Pentraxin-3 and Outcomes in CKD: A Systematic Review and Meta-analysis

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Rationale & Objective: Long pentraxin-3 (PTX-3) serves as a biomarker for prognosticating adverse clinical outcomes in individuals with chronic kidney disease (CKD). The objective of the current meta-analysis was to evaluate the prognostic efficacy of PTX-3 in patients with CKD. In addition, we compared the prognostic effectiveness of PTX-3 and the short pentraxin C-reactive protein (CRP) in the identical cohort of patients with CKD.

Study Design: A systematic review and meta-analysis.

Setting & Participants: Patients with CKD treated with or without dialysis.

Selection Criteria for Studies: A cohort study with a minimum 1-year follow-up.

Data Extraction: Risk measurements, adjusted hazard risk with 95% CI, and modified variables.

Analytical Approach: To aggregate the adjusted effect estimates, a fixed-effects or random-effects model was employed.

Results: Nine studies covering 1,825 patients with CKD were selected in the present review. Six of the 9 studies exclusively included patients receiving hemodialysis. The collected findings indicated that patients with CKD in the highest tertile of PTX-3 demonstrated significantly higher risks of all-cause mortality (HR, 1.92; 95% CI, 1.44-2.56), cardiovascular death (HR, 1.98; 95% CI, 1.28-3.05), infectious death (HR, 5.26; 95% CI, 1.60-17.31), and fatal and nonfatal cardiovascular events (HR, 1.81; 95% CI, 1.35-2.42), as compared with those in the lowest tertile. These significant associations with risk were also observed when effect estimates were presented as per unit change in the PTX-3. Moreover, when comparing the prognostic value of PTX-3 and CRP in the same individuals (5 studies covering 904 patients), PTX-3 proved to be a satisfactory predictor of adverse events in these patients, whereas CRP failed to exhibit such predictive capability, regardless of the type of effect estimate used.

Limitations: A relatively small sample size and some heterogeneity.

Conclusions: Pentraxin 3 is associated with adverse events in individuals with CKD and may be a more reliable predictor of adverse clinical events than CRP in this population.

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Globally, chronic kidney disease (CKD) affects >10% of the population, making it a major concern for public health.[1] Individuals afflicted with CKD, particularly those undergoing dialysis, face elevated susceptibility to unfavorable clinical outcomes and increased mortality rates.[2] A multitude of factors, encompassing inflammation, oxidative stress, and vascular calcification, contribute to the occurrence of associated adverse events. Notably, inflammation assumes an integral role in CKD pathogenesis and progression, rendering it a primary contributor to mortality.[3,4]

Several acute-phase proteins from the pentraxin family, encompassing both short pentraxins like C-reactive protein (CRP) and long pentraxins like pentraxin-3 (PTX-3), have demonstrated their clinical use in disease diagnosis and prediction.[5,6] C-reactive protein, the archetypal acute-phase protein, exhibits a swift surge in the circulatory system on inflammatory stimulation.[7] However, as scientific investigations have progressed, CRP's efficacy in diagnosing and evaluating the risk of particular diseases has diminished.[8,9] Conversely, PTX-3 has emerged as a promising biomarker for indicating inflammation. In contrast to CRP, which is predominantly synthesized by the liver, PTX3 is produced by various tissues and cells, including innate immunity cells that react to proinflammatory stimuli.[10] The extrahepatic synthesis of PTX3 is believed to provide a more precise reflection of the inflammation sites when compared with CRP.[11] Recent studies have indicated that PTX-3 possesses significant diagnostic and prognostic use in a variety of inflammatory and autoimmune conditions.[12,13] Indeed, there is speculation that PTX-3 may surpass CRP as a superior prognostic indicator for forecasting unfavorable clinical outcomes in specific disorders.[11,14] In addition, several studies have also investigated the correlation between circulating PTX-3 and CKD prognosis over the past dozen years. It is crucial to acknowledge that these findings have not consistently aligned with one another. Moreover, the limited sample sizes in previous studies have hindered the ability to establish definitive conclusions.

In this study, our team aimed to perform a meta-analysis to comprehensively assess the predictive value of PTX-3 as a factor for adverse clinical events in individuals with CKD. In parallel, we also performed a pooled analysis of the relationship between CRP and CKD prognoses in the included studies focusing on PTX-3, with a view to comparing their prognostic value in the identical patient population.

PLAIN-LANGUAGE SUMMARY

Systemic inflammatory markers are useful in predicting the prognosis of patients with CKD. Pentraxin-3 (PTX-3) is an emerging biomarker of inflammation compared with other members of the pentraxin family, such as C-reactive protein (CRP). This meta-analysis evaluated the prognostic value of PTX-3 in predicting adverse outcomes in patients with CKD. Also, we compared the prognostic values between PTX-3 and CRP in the subset of studies with data on CRP. We found that patients with CKD with higher circulating PTX-3 levels had a significantly heightened risk of adverse outcomes compared with those with lower PTX-3 levels. By contrast, CRP did not appear to be a good predictor of adverse events. Pentraxin-3 might be a more reliable prognostic marker than CRP in patients with CKD.

METHODS

This study performed a systematic review in accordance with the PRISMA guidelines.[15] The review protocol was registered with INPLASY (registration number: INPLASY202240135).

Search Strategy

A comprehensive search was performed in 3 electronic databases (PubMed, Web of Science, and EMBASE) in June 2023 and the last update was made in November 17, 2023. The search strategy involved combining specific subject terms and free words, namely, (Pentraxin-3 OR PTX-3) AND (chronic kidney disease OR chronic renal failure OR chronic renal disease OR chronic renal insufficiency OR end-stage renal disease OR ESRD OR peritoneal dialysis OR hemodialysis OR dialysis). In addition, relevant studies were meticulously identified from the reference lists.

Selection Criteria

Researches would be deemed as eligible as follows: (1) were prospective cohort researches, or retrospective cohort studies (post hoc analysis); (2) included patients with CKD (hemodialysis, peritoneal dialysis, and nondialysis CKD) as subjects; (3) assessed the relationship between PTX-3 and major unfavorable clinical events, such as cardiovascular events or mortality; (4) reported multivariable-adjusted risk estimates such as hazard risk (HR), odds ratio or relative risk, and their corresponding 95% confidence interval (CI); (5) had a mean follow-up time of 1 year or longer; and (6) were research articles written in English.

Data Extraction and Quality Assessment

The process of research selection, data extraction, and quality evaluation of the literature included in this study was performed independently by 2 researchers. Any disagreements were resolved by a third author (QZ). The collected data consisted of the first author's name, publication year, nation setting, patient types, sample size (percentage of male participants), patient age, measurements of risks, adjusted HR (with a 95% CI), follow-up year, and modified variables. The quality of the methodology was assessed using the Newcastle-Ottawa Scale,[16] which encompasses 3 domains: selection, comparability, and result. The score was between 0 and 9 points, and the scores of 7-9, 4-6, and 0-3 would be deemed as high, moderate, and low quality, separately.

Statistical Analysis

Statistic assay was completed by the Stata 15.0 statistic program (Stata Corp LP). Within the scope of this meta-analysis, a total of 9 studies were selected, each of which reported effect estimates using various methodologies. These methodologies included per unit increase, comparison between the highest and lowest quartiles, comparison between high and low levels, and comparison between the highest tertile and the remaining 2 tertiles. To ensure uniformity in the comparison, all estimates were converted to extreme thirds, specifically the top versus bottom third of circulating PTX-3 or CRP levels, in accordance with a previously established approach.[17,18] It is worth mentioning that the comparison between the third tertile and the other tertiles was treated as a dichotomous categorization, ie, high versus low. In brief, we first assumed that the baseline PTX-3 or CRP levels displayed a log-normal distribution, and the relationship of the 2 proteins with adverse clinical events was linear in the log scale. Then, the conversional HR was speculated as a scaling factor of 2.18 divided by 1.59 times original effect estimates (log transformation) for a contrast of dichotomous categories, and 2.18 divided by 2.54 times for the highest versus lowest quartile. For those studies that reported continuous variables (per unit change) in the circulating concentrations of PTX-3 (ng/mL) or CRP (mg/dL), they were first converted to 1-standard deviation variation, followed by 2.18 as a scale factor. In addition, these continuous variables were also pooled individually. The χ^2 test was employed to assess the between-study inhomogeneity, with a significance level of $P < 0.10$. Statistical heterogeneity was measured using I^2 statistics, where a value >50% indicated significant heterogeneity. In the presence of notable inhomogeneity ($P < 0.10$ or $I^2 > 50\%$), the stochastic effects model was employed; otherwise, the fixed-effects model was used. Subgroup analyses were completed to explore the possible sources of inhomogeneity. Sensitivity analysis was performed by omitting 1 research at a time to evaluate the stability of the combined effect estimates. Publication bias was assessed through the examination of funnel plots and the application of Egger's test.

Unless noted otherwise, P value of <0.05 had significance on statistics.

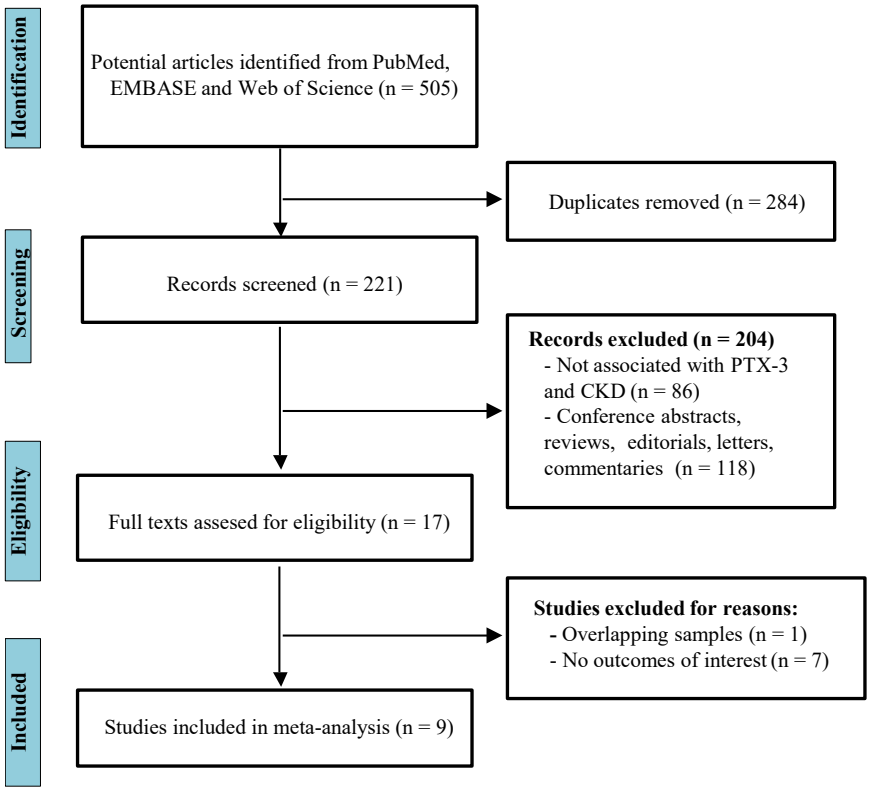

Figure 1. The flow chart of the study selection process.

RESULTS

Literature Search

A total of 505 potentially relevant studies were identified from 3 electronic databases. After removing duplicates (n = 284), the remaining 221 records were assessed based on their title and abstracts. From this assessment, 204 studies were deemed irrelevant and excluded, leaving 17 articles eligible for full-text reading. Among these, 8 articles were excluded because of sample overlap and lack of interesting outcomes. Ultimately, 9 published studies[19-27] were selected for inclusion in this review (Fig 1).

Characteristics of the Included Studies Evaluating the Prognostic Efficacy of PTX-3

The baseline characteristics of the screened studies are presented in Table 1.[19-27] A total of 9 studies, performed between 2007 and 2022, included a combined sample of 1,825 individuals with CKD. Among these articles, 4 studies were performed in Sweden, while the remaining 5 originated from Taiwan, Portugal, Poland, China, and Turkey, respectively. Two studies focused on patients with CKD not receiving dialysis, 6 studies exclusively included patients receiving hemodialysis, and 1 study involved individuals with both nondialysis CKD and hemodialysis. Sample sizes ranged from 78-403, with the proportion of male participants varying between 45.0% and 62.0%.The average baseline age of patients with CKD were between 53.2 and 71.0 years, with an average follow-up time of 1.0-5.0 years. According to the Newcastle-Ottawa Scale, all included studies were of high or moderate quality (44.4% high and 55.6% moderate).

Quantitative Synthesis

To generate consistent comparisons, we converted all these effect estimates into extreme thirds. When we compared those in the lowest tertile, patients with CKD in the highest PTX-3 tertile exhibited remarkably greater risks of all-cause death (HR, 1.92; 95% CI, 1.44-2.56; $P < 0.001$), cardiovascular mortality (HR, 1.98; 95% CI, 1.28-3.05; $P = 0.002$), infectious mortality (HR, 5.26; 95% CI, 1.60-17.31; $P = 0.006$), and lethal and nonlethal cardiovascular events (HR, 1.81; 95% CI, 1.35-2.42; $P < 0.001$) (Fig 2). No statistical heterogeneity was identified in the analyses of cardiovascular death, hence the fixed-effects model was adopted, whereas random-effects models were used for the other analyses because of the high heterogeneity.

For effect estimates presented as continuous variables (per unit increase), the meta-analysis was additionally and individually performed. The pooled results showed that per increase in 1 unit of circulating PTX-3 concentrations increased the risk of all-cause death by 24% (HR, 1.24; 95% CI, 1.08-1.42; $P = 0.002$), cardiovascular death by 28% (HR, 1.28; 95% CI, 1.10-1.48; $P = 0.001$), infectious death by 39% (HR, 1.39; 95% CI, 1.10-1.77; $P = 0.006$),

Table 1. Summary of Clinical Studies Evaluating the Prognostic Efficacy of PTX-3

Reference	Region	Study Design	Patient Types	Sample Size (% Male)	Age (y)	Measurements of Risks	Adjusted HR (95% CI)	Follow-Up (y)	Adjusted Confounders	Overall NOS
Tong,[19] 2007	Sweden	Retrospective cohort	Nondialysis CKD (stage 5)	276 (60.0)	53	Highest tertile vs the other 2 tertiles	Total death: 1.73 (1.08-2.79); and CV death: 2.12 (1.11-4.08)	5.0	Age, sex, inflammation (CRP ≥10 mg/L), and CVD	6
Suliman,[20] 2008	Sweden	Retrospective cohort	HD	200 (54.5)	64	Highest tertile vs the other 2 tertiles	Total death: 1.67 (1.04-2.68)	2.6	Age, sex, dialytic vintage, davies comorbidity score, protein-energy wasting, and hs-CRP	7
Yilmaz,[21] 2014	Turkey	Prospective cohort	Nondialysis CKD (stage 1-5)	403 (56.6)	53.2	Per unit increase	Fatal and nonfatal CV events: 1.02 (1.01-1.03)	3.2	Age, sex, FMD, IL-10, IL-6, hs-CRP, serum albumin, eGFR, smoking, hypertension, diabetes, SBP, HOMA-IR, phosphate, and iPTH	8
Sjöberg,[22] 2014	Sweden	Prospective cohort	HD	188 (55)	66.0	Highest vs lowest quartile	Total death: 2.31 (1.32–4.04)	3.4	Age, sex, CVD, diabetes, vintage, and malnutrition	8
Zhou,[23] 2015	China	Prospective cohort	HD	116 (53.4)	56.4	Per unit increase	Total death: 1.11 (1.01-1.21)	4.8	Age, ABI, smoking, hypertension, diabetes, DBP, Pulse pressure, ACEI/ARB, albumin, and hs-CRP	6
Krzanowski,[24] 2017	Poland	Prospective cohort	HD and nondialysis CKD (stage 5)	78 (60.0)	61.5	Per unit increase	Total death: 1.28 (1.05-1.55); and CV death: 1.28 (1.04-1.57)	5.0	Age and dialysis status	4
Valente,[25] 2019	Portugal	Prospective cohort	HD	246 (54.5)	71.0	Per unit increase	Total death: 1.63 (1.21-2.21)	1.0	Age, dialysis vintage, vascular access, triglycerides, HDL-C, adiponectin, leptin, NT-proBNP, and TIMP-1	6
Feldreich,[26] 2019	Sweden	Prospective cohort	HD	183 (45.0)	63	Per unit increase	CV death: 1.15 (0.76-1.75)	3.6	Age and sex	5
Tsai,[27] 2022	Taiwan	Prospective cohort	HD	135 (48.1)	66.0	Per unit increase	Total death: 1.23 (1.03-1.48); CV death: 1.32 (1.02-1.70); and infectious death: 1.40 (1.10-1.77)	3.0	Age, sex, HD duration, AVF use time, diabetes, hypertension, hyperlipidemia, CAD, serum albumin, and hemoglobin	7

Abbreviations: ABI, ankle-brachial index; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; AVF, arteriovenous fistula; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; CRP, C-reactive protein; CV, cardiovascular; CVD, cardiovascular disease; DBP, diastolic blood pressure; eGFR, estimated glomerular filtration rate; FMD, flow-mediated dilatation; HD, hemodialysis; HDL-C, high-density lipoprotein cholesterol; HR, hazard risk; hs-CRP, high-sensitivity C-reactive protein; iPTH, intact parathyroid hormone; NOS, the Newcastle-Ottawa Scale; NT-proBNP, N-terminal pro-B-type natriuretic peptide; PTX-3, pentraxin-3; SBP, systolic blood pressure; TIMP-1, tissue inhibitor of metalloproteinase-1.

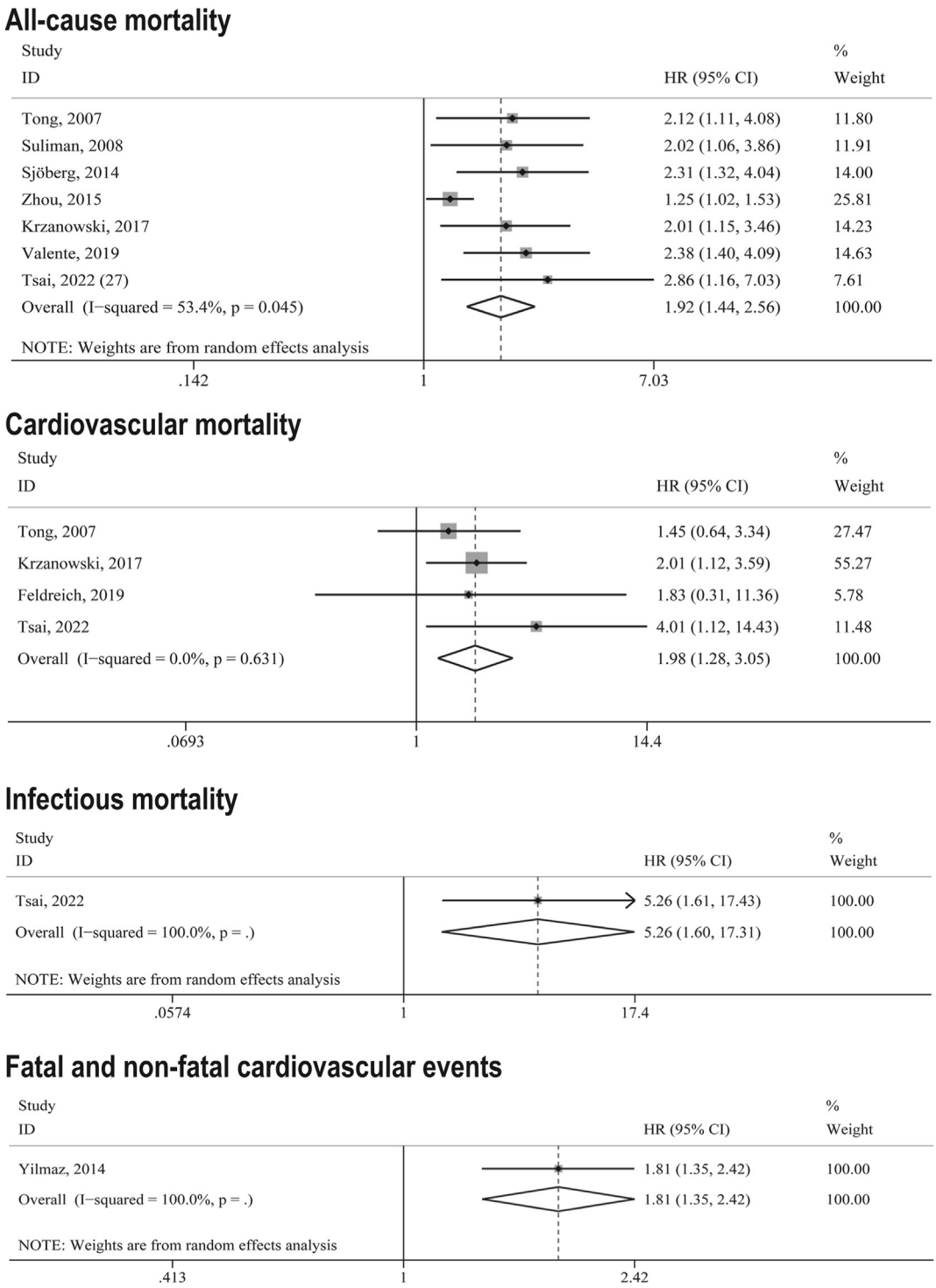

Figure 2. Forest plot of adverse clinical events for patients in the highest versus lowest tertile of circulating pentraxin-3 levels. HR, hazard risk; CI, confidence interval.

and lethal and nonlethal cardiovascular events by 2% (HR, 1.02; 95% CI, 1.01-1.03; $P < 0.001$) (Fig 3). Similar to extreme thirds, the pooled analysis of cardiovascular mortality was performed by a fixed-effects model, whereas the other 3 analyses were finished by random-effects models.

Among the included studies focusing on the predictive value of PTX-3 for adverse clinical events, 5 of these studies also investigated the association between CRP and all-cause or cardiovascular death concurrently.[19,22-25] A summary of the comparison between PTX-3 and CRP for their prognosis within the same

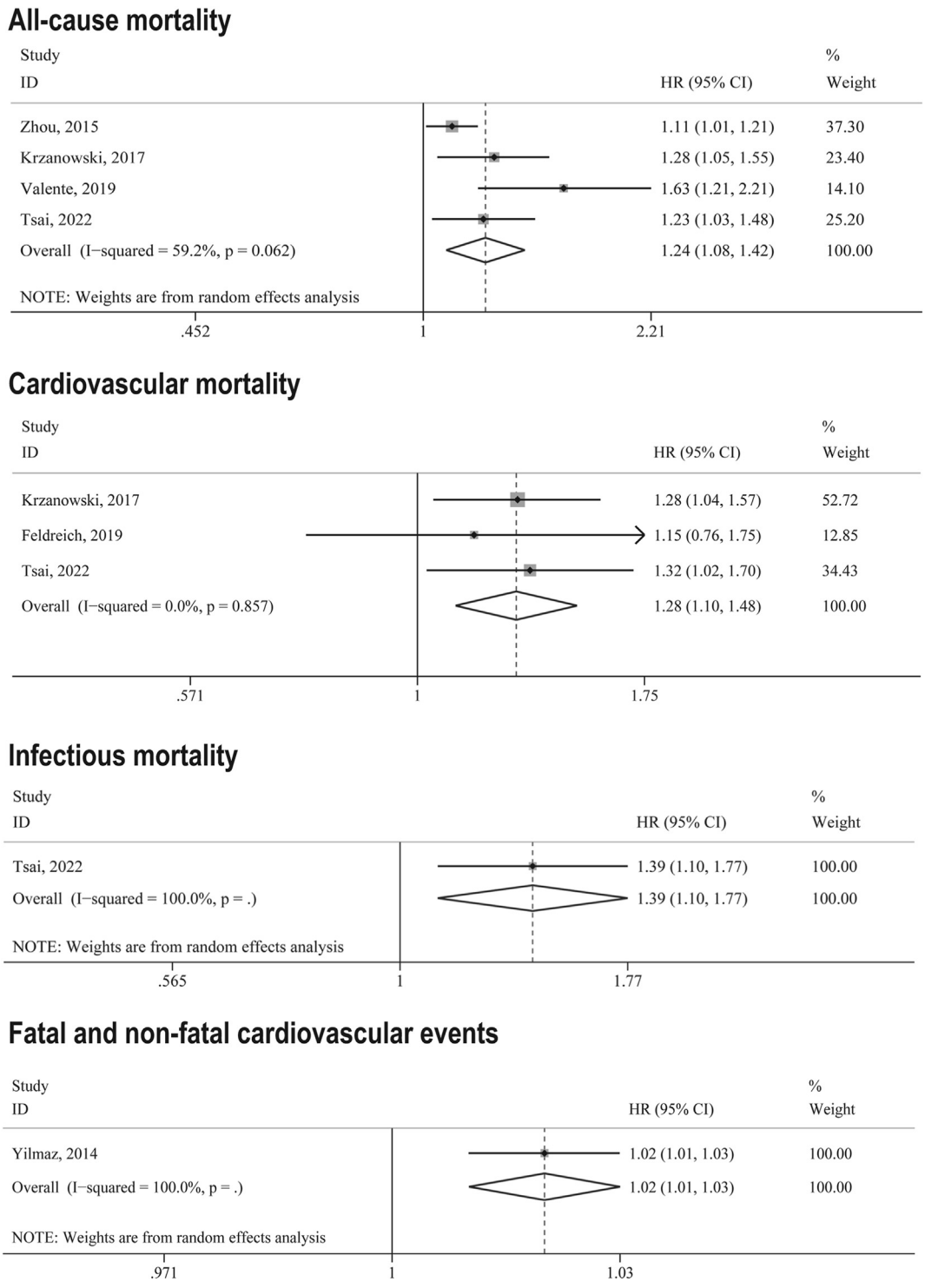

Figure 3. Forest plot of adverse clinical events for patients with per unit increase in circulating pentraxin-3 levels. HR, hazard risk; CI, confidence interval.

population is presented in Table S1. By comparison of the pooled results, we found that PTX-3 significantly predicted the risk of both all-cause and cardiovascular mortality regardless of whether categorical variables (Fig S1) or continuous variables (Fig S2) were used. However, there was no indication that the CRP could predict these outcomes either by categorical variables (Fig S3) or by continuous variables (Fig S4).

Subgroup Analysis

We limited our subgroup analyses to evaluating all-cause mortality in tertiles because of the lack of sufficient

Table 2. Subgroup Analysis of the Association Between Pentraxin-3 and All-Cause Mortality

Subgroup	No. studies	HR	95% CI	*P*	Heterogeneity	
					I^2	*P*
Region						
Europe	5	2.18	1.68-2.82	< 0.001	0.0%	0.99
Asia	2	1.68	0.77-3.64	0.192	67.6%	0.08
Study design						
Prospective cohort	5	1.92	1.33-2.78	0.001	64.6%	0.02
Retrospective cohort	2	2.07	1.31-3.27	0.002	0.0%	0.92
Patient types						
Patients receiving HD	5	1.92	1.32-2.81	0.001	63.7%	0.03
Patients not receiving dialysis	1	2.12	1.11-4.06	0.024	–	–
Patients receiving HD and patients not receiving dialysis	1	2.01	1.16-3.49	0.013	–	–
Sample size						
≥200	3	2.20	1.55-3.11	< 0.001	0.0%	0.92
<200	4	1.82	1.20-2.75	0.005	63.6%	0.04
Patient age						
≥65 y	3	2.42	1.70-3.45	< 0.001	0.0%	0.92
<65 y	4	1.64	1.19-2.28	0.003	46.9%	0.13
Follow-up duration						
≥3 y	5	1.85	1.30-2.64	0.001	57.9%	0.05
<3 y	2	2.23	1.47-3.36	< 0.001	0.0%	0.70
Adjustment for blood pressure parameters or hypertension						
Yes	2	1.68	0.77-3.64	0.192	67.6%	0.08
No	5	2.18	1.68-2.82	< 0.001	0.0%	0.99
Adjustment for diabetes						
Yes	3	1.82	1.05-3.14	0.032	70.1%	0.04
No	4	2.14	1.59-2.87	< 0.001	0.0%	0.97
Adjustment for CRP/hs-CRP						
Yes	3	1.57	1.07-2.30	0.021	48.6%	0.14
No	4	2.29	1.70-3.09	< 0.001	0.0%	0.93

Abbreviations: CI, confidence interval; CRP, C-reactive protein; HD, hemodialysis; HR, hazard risk; hs-CRP, high-sensitivity C-reactive protein.

studies examining other outcomes. Studies were stratified according to study design, location, patient type, ages, sample sizes, average follow-up time, and an adjustment for hypertension, diabetes and CRP/hs-CRP. As indicated in Table 2, we observed that heterogeneity disappeared ($I^2 = 0.0\%$) within some subgroups when stratified. Furthermore, our findings revealed a lack of significant association between PTX-3 and all-cause mortality among Asian patients, and in the stratification adjusted for parameters relating to blood pressure ($P = 0.19$ for both). However, all other stratifications demonstrated statistically significant results, consistent with the overall analysis.

Sensitivity Analysis and Publication Bias

Similarly, sensitivity analyses and publication bias were merely performed in 7 studies evaluating all-cause death with tertiles. The leave-one-out sensitivity analysis did not indicate any single study with a significant effect on the overall effect estimate (Fig 4). However, the funnel plot presented an asymmetric status (Fig 5), and the P value of Egger's test was 0.001, which further suggested a possible publication bias.

DISCUSSION

In this investigation, it was observed that there exists a significant correlation between circulating PTX-3 and adverse clinical outcomes in individuals diagnosed with CKD. Moreover, in the subset of studies that included data on CRP, the association between PTX-3 and unfavorable outcomes exhibited greater strength when compared with the association observed between CRP and clinical outcomes. To the best of our knowledge, this meta-analysis represents the first attempt to explore the relationship between circulating PTX-3 and adverse clinical events in individuals with CKD.

There is an increasing recognition within the academic community that the progression of CKD is accompanied by a persistent low-grade inflammation, which poses a particularly grave concern for individuals undergoing dialysis.[4] Furthermore, the severity of this inflammatory response has been found to play a role in the development of complications associated with CKD, such as cardiovascular disease (CVD) and peripheral artery disease.[28,29] In addition, several studies cited in this review have demonstrated that individuals with more advanced stages

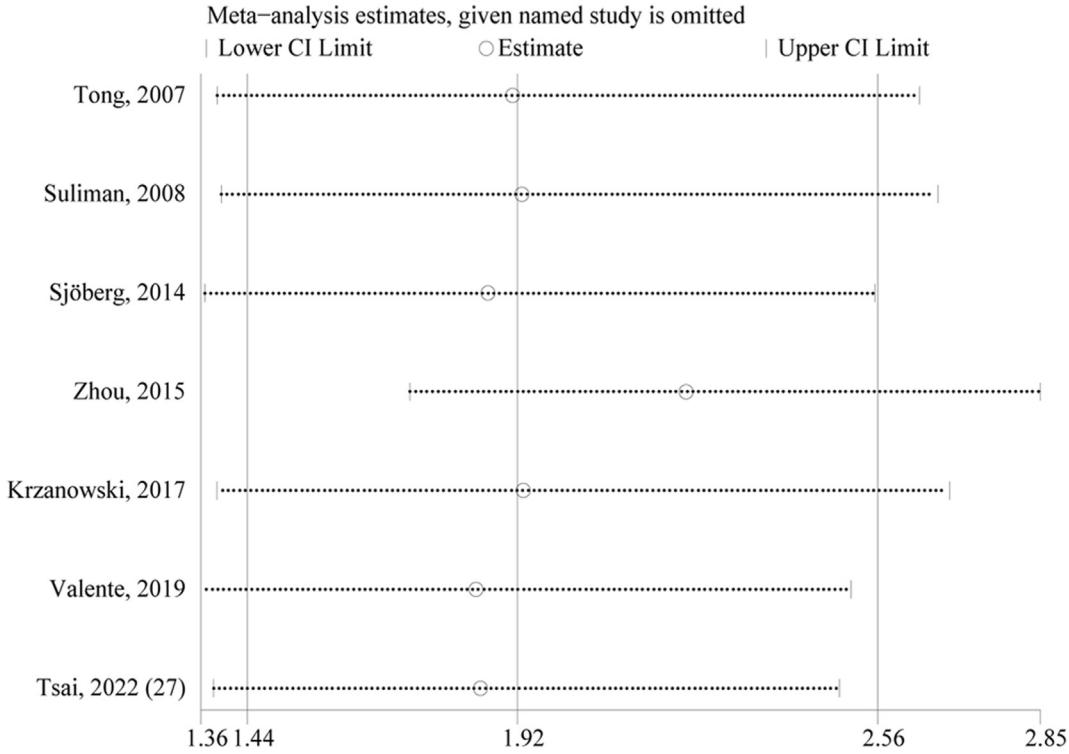

Figure 4. Sensitivity analysis of the association between pentraxin-3 and all-cause mortality. CI, confidence interval.

of CKD exhibit significantly elevated levels of inflammation-related biomarkers, including IL-6, tumor necrosis factorα, CRP, and PTX-3, in contrast to those in the early stages of CKD.[19,21] The included studies also demonstrated that individuals with CKD who also suffered from CVD or peripheral artery disease exhibited more severe systemic inflammation compared with those without these comorbidities.[19,23] However, it appears that PTX-3 is

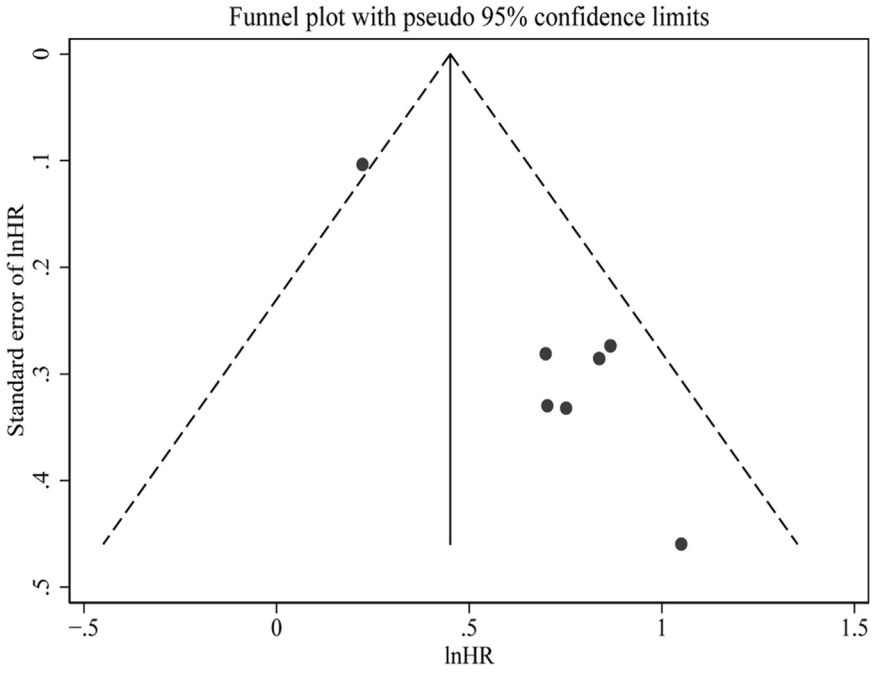

Figure 5. Funnel plot assessing potential publication bias for the association between pentraxin-3 and all-cause mortality risk. HR, hazard risk.

a more effective indicator of CKD severity. This is because of its larger molecular size (40.6 kDa) in comparison with CRP (21.5 kDa), IL-6 (26.0 kDa), and tumor necrosis factor α (17.0 kDa),[19,30] which suggests that PTX-3 remains in the bloodstream for a longer period of time because of impaired renal excretory function in advanced nephropathy. In addition, PTX-3 is synthesized at the site of infection or inflammation by diverse tissue cells, such as dendritic cells, endothelial cells, and macrophages, whereas CRP is predominantly secreted by hepatocytes.[10] Earlier investigation has additionally revealed the secretion of PTX-3 by renal epithelial cells.[31] Consequently, PTX-3 holds promise as a more dependable circulating inflammatory marker, offering potentially valuable diagnostic or prognostic insights for patients with CKD.

Out of the 9 studies included in this review, 5 studies presented the adjusted effect estimates of CRP for adverse events.[19,22-25] However, among the 5 studies examining the relationship between CRP and all-cause death (divided into tertile groups), 3 studies did not yield statistically significant results.[19,24,25] In addition, 3 studies employing per unit change as effect estimates,[23-25] 2 studies also did not demonstrate a statistically significant relationship.[24,25] Furthermore, CRP was not significantly associated with cardiovascular death in 1 study.[24] Comparatively, all the 5 studies demonstrated a significant association between PTX-3 and the risk of all-cause and cardiovascular mortality, using both types of effect estimates. These results indicate that PTX-3 may serve as a superior biomarker for predicting adverse clinical outcomes in patients with CKD compared with CRP. Furthermore, recent research has performed comprehensive evaluations and comparisons between PTX-3 and CRP, examining their diagnostic and prognostic value in various disorders. A recent prospective study has indicated that PTX-3 may possess greater prognostic value as a biomarker when compared with hs-CRP and other inflammation factors in predicting adverse events in individuals with ST-segment elevation myocardial infarction following bare metal stent implantation.[32] Another study has demonstrated that PTX-3 exhibits heightened sensitivity as an early indicator for identifying individuals with coronary artery disease and functioning as a more effective marker for disease progression.[33] Furthermore, a recent meta-analysis has proposed that PTX-3 displays superior sensitivity and specificity in comparison with CRP for evaluating active Takayasu arteritis.[34]

There are inherent limitations in this study. First, despite the incorporation of aggregated data from a total of 9 studies, the relatively constrained number of cases in each individual article, spanning from 78-403, ultimately resulted in a relatively modest pooled sample size. Specifically, only 1 study furnished data on infectious mortality, and lethal and nonlethal cardiovascular incidents, and analogous observations were also made when assessing the prognostic importance of CRP. As a result, the statistical outcomes presented in this review may exhibit diminished persuasiveness. Second, despite the implementation of subgroup analysis, heterogeneity persisted. Moreover, because of the reduced number of studies within each subgroup following stratification, the results in subgroups should be interpreted in a prudent manner. For example, the prognostic value of PTX-3 was not observed in patients from Asia and the subgroup adjusted for blood pressure parameters or hypertension, which were not consistent with the overall pooled result. Third, despite the inclusion of studies with adjusted effect estimates, it is important to acknowledge that the adjusted confounders varied among the studies. Specifically, 2 of the included studies only accounted for 2 potential confounding factors,[24,26] resulting in the exclusion of certain variables from the models. This omission may have influenced the risk estimates, potentially leading to overestimated or underestimated effects. Finally, there is a possibility of publication bias in the pooled analysis. However, it is worth noting that the heterogeneity between the studies could also contribute to the asymmetrical funnel plot.[35]

In summary, this study has provided evidence supporting the significant prognostic value of circulating PTX-3 in predicting adverse clinical outcomes among patients with CKD, encompassing all-cause death, cardiovascular death, infectious death, as well as fatal and nonfatal cardiovascular events. Conversely, CRP does not appear to possess the same level of efficacy as a marker for predicting these events. Consequently, it is imperative that future large-scale prospective research be designed to further assess and compare the prognostic value of these 2 markers within the same patient population.

SUPPLEMENTARY MATERIAL

Supplementary File (PDF)

Figure S1: Forest plot of adverse clinical events for patients in the highest versus lowest tertile of circulating pentraxin-3 levels in the subset of studies with data on C-reactive protein. HR, hazard risk; CI, confidence interval.

Figure S2: Forest plot of adverse clinical events for patients with per unit increase in circulating pentraxin-3 levels in the subset of studies with data on C-reactive protein. HR, hazard risk; CI, confidence interval.

Figure S3: Forest plot of adverse clinical events for patients in the highest versus lowest tertile of C-reactive protein levels. HR, hazard risk; CI, confidence interval.

Figure S4: Forest plot of adverse clinical events for patients with per unit increase in C-reactive protein levels. HR, hazard risk; CI, confidence interval.

Table S1: Summary of Comparison Between Pentraxin-3 and C-Reactive Protein for the Prognosis in the Subset of Studies With Data on C-Reactive Protein.

ARTICLE INFORMATION

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