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REVIEW

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Incidence of major urological cancers in patients on dialysis: a systematic review and meta-analysis

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Abstract

Background Studies have demonstrated an elevated risk of urological malignancies in individuals undergoing dialysis, which consequently leads to unfavorable prognoses and diminished quality of life for patients with end-stage kidney disease. Nevertheless, the absence of standardized recommendations for cancer screening and limited utilization of conventional screening methods within the dialysis population remain prevalent issues. Methods: A meta-analysis was conducted on cohort studies published prior to June 2024, aiming to quantify the cancer risk among individuals undergoing dialysis. Random-effects meta-analyses were employed to combine standardized incidence rates (SIRs) along with their corresponding 95% confidence intervals, considering a *p*-value of less than 0.05 or an I^2 value exceeding 50%. Subgroup analyses, heterogeneity tests, and sensitivity analyses were performed as well. Results: A total of 10 studies, consisting of 12 cohort studies, were ultimately identified, encompassing a collective patient population of 1,362,196 individuals. Compared to the general population, the pooled SIRs for all cancers except non-melanoma skin cancer (NMSC), major urological cancers (MUCs), cancers of the kidney/renal pelvis, bladder cancers and prostate cancers were 1.40 (95% CI: 1.28–1.54), 1.76 (95% CI: 1.45–2.14), 4.73 (95% CI: 3.96–5.64), 1.89 (95% CI: 1.61–2.21) and 0.94 (95% CI: 0.79–1.11), respectively. The cancer risk was notably elevated in specific subgroups of women, younger patients (age at first dialysis, 0–34 years), during the initial year of dialysis, and among Asian patients. SIRs differed when considering different primary renal diseases. However, high heterogeneity was observed among the studies investigating cancers during dialysis, while this heterogeneity did not have a substantial impact on the pooled SIRs for overall cancer, as determined through sensitivity analysis. Conclusions: Compared with the general population, the dialysis population had a significantly increased risk of developing urological malignancies, particularly cancers of the kidney/renal pelvis. Our findings indicate a substantial increase in risks among female, young, Asian patients, during the first year of dialysis and highlight variations in SIRs based on primary renal disease. These results suggest the potential for adopting a more personalized approach to cancer

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screening in chronic dialysis patients. Given the considerable heterogeneity observed, further rigorous investigations are warranted to enhance our understanding in this area.

Keywords Dialysis, Cancer risk, Bladder cancer, Prostate cancer, Kidney neoplasms

Introduction

End-stage renal disease (ESRD) is characterized by kidney function insufficient to sustain long-term survival without kidney transplantation or dialysis. Currently, dialysis is the most common treatment for patients with ESRD, alleviating severe complications and extending survival [1]. As the expected remaining lifespan of most patients undergoing maintenance dialysis continues to increase, cancer has emerged as an increasingly pertinent health concern for these individuals [2, 3]. However, several challenges hinder the effective implementation of cancer screening in ESRD patients, including drug-induced acute kidney injury, limitations in radiologic imaging, and mortality from competing causes such as cardiovascular diseases and infections [4, 5]. Consequently, cancer screening recommendations are not generalizable to ESRD patients [6]. It is crucial to carefully weigh a patient's life expectancy, preferences, eligibility for kidney transplantation, and the potential benefits of screening against its associated risks and costs [7]. Additionally, there should be a heightened focus on addressing cancers that are most prevalent among individuals undergoing dialysis treatment.

Patients undergoing dialysis are recognized to have a heightened susceptibility to cancer compared to the general population [2]an. This elevated risk is attributed to immune system dysfunction, the accumulation of carcinogenic substances due to impaired renal function, compromised DNA repair mechanisms, and chronic inflammation [8, 9]. Among malignancies in ESRD patients, urological cancers (UCs) represent a significant proportion, including kidney, bladder, and prostate cancers [6, 10].

The mortality risk from cancer is notably higher in dialysis patients, who face a 2.6-fold increase compared to the general population [11]. While cardiovascular disease remains the leading cause of death in ESRD patients [4], cancer significantly affects prognosis and quality of life. In a Chinese study, kidney cancer had the highest cancer mortality than the general population [12]. The development of urological cancer in ESRD patients may be exacerbated by factors such as prolonged uremia, chronic infections and inflammation, immune dysregulation, and nutritional deficiencies [9, 13, 14]. Notably, bladder cancer in dialysis patients tends to be pathologically advanced at diagnosis, often necessitating radical cystectomy, which is associated with poor outcomes [15].

Despite the recognized cancer burden in dialysis patients, studies investigating the risk of urological malignancies in this population remain limited. Conflicting findings have been reported regarding the risk of major urology cancers (MUCs)—defined as bladder, prostate, and kidney/renal pelvis cancers [16, 17]. Therefore, this study aims to evaluate and compare the risk of MUCs in a large cohort of dialysis patients, with the goal of informing cancer screening protocols and improving care for this vulnerable population.

Materials and methods

This systematic review and meta-analysis were conducted to investigate the impact of dialysis on the occurrence of major urological cancers in patients with End stage renal disease. The study aimed to compare cancer incidence rates between ESRD patients undergoing dialysis and the general population.

Our methodology and findings followed systematic review and meta-analysis guidelines, including PRISMA 2020 [18]. This systematic review and meta-analysis have been registered in PROSPERO under the unique identifier "CRD42023450318". As a systematic review and meta-analysis, this study did not require any ethical approval or participant consent.

Search strategy

A comprehensive literature search was conducted using the public databases PubMed, Embase, and Web of Science. The search cutoff date for all articles was June 2024. The search was limited to studies involving human subjects and published in English. The search strategy employed key terms such as "Cancer", "dialysis", "Kidney", "Bladder", and "Prostate". These terms were combined using operators like "AND" and "OR." Two members of the review team (JJY and BR), under the supervision of the senior author (LRL), screened all identified abstracts for inclusion.

The literature was initially screened by reviewing the titles and abstracts, with duplicates excluded. A second screening phase was conducted based on predefined inclusion and exclusion criteria followed by a thorough examination of full texts of included studies during the final screening stage.

Inclusion and exclusion criteria

The selected literatures were then thoroughly assessed and included in the meta-analysis based on the inclusion criteria: (a) studies should be population-based cohort studies of patients with ESRD on dialysis; (b) studies collecting information on incidence of urological cancers in

patients on dialysis; (c) studies with sufficient information matched the dialysis population to a standardized population to calculate a standardized incidence ratio of cancers. The following exclusion criteria were used: (a) all those studies on patients who all received kidney transplantation; (b) all those studies on cancers diagnosed before dialysis; (c) all those studies without information on standardized incidence ratio or number of expected cases; (d) all those studies without available data can be extracted; (`e) clinical trials and non-original studies (letters, reviews, editorials, conference abstract). Studies without full text access were also excluded. Studies without full text access were also excluded. Non-melanoma skin cancer (NMSC) was not included due to the high degree of underreporting in clinical and registry data [19].

The quality of the cohort studies was independently evaluated by each investigator using the Newcastle-Ottawa Quality Assessment Scale (NOS) [20]. This tool assesses selection, comparability, and outcomes in non-randomized studies. Each item was rated as 'yes' (1 point), 'no' (0 points), or 'unclear' (0 points). Scores ranged from 0 to 9 and were categorized as follows: high quality (8–9), moderate quality (6–7), and low quality (≤ 5) (Table 1). Discrepancies were resolved through discussion.

Data extraction and outcomes of interest

Using a pre-designed table, two authors independently extracted demographic and outcome data. Conflicts were resolved through senior researcher intervention. Data included study design, first author, publication year, geographic origin, data source, number of patients on dialysis, type of dialysis (hemodialysis or peritoneal dialysis), sex, length of follow-up, person-years, mean age at dialysis initiation, cancer diagnosis, and other relevant parameters. The following outcomes were extracted: (1) SIRs of all cancers except NMSC; (2) SIRs of bladder cancer, prostate cancer and cancers of the kidney/renal pelvis.

The data utilized in this systematic review and meta-analysis were obtained from publicly accessible sources and underwent de-identification to ensure patient confidentiality. The authors adhered to copyright and intellectual property regulations by appropriately citing original sources.

Statistical analysis

In this meta-analysis, the SIR along with 95% confidence intervals (CIs) was employed to assess the relative risk of cancer occurrence. The SIR for a specific cancer type was included if available in ≥ 2 studies. The Cochrane Q test, p-value, and I^2 statistic were used to evaluate heterogeneity. If heterogeneity was statistically significant ($p < 0.05$ or $I^2 > 50\%$), a random-effects model was applied.

Table 1 Results of quality assessment using the Newcastle-Ottawa quality assessment scale

Study/item	Selection				Comparability	Exposure			
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts	total
Taborelli et al.,2019	★	★	★	★	★	★		★	7
Mazzucotelli et al.,2017		★	★	★	★	★		★	6
Hortlund et al.,2017	★	★	★	★	★	★	★	★	8
Loy et al.,2013	★	★	★	★	★★		★	★	8
Vajdic et al.,2006	★	★	★	★	★	★		★	7
Maisonneuve et al.,1999	★	★	★	★	★	★		★	7
Birkeland et al.,2000	★	★	★	★	★	★		★	7
Butler et al.,2015		★	★	★		★		★	5
Port et al.,1989		★	★	★		★		★	4
Cheung et al.,2016	★	★	★	★	★★	★		★	8

Otherwise, a fixed-effect model was use. A p-value < 0.05 was considered statistically significant.

Due to the limited number of studies, Egger's test was performed to assess publication bias. One-way sensitivity analyses were also conducted by sequentially removing individual studies to evaluate their impact on the overall results. All statistical analyses were performed using STATA 17.0 (STATA Corp, College Station, TX, USA).

Result

Study characteristics

The selection process of the identified studies is illustrated in Fig. 1. A total of ten articles derived from 15 data sources were included in the statistical analysis, with the majority of the studies being classified as moderate or high quality [10, 16, 17, 21–24]. These articles encompassed a cohort of 1,362,196 patients on dialysis from Europe, Australia, New Zealand, China, Singapore, and the USA, spanning the period between 1989 and 2019. All included studies were multicenter cohort studies, with the largest study comprising 831,804 patients on dialysis. The details of the included studies are summarized in Table 2.

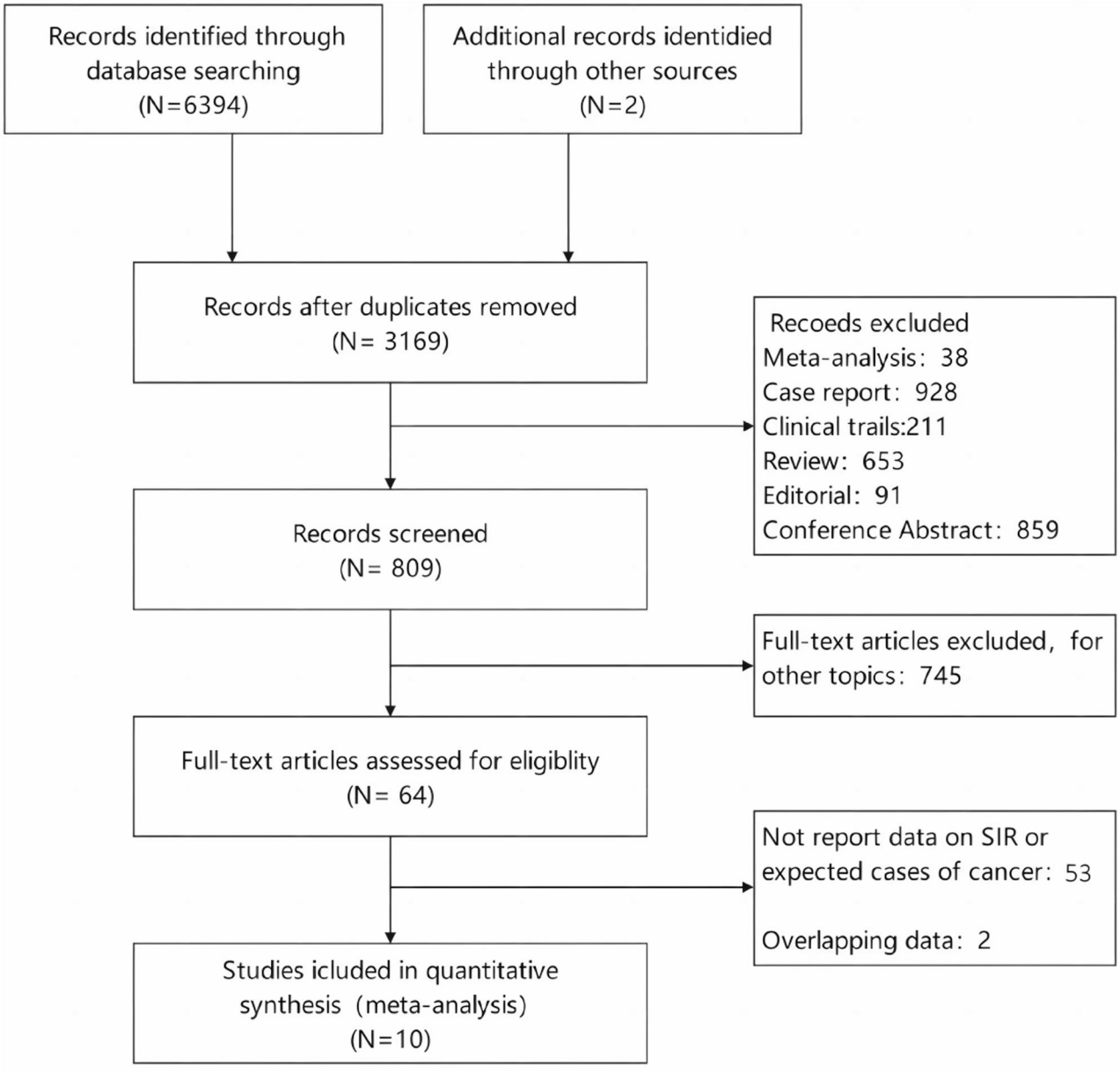

Fig. 1 Flowchart of systematic search and selection process

Table 2 Summary of studies included in the analysis

Study	Type of study	Geographic origin	Number of patients on dialysis	Sex, *n* (%)		Number of all cancers except NMSC, *n* (%)	Number of major urinary system cancers, *n* (%)
				Male	Female		
Taborelli et al.,2019	Retrospective cohort	North-eastern Italy	3,407	2,126 (62.4)	1,281 (37.6)	249 (7.3)	76 (2.2)
Mazzucotelli et al.,2017	Retrospective cohort	Italy	912	597 (65.5)	315 (34.5)	24 (2.6)	10(1.1)
Hortlund et al.,2017	Retrospective cohort	Denmark	24,698	15,346 (62.1)	9,352 (37.9)	1,463 (5.9)	355 (1.4)
Loy et al.,2013	Retrospective cohort	Singapore	5,505	2,875 (52.2)	2,630 (47.8)	267 (4.9)	46 (0.8)
Vajdic et al.,2006	Retrospective cohort	Australian	24,926	14,144 (56.7)	10,782 (43.3)	1,136 (4.6)	249 (1.0)
Maisonneuve et al.,1999	Retrospective cohort	Australia & New Zealand	13,497	7,513 (55.7)	5,984 (44.3)	500 (3.7)	159 (1.2)
Maisonneuve et al.,1999	Retrospective cohort	Europe	296,903	173,375 (58.4)	123,528 (41.6)	6,849 (2.3)	1,762 (0.6)
Maisonneuve et al.,1999	Retrospective cohort	United States	521,404	278,348 (53.4)	243,056 (46.6)	17,695 (3.4)	4254 (0.8)
Birkeland et al.,2000	Retrospective cohort	Denmark	3,592	2,154 (60.0)	1,438 (40.0)	23 (0.6)	16 (0.5)
Butler et al.,2015	Retrospective cohort	United States	456,937	NA	NA	35,767 (7.8)	10,125 (2.2)
Port et al.,1989	Prospective cohort	United States	4,161	2,363 (56.8)	1,798 (43.2)	63 (1.5)	21(0.5)
Cheung et al.,2016	Retrospective cohort	China	6,254	3,403 (54.4)	2,851 (45.6)	212 (3.4)	47 (0.8)
Total			1,362,196	504,607 (37.0)	404,813 (29.7)	64,248 (4.7)	17,120 (1.3)

Patient characteristics

The dialysis population included 504,607 men and 404,813 women, followed up for 2,161,044.1 person-years, with a mean follow-up duration of 2.7 years (range: 2.2–3.9 years). hemodialysis was the predominant type of dialysis reported in the literature, with over 465,923 patients receiving hemodialysis. The mean age at first dialysis was 57.8 years (range: 49–70). Table 3 provides the demographic details of the included studies.

During the period of observation, 64,248 patients developed cancers during dialysis, made up 4.7% of the dialysis population and 17,120 (1.3%) patients developed MUCs, accounted for over 25% of all cancer cases observed in dialysis patients. The expected incidence of all cancers and MUCs was 48,799.8 and 12,621.24, respectively.

During the observation period, 64,248 patients (4.7% of the dialysis population) developed cancers while on dialysis. Among them, 17,120 patients (1.3%) were diagnosed with MUCs, accounting for over 25% of all cancer cases observed in dialysis patients. The expected incidence of all cancers and MUCs was 48,799.8 and 12,621.24, respectively. Among MUC patients, 5042 individuals (7.85%) were diagnosed with kidney/renal pelvis cancers, 4065 patients (6.33%) developed bladder cancer, 8013 patients (12.47%) were diagnosed with prostate cancer. Expected incidence rates for kidney/renal pelvis cancers, bladder cancer, and prostate cancer were 1,298.40 cases, 2,626.23 cases, and 8,696.61 cases, respectively. The average age at malignancy diagnosis was 61.0 years, while the mean time from dialysis initiation to cancer diagnosis was 38.0 months for kidney cancer (range: 20.4–54.0), 47.3 months for bladder cancer (range: 14.7–89.0), 40.3 months for prostate cancer (range: 30.0–58.0), 19.1 months for MUC overall (range: 10.5–27.6).

Evidence synthesis

Meta-analysis for the SIRs for cancers during dialysis suggested a significantly increased risk in cancers developed during dialysis (SIR = 1.40, 95% CI: 1.28–1.54). This included MUCs (SIR = 1.76, 95% CI: 1.45–2.14), kidney/renal pelvis cancers (SIR = 4.73, 95% CI: 3.96–5.64), and bladder cancers (SIR = 1.89, 95% CI: 1.61–2.21). However, the SIR for prostate cancers was not significant (SIR = 0.94, 95% CI: 0.79–1.11). Figure 2 illustrates the forest plot for the overall and cancer-specific SIRs.

All cancers except NMSC and MUCs showed an increased risk of 1.38 and 1.43 times higher than the general population, respectively. Kidney/renal pelvis cancers demonstrated the highest relative risk, occurring 3.97 times more frequently than in the general population, whereas prostate cancers occurred at a similar or slightly lower rate compared to the general population.

However, the Cochrane Q, heterogeneity *p*-value and I^2 statistic showed great heterogeneity in the pooled analysis of SIRs of: all cancers except NMSC (I^2=98.4%, P heterogeneity < 0.001); MUCs (I^2=93.5%, P heterogeneity < 0.001); cancers of the kidney/renal pelvis (I^2=95.6%, P heterogeneity < 0.001); bladder cancer (I^2=75.1%, P heterogeneity = 0.001); prostate cancer (I^2 = 94.7%, P heterogeneity < 0.001). All results showed *p*-value < 0.05 and I^2 > 50%, indicating substantial heterogeneity. Therefore, a random-effect model was used to pool the results.

Table 3 The demographic details of the included studies

Study	Number of all cancers except skin non-melanoma	Number of cancers of the kidney/renal pelvis, *n* (%)	Number of bladder cancers, *n* (%)	Number of prostate cancers, *n* (%)	Length of follow-up time	Mean follow-up time (years)	Person-years	Mean age while dialysis (years)	Mean age at diagnosis of malignancy (years)	Mean time to malignancy discovery (months)	Mean time to kidney cancer discovery (months)	Mean time to bladder cancer discovery (months)	Mean time to prostate cancer discovery (months)
Taborelli et al.,2019	249	25(10.04)	16(6.43)	35(14.06)	1998–2013	2.3	10,798	70	NA	NA	NA	NA	NA
Mazzucotelli et al.,2017	24	2(8.33)	1(4.17)	7(29.17)	1997–2012	2.5	2,400.1	NA	58	20.4	NA	NA	NA
Hortlund et al.,2017	1,463	62(4.24)	142(9.71)	151(10.32)	1977–2013	3.2	79,881	61	NA	NA	NA	NA	NA
Loy et al.,2013	267	30(11.24)	10(3.75)	6(2.25)	1998–2010	3.9	NA	58.1	60.9	43.6	58.9	33.3	NA
Vajdic et al.,2006	1,136	112(9.86)	63(5.55)	74(6.51)	1982–2003	2.7	NA	54	NA	33.6	26.5	30	27.6
Maisonneuve et al.,1999	17,695	1303 (7.4)	933 (5.27)	2,018 (11.40)	1980–1994	2.2	1,152,047	58	NA	NA	NA	NA	NA
Maisonneuve et al.,1999	6,849	680 (9.9)	660 (9.64)	422 (6.16)	1980–1994	2.9	858,532	52	NA	NA	NA	NA	NA
Maisonneuve et al.,1999	500	70 (14.0)	53 (10.60)	36 (7.20)	1980–1994	2.4	34,456	49	NA	NA	NA	NA	NA
Birkeland et al.,2000	23	5(21.74)	11(47.83)	NA	NR-1995	2.3	8,043	50.2	NA	NA	NA	NA	NA
Butler et al.,2015	35,767	2,712(7.58)	2,165(6.05)	5,248(14.67)	1995–2010	2.5	NA	67	NA	NA	NA	NA	NA
Port et al.,1989	63	6(9.52)	2(3.17)	13(20.63)	1973–1984	2.6	NA	52	NA	NA	14.7	NA	10.5
Cheung et al.,2016	212	35 (16.51)	9 (4.25)	3 (1.42)	1994–2014	2.4	14,887	64	63.9	54	89	58	NA
Total	64,248	5,042 (7.85)	4,065 (6.33)	8,013 (12.47)		2.7	21610044.1	57.8	60.9	37.9	47.3	40.4	19.1

Sensitivity analysis

We performed one-way sensitivity analyses after the sequential removal of each study, and the new pooled results demonstrated stable SIRs, indicating that the overall results were not disproportionately influenced by any single study. And the range in estimates of SIRs of all cancers except NMSC, major urinary system cancers, cancers of the kidney/renal pelvis, bladder cancer and prostate cancer are 1.34 to 1.42, 1.39 to 1.47, 3.65 to 4.22, 1.59 to 1.79 and 0.84 to 0.95, respectively (Table 4).

Subgroup analysis

To further explore the risk of MUCs developed during dialysis and assess possible confounding factors, subgroup analyses were performed based on gender, age at first dialysis, time since dialysis initiation, primary renal disease, and ethnicity (Table 5). While no significant change in the high heterogeneity was observed across most subgroup analyses, the results of the subgroup analysis suggest that heterogeneity is partially attributable to differences in patient populations. Across various subgroups, such as ethnicity, gender, follow-up duration, and primary renal disease, the heterogeneity outcomes varied significantly.

For gender, subgroup analysis showed that women were at significantly higher risk for all cancers (SIR = 1.48, 95% CI: 1.30–1.68), kidney cancers (SIR = 4.98, 95% CI: 2.32–10.67), and bladder cancers (SIR = 4.19, 95% CI: 2.14–8.22) compared to male patients, especially for urological cancers. For age at first dialysis, the youngest age group (0–34 years) demonstrated the highest risk for all cancers (SIR = 4.09, 95% CI: 2.59–6.47), kidney cancers (SIR = 38.04, 95% CI: 18.46–78.39), and bladder cancers (SIR = 16.26, 95% CI: 5.27–50.19). Cancer risk decreased with increasing age. For time since dialysis initiation, the risk for all cancers (SIR = 2.16, 95% CI: 1.53–3.04), kidney cancers (SIR = 8.16, 95% CI: 4.45–14.96), and bladder cancers (SIR = 2.33, 95% CI: 1.47–3.67) was highest during the first year of dialysis. For primary renal disease, glomerulonephritis was associated with higher risks for all cancers (SIR = 1.53, 95% CI: 1.34–1.75) and kidney cancers (SIR = 5.03, 95% CI: 3.52–7.18). However, diabetic nephropathy (SIR = 0.89, 95% CI: 0.77–1.03) and glomerulonephritis (SIR = 1.43, 95% CI: 0.82–2.49) did not appear to affect the development of bladder cancers during dialysis. For ethnicity, subgroup analysis revealed that Asian patients had significantly higher risks for all cancers (SIR = 1.54, 95% CI: 1.33–1.78), kidney cancers (SIR = 8.22, 95% CI: 3.58–18.87), and bladder cancers (SIR = 2.75, 95% CI: 1.67–4.53) compared to non-Asian patients. As for prostate cancer, subgroup analyses continued to show no significant association with prostate cancer risk.

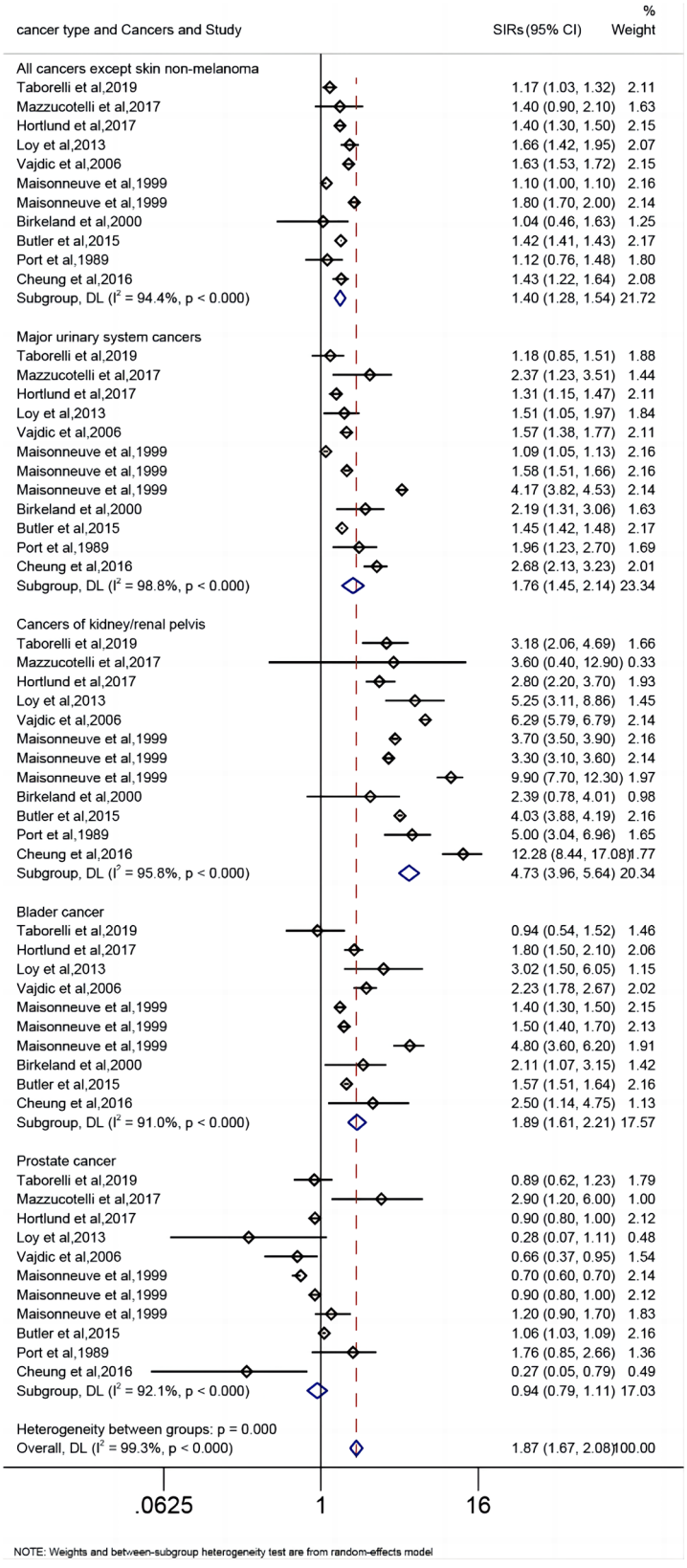

Fig. 2 Forest plot of overall major urological cancers risk, showing the standardized incidence rates (SIRs) and 95% confidence intervals (CI)

Table 4 Sensitivity analysis

	All cancers except skin non-melanoma			Major urinary system cancers			Cancers of the kidney/renal pelvis			Bladder cancer			Prostate cancer		
Study omitted	**SIRs**	**95% confidence intervals**		**SIRs**	**95% confidence intervals**		**SIRs**	**95% confidence intervals**		**SIRs**	**95% confidence intervals**		**SIRs**	**95% confidence intervals**	
Taborelli et al.,2019	1.43	1.30	1.58	1.82	1.49	2.23	4.88	4.06	5.87	1.97	1.68	2.31	0.94	0.78	1.13
Mazzucotelli et al.,2017	1.40	1.27	1.55	1.73	1.42	2.11	4.74	3.96	5.67	1.89	1.61	2.21	0.90	0.76	1.07
Hortlund et al.,2017	1.40	1.26	1.56	1.81	1.48	2.23	5.00	4.15	6.02	1.91	1.60	2.27	0.95	0.77	1.16
Loy et al.,2013	1.38	1.25	1.52	1.78	1.46	2.18	4.70	3.91	5.64	1.85	1.58	2.17	0.95	0.80	1.13
Vajdic et al.,2006	1.37	1.24	1.53	1.78	1.45	2.19	4.52	3.86	5.30	1.84	1.56	2.17	0.96	0.80	1.15
Maisonneuve et al.,1999	1.40	1.28	1.54	1.85	1.49	2.31	4.87	3.89	6.09	2.01	1.64	2.46	0.98	0.86	1.13
Birkeland et al.,2000	1.41	1.28	1.55	1.73	1.42	2.12	4.84	4.04	5.80	1.88	1.60	2.21	0.94	0.79	1.11
Butler et al.,2015	1.39	1.20	1.61	1.81	1.35	2.42	4.81	3.76	6.15	1.99	1.57	2.51	0.91	0.76	1.09
Port et al.,1989	1.42	1.29	1.56	1.75	1.43	2.14	4.71	3.91	5.66	1.89	1.61	2.21	0.90	0.75	1.08
Cheung et al.,2016	1.40	1.27	1.55	1.69	1.38	2.07	4.35	3.65	5.18	1.87	1.59	2.19	0.95	0.80	1.13
Combined	1.40	1.28	1.54	1.76	1.45	2.14	4.73	3.96	5.64	1.89	1.61	2.21	0.94	0.79	1.11

Publication bias

Due to the limited number of studies, Begg's funnel plot was not performed to assess publication bias. However, the results of Egger's test and Begg's test were consistent and showed no evidence of publication bias for any of the SIR estimates for: all cancers except NMSC (P Egger's test = 0.64, P Begg's test = 0.823); MUCs (P Egger's test = 0.451, P Begg's test = 0.346); cancers of the kidney/renal pelvis (P Egger's test = 0.837, P Begg's test = 0.443); Bladder cancer (P Egger's test = 0.283, P Begg's test = 0.154); prostate cancer (P Egger's test = 0.586, P Begg's test = 0.382). Table 6 summarizes the publication bias assessment results.

Discussion

As dialysis patients' survival increases, cancer screening becomes increasingly important for this population [6]. Currently, there are no standard recommendations for cancer screening in the dialysis population, and general population cancer screening among dialysis patients has not been found to be cost-effective [16, 24]. This study was conducted to review recent literature and identify characteristics of urological cancers in dialysis patients, aiming to improve survival rates in an economically feasible manner. The key findings from this study were as following. We found that the cumulative risk of MUCs in dialysis patients was 1.74 times higher than that of the general population after an average follow-up of 2.7 years. This risk exceeded that of overall cancers during dialysis. The increased risk may stem from the nature of CKD, urological anomalies, and specific risk factors in ESRD patients, such as acquired cystic kidney disease, aristolochic acid exposure, cyclophosphamide, and certain analgesics [6, 21]. Routine use of reliable tumor markers like PSA may also facilitate early cancer detection in this population [23].

Among main urological cancers during dialysis, cancers of the kidney/renal pelvis had the highest risk, while the incidence of prostate cancer seemed not related to dialysis [2, 25]. This aligns with previous studies that identified kidney cancer as having the highest relative risk among all cancers in dialysis patients [17, 22, 26]. The mean time to kidney cancer discovery was also the longest among all MUCs. High kidney cancer risk in dialysis patients may be attributed to: increased medical surveillance of the kidneys; high prevalence of acquired cystic kidney disease during dialysis (often developing after 3–7 years and associated with a 1.6-7% incidence of renal cell carcinoma); and risk factors such as aristolochic acid nephropathy, Balkan nephropathy, analgesic nephropathy, oral cyclophosphamide and the slower transit of the urine with high content of toxic waste products (which are linked to transitional cell carcinoma of the urinary tract) [6, 24, 26]. As to prostate cancer, androgen therapy

Table 5 Subgroup analyses of overall cancer risk in patients on dialysis

Characteristic		All cancers except NMSC			Kidney cancers			Bladder cancers			Prostate cancers		
		SIRs (95% CI)	Heterogeneity		SIRs (95% CI)	Heterogeneity		SIRs (95% CI)	Heterogeneity		SIRs (95% CI)	Heterogeneity	
			I^2 (%)	*P*-value[a]		I^2 (%)	*P*-value[a]		I^2 (%)	*P*-value[a]		I^2 (%)	*P*-value[a]
Ethnicity	Asian	1.54 (1.33–1.78)	45	0.178	8.22 (3.58–18.87)	85.6	0.008	2.75 (1.67–4.53)	0	0.71	0.27 (0.10–0.73)	0	0.971
	Non-Asian	1.37 (1.23–1.53)	95.5	<0.001	4.30 (3.59–5.14)	96	<0.001	1.83 (1.56–2.15)	92.6	<0.001	0.97 (0.82–1.15)	93.4	<0.001
Gender	Men	1.37(1.21–1.56)	86.6	<0.001	2.66 (2.01–3.51)	0	0.803	1.48 (1.22–1.81)	0	0.606	0.94 (0.79–1.11)	92.1	<0.001
	Women	1.48(1.30–1.68)	94.1	<0.001	4.98 (2.32–10.67)	63.6	0.064	4.19 (2.14–8.22)	57	0.127	NA	NA	NA
Age	0–34	4.09(2.59–6.47)	93	<0.001	38.04 (18.46–78.39)	86	0.001	16.26 (5.27–50.19)	84.4	0.002	NA	NA	NA
	35–64	1.88(1.41–2.50)	96.9	<0.001	5.50 (4.20–7.21)	94	<0.001	2.59 (1.66–4.06)	97.6	<0.001	NA	NA	NA
	>64	1.21(1.11–1.32)	78.2	0.003	3.07 (2.10–4.49)	90.3	<0.001	1.37 (1.07–1.75)	86.1	0.001	NA	NA	NA
Follow-up time (years)	1	2.16 (1.53–3.04)	99	<0.001	8.16 (4.45–14.96)	96.8	<0.001	2.33 (1.47–3.67)	95.4	<0.001	NA	NA	NA
	2	1.47 (1.22–1.77)	95.4	<0.001	3.97 (2.87–5.50)	74.4	0.004	1.51 (1.36–1.67)	0	0.58	NA	NA	NA
	3–5	1.32 (1.07–1.63)	96.8	<0.001	4.15 (2.94–5.86)	86.9	<0.001	1.92 (1.29–2.86)	92.7	<0.001	NA	NA	NA
	>5	1.03 (0.81–1.30)	96.9	<0.001	6.29 (3.74–10.58)	77.8	0.001	1.91 (0.96–3.79)	93.6	<0.001	NA	NA	NA
Primary renal disease	Diabetic nephropathy	1.07 (0.88–1.31)	94.2	<0.001	2.07 (1.36–3.16)	70.9	0.016	0.89 (0.77–1.03)	0	0.472	NA	NA	NA
	Glomerulon-ephritis	1.53 (1.34–1.75)	87.3	<0.001	5.03 (3.52–7.18)	87.3	0.001	1.43 (0.82–2.49)	87.3	<0.001	NA	NA	NA
	Hypertensive & arteriopathy	1.35 (0.78–2.34)	93.2	<0.001	3.44 (2.18–5.44)	83.5	<0.001	1.76 (1.03-3.00)	92	<0.001	NA	NA	NA
	All other and unknown	1.53 (1.23–1.90)	67.7	0.026	6.56 (3.90–11.05)	58.0	0.068	2.38 (1.61–3.50)	0	0.446	NA	NA	NA

Table 6 Publication bias

	Begg's test	Egger's test
All cancers except skin non-melanoma	0.640	0.823
Major urinary system cancers	0.451	0.346
Kidney/renal pelvis	0.837	0.443
Bladder cancers	0.283	0.154
Prostate cancers	0.586	0.382

for anemia of renal failure may play a possible carcinogenic role, which clinical evidence has not been forthcoming [26].

High heterogeneity was observed in this meta-analysis, similar to other studies [27]. To explore the sources of this heterogeneity and thoroughly analysis, subgroup analyses were performed. As for gender, female dialysis patients were found with higher SIRs for all cancers (SIR = 1.48), kidney cancers (SIR = 4.98), and bladder cancers (SIR = 4.19) compared to males. This suggests a need for enhanced cancer surveillance in women [6, 10, 16, 22, 25]. As for age, younger patients had significantly higher risks for all cancers (SIR = 4.09) and urological cancers, with risk decreasing with age [16, 22]. This may result from a low baseline cancer risk in younger individuals and reduced cancer screening intensity in elderly patients with ESRD [12]. For time since dialysis initiation, the risk of cancers was highest within the first year of dialysis and decreased over time. This trend is consistent with previous research findings and may be attributed to surveillance bias, which arises from more intensive medical monitoring during the initial years of dialysis treatment, leading to both increased detection of pre-existing malignancies and higher rates of cancer diagnosis in the early stages of renal replacement therapy [28]. Furthermore, some studies suggested that long-term dialysis survivors may achieve health outcomes comparable to selected general population individuals without severe complications [16]. For primary renal disease, glomerulonephritis was associated with higher risks for all cancers and kidney cancers, while diabetic nephropathy and hypertensive nephropathy showed lower risks. The specific sites at which primary kidney disease, associated urological abnormalities, or acquired renal cystic disease may contribute to cancer development. Ethnicity also played a role, with Asian patients showing higher SIRs for all cancers, kidney cancers, and bladder cancers. Notably, the heterogeneity analysis within the Asian subgroup did not reveal significant variation among all cancers except NMSC, bladder cancer and prostate cancer. The elevated cancer risk in Asian patients may be attributed to a combination of genetic, environmental, and healthcare-related factors. Notably, the use of aristolochic acid, a compound frequently found in traditional Chinese herbal medicine, could play a significant role. However, confounding variables such as lifestyle, smoking, alcohol

use, and exposure to some carcinogenic agents were not consistently reported across studies, which may limit the interpretation of these findings [7, 29, 30].

Dialysis is associated with increased cancer risk through several potential mechanisms. First, impaired immune function resulting from multiple transfusions and uremic conditions may contribute to carcinogenesis. The accumulation of uremic toxins and carcinogenic compounds due to renal deficiency can trigger antagonistic interactions between pro-inflammatory and immunosuppressive responses, promoting cancer development [11, 19, 31]. Second, chronic dialysis may lead to DNA damage through suppressed DNA repair mechanisms in lymphocytes and decreased antioxidant defense systems [31]. Third, the compromised immune function in dialysis patients predisposes them to chronic infections, particularly viral infections, while dialysis-related chronic inflammation and elevated cytokine levels can further exacerbate DNA damage and impair repair processes [5, 14, 31, 32]. Fourth, the use of various medications, particularly immunosuppressive drugs (e.g., azathioprine and cyclophosphamide) for underlying renal diseases, has been associated with increased cancer incidence [33]. Additionally, certain medications, including some Chinese herbal preparations containing aristolochic acid, can induce both chronic interstitial nephritis and urinary tract cancers, particularly transitional cell carcinoma. Furthermore, dialysis-related factors, including membrane materials and tubing components, may contribute to carcinogenesis. Collectively, these mechanisms, particularly the accumulation of unrepaired DNA damage, create a microenvironment conducive to cancer formation [15, 34].

While this analysis highlights a significantly elevated cancer risk in dialysis patients, the causal relationship between ESRD and carcinogenesis requires careful consideration. Two potential mechanisms may coexist: (1) the uremic microenvironment and dialysis-related factors (e.g., chronic inflammation, DNA repair impairment, carcinogen accumulation) may directly promote tumorigenesis [35], and (2) subclinical malignancies present at the time of ESRD diagnosis could accelerate renal function decline through paraneoplastic effects or chemotherapy-induced nephrotoxicity, creating a diagnostic bias that makes cancer appear dialysis-associated [36, 37]. Notably, the first-year peak cancer incidence post-dialysis initiation, as shown in our time-dependent analysis, supports both hypotheses. This could either reflect intensified surveillance detecting pre-existing malignancies or accelerated carcinogenesis caused by acute uremic stress. Longitudinal studies tracking cancer incidence from pre-ESRD stages would help to clarify this complex relationship [38, 39].

While our study demonstrates temporal associations between ESRD and cancer risk, the observational design does not establish causality. It remains unclear whether the uremic pathophysiology associated with ESRD directly promotes carcinogenesis or if subclinical malignancies contribute to ESRD progression through mechanisms like paraneoplastic nephropathy or chemotherapy-induced nephrotoxicity. Despite robust findings, several limitations must be acknowledged: high heterogeneity across studies, publication bias, limited data for certain cancers, and confounding factors such as lifestyle and medication use. Additionally, some subgroup data were missing, which could have provided further insights into the dialysis-related cancer risks. To clarify this complex relationship, future prospective cohort studies should initiate cancer screening at pre-dialysis stages of chronic kidney disease (CKD), enabling a better understanding of the cause-and-effect dynamics between ESRD and cancer risk.

Conclusion

Our systematic review and meta-analysis reveals an increased risk of urological cancers in dialysis patients, especially kidney/renal pelvis and bladder cancers. Physicians should prioritize screening for these malignancies while carefully considering patient-specific factors, such as life expectancy and individual risk factors. Further large-scale, well-designed prospective studies are necessary to elucidate the link between renal replacement therapy and cancer risk and to refine screening strategies for this vulnerable population.

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Author contributions

Junjiang Ye and Biao Ran: Conceptualization, Data curation, Formal analysis, Writing– original draft; Junjiang Ye: Methodology, Project administration; Yin Huang, Zeyu Chen and Ruicheng Wu: Supervision, Conceptualization; Dengxiong Li, Puze Wang and Bo Chen: Data curation, Investigation, Formal analysis, Methodology, Writing; Ping Han, and Liangren Liu: Review & Editing, Investigation.

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Data availability

This systematic review and meta-analysis have been registered in PROSPERO under the unique identifier "CRD42023450318". Data are available from the corresponding author if justification for the requirement is justified.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication
Not applicable.

Conflict of interest
The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Statement
All the data used in this study can be obtained from the original articles.

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