

Exploring the Relationship Between Smoking and Tumor Characteristics in Bladder Cancer

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Starting date: February-April 2025
Duration: 5 to 6 months
Application deadline: January 31th, 2025

Context

Bladder cancer is a common malignancy, particularly in North America and Europe, where it ranks as the tenth most common cancer worldwide. In 2020, approximately 573,278 new cases and 212,536 deaths were reported globally, with the majority of cases affecting men[1].

Bladder cancer is a complex disease that progresses gradually over time. It is generally classified into two types : muscle-invasive bladder cancer (MIBC), which invades the muscle layer of the bladder and is characterized by stages T2 and above; and non-muscle-invasive bladder cancer (NMIBC), which is confined to the mucosa and submucosal connective tissue, corresponding to stages Tis, Ta and T1, and accounts for approximately 70% of new diagnoses. Treatment for newly diagnosed NMIBC typically involves transurethral resection of the tumor (TURBT), often followed by intravesical chemotherapy and/or immunotherapy in high-risk patients. In contrast, the standard treatment for MIBC patients involves the removal of the bladder via radical cystectomy. Although the 5-year survival rate for NMIBC patients is around 90%, the disease has a significant risk of recurrence within 5 years, ranging from 50% to 70%, and a 10% to 30% risk of progression to MIBC, where the 5-year survival rate falls below 50%[2].

Several risk factors for bladder cancer have been identified, including occupational exposure to carcinogens[3], water contaminants[4], and notably, tobacco smoking[5]. Smoking is recognized as the most important risk factor for bladder cancer, contributing to nearly 50% of cases[6]. Tobacco contains various carcinogens, including 4-aminobiphenyl, 2-naphthylamine, and aromatic amines, which are linked to bladder cancer development in smokers[7]. The risk of bladder cancer increases with both the quantity of cigarettes smoked and the duration of smoking[8]. Some studies suggest that higher smoking intensity is associated with more aggressive bladder tumors at diagnosis, while others find no link between smoking intensity and tumor grade or stage[9]. Investigating the link between smoking and tumor characteristics is crucial, as understanding how smoking quantity and duration influence tumor aggressiveness could help physicians better identify patients at higher risk for more severe forms of cancer, enabling more tailored and effective treatment strategies.

Given the varied and inconsistent results in the literature, and the fact that most studies have focused on the association between smoking and tumor stage or grade, the relationship between smoking habits and clinicopathological factors (including age, tumor stage and grade, tumor size, number of tumors, presence of concomitant CIS, and histological type) at diagnosis remains unclear and warrants further investigation. This project will utilize data from the COBLAnCE cohort (a COhort to study BLadder CancEr)[10], a large prospective French cohort of 1,800 bladder cancer patients (both NMIBC and MIBC) enrolled between 2012 and 2018.

Objectives

The goal of the internship is to investigate the association between smoking habits (including smoking status, age at smoking initiation, smoking intensity and smoking duration) and clinicopathological variables at diagnosis. These variables include age, gender, tumor stage, grade, tumor size, number of tumors, presence of concomitant CIS and histological type among NMIBC and MIBC patients. The main objectives of the internship will be:

- to become familiar with the COBLAnCE cohort and its data,
- to analyze the association between smoking habits and clinicopathological variables at diagnosis,
- to prepare a research paper presenting the findings obtained during the internship.

Candidate Profile

- Master's student in Epidemiology or Biostatistics
- Experience with the R/SAS programming language
- Proficiency in English

How to apply?

As part of our proactive policy to promote the integration of people with disabilities, all applications received are considered on an equal basis. To submit an application for this vacancy, please send your curriculum vitae and a cover letter by email to Maryam KARIMI (Maryam.KARIMI@gustaveroussy.fr), indicating the reference “InternCOBLAnCE2025” in the object of the email.

References

- [1] Hyuna Sung, Jacques Ferlay, Rebecca L. Siegel, Mathieu Laversanne, Isabelle Soerjomataram, Ahmedin Jemal, and Freddie Bray. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: a cancer journal for clinicians*, 71(3):209–249, May 2021.
- [2] Ashish M. Kamat, Noah M. Hahn, Jason A. Efstathiou, Seth P. Lerner, Per-Uno Malmström, Woonyoung Choi, Charles C. Guo, Yair Lotan, and Wassim Kassouf. Bladder cancer. *Lancet (London, England)*, 388(10061):2796–2810, December 2016.
- [3] Javier García-Pérez, Marina Pollán, Elena Boldo, Beatriz Pérez-Gómez, Nuria Aragonés, Virginia Lope, Rebeca Ramis, Enrique Vidal, and Gonzalo López-Abente. Mortality due to lung, laryngeal and bladder cancer in towns lying in the vicinity of combustion installations. *The Science of the Total Environment*, 407(8):2593–2602, April 2009.
- [4] Mario I. Fernández, J. Francisco López, Bruno Vivaldi, and Fernando Coz. Long-term impact of arsenic in drinking water on bladder cancer health care and mortality rates 20 years after end of exposure. *The Journal of Urology*, 187(3):856–861, March 2012.
- [5] Neal D Freedman, Debra T Silverman, Albert R Hollenbeck, Arthur Schatzkin, and Christian C Abnet. Association between smoking and risk of bladder cancer among men and women. *JAMA : the journal of the American Medical Association*, 306(7):737–745, August 2011.
- [6] Kalyan Saginala, Adam Barsouk, John Sukumar Aluru, Prashanth Rawla, Sandeep Anand Padala, and Alexander Barsouk. Epidemiology of Bladder Cancer. *Medical Sciences (Basel, Switzerland)*, 8(1):15, March 2020.
- [7] Gerd P. Pfeifer, Mikhail F. Denissenko, Magali Olivier, Natalia Tretyakova, Stephen S. Hecht, and Pierre Hainaut. Tobacco smoke carcinogens, DNA damage and p53 mutations in smoking-associated cancers. *Oncogene*, 21(48):7435–7451, October 2002.
- [8] Maximilian Burger, James W. F. Catto, Guido Dalbagni, H. Barton Grossman, Harry Herr, Pierre Karakiewicz, Wassim Kassouf, Lambertus A. Kiemeney, Carlo La Vecchia, Shahrokh Shariat, and Yair Lotan. Epidemiology and risk factors of urothelial bladder cancer. *European Urology*, 63(2):234–241, February 2013.
- [9] André L. A. Barbosa, Sita H. H. M. Vermeulen, Katja K. Aben, Anne J. Grotenhuis, Alina Vrieling, and Lambertus A. Kiemeney. Smoking intensity and bladder cancer aggressiveness at diagnosis. *PLoS ONE*, 13(3):e0194039, March 2018.
- [10] Thierry Lebreton, Julia Bonastre, Aldéric Frassin, Yann Neuzillet, Stéphane Droupy, Xavier Rebillard, Dimitri Vordos, Laurent Guy, Arnaud Villers, Marc Schneider, Patrick Coloby, Jean Lacoste, Arnaud Méjean, Jacques Lacoste, Jean-Luc Descotes, Pascal Eschwege, Guillaume Loison, Hélène Blanché, Odette Mariani, Bijan Ghaleh, Anthony Mangin, Nanor Sirab, Karine Groussard, François Radvanyi, Yves Allory, and Simone Benhamou. Cohort profile: COBLAnCE: a French prospective cohort to study prognostic and predictive factors in bladder cancer and to generate real-world data on treatment patterns, resource use and quality of life. *BMJ open*, 13(12):e075942, December 2023.