ege University Faculty of Medicine, Department of Medical Oncology, İzmir, Turkey*
[6]*Sanko University Faculty of Medicine, Department of Chest Diseases, Gaziantep, Turkey*

Abstract

Objective: To evaluate the relationship between smoking status and clinicopathological characteristics and oncological outcome in bladder cancer (BC) patients and those with concomitant BC and lung cancer (LC) who developed BC or LC as a second primary cancer during their survivorship.
Materials and Methods: A total of 2621 BC patients registered in the Turkish Urooncology Association Bladder Cancer Database between 2001 and 2021 were retrospectively analyzed. Patients were divided into two groups: those with BC only (BC group, n=2568) and those with concomitant BC and LC (BLC group, n=53). Data on patient demographics and smoking status (active smoker, former smoker, non-smoker) were recorded, as were the clinicopathological characteristics and oncological outcomes with respect to smoking status.
Results: Active smokers comprised 50.5% and 49.1% of patients in the BC and BLC groups, respectively. The percentage of former smokers was 14.3% and 13.2% and percentage of non-smokers was 31.4% and 18.9% in the BC and BLC groups, respectively. In both BC and BLC groups, a higher percentage of males than females were active smokers (45.8% vs. 4.6% in BC and 47.2% vs. 1.9% in BLC). In the BLC group, the percentages of active smokers, former smokers and non-smokers in the BC first group were 56.0%, 24.0% and 20.0%, respectively, whereas the corresponding ratios in the LC first group were 50.0%, 8.3%, and 41.7%, respectively. The presence of smoking (active or former) vs. non-smoker status was associated with more advanced clinicopathological characteristics and poor oncological outcomes in both BC and BCL groups.
Conclusions: This population-based registry study in patients with BC revealed the presence of smoking history (active or former) in almost two-thirds of patients in both BC and BLC groups, which was associated with more advanced clinicopathological characteristics and poor oncological outcomes in both BC and BCL groups.
Keywords: Smoking status, bladder cancer, lung cancer, second primary cancer, clinicopathological features, oncological outcome

Introduction

Tobacco smoking is considered among the most important threats to public health and is one of the major preventable causes of death. It was reported that more than 1 billion people smoked tobacco regularly in 2019, and approximately 8 million deaths were related to smoking (1). In Turkey, the prevalence of tobacco smoking in adults was 31.3% in 2019, while an estimated 77000 and 11000 deaths in 2017 were attributed to tobacco smoking and secondhand smoke exposure, respectively (2,3).

Although different forms of tobacco (i.e., cigars, electronic cigarette hookah, bidis) are available in the market, none are considered safe, and each may lead to significant cardiovascular and respiratory (i.e., restrictive or obstructive lung diseases) problems (4). Furthermore, one of five cancer cases is directly caused by smoking (5). The International Agency for Research

Cite this article as: Bolat D, Tinay İ, Aslan G, Özkök S, Göker E, Akkoçlu A. Smoking Status in Relation to Clinicopathological Characteristics, Oncological Outcome, and Presence of Second Primary Lung Cancer in Patients with Bladder Cancer: A Population-based Registry Study. Bull Urooncol 2023;22(4):144-149.

Address for Correspondence: Deniz Bolat, University of Health Sciences Turkey, Izmir Faculty of Medicine, Tepecik Training and Research Hospital, Department of Urology, Izmir, Turkey
Phone: +90 505 638 30 10 **E-mail:** drbolat@hotmail.com **ORCID-ID:** orcid.org/0000-0001-7338-8737
Received: 23.02.2023 **Accepted:** 06.05.2023

on Cancer (IARC) declared tobacco smoking a group 1 carcinogen in humans and associated it with cancers of the oral cavity, pharynx, larynx, lung, nasal cavity/accessory sinuses, esophagus, stomach, colorectum, liver, pancreas, kidney, ureter, urinary bladder, ovary, cervix, and myeloid leukemia (6).

Both lung cancer (LC) and bladder cancer (BC) are among the most common and mortal cancers globally (7). Tobacco smoking is the strongest modifiable risk factor for both cancer types. Approximately 85% of LCs result from smoking, and smoking accounts for nearly 50% of the BC burden (8,9).

Cigarette smoking is commonly continued after an initial diagnosis of smoking-associated cancer, despite being a strong and modifiable oncological risk factor (10,11,12,13). Smoking and/or alcohol consumption are causally linked to more than one-third of all second primary cancers (SPCs) in the United States, whereas the risk of developing a second smoking-associated cancer is also higher in survivors of smoking-associated cancers than in the general population (12).

BC and LC are the two most frequently diagnosed and mortal cancers that share tobacco smoking as a common risk factor. Therefore, this population-based registry study aimed to evaluate the relationship between smoking status and clinicopathological characteristics and oncological outcome in BC patients and in those with concomitant BC and LC who developed BC or LC as a SPC during their survivorship.

Materials and Methods

Study Population

A total of 2621 BC patients registered in the Turkish Urooncology Association Bladder Cancer Database between 2001 and 2021 were retrospectively analyzed. The database included the demographic, pathologic, and clinical parameters of patients with non-muscle-invasive and muscle-invasive BCs. Patients were divided into two groups: those with BC only (BC group, n=2568) and those with concomitant BC and LC (BLC group, n=53). The BLC group was further divided into two subgroups based on the type of SPC, including those who developed LC as an SPC during BC (BC first, n=25) and those who developed BC as an SPC during LC (LC first, n=12). Patients with missing data, those with benign lesions and/or metastatic lesions of the lung, and those with benign lesions of the bladder were excluded from the analysis.

In accordance with the registry database design of the study, ethics committee approval was not required.

Assessments

Data on patient demographics (age at diagnosis, gender) and smoking status (active smoker, former smoker, non-smoker) were recorded in each group. Clinicopathological characteristics and oncological outcomes (advanced tumor stage at diagnosis, high grade tumor at diagnosis, nodal disease, metastasis at the time of initial diagnosis, complications, postoperative recurrence, postoperative metastasis, need for additional treatment [radiotherapy (RT)/computed tomography (CT), and mortality] were evaluated with respect to smoking status in the BC and BLC groups. In the BLC group, smoking status was also evaluated with respect to primary diagnosis (LC first and BC first).

Statistical Analysis

Statistical analysis was performed using Python and Pandas (14,15), Numpy (16), Scipy (16), and JupyterLab (17) as the coding interface. The normality of distribution was evaluated using visual (Histograms, QQ Plots) and analytical methods (Kolmogorov-Smirnov, Shapiro-Wilk, and D'Agostino's κ^2 tests). Descriptive statistics were reported, and the data were expressed as mean (standard deviation), median (interquartile range), and n (%) where appropriate. This is a sectional study; therefore, no hypothesis tests or p-values were presented.

Results

Patient Demographics and Smoking Status

Of 2621 BC patients included in the registry database, 2568 (97.9%) were diagnosed with BC only (BC group), whereas 53 (2.1%) were diagnosed with concomitant BC and LC (BLC group). Males comprised 85.7% (2201/2568) and 96.2% (51/53) of patients in the BC and BLC groups, respectively (Table 1).

In the BC group, the mean age at cancer diagnosis was 68 years overall, and it was 66 years, 67 years, and 68 years in active smokers, former smokers, and non-smokers, respectively (Table 1).

In the BLC group, the mean age at cancer diagnosis was 70 years overall, and it was 68 years, 77 years, and 70 years for active smokers, former smokers, and non-smokers, respectively (Table 1).

Active smokers comprised 50.5% (1296/2568) and 49.1% (26/53) of patients in the BC and BLC groups, respectively. The percentage of former smokers was 14.3% (367/2568) and 13.2% (7/53) and the percentage of non-smokers was 31.4% (807/2568) and 18.9% (10/53) in the BC and BLC groups, respectively (Table 1, Figure 1).

Accordingly, a history of smoking (current or former) was evident in 1663 (64.8% overall, 67.3% of those with available data) patients with BC only and in 33 (62.3% overall, 76.7% of those with available data) patients with concomitant bladder and LC (Table 1).

In both BC and BLC groups, a higher percentage of males than females were active smokers (45.8% vs. 4.6% in BC and 47.2% vs. 1.9% in BLC) and former smokers (13.5% vs. 0.8% in BC and 11.3% vs. 1.9% in BLC) (Table 1, Figure 2).

Demographics and Smoking Status in the BLC Group with Respect to SPC

In the BLC group of 53 patients with concomitant BC and LC, data on the type of SPC were available in 37 patients. The first diagnosed cancer was BC, and LC appeared as an SPC in 25 (67.6%) patients, whereas LC diagnosis preceded the development of BC as an SPC in 12 (32.4%) patients (Table 2).

The mean patient age at diagnosis was 71 years and 70 years in the BC first and LC first groups, respectively. LC was detected a

mean of 3.7 years after the diagnosis of BC, and BC was detected a mean of 4.2 years after the diagnosis of LC (Table 2).

The percentages of active smokers, former smokers and non-smokers in the BC first group were 56.0%, 24.0% and 20.0%, respectively, while the corresponding ratios in the LC first group were 50.0%, 8.3%, and 41.7%, respectively (Table 2, Figure 1).

Clinicopathological Characteristics and Oncological Outcomes

Figure 3 illustrates the clinicopathological characteristics and oncological outcomes with respect to smoking status (active smokers, former smokers and non-smokers, respectively) in the BC group, including advanced tumor stage at diagnosis (57.2%, 55.2%, 49.3%), high-grade tumor at diagnosis (72.8%, 72.5%, 61.5%), nodal disease (37.0%, 36.7%, 34.6%), metastasis at the time of initial diagnosis (3.8%, 2.2%, 1.9%), complications (43.3%, 20.4%, 36.0%), postoperative recurrence (23.7%, 28.0%, 19.6%), postoperative metastasis (11.8%, 25.7%, 14.5%), need for additional treatment (RT/CT; 66.1%, 63.6%, 52.1%), and mortality (14.2%, 26.5%, 12.1%) (Figure 3).

Figure 4 illustrates clinicopathological characteristics and oncological outcomes with respect to smoking status (active smokers, former smokers and non-smokers, respectively) in the BLC group, including advanced tumor stage at diagnosis (42.4%, 28.6%, 28.6%), high-grade tumor at diagnosis (65.6%, 55.6%, 28.6%), nodal disease (15.4%, 0.0%, 0.0%), metastasis at the

Table 1. Patient demographics and smoking status in the study groups

		Cancer registry (n=2621)	
		Bladder cancer (n=2568)	**Bladder cancer + lung cancer (n=53)**
Gender, n (%)			
Male		2201 (85.7)	51 (96.2)
Female		367 (14.3)	2 (3.8)
Age at diagnosis (year), mean	Total	68	70
	Active smoker	66	68
	Former smoker	67	77
	Non-smoker	68	70
Smoking status, n (%)			
Active smoker	Total	1296 (50.5)	26 (49.1)
	Male	1177 (45.8)	25 (47.2)
	Female	119 (4.6)	1 (1.9)
Former smoker	Total	367 (14.3)	7 (13.2)
	Male	347 (13.5)	6 (11.3)
	Female	20 (0.8)	1 (1.9)
Non-smoker	Total	807 (31.4)	10 (18.9)
	Male	622 (24.2)	10 (18.9)
	Female	185 (7.2)	0 (0.0)
Missing data	Total	98	10
	Male	55	10
	Female	43	0
History of smoking (current or former)	Total	1663 (64.8)	33 (62.3)
	In those with available data (n=2470 and n=43)	1663 (67.3)	33 (76.7)

Table 2. Demographics and smoking status in patients with concomitant bladder and lung cancer with respect to the type of SPC

		Bladder cancer + lung cancer (n=53)	
		Bladder cancer first	**Lung cancer first**
Total (n=37), n (%)[a]		25 (67.6)	12 (32.4)
Age at diagnosis (year), mean		71	70
Time between two diagnoses (year), mean		3.7	4.2
Smoking status, n (%)	Active smoker	14 (56.0)	6 (50.0)
	Former smoker	6 (24.0)	1 (8.3)
	Nonsmoker	5 (20.0)	5 (41.7)

[a]Unknown in 16 patients, SPC: Second primary cancer

time of initial diagnosis (12.5%, 0.0%, 0.0%), complications (73.3%, 33.3%, 20.0%), postoperative recurrence (16.7%, 66.7%, 20.0%), postoperative metastasis (23.8%, 33.3%, 0.0%), need for additional treatment (RT/CT; 41.2%, 33.3%, 0.0%), and mortality (26.7%, 33.3%, 0.0%) (Figure 4).

Discussion

This population-based registry study in BC patients revealed the presence of smoking history (active or former) in almost two-thirds of patients in both BC and BLC groups, which was associated with an increased risk of advanced tumor stage, high-grade tumor and metastasis at the time of initial diagnosis, more invasive surgeries and related postoperative complications, recurrence and metastasis, and a higher rate of mortality compared with non-smoker status. The association of smoking with poor prognostic factors and mortality was more marked in the BLC group than in the BC group, whereas the postoperative recurrence, metastasis, and mortality rates remained high even after smoking cessation in both the BC and BLC groups. Younger age at diagnosis (2 years earlier overall and 10 years earlier for former smokers) in the BC than in the BLC groups, and for active smokers than non-smokers in both BC and BLC groups.

The current population of Turkey is 85 million, and there are approximately 65.000 LC survivors (18). Our findings revealed the presence of LC as a SPC in 2.1% of patients with BC, which seems to indicate that LC is approximately 28-fold more common in patients with BC than in the general population. This situation is related to smoking, which is a common risk factor for both cancers.

Tobacco use is considered to be the main cause of 90% and 79% of LCs in males and females, respectively, and approximately half of BC cases as well (19,20). Similarly, our findings also indicate that almost two-thirds of patients with BC or concomitant bladder and LC have smoked at some point in their lives.

Overall, 75% of new BC cases occur in men, with an M:F ratio ranging 6:1 to 2:1 in different regions worldwide (21). Similarly, LC incidence is also 2-3 times higher in men than in women in different countries of the world (22). This is related to the fact that men smoke more than women (23). In the current study, BC alone or together with LC was also more common in men than in women. Moreover, both BC and concomitant BC + LC were 2-fold more common in smoker men than in non-smoker men.

Although nicotine itself is not carcinogenic, many substances in cigarette smoke, such as polycyclic aromatic hydrocarbons and 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone, have been deemed carcinogenic by the IARC. The activation of these substances is considered to be responsible for the formation of DNA adducts and subsequent gene methylation, DNA sequence alterations, DNA segment amplification/deletion, or whole chromosome gains/losses (24).

Recent studies have reported the association of continued smoking with a higher risk of SPC and adverse outcomes, whereas smoking cessation lowered the incidence of SPC in survivors of LC (13,25). Barclay et al. (13) described the incidence of second- and higher-order smoking-related primary cancers in LC survivors and noted that BC is the second most common smoking-related SPC after non-small cell LC among survivors of primary LC. The standardized incidence ratios (SIRs) for second

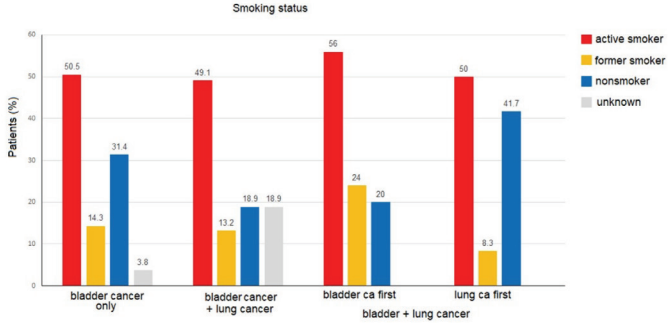

Figure 1. Smoking status in "bladder cancer only" and "bladder cancer plus lung cancer" groups

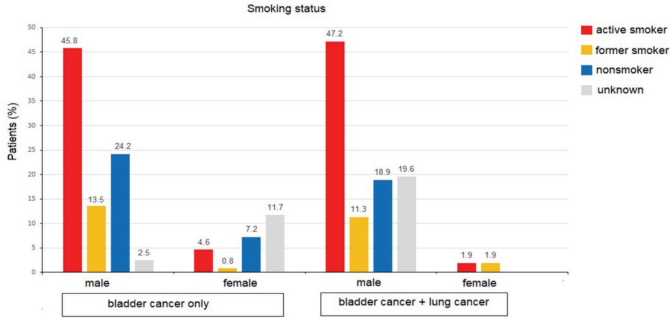

Figure 2. Smoking status with respect to gender in "bladder cancer only" and "bladder cancer plus lung cancer" groups

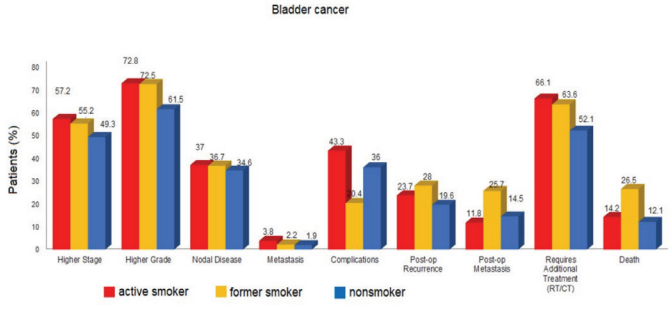

Figure 3. Clinicopathological characteristics and oncological outcomes with respect to smoking status in bladder cancer patients

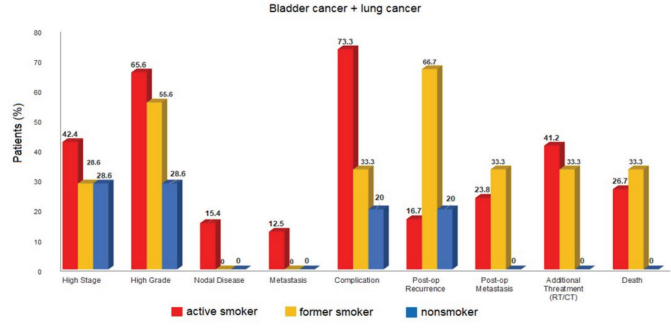

Figure 4. Clinicopathological characteristics and oncological outcomes with respect to smoking status in patients with concomitant bladder and lung cancers

primary BC were found to be similar to the general population at the beginning and end of follow-up, which appears to peak at approximately 5 years, with an SIR of 1.8 [95% confidence interval (CI) 1.5 to 2.2], from first primary LC diagnosis (13). Zheng et al. (11) investigated the sex-specific risks for any SPCs following urothelial cancers and, in reverse order, for urothelial cancers as SPCs following any cancer in 46234 BC patents. The authors noted that after BC, the SIR for LC as an SPC was 2.08 (95% CI 1.93-2.25) and 2.82 (95% CI 2.43-3.26) in males and females, respectively. However, the second BC risk after LC was 1.31 (95% CI 1.12-1.52) in males and 1.81 (95% CI 1.34-2.4) in females. The authors also emphasized that this association was most likely related to smoking (11). In a study by Shiels et al. (12) from five cohorts including stage I LC (n=2,552), BC (n=6,386), kidney cancer (n=3,179) and with head/neck cancer (n=2,967) patients, smoking before the first cancer diagnosis was found to increase the risk of SPC in cancer survivors, in relation to the increased smoking prevalence. In our study, 37 of 2568 patients with BC also had LC. Of these, 67.6% were diagnosed with LC after a mean of 3.7 years of initial BC diagnosis. In the remaining 32.4%, BC developed a mean of 4.2 years after the diagnosis of LC. Moreover, we found that secondary primary lung or BC occurred in approximately half of the patients with primary cancer who smoked over the years. According to our results, it seems that if patients survive to primary bladder or LC, they will develop the other one of these cancers in about 4 years. Thus, these patients will begin to struggle with two aggressive cancers in their early 70s.

A growing body of evidence indicates the association of smoking with adverse outcomes in BC patients treated with transurethral resection and/or radical cystectomy, although not uniformly. Rink et al. (26) suggested the potential of smoking in causing unfavorable outcomes after radical cystectomy and the likelihood of smoking cessation to attenuate these effects. Recently, in a cohort study of 1472 adult NMIBC patients (two-thirds were former or current cigarette smokers at the time of diagnosis), the recurrence risk was reported to increase with longer duration and increasing pack-years of cigarette smoking in an exposure-response manner (~ two-fold greater risk for ≥40 years of smoking and ≥40 pack-years). Pipe, cigar, marijuana, and e-cigarette usage were not associated with an increase in recurrence risk (27). Moreover, in a systematic review and meta-analysis by Cacciamani et al. (28), smoking status was found to be associated with lower neoadjuvant chemotherapy response rates, higher overall and cancer-specific mortality, and higher rate of BC recurrence after radical cystectomy. In a meta-analysis by Tellini et al. (29), it was demonstrated that smoking status at the time of radical cystectomy is related to an increased risk for major postoperative complications, infections, and mortality. Besides the increased risk of mortality and subsequent malignancies, cigarette smoking in cancer patients is also known to increase surgical complications and chemotherapy-related and radiation-related toxicities (30,31). In our study, BC was at a more advanced stage at the time of diagnosis in smokers along with a more aggressive course in these patients. Our observations regarding postoperative complications, prognosis, response to treatments, and survival outcomes were consistent with those of previous studies. Additionally, we found that even if patients with concomitant bladder and LCs quit smoking, BC relapsed and metastasized more frequently.

Study limitations

This study has certain limitations. First, we did not consider the amount and duration of smoking because it is self-reported and may cause bias. Secondly, although there are many forms of tobacco in the market, we considered all in one as tobacco smoking. Third, in our cohort, we considered cancer-specific and other causes of mortality as a single parameter. However, smoking also increases the risk of non-cancer-related deaths, primarily by affecting the cardiovascular system. Fourth, concomitant cancers have some genetic mutations that affect tumor suppressor genes. Smoking is not solely responsible for bladder and LCs. Due to the lack of genetic information in our database, we could not analyze the impact of genetic factors on this patient population. Lastly, while this is a population-based study with a high number of participating centers and patients, increasing the strength of the study, our results may not be generalizable because all participating centers were referral centers in their region and across Turkey.

Conclusion

In conclusion, this population-based registry study in patients with BC revealed the presence of smoking history (active or former) in almost two-thirds of patients in both BC and BLC groups, which was associated with more advanced clinicopathological characteristics at diagnosis and poor oncological outcomes in both BC and BCL groups. The association of smoking with poor prognostic factors and mortality was more marked in the BLC group than in the BC group, whereas the postoperative recurrence, metastasis, and mortality rates remained high even after smoking cessation in both the BC and BLC groups. Tobacco smoking is a common risk factor for both bladder and LCs. If survivors of one of these cancers continue to smoke, the risk of developing another cancer is high. Patients with BC who smoke have adverse pathological outcomes, worse treatment response, and lower survival rates. Therefore, healthcare providers should counsel cancer patients regarding the importance of smoking cessation.

Acknowledgements

Publication: The results of the study were not published in full or in part in form of abstracts.

Contribution: There is not any contributors who may not be listed as authors.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: Astra Zeneca-Turkiye provided unconditional support for updating the Turkish Association of Urooncology Bladder Cancer Database.

Ethics

Ethics Committee Approval: In accordance with the registry database design of the study, ethics committee approval was not required.

Informed Consent: Database report.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: D.B., Concept: D.B., İ.T., G.A., S.Ö., E.G., A.A., Design: D.B., İ.T., G.A., S.Ö., E.G., A.A., Data Collection or Processing: D.B., İ.T., G.A., Analysis or Interpretation: D.B., İ.T., G.A., S.Ö., E.G., A.A., Literature Search: D.B., Writing: D.B.

References

1. GBD 2019 Tobacco Collaborators. Spatial, temporal, and demographic patterns in prevalence of smoking tobacco use and attributable disease burden in 204 countries and territories, 1990-2019: a systematic analysis from the Global Burden of Disease Study 2019. Lancet 2021;397:2337-2360.
2. Turkish Statistical Institute. TUIK Data Portal. Accessed August 8, 2022. https://www.tuik.gov.tr/Home/Index.
3. Institute for Health Metrics and Evaluation GBD Results. Accessed August 8, 2022. http://ghdx.healthdata.org/gbd-results-tool.
4. Hussain A, Dulay P, Rivera MN, et al. Neoplastic Pathogenesis Associated with Cigarette Carcinogens. Cureus 2019;11:e3955.
5. Agudo A, Bonet C, Travier N, et al. Impact of cigarette smoking on cancer risk in the European prospective investigation into cancer and nutrition study. J Clin Oncol 2012;30:4550-4557.
6. International Agency for Research on Cancer Personal habits and indoor combustions. Volume 100 E: a review of human carcinogens 2012.
7. Sung H, Ferlay J, Siegel RL, et al. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 2021;71:209-249.
8. Warren GW, Cummings KM. Tobacco and lung cancer: risks, trends, and outcomes in patients with cancer. Am Soc Clin Oncol Educ Book 2013:359-364.
9. Laaksonen MA, MacInnis RJ, Canfell K, et al. The future burden of kidney and bladder cancers preventable by behavior modification in Australia: A pooled cohort study. Int J Cancer 2020;146:874-883.
10. Muller J, Grosclaude P, Lapôtre-Ledoux B, et al. Trends in the risk of second primary cancer among bladder cancer survivors: a population-based cohort of 10 047 patients. BJU Int 2016;118:53-59.
11. Zheng G, Sundquist K, Sundquist J, et al. Bladder and upper urinary tract cancers as first and second primary cancers. Cancer Rep (Hoboken) 2021;4:e1406.
12. Shiels MS, Gibson T, Sampson J, et al. Cigarette smoking prior to first cancer and risk of second smoking-associated cancers among survivors of bladder, kidney, head and neck, and stage I lung cancers. J Clin Oncol 2014;32:3989-3995.
13. Barclay ME, Lyratzopoulos G, Walter FM, et al. Incidence of second and higher order smoking-related primary cancers following lung cancer: a population-based cohort study. Thorax 2019;74:466-472.
14. Reback J, McKinney W, Den Van Bossche J, et al. Pandas-dev/pandas: Pandas 1.0. 3. Zenodo 2020.
15. McKinney W. Data structures for statistical computing in python. Proceedings of the 9th Python in Science Conference: Austin TX 2010;51-56.
16. Virtanen P, Gommers R, Oliphant TE, et al. SciPy 1.0 Contributors. SciPy 1.0: fundamental algorithms for scientific computing in Python. Nat Methods 2020;17:261-272.
17. Kluyver T, Ragan-Kelley B, Pérez F, et al. Jupyter Notebooks-a publishing format for reproducible computational work flows. 2016. https://eprints.soton.ac.uk/403913/1/STAL9781614996491-0087.pdf
18. Cangır AK, Yumuk PF, Sak SD, et al. Lung Cancer in Turkey. J Thorac Oncol 2022;17:1158-1170.
19. Ozlü T, Bülbül Y. Smoking and lung cancer. Tuberk Toraks 2005;53:200-209.
20. Mori K, Mostafaei H, Abufaraj M, et al. Smoking and bladder cancer: review of the recent literature. Curr Opin Urol 2020;30:720-725.
21. Cumberbatch MGK, Jubber I, Black PC, et al. Epidemiology of Bladder Cancer: A Systematic Review and Contemporary Update of Risk Factors in 2018. Eur Urol 2018;74:784-795.
22. Barta JA, Powell CA, Wisnivesky JP. Global Epidemiology of Lung Cancer. Ann Glob Health 2019;85:8.
23. Navas-Acien A. Global Tobacco Use: Old and New Products. Ann Am Thorac Soc 2018;15(Suppl 2):69-75.
24. Hecht SS. Tobacco smoke carcinogens and lung cancer. J Natl Cancer Inst 1999;91:1194-1210.
25. Tabuchi T, Ito Y, Ioka A, Nakayama T, Miyashiro I, Tsukuma H. Tobacco smoking and the risk of subsequent primary cancer among cancer survivors: a retrospective cohort study. Ann Oncol 2013;24:2699-2704.
26. Rink M, Crivelli JJ, Shariat SF, et al. Smoking and Bladder Cancer: A Systematic Review of Risk and Outcomes. Eur Urol Focus 2015;1:17-27.
27. Kwan ML, Haque R, Young-Wolff KC, et al. Smoking Behaviors and Prognosis in Patients With Non-Muscle-Invasive Bladder Cancer in the Be-Well Study. JAMA Netw Open 2022;5:e2244430.
28. Cacciamani GE, Ghodoussipour S, Mari A, et al. Association between Smoking Exposure, Neoadjuvant Chemotherapy Response and Survival Outcomes following Radical Cystectomy: Systematic Review and Meta-Analysis. J Urol 2020;204:649-660.
29. Tellini R, Mari A, Muto G, et al. Impact of Smoking Habit on Perioperative Morbidity in Patients Treated with Radical Cystectomy for Urothelial Bladder Cancer: A Systematic Review and Meta-analysis. Eur Urol Oncol 2021;4:580-593.
30. Hanna N, Mulshine J, Wollins DS, et al. Tobacco cessation and control a decade later: American society of clinical oncology policy statement update. J Clin Oncol 2013;31:3147-3157.
31. U.S. Department of Health and Human Services. The health consequences of smoking: 50 years of progress—A report of the Surgeon General, 2014. https://www.hhs.gov/sites/default/files/consequences-smoking-exec-summary.pdf.