

Triglyceride glucose index can predict the risk of contrast-induced nephropathy undergoing percutaneous coronary intervention: A systematic review and meta-analysis

Shuxiong Ge, Jinlin Yan, Hui Wang

Abstract

Objective: To investigate the association between triglyceride glucose index and contrast-induced nephropathy in patients after percutaneous coronary intervention.

Methods: The meta-analysis was conducted in Ningbo in 2024 from May to July and comprised literature search across PubMed, Embase and Web of Science databases for relevant studies published up to May 2024 and evaluated the adverse outcomes of contrast-induced nephropathy in patients after percutaneous coronary intervention. The pooled odds ratios with 95% confidence intervals were calculated by random-effects model, assessing the strength of association between triglyceride glucose index and contrast-induced nephropathy. Subgroup analysis assessed the sources of heterogeneity. Data was analysed using Stata 17.

Results: Of the 212 studies identified initially, 6(2.8%) were included, comprising 4,521 individuals; 2,996(66.3%) men and 1,525(33.7%) women. High triglyceride glucose index increased the risk of contrast-induced nephropathy in the patients compared to those with low triglyceride glucose index ($p<0.05$). There was a significant association between triglyceride glucose index and an increased risk of contrast-induced nephropathy ($p=0.012$). There was some obvious heterogeneity in the meta-analysis ($I^2=79.9\%$).

Conclusion: Triglyceride glucose index in patients undergoing percutaneous coronary intervention was found to be associated with marked increase in the risk of contrast-induced nephropathy. Pretreatment of high-risk patients could reduce the risk.

Keywords: Triglyceride glucose index, Contrast-induced nephropathy, Meta-analysis, Percutaneous coronary intervention, Predictor. (JPMA 76: 1726; 2026) DOI: <https://doi.org/10.47391/JPMA.23287>

Introduction

Contrast-induced nephropathy (CIN) is a common and serious disease, which refers to acute renal failure complications caused by contrast agents during arteriography or interventional surgery. The diagnostic criteria for CIN is an increase in serum creatinine of $\geq 26.5\text{mmol/l}$ (0.3mg/dl) or $>50\%$ compared to preoperative creatinine.¹ Despite improved understanding of CIN among the clinicians and the increasing awareness of risk assessment, the incidence of CIN continues to rise with the increasing use of contrast agents in clinical practice. Previous studies have reported that the incidence of CIN after percutaneous coronary intervention (PCI) was 15-35%.² Many potential factors increase the risk of CIN, including advanced age, congestive heart failure (CHF), diabetes mellitus (DM), chronic renal insufficiency, and the type and amount of contrast agent.³ Although CIN is a self-

limiting disease, it can prolong hospitalisation, and increase the risk of mortality and economic burden during hospitalisation. Therefore, early identification of high-risk patients with CIN and timely preventive measures are essential for reducing complications in patients post-PCI.

Insulin resistance (IR) is a pathophysiological process of cellular metabolic imbalance, characterised by the reduced efficiency of glucose uptake and utilisation by insulin-sensitive tissues and cells in the body. Studies have supported a profound relation between IR and acute kidney injury (AKI).⁴ The hyperinsulinaemic-euglycaemic clamp test is considered the gold standard method for diagnosing IR, which has the disadvantages of being cumbersome, costly and time-consuming.⁵ Triglyceride glucose index (TyG) is a novel index based on fasting triglyceride (TG) and fasting blood glucose (FBG), and showing a powerful ability to predict IR, with studies indicating that TyG is strongly associated with CIN in patients post-PCI.⁶ In addition, patients with high TyG are more likely to develop CIN.⁷ Although some studies have demonstrated that the TyG is a potential biomarker to predict the adverse outcome of CIN in patients undergoing PCI, but the evidence for TyG's assessment of CIN was not strongly robust because the studies were limited by their

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single-centre design and small sample size.^{6,8} Furthermore, the absence of randomised controlled trials (RCTs) further weakens the validity of such findings. The current study was planned to use the existing data for the evaluation of the accuracy of high TyG in terms of predicting CIN post-PCI.

Materials and Methods

The meta-analysis was conducted in Ningbo in 2024 from May to July and comprised literature search across PubMed, Embase and Web of Science databases for relevant studies published up to May 2024. The review was carried out in accordance with Cochrane Collaboration methods and Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.⁹ The search was performed using the following key words: "(triglyceride-glucose index or TyG) and (contrast-induced nephropathy or CIN or Acute Kidney Injury or AKI)". The studies were screened by two reviewers independently to identify the eligible publications, and any disagreement was resolved with mutual discussion.

To be included, the studies had to satisfy the following criteria: patients were precisely diagnosed CIN after PCI or arteriography; provided the number of patients positive with CIN in different TyG stages; and designed as a cohort control project. Exclusion criteria entailed the following elements: review articles, case reports, comments, cell and animal research; lack of correlation information for calculating odds ratio (OR). In studies having identical or overlapping data, only the largest patient cohort was selected for analysis to avoid duplicate information.

Crude data was collected from the selected studies by two researchers independently, including the name of the first author, the year of publication, country, age, the sample size, cut-off value, with or without DM, the number of patients with CIN in different TyG categories, and multivariate OR values of TyG. In the event of missing data, communication was initiated with the primary corresponding author via email in order to acquire adequate information.

Quality assessment of the eligible studies for meta-analysis was done using the Newcastle-Ottawa scale (NOS).¹⁰ The NOS scores ranged 0-9, and studies with score ≥ 6 were considered to have high-quality methodology.

Data was analysed using Stata 17 OR and 95% confidence intervals (CIs) were used to estimate the association between TyG and CIN in patients who underwent PCI. The statistical significance of OR was calculated by Z test, and $p < 0.05$ indicated significance. Heterogeneity across the studies was assessed using Cochran's Q and I². In case of

$p > 0.05$, a fix-effect model was applied. Otherwise a random-effect model was used. Subgroup analysis and meta-regression were conducted to explore potential sources of heterogeneity. Publication bias was inspected using Begg's rank correlation test and Egger's regression test.¹¹ To evaluate the robustness of the summary estimates and to identify potential sources of heterogeneity, a sensitivity analysis was conducted by systematically eliminating the included studies one by one from the pooled analysis. This Meta-Analysis was prospectively registered with INPLASY with the registration number of INPLASY202460115.

Results

Of the 212 studies identified initially, 6(2.8%) were included (Figure 1)^{6-8,12} comprising 4,521 individuals; 2,996(66.3%) men and 1,525(33.7%) women (Table 1).

The pooled OR was 2.32 (95%CI: 1.58-3.40, $p < 0.05$) for predicting CIN, as assessed by the random effect model with heterogeneity ($I^2 = 79.9\%$) (Figure 2). Multivariate regression analysis revealed a significant association between TyG and an increased risk of CIN (OR=2.36, 95%CI: 1.74-3.21, $p = 0.012$) (Table 2, Figure 3).

There was significant heterogeneity in terms of country, study design, participants, DM comorbidity, sample size, and cut-off < 9 (Figure 4). The heterogeneity of meta-regression analysis was noted (Supplementary Figure 1).

Quality assessment suggested 5(83.3%) of the studies had high quality (Table 1).

Publication bias was assessed using a funnel plot. There

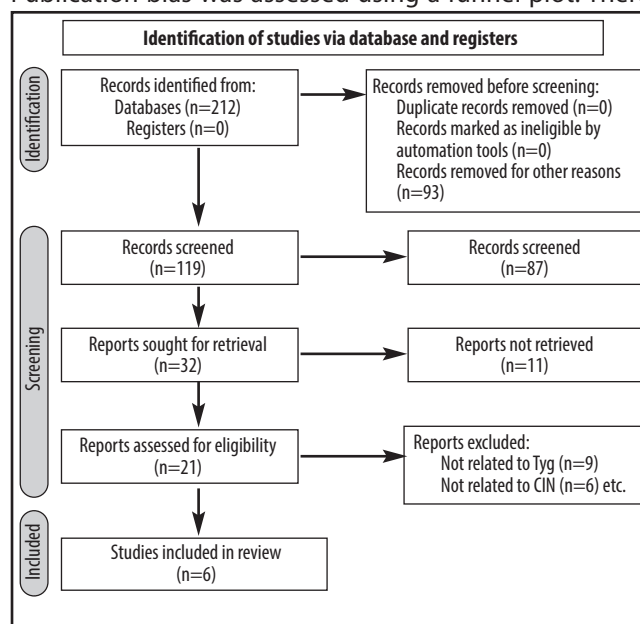
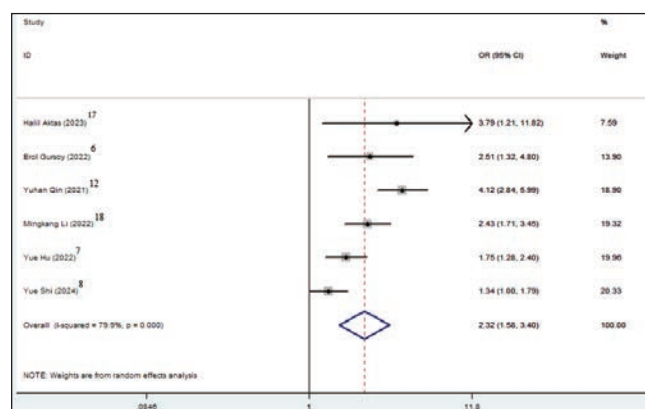


Figure-1: Search flowchart for meta-analysis.

Table-1: Characteristics of the included studies (n=6).

	Author	Year	Nation	Study Design	Participants(n)	Age(years)	M
1	Halil Aktas ¹⁷	2023	Turkey	prospective study	272	60.47±12.25	216
2	Erol Gursoy ⁶	2022	Turkey	retrospective study	350	-	183
3	Yuhan Qin ¹²	2021	China	retrospective study	928	68.32± 8.95	658
4	Mingkang Li ¹⁸	2022	China	retrospective study	1108	66.4 ± 10.4	692
5	Yue Hu ⁷	2022	China	retrospective study	1073	-	680
6	Yue Shi ⁸	2024	China	retrospective study	790	67.65	567
	n1	n2	m1	m2	DM	cut-off	NOS
	14	4	122	132	NO	8.87	8
	42	14	160	134	NO	8.65	7
	155	42	309	345	YES	9.04	7
	113	53	440	502	NO	8.85	7
	141	72	454	406	YES	8.98	7
	136	102	394	396	YES	9.15	7

DM: Diabetes mellitus, NOS: Newcastle-Ottawa scale.

**Figure-2:** Forest plots of odds ratio (OR) for the relation between triglyceride glucose index (TyG) and contrast-induced nephropathy (CIN) in patients receiving percutaneous coronary intervention (PCI).**Table-2:** Multivariate regression odds ratio (OR) for contrast-induced nephropathy (CIN) incidence.

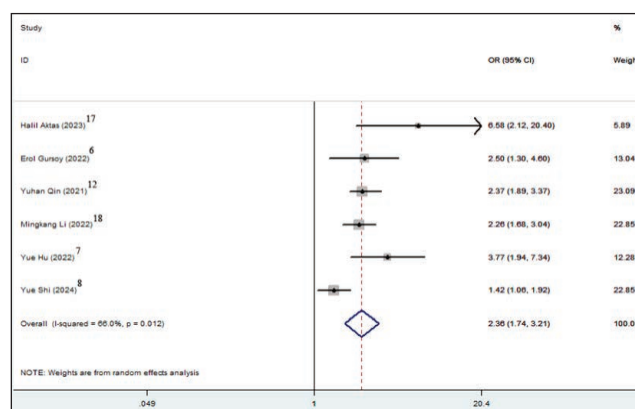
Author	OR	95%CI
1 Halil Aktas ¹⁷	6.583	2.12-20.40
2 Erol Gursoy ⁶	2.5	1.30-4.60
3 Yuhan Qin ¹²	2.37	1.89-3.67
4 Mingkang Li ¹⁸	2.26	1.68-3.04
5 Yue Hu ⁷	3.77	1.94-7.34
6 Yue Shi ⁸	1.42	1.06-1.92

CI: Confidence interval.

was no significant publication bias in the meta-analysis (Figure 5). Sensitivity analysis evaluated the reliability of the studies analysed, and showed that the pooled OR of TyG was not significantly affected by omitting any single study (Figure 6).

Discussion

The growing popularity of endovascular interventional therapy has led to increased CIN awareness, as it can have severe consequences. IR is considered a risk factor for CIN

**Figure-3:** Multivariate regression analysis regarding the correlation between triglyceride glucose index (TyG) and contrast-induced nephropathy (CIN) in patients receiving percutaneous coronary intervention (PCI).

and has an impact on its incidence. The TyG index, which serves as a biomarker for IR, plays a significant role in predicting the occurrence of CIN.¹² The current meta-analysis, to our knowledge, is the first to establish a correlation between TyG and CIN, and provides evidence for the predictive value of elevated TyG levels in CIN post-PCI.

The occurrence of CIN is a frequently encountered complication, and numerous biomarkers have demonstrated their efficacy in the prediction of CIN. A meta-analysis conducted by Tong et al. demonstrated that neutrophil gelatinase-associated lipocalin (NGAL) was a reliable marker for predicting CIN. The analysis revealed that NGAL had a higher diagnostic accuracy in urine compared to blood.¹³ Another meta-analysis suggested that cystatin C and NGAL could be used as predictors of CIN, with cystatin C showing a higher diagnostic value than NGAL.¹⁴ Additionally, cystatin C levels are less influenced by factors, such as muscle mass, age, gender, or nutritional status, compared to blood creatinine levels. Therefore, they

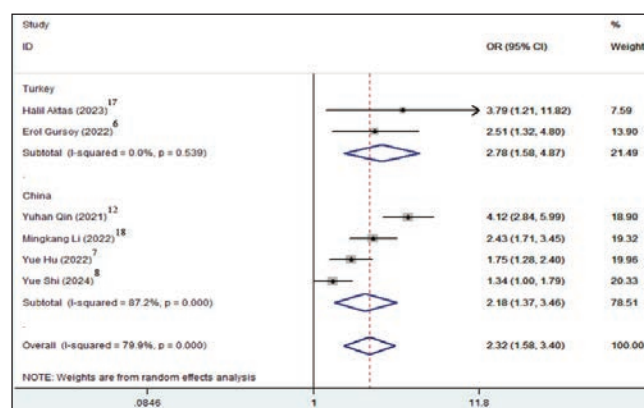


Figure 4A:

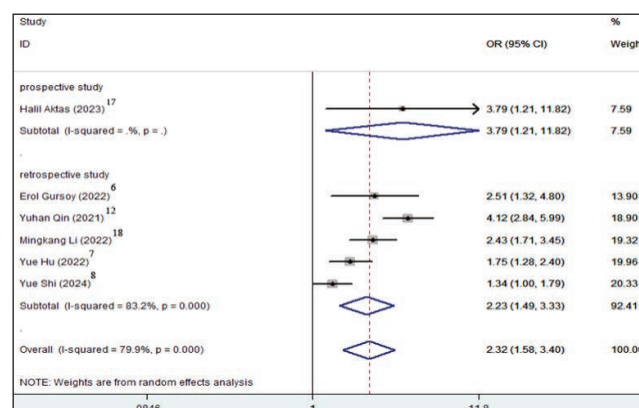


Figure 4B:

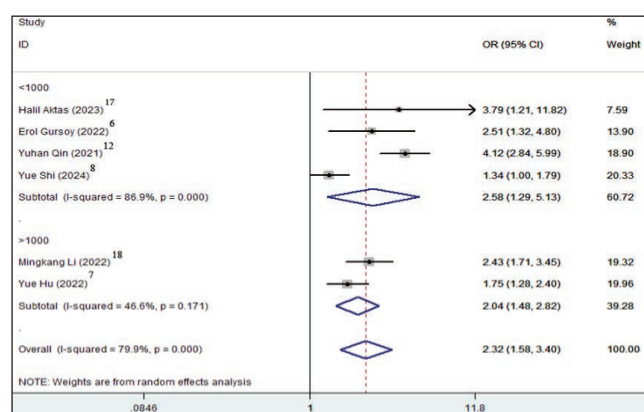


Figure 4C:

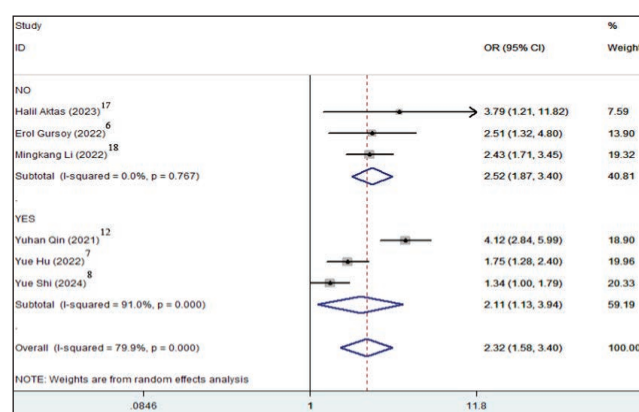


Figure 4D:

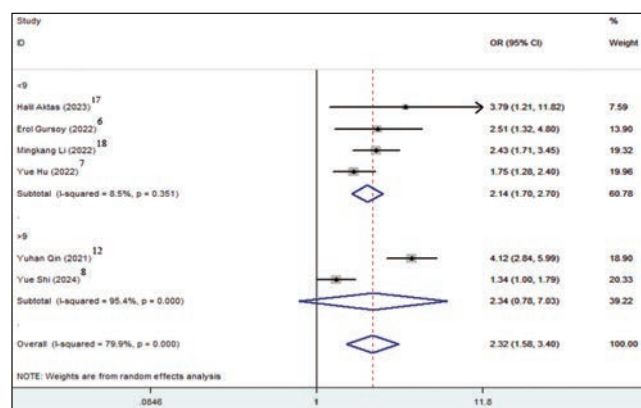
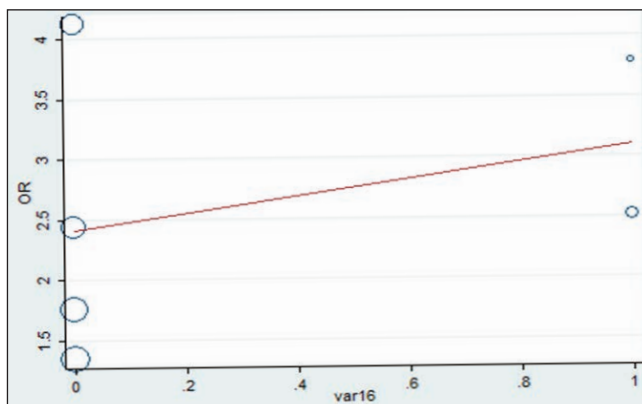


Figure 4E:

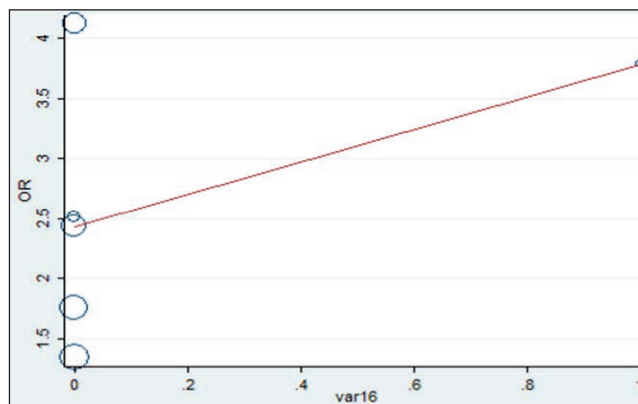
Figure 4: Subgroup analyses regarding heterogeneity between triglyceride glucose index (TyG) and contrast-induced nephropathy (CIN) in the studies subjected to meta-analysis. A: Country; B: Study type; C: Sample size; D: Diabetes comorbidity; E: Cut-off value

provide a more reliable prediction of kidney function deterioration. It has been suggested that the elevation of cystatin C can serve as an early biomarker for CIN following exposure to contrast media, and it can be utilised as an independent predictor of CIN.¹⁵ Furthermore, in patients with heart failure and reduced left ventricular ejection

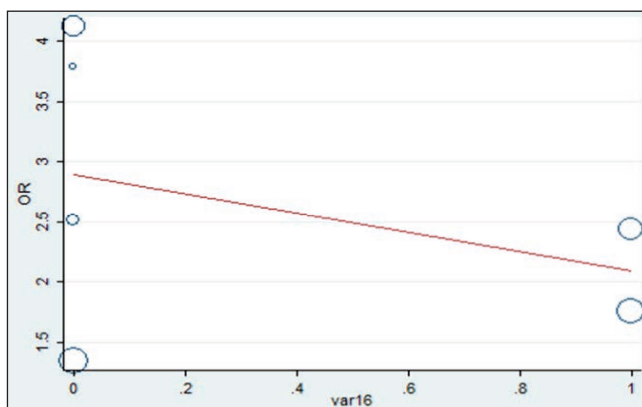
fraction (LVEF), elevated levels of neutrophil-to-lymphocyte ratio (NLR) have been found to be associated with the progression of renal dysfunction. NLR serves as a predictive marker for the deterioration of kidney function in DM patients.¹⁶ Although numerous studies have been conducted on the early prediction of CIN, a majority of



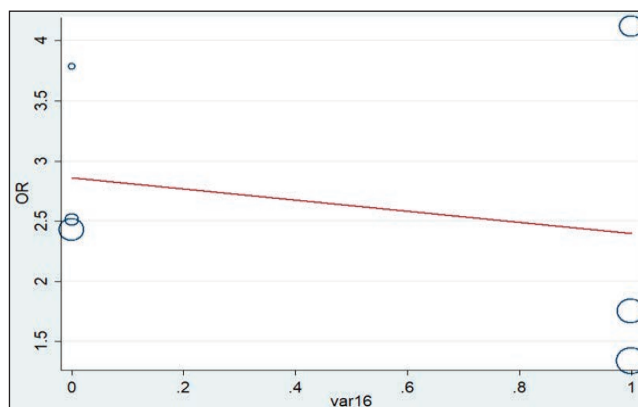
Supplement Figure-1A:



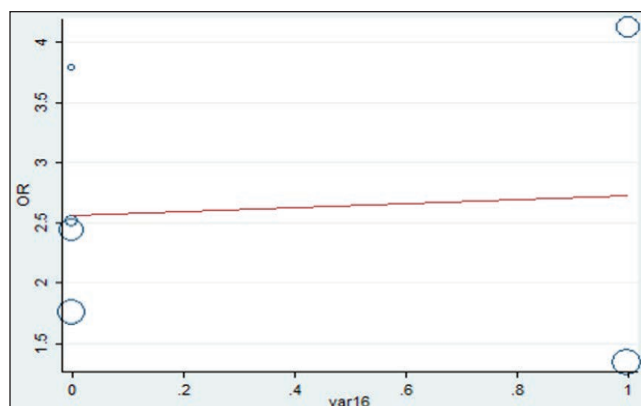
Supplement Figure-1B:



Supplement Figure-1C:



Supplement Figure-1D:



Supplement Figure-1E:

Supplement Figure-1: Meta regression analysis the heterogeneity between TyG and CIN in eligible articles.

A: Country; B: Study type; C: Sample size; D: Diabetes comorbidity; E: Cut-off value.

them were single-centre clinical and retrospective studies, which remain controversial and necessitate further evaluation to discover novel indicators or improve the value of existing indicators for early CIN prediction.^{17,18}

As a novel index for predicting CIN, TyG demonstrates clinical value. Halil Aktas et al. found that high TyG

increased CIN risk after PCI in non-diabetic patients with non-ST segment elevation.¹⁷ Similarly, Yuhan Qin et al. investigated the role of TyG in predicting CIN in patients with type 2 DM undergoing PCI. Their findings indicated that high TyG levels were an independent risk factor for predicting CIN, and played a significant role in predicting acute renal function injury.¹² Li et al. investigated the use

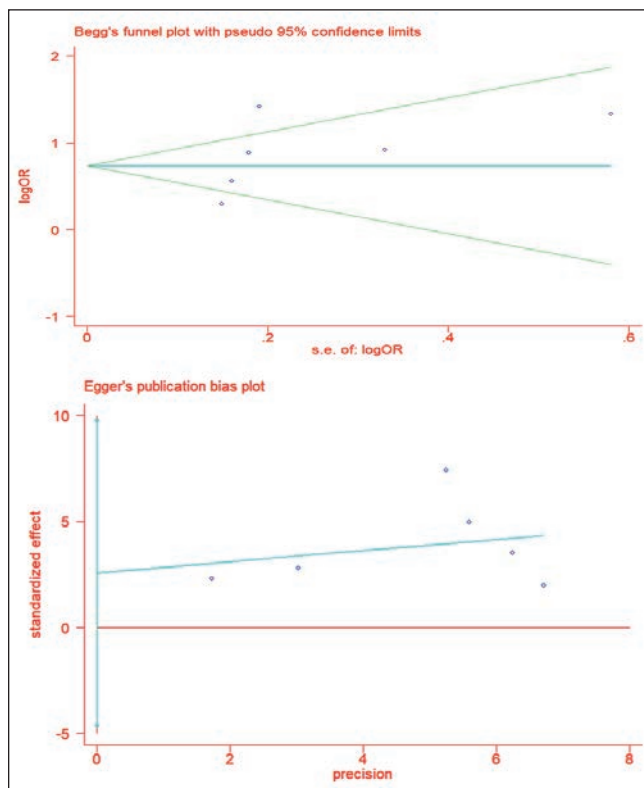


Figure-5: Begg's and Egger's funnel plot for publication bias of OR in eligible articles.

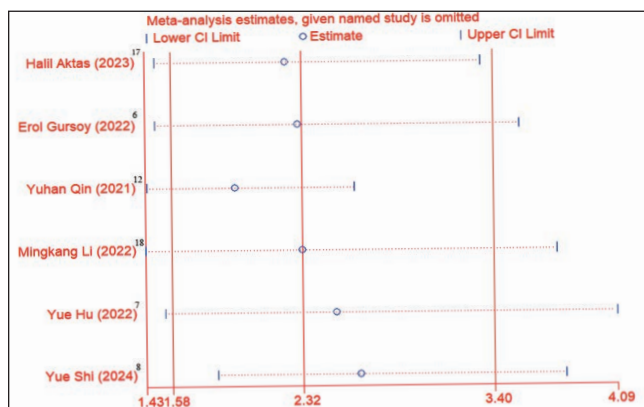


Figure-6: Sensitivity analysis of the association between TyG and CIN. of drug-eluting stents in non-ST-segment elevation patients with acute coronary syndrome.¹⁸ They discovered a significant association between high TyG levels and CIN. Furthermore, they observed that elevated TyG levels increased the risk of CIN. Despite the development of diagnosis and treatment technology, serum creatinine (SCr) level is still the reference standard test for clinical diagnosis of CIN. Therefore, there is an urgent need for simple, accessible and inexpensive detection indicators to predict CIN.

DM is an established independent risk factor for CIN and has a strong association with CIN. The incidence of CIN is

2% in patients without diabetes and normal renal function, and 16% in patients with DM and normal renal function.¹⁹ Patients with diabetic nephropathy are more susceptible to CIN due to changes in glomerular filtration rate (GFR), renal haemodynamics, and increased production of reactive oxygen species (ROS).²⁰ The main features of DM include insufficient insulin secretion and IR, which are implicated in the dysregulated processes of metabolic and cardiovascular diseases.²¹ In multivariate regression analysis, the current meta-analysis found that TyG increased the risk of CIN in patients post-PCI ($p=0.012$) after adjusting for confounding factors, including DM, hypertension, heart failure and so on. The current study showed that TyG still had a high predictive value after adjusting for DM.

The pathophysiological mechanism of CIN has not been fully elucidated. Numerous clinical and experimental studies have confirmed the association between renal medullary ischaemia, hypoxia, direct toxicity of contrast agent, oxidative stress, and inflammatory response with the onset and progression of CIN.²² Evidence has shown that IR elevates the risk of renal impairment in vascular disease.²³ IR affects the prevalence of CIN related to various mechanisms. Firstly, there is renal medullary ischaemia. In the state of IR, the activation of nitric oxide synthase is reduced through the PI3K pathway, resulting in decreased renal blood flow and subsequently decreased renal function.²⁴ Upon the administration of contrast agents, renal vasoconstriction occurs, leading to the redistribution of blood flow from the renal medulla to the renal cortex. This exacerbates renal ischaemia and hypoxia.²⁵ Secondly, oxidative stress plays a role. IR induces mitochondrial deoxyribonucleic acid (DNA) gene mutation in various tissue cells, such as skeletal muscle, liver and fat, causing mitochondrial dysfunction and oxidative stress in the body. This leads to an increase in the generation of ROS, which can directly damage mitochondrial DNA, the mitochondrial cell membrane and macromolecular substances within the mitochondria, ultimately resulting in mitochondrial dysfunction.²⁶ Additionally, ROS can activate pathways, such as NF- κ B and JNK, further aggravating IR.

There was moderate heterogeneity in the current meta-analysis, which is related to differences in study design criteria. In order to find the source of heterogeneity, subgroup analysis was conducted. Firstly, the sample sizes of the study groups varied, with 4 articles having a sample size of less than 1,000 and 2 articles having a sample size of more than 1,000. This discrepancy in sample size introduced selection bias, which can limit the rationality and accuracy of predictions. Secondly, different cut-off values for TyG influenced the diagnosis of CIN. The

fluctuation of TyG values was found to be influenced by individual factors, regional factors, and complications. Establishing a stable cut-off interval is crucial for improving the diagnosis. Heterogeneity was also observed with respect to country, DM status, and study type. Multicentre RCTs with large sample sizes are recommended to validate the predictive value of TyG for CIN.

The current meta-analysis has some limitations. First, all the incorporated studies were retrospective and observational in approach. Second, there was no uniform criterion for defining the cut-off value, which may have influenced the findings. Third, despite adjusting for potential covariates, the confounding factor of accompanying DM could have rendered the result less valid. Finally, some key factors of CIN, such as dose and type of contrast agent and preoperative hydration, were not taken into account in the analysis.

Conclusion

TyG could serve as an underlying predictive marker of CIN in patients undergoing PCI.

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Conflict of Interest: None.

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Author Contribution:

SG, JY & HW: Concept, design, data acquisition, analysis, interpretation, drafting, revision, final approval and agreement to be accountable for all aspects of the work.