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The Geriatric Nutritional Risk Index as a Predictor of Outcomes in Urological Cancers: A Systematic Review and Meta-Analysis

Yuefen Chen[a] Mei Wen[b] Zhe Yu[a] Fengjiao Xu[a]

[a]Comprehensive Medical Treatment Ward, Nanfang Hospital, Southern Medical University, Guangzhou, China;
[b]Department of Hepatobiliary Surgery, Nanfang Hospital, Southern Medical University, Guangzhou, China

Keywords
Urothelial cancer · Prostate cancer · Renal cell carcinoma · Bladder cancer · Nutrition · Survival

Abstract

Introduction: The geriatric nutritional risk index (GNRI) is being used to predict outcomes of several malignancies. However, its utility for urinary tract cancer has not been systematically analyzed. We present the first meta-analysis examining the association between GNRI and the prognosis of urological cancers. ***Methods:*** This PROSPERO registered review searched Embase, PubMed, Web of Science, and Scopus up to 25 November 2024 for studies examining the relationship between GNRI and overall survival (OS), cancer-specific survival (CSS), and progression-free survival (PFS) after urological cancers. ***Results:*** A total of 20 studies were eligible. Three studies were on bladder cancer, four on prostate cancer, seven on renal cell carcinoma (RCC), and six on urothelial cancers. Meta-analysis showed that low GNRI was a statistically significant predictor of poor OS in prostate cancer (OR: 3.02; 95% CI: 1.61, 5.67). Pooled analysis showed that low GNRI was associated with poor OS (OR: 2.17; 95% CI: 1.46, 3.22) and CSS (OR: 2.60; 95% CI: 1.57, 4.30) in RCC but not PFS (OR: 1.50; 95% CI: 1.00, 2.24). Pooled analysis also found that low GNRI was a predictor of worse OS (OR: 2.24; 95% CI: 1.52, 3.29) and CSS (OR: 3.07; 95% CI: 1.38, 6.86) in urothelial carcinoma. A narrative review on bladder cancer and GNRI showed mixed results. ***Conclusion:*** GNRI may have a role in predicting outcomes of urological malignancies. Low GNRI was independently associated with worse OS after prostate, renal cell, and urothelial carcinoma. Further, it also predicted CSS after RCC and urothelial carcinoma.

Introduction

Urological cancers include a gamut of malignancies that can originate anywhere from the kidneys up to the urethra or in the male reproductive system [1]. Urological cancers can include renal, ureteral, bladder, prostate, urethral, penile, or testicular cancer. Among these, bladder cancer is among the commonest types of urinary tract cancers with 1.6 million patients diagnosed with it in 2022 alone [2]. On the other hand, renal cell carcinomas (RCCs) constitute around 80–90% of all primary renal neoplasms [3]. Prostate cancer is the second most common cancer seen in men with about 1,414,000 new cancer cases and 375,304 deaths in 2020 [4]. Despite advances in diagnosis and therapeutics, survival after

Yuefen Chen and Mei Wen are co-first authors and they contributed equally to this work.

karger@karger.com
www.karger.com/uin

Correspondence to:
Fengjiao Xu, 13751887453@163.com

urological cancers remain poor, and there is a need to identify prognostic factors that can be altered to improve survival [5].

Malnutrition has been identified in around 71% of cancer patients [6]. A large proportion of cancer patients are malnourished primarily due to heightened energy and nutritional requirements due to malignancy, inadequate diet, and nutritional intake as well as due to diminished physical activity [7]. Poor nutrition in cancer has been associated with surgical complications, chemotherapy-related toxicities, poor treatment response, reduced quality of life, and dismissal survival [8]. Therefore, recognizing malnutrition early in the treatment course can help in the identification and stratification of high-risk patients who would benefit from therapies targeting nutritional status and in turn improve outcomes. However, recognizing and classifying patients as malnourished has been a matter of controversy. A plethora of nutritional assessment tools are at the disposal of the treating physician, but no single optimal nutrition assessment tool has been identified to date. On the one hand, there are simple indices [9, 10] like albumin and body mass index while on the other hand, there are complex tools like Patient-Generated Subjective Global Assessment and the Subjective Global Assessment tools, which are extremely time-consuming and difficult to apply in routine practice [11]. Hence, tools like the prognostic nutritional index, geriatric nutritional risk index (GNRI), Mini-Nutrition Assessment, Malnutrition Universal Screening Tool, and the controlling nutritional status score have been developed with combined easily available indices to provide rapid nutritional assessment of cancer patients [9].

The GNRI is a widely used nutritional marker that was first proposed in 2005 [12]. It is derived from albumin and body weight data and used to predict the prognosis of several different diseases [13–16]. The GNRI is an independent prognostic indicator of several malignancies like lung [17], head and neck [18], colorectal [19], and gastric cancer [20]. However, its utility has never been reviewed for urological cancers. In this study, we examined the prognostic ability of GNRI for several different types of urological cancers.

Materials and Methods

We prepared the study in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement reporting guidelines (online suppl. File 1; for all online suppl. material, see https://doi.org/10.1159/000544793) [21]. Pre-registration was done on the International Prospective Register of Systematic Reviews, PROSPERO (CRD42024616395).

Information Sources

Literature was searched by two reviewers on the databases of Embase (http://embase.com), PubMed (https://pubmed.ncbi.nlm.nih.gov), Web of Science (https://www.webofscience.com/wos), and Scopus (https://www.scopus.com). The search began on 22 November 2024 and was last updated on 25 November 2024. We searched all articles without any restrictions on language and date of publication. The searched studies published only as full-texts.

The reviewers utilized free and MeSH keywords to formulate a common search query for all databases. The search query used was "((((((((((prostate) OR (renal)) OR (urethral)) OR (urinary bladder)) OR (renal)) OR (kidney)) OR (urothelial)) OR (ureter)) OR (testicular)) OR (penile)) AND ((geriatric nutritional risk index) OR (GNRI))". To supplement the search, we examined Google Scholar as a source for gray literature. Further, the references of included papers were also scrutinized.

Study Selection

Studies were selected for the review in three phases. In the first phase, all search results were combined and duplicated studies were removed by EndNote software (version X9.3.3, Thomson Reuters, PA, USA). In the second phase, two reviewers independently screened the remaining results by reading the titles and abstracts. Important studies were selected and downloaded for phase 3. In the third phase, the same reviewers conducted the final selection of studies by reading the full texts. Any disagreement was resolved through consensus.

Eligibility Criteria

Studies had to fulfill the following criteria for inclusion:

1. Studies that were cohort, case control, or secondary analysis of randomized controlled trials
2. Studies examining the association between GNRI and any type of urinary tract cancer (renal, bladder, prostate, urethral, or urothelial)
3. Studies reporting overall survival (OS), cancer-specific survival (CSS), or progression-free survival (PFS)
4. Studies reporting the effect size of the association with 95% confidence intervals (CI)

The investigations that met the following criteria were excluded:

1. Studies not reporting data on urinary tract cancers

2. Studies with insufficient outcomes or not reporting complete data
3. Review articles, meta-analyses, case reports, commentaries

Risk of Bias

Study quality was judged by the Newcastle Ottawa Scale (NOS) [22]. Two reviewers conducted the risk-of-bias analysis with disagreements being resolved by consensus. Studies were judged for criteria for participant selection, comparability of groups, and outcomes. NOS gives four stars, two stars, and three stars for these domains, respectively. The greater the number of stars, the better the quality of study.

Data Management

We used a pre-piloted Excel sheet for data extraction. Both reviewers were involved in the data extraction process. Data extracted was first author name, year of publication, location, study design, sample size, demographic details like age and gender, timing of GNRI, its cutoff, method of cutoff, type of treatment for the cancer, adjusted factors for the effect size, and follow-up.

Outcome data of interest were OS, CSS, and PFS. Adjusted data were preferred over crude data. However, if the study did not report adjusted data, we used an unadjusted association between GNRI and outcomes for the meta-analysis.

Statistical Analysis

"Review Manager" (RevMan, version 5.3) was used for all the meta-analyses. Meta-analysis was conducted if studies reported similar outcomes; otherwise, a narrative review was conducted. A pooled odds ratio (OR) with 95% CI was generated for the association between GNRI and OS, CSS, and PFS. Effect size data were entered utilizing the generic inverse variance function of the meta-analysis software. OR >1 indicated worse OS/CSS/PFS. For studies reporting outcomes of higher GNRI versus lower GNRI, the effect size was divided by 1 to establish higher GNRI as the reference group. Heterogeneity among studies was assessed through Cochran's Q statistic and the I^2 index. I^2 of over 50% and/or $p < 0.05$ indicated a large degree of heterogeneity. However, given the methodological differences between studies, we preferred an inverse-variance random-effect model irrespective of the quantified inter-study heterogeneity. A sensitivity analysis involving the removal of one study at a time was conducted to assess the credibility of the results. It was done only if there were ≥3 studies in the meta-analysis. Owing to the small number of studies, funnel plots were not generated for publication bias.

Results

Search Results

The initial search led to 1,029 articles from Embase, PubMed, Web of Science, and Scopus. No new studies were identified from Google Scholar and reference searching. After phase 1, we were left with 458 articles. Following this, phase 2 (initial screening) was conducted. This led to 32 studies for phase 3. A high degree of inter-reviewer agreement was observed (kappa = 0.9). All 32 articles were available as full texts and underwent the final phase 3 screening. The reviewers finally selected 20 studies [23–42] (Fig. 1). There was no disagreement between reviewers for the final selection of studies.

Study Characteristics

All included studies were published as English-language full-text articles between the years 2015 and 2024. Details extracted from studies are shown in Table 1. Three studies were on bladder cancer, four were on prostate cancer, seven were on RCC, and six were on urothelial cancers. The location of urothelial cancers included the upper urinary tract and bladder and were studied as a single group in the included studies. Only one study was on the Western population (the USA) while all remaining studies were from Japan, China, and Taiwan. All studies were retrospective cohort in design. The included patients were elderly in all studies with the mean or median age being >60 years. A male predominance was noted across the majority of studies. GNRI cutoff was 98 in 9 studies, was 92 in 7 studies, and varied between 80 and 101.6 in the remaining studies. The percentage of malnourished patients as per GNRI scores ranged from 13.5 to 55.8%. Treatment plans varied among studies. In the three studies on bladder cancer, two performed cystectomy while one performed transurethral resection. In the four studies on prostate cancer, one used androgen-deprivation therapy, one used androgen receptor signaling inhibitors, another used androgen-deprivation therapy or combined androgen blockade, and the last one included castration-resistant patients receiving docetaxel. Of the seven studies on RCC, four were on surgically treated patients. One study used targeted therapies mainly tyrosine kinase inhibitors, while the other two used immune checkpoint inhibitors. Among the studies on urothelial cancers, two were on surgery while four were on chemotherapy (two of which included immune checkpoint inhibitors). All studies except for two studies reported adjusted outcomes. Follow-up was generally more than 1 year in all studies. Only two studies, which reported unadjusted data,

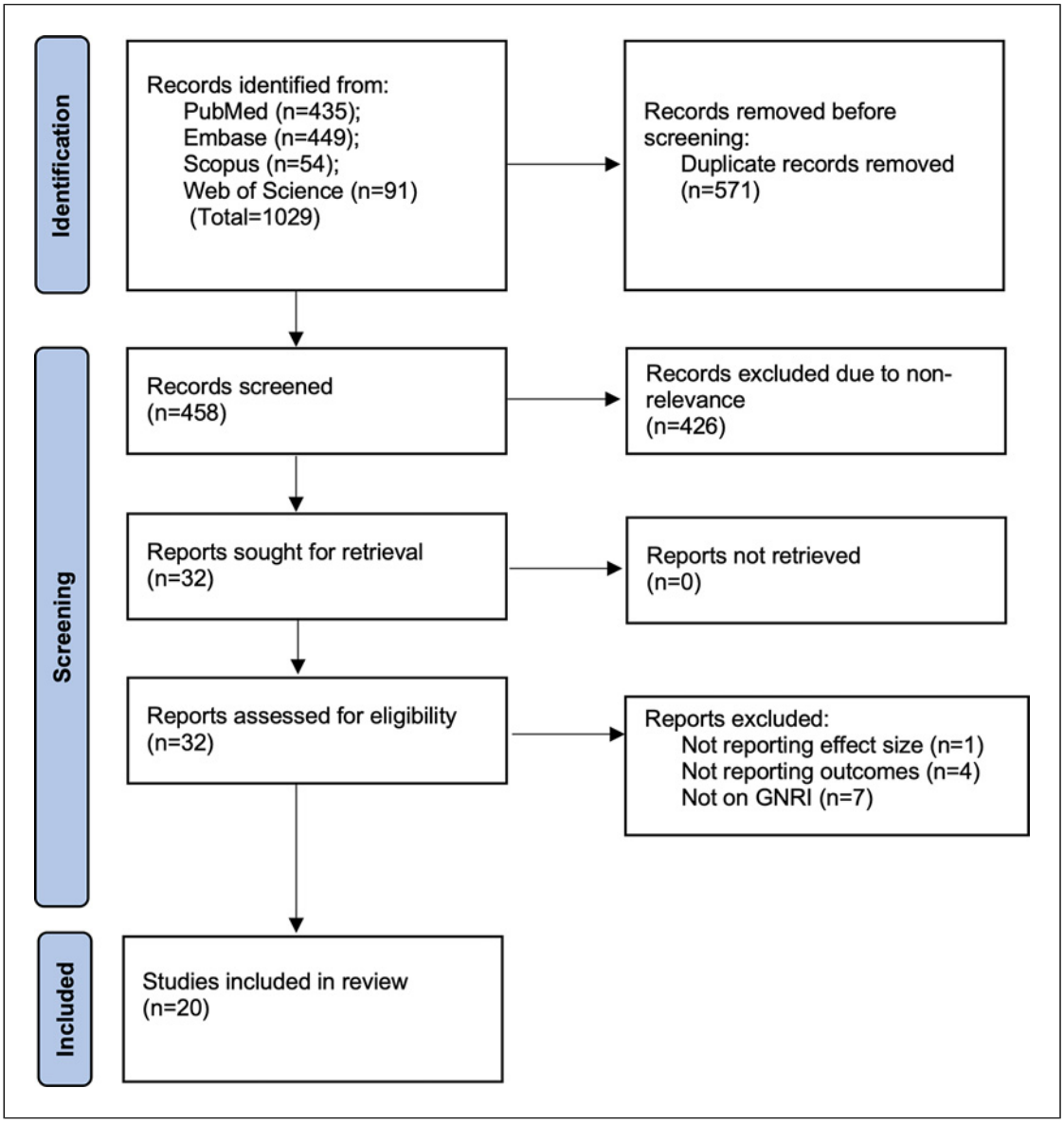

Fig. 1. PRISMA flowchart of the search.

received an NOS score of 6. Five studies received a score of 7 while all other studies received a score of 8 indicating high-quality articles.

Bladder Cancer

The outcomes reported by the three studies on bladder cancer were not amenable for a meta-analysis; hence, only a narrative review was conducted. Riveros et al. [29] used GNRI as a continuous variable and noted that per unit decrease in GNRI was associated with an increased risk of 30-day mortality (OR: 1.05; 95% CI: 1.01, 1.08). Pan et al. [23] in their cohort of bladder cancer patients undergoing cystectomy found that OS was not significantly associated with GNRI (hazard ratio [HR]: 0.783; 95% CI: 0.602–1.017). Lastly, Wu et al. [24] reported only the association between GNRI and PFS. The authors found that low GNRI was an independent predictor of worse PFS (HR: 2.155; 95% CI: 1.135–4.091).

Prostate Cancer

Data on OS were reported by all four studies on prostate cancer. Meta-analysis showed that low GNRI was a statistically significant predictor of poor OS in prostate cancer (OR: 3.02; 95% CI: 1.61, 5.67) (Fig. 2).

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Table 1. Details of included studies

Study	Location	Design	Sample size	Age	Male, %	Timing of GNRI	Cutoff	Method of cutoff	% with low GNRI	Treatment	Adjusted factors	F/U	NOS score
Bladder													
Riveros et al. [29] (2022)	USA	R	1,564	74.5	80.8	Before surgery	98	Std value	50	Radical cystectomy	Age, sex, frailty, ASA score, BMI, bleeding disorder, steroid use for a chronic condition, smoking history, preoperative creatinine, anemia and transfusion, and procedure characteristics (operative time and procedure type)	30 days	7
Pan et al. [23] (2023)	China	R	442	72.1	85	NR	100	Std value	42.5	Radical cystectomy	Age, sex, BMI, smoking, hypertension, tumor depth, perineural invasion, metastasis	Mean 67.5 months	8
Wu et al. [31] (2024)	China	R	162	69	77.8	Before surgery	93.8	X-tile software	27.8	Transurethral resection	Age, gender, restaging transurethral resection of the bladder tumor, smoking, alcohol consumption, hypertension, diabetes, hematuria, lower urinary tract irritative symptoms, ASA, tumor size, tumor number, pathological grade, concomitant carcinoma in situ, and type of intravesical therapy	Median 43 months	8
Prostate													
Okamoto et al. [30] (2019)	Japan	R	339	72	100	NR	92	Std value	19	Androgen-deprivation therapy	Age, year of diagnosis, ECOG-PS, and PSA level	Median 26 months	8

Table 1 (continued)

Study	Location	Design	Sample size	Age	Male, %	Timing of GNRI	Cutoff	Method of cutoff	% with low GNRI	Treatment	Adjusted factors	F/U	NOS score
Chang et al. [27] (2021)	Taiwan	R	170	76	100	NR	92	Std value	26.5	Castration–resistant receiving Docetaxel	ECOG-PS, hormone-sensitive period, lactate dehydrogenase, alkaline phosphatase, high-risk and high-volume metastasis, docetaxel dose, PSA	Median 22.5 months	8
Naiki et al. [28] (2023)	Japan	R	175	74	100	Treatment initiation	98	Std value	37.7	Abiraterone acetate plus androgen-deprivation therapy or combined androgen blockade	Age, ECOG-PS, PSA, liver metastasis, serum C reactive protein, agent at start of treatment	Median 26–38 months	8
Takahara et al. [33] (2024)	Japan	R	160	79	100	NR	101.6	ROC curve	NR	Androgen receptor signaling inhibitors	Initial PSA, hemoglobin, time to castration resistance	Median 23 months	7
Renal cell													
Gu et al. [26] (2015)	China	R	300	56.2	67.7	Before therapy	98	Std value	31.7	Targeted therapies	Age, sex, Heng risk stratification, Charlson comorbidity index, prior nephrectomy, systemic inflammation score, and geographic location	Median 30.8 months	8
Tang et al. [25] (2021)	China	R	694	NR	63.7	Before surgery	98	Std value	NR	Curative surgery	Gender, age, pathological T stage, pathological N stage, Fuhrman grade, tumor size, surgical type, pathological type, coagulation necrosis, tumor thrombus, smoking history, and prognostic nutritional index	Median 60.9 months	8
Kang et al. [42] (2022)	Korea	R	4,591	NR	73.3	Before surgery	98	Std value	15.9	Radical nephrectomy	Age, BMI, diabetes, tumor stage, Fuhrman grade, ECOG-PS	Median 37 months	8

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Table 1 (continued)

Study	Location	Design	Sample size	Age	Male, %	Timing of GNRI	Cutoff	Method of cutoff	% with low GNRI	Treatment	Adjusted factors	F/U	NOS score
Fujiwara et al. [41] (2023)	Japan	R	56	62	75	Before therapy	92	Std value	23	Nivolumab	Age, sex, Karnofsky Performance Status, duration from diagnosis to treatment, hemoglobin, calcium, blood cell count, lactate dehydrogenase, International Metastatic Renal Cell Cancer Database Consortium classification, number of metastatic lesion, line of therapy, histology	Median 28.6 months	8
Makino et al. [40] (2023)	Japan	R	213	63	72.8	Before surgery	98	Std value	NR	Surgery	Nil	Median 4.45 years months	6
Watari et al. [39] (2023)	Japan	R	119	70	78.2	NR	98	Std value	49.6	Immune checkpoint inhibitors	Age, sex, Karnofsky Performance Status, anemia	Median 11 months	7
Zhou et al. [34] (2024)	China	R	645	NR	64	Before surgery	98	X-tile software	13.5	Surgery	Age, diabetes, smoking, tumor size	Median 37 months	8
Urothelial													
Etani et al. [38] (2020)	Japan	R	52	71	82.7	Before therapy	92	Std value	55.8	Chemotherapy and pembrolizumab	Age, ECOG-PS, gender, metastasis, neutrophil lymphocyte ratio, serum C reactive protein	NR	7
Naiki et al. [36] (2021)	Japan	R	68	71	80.9	Before therapy	92	Std value	36.8	Chemotherapy	Age, ECOG-PS, visceral metastasis, neutrophil lymphocyte ratio, serum C reactive protein	Median 12.9 months	8
Isobe et al. [35] (2021)	Japan	R	94	77	81.9	Before therapy	92	Std value	40.4	Chemotherapy and immune checkpoint inhibitors	Age, sex, choice of treatment, metastasis, neutrophil lymphocyte ratio, serum C reactive protein	NR	7

Table 1 (continued)

Study	Location	Design	Sample size	Age	Male, %	Timing of GNRI	Cutoff	Method of cutoff	% with low GNRI	Treatment	Adjusted factors	F/U	NOS score
Chang et al. [37] (2023)	Taiwan	R	488	69	41.8	Before surgery	92	Std value	20.9	Surgery	Age, sex, ECOG-PS, comorbidity, smoking, renal function, uremia, surgical margin, pathological T and N stage, tumor grade, lymphovascular invasion	Median 23.2 months	8
Wu et al. [31] (2023)	China	R	458	70	49.1	Before surgery	98	Std value	32.3	Surgery	Sex, side, site, approach, multifocality, distal ureteral management, and carcinoma in situ	Median 36.8 months	8
Morikawa et al. [32] (2024)	Japan	R	61	74	62.3	Before therapy	80	ROC curve	NR	Enfortumab vedotin	Nil	NR	6

ASA, American Society of Anesthesiologists; GNRI, geriatric nutritional risk index; Std, standard; NOS, Newcastle Ottawa Scale; F/U, follow-up; ECOG-PS, Eastern Cooperative Oncology Group performance status; PSA, prostate-specific antigen; BMI, body mass index; ROC, receiver operating characteristics.

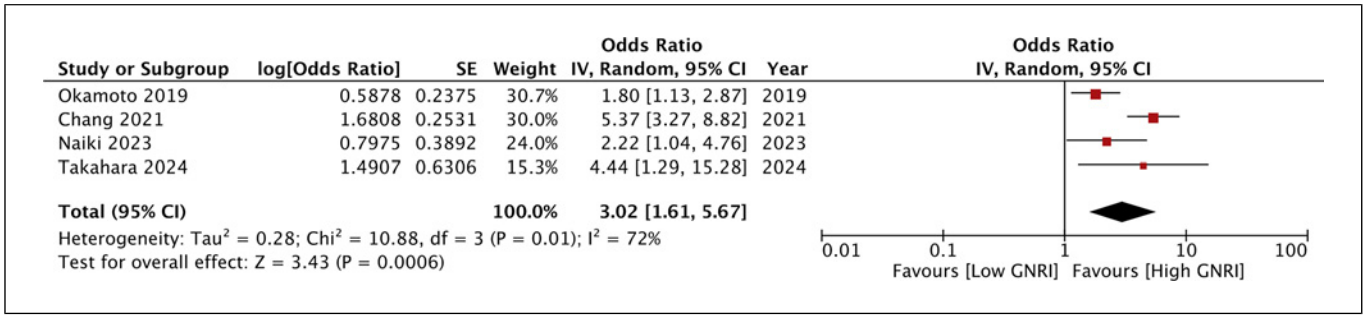

Fig. 2. Meta-analysis of the association between GNRI and OS after prostate cancer.

High heterogeneity was noted in the meta-analysis as I^2 was 72%. Sensitivity analysis showed that no study was an outliner and a positive association persisted in the removal of one study at a time (Table 2). However, heterogeneity was reduced to nil on the exclusion of the study of Chang et al. [27]. No data were available for a meta-analysis on CSS and PFS.

Renal Cell Carcinoma

Data were available for OS, CSS, and PFS from the studies on RCC. A pooled analysis of six studies showed that low GNRI was associated with poor OS in RCC (OR: 2.17; 95% CI: 1.46, 3.22) (Fig. 3). Low inter-study heterogeneity was seen (I^2 = 30%). Results did not change in significance on sensitivity analysis (Table 2). Further, the meta-analysis showed that low GNRI predicted CSS (OR: 2.60; 95% CI: 1.57, 4.30) but not PFS (OR: 1.50; 95% CI: 1.00, 2.24) (Fig. 4). The outcomes of PFS turned significant on the exclusion of Kang et al. [42] (Table 2).

Urothelial Carcinoma

Four and three studies each reported data on OS and CSS, respectively. No meta-analysis was possible for PFS. The pooled analysis found that low GNRI was a predictor of worse OS (OR: 2.24; 95% CI: 1.52, 3.29) and CSS (OR: 3.07; 95% CI: 1.38, 6.86) in urothelial carcinoma. High heterogeneity was noted in both meta-analyses with I^2 at 36% and 83%, respectively. The CSS results turned nonsignificant on sensitivity analysis following the exclusion of Etani et al. [38] (Table 2).

Discussion

Our review for the first time in literature explored the association between GNRI and outcomes of urological cancers. After a detailed literature search, we retrieved 20 studies examining the prognostic impact of GNRI on prostate, bladder, renal cell, and urothelial carcinoma. In general, GNRI was found to independently predict OS after prostate, renal cell, and urothelial carcinoma. GNRI was also a prognostic factor for CSS after RCC and urothelial carcinoma. Data on DFS were limited and meta-analysis for RCC failed to demonstrate an association between GNRI and DFS.

GNRI has generated significant interest as a prognostic marker for several malignancies in the past few years. Numerous meta-analyses have validated the prognostic role of GNRI as a reliable and easy-to-use malnutritional marker. Shen et al. [17] combined data from eleven studies to show that GNRI predicted poor OS (HR: 1.96; 95% CI: 1.66, 2.30) and disease-free survival (HR: 1.74; 95% CI: 1.36, 2.23) in non-small cell lung cancer. Yiu et al. [43] in a recent review of 10 studies including 2,793 patients demonstrated that GNRI was associated with worse OS in head and neck cancer patients (HR: 2.84; 95% CI: 2.07, 3.91). Another systematic review of ten studies by Mao and Lan [19] found that patients with low GNRI had significantly poor OS (HR: 2.41; 95% CI: 1.72, 3.41) and DFS (HR: 1.92; 95% CI: 1.47, 2.49) as compared to those with high GNRI. Xie et al. [44] collated data from 9 studies on patients with gastrointestinal malignancies and noted that low GNRI was predictive of worse OS (HR: 1.94; 95% CI: 1.65–2.28), PFS (HR: 2.45; 95% CI: 1.50–4.00), and postoperative complications (OR = 2.19; 95% CI: 1.57–3.05) but not CSS (HR = 1.60; 95% CI: 0.91–2.82).

Our review concurs with these results and extends the validity of GNRI to the group of urological cancers. We performed a broad literature search with the aim of including studies on all types of urological cancers and comprehensively reviewing the role of GNRI. However, we were limited by adequacy of the literature for each subtype of cancer. Nevertheless, a meta-analysis was

Table 2. Results of sensitivity analysis

Excluded study	OR (95% CI)	I^2
Prostate: OS		
Okamoto et al. [30] (2019)	3.86 (2.12, 7.03)	45
Chang et al. [27] (2021)	2.06 (1.41, 3.01)	0
Naiki et al. [28] (2023)	3.36 (1.45, 7.76)	81
Takahara et al. [33] (2024)	2.81 (1.34, 5.88)	81
Renal cell: OS		
Gu et al. [26] (2015)	2.24 (1.35, 3.70)	44
Tang et al. [25] (2021)	2.67 (1.82, 3.94)	0
Makino et al. [40] (2023)	2.20 (1.38, 3.50)	44
Watari et al. [39] (2023)	2.14 (1.36, 3.37)	41
Fujiwara et al. [41] (2023)	1.94 (1.35, 2.78)	14
Zhou et al. [34] (2024)	2.08 (1.29, 3.37)	36
Renal cell: CSS		
Kang et al. [42] (2022)	2.95 (1.57, 5.52)	0
Watari et al. [39] (2023)	2.54 (1.45, 4.46)	0
Zhou et al. [34] (2024)	2.31 (1.16, 4.58)	0
Renal cell: PFS		
Tang et al. [25] (2021)	1.75 (1.28, 2.40)	27
Kang et al. [42] (2022)	1.46 (0.75, 2.82)	74
Watari et al. [39] (2023)	1.55 (0.93, 2.58)	76
Zhou et al. [34] (2024)	1.30 (0.87, 1.93)	59
Urothelial: OS		
Isobe et al. [35] (2021)	2.34 (1.28, 4.27)	51
Naiki et al. [36] (2021)	1.90 (1.43, 2.54)	3
Wu et al. [31] (2023)	2.80 (1.83, 4.30)	0
Morikawa et al. [32] (2024)	2.23 (1.39, 3.59)	53
Urothelial: CSS		
Etani et al. [38] (2020)	3.02 (0.99, 9.27)	92
Chang et al. [37] (2023)	2.07 (1.18, 3.63)	37
Wu et al. [31] (2023)	4.78 (3.06, 7.47)	0

OS, overall survival; CSS, cancer-specific survival; PFS, progression-free survival.

possible for prostate, renal cell, and urothelial carcinoma, and low GNRI was found to worsen the risk of OS by about two or three times. Most of the results were robust on sensitivity analysis, thereby improving the credibility of the marker. Limited data also showed that low GNRI was predictive of worse CSS after RCC and urothelial carcinoma. Data on DFS were scarce and a meta-analysis was possible only for RCC, which failed to demonstrate a significant outcome. For bladder cancer, we could retrieve only three studies with all reporting variable outcomes. Overall, GNRI was associated with an increased risk of early mortality and PFS after bladder cancer but no OS. It must be reiterated that literature on bladder cancer was scarce and further investigations are needed to validate the utility of GNRI for this cancer subtype.

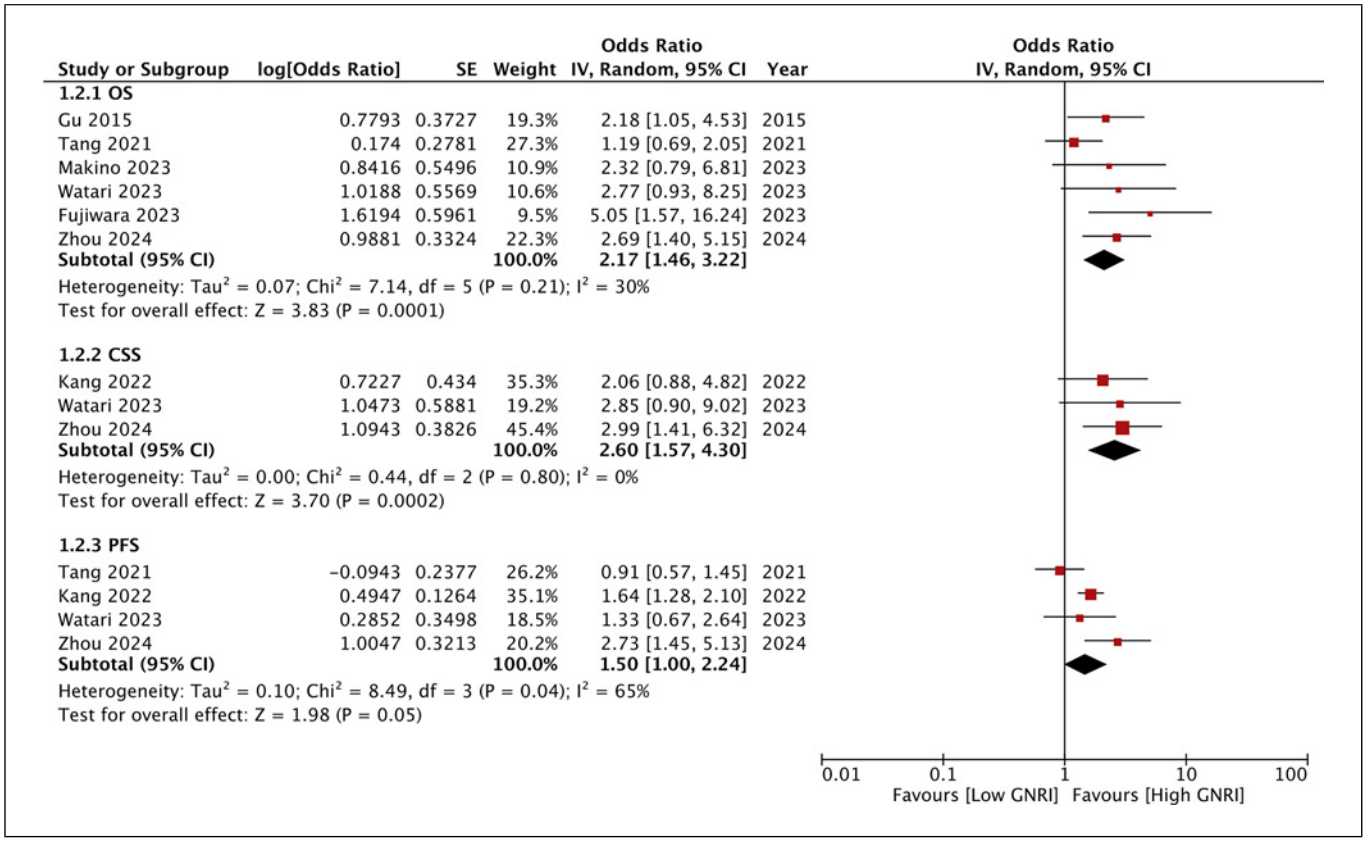

Fig. 3. Meta-analysis of the association between GNRI and OS, CSS, and PFS after RCC.

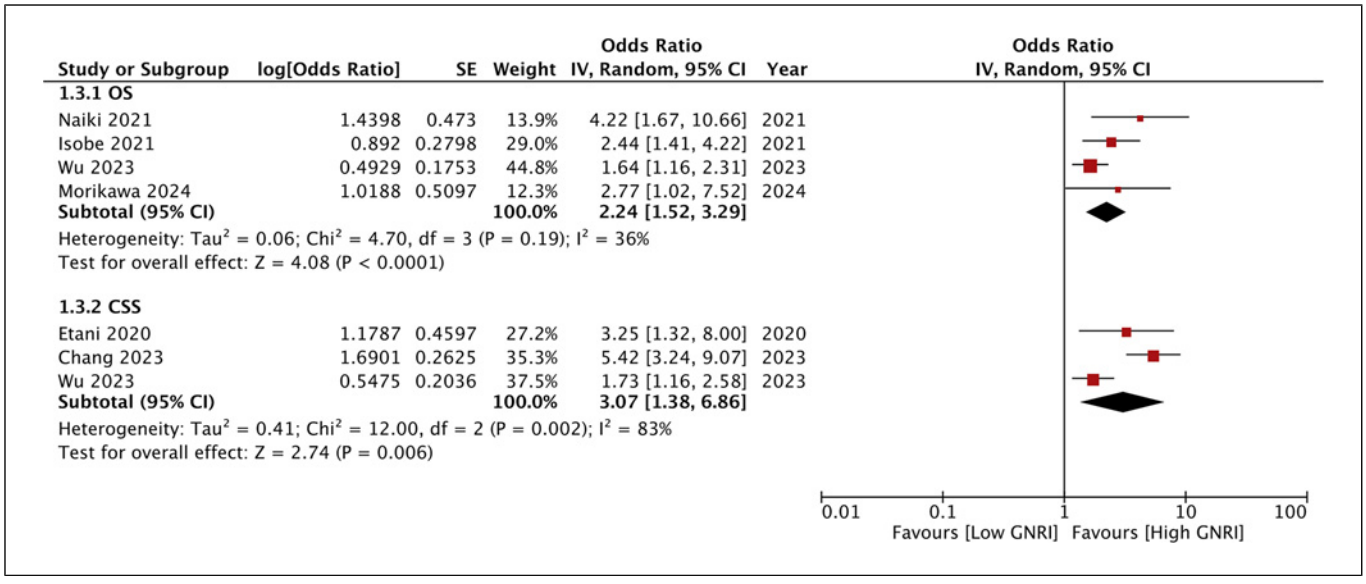

Fig. 4. Meta-analysis of the association between GNRI and OS and CSS after urothelial carcinoma.

The prognostic ability of GNRI is derived from its components, which are albumin and body weight [12]. Hypoalbuminemia is synonymous with malnutrition and is a direct indicator of the baseline nutritional status of the individual. As a standalone marker, low albumin levels have been linked with poor prognosis in cancer patients [45]. Low preoperative albumin levels are linked with increased complications and mortality in patients undergoing surgery for bladder and urothelial cancer [46, 47]. Serum albumin levels have also been found to independently predict the prognosis of prostate cancer undergoing chemotherapy [48]. Chen et al. [49] in a meta-analysis have noted that low pretreatment serum albumin leads to worse OS, CSS, and PFS after RCC. Further, owing to the high frequency of malnutrition in patients with malignancies, a large number of individuals progress to cachexia, which presents as muscle wasting and diminished immune, physical, and mental function [50]. Malnutrition and cachexia are associated with reduced chemotherapeutic effects, increased adverse events and treatment interruptions, and even poorer OS [51]. Second, albumin has a prominent immunomodulatory role wherein reduced levels lead to attenuation of macrophage activation and cell-mediated immunity against cancer cells [7]. Despite strong evidence on the prognostic role of albumin, its use as a standalone marker has limitations as albumin levels can vary with hydration status, diet, and concomitant diseases. GNRI overcomes these limitations by combining it with another variable i.e., body weight. Using the ratio of current body weight to ideal body weight, GNRI factors in body mass index, which is a known indicator of worse survival after cancer [52]. Recent studies have shown that high body mass index increases progression and postoperative complications of bladder cancer [53, 54] and also worsens survival after prostate cancer [55].

Our review should be interpreted with the following limitations. The primary limitation was the limited number of studies for each cancer sub-type, which precluded a detailed subgroup analysis for various moderators. There were important differences between studies regarding GNRI cutoffs, follow-up, and treatment protocols, which could skew the results. Further, the limited number of studies did not allow a detailed analysis of DFS, and more studies are needed to analyze the predictive ability of GNRI for PFS. Second, all data were retrospective and derived from medical records. Several patients with incomplete data were excluded from the individual studies. Also, erroneous data recording is a possibility in such studies, which can alter the results. Third, most data were on the Asian population with only one study from the USA. Hence, results cannot be generalized at this stage. Lastly, all studies used single-point measurements of GNRI and no information was available on change in GNRI and its impact on outcomes. Investigations are needed on the impact of nutritional supplements on GNRI and how it changes OS and PFS.

Conclusions

GNRI may have a role in predicting outcomes of urological malignancies. Low GNRI was independently associated with worse OS after prostate, renal cell, and urothelial carcinoma. Further, it also predicted CSS after RCC and urothelial carcinoma. More studies are needed to supplement the available evidence.

Statement of Ethics

Statement of Ethics is not applicable because this study is based exclusively on published literature.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Project was conceptualized by Y.C. and M.W. Data were curated by Z.Y. and F.X. Systematic review was conducted by M.W., Z.Y., and F.X. Statistical analysis was done by Z.Y. Original manuscript draft was prepared by Y.C. with review and editing by all authors. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

Studies included in the review are available on the databases of Embase (http://embase.com), PubMed (https://pubmed.ncbi.nlm.nih.gov), Web of Science (https://www.webofscience.com/wos), and Scopus (https://www.scopus.com). All data analyzed in the study are presented in the tables and figures. Any other information can be obtained from the corresponding author on reasonable request.

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