BMC Nephrology

RESEARCH

Open Access

Metabolic syndrome and increased susceptibility to renal cell carcinoma – a meta-analysis

Yanyu Zhou[1], Yujun Chen[1,2], Heng Yang[1], Zhiqi Xu[1], Jinbiao Zhuang[1], Qitao Bian[1] and Gongxian Wang[1,2*]

Abstract

Background Metabolic syndrome (MetS) has been demonstrated to be associated with various types of cancer, but its specific relationship with kidney cancer remains inconclusive. Therefore, this study conducts a Meta-analysis to systematically evaluate the potential link between metabolic syndrome and the risk of kidney cancer development.

Methods Observational studies were retrieved from PubMed, Embase, Cochrane Library, and Web of Science. Two independent reviewers extracted study characteristics and assessed the quality of the studies. A random-effects model was employed to account for heterogeneity, and subgroup analyses were conducted to explore the impact of study characteristics on the results. Publication bias was evaluated using funnel plot symmetry and Egger's regression test.

Results Six studies were included, with 10 results extracted for the Meta-analysis. The findings indicated that MetS is an independent risk factor for kidney cancer (HR: 1.44, 95% CI: 1.31–1.59, $P<0.001$). Heterogeneity between studies was significant (Cochran's Q test, $P<0.001$; $I^2=83.7\%$), indicating substantial variability. Subgroup analyses revealed consistent associations across gender, follow-up duration, and MetS diagnostic criteria ($P>0.05$), but significant variations by race and study design ($P<0.05$). The funnel plot appeared symmetrical, and Egger's regression test ($P=0.425$) confirmed a low risk of publication bias.

Conclusion MetS is independently associated with an increased susceptibility to RCC in the adult population, although the strength of this association varies across different study designs and regions due to the observed heterogeneity.

Keywords Metabolic syndrome, Renal cell cancer, Meta-analysis

Background

Kidney cancer, clinically referred to as Renal Cell Carcinoma (RCC), ranks second only to prostate cancer and bladder cancer in incidence within the male urinary system, accounting for 3% to 5% of malignant tumors in adults [1]. However, it has the highest lethality among urological tumors [2]. Due to its asymptomatic nature in early stages, advanced kidney cancer often leads to a worse prognosis, imposing a significant burden on patients' physical and mental health as well as on the healthcare system [3]. Given these challenges, identifying

*Correspondence:
Gongxian Wang
wanggx-mr@126.com
[1] Department of Urology, the 1st Affiliated Hospital, Jiangxi Medical College, Nanchang University, 17 YongWai Street Surgery Building, 17th Floor, Nanchang, Jiangxi 330006, China
[2] Jiangxi Provincial Key Laboratory of Urinary System Diseases, Nanchang, Jiangxi 330000, China

risk factors for the prevention and early detection of kidney cancer is of paramount importance.

Metabolic syndrome (MetS) is a collection of clinical syndromes characterized by metabolic disorders such as obesity, hyperglycemia, hypertension, and dyslipidemia [4]. Although the diagnostic criteria for MetS vary across different countries, major guidelines include those from the International Diabetes Federation (IDF), National Cholesterol Education Program Adult Treatment Panel III (NCEP ATP III), and the Chinese Diabetes Society (CDS), among others. Recently, the incidence of MetS has been rising among younger populations, with a prevalence of approximately 25% in Chinese adult males [5]. The situation in Europe and the United States is also concerning. In the United States, the prevalence rate among older adults exceeds 40% [6], while in Europe and Latin America, the rate is around 25% [7], MetS is not only a significant risk factor for cardiovascular diseases, but it is also closely associated with the development of various cancers, including prostate, colorectal, breast, and kidney cancers [8–11].

Current research on the relationship between RCC and MetS has yielded mixed findings [12–14], possibly due to differences in study design, follow-up duration, and diagnostic criteria for MetS. In 2022, a meta-analysis demonstrated that MetS is associated with an increased risk of kidney cancer [15]; however, the study did not account for the potential impact of differing diagnostic criteria for MetS on the outcome. Moreover, several new prospective studies have recently examined this association in greater detail [10, 16, 17]. By synthesizing the latest evidence, this meta-analysis aims to clarify the strength and consistency of this association, address methodological limitations in previous studies, and provide a more comprehensive understanding of how metabolic syndrome influences the risk of RCC.

Material and methods

Search strategy

This meta-analysis adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement [18] was followed in this systematic review and meta-analysis. The methodology for analysis and reporting was conducted in accordance with the Cochrane Handbook for Systematic Reviews and Meta-Analyses [19]. These frameworks ensure rigorous and transparent reporting, which enhances the reliability and reproducibility of our findings.

The study performed a comprehensive literature search across four major databases: PubMed, Web of Science, Cochrane, and Embase. The final database search was conducted on August 1, 2024, with no restrictions applied to publication language. The search strategy used in PubMed is as follows:

MeSH Terms: Kidney Neoplasms, Metabolic Syndrome, Cohort Study, Case–Control Study.

Title/Abstract: Renal Neoplasm OR Cancer of Kidney OR Kidney Cancer OR Cancer of the Kidney OR Renal Cell Cancer OR Renal Cancer, Reaven Syndrome X OR Metabolic Syndrome X OR Insulin Resistance Syndrome X OR Metabolic X Syndrome OR Dysmetabolic Syndrome X.

Study inclusion

The inclusion criteria for this study are as follows: 1. Participants were aged 18 years or older at the start of the study and had not been diagnosed with cancer; 2. The exposure variable was metabolic syndrome (with varying diagnostic criteria), and the outcome variable was renal cell carcinoma; 3. The study design could be either prospective or retrospective. The exclusion criteria are as follows: 1. Studies that measured risk using odds ratios (OR) or relative risks (RR); 2. Studies that did not specify the diagnostic criteria for metabolic syndrome; 3. Reviews, meta-analyses, preclinical studies, and studies that did not assess the impact of MetS.

Data collection and evaluation of study quality

To ensure minimize potential bias, the database search, collection, and assessment of study quality were conducted independently by two authors. Each step was carried out separately to maintain objectivity, with both authors cross-checking their findings to ensure consistency and accuracy in the results. In cases of disagreement, the two authors engaged in in-depth discussions to resolve the issue. If they were unable to reach a solution, the corresponding author was involved to provide additional perspectives and help facilitate consensus. Data extracted included study characteristics, patient demographics, diagnostic criteria for MetS, study periods, HR and their corresponding 95% confidence intervals (CIs). Study quality was assessed using the Newcastle–Ottawa Scale (NOS), which scores studies from 1 to 9 stars. The NOS evaluates the quality of observational studies across three domains: patient selection, comparability of cohorts with and without exposure, and outcome validation strategies. A score of 7 or above is generally regarded as an indicator of high-quality studies.

Statistical methods

HR (95%CI) was used to assess the association between MetS and RCC. The standard errors (SEs) were calculated from the data provided by the 95% CIs or p-values, and the HRs were logarithmically transformed to ensure a normal distribution of the data.

Heterogeneity between studies was evaluated using Cochrane's Q test and the I^2 statistic. A *P*-value for heterogeneity < 0.10 or I^2 > 50% was considered indicative of significant heterogeneity among the studies. To account for this heterogeneity, a random-effects model was employed. Sensitivity analysis, performed by excluding one dataset at a time, was conducted to confirm the robustness of the findings. A series of subgroup analyses were carried out to explore the effects of study characteristics on the associations, based on variables such as gender, ethnicity, follow-up period, study design, and the diagnostic criteria for MetS. The primary variation in diagnostic criteria for MetS was related to the measurement of obesity, which was classified based on Body Mass Index (BMI) or Waist Circumference (WC). As a result, studies were grouped accordingly into BMI-based or WC-based criteria. Publication bias was evaluated through visual inspection of funnel plot symmetry and by applying Egger's regression test.

A $P < 0.05$ was considered statistically significant. All the statistical analyses were performed using STATA statistical software version 12.0.

Results

Identification of related studies

Figure 1 shows the process of the literature search. A total of 623 articles were retrieved from four databases (Pubmed: 19, Web of Science: 554, Embase: 50, Cochrane's Library: 0). 25 duplicates were excluded, 583 articles were excluded by title and abstract, and 9 articles were excluded by reading the full-text content. Nine articles were excluded and a total of six papers were included in the study [10, 14, 16, 17, 20, 21].

Summary of study characteristics

Table 1 presented the characteristics of the individual studies. These studies were conducted in the United Kingdom, China, and South Korea, and were categorized as prospective or retrospective in design. Two studies reported results exclusively for male patients [14, 20], while four other studies performed subgroup analyses based on gender. The sample sizes ranged from 61,758 to 9,932,670 participants, with a total of 11,313,741 participants across all studies. All studies had a follow-up period of more than 5 years. The diagnostic criteria for MetS varied, including NCEP-ATP III, IDF, CDS, American Heart Association/National Heart, Lung, and Blood Institute (AHA/NHLBI), and the Korean Society for the Study of Obesity (KSSO). One of the papers, although

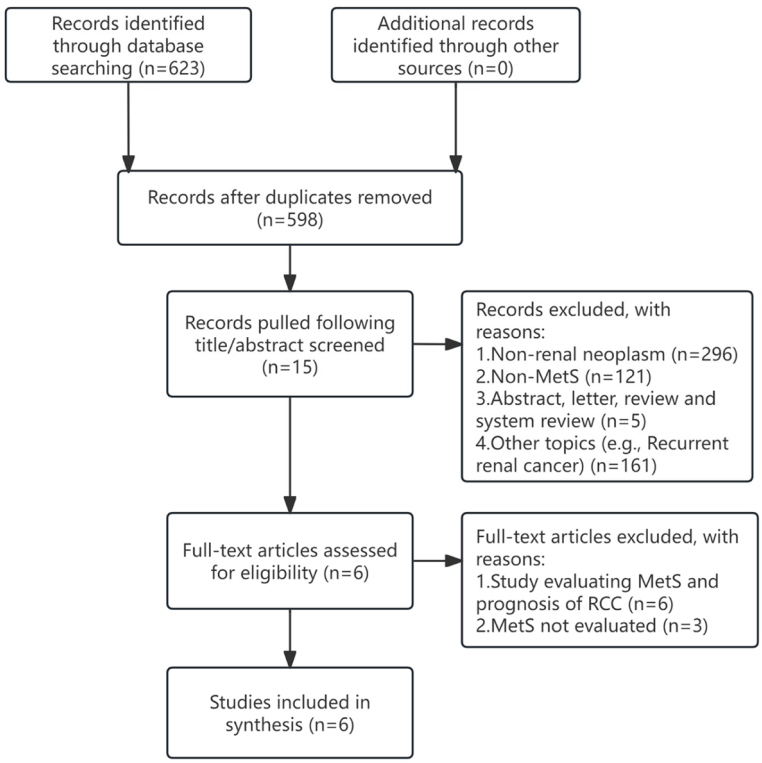

Fig. 1 PRISMA diagram of literature search and study inclusion

Table 1 Characteristic of the included studies

Author	Year	Study design	Ethnicity	Sample size	Median Follow-up(years)	Diagnostic criteria of MetS	Diagnostic criteria of obesity	NOS score
Wang L	2024	PC	UK	355678	11	NCEP-ATP III	WC	8
Jiang R	2023	PC	China	97975	13.03	IDF	WC	8
Lee H Y	2023	PC	Korea	9932670	8.26	AHA/NHLBI	WC	8
Xin L	2020	PC	China	104274 (M)	8.88	CDS	BMI	8
Oh T R	2019	RC	Korea	761386	5.94	KSSO	WC	8
Ko S	2016	RC	Korea	61758 (M)	10.4	NCEP-ATP III	BMI	7

PC Prospective Cohort, *RC* Retrospective Cohort, *M* Male, *WC* Waist Circumference, *BMI* Body Mass Index, *NCEP-ATP III* National Cholesterol Education Program Adult Treatment Panel III, *IDF* International Diabetes Federation, *AHA/NHLBI* American Heart Association/National Heart, Lung, and Blood Institute, *CDS* Chinese Diabetes Society, *KSSO* Korean Society for the Study of Obesity

using the NCEP-ATP III diagnostic criteria [14], replaced the reference for obesity from WC to BMI. The NOS scores for study quality ranged from 7 to 8, indicating high quality. A multifactorial analysis was conducted for all findings, controlling for confounding variables such as age, sex, smoking, alcohol intake, BMI, and exercise, to varying extents in the multivariate analyses.

Association between MetS and RCC

Of the six papers included, two studies reported results exclusively for male populations [14, 20], and four of the studies examined the association between MetS and RCC based on the sex of the participants, so a total of 8 results were extracted from these studies, and 10 final results were included in the meta-analysis. Significant between-study heterogeneity was observed (P for Cochrane's Q test < 0.001, $I^2 = 83.7\%$). Pooled results using a random-effects model indicated that MetS was independently associated with an increased risk of RCC in the adult population (HR: 1.44, 95% CI: 1.31 to 1.59, $P < 0.001$; Fig. 2). Sensitivity analyses, conducted by omitting one

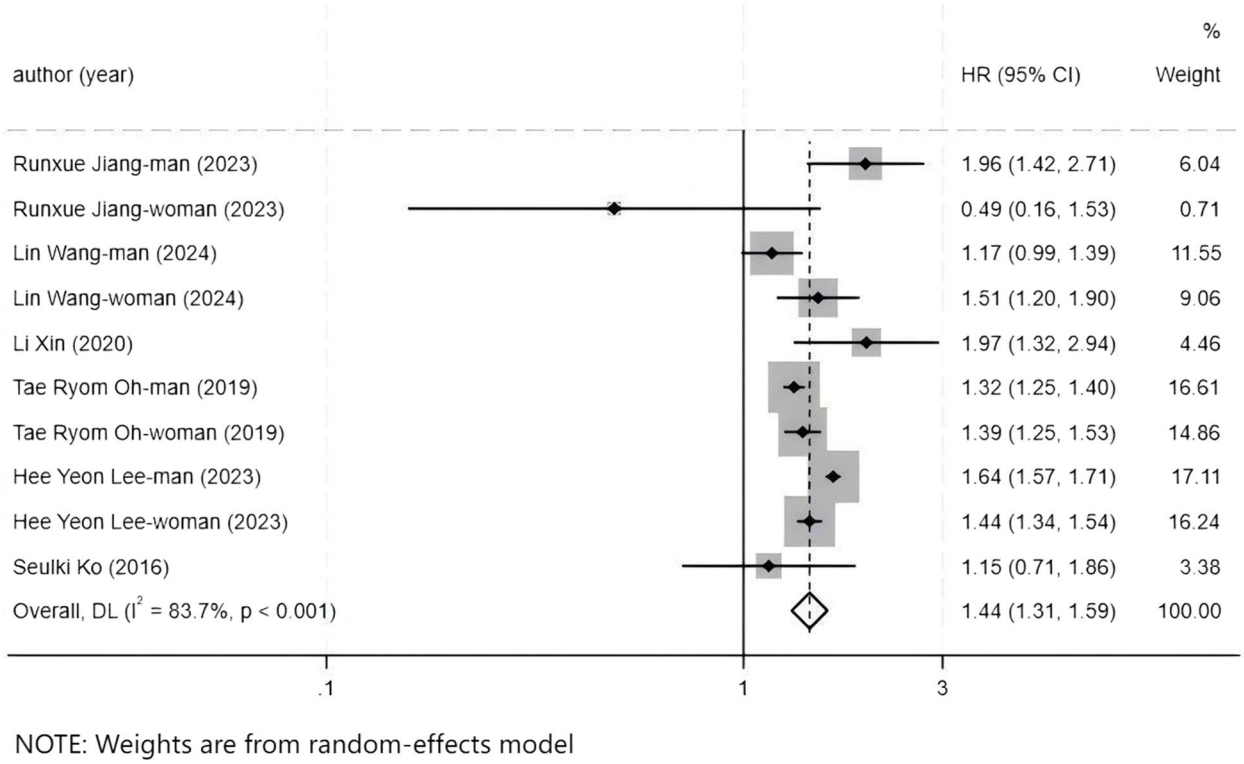

Fig. 2 Forest plots for the meta-analysis of the association between MetS and RCC

dataset at a time, yielded similar results (HR: 1.39 to 1.48, all $P < 0.05$; Fig. 3).

Table 2 presents the results of the subgroup analysis. The predefined subgroup analysis demonstrated a consistent association between MetS and RCC in both men (HR: 1.47 [1.26, 1.72], $P < 0.001$) and women (HR: 1.42 [1.35, 1.51], $P < 0.001$; P for subgroup difference = 0.068). However, the association varied significantly across different geographic regions, including China (HR: 1.63 [1.01, 2.63], $P = 0.045$), England (HR: 1.31 [1.02, 1.69], $P = 0.032$), and Korea (HR: 1.43 [1.28, 1.60], $P < 0.001$; P for subgroup difference = 0.022), indicating that the strength of association was not consistent among region. Similarly, significant differences were observed between prospective and retrospective studies, with prospective studies showing a stronger association (HR: 1.50 [1.33, 1.70], $P < 0.001$) compared to retrospective studies (HR: 1.34 [1.27, 1.41], $P < 0.001$; P for subgroup difference < 0.001). In contrast, a consistent association was observed in subgroup analyses based on the diagnostic criteria for MetS and the duration of follow-up (P for subgroup difference in both cases > 0.05).

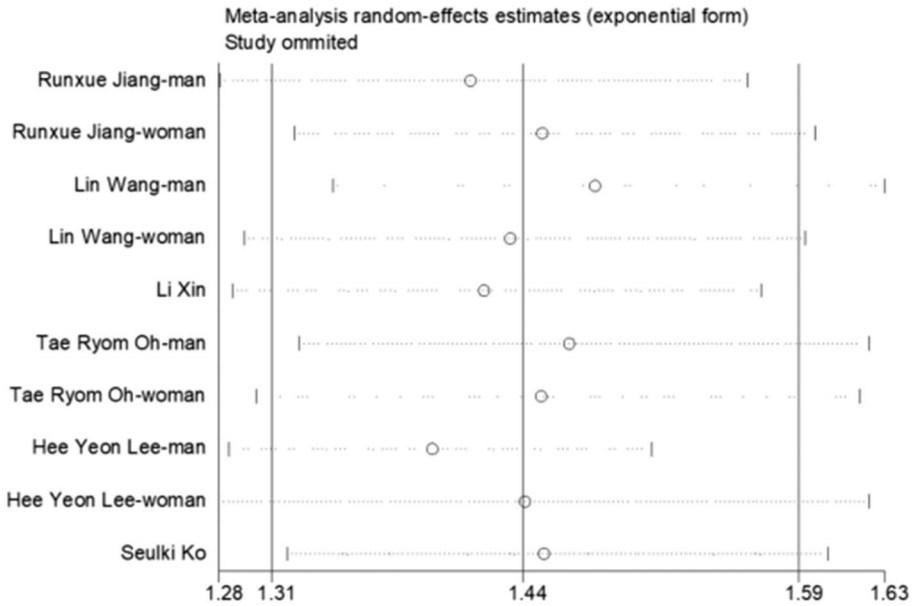

Fig. 3 Sensitivity analysis of the meta-analysis results

Table 2 Subgroup analysis results for various factors

		Random-effects model		Fixed-effects model		Heterogeneity		Heterogeneity between groups
Analysis	**N**	**HR (95%CI)**	***P***	**HR (95%CI)**	***P***	I^2	***Ph***	***P***
Subgroup 1: PC	7	1.50 (1.33, 1.70)	< 0.001	1.57 (1.51, 1.62)	< 0.001	79.00%	< 0.001	< 0.001
RC	3	1.34 (1.27, 1.41)	< 0.001	1.34 (1.27, 1.41)	< 0.001	0.00%	0.606	
Subgroup 2: man	6	1.47 (1.26, 1.72)	< 0.001	1.51 (1.46, 1.56)	< 0.001	89.50%	< 0.001	0.068
woman	4	1.42 (1.32, 1.53)	< 0.001	1.42 (1.35, 1.51)	< 0.001	25.00%	0.261	
Subgroup 3: BMI	2	1.43 (1.29, 1.58)	< 0.001	1.49 (1.45, 1.53)	< 0.001	86.60%	< 0.001	0.707
WC	8	1.53 (0.90, 2.59)	0.113	1.58 (1.16, 2.15)	0.004	65.00%	0.091	
Subgroup 4: UK	2	1.31 (1.02, 1.69)	0.032	1.28 (1.12, 1.47)	< 0.001	67.90%	0.078	0.022
China	3	1.63 (1.01, 2.63)	0.045	1.84 (1.44, 2.35)	< 0.001	63.30%	0.066	
Korea	5	1.43 (1.28, 1.60)	< 0.001	1.49 (1.45, 1.54)	< 0.001	89.70%	< 0.001	
Subgroup 5: Follow-up ≥ 10	5	1.35 (1.05, 1.74)	0.021	1.34 (1.18, 1.51)	< 0.001	67.70%	0.016	0.071
Follow-up < 10	5	1.47 (1.32, 1.64)	< 0.001	1.50 (1.45, 1.54)	< 0.001	89.90%	< 0.001	

Publication bias

Funnel plots assessing the association between MetS and RCC appeared symmetrical upon visual inspection (Fig. 4), suggesting a low risk of publication bias. This observation was further supported by the results of Egger's regression test (p = 0.425), which confirmed the absence of significant publication bias.

Discussion

In this study, a total of 10 outcomes from 6 studies were included, and the initial analysis demonstrated that MetS was independently associated with an increased risk of developing kidney cancer. Sensitivity analyses did not significantly alter the results, indicating that the findings were relatively stable. High intergroup heterogeneity was observed among the 10 outcomes, as revealed by the subgroup analyses. These analyses showed greater variability between different study designs and ethnic groups, which were identified as the primary sources of intergroup heterogeneity. In contrast, subgroup analyses by gender, follow-up duration, and diagnostic criteria for MetS consistently demonstrated an association between MetS and RCC. Finally, the results of all subgroup analyses confirmed that MetS was a risk factor for RCC, with HRs consistently greater than 1.

The methodology of this study is similar to that of Du et al.; however, the eight studies included in their analysis employed varying diagnostic criteria for metabolic syndrome [15]. Furthermore, these studies used three distinct measures of risk—HR, Standardized Incidence Ratio (SIR) and Relative Risk (RR). Du et al. did not address the heterogeneity introduced by these variations in diagnostic criteria. Moreover, it is generally inappropriate to combine different risk measures within the same meta-analysis model. A key difference in the diagnostic criteria for metabolic syndrome lies in the assessment of obesity, which is measured using either WC or BMI [14]. Although no universally accepted diagnostic standard exists, it is crucial to account for its potential impact on the results during analysis. In the current study, further adjustments were made to address these issues. A large cross-sectional study from the United States demonstrated a significant association between MetS and kidney cancer (OR = 5.44 [5.17–5.72]) [22]. Another study showed that kidney cancer was associated with MetS by calculating a composite score of all five metabolic factors [23], conversely, some studies have reported no association between MetS and kidney cancer [13], however, these studies did not meet the inclusion criteria for the current analysis and were excluded. The two studies, Oh et al. (2019) with 761,386 participants and Ko et al. (2016) with 61,758 participants, may have overlapping populations [17, 21]. However, we did not exclude either study because the first cohort included both males and females, whereas the Ko et al. (2016) cohort only included males. In our analysis, we extracted sex-stratified results from each study. Furthermore, the two studies differ in sample size and the diagnostic criteria for metabolic syndrome.

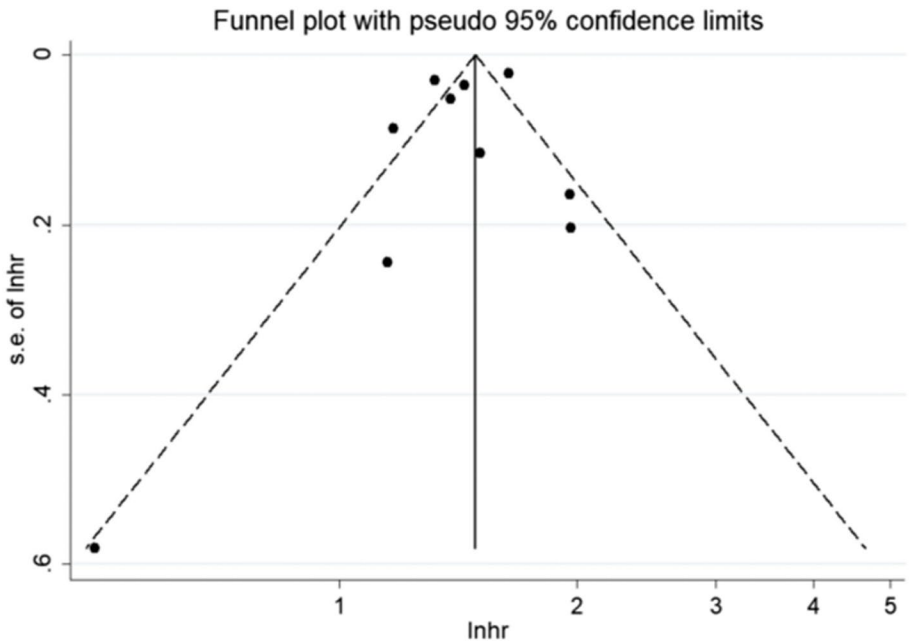

Fig. 4 Funnel plot for assessing publication bias

Finally, although there may be overlap in the male populations, we performed sensitivity analyses by sequentially excluding each cohort to evaluate the impact.

Currently, numerous pathophysiologic mechanisms related to MetS have been identified that promote the development of renal cancer. Diabetes mellitus is closely associated with insulin resistance (IR), and elevated insulin levels can inhibit the synthesis of insulin-like growth factor (IGF)-binding proteins, resulting in increased IGF activity. Insulin-like growth factor plays a crucial role in tumor initiation and progression by promoting mitosis, enhancing cell migration, and inhibiting apoptosis through the activation of the MAPK and PI3K pathways, particularly via the binding of IGF-1 and IGF-1R [24]. Kidney cells are histologically characterized by sterol storage, suggesting that lipid metabolism plays a pivotal role in renal cancer formation. Laboratory studies studies have demonstrated [25] that statins can inhibit tumor cell growth and invasion, possibly due to their effect on lowering lipid levels, thereby inhibiting renal cancer progression. Antihypertensive medications, in addition to lipid-lowering drugs, may also have an impact on kidney cancer. Research has shown that certain antihypertensive drugs, such as calcium channel blockers and diuretics, are associated with an increased risk of papillary renal cell carcinoma (pRCC) [26], whereas their relationship with clear cell renal cell carcinoma (ccRCC) is not significant. This may be due to the long-term effects of diuretics on renal tubular cells, alterations in renal hemodynamics, and the potential carcinogenic transformation of certain diuretics in the body [27, 28]. Additionally, a large-scale prospective cohort study has shown that calcium channel blockers are associated with an increased cancer risk, and a dose–response relationship exists [29]. However, the reasons for the lack of association with ccRCC and the absence of a clear link between other antihypertensive medications and kidney cancer remain unclear. Patients with MetS have reduced levels of lipocalin, which may be linked to obesity and insulin resistance. Low circulating lipocalin is involved in the pathogenesis of various obesity-associated cancers [30, 31]. Moreover, tissue cells in obese individuals are often hypoxic, leading to a chronic inflammatory state in systemic tissues and the release of inflammatory cytokines, which create a microenvironment favourable for tumor survival [32, 33]. Metabolic disorders are also associated with chronic systemic inflammation and oxidative stress, both of which contribute to the carcinogenic process [34].

As seen in the previous text, the impact of medications on cancer is complex, especially for antihypertensive drugs like diuretics and calcium channel blockers. On one hand, these medications reduce blood pressure, alleviating the negative effects of hypertension on kidney cancer. On the other hand, long-term use of these drugs may promote cancer development, particularly in relation to a specific histological subtype of kidney cancer. The underlying mechanisms remain unclear. Unfortunately, the studies included in this article did not account for the use of medications, which undoubtedly affects the interpretation of the results. In studies examining the relationship between MetS and kidney cancer survival, there has been disagreement. Some studies suggest that MetS may shorten cancer survival [35, 36], while others indicate that it may actually contribute to better survival outcomes [37, 38], possibly due to the use of anti-metabolic disorder medications in these patients.

Although this study found that different diagnostic criteria for MetS did not have a significant impact on the results, the importance of diagnostic criteria should not be overlooked. The subgroup analysis in this study was based solely on the concept of obesity; however, MetS consists of four metabolic disturbances: glucose, lipid, blood pressure, and obesity. Some studies have shown that as the number of metabolic disturbances increases, the risk of renal cell carcinoma also rises [10], and even the combination of different components may result in varying levels of risk [16, 39]. As studies on MetS progress, its core mechanism—IR—is well recognized, but clinically, measuring IR is complex [40]. Therefore, most studies on MetS use surrogate markers for IR, such as METS-IR, TyG, and TyG-BMI [41–43], which incorporate multiple metabolic indicators to best represent IR. However, the relationship between these surrogate markers and the risk of renal cell carcinoma remains unclear. Further research is needed to clarify the role of these markers in assessing the relationship between MetS and renal cancer.

The results of this meta-analysis confirm the conclusions of most previous studies, showing that MetS is a potential risk factor for RCC in both male and female populations. This also suggests that clinical interventions, such as adjusting dietary habits, improving lifestyle, and implementing early interventions, may help reduce cancer risk in high-risk populations, while also providing new strategies for the treatment of RCC patients.

The study also has some limitations. First, none of the studies accounted for the use of medications, such as those for hypertension or diabetes, which may have influenced the results. In addition, there was significant heterogeneity across the included studies. Although sensitivity and subgroup analyses were conducted, this heterogeneity remains a potential issue that may impact the interpretation of the meta-analysis results. Finally, the power of Egger's regression test is relatively low when the number of studies is small, meaning that publication bias might not be reliably detected.

Conclusion

Based on the results of this meta-analysis, MetS is independently associated with an increased risk of RCC in adults, although the strength of this association varies across different study designs and regions due to the observed heterogeneity, suggesting that individuals with MetS may represent a high-risk population for RCC. Future research should focus on determining whether the use of medications aimed at treating metabolic disorders could potentially reduce or increase this risk.

Abbreviations

MetS	Metabolic syndrome
RCC	Renal Cell Carcinoma
IDF	International Diabetes Federation
NCEP ATP III	National Cholesterol Education Program Adult Treatment Panel III
CDS	Chinese Diabetes Society
AHA/NHLBI	American Heart Association/National Heart, Lung, and Blood Institute
KSSO	Korean Society for the Study of Obesity
NOS	Newcastle-Ottawa Scale
BMI	Body Mass Index
WC	Waist Circumference
SIR	Standardized Incidence Ratio
IR	Insulin resistance
PC	Prospective Cohort
RC	Retrospective Cohort

Acknowledgements

Not applicable.

Clinical trial number

Not applicable.

Authors' contributions

ZY and CY contributed in conception and design of the work; Data analysis was performed by ZY, BQ and YH. The first draft of the manuscript was written by ZY, XZ and ZJ. It was critically revised by WG. All authors reviewed and commented on previous versions of the manuscript. They approved the final manuscript and agreed to take responsibility for the accuracy and integrity of the work, ensuring that any issues are properly investigated and resolved.

Funding

This study was supported by the National Natural Science Foundation of China (No. 82060467, 81460389).

Data availability

The datasets used during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

Not applicable. This study is a meta-analysis based on previously published data, and it does not involve the collection of new data from human participants, human tissue, or animals.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Received: 14 October 2024 Accepted: 6 February 2025
Published online: 26 February 2025

References

1. Xia C, Dong X, Li H, Cao M, Sun D, He S, et al. Cancer statistics in China and United States, 2022: profiles, trends, and determinants. Chin Med J (Engl). 2022;135(5):584–90. https://doi.org/10.1097/cm9.0000000000002108.
2. Lane BR, Tiong HY, Campbell SC, Fergany AF, Weight CJ, Larson BT, et al. Management of the adrenal gland during partial nephrectomy. J Urol. 2009;181(6):2430–6. https://doi.org/10.1016/j.juro.2009.02.027. discussion 6–7.
3. Safiri S, Kolahi AA, Mansournia MA, Almasi-Hashiani A, Ashrafi-Asgarabad A, Sullman MJM, et al. The burden of kidney cancer and its attributable risk factors in 195 countries and territories, 1990–2017. Sci Rep. 2020;10(1):13862. https://doi.org/10.1038/s41598-020-70840-2.
4. Reaven GM. Banting lecture 1988. Role of insulin resistance in human disease. Diabetes. 1988;37(12):1595–607. https://doi.org/10.2337/diab.37.12.1595.
5. Qin X, Qiu L, Tang G, Tsoi MF, Xu T, Zhang L, et al. Prevalence of metabolic syndrome among ethnic groups in China. BMC Public Health. 2020;20(1):297. https://doi.org/10.1186/s12889-020-8393-6.
6. Ford ES, Li C, Zhao G. Prevalence and correlates of metabolic syndrome based on a harmonious definition among adults in the US. J Diabetes. 2010;2(3):180–93. https://doi.org/10.1111/j.1753-0407.2010.00078.x.
7. Zanchetti A, Hennig M, Baurecht H, Tang R, Cuspidi C, Carugo S, et al. Prevalence and incidence of the metabolic syndrome in the European Lacidipine Study on Atherosclerosis (ELSA) and its relation with carotid intima-media thickness. J Hypertens. 2007;25(12):2463–70. https://doi.org/10.1097/HJH.0b013e3282f063d5.
8. Healy LA, Howard JM, Ryan AM, Beddy P, Mehigan B, Stephens R, et al. Metabolic syndrome and leptin are associated with adverse pathological features in male colorectal cancer patients. Colorectal Dis. 2012;14(2):157–65. https://doi.org/10.1111/j.1463-1318.2011.02562.x.
9. Xiang YZ, Xiong H, Cui ZL, Jiang SB, Xia QH, Zhao Y, et al. The association between metabolic syndrome and the risk of prostate cancer, high-grade prostate cancer, advanced prostate cancer, prostate cancer-specific mortality and biochemical recurrence. J Exp Clin Cancer Res. 2013;32(1):9. https://doi.org/10.1186/1756-9966-32-9.
10. Jiang R, Wang X, Li Z, Cai H, Sun Z, Wu S, et al. Association of metabolic syndrome and its components with the risk of urologic cancers: a prospective cohort study. BMC Urol. 2023;23(1):150. https://doi.org/10.1186/s12894-023-01324-4.
11. Colonna SV, Douglas Case L, Lawrence JA. A retrospective review of the metabolic syndrome in women diagnosed with breast cancer and correlation with estrogen receptor. Breast Cancer Res Treat. 2012;131(1):325–31. https://doi.org/10.1007/s10549-011-1790-x.
12. Jiang R, Li Z, Wang X, Cai H, Wu S, Chen S, et al. Association of metabolic syndrome and its components with the risk of kidney cancer: A cohort-based case-control study. Technol Health Care. 2023;31(4):1235–44. https://doi.org/10.3233/thc-220482.
13. van Kruijsdijk RC, van der Graaf Y, Peeters PH, Visseren FL. Cancer risk in patients with manifest vascular disease: effects of smoking, obesity, and metabolic syndrome. Cancer Epidemiol Biomarkers Prev. 2013;22(7):1267–77. https://doi.org/10.1158/1055-9965.Epi-13-0090.
14. Ko S, Yoon SJ, Kim D, Kim AR, Kim EJ, Seo HY. Metabolic risk profile and cancer in Korean men and women. J Prev Med Public Health. 2016;49(3):143–52. https://doi.org/10.3961/jpmph.16.021.
15. Du W, Guo K, Jin H, Sun L, Ruan S, Song Q. Association Between Metabolic Syndrome and Risk of Renal Cell Cancer: A Meta-Analysis. Front Oncol. 2022;12:928619. https://doi.org/10.3389/fonc.2022.928619.
16. Wang L, Du H, Sheng C, Dai H, Chen K. Association between metabolic syndrome and kidney cancer risk: a prospective cohort study. Lipids Health Dis. 2024;23(1):142. https://doi.org/10.1186/s12944-024-02138-5.
17. Lee HY, Han KD, Woo IS, Kwon HS. Association of Metabolic Syndrome Components and Nutritional Status with Kidney Cancer in Young Adult Population: A Nationwide Population-Based Cohort Study in Korea. Biomedicines. 2023;11(5):1425. https://doi.org/10.3390/biomedicines11051425.

18. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71.
19. JPT H, J T, J C, M C, T L, MJ P, et al., editors. Cochrane Handbook for Systematic Reviews of Interventions version 6.4. Cochrane: Cochrane Collaboration. https://training.cochrane.org/handbook/current. Accessed Aug 2024.
20. Li X, Li N, Wen Y, Lyu ZY, Feng XS, Wei LP, et al. Metabolic syndrome components and renal cell cancer risk in Chinese males: a population-based prospective study. Zhonghua Yu Fang Yi Xue Za Zhi. 2020;54(6):638–43. https://doi.org/10.3760/cma.j.cn112150-20190711-00558.
21. Oh TR, Han KD, Choi HS, Kim CS, Bae EH, Ma SK, et al. Metabolic Syndrome Resolved within Two Years is Still a Risk Factor for Kidney Cancer. J Clin Med. 2019;8(9):1329. https://doi.org/10.3390/jcm8091329.
22. Suarez Arbelaez MC, Nackeeran S, Shah K, Blachman-Braun R, Bronson I, Towe M, et al. Association between body mass index, metabolic syndrome and common urologic conditions: a cross-sectional study using a large multi-institutional database from the United States. Ann Med. 2023;55(1):2197293. https://doi.org/10.1080/07853890.2023.2197293.
23. Häggström C, Rapp K, Stocks T, Manjer J, Bjørge T, Ulmer H, et al. Metabolic Factors Associated with Risk of Renal Cell Carcinoma. PLoS ONE. 2013;8(2):e57475. https://doi.org/10.1371/journal.pone.0057475.
24. Tracz AF, Szczylik C, Porta C, Czarnecka AM. Insulin-like growth factor-1 signaling in renal cell carcinoma. BMC Cancer. 2016;16:453. https://doi.org/10.1186/s12885-016-2437-4.
25. Woodard J, Sassano A, Hay N, Platanias LC. Statin-dependent suppression of the Akt/mammalian target of rapamycin signaling cascade and programmed cell death 4 up-regulation in renal cell carcinoma. Clin Cancer Res. 2008;14(14):4640–9. https://doi.org/10.1158/1078-0432.Ccr-07-5232.
26. Colt JS, Hofmann JN, Schwartz K, Chow WH, Graubard BI, Davis F, et al. Antihypertensive medication use and risk of renal cell carcinoma. Cancer Causes Control. 2017;28(4):289–97. https://doi.org/10.1007/s10552-017-0857-3.
27. Schouten LJ, van Dijk BA, Oosterwijk E, Hulsbergen-van de Kaa CA, Kiemeney LA, Goldbohm RA, et al. Hypertension, antihypertensives and mutations in the Von Hippel-Lindau gene in renal cell carcinoma: results from the Netherlands Cohort Study. J Hypertens. 2005;23(11):1997–2004. https://doi.org/10.1097/01.hjh.0000186023.74245.48.
28. Grossman E, Messerli FH, Goldbourt U. Does diuretic therapy increase the risk of renal cell carcinoma? Am J Cardiol. 1999;83(7):1090–3. https://doi.org/10.1016/s0002-9149(99)00021-1.
29. Pahor M, Guralnik JM, Ferrucci L, Corti MC, Salive ME, Cerhan JR, et al. Calcium-channel blockade and incidence of cancer in aged populations. Lancet. 1996;348(9026):493–7. https://doi.org/10.1016/s0140-6736(96)04277-8.
30. Horiguchi A, Ito K, Sumitomo M, Kimura F, Asano T, Hayakawa M. Decreased serum adiponectin levels in patients with metastatic renal cell carcinoma. Jpn J Clin Oncol. 2008;38(2):106–11. https://doi.org/10.1093/jjco/hym158.
31. Ghadge AA, Khaire AA, Kuvalekar AA. Adiponectin: A potential therapeutic target for metabolic syndrome. Cytokine Growth Factor Rev. 2018;39:151–8. https://doi.org/10.1016/j.cytogfr.2018.01.004.
32. Zhang GM, Zhu Y, Ye DW. Metabolic syndrome and renal cell carcinoma. World J Surg Oncol. 2014;12:236. https://doi.org/10.1186/1477-7819-12-236.
33. Harvey AE, Lashinger LM, Hursting SD. The growing challenge of obesity and cancer: an inflammatory issue. Ann N Y Acad Sci. 2011;1229:45–52. https://doi.org/10.1111/j.1749-6632.2011.06096.x.
34. Reuter S, Gupta SC, Chaturvedi MM, Aggarwal BB. Oxidative stress, inflammation, and cancer: how are they linked? Free Radic Biol Med. 2010;49(11):1603–16. https://doi.org/10.1016/j.freeradbiomed.2010.09.006.
35. Eskelinen TJ, Kotsar A, Tammela TLJ, Murtola TJ. Components of metabolic syndrome and prognosis of renal cell cancer. Scand J Urol. 2017;51(6):435–41. https://doi.org/10.1080/21681805.2017.1352616.
36. Qin G, Sun Z, Jin Y, Ren X, Zhang Z, Wang S, et al. The association between the triglyceride-glucose index and prognosis in postoperative renal cell carcinoma patients: a retrospective cohort study. Front Endocrinol. 2024;15:1301703. https://doi.org/10.3389/fendo.2024.1301703.
37. Liu Z, Wang H, Zhang L, Li S, Fan Y, Meng Y, et al. Metabolic syndrome is associated with improved cancer-specific survival in patients with localized clear cell renal cell carcinoma. Transl Androl Urol. 2019;8(5):507–18. https://doi.org/10.21037/tau.2019.10.04.
38. Zuo MN, Du YQ, Yu LP, Dai X, Xu T. Correlation between metabolic syndrome and prognosis of patients with clear cell renal cell carcinoma. Beijing Da Xue Xue Bao Yi Xue Ban. 2022;54(4):636–43. https://doi.org/10.19723/j.issn.1671-167X.2022.04.009.
39. Eskelinen T, Kotsar A, Tammela TLJ, Murtola TJ. Components of metabolic syndrome and prognosis of renal cell cancer. Eur Urol Suppl. 2017;16(5):e2168. https://doi.org/10.1016/S1569-9056(17)31326-X.
40. DeFronzo RA, Tobin JD, Andres R. Glucose clamp technique: a method for quantifying insulin secretion and resistance. Am J Physiol. 1979;237(3):E214–23. https://doi.org/10.1152/ajpendo.1979.237.3.E214.
41. Xia W, Cai Y, Zhang S, Wu S. Association between different insulin resistance surrogates and infertility in reproductive-aged females. BMC Public Health. 2023;23(1):1985. https://doi.org/10.1186/s12889-023-16813-2.
42. Cao S, Meng L, Lin L, Hu X, Li X. The association between the metabolic score for insulin resistance (METS-IR) index and urinary incontinence in the United States: results from the National Health and Nutrition Examination Survey (NHANES) 2001–2018. Diabetol Metab Syndr. 2023;15(1):248. https://doi.org/10.1186/s13098-023-01226-3.
43. Shi YY, Zheng R, Cai JJ, Qian SZ. The association between triglyceride glucose index and depression: data from NHANES 2005–2018. BMC Psychiatry. 2021;21(1):267. https://doi.org/10.1186/s12888-021-03275-2.

Publisher's Note