

OBESITY PROFILE AS A RISK FACTOR IN RENAL CELL CARCINOMA PATIENTS: A LITERATURE REVIEW

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ABSTRACT

Objective: This study aims to determine the profile of obesity as a risk factor for developing RCC. **Material & Methods:** This study is a library research study with journals, articles, and opinions of related experts taken from Google Scholar and Pubmed which was uploaded in 2019-2023. **Results:** 7 articles met the inclusion, exclusion and topic relevance criteria. Several journals stated that obesity is a strong risk factor for the development of renal cell carcinoma (RCC), although opposite results were found in one study regarding obesity and the prognostic outcome of RCC patients. **Discussion:** The mechanism of obesity in increasing the risk of RCC is a complex process, which involves the process of insulin resistance, inflammation by pro-inflammatory cytokines, angiogenesis, and proliferative effects as a result of the role of insulin as one of the most important anabolic hormones capable of stimulating cell proliferation, and is exacerbated by imbalanced cell anti-apoptotic mechanisms. **Conclusion:** No relationship was found between the lipid profile and the incidence of RCC. Little research has been done on lipid profiles for RCC, considering that the largest RCC subtype, ccRCC, is characterized by the accumulation of lipids and glycogen, which has implications for changes in fatty acid and glucose metabolism in its etiology. Further studies are needed to examine the effect of lipid profiles on the risk of renal cell carcinoma.

Keywords: Carcinogenesis, obesity profile, renal cell carcinoma.

ABSTRAK

Tujuan: Penelitian ini bertujuan untuk mengetahui profil obesitas sebagai faktor risiko terjadinya RCC. **Bahan & Cara:** Studi tinjauan literatur ini merupakan studi dengan jurnal, artikel, dan opini dari pakar terkait yang diambil dari Google Scholar dan Pubmed yang diunggah pada tahun 2019-2023. **Hasil:** 7 artikel memenuhi kriteria inklusi, eksklusi dan relevansi topik. beberapa jurnal menyatakan bahwa obesitas merupakan faktor risiko yang kuat untuk perkembangan karsinoma sel ginjal (RCC), meskipun hasil yang berlawanan ditemukan dalam satu penelitian mengenai obesitas dan hasil prognostik pasien RCC. **Diskusi:** Mekanisme obesitas dalam meningkatkan risiko RCC merupakan proses yang kompleks, yang melibatkan proses resistensi insulin, inflamasi oleh sitokin pro-inflamasi, angiogenesis, dan efek proliferatif akibat peran insulin sebagai salah satu hormon anabolik terpenting yang mampu merangsang proliferasi sel, dan diperburuk oleh mekanisme anti-apoptosis sel yang tidak seimbang. **Simpulan:** Tidak ditemukan hubungan antara profil lipid dan kejadian RCC. Sedikit penelitian yang dilakukan mengenai profil lipid untuk RCC, mengingat subtype RCC terbesar, ccRCC, ditandai dengan akumulasi lipid dan glikogen, yang berimplikasi pada perubahan metabolisme asam lemak dan glukosa pada etiologinya. Penelitian lebih lanjut diperlukan untuk menguji pengaruh profil lipid terhadap risiko karsinoma sel ginjal.

Kata kunci: Faktor risiko, karsinoma sel ginjal, profil obesitas.

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INTRODUCTION

Renal cell carcinoma (RCC) is considered the deadliest cancer among genitourinary malignancies in general which accounts for about 4% of all new cancers worldwide. Kidney cancer (ie, renal cell cancer (RCC)) has an estimated incidence

of 270.000 worldwide and accounts for nearly 116.000 deaths annually.¹ In the United States, estimates show there were 65.150 new cases and 13.680 deaths from kidney cancer and renal pelvic cancers in 2017 with approximately 35% presenting as metastatic disease.² Obesity and hypertension are associated with an increased risk of developing RCC

based on epidemiological studies.¹ Obesity is characterized by an overgrowth of white adipose tissue (WAT) and a body mass index (BMI) exceeding 30 kg/m² making it a debilitating disease worldwide.³ As the second most common process involved in carcinogenesis after smoking, by 2025, the worldwide incidence of obesity is expected to reach 21% in women.⁴⁻⁵ Obesity is reported to be attributable to 40% of cancer deaths in the United States including RCC.⁶ Screening is needed to assess the risk of developing RCC based on a risk factor that is closely related to carcinogenesis, namely obesity.⁷⁻⁸

OBJECTIVE

This study aims to determine the profile of obesity as a risk factor for developing RCC.

MATERIAL & METHODS

This study is a library research study where the subjects of this research are journals, articles, and opinions of related experts taken from Google Scholar and Pubmed. The research method used includes general processes such as synthesis, analysis, review, and study of various references which are secondary data as the main object. Study inclusion criteria include articles uploaded in 2019-2023, articles with original study design (non-

review), such as observational studies, cohort studies, clinical experimental studies, and case-control studies, articles with full access and free of charge and articles made in Indonesian or English and using key phrases: "obesity", "abdominal obesity", "obesity profile", "BMI", "waist circumference", "lipid profile", "renal cancer", "renal cell carcinoma" and "dyslipidemia". Exclusion criteria in this study were literature in the form of only abstracts, conferences, editorial comments, inappropriate results, inaccessible literature, literature irrelevant to research variables, duplication of previous literature publications, and not using English or Indonesian. The data analysis technique in this study used content analysis.

RESULTS

The literature search was carried out and yielded articles (Fig. 1). Literature selection was based on exclusion criteria and left 95 articles which were then processed, leaving 7 articles that met the inclusion, exclusion and topic relevance criteria, while 88 literature were excluded because they were not relevant. All of these articles are original research (non-review) published in 2019-2023, where out of 7 articles, 2 are prospective cohort studies, 4 are retrospective observational studies and 1 is a multicenter Mendelian randomized study.

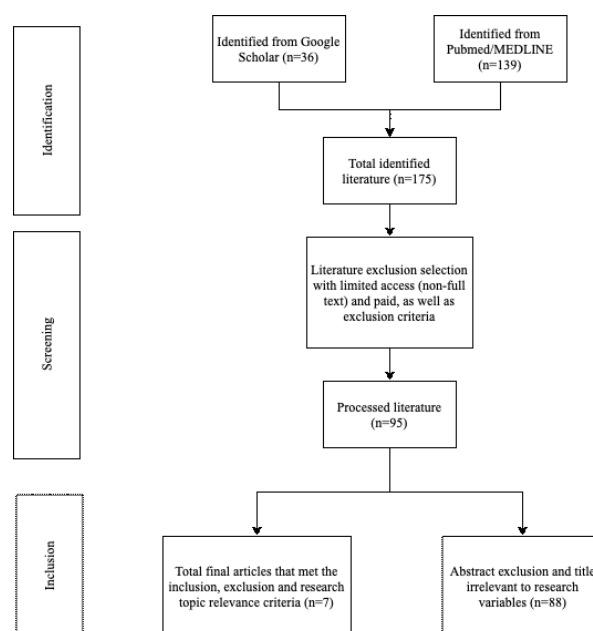


Figure 1. Flow of study selection process.

DISCUSSION

There are several risk factors that lead to kidney cancer, such as BMI and cholesterol. High cholesterol can also increase the likelihood of cardiovascular disease. A multi-center study conducted in Korea was published by Jeong et al. using retrospective data through medical records collected from 1988 to 2015 with male and female subjects with an average age ranging from 54-57 years, which found a total of 7,047 patient was diagnosed with RCC who then underwent partial/radical nephrectomy. The distribution of patients according to BMI measurements (HR = 0.8; 95% CI: 0.53-1.48, P=0.65) was different from previous studies. This study describes the relationship between BMI and the incidence of renal tumors in men and women by using a linear-by-linear association. In that study, it was found that men with normal BMI had a lower incidence of RCC than those with high BMI (74.8% vs 80.0% P = 0.003). However, the incidence of RCC showed no significant difference between women with normal BMI and those with high BMI (74.2% vs 74.3%, P=0.971).⁹

In the study of Landberg et al., weight gain has been associated with several types of cancer, including RCC. This research was conducted as a cohort on male military conscription members in Sweden in 1952 - 1956 between the ages of 18 - 19 years. The oncogenic effects of chronic inflammation, the influence of hormones such as leptin and adiponectin, and overstimulation of insulin receptors and IGF-I are supporting materials in this study which also explored insulin resistance, growth factors, and adipokines such as adiponectin, which have anti-inflammatory and antiproliferative properties. Based on the results of this study, the increased risk of RCC for obese and overweight individuals remained significant even after adjustment for physical work capacity and muscle strength, although BMI may not be an ideal measure of adiposity in these groups. This study suggests a link between higher BMI during adolescence may increase the risk of DNA errors and the development of malignancy thereby increasing the risk of RCC. This study also shows that overweight and obesity play a role in the pathogenesis of adolescent RCC so that reducing obesity in children and adolescents can prevent the occurrence of RCC.¹⁰

A large multicenter study by Johansson et al. found a significant association between obesity and

the risk of RCC. In this study, the population of RCC patients was 10,784. Patients with overweight and obese body mass index have a 1.5 times higher risk of experiencing RCC (table 4.2). In this study, it was estimated that for every one standard deviation increase in BMI obtained (equivalent to 5 kg/m²), the risk of RCC increased by 56%. The highest increased risk was found in patients with hip circumference above the normal limit, 70 cm for women and 80 cm for men, which was 1.6 times.¹¹ However, a strong association of obesity as a risk factor for the incidence of RCC was not found in his analysis of the deviation of lipid profile values (i.e. HDL, LDL, triglycerides, and total cholesterol) from normal limits as occurs in conditions of dyslipidemia, even though obesity and dyslipidemia are co-morbidities. Relatively prevalent co-occurring morbidity.¹²

Research conducted by Hao et al. with patient data totaling 308 patients using the retrospective observational method with a total of 193 men and 115 women; 128 patients aged >60 years and 180 patients aged <60 years. The median age of the patients was 59 years. The age range of patients 27-79 years who have been diagnosed with Clear Cell RCC. The results of this study indicate that low serum HDL-C preoperatively is a risk factor for the occurrence of Clear Cell RCC. Multivariate analysis showed that higher serum HDL-C levels were associated with better overall survival (HR = 0.32; 95% CI (0.13, 0.78); P=0.013) and Cancer-Specific Survival (CSS) is better (HR = 0.42; 95% CI (0.15, 0.99); P=0.04).¹³

The study of Callahan et al., aimed to see the relationship between kidney cancer and histological differences in risk factors. This study has a subject age range of 18-54 years, 55-64 years, 65-75 years, and 75-99 years with more males than females. Characteristics of subjects in the study Subjects met racial/ethnic criteria (black, white, Hispanic, Asian/Pacific), and had been diagnosed with cancer for 1 year. Using a nested case-control study design with the Kaiser Permanente Northern California (KPNC) health care network. In this study, obesity (BMI>30kg/m²) was associated with clear cell RCC (OR 1.5 95% CI 1.1-2.1) and chromophobe RCC (OR 2.5, 95% CI 0.8-8.1), Papillary RCC (OR 1.0, 95% CI 0.5-1.9). These results indicate that there is a significant relationship between obesity and the incidence of Renal Cell Carcinoma.⁵

Study of Lee et al. aims to determine the relationship between metabolic syndrome (MetS)

and kidney cancer and the impact of age and gender on this relationship. A total of 9,932,670 subjects were followed from 2009 to 2019 from the Korea National Health Insurance Service database with kidney cancer outcomes significantly associated with MetS (HR 1.56), with the younger age group having a higher association. Young men showed a higher HR for kidney cancer compared to older men (HR = 1.94 (95% CI = 1.7-2.21) vs. HR = 1.53 (95% CI = 1.44) -1.62) and HR = 1.3 (95% CI = 1.2-1.41)) (p<0.005)) in terms of the association of kidney cancer with obesity and central obesity. In contrast to the results for men, young women showed lower HR (HR = 1.21 (95% CI = 0.72 -2.01) vs HR = 1.33 (95% CI = 1.21 -1.47) and HR 1.25 (95% CI = 1.11 -1.4) (P < 0.005)). Overall, populations with kidney cancer had higher BMI, LP, glucose, BP, and TG, but lower HDL than populations without kidney cancer. BMI and LP showed a positive relationship with kidney cancer, and MetS showed a higher relationship with kidney cancer in the young population (20-39 years) than the other population (Male (HR $\geq$ 1.52 (95% CI = 1.43 - 2) .9)) and women (HR $\geq$ 1.42 (95% CI = 1.31 - 2.22)).

Compared to other age groups, the younger group showed a stronger association between kidney cancer and obesity, central obesity, low HDL and high TG. The positive association between MetS without obesity and kidney cancer was higher in the younger age group than in other age groups. Significant associations between kidney cancer in young men and sex, MetS, obesity, and central obesity were found. Obesity and overweight in young adults compared to older people for kidney cancer is an emphasized risk factor for kidney cancer in this study. Research subjects that only use the Korean population lead to the need for validation from other populations. However, this study is considered representative because it is a population-based study that evaluates the association of MetS with kidney cancer based on age and sex, but not much is known about the relationship between obesity and kidney cancer subtypes.¹⁴

Modifiable risk factors for renal cell carcinoma can reduce the incidence of renal cell carcinoma. The study published by J. Gelfond et al. used a database of 493 male (64.4%) and 261 female (34.6%) patients with prostate, lung, colorectal, and ovarian cancer with primary outcome kidney cancer with age between 59 - 67 years. This study uses questionnaires and medical records as primary and secondary data in this study. A total of 748 patients

had kidney cancer. Race/ethnicity in white-non-Hispanic were 681(90.3%), black-non-Hispanic 35(4.6%), and Hispanic 17(2.3%). This study shows that the higher the patient's BMI will increase the occurrence of kidney cancer (HR = 1.05; 95% CI: 1.02-1.07, P<0.00001). Obesity as a modifiable risk factor has a relationship with an increased incidence of kidney cancer.¹⁵

Several journals stated that obesity is a strong risk factor for the development of renal cell carcinoma (RCC), although opposite results were found in one study regarding obesity and the prognostic outcome of RCC patients. The mechanism of obesity in increasing the risk of RCC is a complex process, which involves the process of insulin resistance, inflammation by pro-inflammatory cytokines, angiogenesis, and proliferative effects as a result of the role of insulin as one of the most important anabolic hormones capable of stimulating cell proliferation, and is exacerbated by imbalanced cell anti-apoptotic mechanisms.

CONCLUSION

Several journals have discussed lipid profiles as a predictive factor for survival in renal cell carcinoma patients, so total cholesterol (TC) examination is very good as a predictive factor in RCC patients. However, no relationship was found between the lipid profile and the incidence of RCC. Little research has been done on lipid profiles for RCC, considering that the largest RCC subtype, ccRCC, is characterized by the accumulation of lipids and glycogen, which has implications for changes in fatty acid and glucose metabolism in its etiology. Further studies are needed to examine the effect of lipid profiles on the risk of renal cell carcinoma.

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