Epidemiology of the Small Renal Mass and the Treatment Disconnect Phenomenon

Robert M. Turner II, MD[a,*], Todd M. Morgan, MD[b], Bruce L. Jacobs, MD, MPH[c]

KEYWORDS

• Kidney cancer • Epidemiology • Incidence • Mortality • Treatment disconnect

KEY POINTS

- The incidence of kidney cancer has steadily increased over recent decades, with most new cases found when asymptomatic and small.
- Smoking, hypertension, and obesity are associated with an increased risk of kidney cancer.
- Despite earlier detection and increasing treatment, the morality rate of kidney cancer has not decreased.
- The treatment disconnect phenomenon in kidney cancer highlights a need to reduce overtreatment of small, indolent tumors.

INTRODUCTION

The epidemiology of kidney cancer has evolved in recent decades in response to the changing clinical presentation of the disease. Although historically associated with symptoms at presentation, fewer than 10% of renal cancers today present with the classic triad of hematuria, pain, and a palpable mass.[1] Most renal masses are now screen-detected as small, asymptomatic, incidental findings on imaging studies performed for unrelated reasons. As a consequence of the increased adoption of cross-sectional imaging, the incidence of renal cancer has increased and there has been a stage migration toward earlier stage tumors. The rising incidence of kidney cancer is also thought to be, in part, due to the rising prevalence of associated risk factors and 3 public health epidemics: smoking, hypertension, and obesity.

Although early detection and treatment of early-stage kidney cancer should theoretically result in improved survival outcomes, there has been an apparent rise in mortality rates over the past 20 years.[2,3] This paradox has held true even after accounting for stage and size migration. Termed treatment disconnect, this phenomenon has affected contemporary management and policy

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[a] Department of Urology, University of Pittsburgh Medical Center, Mercy Professional Building, 1350 Centre Avenue, Suite G100A, Pittsburgh, PA 15219, USA; [b] Department of Urology, University of Michigan, 1500 E. Medical Center Drive, CCC 7308, Ann Arbor, MI 48109, USA; [c] Department of Urology, University of Pittsburgh Medical Center, Shadyside Medical Building, 5200 Centre Avenue, Suite 209, Pittsburgh, PA 15232, USA
* Corresponding author.
E-mail address: turnerrm@upmc.edu

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perspectives related to kidney cancer. This article reviews the changing epidemiology of kidney cancer, public health epidemics associated with its rising incidence, potential explanations for the treatment disconnect phenomenon, and their implications on public policy.

RISK FACTORS

Smoking

Tobacco smoke is the most common human carcinogen and is noted to be the predominant risk factor in 20% to 25% of renal cell carcinoma cases.[4] It is estimated that there were more than 1 billion smokers worldwide in 2015.[5] In a recent meta-analysis of 109 case-control studies and 37 cohort studies, the risk of developing renal cell carcinoma was higher for current smokers (relative risk [RR] 1.36, 95% CI 1.19–1.56) and former smokers (RR 1.16, 95% CI 1.08–1.25) compared with nonsmokers.[6] The association between smoking and kidney cancer seems to be slightly greater in men than woman, and there seems to be a dose-related effect, with greater risk noted in those who smoke more than 20 cigarettes per day compared with fewer than 10 per day.[7] The role of secondhand smoke exposure is unknown.[6]

Importantly, smoking cessation may mitigate the risk of kidney cancer.[7] In a population-based case-control study in Iowa, there was an inverse linear relationship between the risk of renal cell carcinoma and the number of years after cessation of smoking.[8] Additionally, those with a distant (30 or more years prior) tobacco history experienced a 50% reduction in risk compared with current smokers (odds ratio [OR] 0.5, 95% CI 0.4–0.8).

Hypertension

Hypertension is another well-known and potentially modifiable risk factor for the development of kidney cancer. A recent longitudinal study of 156,774 women enrolled in the Women's Health Initiative (WHI) observational study and clinical trial demonstrated an excess risk of kidney cancer with increasing systolic blood pressure levels, a relationship that persisted after adjustment for age, smoking, race, and body mass index (BMI) (**Table 1**).[9] An elevated diastolic blood pressure (≥90 mm Hg) was also independently associated with kidney cancer. Similar relationships have been observed in men as well.[10,11] Furthermore, the duration of hypertension seems to be closely associated with development of kidney cancer.[12] Although some evidence suggests that controlling blood pressure can help lower renal cancer risk, the role of hypertensive drug therapy in reducing this risk is unclear.[13,14]

Table 1
Cox regression of kidney cancer incidence with a model combining body mass index and blood pressure in the Women's Health Initiative Studies

Variables	Hazard Ratio (95% CI)
Age	1.03 (1.01–1.04)
Body mass index (kg/m^2)	
18.5–24.9	Reference
25–29.9	1.28 (1–1.65)
30–34.9	1.39 (1.04–1.86)
35–39.9	1.79 (1.24–2.58)
40 or more	2.30 (1.49–3.54)
Smoking	
No	Reference
Yes	1.62 (1.15–2.28)
Systolic blood pressure (mm Hg)	
120.0 or less	Reference
120.1–130.0	1.33 (1.01–1.75)
130.1–140.0	1.24 (0.92–1.67)
140.1–150.0	1.93 (1.42–2.63)
150.1–160.0	1.48 (0.97–2.26)
160.0 or more	1.54 (0.96–2.25)
Diabetes	
No	Reference
Yes	0.97 (0.65–1.45)

Multivariable model adjusted for age, race or ethnicity, BMI, smoking, systolic blood pressure, and diabetes.

Data from Sanfilippo KM, McTigue KM, Fidler CJ, et al. Hypertension and obesity and the risk of kidney cancer in 2 large cohorts of US men and women. Hypertension 2014;63(5):934–41.

Hypertension is more prevalent among blacks than whites and is thought to play a role in the racial disparity of renal cancer incidence. Data from the National Health and Nutrition Examination Survey (NHANES) between 1999 and 2004 showed age-adjusted prevalences of 39% and 28% for black and white men, respectively; and 41% and 27% for black and white women, respectively.[15] In an updated analysis of data through 2012, the prevalence of hypertension remained greater in blacks than whites (OR 1.86, 95% CI 1.64–2.12).

The association between hypertension and kidney cancer also seems to be stronger in blacks than whites. In a population-based case-control study from 2002 to 2007, renal cancer risk increased with increasing time since the diagnosis of hypertension, with a greater effect in blacks.[13] A similar pattern was observed for decreasing levels