



C-reactive protein to albumin ratio as a predictor of contrast-induced nephropathy; a systematic review and meta-analysis

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ABSTRACT

Introduction: The C-reactive protein-to-albumin ratio (CAR) is a marker of inflammation that has been found to be more informative in assessing inflammation conditions in cardiovascular patients than the C-reactive protein (CRP) or albumin (ALB) levels only. Since inflammation has been identified as a factor causing contrast-induced nephropathy (CIN), this research seeks to establish the correlation between the CAR and the risk of CIN.

Materials and Methods: This systematic review and meta-analysis was conducted according to the PRISMA protocol. The Cochrane, PubMed, ProQuest, and Web of Science databases, as well as the Google Scholar search engine, were searched with no time limit up to August 8, 2024. Data were analyzed using STATA 14 software at a significance level of $P < 0.05$ for all tests.

Results: The findings of five reviewed studies with a total number of 1,442 participants showed a statistically significant positive correlation between CAR (OR: 2.11, 95% CI: 1.41, 3.14) and CRP (OR: 1.11, 95% CI: 1.02, 1.20), with an increase in the risk of CIN. However, no statistically significant associations were found between the patient age (OR: 1.02, 95% CI: 0.96, 1.09), albumin level (OR: 0.64, 95% CI: 0.14, 2.90), hypertension (OR: 2.12, 95% CI: 0.86, 5.21), and diabetes mellitus (OR: 0.80, 95% CI: 0.28, 2.29) variables and the risk of CIN.

Conclusion: Elevated CAR and CRP are CIN risk factors that can be evaluated to provide a good prognosis of this condition. Nevertheless, albumin levels were not significantly related to the development of CIN.

Registration: This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO (ID: CRD42024580053) and Research Registry (UIN: reviewregistry1874) websites.

Implication for health policy/practice/research/medical education:

In this meta-analysis we found that C-reactive protein-to-albumin ratio (CAR) and C-reactive protein (CRP) are proteins that raise contrast-induced nephropathy (CIN risk), therefore, their value can be conducted to diagnose the condition. However, the correlation between the albumin levels and the incidence of CIN was not statistically significant. Consequently, increased levels of CAR and consequently can be regarded as significant risk factors for contrast-induced acute kidney injury prediction in patients with type 2 diabetes. Specifically, CAR levels are elevated in patients with contrast-induced acute kidney injury than in those with CRP only, suggesting that CAR is a serious risk factor for CIN.

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Introduction

Contrast-induced nephropathy (CIN) is defined as an increase of more than 0.5 mg/dL in serum creatinine levels within 48 hours after administering an intravascular

contrast agent or a 25% or greater increase compared to baseline serum creatinine levels (1,2). The incidence of CIN can vary from approximately 0% to 50% (3,4). Currently, CIN accounts for about 11% of acute kidney

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injuries, ranking second after drug-induced and ischemic acute kidney injury (AKI) (5, 6). Risk factors for CIN include kidney failure, diabetes, advanced age, type and dose of contrast agent, and accompanying cardiovascular diseases (7,8). Several pathophysiological factors have been proposed for the development of CIN. However, the reason for the variability in CIN development among patients with similar risk factors or those exposed to equal amounts of contrast agents remains unclear (9,10).

Inflammation is known to affect the development of CIN (11). High-sensitivity C-reactive protein (hs-CRP) measures systemic inflammation and has been linked to postoperative AKI in high-risk patients (12-15). Indeed, hs-CRP can potentially be a diagnostic and therapeutic marker for CIN prediction and management (15). On the other hand, low albumin levels may be associated with the development of CIN (16). A recently introduced marker of inflammation, the CRP/ALB ratio (CAR), has been proven to be better than CRP and albumin levels in identifying inflammation conditions in cardiovascular diseases (17-19). The CAR, which has been recently proposed as a new parameter of inflammation, provides a more accurate prognosis for individuals with various inflammatory diseases, including cardiovascular diseases, sepsis, ulcerative colitis, cancer, acute pancreatitis, and hepatitis B (17,20,21).

Contrast-induced acute kidney injury is associated with prolonged hospital stays, increased complications, and mortality (22-24), and this topic has so far been reviewed in no meta-analysis study. Therefore, the present study aimed to consider the association amongst the CAR and the risk of CIN using a systematic review and meta-analysis approach.

Materials and Methods

Study design

This systematic review and meta-analysis were designed and conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (25). The study protocol was registered on the PROSPERO (International Prospective Register of Systematic Reviews) website.

Search strategy

The Google Scholar search engine and the Cochrane, PubMed, ProQuest, and Web of Science databases were searched by two authors until August 8, 2024, with no time limit. Keywords used in the search included Medical Subject Headings (MeSH) terms and their equivalents, namely Contrast-Induced Nephropathy, C-reactive protein, High Sensitivity C-reactive protein, hsCRP, Albumins, Albumin, and CAR. In the advanced search stage, the keywords were combined using the “AND” and “OR” Operators. A manual search was also performed by reviewing the references of the primary studies (See [Supplementary file 1](#)).

PICO components

- Population: Studies evaluating the association between CAR and the risk of CIN.
- Intervention/Exposure: Increased CAR.
- Comparison: Individuals who did not develop CIN.
- Outcomes: The primary outcome was the odds ratio of the association between CAR and the risk of CIN. Secondary outcomes included the odds ratios of the associations between CRP, diabetes, hypertension, albumin, and age with the risk of CIN.

Inclusion and exclusion criteria

Observational studies evaluating the association between CAR and the risk of CIN were included in the current meta-analysis. Duplicate studies, conference abstracts, non-observational studies, those of low qualitative quality, studies without full-text access, and studies lacking sufficient data for analysis were excluded from this study.

Quality assessment

Two authors assessed the quality of the studies using the Newcastle-Ottawa Scale (NOS), consisting of nine questions with a total score ranging from 0 to 10, indicating the lowest and highest quality, respectively. The cut-off point for this tool was a score of 6, and high-quality studies were scored 6 or higher (26).

Data extraction

The following data, namely author name, sample size, study type, year, country, age, study duration, type of disease, and the odds ratios of the associations between CAR, CRP, diabetes, hypertension, albumin, and age with the risk of CIN, along with the upper and lower limits of each, were extracted from the selected studies by two authors. The extracted data were then entered into SPSS version 19.

Statistical analysis

The log OR (odds ratio) was used for each study. The studies were then combined for data analysis. The I^2 index was used to assess heterogeneity. A random-effects model was employed due to significant heterogeneity ($I^2 = 87.6\%$). Additional analyses were conducted using meta-regression and sensitivity analysis. Data were analyzed using STATA 14 software at a significance level of $P < 0.05$ for all tests.

Results

In the mentioned databases, 652 articles were extracted after the search. Among the titles, 319 duplicate articles were excluded from the analysis. The abstracts were screened for 333 included articles, 49 of which were excluded due to the unavailability of full texts or incomplete abstract data. Then, 93 out of 284 full-text articles were excluded due to insufficient data for the analysis. In the next stage, 186 out of 191 screened articles

were excluded for the other exclusion criteria. Finally, five articles of good quality were selected for the systematic review and meta-analysis (Figure 1).

Although the present study did not limit the search by geographical locations, all the published studies reviewed in the present study were conducted in Turkey. Out of the five analyzed investigations, two and three studies were cross-sectional and cohort research, respectively. In total, 1,442 patients were investigated in these studies, and the average participants' ages ranged from 51 to 70 years (Table 1).

As shown in Figure 2, CAR (OR: 2.11, 95% CI: 1.41, 3.14) was positively associated with CIN, with an odds ratio of 1.19, indicating the increased risk of CIN with the increase of CAR.

The elevated levels of CRP were accompanied by a significantly increased risk of CIN (OR: 1.11, 95% CI: 1.02, 1.20). However, the analysis of the correlation between the risk of CIN and the patients' ages (OR: 1.02, 95% CI: 0.96, 1.09), albumin level (OR: 0.64, 95% CI: 0.14, 2.90), hypertension (OR: 2.12, 95% CI: 0.86, 5.21), and diabetes mellitus (OR: 0.80, 95% CI: 0.28, 2.29) did not reveal statistically significant differences (Table 2).

In the meta-regression analysis, no statistically significant relationships were detected among "CAR and

CIN risk" and factors such as sample size ($P = 0.583$) and year of publication ($P = 0.378$) (Figures 3 and 4).

The results of the current research were most influenced by the studies of Altıparmak et al (31) and Satılmış et al (27), as revealed by the sensitivity analysis (Figure 5).

Discussion

The findings of this meta-analysis with 1,442 participants reveal that high levels of CAR and CRP are associated with increased CIN risk. Nevertheless, no noteworthy association was detected between albumin levels and the rates of CIN. Furthermore, no significant associations were established amongst age, hypertension, diabetes mellitus, and CIN.

In an attempt to determine the effectiveness of the CAR in the prognosis of CIN development in emergency department patients, Temel et al established that high CAR was a risk factor for increased CIN risk (OR: 2.32, 95% CI: 1.39, 3.89) (30). In a cross-sectional investigation, Satılmış et al assessed the correlation amongst the CAR and the development of CIN in individuals with non-ST-elevating myocardial infarction. The results of logistic regression analysis showed that the increase in CAR was associated with the increased risk of CIN (OR: 1.24, 95% CI: 1.10-1.39) (27). In a retrospective study, Kelesoglu et

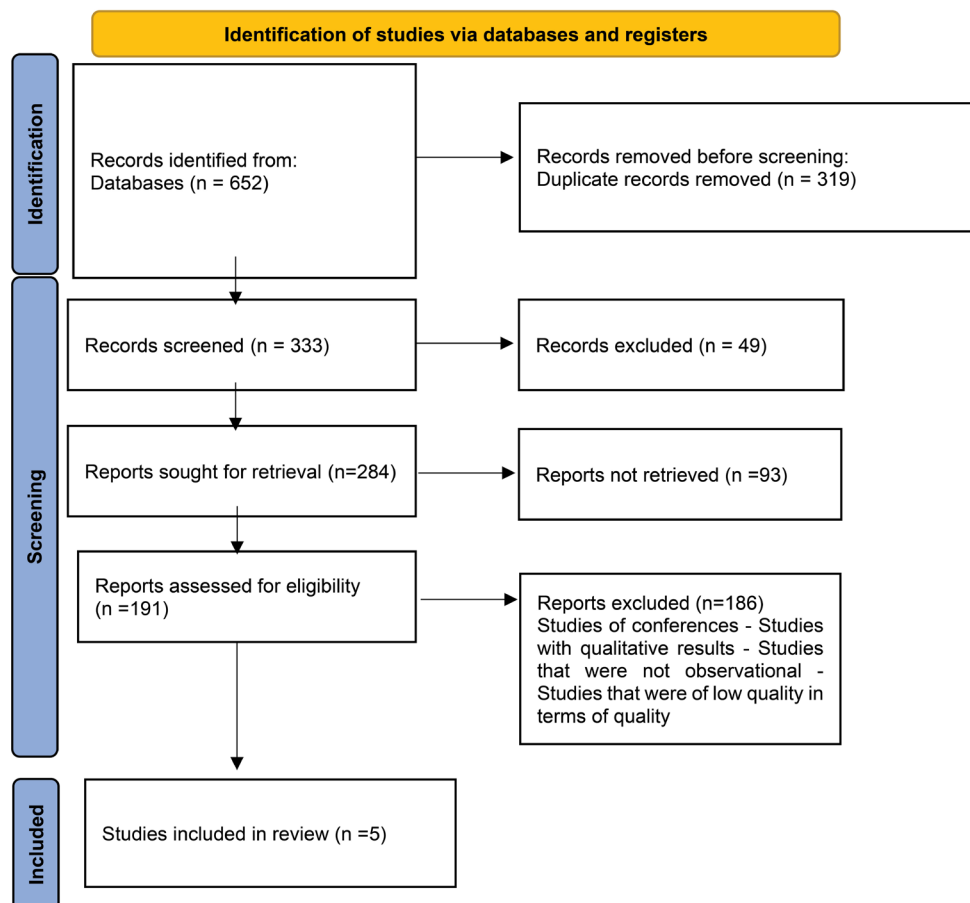


Figure 1. The PRISMA flowchart of study selection.

Table 1. Part of the information of the reviewed studies

Name, year	Type of study	Sample size	Age (year)	Sample size in CIN group	Age in CIN group	Sample size in comparison group	Age in comparison group	Duration of study	Patients	CRP/Albumin	CAR	Low limit	Up limit
Satilmis S, 2020 (27)	Cross-sectional	205	61.3	21	64.4	184	61	Between Aug 1, 2015, and Aug 21, 2018	Non-ST-elevation myocardial infarction	8.54	1.24	1.11	1.39
Yasar E, 2022 (28)	Cohort	148	NR	26	67.6	122	70.4	From Oct 2020 through Sep 2021	Acute stroke	0.52	2.84	1.81	4.47
Kelesoglu S, 2024 (29)	Cohort	410	NR	69	65	341	51	Between Jan 2016 and Mar 2022	Carotid artery stenosis	2.4	1.77	1.36	2.29
Temel TZ, 2023 (30)	Cohort	125	65.96	112	65.74	13	67.85	Between Jan 1, 2018 and Jan 1, 2021	Emergency Department Patients	0.02	2.32	1.39	3.89
Altıparmak IH, 2023 (31)	Cross-sectional	554	NR	87	59	467	56	Between Jul 2020 and Jan 2022	Stable angina pectoris	0.04	3.71	2.13	6.46

NR: Not reported; CRP: C-reactive protein; CAR: CRP/Albumin.

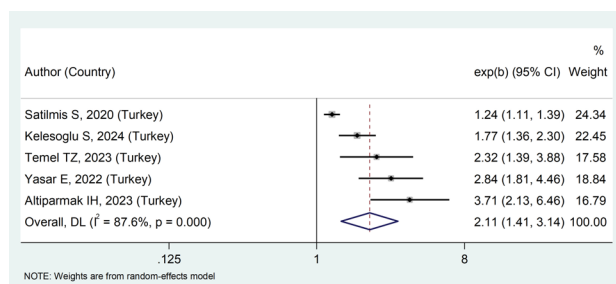
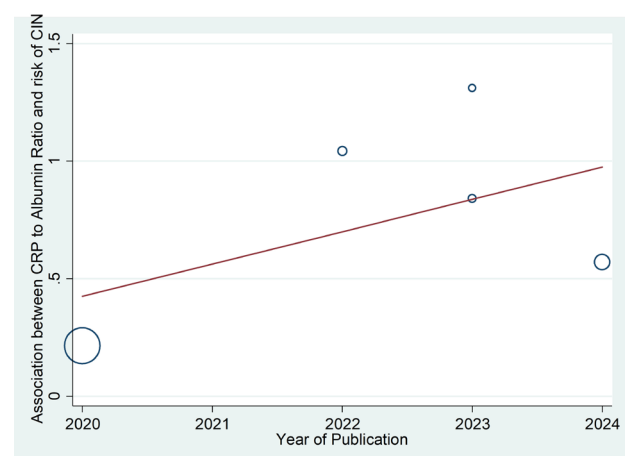
Table 2. Association between secondary outcomes and risk of contrast-induced nephropathy

Variables	OR	Low limit	Up limit	I ² (%)	P value
CRP	1.11	1.02	1.20	53.6	0.142
Age	1.02	0.96	1.09	91.9	<0.001
Albumin	0.64	0.14	2.90	0	-
Hypertension	2.12	0.86	5.21	51.2	0.152
Diabetes mellitus	0.80	0.28	2.29	68.2	0.043

al investigated the relationship between the CAR/ and the development of CIN after carotid angiography. The authors found higher neutrophil-to-lymphocyte ratios (OR: 1.098, 95% CI: 1.051, 1.148), higher hs-CRP (OR: 1.166, 95% CI: 1.094, 1.243), and higher CAR (OR: 1.786, 95% CI: 1.415, 2.254) in patients with CIN than in those without CIN (29). The results of these studies are similar to the current study, confirming that increased levels of CAR can act as a risk factor and a prognosis factor for the progression of CIN. It might be possible to prevent CIN and decrease the burden of the disease by evaluating and regulating CAR levels.

Aksoy et al sought to evaluate the relationship between

the CAR and new-onset atrial fibrillation (AFib) after coronary artery bypass grafting (CABG). They found that CAR was a risk factor for AFib after CABG (OR: 1.82, 95% CI: 1.53, 2.16) (32). In a prospective cohort study with 62,067 participants, Yang et al assessed the relationship between the Hs-CAR - and cardiovascular disease risk. The authors found that high CAR levels could enhance the risk

**Figure 2.** Forest plot of the relationship between CAR and the risk of contrast-induced nephropathy, with its 95% confidence interval.**Figure 3.** Meta-regression plot of the association among CAR and the risk of contrast-induced nephropathy with the year of publication of the studies.

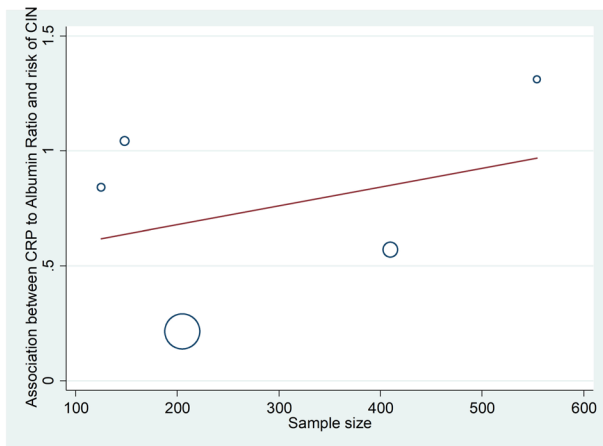


Figure 4. Meta-regression plot of the relationship between CAR and the risk of contrast-induced nephropathy with the sample size.

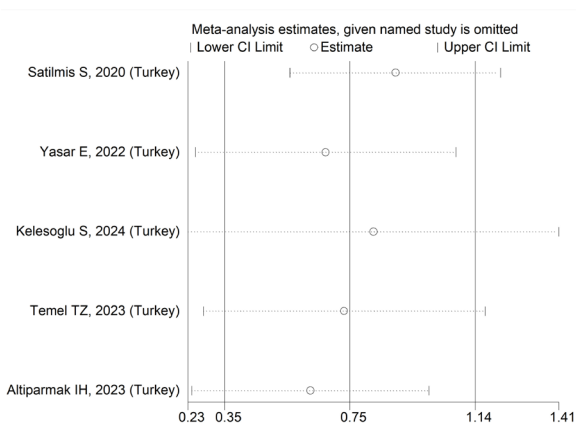


Figure 5. Plot of sensitivity analysis.

of cardiovascular diseases and the prognosis performance of CAR for cardiovascular diseases (HR: 1.26, 95% CI: 1.15, 1.38) was better than hs-CRP or albumin alone (33). These studies indicate that CAR is not only a prognosis for CIN development but also a risk factor predictor for other diseases, including cardiovascular diseases and AFib. Hence, the measurement of CAR levels is an important determinant for the prognosis and management of diseases such as CIN, which will lower hospital expenses caused by such diseases. Similar to the findings of Yang et al, the present study demonstrated that CAR had better predictive accuracy than CRP or albumin alone because no relationship was detected between albumin levels and CIN incidence.

In a previous meta-analysis, Wu et al evidenced that a high pretreatment CAR was significantly linked to lower overall survival (HR: 2.21, 95% CI: 1.86, 2.62) and progression-free survival (HR: 1.85, 95% CI: 1.36, 2.52) in patients with urological cancers (34). In a meta-analysis, Utsumi et al reported that the preoperative CAR/was inversely associated with overall survival (HR: 2.44, 95% CI: 1.98, 2.90) and recurrence-free survival (HR: 2.73, 95% CI: 2.01, 3.70) in patients with biliary tract cancers (35). In

a recent meta-analysis by Xu et al, high pretreatment CAR was significantly higher in patients with malignancies, which was a predictor of poor overall survival (HR: 1.99, 95% CI: 1.65, 2.40) (36). In their meta-analysis designed to assess the ability of CAR as a predictor of renal cell carcinoma outcomes, Zhou et al concluded that high pre-treatment CAR was inversely correlated with overall survival (HR: 2.14, 95% CI: 1.64, 2.79) and progression-free survival (HR: 1.75, 95% CI: 1.31, 2.35) (37). Similar to the present study, the reviewed meta-analysis studies support our conclusions, suggesting that high CAR levels are a risk factor for cancer patients' survival, decreasing their lifespan.

Conclusion

CAR and CRP are proteins that raise CIN risk, hence, their value can be expended to diagnose the condition. However, the correlation between the albumin levels and the incidence of CIN was not statistically significant. Therefore, increased levels of CAR and CRP can be regarded as significant risk factors for contrast-induced acute kidney injury prediction in patients with type 2 diabetes. Specifically, CAR levels are elevated in patients with CIN than in those with CRP only, suggesting that CAR is a serious risk factor for CIN.

Limitations of the study

A limitation of this study was that all the published studies were conducted in Turkey, although no geographical constraints were used during the search process. Additionally, the number of female and male participants was not reported in the reviewed studies; hence, the relationship between the CAR and CIN risk was not assessed separately for male and female patients. Because the present analysis was based on a few studies, the authors were not able to carry out a subgroup analysis.

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Ethical issues

This study has been compiled based on the PRISMA checklist, and its protocol was registered on the PROSPERO website (ID: [CRD42024580053](#)) and Research Registry website with (Unique Identifying Number (UIN) [reviewregistry1874](#)). Besides, ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

Authors' contribution

Conceptualization: Sam Mirfendereski, Ali Hasanpour Dehkordi.

Data curation: Sam Mirfendereski, Mahdiah Ahmadnia.

Formal analysis: All authors.

Investigation: All authors.

Methodology: Mahdiah Ahmadnia.

Resources: Mahdiah Ahmadnia

Supervision: All authors.

Validation: All authors.

Visualization: All authors.

Writing—original draft: All authors.

Writing—review & editing: Sam Mirfendereski, Ali Hasanpour Dehkordi.

Conflicts of interest

The authors declare that they have no competing interests.

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None.

Supplementary files

Supplementary file 1 contains search strategy in databases.

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