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Are Your Painkillers Putting Your Kidneys at Risk? A Meta-Analysis of Non-Aspirin NSAIDs and Kidney Cancer

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ABSTRACT

Background: Kidney cancer cases are rising globally, with over 400,000 new cases reported annually. Nonsteroidal anti-inflammatory drugs (NSAIDs), widely used for pain relief, have been linked to an increased risk of kidney cancer, particularly renal cell carcinoma, with long-term use of non-aspirin NSAIDs. This association may be due to chronic kidney damage and prostaglandin-mediated DNA alterations, though the evidence remains inconsistent. However, evidence remains inconsistent, and clarifying this relationship is clinically important given the widespread and often prolonged use of non-aspirin NSAIDs. Objectives: This meta-analysis reviews recent studies (2014–2024) to reassess the relationship between non-aspirin NSAIDs and kidney cancer Methods: This meta-analysis followed PRISMA 2020 guidelines, reviewing case-control studies (2014–2024) on non-aspirin NSAIDs and kidney cancer risk from PubMed, Scopus, Web of Science, and Cochrane. Data extraction, bias assessment (ROBINS-E), and quantitative analysis (Review Manager 5.4) were conducted, with significance set at $p<0.05$ and heterogeneity assessed via I^2. **Results:** Out of 190 studies, two studies met inclusion criteria. The risk of bias was low in both included studies. Meta-analysis revealed an OR of 2.08 [95% CI: 0.77–5.65], indicating no significant association (p=0.15). Substantial heterogeneity was observed (I^2=95%), likely reflecting marked differences in sample sizes between the included case-control studies. These findings highlight the need for further research to better understand the relationship between non-aspirin NSAID use and kidney cancer risk and to address the observed inconsistencies. Conclusion: This meta-analysis suggests a potential link between non-aspirin NSAIDs and kidney cancer, though results lacked statistical significance. Future studies should focus on larger, more homogeneous populations with standardized definitions of non-aspirin NSAID exposure duration and clearly defined latency periods for kidney cancer outcomes.

Keyword: Cancer risk, Kidney cancer, Non-aspirin NSAIDs, Renal cell carcinoma

ABSTRAK

Latar Belakang : Kasus kanker ginjal meningkat secara global, dengan lebih dari 400.000 kasus baru dilaporkan setiap tahun. Obat nonsteroidal anti-inflammatory (NSAIDs), yang banyak digunakan untuk meredakan nyeri, telah dikaitkan dengan peningkatan risiko kanker ginjal, khususnya karsinoma sel ginjal, terutama pada penggunaan jangka panjang NSAID non-aspirin. Asosiasi ini mungkin disebabkan oleh kerusakan ginjal kronis dan perubahan DNA yang dimediasi prostaglandin, meskipun buktinya masih tidak konsisten. Namun, bukti yang ada masih tidak konsisten, dan klarifikasi hubungan ini penting secara klinis mengingat penggunaan NSAID non-aspirin yang luas dan sering kali berlangsung dalam jangka panjang. Objectives: Meta-analisis ini meninjau studi-studi terbaru (2014–2024) untuk menilai hubungan antara NSAID non-aspirin dan kanker ginjal. Methods: Meta-analisis ini mengikuti pedoman PRISMA 2020, meninjau studi case-control (2014–2024) mengenai risiko kanker ginjal terkait NSAID non-aspirin dari PubMed, Scopus, Web of Science, dan Cochrane. Ekstraksi data, penilaian bias (ROBINS-E), dan analisis kuantitatif (Review Manager 5.4) dilakukan, dengan batas signifikansi $p<0.05$ dan heterogenitas dinilai menggunakan I^2. Results: Dari 190 studi, dua studi memenuhi kriteria inklusi. Risiko bias rendah pada kedua studi. Meta-analisis menunjukkan OR 2.08 [95% CI: 0.77–5.65], yang mengindikasikan tidak ada asosiasi yang signifikan (p=0.15). Heterogenitas yang tinggi ditemukan (I^2 = 95%), yang kemungkinan mencerminkan perbedaan ukuran sampel yang mencolok antar studi case-control yang disertakan. Temuan ini menekankan perlunya penelitian lebih lanjut untuk

memahami hubungan antara penggunaan NSAID non-aspirin dan risiko kanker ginjal serta untuk mengatasi inkonsistensi yang terlihat. Conclusion: Meta-analisis ini menunjukkan adanya potensi hubungan antara NSAID non-aspirin dan kanker ginjal, meskipun hasilnya tidak mencapai signifikansi statistik. Penelitian selanjutnya sebaiknya berfokus pada populasi yang lebih besar dan lebih homogen, dengan definisi durasi paparan NSAID non-aspirin yang terstandarisasi serta periode laten yang didefinisikan secara jelas antara penggunaan NSAID non-aspirin dan terjadinya kanker ginjal.

Kata Kunci : *Kanker ginjal, Karsinoma sel ginjal, Non-aspirin NSAIDs, Risiko kanker*

1. Introduction

Kidney cancer continues to rise each year, with around 400,000 new cases reported annually and an estimated 175,000 deaths within the same period. Its causes are complex and influenced by many factors. Some evidence suggests that both incidence and mortality may be higher in lower-resource settings, potentially linked to exposures like tobacco use, excess body weight, and elevated blood pressure, and other factors. Despite these observations, the precise underlying cause of kidney cancer remains not fully understood.[1] Numerous meta-analyses published about a decade ago reported that the use of certain analgesics, including aspirin and non-aspirin NSAIDs, was significantly associated with a higher risk of kidney cancer. However, these findings remain inconsistent, as other studies found no clear association involving non-aspirin NSAID use and the development of kidney cancer.[2]

Nonsteroidal anti-inflammatory drugs (NSAIDs) are widely used because they reduce fever, relieve inflammation, and ease pain. These medications are grouped based on their chemical structure and their selectivity, which includes acetylated salicylates such as aspirin, propionic acid derivatives such as ibuprofen and naproxen, and selective COX 2 inhibitors such as celecoxib. NSAIDs act by blocking the COX enzyme, which is needed to produce eicosanoids like prostaglandins that play key roles in inflammation, pain regulation, and blood vessel dilation. COX-1 plays a role in maintaining the gastric lining and supporting renal function, while COX-2 is generated as part of the inflammatory response. Most NSAIDs block both COX-1 and COX-2, whereas COX-2–selective agents act only on COX-2 and therefore reduce inflammation with fewer gastrointestinal effects.[3] Although NSAIDs are effective and widely used, long-term use of non-aspirin NSAIDs has been associated with a higher risk of kidney cancer, especially renal cell carcinoma. This association may be related to chronic kidney injury and DNA changes influenced by prostaglandins.[4] Interestingly, NSAIDs can also have anti-tumor effects, particularly in colorectal cancer. These effects are thought to occur mainly through COX 2 inhibition, although COX independent pathways may also play a role. Research indicates that NSAIDs may help suppress early cancerous changes, encourage tumor regression, and modestly reduce the recurrence of colorectal adenomas.[5]

The effects of NSAIDs on the kidneys show how these medications can provide benefits while also posing risks. By blocking COX enzymes, NSAIDs lower the production of prostaglandins, which play an important role in maintaining kidney blood flow through vasodilation. In people who are already at higher risk, this reduction in prostaglandins can result in stronger vasoconstriction, lower renal blood flow, and decreased glomerular filtration. If this continues, it may progress to renal ischemia and acute tubular necrosis. Fortunately, these problems are often reversible once NSAIDs are stopped.[6] Acute kidney injury (AKI) may also increase the likelihood of kidney cancer through several biological mechanisms related to tissue damage and repair. When the kidneys are injured, the body activates renal progenitor cells to replace the damaged tissue. This rapid cell growth, combined with oxidative stress and inflammation, can create conditions that favor genetic mutations. Important pathways involved in cancer development, such as HIF, mTOR, and Notch, may also become activated during this process. Repeated or long-standing episodes of AKI can lead to continuous tissue injury, which may play a role in the formation of renal tumors, particularly papillary renal cell carcinoma.[7]

The use of pain-relieving medications is very common in everyday life, especially since drugs like aspirin, non-aspirin NSAIDs, and other analgesics can be easily purchased without a prescription. This easy access increases the possibility of misuse, which can have harmful effects. Regular or prolonged use of these medications, including both aspirin and non-aspirin types, can cause kidney damage and may eventually lead to chronic kidney failure. In addition, some reports from patients suggest that frequent use of these analgesics could be linked to a higher risk of developing kidney cancer.[2] Supporting this concern, a study by Babelghaith

et al. (2019) found that patients used NSAIDs for about 7 years, with 45% taking them daily and 38% as needed. Despite such widespread use, only a quarter of these patients received advice on the risks from healthcare providers.[8] Therefore, it is important to conduct further observational research on the causes of kidney cancer to aid in its prevention.

The aim of this meta-analysis is to provide an updated review of previous meta-analyses regarding the risk associated with the use of non-aspirin NSAIDs and kidney cancer. Because the existing evidence remains inconsistent, clarifying this relationship is clinically important given the widespread and often prolonged use of non-aspirin NSAIDs. Specifically, this study examines whether recent observational studies conducted within the past decade (2014–2024) corroborate the findings of earlier research, which identified non-aspirin NSAIDs as a risk factor for kidney cancer, or if the results differ. This study focuses exclusively on non-aspirin NSAIDs to ensure a more precise analysis.

2. Method

2.1 Search Strategy and Selection Criteria

A meta-analysis and systematic review were conducted to evaluate the relationship between non-aspirin NSAID use and kidney cancer risk. Relevant studies were identified through searches in PubMed, Scopus, Web of Science, and Cochrane databases from January 2014 to December 2024. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 guidelines were followed throughout the review process. The search strategy used was a modification of: (non-aspirin NSAID OR "non-aspirin nonsteroidal anti-inflammatory agents") AND (neoplasms OR "kidney neoplasms" OR "renal cell carcinoma" OR "kidney cancer").

2.2 Eligibility Criteria

This review included original case-control studies that examined the association between non-aspirin NSAID use and kidney cancer risk, in accordance with the PICO framework (Figure 1). Studies were eligible if they met the following criteria: 1) case-control design, and 2) evaluation of non-aspirin NSAID exposure in relation to kidney cancer risk. Studies were excluded if they did not address non-aspirin NSAID use and kidney cancer, were not written in English, or lacked full-text availability. Systematic reviews and meta-analyses were excluded, although reference lists were manually screened to identify additional primary studies.

2.3 Data Extraction and Analysis

Two independent authors screened all titles and abstracts after removing duplicates. Full texts of potentially eligible studies were then reviewed by the same authors. Any disagreements were resolved through discussion with all team members. Extracted data included: 1) year of publication, 2) authors, 3) study design, 4) outcomes, 5) number of cases and controls, 6) exposure definitions, 7) odds ratios or hazard ratios, 8) adjustment variables, and 9) conclusions. Data extraction was conducted by two authors and cross-checked by the primary author. The study selection process is illustrated in Figure 1.

2.4 Quality Assessment

Risk of bias was evaluated using the ROBINS-E tool, which assesses seven domains: confounding, measurement of exposure, selection of participants, post-exposure interventions, missing data, outcome measurement, and selection of reported results. Each study was categorized as low risk of bias, some concerns, or high risk of bias across these domains.[9]

2.5 Meta-analysis

Review Manager 5.4 (RevMan) was used for quantitative analysis. The primary effect size was pooled odds ratio (OR) with a 95% confidence interval (CI). A p-value of less than 0.05 was considered statistically significant. Heterogeneity across studies was assessed using the I^2 statistic, defined as high when greater than 50%, moderate between 26% and 50%, and low when less than 26%.

3. Results

3.1 Study selection and characteristics

The literature search (Figure 1) presents a detailed flow diagram outlining the study selection process, including all exclusions made during screening. A total of 190 studies were identified across four databases. After removing duplicates and irrelevant records, 78 records were screened, of which 37 were excluded. Forty-one reports were sought for retrieval, and 31 were assessed for eligibility. Ultimately, two studies met the

inclusion criteria and were included in this systematic review and meta-analysis. The characteristics and key findings of these two studies are summarized in Table 1.

3.2 Data extraction and Risk of bias in studies

The included studies consisted of two case-control studies. The risk of bias assessment is shown in Figure 2. Using the ROBINS-E tool, both case-control studies were judged to have a low risk of bias.

3.3 Description of study outcomes

This review evaluates the association between non-aspirin NSAID use and the risk of kidney cancer. Both included studies were case-control designs assessing the odds ratio of kidney cancer occurrence in relation to non-aspirin NSAID exposure.

Table 1. Study Summaries

No	Author (Year)	Country	Design of Study	Outcome	No Cases	Exposure definition	RR (95% CI) OR (95% CI)	Conclusions
1	Bruinsma.t et al., 2021[10]	Australia	Population-based case-control	Kidney cancer	Cases: 1064 Control:724	Regular analgesic use. Duration and Frequency of use.	Paracetamol (OR 1.41, 95%CI 1.13–1.77). NSAIDs (OR 1.71, 95% CI 1.23–2.39)	An elevated risk of RCC was observed with paracetamol use, whereas NSAIDs showed an increased risk only among female users.
2.	Nayan et al., 2017 [11]	Canada	Population-based case-control	Kidney cancer	Cases :10,377 Control:35,939	6 months of exposure, 3 years versus <3 years, Ever exposure versus never	NSAIDs OR (95% CI) A. 1.00 (4.8 103) B. 1.04 (5.3 102) C. 0.92 (2.5 102)	Kidney cancer risk was not shown to increase with NSAID exposure, regardless of the length of usage.

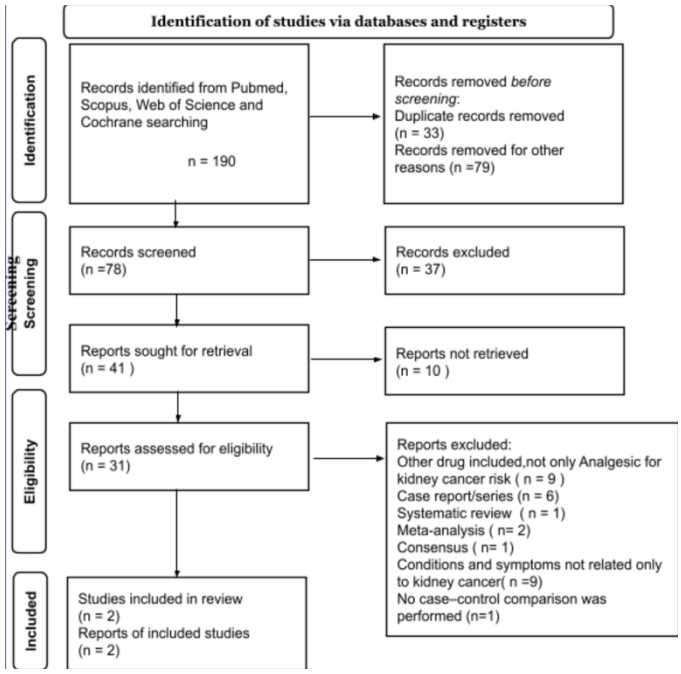

Figure 1. PRISMA (Preferred Reporting Items for Systematic Review and Meta-analysis) flow diagram

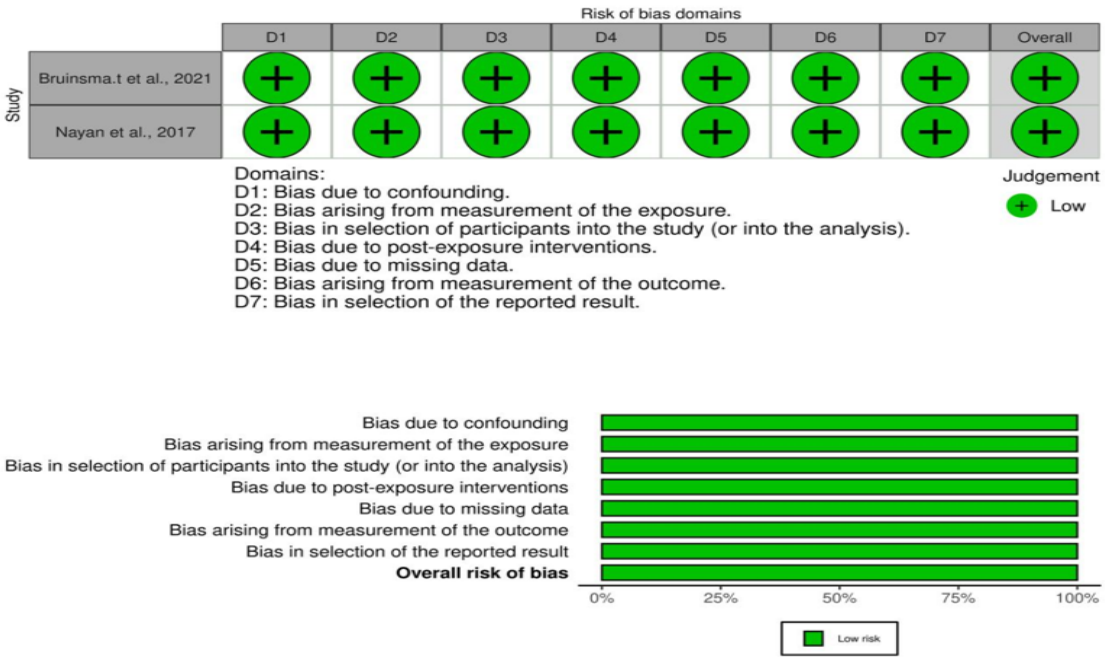

Figure.2 Risk of bias assessments of observational studies by Robins-E

3. 3 Relationship between Non-Aspirin NSAIDs and Kidney Cancer

The meta-analysis evaluating the association between non-aspirin NSAID use and kidney cancer reported an odds ratio of 2.08 (95% CI: 0.77–5.65). This estimate is not statistically significant, as shown by the overall effect test ($Z = 1.44$, $P = 0.15$), indicating insufficient evidence to establish a meaningful relationship. Substantial heterogeneity was observed ($Tau^2 = 0.49$; $Chi^2 = 18.85$, $df = 1$, $P < 0.0001$; $I^2 = 95\%$), suggesting considerable variability between studies. This high heterogeneity likely reflects marked differences in sample sizes among the included case-control studies. Although the pooled OR of 2.08 suggests a possible increased

risk, the wide confidence interval and lack of statistical significance prevent reliable interpretation or generalization. (Figure 3.) This conclusion is consistent with the findings of Kang et al. (2017), who also reported that non-aspirin NSAID use was not significantly associated with kidney cancer risk. In contrast, their study demonstrated that aspirin (HR 1.28) and statins (HR 1.55) were significantly associated with increased kidney cancer risk over a 10-year follow-up period.[12]

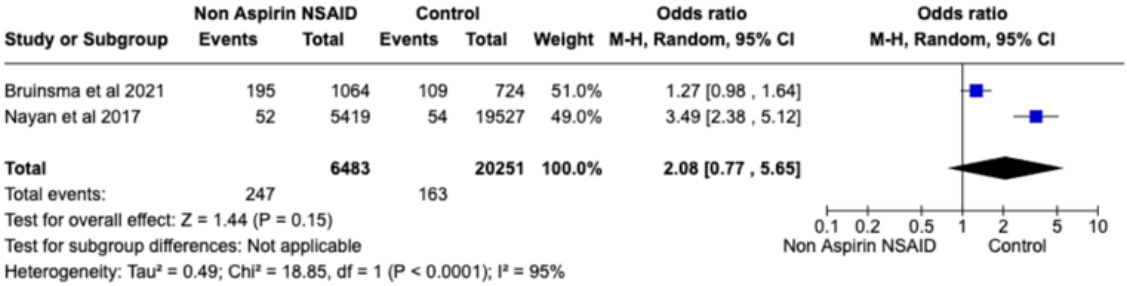

Figure 3. Forrest Plot Non Aspirin NSAID exposure and Kidney Cancer Occurrence

4. Discussion

Renal cell carcinoma (RCC) represents the predominant form of kidney cancer in adults, comprising over 90% of all diagnosed cases. RCC represents more than 3% of adult cancers and most often occurs between 50 and 70 years of age, with men affected about twice as frequently as women.[10,11] Tobacco use is the strongest risk factor for RCC, whether through cigarettes, pipes, or cigars. Obesity, especially in women, also contributes significantly. Research suggests that eliminating smoking and reducing excess body weight could prevent a substantial proportion of kidney cancer cases. Other risk factors include high blood pressure, chronic kidney failure, and occupational exposure to chemicals such as trichloroethylene. In contrast, moderate alcohol consumption, nutritional intake high in plant-based foods, and regular intake of fatty fish have been linked to reduced kidney cancer risk. Hereditary influences are also significant, with alterations in the VHL gene found in both sporadic and familial clear cell RCC (CCRCC). In papillary RCC (PRCC), hereditary cases frequently involve mutations in the MET gene, while sporadic PRCC displays a wider and more diverse range of molecular abnormalities.[13–17]

NSAIDs are widely used by the general population because they treat many common conditions.[3] They are among the most frequently consumed medications worldwide. [18] In many countries, people can purchase NSAIDs without a prescription, which has likely contributed to the steady increase in their use over the past twenty years. [19] In the United States alone, an estimated 72 million people regularly used NSAIDs in 2010, taking them at least three times a week for a minimum of three months.[20] Several pain-relieving drugs, including aspirin and non-aspirin NSAIDs, have been linked to lower risks of cancers such as breast, prostate, and colorectal cancer. However, their effect on kidney cancer, particularly renal cell carcinoma, is still unclear. Long-term use of older analgesics that contain phenacetin, a drug now banned, can cause analgesic nephropathy, which may progress to chronic kidney failure. A meta-analysis by Choueiri et al. in 2014 found that evidence from 20 observational studies suggests that acetaminophen and non-aspirin NSAIDs may be associated with an increased risk of kidney cancer. The authors also noted several limitations, such as differences in patient risk factors, variations in the types of analgesics used, differences in how long the medications were taken, and the inclusion of several kidney cancer subtypes, not only RCC.[2] Similar concerns were highlighted in a recent umbrella review by Wang et al. in 2024, which reported that although NSAIDs may reduce the risk of some cancers, regular use of non-aspirin NSAIDs could increase the risk of kidney cancer, especially when taken for long periods or at high doses.[21]

NSAIDs can cause AKI by blocking the enzymes COX 1 and COX 2. These enzymes are needed to produce prostaglandins such as PGE2 and PGI2, which help maintain kidney blood flow, especially when circulation is reduced. When this protective mechanism is inhibited, kidney blood flow and filtration decrease. This effect is more pronounced in people who already have conditions like heart or liver disease, or in those who take diuretics or RAAS inhibitors. NSAIDs can also interfere with electrolyte balance and fluid regulation, which further strains the kidneys and increases the risk of AKI. NSAIDs can also contribute to CKD when used for long periods. Long-term reduction of prostaglandin production affects the ability of the kidneys to maintain normal blood flow and function. This can result in persistent changes in kidney circulation and gradual structural damage. Prolonged NSAID exposure has been linked to tubulointerstitial nephritis (TIN), which involves inflammation and scarring in the kidney tissues and leads to worsening kidney function. Over time, changes such as thinning of the glomerular basement membrane and loss of podocytes can accelerate the

development of CKD. The risk is higher in people with existing health problems or in those who take NSAIDs together with other medications that can harm the kidneys.[22]

AKI and CKD can both contribute to the development of cancer through processes related to tissue damage and repair. These conditions can lead to DNA injury and mutations in kidney cells. During AKI, reduced oxygen levels and inflammation stimulate the growth of renal progenitor cells, and these cells may accumulate mutations during the repair process, which can eventually form precancerous or malignant cells. CKD involves ongoing and persistent kidney injury that results in long-term inflammation and metabolic stress, creating an environment that increases the likelihood of tumor formation. Both AKI and CKD activate cellular pathways such as hypoxia inducible factor (HIF) and the mechanistic target of rapamycin (mTOR), which promote abnormal cell growth and help explain how kidney injury can lead to cancer development.[7] In contrast, some studies suggest that NSAIDs may play a protective role against kidney cancer and other types of cancer by blocking cyclooxygenase (COX) enzymes, especially COX 2, which is often highly expressed in tumors. COX 2 produces prostaglandins such as PGE2 that support tumor growth by encouraging cell proliferation, reducing cell death, and promoting the formation of new blood vessels. By lowering prostaglandin production, NSAIDs interfere with these cancer promoting processes. NSAIDs also reduce chronic inflammation, affect important cancer related pathways such as NF kappa B and Akt, and influence the tumor environment by modifying immune responses and limiting blood vessel formation. These combined effects may help prevent the initiation and progression of tumors.[10]

Our meta-analysis of two case control studies, Bruinsma et al. (2021) and Nayan et al. (2017), reported a pooled odds ratio (OR) of 2.08 with a 95% confidence interval (CI) of 0.77 to 5.65. This indicates a potential association between the use of acetaminophen and non-aspirin NSAIDs and an increased risk of kidney cancer. However, as the confidence interval includes 1.0 and the p-value is 0.15, the result is not statistically significant, suggesting the association may be due to chance. The analysis also revealed significant heterogeneity among the studies. A Tau^2 value of 0.49 and a Chi^2 statistic of 18.85 with 1 degree of freedom ($p < 0.0001$) indicate substantial variability. Furthermore, an I^2 value of 95% confirms that the observed effect sizes vary considerably between the studies. These findings highlight the limitations of the meta-analysis, including high heterogeneity and lack of statistical significance. As a result, the pooled estimate should be interpreted cautiously, emphasizing the need for further research to clarify the potential relationship between these analgesics and kidney cancer risk.

In contrast to the 2014 meta-analysis by Choueiri et al., which found that the use of acetaminophen and non-aspirin NSAIDs was linked to a higher likelihood of developing kidney cancer, with pooled relative risks (RR) of 1.28 (95% CI: 1.15–1.44) and 1.25 (95% CI: 1.06–1.46), respectively, our meta-analysis differs. In their study, aspirin use showed no overall increased risk (pooled RR: 1.10, 95% CI: 0.95–1.28), except in non-US studies, where a slight increase was observed (5 studies, pooled RR: 1.17, 95% CI: 1.04–1.33).[2] However, there are very few recent observational studies in the past 10 years directly analyzing the impact of non-aspirin NSAID use on kidney cancer. As a result, our meta-analysis only included 2 case-control studies. The findings showed an odds ratio (OR) greater than 1, indicating a potential association between non-aspirin NSAID use and kidney cancer, but this result was not statistically significant. This could be due to the small number of studies included, wide methodological differences, and other factors. Nonetheless, in the past decade, only a limited number of studies have explored this relationship.

The individual study findings also demonstrate variation. Bruinsma et al. (2021) reported that regular paracetamol use was associated with an increased risk of renal cell carcinoma (RCC) (OR 1.41, 95% CI: 1.13–1.77), with a stronger association observed among women using non-aspirin NSAIDs (OR 1.71, 95% CI: 1.23–2.39), while no association was seen in men (OR 0.83, 95% CI: 0.58–1.18; p-interaction = 0.003). They found no dose-response trend for paracetamol duration ($p = 0.77$) and only weak evidence for non-aspirin NSAID use in women ($p = 0.054$).[10] Conversely, Nayan et al. (2017) reported that long-term use of aspirin or NSAIDs was not associated with kidney cancer. Instead, their study identified long-term antihypertensive use (ACE inhibitors, ARBs, and calcium channel blockers) as significantly associated with kidney cancer risk, while NSAIDs, SSRIs, and statins showed no such association.[11]

Besides differences in population size among the included studies, the observed variability may also be explained by differences in confounder control and methodological approaches. The CONFIRM study by Bruinsma et al. adjusted for key kidney cancer risk factors, including age, sex, body mass index, smoking, hypertension, diabetes, alcohol intake, and family history, with confounder selection guided by directed acyclic

graphs to minimize bias. To reduce reverse causation, NSAID exposure was defined as regular use initiated at least two years before diagnosis; however, exposure assessment relied on self-reported data and may remain susceptible to recall bias. [10] In contrast, the population-based study by Nayan et al. used prescription claims data to objectively quantify cumulative NSAID exposure, substantially reducing recall bias and allowing detailed modeling of exposure duration, while also adjusting for multiple comorbidities, healthcare utilization, and duration of hypertension to limit confounding by indication and detection bias. However, this study was restricted to individuals aged 66 years and older, which may limit generalizability to younger NSAID users, and demonstrated that effect estimates varied depending on the exposure modeling strategy. [11] Overall, these differences in population characteristics, exposure assessment, confounder adjustment, and latency considerations likely contributed to the substantial heterogeneity observed in this meta-analysis.

4.1 Limitations and Future Research Directions

Our meta-analysis study suggests a potential association between the use of non-aspirin NSAIDs and the occurrence of kidney cancer, although the results were not statistically significant. Several factors may explain this outcome. First, there is a lack of studies conducted in the last decade, limiting the number of studies included in the quantitative analysis. Second, there is considerable variability among the studies in terms of the types of NSAIDs analyzed, their dosages, and their intended uses, contributing to heterogeneity in the findings. Additionally, kidney cancer encompasses various subtypes, such as clear cell carcinoma and others. However, many studies did not specify whether the outcomes assessed were specific to one subtype or all types collectively. The limited number of observational studies identified between 2014 and 2024 further restricts the scope of the analysis. Moreover, some studies did not clearly differentiate whether the association between NSAIDs/non-aspirin NSAIDs and kidney cancer was due solely to NSAID use or influenced by other contributing factors. Due to the scarcity of recent studies, only two types of observational studies were included in our meta-analysis, reflecting the limited research available in the past decade on this topic. Despite these limitations, our study provides an updated overview of research over the last 10 years, compared to earlier meta-analyses from 2014. While the statistical significance of our findings is limited, the identification of non-aspirin NSAIDs as a potential risk factor for kidney cancer underscores the need for further research. Future research should prioritize larger and more homogeneous studies with standardized definitions of non-aspirin NSAID exposure, including duration and timing of use, as well as clearly defined latency periods between NSAID consumption and the diagnosis of kidney cancer, to enable clearer and more reliable conclusions. This approach will be essential for establishing clinical guidelines for NSAID use and gaining a better understanding of the causes and etiology of kidney cancer.

5. Conclusion

This meta-analysis explored the relationship between non-aspirin NSAIDs and kidney cancer risk, highlighting the limited number of recent studies. Although no statistically significant association was observed, the elevated pooled effect estimate suggests a possible increased risk between non-aspirin NSAIDs and kidney cancer. These preliminary findings should be interpreted with caution and validated by larger, well-designed studies. Future studies should focus on larger, more homogeneous populations with standardized definitions of non-aspirin NSAID exposure duration and clearly defined latency periods for kidney cancer outcomes.

References

[1] Cirillo L, Innocenti S, Becherucci F. Global epidemiology of kidney cancer. Nephrol Dial Transplant. 2024;39(6):920–8.
[2] Choueiri TK, Je Y, Cho E. Analgesic use and the risk of kidney cancer: a meta-analysis of epidemiologic studies. Int J Cancer. 2014;134(2):384–96.
[3] Ghlichloo I, Gerriets V. Nonsteroidal anti-inflammatory drugs (NSAIDs). StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024.
[4] Susman E. Beware of non-aspirin NSAIDs for kidney cancer patients. Oncol Times. 2016;38(6):21. doi:10.1097/01.COT.0000482228.48342.79
[5] Hamieh L, Moreira RB, Lin X, Simantov R, Choueiri TK, McKay RR. Impact of aspirin and non-aspirin NSAIDs on outcomes in patients with metastatic renal cell carcinoma. Kidney Cancer. 2018;2(1):37–46.
[6] Klomjit N, Ungprasert P. Acute kidney injury associated with non-steroidal anti-inflammatory drugs. Eur J Intern Med. 2022;101:21–8.
[7] Peired AJ, Lazzeri E, Guzzi F, Anders HJ, Romagnani P. From kidney injury to kidney cancer. Kidney Int. 2021;100(1):55–66.

[8] Babelghaith SD, Alarifi MN, Wajid S, Alhawassi TM, Alqahtani SK, Alghadeer SM. Knowledge of patients on safe medication use in relation to NSAIDs. Saudi J Anaesth. 2019;13(2):106–11. doi:10.4103/sja.SJA_557_18
[9] Higgins JPT, Morgan RL, Rooney AA, Taylor KW, Thayer KA, Silva RA, et al. A tool to assess risk of bias in non-randomized follow-up studies of exposure effects (ROBINS-E). Environ Int. 2024;108602.
[10] Bruinsma FJ, et al. Analgesic use and the risk of renal cell carcinoma: findings from the CONFIRM study. Cancer Epidemiol. 2021;75:102036. doi:10.1016/j.canep.2021.102036
[11] Nayan M, et al. Medication use and kidney cancer risk: a population-based study. Eur J Cancer. 2017;83:203–10. doi:10.1016/j.ejca.2017.07.001
[12] Kang M, Ku JH, Kwak C, Kim HH, Jeong CW. Effects of aspirin, NSAIDs, statin, and COX-2 inhibitor on the development of urological malignancies: a population-based study with 10-year follow-up in Korea. Cancer Res Treat. 2018;50(3):984–91. doi:10.4143/crt.2017.248
[13] Pandey J, Syed W. Renal cancer. StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025.
[14] Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. CA Cancer J Clin. 2020;70(1):7–30. doi:10.3322/caac.21590
[15] Alaghehbandan R, Perez Montiel D, Luis AS, Hes O. Molecular genetics of renal cell tumors: a practical diagnostic approach. Cancers (Basel). 2019;12(1):1. doi:10.3390/cancers12010001
[16] Akhtar M, Al-Bozom IA, Al Hussain T. Papillary renal cell carcinoma (PRCC): an update. Adv Anat Pathol. 2019;26(2):124–32. doi:10.1097/PAP.0000000000000222
[17] Nabi S, Kessler ER, Bernard B, Flaig TW, Lam ET. Renal cell carcinoma: a review of biology and pathophysiology. F1000Res. 2018;7:307. doi:10.12688/f1000research.14945.1
[18] Godersky ME, Vercammen LK, Ventura AS, Walley AY, Saitz R. Identification of non-steroidal anti-inflammatory drug use disorder: a case report. Addict Behav. 2017;70:61–4. doi:10.1016/j.addbeh.2017.02.008
[19] Mullan J, Weston KM, Bonner C, McCaffery K, Williams KM. Consumer knowledge about over-the-counter NSAIDs. Aust N Z J Public Health. 2017;41(2):210–4. doi:10.1111/1753-6405.12589
[20] Zhou Y, Boudreau DM, Freedman AN. Trends in the use of aspirin and NSAIDs in the general U.S. population. Pharmacoepidemiol Drug Saf. 2014;23:43–50. doi:10.1002/pds.3463
[21] Wang P, Chen B, Huang Y, et al. The relationship between NSAIDs and cancer incidence: an umbrella review. Heliyon. 2024;10(1):e23203. doi:10.1016/j.heliyon.2023.e23203
[22] Drożdżal S, Lechowicz K, Szostak B, et al. Kidney damage from NSAIDs—myth or truth? A review of selected literature. Pharmacol Res Perspect. 2021;9(4):e00817. doi:10.1002/prp2.817
[23] Primasari D, et al. Perbedaan perkembangan pada anak dengan penyakit jantung bawaan sianotik dan non-sianotik. J Kedokt Diponegoro. 2012;1(1).