LIFESTYLE RISK FACTORS IN THE DEVELOPMENT OF KIDNEY CANCER: A RUSSIAN EXPERIENCE

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STIL ŽIVOTA KAO FAKTOR RIZIKA ZA NASTANAK KARCINOMA BUBREGA: ISKUSTVA IZ RUSIJE

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ABSTRACT

The objective of our study was the evaluation of major lifestyle risk factors for the development of renal cell carcinoma (RCC) and the assessment of chances of developing this disease among inhabitants in the region, in the presence of and with combinations of the studied risk factors. Risk factors for developing RCC that are associated with lifestyle (smoking, obesity and hypertension) were observed in 500 patients with RCC aged 30-64 years who were investigated at the Krasnoyarsk Oncology Dispensary (study group) and 858 participants in the Krai (control group). The results of our study showed that smoking increases the risk of developing RCC 2.9 times and arterial hypertension 3.3 times in men; in women, obesity and hypertension increased these risks 2.6 and 3.2 times, respectively. All three risk factors were combined in 13.6% of men and in 8.4% of women with RCC. Our data may be useful for the prevention, development of screening programmes and early diagnosis of RCC.

Keywords: *risk factors, renal cell carcinoma, kidney cancer, smoking, obesity, arterial hypertension*

SAŽETAK

Cilj ovog istraživanja bio je evaluacija najznačajnijih faktora rizika koji potiču od stila života na razvoj karcinoma bubrežnih ćelija (KBĆ) i procena šanse za razvoj bolesti u regionu, u zavisnosti od prisutnosti ispitivanih faktora rizika. Faktori rizika za razvoj karcinoma bubrežnih ćelija koji su povezani sa stilom života (upotreba nikotina, gojaznost i hipertenzija) su posmatrani kod 500 pacijenata obolelih od karcinoma bubrežnih ćelija starosti 30-64 godina u Onkološkoj klinici Krasnojark (eksperimentalna grupa) i 858 ispitanika u kontrolnoj grupi u Krai. Rezultati studije su pokazali da upotreba nikotina 2,9 puta, dok hipertenzija 3,3 puta povećava rizik za razvoj karcinoma bubrežnih ćelija kod muškaraca; sa druge strane kod žena gojaznost i hipertenzija povećavaju ovaj rizik za 2,6 i 3,2 puta. Sva tri faktora rizika su bila prisutna kod 13,6% muškaraca i 8,4% žena sa karcinomom bubrežnih ćelija. Ovi podaci mogu biti od koristi za prevenciju bolesti, razvoj programa za skrining i ranu dijagnozu karcinoma bubrežnih ćelija.

Ključne reči: *faktori rizika, karcinom bubrežnih ćelija, karcinom bubrega, upotreba nikotina, gojaznost i hipertenzija*

INTRODUCTION

Renal cell carcinoma (RCC) is a multifactorial disease. Approximately 100 risk factors for the development of this malignant neoplasm have been described in the literature (1). However, in accordance with principles of evidence-based medicine, only three of these factors have been confirmed in large non-randomized, well-planned controlled trials (level of evidence: 2a): smoking, obesity and arterial hypertension (2). Smoking is a risk factor for development of RCC, as proven by the International Agency for Research on Cancer (3, 4). A large meta-analysis conducted in 24 centres showed that compared with non-smokers, there is a greater risk of developing RCC in ever-smokers. The risk of developing this SNR increases in proportion to the number of cigarettes smoked per day. Compared to those who never smoked, people who smoke more than 20 cigarettes a day increase the risk of developing RCC by 60-100%. The risk of developing RCC decreases only 10 years after quitting smoking (5). On the other hand, regarding excess body weight, the relationship between increase in body mass index (BMI) and risk of RCC development has been proven, and this risk is more pronounced in women than in men and depends on the degree of obesity. Thus, for every 5 unit (kg/m²) increase in BMI, the risk of developing RCC increases by 24% in men and 34% in women (6, 7). The mechanism of this effect is associated with chronic hypoxia, insulin resistance development in tissues and compensatory hyperinsulinaemia, endocrine status changes with hyperproduction of adipokines, oestrogen,

growth factors, immune response changes and cholesterol metabolism, increased lipid peroxidation and oxidative stress (8, 9). The association of arterial hypertension (AH) and the means used for its treatment, with the development of RCC, has been established in a number of epidemiological studies (10-12). The biological mechanism of this connection is not fully understood but is most likely associated with chronic renal hypoxia, lipid peroxidation, and formation of free radicals (13, 14). The risk of RCC in patients with AH is increased by 60% according to one author (11), and another group of researchers (12) found a 24% increase in risk in women and 15% in men. To date, the role of antihypertensive drugs in the development of RCC has not been determined, but it has been established that controlled BP reduces the risk of developing RCC (11, 12).

The aim of the study was to examine the major lifestyle risk factors for the development of RCC and to evaluate the chances of developing this disease among inhabitants of the region in the presence and combination of studied risk factors.

MATERIALS AND METHODS

The three major lifestyle-associated risk factors (smoking, obesity and hypertension) for the development of RCC were studied in 500 patients with RCC, age range 30-64 years old, at the Krasnoyarsk oncological dispensary (study group) and in 858 participants of the Krasnoyarsk Territory (control group). Study participants were from similar sex and age groups from a study of the main behavioural risk factors for the development of chronic non-communicable diseases within the framework of the targeted programme 'Prevention and control of socially significant diseases' (15). Evaluation of smoking-related indicators was carried out on the basis of questionnaire, which included questions about the existence of bad habits, quality of tobacco products, smoking experience and the number of cigarettes smoked per day. These questions are used in most major sociological studies on tobacco consumption in our region, Russia, Europe and the United States (5, 16, 17).

Body weight estimation was carried out using body mass index (BMI), developed by Quetelet *et al.,* and calculated by the formula (m=body weight in kg; h=growth in metres):

$$I = \frac{m}{h^2}$$

Interpretation of BMI values was carried out in accordance with WHO recommendations (18).

Arterial hypertension (AH) was observed in patients with RCC and study participants who had a history of hypertension, or a persistent increase in blood pressure values of more than 140/90 mm Hg (19).

Statistical analyses

All data are presented as frequency in percent (%). To assess the risk of developing RCC in the presence of a number of predisposing factors, odds ratios (ORs) were calculated with 95% confidence intervals (95% CI). In each case, confidence intervals were calculated for the OR. The chances were considered statistically significant if the unit did not fall within the confidence interval.

RESULTS

Smoking

Among the study group patients, 245 (49.0%) were identified as smokers, and of these, there were 211 men (73.8%) and 34 women (15.9%). In the control group (regional population), 285 (33.2%) were smokers, including 208 men (49.2%) and 77 women (17.7%). The data obtained indicate a statistically significant (p<0.05) prevalence of smoking among patients with RCC. This predominance is formed mainly by male smokers in the study group (smoking rate was 1.5 times higher than in the control group men). For females, there were no significant differences in smoking rates in the compared groups. Age-specific analysis of the prevalence of smoking in the compared groups revealed a significant predominance of smokers among men in the study group. Additionally, compared to the control group, among men with RCC in the age groups 35-39, 45-49, 50-54, 55-59, and 60-64 years and women aged 35-39 years, the prevalence of smoking was significant (p<0.05) (Figure 1).

Regarding the quality of tobacco products used by patients with RCC, it was found that most of the patients who used tobacco smoked cigarettes: men 65.4%, women 70.6%; 3.3% of men and 0% of women smoked cigarettes; 2.8% of men and 0% of women smoked cigarettes; other kinds of tobacco products were used by 6.6% of men and 5.9% of women.

Among the control group, the majority of smokers had a smoking history of up to 10 years, and among those in the study group, the smoking history was 20-29 years. In this case, among patients with RCC compared with the control group, the proportion of people who had smoked for less than 10 years was much lower, and those who had smoked for more than 30 years were predominant.

For males, there were significant smoking differences in 2 subgroups: smoking experience of up to 10 years and smoking experience of 30-39 years. In the first subgroup, smoking experience in the study group was significantly lower (3.8 times), and in the second subgroup was 2.8 times higher (p<0.05).

Among women, significant differences in smoking experience were found in all subgroups. In the subgroup with smoking experience of up to 10 years, the proportion of women in the control group was 7.3 times higher than that of the study group, and in the subgroup with 10-19 years of experience, there was a similar trend with a difference in indices of 2.2. In subgroups with smoking experience of 20-29 years, 30-39 years, and 40 years or more, the propor-
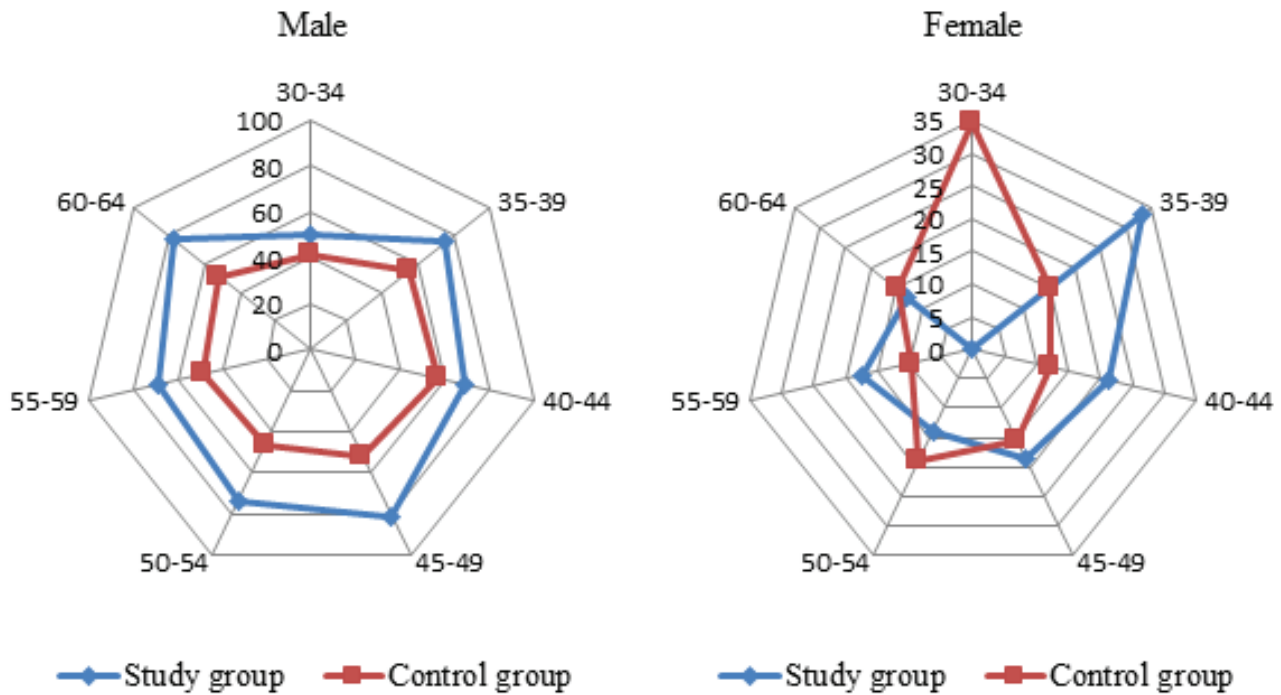
Figure 1. Prevalence of smoking in men and women in the compared groups.

tion of women in the study group was much higher; 1.8, 2.9, and 7.9 times, respectively, than a similar indicator in the control group.

Furthermore, 47.3% of patients with RCC smoked 10 to 20 cigarettes a day. The same number of cigarettes smoked was smoked by men with RCC, and among women surveyed, the prevalence of smoking was up to 10 cigarettes a day (50.0%). Comparative analysis of the number of smoked cigarettes did not reveal significant differences for this indicator for the groups compared.

Obesity

Compared with the control group, we found two statistically significant trends in our age-specific analysis of BMI: the prevalence of men with normal body weight (BMI 18.5-25) and the reduced in overweight (BMI 25-30) among RCC patients aged 35-39, 40-44 and 50-54 years (Figure 2).

Age-specific analysis of BMI in the compared groups of women revealed a 4.2 times predominance of persons with excess weight in the 30-34 years age group (BMI 25-30). In
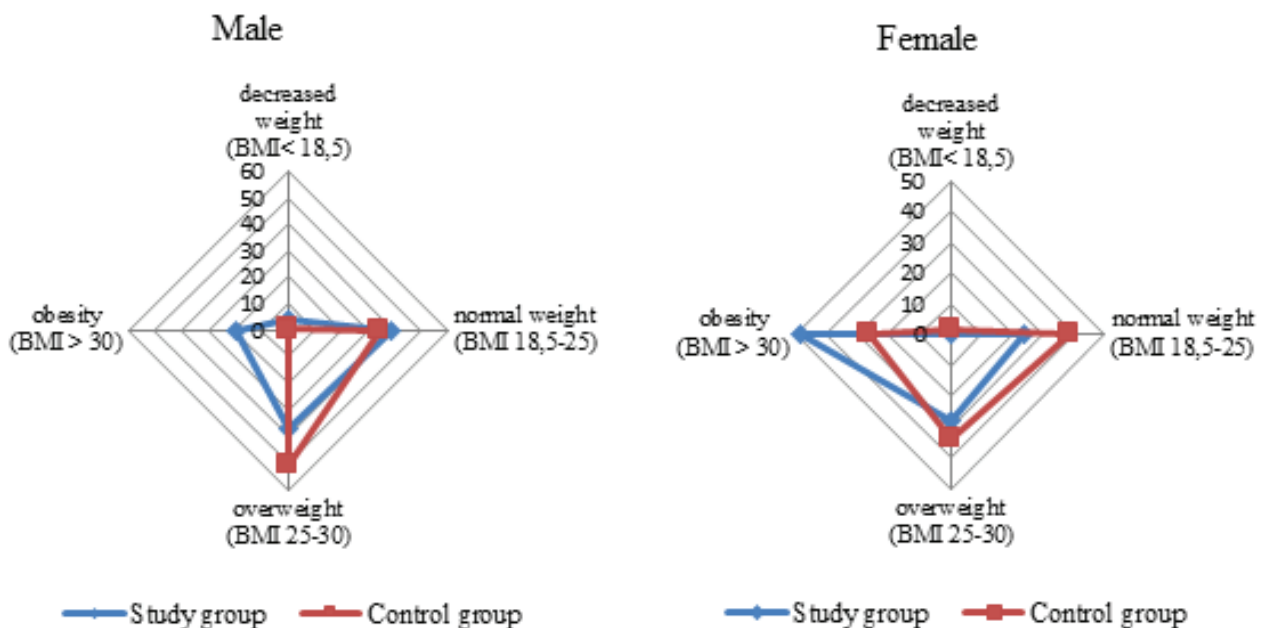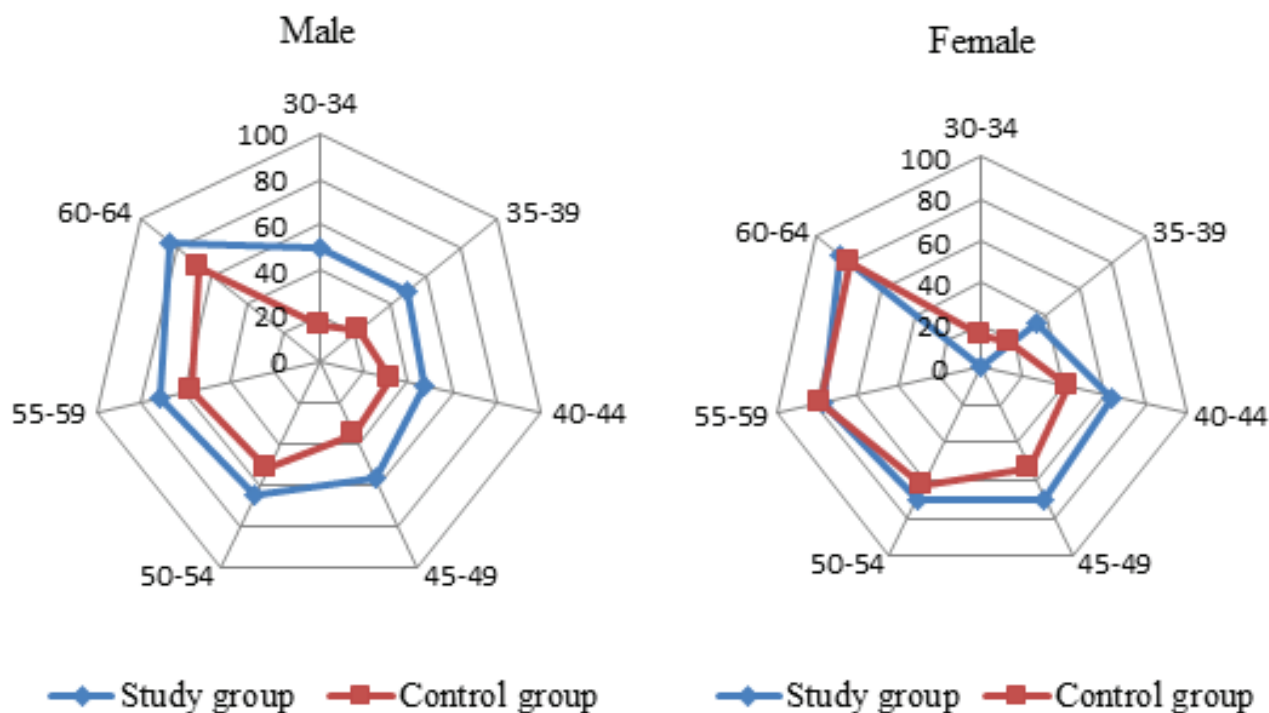

Figure 2. BMI distribution of men and women in the compared groups.

Figure 3. Prevalence of AH in men and women in the compared groups.

the 35-39 years age of the study group, there were 31.6% more people with a body mass deficit (BMI<18.5), 21.7% fewer women with normal body weight (BMI 18.5-25) and 18.3% more obese people (BMI>30) than in the control group. In the 40-44 years age in the study group, the number of persons with normal body weight was reduced by 43.8%, and there were 39.7% more women with obesity than in the control group. In the 60-64 years age group, there were 18.4% fewer overweight women in the study group and an 18.9% increase in the number of obese people compared to the control group. Despite the multidirectional character of age-specific trends, the final data show that in comparison with the control group, there was a predominance of obese women in the study group and a decrease in the proportion of people with normal body weight (Figure 2).

Arterial hypertension

In the study group, the average prevalence of arterial hypertension (AH) was 66.1% and 75.7% among men and women, respectively. In general, the prevalence of hypertension in patients of both sexes with RCC was 70.2%, which was significantly higher than the 43.4% in the control group (p<0.05). The prevalence of hypertension tended to increase with age among both men and women.

Age-specific analysis of the prevalence of hypertension in men and women in the compared groups is shown in Fig. 3. For both sexes, there was a statistically significant prevalence (p<0.05) of hypertension among patients with RCC in age groups 35-39, 40-44, and 45-49 and in men with RP at ages 30-34 and 60-64.

Combination of risk factors

The combination of all three risk factors for RCC was identified in 11.4% (13.6% of men, 8.4% of women), smoking and obesity in 14.4% (16.1% of men, 12.1% of women), smoking and hypertension in 34.8% (58.3% of men, 9.3% of women), and obesity and hypertension in 29.0% (17.8% of men, 43.9% of women).

Risk assessment of RCC development

In assessing the impact of risk factors on the development of RCC in men, it was found that the likelihood of developing disease was 2.9 times higher among smokers and 3.3 times higher among patients with AH. In women, the incidence of RCC increased by a factor of 2.6 in the presence of obesity and by 3.2 times with elevated BP fig-

Table 1. The ratio of the chances of developing RCC among participants of the region, depending on risk factor

Risk factor	Sex	OR	95% CI	
			Lower bound	Upper bound
Smoking	Male	2.894*	2.091	4.007
	Female	0.881	0.566	1.369
Obesity	Male	1.494	0.998	2.238
	Female	2.621*	1.860	3.693
Arterial hypertension	Male	3.256*	2.378	4.458
	Female	3.232*	2.245	4.653

Note: * - significant odds ratios.

ures. There was no significant difference in the likelihood of developing RCC in men with obesity and in women who smoked (Table 1).

Among men with smoking as a risk factor, the risk of developing RCC was confirmed for 4 age groups: 45-49 (OR 5.313 (95% CI 2.430-11.612)), 50-54 (OR 3.180 (95% CI 1.606-6.297)), 55-59 OR 2.257 (95% CI 1.077-4.731)) and 60-64 years (OR 3.135 (95% CI 1.217-8.073)). For hypertension, a significant odds ratio of 2.4 times (95% CI 1.2-5.0) was found only for ages 45-49 years. Among female patients, significant chances of developing RCC were found in obese patients in 2 age groups: 40-44 (OR 6.267 (95% CI, 1.778-22.081)) and 60-64 years (OR 2.182 (95% CI 1.044-4.559)).

DISCUSSION

From a medical and demographic point of view, Krasnoyarsk Territory is the largest part of the Russian Federation with a regressive type of population and gender disproportion (the prevalence of women is 14.5%), in addition to high mortality among able-bodied people (30.6%), most of whom are men (78.2%). Oncological diseases make a significant contribution to the mortality of the working-age population in our region as the third-most common cause of death (20). The mortality from RCC is significant to the region's medical, demographic and economic losses for a number of reasons: against a background of high mortality (JV 4.54, in the Russian Federation, 3.43 per 100,000 population), low, active detection rates were 7.5% (RF 11.1%), and early diagnosis of the disease was 46.2% (RF 55.8%).

Using the analysis of major lifestyle risk factors for developing RCC, we demonstrated the prevalence of smoking in men in virtually all analysed age groups and for women with RCC at ages 35-39 years. According to the quality of tobacco products used by patients with RCC, our data are comparable with the results of regional and Russian (15, 16) sociological polls of the population: 59.8% of men smoke, and 81.5% of women use factory-produced cigarettes in Russia (in our study 65.4% and 70.6%, respectively); 2.2% of men and 0.7% of women smoked cigarettes (our study; 3.3% and 0.0%); 1.8% of men and 1.4% of women smoked cigarettes (our study; 2.8% and 0%); and other kinds of tobacco products are used by 8.3% of men and 3.8% of women (our study 6.6% and 5.9%). Compared to the regional population (control group), smoking experience was significantly higher among patients with RCC, which was confirmed by the prevalence in this group of people who smoked for more than 20 years and the proportion of people who smoked for less than 10 years.

Overall, 31.6% of patients with RCC were obese; women, 65.2% and men, 34.8%. In the control group, the proportion of obese individuals was 20.0% (women, 66.3%; men, 33.7%). The most interesting and significant trend was revealed in the analysis of BMI, where compared with the control group, there was a predominance of obese females in the study group. No less important is the fact that this trend was formed mainly at the expense of age groups 40-44 and 60-64.

There was a prevalence of AH among men with RCC in almost all age groups and in women at younger ages (35-39, 40-44, 45-49 years).

Still, the importance and actuality of combined risk factors for the development of RCC is present in the literature. For example, when smoking and obesity are combined, the gender significance of the factors increases; in men, the risk of developing the disease increases by 47.0%, and in women by 33.9% (1). Krasnoyarsk residents have found that for men, risk factors such as smoking and hypertension (increased risk of developing RCC is 2.9 and 3.3 times, respectively) are more significant, and for women, obesity and hypertension (in 2.6 and 3.2 times respectively). All three risk factors are combined in 13.6% of men and in 8.4% of women with RCC.

CONCLUSION

A comprehensive analysis of the given risk factors for the development of RCC indicates that most attention should be paid to lifestyle-related factors: smoking, obesity and hypertension. On the other hand, these factors are preventable through primary and secondary prevention procedures, and they may be a useful tool for the screening and early diagnosis of RCC.

CONFLICT OF INTEREST

The authors declare no conflict of interest regarding this manuscript.

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