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## Review

# Hypertension, serum lipids and cancer risk: A review of epidemiological evidence

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## ABSTRACT

Although the association between blood pressure, serum lipids and cancer risk has been investigated, the results are controversial. The aim of this literature review was to examine the epidemiological evidence and provide overview of the association between blood pressure, serum lipids and cancer risk. The arterial hypertension is closely linked with renal cell cancer development. Risk of renal cell cancer was 2–4 times higher for persons with arterial hypertension, independently of sex. In some studies arterial hypertension as one of the components of the metabolic syndrome, was associated with a higher risk of colorectal, prostate cancer and malignant melanoma. Studies suggest that a higher total serum cholesterol level is linked with higher risk of colorectum, colon, prostate and testicular cancer and lower risk of stomach, liver and hematopoietic and lymphoid tissues cancer. There was positive association between serum triglycerides and esophageal, colorectal, lung, renal, thyroid cancer. Given that hypertension is a common risk factor worldwide and its control remains inadequate, our analysis supports the relevance of public health programs aimed at reducing hypertension to reduce the incidence of a number of cancers including renal cell cancer. Effective cholesterol control may lower the risk of cancer, but further studies with longer follow-up and repeated measurements of cholesterol and other lipids are needed.

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## 1. Introduction

Arterial hypertension (AH) and plasma lipid profile levels (low high-density lipoprotein (HDL) and/or raised triglyceride (TG)) are among other acknowledged key risk factors for atherosclerosis and coronary heart disease. Changes in lifestyle factors including unhealthy diet, harmful use of alcohol, lack of physical activity, excess weight and aging of population determined the increased prevalence of chronic conditions such as high blood pressure and high blood cholesterol worldwide [1,2]. In 2008, worldwide, approximately 40% of adults aged 25 and above had been diagnosed with hypertension [1]; the global prevalence of elevated plasma cholesterol levels among adults was 39% (37% for males and 40% for females) [3]. The influence of blood pressure and cholesterol on cancer risk has been an area of investigation for long-time. Many studies and meta-analyses had separately reported these factors as important etiologic factors for the development and progression of certain types of cancer.

The aim of this literature review was to examine the epidemiologic evidence and provide overview of the association between blood pressure, serum lipids and cancer risk.

## 2. Association between arterial hypertension and cancer

### 2.1. Kidney cancer

Arterial hypertension (AH) is the most important modifiable risk factor for cardiovascular, cerebrovascular and renal disease. Epidemiological evidence shows that there are several factors which play an important role in the development, evolution and prognosis of AH, some of them non-modifiable, such as age, sex, ethnicity and heredity, and others modifiable, such as body weight, salt intake, alcohol intake, use of hormonal contraceptives and drugs retaining sodium, sedentary life and psychosocial factors [4,5]. There is increasing evidence that AH affects the potential for the development of kidney cancer. Worldwide, kidney cancer is the 13th most common malignancy, with approximately 271,000 new cases diagnosed in 2008, and renal cell carcinoma (RCC) accounts for about 90%–95% of them [6]. The Czech Republic, Lithuania, Latvia, Estonia, and Iceland have the highest RCC rates in Europe. An increase in RCC incidence has been observed globally during the last decades, although in some European countries RCC incidence is declining in recent years [6]. Tumor causes are varied, but it is established that smokers as well as overweight and obese patients have increased risk [6]. Many cohort [5–12] and case-control [13] studies linked RCC with a history of AH (Table 1).

In Sweden 363,992 men were investigated in a cohort study, 759 persons with RCC were identified. RCC risk increased with increasing systolic and diastolic blood pressure and severity of AH [7]. The risk of RCC was more than two-fold higher for men who had increased diastolic blood pressure of 90 mm Hg or more compared to below 70 mm Hg. Relative risk of developing kidney cancer was 60%–70% higher in men with systolic blood pressure of 150 mm Hg or more than those <120 mm Hg.

European Prospective Investigation into Cancer and Nutrition (EPIC) study of 296,638 men and women recruited in 1992–1998 investigated the relation between blood pressure, antihypertensive medication, and RCC [10]. Renal cancer was diagnosed for 250 subjects during the study period. The researchers found that increased arterial blood pressure is associated with an increased risk of RCC development independently of sex, body mass index, smoking and use of antihypertensive medication. Furthermore, the risk of RCC was higher in men, whose blood pressure rose by more than 14 mm Hg during the six year period as compared to men whose blood pressure changed less. A reduced risk was observed in those whose blood pressure decreased during 6 years.

In 2002–2007, Colt and colleagues studied the incidence of AH and kidney cancer links in Detroit and Chicago (USA) cities depending on the race using a case-control study methodology. Kidney cancer was diagnosed in 843 whites and 358 blacks during the period of the study, the controls were 707 whites and 519 blacks. The study results showed that AH increased the chance for kidney cancer development 2 times (95% CI, 1.7–2.5), 1.9 times in whites, and 2.8 times in blacks. The kidney cancer risk increased with a longer duration of AH. After 25 years of tracking it reached 4.1 times in blacks and 2.6 times in whites. The possibility of developing kidney cancer was even greater for individuals with poor AH control [13]. It is possible that a high incidence of kidney cancer in Lithuania among men and women [6] could be due to a high prevalence of AH that is poorly treated [24].

A combined analysis of the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS) cohorts in the United States examined AH, use of diuretics, BMI, change of weight and smoking as independent RCC risk factors in a prospective study, which included 48,953 men and 118,191 women working in the health care system. The study results showed that the relative risk to suffer from kidney cancer in men and women with AH was 1.8 (95% CI, 1.2–2.7) and 1.9 (95% CI, 1.4–2.7) times higher, respectively. No increased risk to suffer from RCC in men taking thiazide diuretics had been determined [5]. Other researchers also identified a significant direct relationship between AH and RCC development [9,12,25]. The issue of whether use of diuretics and antihypertensive drugs is also associated with an increased risk of kidney cancer development remains unresolved, although some studies suggest that antihypertensive treatment may not be a risk factor as long as blood pressure is effectively controlled [4,5,7,10,26,27]. Despite the high correlation between obesity, AH and RCC risk, these factors have been shown as independent of each other risk factors. The risk to suffer from kidney cancer is higher among those who are obese and have AH than those who have one of these risk factors [7,10]. The US Multiethnic Cohort study estimated that more than 15% of RCC in male cases and 24% of RCC in female cases could be attributed to hypertension [8]. However, the biological mechanism of relationship between the AH and kidney cancer is still not clear, association with chronic renal hypoxia and lipid peroxidation formation of reactive oxygen cultivars has been linked to tumor development and might be partly responsible for the increased RCC risk [28,29].

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