

Can a diagnosis of bladder cancer motivate positive lifestyle changes – and prevent recurrent disease?

Caitlin Lim¹, John R. Cohn², Joshua A. Cohn^{1,3}

¹Department of Urology, Einstein Healthcare Network, Philadelphia, PA, USA; ²Department of Medicine, Division of Pulmonary, Allergy and Critical Care Medicine, Korman Respiratory Institute, Thomas Jefferson University, Philadelphia, PA, USA; ³Department of Surgical Oncology, Division of Urologic Oncology, Fox Chase Cancer Center, Philadelphia, PA, USA

Correspondence to: Joshua A. Cohn. Department of Urology, Einstein Healthcare Network, Philadelphia, PA, USA. Email: cohnjosh@einstein.edu; Caitlin Lim. Department of Urology, Einstein Healthcare Network, Philadelphia, PA, USA. Email: LimCaitl@einstein.edu.

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According to the American Centers for Disease Control and prevention (CDC), tobacco use remains the single largest preventable cause of death and disease in the United States. Cigarette smoking kills more than 480,000 Americans each year, with more than 41,000 of these deaths from exposure to secondhand smoke. In addition, smoking-related illness in the United States costs more than \$300 billion a year, including nearly \$170 billion in direct medical care for adults, and \$156 billion in lost productivity (1).

Urology patients are not exempt from this scourge. In 2018, there will be an estimated 81,190 new cases of bladder cancer in the United States, with over 17,000 patients expected to die from their disease (2). Worldwide, bladder cancer is the ninth most frequently diagnosed malignancy, with the incidence directly paralleling the prevalence of tobacco-smoking (3). Smoking is the single most modifiable risk factor for the development of bladder cancer, with ever-smokers having a 2.5 times greater risk for bladder cancer than never-smokers. Smokers also remain at risk for coronary artery disease (CAD), lung cancer, chronic obstructive pulmonary disease (COPD) and other tobacco-related illnesses (4,5).

In contrast to tobacco use, alcohol consumption has not been clearly linked to an increased incidence of bladder cancer. However, it has been shown that both excessive alcohol and smoking have a negative impact on post-

operative recovery and overall health. Individuals undergoing intensive alcohol cessation programs were five times less likely to experience a post-operative complication in a meta-analysis of two randomized controlled trials (6). Similarly, individuals randomized to targeted smoking cessation therapy four weeks before and after surgery experienced a 49% reduced risk of postoperative complications following general and orthopedic surgical procedures (7). Shared pathophysiologic processes related to tobacco and alcohol abuse, such as altered or impaired angiogenesis, tissue perfusion, and oxygen delivery (8,9), may in part explain the common perioperative benefits associated with cessation of either substance.

Treatment modalities for muscle-invasive bladder cancer (MIBC) include radical surgery (i.e., radical cystectomy, RC), as well as radical transurethral resection (TURBT) combined with chemotherapy and radiation (i.e., bladder preservation therapy, BPT), depending on stage and other pathologic features, as well as a patient's fitness for surgery (10). However, despite increasing indications for BPT, RC remains the gold standard in surgical management of MIBC (11). With a mortality rate of 1–3%, and twice that at smaller institutions, and a greater than 60% 90-day complication rate associated with RC, perioperative optimization of modifiable risk factors is of utmost importance (12,13).

The effects of smoking cessation programs for lung cancer have been widely evaluated, and data suggests the diagnosis of a smoking-related cancer represents an important opportunity for intervention (14-16), yielding both immediate and long-term health benefits (17). Specifically, smoking cessation in patients with lung cancer was shown to positively affect perioperative outcomes (18), overall survival (19), response to secondary therapies (i.e., chemotherapy and radiation) (20,21), and overall quality of life (22). Fortunately, there are multiple established approaches to smoking cessation in lung cancer (17), which generally adhere to the principles outlined by the Agency in Healthcare Quality and Research's well-researched and thoughtful "Treating Tobacco Use and Dependence Guideline" (23). However, despite extensive study of cessation methods and knowledge of the benefits of smoking cessation, success is often elusive.

Perhaps with lung cancer more than any other tobacco-linked disease process, it is reasonable to presume that the connection between smoking and the disease is widely known due to warning labels on tobacco products. As a result, in 2018 the CDC reported that "Cigarette smoking among U.S. adults (aged ≥ 18 years) declined from 20.9% in 2005 to 15.5% in 2016." Yet despite this encouraging trend, nearly 38 million American adults smoked cigarettes ("every day" or "some days") in 2016 (24). Furthermore, even the most intensive interventions in smoking cessation in patients with lung cancer may fail 60% of the time (14). This underscores the disconnect between knowledge and action, and the complexity of continued tobacco use even in patients who have developed a disease they know to be directly related to smoking.

In facing such a challenge, knowledge of general and disease-specific motivations for continued tobacco use may maximize the likelihood of successful smoking cessation. As part of the STOP-OP study (stop smoking and alcohol drinking before operation for bladder cancer), an on-going multi-center randomized control trial (RCT) in Europe, Lauridsen *et al.* explored the implications of an intensive smoking and alcohol cessation program prior to RC and its effect on post-operative outcomes (25). While randomized as far as patient participation, blinding was not feasible due to intensive counseling and data collection. The investigators describe an interventional program in which they sought to better understand the patient perspective regarding their diagnosis and management of bladder cancer as it relates to their efforts in smoking and alcohol use cessation. The intent of STOP-OP was to explore a

patient-centered approach towards tobacco and alcohol cessation in the setting of bladder cancer. Unfortunately, results were mixed, even with intense counseling and just weeks of follow up. Specifically, of the eleven patients interviewed in this qualitative study (six of whom had been randomized to intensive smoking and alcohol cessation intervention), only five participants had stopped smoking or reduced alcohol intake at the time of the interview.

These data underscore the need to provide adequate support and long-term treatment follow-up if the benefits of long-term cessation are to be achieved, but also the high likelihood of failure even with resources that most urologists do not possess. Improved patient-oriented cessation programs and treatments are of the utmost importance; however, efforts must take place in an environment where adequate infrastructure to achieve successful intervention can be undertaken. It is unrealistic to expect the average physician, let alone a busy surgeon, to undertake the repeated personal engagement that these subjects experienced.

There are other limitations to this qualitative study, including the small number of participants (eleven), and limited patient demographics. Therefore, it is uncertain how easily such an approach would be implemented given the differences in health care systems, physician and nurse resources, and heterogeneous patient demographics in other care systems.

Perhaps the primary reason to remain guarded regarding the results of STOP-OP is prior experience with similar efforts in other disease processes. For example, a 2015 Cochrane review investigating the effectiveness of smoking cessation programs on patients diagnosed with lung cancer revealed a lack of RCT to support any such programs (26), and limited perioperative benefit was observed in a similar intervention prior to colorectal surgery (27).

The STOP-OP study, and the qualitative undertaking by Lauridsen *et al.*, brings to light several aspects of what inevitably needs to be a more thoroughly investigated subject both in bladder cancer and across multiple disease processes. To this end, these data may help guide further development of cessation resources that can be incorporated into urologic practice. If standardized programs become available, urology clinics may choose to institute a more dedicated screening, education, and/or cessation protocol for their patients. However, smoke-ending strategies with the highest likelihood of success have become complex, and it is unrealistic to expect urologists to master these strategies and remain current (28).

Implementation of limited smoking and alcohol cessation intervention into regular urology practice is plausible, although the likelihood of success with such interventions in isolation may be relatively low. While Lauridsen *et al.*'s qualitative analysis of STOP-OP study participants presents an interesting perspective on smoking and alcohol cessation and the perioperative implications of such interventions, much more work needs to be undertaken in order to ensure an effective, but realistic approach toward patient education and intervention is accomplished. The hazards of tobacco have been recognized for decades, but patients still continue to smoke in unfortunately large numbers. Urologists are not likely to have the resources to be the foundation of tobacco cessation interventions, but they can still play a key role in patient identification and guidance of their patients to resources that show they can work.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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