

# Gender-Related Approach to Kidney Cancer **Francesca Carolina\***

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**Citation:** Carolina F (2023) Gender-Related Approach to Kidney Cancer. Archives Can Res, Vol.11 No. 2: 109.

## Abstract

Different non-reproductive cancer forms have been linked to sex and gender discrepancies. Males have a greater mortality rate and are two times more likely than females to acquire kidney cancer. Examining genetics and genomes, together with additional risk factors including hypertension and obesity, lifestyle choices, and female sex hormones, can help explain these discrepancies. Understanding the hormonal signalling pathways can help us understand the distinctions between the sexes better. At the diagnostic, histological, and therapeutic levels, there are gender and sex-based discrepancies that can be seen, and these differences can significantly affect the result. The current understanding of disparities in the clinical presentation of kidney cancer patients based on sex and gender is summarised in this review, along with potential scientific explanations for these findings. The advancement of sex-specific prognostic and diagnostic tools as well as individualised therapy may be facilitated by underlying sex-based distinctions.

Men are diagnosed with kidney cancer more commonly than women are, and they also have more aggressive histologies, larger tumours, higher grades and stages, and worse oncological outcomes. The use of sex steroid hormones and smoking appear to play a part in the explanation of these gender differences. A further factor affecting the gender-related response to oncological therapy, such as anti-angiogenic medicines and immunotherapy, is the expression of genes implicated in tumour growth and immune response in kidney cancer. This report summarises recent developments in our understanding of the molecular and genetic pathways behind kidney cancer, which may help to explain some of the gender discrepancies. Other crucial processes, meanwhile, that fully explain the startling clinical gender-related disparities in kidney cancer are now unknown. The most pertinent articles on the link between gender and kidney cancer were reviewed and summarised. Bench and clinical studies on gender-related signs and inequalities, as well as their effects on the clinical therapy of kidney cancer, should be advanced.

**Keywords:** Sex and gender; Kidney cancer; Outcomes; Renal Cell Carcinoma, Hormones Profile and Inflammation; Sex-specific disease biomarkers; Drug response and resistance

**Received:** 30-Jan-2023, Manuscript No. ipacr-23-13453; **Editor assigned:** 01-Feb-2023, Preqc No. PQ- ipacr-23-13453; **Reviewed:** 15-Feb-2023, QC No ipacr-23-13453; **Revised:** 20-Feb-2023, Manuscript No. ipacr-23-13452 (R); **Published:** 27-Feb-2023, DOI: 10.36648/2254-6081-11.2-152

## Introduction

The terms "sex" and "gender" are frequently used interchangeably, which has led to misunderstandings and misperceptions in recent years. As defined by the World Health Organization, we shall refer to biological and physiological traits in this review as "sex," and socially produced qualities as "gender" (WHO). For a large number of malignancies, sex-related variations in incidence and death have been documented. Males have a higher incidence

and worse survival outcomes than females for the majority of cancer sites, including the bladder, kidney, colorectum, liver, oesophagus, head and neck, brain, skin, and blood, according to an analysis of the United States Cancer Statistics (USCS) public use database from 2001 to 2016. However, despite the fact that cancer professionals are urging greater focus and research, gender is frequently ignored in the therapeutic care of patients.

Kidney cancer accounts for 5% and 3% of all new cases globally,

respectively, and is the sixth most common cancer in men and the tenth most common disease in women. With a male to female incidence ratio of 2.0, it ranks behind head and neck, oesophagus, bladder, and liver as the fifth non-reproductive cancer. The sex-based variations in cancer incidence will be covered first in this review, followed by their effects on genetics and genomes as well as the risk factors that cause them. Then, in order to address the sex discrepancy problem, we will look at the hormone signalling pathways in kidney cancer. Then, we'll look at the surgical, oncological, and functional outcomes for tumours in male and female patients as well as their features, therapy, and prevention. Finally, we will talk about how the clinical care of kidney cancer patients should place a strong emphasis on sex-related specificities.

A common malignant tumour that makes up around 5% of all cancer cases is kidney cancer. Males are twice as likely as females to acquire kidney cancer, while it can afflict either gender. Evidence suggests that the cause of this gap is a result of the patient's diseases or genetic abnormalities. The clinical features of the tumours then mirror this, with men having bigger, more aggressive tumours. For doctors to be able to provide patients with tailored medicine that would better meet their requirements in terms of prevention, diagnosis, and treatment, it is crucial to understand the sex- and gender-based distinctions in kidney cancer.

A collection of cancers that begin in the kidney is referred to as renal cancer or kidney cancer. Back pain, a bulge in the abdomen, and blood in the urine are just a few symptoms. Other symptoms include fatigue, weight loss, and fever. It is possible for complications to move to the brain or lungs. Renal cell cancer (RCC), transitional cell cancer (TCC), and Wilms tumour are the three main kinds of kidney cancer. About 80% of kidney malignancies are RCC, and the majority of the remainder are TCC. [8] Smoking, using certain painkillers, having had bladder cancer in the past, being overweight, having high blood pressure, using certain chemicals, and having a family history are risk factors for RCC and TCC. Family histories of the condition as well as specific genetic diseases like WAGR syndrome are risk factors for Wilms' tumour. On the basis of symptoms, urine testing, and diagnostic imaging, a diagnosis may be suspected. By tissue biopsy, it is verified [1-5].

Surgery, radiation therapy, chemotherapy, immunotherapy, and targeted therapy are all possible forms of treatment. In 2018, kidney cancer killed 175,000 people worldwide and affected 403,300 new cases. Normal onset occurs after the age of 45. Males are more frequently impacted than females. In the United States, 75% of people survive five years, compared to 71% in Canada, 70% in China, and 60% in Europe. The five-year survival rate for kidney-confined cancer is 93%, 70% for cancer that has migrated to nearby lymph nodes, and 12% for cancer that has spread broadly. The 13th most prevalent type of cancer, kidney cancer accounts for 2% of all cancer cases and fatalities worldwide. Since 1930, the prevalence of kidney cancer has risen steadily. Urban populations are more likely than rural ones to experience renal cancer.

## RCC Epidemiology and Gender

According to epidemiological research, men have a two-fold higher lifetime chance of having kidney cancer than women. A 2:1 male/female case incidence ratio that was consistent by age, year, and area was found in an examination of global cancer incidence statistics for the years 1978–2007. According to an investigation of the Surveillance, Epidemiology and End Results (SEER) database covering the years 2001 to 2016, males had a rate that was equivalent to females' but had an age-adjusted incidence rate that was twice as high. Between 1990 and 2013, the age-standardized incidence of kidney cancer increased by 23.04% globally, with a 31.19% rise in males and an 8.79% increase in females, according to data from global vital registries. The anticipated age-standardized incidence rates for kidney cancer worldwide in 2020 were 4.6 for both sexes, 6.1 for men and 3.2 for women, according to the Global Cancer Observatory: CANCER TODAY. For the years 2013 to 2017, the American Cancer Society's Cancer Statistics Center reported incidence rates of 16.9 for both sexes, 22.9 for men and 11.7 for women (average annual rate per 100,000, age adjusted to the US standard population of 2000). The European Cancer Information System recorded incidence rates for 2020 for Europe of 18.4 for both sexes, 25.9 for men and 12.5 for women (average annual rate per 100,000, age adjusted).

Males are more likely than females to have RCC. Men showed a 1.85-fold higher incidence of RCC than women in a recent retrospective research by Gelfond et al. RCC, however, displayed the least variation in the male to female sex ratio globally over the previous 30 years when compared to other solid tumours. Since the male to female incidence ratio of RCC is 2:1 and remains steady with age throughout time, sociocultural factors and health-related behaviours (such as smoking, hypertension, and obesity) are not the only causes of this discrepancy. The incidence of RCC is two times higher in men than in women between the ages of 40 and 60, according to some studies, albeit this difference tends to gradually vanish by the age of 70. In addition, women tend to be considerably older than men at the time of diagnosis (3 years, median). These findings point to a potential early protective role for female hormones like oestrogen [6-10].

It has been acknowledged that hypertension, which is more prevalent in males than in women, is a modifiable risk factor for RCC. Men with hypertension are 1.32 times more likely than women to develop RCC. However, it seems that females are more severely affected by hypertension's effects on RCC formation. Regarding additional risk factors, men are more likely than women to smoke cigarettes, a recognised carcinogen. However, there is no discernible variation in how body mass index (BMI) affects the incidence of RCC according to gender. According to a recent retrospective study by Lotan et al., there is a population that is very susceptible to RCC and should be screened. Males over 60, current smokers, and obese people made up this group.

The heritability of kidney cancer is believed to be approximately 38%, indicating that genetics is a significant driver of kidney carcinogenesis. People with a family history of cancer are more likely to get kidney cancer. Genetic sexual dimorphisms are absent in the vast majority of hereditary and sporadic kidney tumours,

nevertheless. Angiomyolipomas are the usual lesions and are more common in females with tuberous sclerosis complex (mutation in TSC1, 9q34.13 or TSC2, 16p13.3). Angiomyolipomas commonly exhibit loss of heterozygosity in TSC2 or TSC1 from a genetic perspective. Renal cell carcinoma (RCC), which mostly affects females, develops in less than 5% of tuberous sclerosis complex individuals. The primary histotype of kidney cancer is papillary RCC (pRCC), type 1 in hereditary papillary renal carcinoma and type 2 in hereditary leiomyomatosis and renal cell cancer (mutation in fumarate hydratase, FH, 1q43). Hereditary papillary renal cancer has a 2.4:1 male to female ratio; however it is yet unclear what causes this variation. Although symptomatic uterine tumours usually lead to the diagnosis of renal cell carcinoma and inherited leiomyomatosis, there is little information available regarding the sex predominance of RCC in this disease. It's interesting to note that post-gynecological surgery, such as a hysterectomy, which has been linked to a higher risk of kidney cancer, increases lipid peroxidation, which can lead to DNA damage and encourage mutations in tumour suppressor and protooncogene genes.

## Discussion

Renal cell carcinoma (RCC) accounts for between two and three percent of all cancers, has a higher prevalence in Western nations, and accounts for 5% of cancers in men and 3% in women. The incidence of RCC has increased globally over the past 20 years by roughly 2%, with Africa and Asia having the lowest rates. In the European Union in 2012, there were 34,700 RCC-related fatalities and about 84,400 new cases of RCC. RCC incidence has been revealed to have increased 2.1-fold between 1990 and 2013, despite the fact that there aren't any suggestions for a routine RCC screening at the moment. This might be the outcome of more frequently discovering localised RCC due to advancements

in imaging techniques. There are gender-related differences that have been linked to RCC surgical, functional, and oncological outcomes as well as tumour features. This study reviews the most recent and clinically applicable discoveries on this subject.

## Conclusion

Men typically have a more advanced disease at the time of diagnosis and are at a higher risk of developing RCC. In comparison to men, women are more likely to have favourable histological RCC subtypes, better oncological outcomes, and benign histology after NSS. Contrarily, the female gender appears to be associated with a worse response to therapy and a shorter survival in the context of metastatic RCC. However, it is important to note that the majority of the data come from studies that were published in the developed world. It is conceivable that in nations where women have less access to medical care, including computed tomography or ultrasonography, they would be more likely to be diagnosed with RCC at an advanced stage than men. This may be especially true in nations where women's civic rights and freedoms are restricted, given that RCC frequently has no symptoms at all.

The biochemical, genetic, and molecular mechanisms that account for the gender-specific variations in RCC are currently not fully understood. The possibility of incorporating gender characteristics in risk-predictive nomograms may arise from a greater understanding of gender-related mechanisms, a process that is now under way. In order to get toward gender-specific, individualised therapy options for patients, efforts should be made to speed up progress in bench and clinical research on the gender impact in kidney cancer.

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