

Risk Factors for Kidney Cancer

<Review>

Masakazu Washio, Fumio Sakauchi, Tomoko Sonoda, Toshiko Ikeda, and Mitsuru Mori

*Department of Public Health, Sapporo Medical University School of Medicine
South 1, West 17, Chuo-ku, Sapporo, Hokkaido, 060-8556, Japan*

ABSTRACT

The incidence of kidney cancer and resulting mortality has been increasing in recent years. Its incidence is highest in Western and Northern Europe and North America, moderate in Japan, and low elsewhere in Asia. Although the incidence of kidney cancer in Japan is lower than in the other developed countries, there is no doubt that there has been an increasing occurrence of this disease recently in Japan, which may be partly due to the adoption of a Western life style.

Obesity/overweight is associated with an increased risk of several kinds of cancers, including Kidney cancer. The prevalence of obesity/overweight is lower in Japan compared with in western countries; however, there has been a rapid increase due to the phenomenon of the Japanese adopting Western life styles and dietary habits. This in turn has led to a sharp increase in insulin resistance syndromes such as hypertension, dyslipidemia and diabetes melli-

tus. Hypertension is a risk factor for kidney cancer as well.

Smoking tobacco smoking is also a risk factor for Kidney cancer and although smoking by people under the age of 20 years is prohibited by law in Japan, 36.6% of male high school students and 16.2% of female high school students smoke more than once a month. As adolescent smoking is a public health priority, an anti-smoking education and program to be introduced to school children at an early age is urgently required.

As it is possible to intervene in order to reduce the prevalence and degree of obesity and smoking, health education would seem to be crucial tool in the fight against renal cancer. In this paper, we discuss the risk factors for kidney cancer (i.e., renal cell carcinoma) including life styles.

Key words : Kidney cancer, Risk factor, Westernization of life style, Obesity, Smoking

Corresponding author:

Masakazu Washio MD. PhD.

Department of Public Health, Sapporo Medical University School of Medicine

South 1, West 17, Chuo-ku, Sapporo, Hokkaido, 060-8556, Japan

TEL: (81)-11-611-2111 (ext. 2742) FAX: (81)-641-8101

E-mail: 918washi@sapmed.ac.jp

1. Introduction

In adults, 70–90% of cases of kidney cancer are renal cell carcinoma, which arises from cells of the proximal convoluted renal tubule^{1,2,3}. Renal cell carcinoma accounts for 2–3% of all malignancies in Western countries^{2,3,4} and 2% in Japan⁵. The incidence of kidney cancer and resulting mortality has been increasing in recent years^{1,2,3}. In Japan, the age-adjusted incidence of kidney cancer has also increased; in 1975, 2.5/100,000 person-years for males and 0.8/100,000 person-years for females; in 1993, 5.7/100,000 person-years for males and 2.1/100,000 person-years for females; in 1996, 8.8/100,000 person-years for males and 3.2/100,000 person-years for females⁵. Thus, kidney cancer is more common in males than females^{1,2,3,5}. The early diagnosis of kidney cancer with the increasing use of renal imaging techniques such as ultrasonography and computer tomography may partly explain the increase in rates of kidney cancer⁵. Such incidental kidney cancer increased from 1980s and the rate of incidental cancer in the total cases of kidney cancer is 70–80% in these days⁵.

The incidence of kidney cancer is highest in Western, and Northern Europe and North America, intermediate in Japan, and low elsewhere in Asia^{1,2,3}. We cannot explain the lower incidence of kidney cancer in Japan compared with in other developed countries by a different frequency of using imaging techniques because in Japan, these techniques are more common than the other developed countries. The difference in life styles between Japan and Western countries may partly explain the difference in the incidence of kidney cancer. Although the incidence of kidney cancer in Japan is lower than in the other developed countries, there is no doubt that it has been increasing steadily in recent years⁵, and we speculated that this is partly due to the adoption of the Western life styles in Japan.

In this paper, we discuss the risk factors for kidney cancer (i.e., renal cell carcinoma) including life styles.

2. Tobacco

It is well known that tobacco smoking is associated with an increased risk of malignancies of organs in direct contact with the smoke such as the lung⁶. Although the kidney is an organ which does not have direct contact with the smoke⁶, smoking tobacco is also a risk factor for kidney cancer^{6,7,8,9,10,11}. McLaughlin *et al*⁷ found a statistically significant dose-response association in both sexes regardless of the measure used: cigarettes per day, duration of use or pack years⁷. In addition, the increased risk of kidney cancer remains even after stopping smoking^{7,8,9,26,27}. McLaughlin *et al*⁷ found that the increased risk of kidney cancer among ever-smokers was more than half of the risk among current smokers. However, there was an inverse relationship between kidney cancer risk and time since smoking cessation⁹.

Vecchia *et al*⁹ demonstrated that the risk of kidney cancer was inversely related with age at which smoking tobacco began. Although smoking by young people under 20 years is prohibited by law in Japan, 36.6% of male high school students and 16.2% of female high school students smoke more than once a month¹². As adolescent smoking is a public health priority, there is an urgent requirement for the development of an anti-smoking educational program to be introduced to school children at an early age.

3. Obesity/overweight

Obesity is associated with an increased risk of several kinds of cancers including kidney cancer¹. Yu *et al*¹⁰ reported that obesity 10 years ago was associated with an increased risk of kidney cancer in a case control study although obesity 1 year ago failed to show an increased risk. Mellemggaard *et al*¹³ reported that obesity was a risk factor for kidney cancer in a cohort study (Table 1). In their paper¹³, the increased risk of kidney cancer due to obesity was greater in women than in men while Yuan *et al*¹⁴ reported that the risk was similar between sexes. Obesity is associated with an increased risk of kidney cancer regardless of the presence

Table 1 Obesity and the risk of kidney cancer.

Author	Published year	Relative Risk	
Mellemgaard et al ¹³⁾ Obesity +/-	1991	Men	1.52
		Women	2.67
Yuan et al ¹⁴⁾ BMI ≥ 30 /BMI < 22	1998	Men	4.6
		Women	4.0
		Hypertension	7.0
		No hypertension	3.2
Chow et al ¹⁵⁾ BMI ≥ 25.96 /BMI < 22.85	2000	-49yr (Men)	2.5
		50-59yr (Men)	1.8
		60 + yr (Men)	1.2

of hypertension¹⁴⁾, but hypertensive subjects shows a greater risk¹⁴⁾ and the risk decreases in the aged group¹⁵⁾.

The prevalence of obesity by WHO criteria (a body mass index of 30.0 or greater) is low (3%) in Japan compared with in Western countries (8% in Sweden, 20% in UK, 23% in USA)¹⁶⁾. However, it has rapidly increased due to the phenomenon of following Westernization of dietary habits^{16, 17, 18)}, which has led to the development of insulin resistance syndromes such as hypertension, dyslipidemia and diabetes mellitus^{16, 17, 18)}.

The WHO Expert Committee in 1995 proposed the term of overweight (a body mass index of 25.0 and greater) and drew attention to the association of an overweight body with increased mortality¹⁹⁾. Overweight people now constitute more than half of adult population in Western countries and in Japan the figure is 20-25%¹⁶⁾. Yuan et al¹⁴⁾ reported that compared with those with BMI of 21 or smaller, those with body mass index of 24-25 were 1.5-fold more likely to develop kidney cancer while those with body mass index of 26-27 were 1.7-fold more likely to do so. Since obesity/overweight is a risk factor for kidney cancer as well as other cancers¹⁾ and heart diseases^{20, 21)}, a health education program designed to prevent it should be instigated immediately.

4. Kidney diseases

Kidney infections as well as kidney stones have been reported to be risk factors for kidney cancer^{2,3,4,5,11)}. Kidney cyst also increases the risk of kidney cancer¹⁰⁾. Acquired renal cysts, which occur in end-stage renal disease with poorly functioning kidneys, is associated with the development of kidney cancer^{2,3,4,5,22)}. Acquired renal cysts were found in almost all of a group of dialysis patients who received dialysis therapy for more than 4 years⁵⁾. The relative risk is high in younger patients and decreases with age²²⁾.

5. Hypertension and anti-hypertensive agents

Hypertension^{14,15,23,24)} as well as anti-hypertensive medication^{14,23,24,25)} has been reported to be a risk factor of kidney cancer (Table 2). Lindbald et al²⁵⁾ found an increased risk of kidney cancer among the users of diuretics (men: standardized incidence rate, 1.28; 95% confidence interval 1.07-1.54, women: SIR 1.42; 95% CI 1.17-1.71). However, epidemiologic studies have not been able to distinguish the effect of hypertension from those of anti-hypertensive medication on the risk of developing kidney cancer²⁶⁾. Administration of diuretics or non-diuretic anti-hypertensive agents for reasons other than hypertension is not associated with an increased risk of kidney cancer. Hypertension is often associated with obesity²⁷⁾, and may necessitate the use of these drugs¹⁴⁾.

Table 2 Antihypertensive agents and the risk of kidney cancer

Author	Published year	Agent	Relative Risk	
Fraser et al ²³⁾	1990	Anti-hypertensive agents	4.51	
Lindbald et al ²⁵⁾	1993	Diuretics	Men	1.28
			Women	1.42
Weinmann et al ²⁴⁾	1994	Any diuretics	1.9	
		Thiazides	1.9	
		Loop	3.1	
		Potassium-sparing	2.1	
		Chlorthalidone	1.4	
		Any non-diuretic agents	2.0	
		Beta-blockers	2.5	
Other non-diuretic agents	2.1			
Yuan et al ¹⁴⁾	1998	Any diuretics	1.9	
		Thiazides	1.9	
		Potassium-sparing	2.0	

6. Analgesics

There are several reports stating that the heavy or long-term use of analgesics is a risk factor of kidney cancer^{28, 29)}. Gago-Dominguez et al²⁸⁾ showed that a small dose of aspirin for cardiovascular disease prevention did not increase the risk of kidney cancer, although the regular use of analgesics was associated with an increased risk. Contrary to this however, Chow et al³⁰⁾ reported that the use of analgesics was not associated with an increased risk of kidney cancer.

7. Conclusion

The incidence of kidney cancer and resulting mortality has been increasing in recent years^{1,2,3)}. Western, and Northern Europe and North America have the highest incidence, in Japan, the incidence is less and elsewhere in Asia it is low^{1,2,3)}. Although the incidence of kidney cancer in Japan is lower than in the other developed countries, there is no doubt that over recent years the incidence rate has been increasing⁵⁾, and it is speculated that this may be partly due to the westernization of Japanese life

styles

Obesity/overweight is associated with an increased risk of several kinds of cancers, including kidney cancer¹⁾. The prevalence of obesity/overweight is lower in Japan compared with in Western countries¹⁶⁾; however, it has increased rapidly due to the westernization of life styles and dietary habits^{16,17,18)}. This in turn has led to the development of the insulin resistance syndrome such as hypertension, dyslipidemia and diabetes mellitus^{16, 17, 18)}. Hypertension^{14,15,23,24)} is a risk factor for kidney cancer as well.

Tobacco smoking is also a risk factor for kidney cancer^{6,7,8,9,10,11)}. Although smoking under the age of 20 years is prohibited by law in Japan, 36.6% of male high school students and 16.2% of female high school students smoke more than once a month¹²⁾. As adolescent smoking is a public health priority, there is an urgent need for anti-smoking education program aimed at school children of an early age.

The kidney cancer risk factors of obesity and smoking could be avoided if an adequate health education program were to be implemented. Since it may be difficult to change ac-

quired life styles in adults, health education not only for adults but also for children seems to be very important.

REFERENCES

1. Stewart BW, Kleihues P. World cancer report. Lyon: International Agency for Research on Cancer Press; 2003.
2. McLaughlin JK, Blot WJ, Devesa SS, Fraumeni JF Jr. Renal Cancer. In: Schottenfeld D, Fraumeni JF Jr, editors. Cancer epidemiology and prevention. New York: Oxford University Press; 1996. p1142-1155.
3. Lindbland P, Adami HO. Kidney cancer. In: Adami HO, Hunter D, Trichopoulos D, editors. Textbook of cancer epidemiology. New York: Oxford University Press; 2002. p467-485.
4. Brosman SA. Tumors of the kidney and urinary tract. In: Massry SG, Glassock RJ, editors. Textbook of nephrology. 2nd ed. Baltimore: Williams and Wilkins; 1989. p942-961.
5. Toma H. Epidemiology of kidney cancer. In: Toma H, Nakazawa H, editors. All about kidney cancer: basic medicine and clinical practice. Tokyo: Medical View; 2003. p2-10 (in Japanese).
6. Gajalaskshmi CK, Jha P, Ranson K, Nguyen S. Global patterns of smoking and smoking-attributable mortality. In: Jha P, Chaloupka F, editors. Tobacco control in developing countries. Oxford: Oxford university press; 2000. p11-39.
7. McLaughlin JK, Silverman DT, Hsing AW, Ross RK, Schoenberg JB, Yu MC, Stemhagen A, Lynch CF, Blot WJ, Fraumeni JF Jr. Cigarette smoking and cancers of the renal pelvis and ureter. *Cancer Res* 1992; 52: 254-257.
8. McLaughlin JK, Gao YT, Gao RN, Zheng W, Ji BT, Blot WJ, Fraumeni JF Jr. Risk factors for renal-cell cancer in Shanghai, China. *Int J Cancer* 1992; 52: 562-565.
9. La Vecchia C, Negri E, D'Avanzo B, Franceschi S. Smoking and renal cell carcinoma. *Cancer Res* 1990; 50: 5231-5233.
10. Yu MC, Mack TM, Hanisch R, Cicioni C, Henderson BE. Cigarette smoking, obesity, diuretic use, and coffee consumption as risk factors for renal cell carcinoma. *J Natl Cancer Inst* 1986; 77:351-356.
11. McLaughlin JK, Mandel JS, Blot WJ, Schuman LM, Mehl ES, Fraumeni JF Jr. A population-based case-control study of renal cell carcinoma. *J Natl Cancer Inst* 1984; 72: 275-284.
12. Statistics and Information Department, Minister's Secretariat, Japanese Ministry of Health, Labour and Welfare. Health Promotion. *Kokumin Eisei no Doko (J Health Welfare Stat)* 2003; 50(9): 78-86 (in Japanese).
13. Mellempgaard A, Moller H, Olsen JH, Jen-sen OM. Increased risk of renal cell carcinoma among obese women. *J Natl Cancer Inst* 1991; 83: 1581-1582.
14. Yuan JM, Castela JE, Gago-Dominguez M, Ross RK, Yu MC. Hypertension, obesity and their medications in relation to renal cell carcinoma. *Br J Cancer* 1998; 77: 1508-1513.
15. Chow WH, Gridley G, Fraumeni JF Jr, Jarvholm B. Obesity, hypertension, and the risk of kidney cancer in men. *N Engl J Med* 2000; 343: 1305-1311.
16. Yamada Y, Ishizaki M, Tsuritani I. Prevention of weight gain and obesity in occupational populations: a new target of health promotion services at worksites. *J Occup Health* 2002; 44: 373-384.
17. Kiyohara Y, Nakayama K, Iwamoto H, Kato I, Ueda K, Fujishima M. Chronological trends in the prevalence of obesity and the effects on life longevity in a community population: the Hisayama Study. *Himan Kenkyu (J Jpn Soc Stud Obes)* 1998; 4: 12-16 (in Japanese).
18. Egusa G, Okubo M, Yamamoto M, Kawamura T, Yamakido M. Chronological trends in the prevalence of obesity and its complication: special references with westernized life style. *Himan Kenkyu (J Jpn Soc Stud Obes)* 1998; 4: 17-21 (in Japanese).
19. Physical status: the use and interpretation

- of anthropometry. Report of a WHO Expert Committee. World Health Organ Tech Rep Ser 1995; 854: 1-452.
20. Kaplan NM. The deadly quartet, Upper-body obesity, glucose intolerance, hypertriglyceridemia, and hypertension. *Arch Intern Med* 1989; 149: 1514-1520.
 21. Washio M, Hayashi R, Fukuoka Heart Study Group. Past history obesity (overweight by WHO criteria) is associated with an increased risk of non-fatal acute myocardial infarction: a case-control study in Japan. *Circ J* 2004; 68: 41-46.
 22. Maisonneuve P, Agodoa L, Gellert R, Stewart JH, Bucciante G, Lowenfels AB, Wolfe RA, Jones E, Disney AP, Briggs D, McCredie M, Boyle P. Cancer in patients on dialysis for end-stage renal disease: an international collaborative study. *Lancet* 1999; 354: 93-99.
 23. Fraser GE, Phillips RL, Beeson WL. Hypertension, antihypertensive medication and risk of renal carcinoma in California Seventh-day Adventists. *Int J Epidemiol* 1990; 19: 832-838.
 24. Weinmann S, Glass AG, Weiss NS, Psaty BM, Siscovick DS, White E. Use of diuretics and other antihypertensive medications in relation to the risk of renal cell cancer. *Am J Epidemiol* 1994; 140: 792-804.
 25. Lindblad P, McLaughlin JK, Mellempgaard A, Adami HO. Risk of kidney cancer among patients using analgesics and diuretics: a population-based cohort study. *Int J Cancer* 1993; 55: 5-9.
 26. Yu MC, Ross RK. Obesity, hypertension, and renal cancer. *N Engl J Med* 2001; 344: 531-532.
 27. Yoshikawa A, Nishio I. Obesity and hypertension. In: Goto Y, editor. *Himan-sho (Obesity)*. Tokyo: Nihon Rinsho-sha; 1995. p271-275 (in Japanese).
 28. Gago-Dominguez M, Yuan JM, Castelao JE, Ross RK, Yu MC. Regular use of analgesics in a risk factor for renal cell carcinoma. *Br J Cancer* 1999; 81: 542-548.
 29. McCredie M, Stewart JH, Day NE. Different roles for phenacetin and paracetamol in cancer of the kidney and renal pelvis. *Int J Cancer* 1993; 53: 245-249.
 30. Chow WH, McLaughlin JK, Linet MS, Niwa S, Mandel JS. Use of analgesics and risk of renal cell cancer. *Int J Cancer* 1994; 59: 467-470.

(Accepted for publication, Dec. 18, 2003)