



## EPIDEMIOLOGY AND FACTORS CONTRIBUTING TO THE OCCURRENCE OF RENAL PARENCHYMAL TUMORS

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**Summary:** Renal cancers represent 2-3% of the total number of carcinomas. Renal cancer occupies the third position among all tumors of the urinary tract following prostatic carcinoma and urinary bladder tumors. There are great geographic differences and incidence ranges from 1 to 20 in various countries. Kidney cancer is more frequent in urban population. The sex ratio is two males/one female. The increase in renal cancer incidence may be related to predisposing factors.

**Key words:** *Renal parenchymal tumors, epidemiology, predisposing factors*

### Introduction

Renal cancers represent 2 to 3% of the total number of carcinomas (Table 1). Renal cancer occupies the third position among all tumors of the urinary tract following prostatic carcinoma and urinary bladder tumors. The total incidence in Europe is 5.4 - 20 per 100 000 men and 3.3 - 11.1 per 100 000 women (Table 2) (15, 20).

There are great geographic differences and the incidence ranges from 1 to 20 in various countries. Kidney cancer is more frequent in urban population of North America, of Scandinavian countries and in Western Europe, where the incidence ranges from 5 to 12 per 100 000 inhabitants (Table 2).

The incidence of renal cancer is small in Asia, in Eastern Europe, in Japan and Israel (1 to 5/100 000) (21, 32).

The average age is 62 years (according to the questionnaire of the French Association of Urologists in 1994: 83% of patients are older than 50) (7).

The sex ratio is two males/one female (26).

In 1995, in France, there were 4 910 newly diagnosed cases of renal cancer and 3060 lethal outcomes during that year (Table 3) (1,3).

This corresponds to the global incidence (which was not corrected as to age) of 11.9/100 000 males and 5.5/100 000 females.

The renal cancer incidence varies depending on the sex and climate, keeping in mind the age (application of standardized rates).

In Europe, the average incidence is 12.2 per 100 000 males and 5.5 per 100 000 females.

The renal cancer incidence in France corresponds to the average European incidence.

Countries with low incidence, for males between 5 and 7 per 100 000, are Portugal, Greece and Spain.

In countries with the greatest incidence, for males is higher than 15 new cases per population of 100 000 per year in Finland, Germany and Austria (Table 2) (13, 14,15, 28).

The Cancer Register in the USA in 1996 registered 36 000 newly diagnosed cases of renal cancer and 12 000 lethal outcomes (32). It is estimated that the number of lethal outcomes due to renal cancer in the world will be 100 000 in the year of 2000.

### Increased incidence of renal cancer after 1970

The global incidence of "all cancers" increases as the years pass by. The International Center for the Fight Against Cancer follows the incidence of cancer since 1975 in 24 countries and registered the incidence increase of 20% since 1980 until 1985 (10, 32). Out of these 20%, 9% accounts for population growth and prolonged life span, and the remaining 11% are explained by the methodology differences during the time period and/or by real increases of the risks for renal cancer occurrence.

According to the study of Menegoz, the renal cancer incidence in males in France has progressed for 20 years from 7.8 to 12.2 per 100 000 inhabitants (27).

In the USA the number of renal cancer increased for 38% since 1974 to 1990 (20). At the same time the survival rate shows favorable trends, from 52% in 1974 to 58% in 1990 (20).

The increase of renal cancer incidence may be related

to predisposing factors such as obesity, exposure to some heavy metals, smoking, etc.

Table 1. Cancers in France: new cases in 1995 (34)

Males		Females	
Prostate	26474	Breast	33867
Lungs	18713	Colon-rectum	15298
ENT	18107	Uterus	7917
Urinary bladder	7815	Ovary	3150
Stomach	4571	Lungs	3137
Esophagus	4171	Lymphoma	2966
Larynx	4044	Stomach	2742
Lymphoma	3791	Urinary bladder	2290
Liver	3536	CNS	1986
Kidney	3305	Kidney	1605
Total	134729	Total	105058

Table 2. Incidence rate and number of renal cancer cases in Europe in 1990 (15).

	Incidence (Rate per 100 000 adjusted for European population)		Total number of cases
	Males	Females	
	Portugal	5.4	
Greece	5.9	2.1	463
Spain	7.5	2.6	2 000
Ireland	8.4	3.7	185
G.Britain	9.8	4.5	4589
Italy	11.4	4.3	5026
Belgium	11.8	6.7	1017
France	12.3	4.9	5164
Denmark	12.7	7.9	623
Luxembourg	12.9	6.2	38
Holland	14.6	7.4	1617
Sweden	14.7	8.8	1287
Finland	16.8	9.0	661
Germany	17.3	7.7	10840
Austria	20.0	11.1	1324
European countries	12.2	5.5	35264

Table 3. Incidence rate per 100 000 cases (European standard) and the number of new renal cancer cases in France in 1975, 1985 and 1995 (27)

	Males			Females		
	1975	1985	1995	1975	1985	1995
Incidence						
- rate	7.8	10.3	12.2	4.1	4.4	4.8
- No.of cases	1909	2606	3305	1306	1412	1605
Mortality						
- rate	5.1	6.5	6.7	2.4	2.7	2.8
- No. of cases	1204	1716	1906	816	1018	1154

### Predisposing factors

Factors, which relate to the patient himself or his environments, are defined in several international epidemiology questionnaires.

#### A - The patients

The patient presents a risk for the occurrence of

renal cancer in 5 situations: patient who is on hemodialysis and has multicystic renal dysplasia, patient who had renal transplantation, patient who originates from "family with risk" (von Hippel Lindau, phacomatoses), obese patients and patient with hypertension.

1. The patient on hemodialysis who has multicystic renal dysplasia, renal cancer in such a case has its features: it occurs in early age (around 45), depends on the period the patients spent on dialysis (80% of cases occur after 3 years), the incidence is higher than in the general population, males predominate (7/1), multicentric tumors are registered in one out of two cases, bilaterally is present in 9% of cases, according to pathohistological analysis, tubulo papillary cancers are predominant (3,4,5,18,19,25).

2. Carcinoma of the patient's own kidney in patients who had renal transplantation

During the follow-up of 129 patients who had renal transplantation 5 carcinomas of the patient's own kidney were detected. No predisposing factor was determined (no effect of dialysis effect, time of renal transplantation, the type of immunosuppressive therapy) (12). The prevalence of cancer of patient's own kidneys ranges according to some studies from 0.04% to 3.9% (12, 17, 24, 27).

3. Family diseases

a. Von Hippel-Lindau disease, phacomatoses with dominant autosomal transmission is characterized by polymorphous and multifocal tumor evolution; heman-gioblastoma of the central nervous system and the retina, cysts and kidney cancer, pheochromocytomas, pancreatic cysts and tumors. This disease occurs in one case per 36 000 newborns.

The disease is related to the loss of the short arm of chromosome 3. This corresponds to the loss of suppressor gene VHL (positioned in the 3 p 25-26). Renal cancer occurs in 25-45% of cases. It is characterized by multicentricity, bilaterality, early occurrence (average age 42), cause of death and one predominant histologic type (clear cell carcinoma).

b) Other phacomatoses

- tuberous sclerosis (Bourneville) (31)
- Sturge-Weber's syndrome

4. Obese patients

The influence of diet on the occurrence renal carcinoma was studied in recent multidisciplinary studies (23, 35, 39, 54); 1985 patients with renal cancer were compared with 1526 cases that represented the control group.

The following results were obtained:

- total energetic intake represents a relative risk (as a predisposing factor) of 1.7 (1.4 to 2.2). Increased risk of 72% was found in overweight individuals in relation to slim persons (33). According to Mellegaard, body weight is the basic favorable factor in females, with a relative risk, which is three times higher in overweight

females. Beside this, the rate of weight gain (kg/age) seems to be a special risk factor in females (35);

- protein and lipid intake present two possible risk factors. As a rule, they depend on the total intake of calories (33).

Meat, milk and fats are not independent risk factors for the occurrence of renal cancer.

There is also a protective effect of fruits and of most vegetables with prominent effect of oranges and green vegetables (33).

As to vitamins and oligoelements, small intake of vitamin E and magnesium increases the risk of renal cancer occurrence.

Coffee is one of risk factors for the occurrence of renal cancer in females (relative risk 1.7). Wolk did not find a connection between alcoholism and occurrence of renal cancer (53). Some studies even indicate that there is a protective effect alcohol drinking individuals, especially if it is the red wine.

Table 4. Diet and risk of renal cancer occurrence (14)

Energy or food	RISK DISTRIBUTION			
	1	2	3	4
Calories	1	1.38	1.53	1.74
Proteins	1	1.20	1.15	1.18
Total lipids	1	1.08	1.29	1.16
Monosaturated fats	1	1.14	1.28	1.06
Polyunsaturated fats	1	0.87	0.86	0.87
Vitamin E	1	0.85	0.85	0.90
Magnesium	1	0.76	0.70	0.79
Milk-yogurt	4	1.04	0.96	1.27
Vegetables	1	1.18	0.99	0.81
Oranges and green vegetables	1	0.96	1.06	0.70

For other cancers (colon, rectum, breast, prostate) predisposing factors may be excessive intake of calories, wrong diets, overweight, cellulose poor diet (14).

The collection of these dietetic mistakes in western countries is the basis for prevention of all cancers (13, 26).

### 5. Patients with hypertension

There is a relation between arterial hypertension and body mass (7, 33). Arterial hypertension cannot be an independent risk factor. However, there is an interaction between the body mass index and arterial hypertension (8) and in those conditions, the relative risk is 1.9 in males and 3.2 in females.

#### B - Environment

##### 1. Professional environment

In 1995 Mandel published an international study with a control group with the aim to define the existing risk factors according to the type of patient's profession: the study group included 4 000 patients and the control group included 2 300 individuals.

There are environmental risk factors related to patient's profession (27, 29, 34). Various professional risks are as follows:

- work with blast furnaces or in industry using coke ovens (30). All those workers carry a relative risk of 1.7
- ferrous metallurgy 1.6
- exposure to asbestos (28) 1.4
- exposure to cadmium 2.0
- exposure to oil derivatives 1.6

##### 2. Hormonal status

Several elements influence the opinion that hormonal status plays a role in the genesis of renal cancer: lower incidence in females, existence of hormonal receptors in normal kidneys as well as in kidneys with cancer, renal cancer induction by estrogens.

Libland made a study on 1 500 patients. The patients who underwent hysterectomy with omentectomy carry a greater risk (6, 24).

Other factors seem as "protectors": advanced age in females at delivery of first child, onset of menstrual cycle after the age of 13, use of oral contraceptives in females who are not smokers (relative risk is 0.5 per 1 in women who never used oral contraceptives).

##### 3. Toxins

Tobacco and certain analgetics are risk factors, which were verified in cases of tumors of the urothelium. It seems that tobacco is the only cancerogenic factor for the renal parenchyma.

###### a) Tobacco

Epidemiological studies indicated that the incidence of renal cancer is doubled in females (8, 22, 29).

The study of Muscat on 1 500 cases, out of which 779 were controls, confirms that the risk is doubled only in males (5). In females there is not risk factor regardless of the type of cigarettes, whether they are filter cigarettes or not, and regardless of the quantity of cigarettes smoked for one year (25). Smokers who smoke filter cigarettes carry the same risk as the control group.

Individuals who chew tobacco are exposed to a relative risk of 3.2 (29).

What is expected in the coming years is to influence the public to stop smoking because tobacco is responsible for 3/4 of lung cancer cases, 2/3 of ENT cancer cases, 1/3 of esophageal cancer and of numerous other cancers, such as pancreatic cancer, urinary bladder or renal cancer (12, 23).

###### b) Analgetics

Phenacetin and other analgetics were the subject of study in order to determine their possible responsibility for the occurrence of renal cancer (31, 32). It seems that none of the analgetics cause renal cancer, regardless of their quantity or duration of administration. Even aspirin is not at all related to renal cancer (32). However, when all studies related to this topic are taken into account, these epidemiological data represent the results of studies, which are delicate for interpretation.

Other factors, such as urinary infection, renal lithiasis or diabetes were not taken into account for the estimation of the occurrence of renal cancer.

## Renal cancer

According to the results of the national epidemiological study in France, which included 970 patients with renal cancer during the period 1993-1994 (9) we may point out the following results:

The average age of the patients was 62 years.

The sex distribution was 2 males/1 female.

The rate of cancer detection was 40% (these tumors were intracapsular in 80%).

Radical nephrectomy was performed in 90% of cases. Conservative surgery was performed in 7% of cases. Medicaments therapy was administered in 5% of cases.

The distribution of tumor according to stage was: pT1 - 8%, pT2 - 53%, pT3 - 21%, pT3b - 18%.

The invasion of lymph nodes was registered in 12% of cases.

Visceral metastases were found in 6% of cases.

Clear cell carcinoma dominates in the histological structure (26).

The average size of the tumors was 6.4 cm. The tumor mass was larger in patients who had symptoms and in those patients with poor prognosis (invasion of the adrenals, invasion of the vena cava inferior, visceral metastases or lymph node metastases). The invasion of the adrenal gland as well as the invasion of the vena cava inferior were registered in 4% of cases.

Multicentricity of the tumors was observed in 14% of cases. The size and the type of cells did not effect the multicentricity.

Tumor grade was analyzed in 66% of cases. It was in correlation with the invasion of the perirenal fatty tissue and invasion of the lymph nodes. This French epidemiological questionnaire enabled to detect 20% of new renal cancer cases in 1994.

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## **EPIDEMIOLOGIJA I FAVORIZIRAJUĆI FAKTORI U NASTANKU TUMORA BUBREŽNOG PARENHIMA**

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*Kratak sadržaj: Karcinom bubrega čini 2–3% svih karcinoma. Po učestalosti među tumorima urogenitalnog sistema nalazi se na trećem mestu, posle karcinoma prostate i mokraćne bešike. Dva puta je češći kod muškaraca. Incidenca karcinoma bubrega varira u zavisnosti od pola i podneblja imajući u vidu starosnu dob. U radu autor, koristeći najnovije reference, analizira epidemiologiju i faktore rizika u nastanku karcinoma bubrežnog parenhima.*

*Ključne reči: Karcinom bubrežnog parenhima, epidemiologija, predisponirajući faktori*

*Received: December 30, 1998*