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REVIEW

The Potential of Prognostic Biomarkers of Uric Acid Levels in Coronary Heart Disease Among Aged Population: A Scoping Systematic Review of the Latest Cohort Evidence

Sidik Maulana [1], Aan Nuraeni[2], Bambang Aditya Nugraha[3]

[1]Faculty of Nursing, Universitas Padjadjaran, Bandung, Indonesia; [2]Department of Critical Care and Emergency Nursing, Faculty of Nursing, Universitas Padjadjaran, Bandung, Indonesia; [3]Department of Medical-Surgical Nursing, Faculty of Nursing, Universitas Padjadjaran, Bandung, Indonesia

Correspondence: Aan Nuraeni, Department of Critical Care and Emergency, Faculty of Nursing, Universitas Padjadjaran, Sumedang, Indonesia, Tel + 6285624217606, Fax +022-7795596, Email aan.nuraeni@unpad.ac.id

Background: This study sought to determine whether uric acid levels have a relationship with and can potentially be used as a prognosis for coronary heart disease (CHD) biomarkers using a scoping review.

Methods: This study was conducted following Arksey and O'Malley's scoping review framework. It was reported as obeying the Preferred Reporting Item for Systematic Review and Meta-analysis for Scoping Review (PRISMA-ScR). The subject was extensively searched for in PubMed, CINAHL, and ScienceDirect. The inclusion criteria in the study were that the sources were journal articles written in English and were available in full text. The age of the subject in the item is the elderly population to capture the relationship between uric acid levels and the prognosis of CHD. The publication time limit was 2010 to 2020. The study was analyzed using thematic analysis.

Results: We identified 592 studies in our initial search, and 21 studies with a cohort design were included in this study's analysis. The majority of the evidence suggests an independent correlation with a poor prognosis of CHD in the elderly population. The prognosis of gout includes the prognosis of clinical outcome, severity, and mortality, all of which influence the prognosis value, which becomes a marker.

Conclusion: Uric acid levels have been identified as a potential biomarker for poor CHD prognosis. Nurses and other healthcare workers should learn how to control poor CHD prognosis.

Keywords: biomarker, coronary heart disease, prognosis, uric acid

Introduction

Uric acid's potential role is a two-edged sword; it is a determinant of the antioxidant system or a parameter of metabolic syndrome.[1] Uric acid is a potent antioxidant in bodily fluids. On the one hand, it depletes approximately more than 70% of plasma's total antioxidant capacity, protecting against CHD,[2–4] while, on the other, because it is one of the metabolic syndrome parameters, it positively correlates with CHD.[1]

Recent pathophysiological studies have provided evidence that elevated uric acid levels (hyperuricemia) contribute to a poor coronary heart disease (CHD) prognosis. It is not clear how uric acid is correlated with CHD, but several studies suggest that elevated uric acid, also known as hyperuricemia, increases CHD risk by inducing endothelial dysfunction, oxidative stress, and interconnected inflammatory mechanisms.[5,6] The clinical manifestations of CHD contribute to increased circulating uric acid levels in the arterial tissue, including coronary arteries.[7] Impaired tissue reperfusion due to CHD activates circulating xanthine oxidase enzymes in the endothelium, leading to an increase in uric acid levels and, as a result, endothelial dysfunction.[7] Thus, circulating uric acid as a result of reperfusion disorders has the potential to be a new biomarker in determining the prognosis of CHD.

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Several epidemiological studies have found a correlation between uric acid levels and coronary heart disease.[8–10] These findings support the model's improvement in predicting CHD prognosis by taking uric acid levels into account. Recent meta-analysis studies on uric acid levels and CHD continue to provide a review of the relationship between uric acid levels and the risk of CHD morbidity and mortality.[11–13] There are, however, no reviews that lead to the determination of clinical considerations related to uric acid as a biomarker to determine the prognosis of CHD, nor are there any that lead to the coverage of the elderly population. The study has a high priority in determining the considerations in establishing uric acid levels a biomarker of CHD prognosis, given the rising trend of the global elderly population. This study has implications for the nursing care process for the elderly with CHD by increasing uric acid levels, focusing on secondary prevention, and reducing the burden of patient care.

Furthermore, the condition of rising uric acid in the community affects a sizable number of people worldwide.[14] The prevalence of gout increases with age, and the factor of decreased estrogen in the elderly affects the decrease in renal uric acid excretion and urate transporter 1 (URAT1); thus, serum uric acid levels rise.[15] Furthermore, decreased kidney function due to degenerative processes raises serum uric acid levels, as a result of which the elderly with decreased metabolic function are more likely to increase uric acid.

Given the above conditions, this study update adds to the body of evidence regarding uric acid levels as a biomarker in predicting CHD prognosis in the elderly population. It is hoped that this review study can provide an evidence base for prognostication aids to help nurses and other health professionals offer effective secondary prevention in CHD patients. Therefore, the study aimed to summarize and explore the potential of the prognostic biomarker of the uric acid level in coronary heart disease among the elderly population. This review provides a theoretical basis for poor prognosis prevention.

Methods
Study Design
This study was conducted following Arksey and O'Malley's scoping review framework,[16] which allows for the inclusion of extensive study designs to offer a full outline of the research topic. It was reported as obeying the Preferred Reporting Item for Systematic Review and Meta-analysis for Scoping Review (PRISMA-ScR).[17] The scoping review methodology is suited for this subject because it allows for a thorough study of the relationship between CHD and poor prognostics among the elderly population. The review began with a broad research subject, restricted during the study process to allow a more thorough evaluation of the relationship between outcomes.[18] The initial research question guided the initial search procedure and the study's primary outcome is to look into the relationship between uric acid levels and CHD prognosis, while the secondary outcome is to find the prognostic value that causes poor CHD prognosis. The objective of the present scoping review is to evaluate the latest cohort evidence on the potential of prognostic biomarkers of uric acid in CHD among the aged population. Therefore, the search was limited to the last ten years, 2010–2020.

Search Strategy
Three databases were used for the literature search: PubMed, CINAHL, and Science Direct. A literature search was conducted using keywords: coronary heart disease, uric acid, and prognosis.

Eligibility Criteria
The PICOS framework was used to determine the study strategy. Furthermore, full-text articles with a publication time limit of 2010 to 2020 had to be available in English.

P (Population): CHD patients
I (Interest): uric acid levels as a biomarker of CHD prognosis
C (Comparison): no comparison
O (Outcomes): the relationship or influence of interest on the prognosis of CHD
Study design: a cohort study

Data Collection and Analysis

Three reviewers carried out the study selection process, and the included studies followed the PRISMA flow chart: (1) identifying duplicate articles; (2) screening of titles and abstracts; (3) checking full-text availability; and (4) screening full texts based on the study method and critical assessment criteria.

Data were manually extracted from the study results using Microsoft Excel (tabulation method). The included studies' quality was evaluated using the Joanna Briggs Institute (JBI) critical assessment. Three authors used the JBI critical assessment checklist for cohort studies to assess and report the risk of bias. Thematic descriptive analysis was used for each outcome analysis.

Results

Description of Study Findings

In the initial search results, 592 studies were found in the electronic databases. The authors screened 33 full-text articles and excluded ten studies with a cross-sectional design and two cohort studies that did not meet the critical appraisal cut-off. As a result, the authors included 21 cohort studies in this scoping review study.[20–40] Figure 1 depicts the number of studies retrieved using the PRISMA flow chart diagram.

Study Characteristics

The authors identified a cohort study on the mean of the elderly population. They used a prospective and retrospective cohort design to examine the relationship between uric acid and CHD prognosis. Turkey (n= 3), Singapore (n= 1), Israel (n= 1), Taiwan (n= 4), Germany (n= 2), Ukraine (n= 1), USA (n= 1), China (n= 1), Japan (n= 2), South Africa (n= 1), Denmark (n= 1), Spain (n= 1), France (n= 1), and Korea (n= 1) were the countries studied (See Table 1). The study included 82,727 CHD patients in various stages, including Acute Coronary Syndrome (ACS), stable angina, asymptomatic angina, ST-Elevation Myocardial Infarction (STEMI), and Acute Myocardial Infarction (AMI). They all underwent angiography and PCI procedures for both diagnosis and treatment due to stenosis and recurrent PCI due to restenosis. The study's follow-up period ranged between 1.2 and 8.1 years (see Table 2).
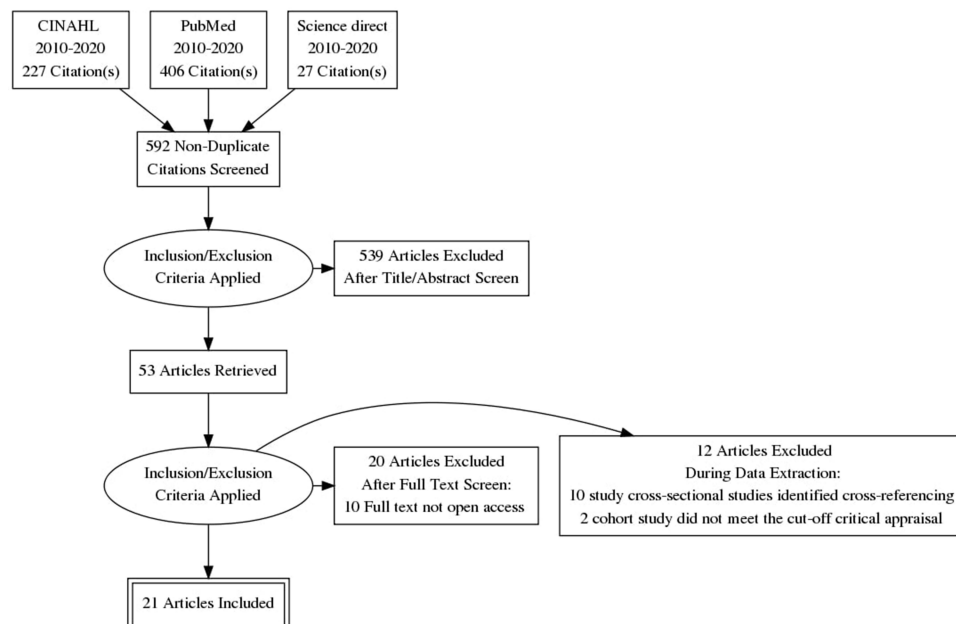

Figure 1 PRISMA flow diagram.
Note: Adapted from Liberati A, Altman D, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. Journal of Clinical Epidemiology. 2009;62(10)e1–e34[19]

Table 1 Characteristics of Study

Study	Country	Age (Mean)	Participant	Follow-Up (Years)	Critical Appraisal
(Sinan Deveci et al., 2010)[40]	Turkey	59.4 ± 10.24	1012 patients with symptoms of CAD	N/I	7/11
(Duran et al., 2012)[30]	Turkey	59 ± 12	520 patients with ACS	N/I	6/11
(Teng et al., 2012)[32]	Singapura	45 ± 74	52.322 CHD patients	8.1	10/11
(Eisen et al., 2013)[34]	Israel	45-74	3122 stable CAD	8	11/11
(Lin et al., 2013)[26]	Taiwan	Male (M)= 64.8 Female (F)= 66.9	1054 Angiographic confirmed CAD patients with >50% stenosis	3.1	11/11
(Ndrepepa et al., 2013)[22]	Germany	M= mean: 65.6-67.1 F= mean: 69.8-74.3	13.273 CAD patients	N/I	7/11
(Li et al., 2013)[21]	Taiwan	BMI> 25 group 64.0 ± 10.3 (SUA< 6.6) 64.5 ± 10.9 (SUA≥ 6.6) MI< 25 group 66.5 ± 10.5 (SUA< 6.6) 67.6 ± 10.7 (SUA≥ 6.6)	1,202 Angiography-confirmed CAD patients	5.4	9/11
(Berezin & Kremzer, 2013)[33]	Ukraine	58.34 ± 9.60	126 asymptomatic CAD patients	N/I	6/11
(Calvo et al., 2014)[38]	USA	White: 64.6 Filipino: 59.3	202 white women and 166 postmenopausal Filipino women (N= 368)	4.6	10/11
(Yu et al., 2014)[31]	China	Low: 61.8 ± 11.6 Moderate: 64.6 ± 10.2 High: 64.6 ± 10.2	347 patients	1.10	9/11
(Liu et al., 2014)[25]	Taiwan	Gout group: 61.08 ± 13.69 Control group: 60.72 ± 12.90	444 patients with STEMI	49 ± 28 month	8/11
(Baumann et al., 2016)[20]	Germany	62.5 ± 13.4	803 STEMI patients undergoing primary PCI	N/I	8/11
(Ando et al., 2016)[23]	Japan	69.1 ± 10.9	385 patients undergoing PCI	N/I	8/11
(Kawabe et al., 2016)[36]	Japan	M= 64.5 ± 11.7 F= 72.1 ± 10.6	1380 patients with ACS	1.2 (437 days)	8/11
(Ranjith et al., 2017)[35]	South Africa	51.7 ± 11.5	2683 patients with AMI	N/I	7/11

(*Continued*)

Table 1 (Continued).

Study	Country	Age (Mean)	Participant	Follow-Up (Years)	Critical Appraisal
(Larsen et al., 2018)[29]	Denmark	59.4	1039 patients with suspected or definite AMI		9/11
(Liu et al., 2017)[24]	Taiwan	57	951 STEMI patients undergoing PCI	N/I	6/11
(Lopez-Pineda et al., 2018)[28]	Spain	68 ± 13	1119 patients with ACS	3	10/11
(Gaubert et al., 2018)[37]	France	67.8 ± 9.4	80 patients with first episode of non-ST segment ACS	N/I	7/11
(Joo et al., 2018)[27]	Korea	Normal uric acid = 64.6 ± 9.9 High uric acid = 65.3 ± 10.3	317 restenotice patients undergoing repeated PCI	1088 days (3)	10/11
(Karabağ et al., 2019)[39]	Turkey	62.2 ± 10.96	331 patients with stable angina pectoris	505 ± 13 days	10/11

Risk of Bias

According to the risk of bias assessment, the overall quality of the 23 cohort studies had low risk of bias. Figure 2 shows that several studies had a high risk of bias reporting follow-up studies (11 studies/47.8%).

The Correlation Between Uric Acid Levels and CHD Prognosis

This study found various evidence of the causality of uric acid and CHD prognosis, with the identified prognostic components including clinical outcome, severity, and mortality. A clinical outcome refers to the incidence (first or new diagnosis), prevalence, and recurrence.[41] Severity is defined as an outcome that refers to the degree of obstruction as measured by various clinical vessel score indice, while mortality is defined as the number of deaths recorded in the death record or during the study's follow-up period. The findings yielded a three-component thematic model explaining the role of uric acid levels in a poor prognosis: clinical outcome, severity, and mortality. The review found that each component of the thematic model of uric acid levels as a prognostic biomarker of CHD was interrelated in the poor prognosis of coronary heart patients. The review's findings show that clinical outcomes and severity impact each other, and both have an impact on the risk of CHD death (see Table 1).

Theme 1: Clinical Outcome Prognosis

The primary studies have found a correlation between uric acid levels and clinical outcome prognosis. Measurement of CCV, calcification; plaque components, endothelial dysfunction with Reactive Hyperemia (RH), the severity of atherosclerosis, MAE (non-fatal myocardial infarction and revascularization), and MACE were identified as studies that provided evidence of a significant clinical outcome relationship (heart failure, AF, complete heart block, cardiogenic shock, ventricular arrhythmias, infarction recurrence and angina, and cerebrovascular events).[33] Meanwhile, two studies concluded that they had a significant effect on the prognosis of CHD clinical outcomes. MACE and CAC severity were identified as clinical outcomes with no significant relationship.[19]

There are several modalities for determining the clinical outcome prognosis of CHD, including angiography, CT, echocardiogram, ECG, cardiac enzyme biochemistry, non-invasive peripheral arterial tonometry (PAT), endo PAT, and Integrated Backscatter Intravascular Ultrasound (IB-IVUS). Each modality was only used to assess a subset of clinical outcomes (see Table 2).

Table 2 Summary of Finding

Study	Measurement	Measurement Methods	Findings
(Sinan Deveci et al., 2010)[40]	The severity with clinical vessel score indicator	Angiography	Uric acid has a significant relationship with severity prognosis (p< 0.001). Improved severity prognosis associated with increased uric acid based on quartile increase in uric acid, p=0.015
(Duran et al., 2012)[30]	Coronary Collateral Vessel (CCV) with Rentrop classification	Angiography	The presence of CCV was associated with lower serum uric acid levels (p<0.001) CCV development was associated with lower uric acid levels (p= 0.003)
(Teng et al., 2012)[32]	Mortality	International Classification of Diseases (ICD)-10	Patients with gout have a higher risk of mortality from CHD than non-gout (HR 1.38, 95 CI 1.10-1.73)
(Eisen et al., 2013)[34]	Heart failure	New York Heart Association (NYHA) Classification	Uric acid levels are associated with heart failure with HR adjusted for age (HR 1.16; 95% CI 0.94-1.45) and (HR 1,28; 95% CI 1.04-1.59) in tertiles 2 and 3. Meanwhile, HR adjusted for several confounders (HR 1.18; 95% CI 0.95-1.47) dan (HR 1.25 95% CI 1.00-1.56) in tertile 2 and 3.
(Lin et al., 2013)[26]	Mortality	Death certificate	Elevated uric acid causes a 2.08-fold independent mortality risk mortality (HR 2.08; 95% CI 1.19-3.65; p= 0.01) viewed from the highest quartile.
(Ndrepepa et al., 2013)[22]	1-year mortality	Hospital records and death certificates	Uric acid is an independent predictor of 1-year mortality (HR 1.17; 95% CI 1.03-1.31; p= 0.012; male) dan (HR 1.25; 95% CI 1.06-1.48; p=0.007; Female)
(Li et al., 2013)[21]	Mortality	The death certificate and database	Independently, higher uric acid levels cause higher mortality in obese CHD patients (HR 1.79; 95% CI 1.14-2.82; P= 0.023), but obesity is not a predictor (HR 0.91; 95% CI 0.62-1.32)
(Berezin & Kremzer, 2013)[33]	Calcification with Agatston score index	Contrast-enhanced spiral Computed Tomography (CT) angiography	The uric acid level is an independent predictor of CHD (HR 1.12; 95% CI 1.01-1.52; p< 0.001)
(Calvo et al., 2014)[38]	Severity and progression Coronary Artery Calcium (CAC) with Agatston index score	Electron Beam Computed Tomography (EBCT)	Uric acid levels independently caused CAC severity in the Filipino group (OR 1.34; 95% CI 1.05-1.71) and not for the white group (OR 0.94; 95% CI 0.71-1.25) Uric acid levels independently led to CAC development in both groups (OR 1.26; 95% CI 1.02 – 1.56).

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Table 2 (Continued).

Study	Measurement	Measurement Methods	Findings
(Yu et al., 2014)[31]	Severity, Major Advance Cardiac Events (MACE), Mortality	Angiography and SYNergy between PCI with TAXUSTM and Cardiac Surgery (SYNTAX) score	Uric acid levels were independently correlated with high SYNTAX scores (B= 0.33, 95% CI 0.023-0.042, p<0.001). Comparison with normal uric acid levels, high uric acid levels tend to increase SYNTAX scores (p<0.0001) Uric acid levels are positively correlated with MACE (p<0.001) Kaplan-Meier analysis showed that event-free survival was higher in the high uric acid group (p< 0.001)
(Liu et al., 2014)[25]	Adverse non-fatal cardiac event (Unstable angina, symptomatic arrhythmias, repeated revascularization, recurrent infarction, rehospitalization due to heart failure)	Electrocardiography (ECG), cardiac enzyme checks, hospital documentation	Gout is independently associated with short and long term adverse non-fatal cardiac events (HR 1,88, 95% CI 1.09-3.24, p= 0.024; HR 1.82. 95% CI)
(Baumann et al., 2016)[20]	Major Adverse Cardiac Events (MACE)	Coronary angiography, echocardiography	Uric acid was not a significant predictor of MACE (AUC: 0.59; 95% CI 0.51-0.65; p= 0.83)
(Ando et al., 2016)[23]	Coronary plaque components	Integrated Backscatter Intravascular Ultrasound (IB-IVUS)	Uric acid levels were correlated with the percentage of lipid volume (r= 0.371, p < 0.001) and inversely with fiber volume (r = -0.347, p < 0.001). Uric acid levels were independently correlated with lipid-rich plaque (OR 2.43; 95% CI 1.75-3.47).
(Kawabe et al., 2016)[36]	Major Adverse Cardiac Events (MACE): mortality, heart failure, infarction, and stroke	Computed Tomography (CT)/ Magnetic Resinance Imaging (MRI)	Uric acid level was an independent predictor of MACE in women (HR 2.84; 95% CI 1.19-6.77; p= 0.018), but not significant in men (HR 1.32; 95% CI 0.66-2.64; p= 0.422)
(Ranjith et al., 2017)[35]	Major Adverse Cardiac Events (MACE): heart failure, mortality, AF, complete heart block, cardiogenic shock, ventricular arrhythmias, recurrence of infarction and angina, and cerebrovascular events	N/I	Hyperuricemia significantly and independently caused mortality risk (OR 1.7; 95% CI 1.0-2.8; p= 0.042) High above-normal uric acid levels in tertiles correlated with a significant increase in MACE (p<0.001), especially for heart failure (p<0.001) and mortality (p=0.006).
Larsen et al., 2018)[29]	Severity of CAC	Non-contrast CT Scan	There is no relationship between uric acid and CAC severity.
(Liu et al., 2017)[24]	Death on Killip class	Records of patients who come to the ED	In Killip class I, hyperuricemia was associated with mortality at one year (HR 5.176; 95% CI 1.488-18007; p= 0.01) and for 30 days (HR 11.204; 95% CI 1.123-111.8; p= 0.047), but had no association. on Killip class II-IV

(*Continued*)

Table 2 (Continued).

Study	Measurement	Measurement Methods	Findings
(Lopez-Pineda et al., 2018)[28]	Mid-term and long-term clinical outcomes and results after addition to the GRACE score	Cardiology notes, echocardiography	Independently, hyperuricemia was associated with cardiovascular death (HR 1.91; 95% CI 1.32-2.28; p < 0.01), all disease mortality (HR 1.59; 95% CI 1.18-2.15; p < 0.01), major cardiovascular events (HR 1.36; 95% CI 1.11-1.67; p<0.01). Addition of hyperuricemia to GRACE increased the risk of 38% of the total participants.
(Gaubert et al., 2018)[37]	Endothelial dysfunction with reactive hyperemia (RH) and severity of atherosclerosis	Non-invasive peripheral arterial tonometry (PAT) and angiography	The uric acid level had a significant relationship with Reactive Hyperemia Index/RHI (β= -0.17, p<0.001), and the uric acid level was associated with the Gensini score and SYNTAX score (p<0.001)
(Joo et al., 2018)[27]	Major adverse event (MAE): the cause of all mortality, non-fatal myocardial infarction, and revascularization.	Angiography	Uric acid was not an independent predictor of MAE (HR 1.110; 95% CI 0.980-1.257; p= 0.100)
(Karabağ et al., 2019)[39]	SYNTAX score II (SII) and long-term mortality	Angiography	Uric acid and SYNTAX independent predictors of long-term mortality (HR 1.24, 95% CI 1.046-1.482, p= 0.014; HR 1.042, 95% CI 1.007-1.079, p= 0.018)

Theme 2: Severity Prognosis

According to the study findings, there was a significant relationship between uric acid levels and prognosis severity.[31,40] There were differences found in the indicators and modalities used to assess prognosis when using the clinical vessel score indicator, measured with angiography, and angiography with the SYNTAX score index.[31,40]

Theme 3: Mortality Prognosis

This study found evidence that uric acid levels were independently associated with the prognosis of CHD mortality. The hazard ratio of uric acid causing death is between 1.110 and 5.176 times.[21,22,24,26,28,31,32,35,36,39] Several studies, however, call the evidence for a correlation into question, claiming that there is no significant relationship between uric acid levels
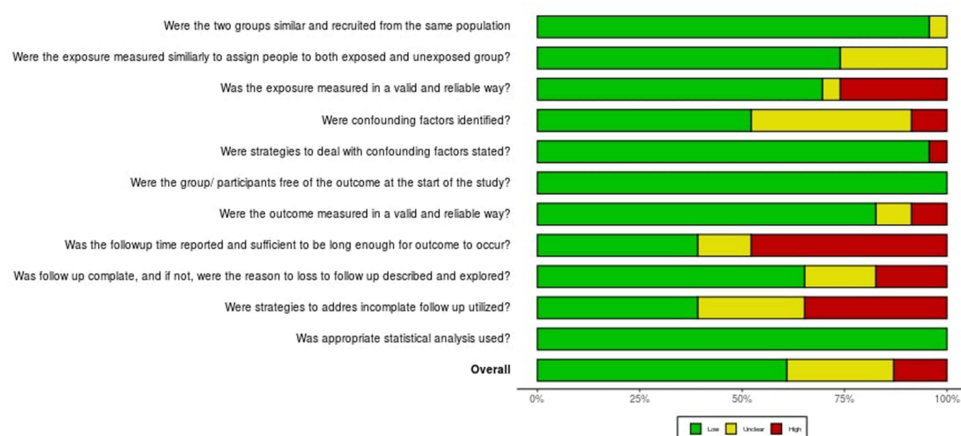

Figure 2 Risk of bias.

Table 3 Cut off Uric Acid as a Predictor of Poor Prognosis

Study	Type of Prognosis	Value	Sensitivity	specificity
(Sinan Deveci et al., 2010)[40] (Duran et al., 2012)[30]	Clinical vessel score CCV	6.86 mg/dl 5.8 mg/dl	- -	- -
(Ndrepepa et al., 2013)[22]	Mortality	Male= 6.8 mg/dl female= 6.2 mg/dl	Male= 59% Female= 61%	Male= 59% female= 62%
(Berezin & Kremzer, 2013)[33]	Arterial calcification	35.9 mmol/dl	80.0%	59.2%
(Karabağ et al., 2019)[39]	SYNTAX score II (SSII)	>4.45	82%	35%

and CHD mortality prognosis.[19,27] Hospital records or death certificates are used to determine a person's mortality prognosis.

Value of Prognosis

The secondary aim of this scoping review is to identify the prognostic value that causes poor CHD prognosis. In each study, the prognostic value ranged from 4.45 to 6.86 mg/dL (see Table 3). According to the area under the ROC curve taken from the study by Ndrepepa et al (2013), the predictive accuracy of uric acid in causing death for one year was 0.625; 95% CI 0.594–0.656, p< 0.001.[22] The uric acid levels that predicted mortality were 6.2 mg/dl (61% sensitivity; 62% specificity) in women and 6.8 mg/dl in men (sensitivity 59%; specificity 59%).

According to Berezin and Kremzer (2013), the accuracy of uric acid leading to the clinical prognosis of calcifications was 35.9 mmol/L with a sensitivity of 80.0% and a specificity of 59.2% based on ROC analysis.[33] The uric acid value associated with an increase in the SYNTAX score, according to Karabağ et al (2019), was >4.45 with an 82% sensitivity and a 35% specificity (ROC 0.604; 95% CI 0.538–0.670; p= 0.001).[39]

Discussion

This study is the first scoping review related to identifying the correlation between uric acid levels and the prognosis of CHD. The review of several cohort studies show that (1) uric acid levels are associated with CHD prognosis in the elderly population, (2) CHD prognosis related to uric acid levels includes clinical outcome, severity, and mortality prognosis, and (3) distinct prognostic values are for clinical outcome prognosis, severity, and mortality.

Previous meta-analyses have identified a correlation between uric acid levels and a variety of CHD outcomes. Previous research by[5] revealed a correlation between uric acid levels and the risk of poor clinical outcomes in the form of coronary artery calcification in the CHD patient population; with every 1 mg/dl uric acid increase, the risk of CAC increased by 31%. Furthermore, the study by[12] found a correlation between uric acid levels and the prognosis of CHD mortality; with every 1 mg/dl uric acid increase, mortality increased by 9%, but the missing adjustment needed for diuretic use and renal functioning was identified as a shortcoming in their meta-analysis. The elderly are more likely to suffer renal function disorders, diabetes, and hypertension than the younger population.

According to Zuo et al's (2016) study subgroup analysis, uric acid increased CHD mortality in women (RR 1.47; 95% CI 1.21–1.73) more than in men (RR 1.47; 95% CI 1.00–1.19). Based on the following two meta-analyses, there is no available synthesis of whether uric acid is associated with prognosis. Although neither meta-analysis explicitly stated the correlation with prognosis, the study shares some similarities with the previous meta-analysis, which looked at the correlation of uric acid levels with one component of poor CHD prognosis from cohort studies. This scoping review provides more comprehensive evidence to reach a descriptive conclusion and includes the relationship between uric acid levels and the prognosis of CHD, including clinical outcome prognosis, severity, and mortality among the elderly population recruited from various studies. The elderly are prone to reduced metabolism, one of which is uric acid metabolism. Thus, according to the final CHD prognosis prediction model, age is a predictor of poor CHD prognosis.[42]

Although the role of uric acid levels in the prognosis of CHD is unclear, several studies have described its mechanism, which may be used as a reference. Firstly, uric acid causes calcification, slowing coronary blood flow.[43,44] Furthermore, increased uric acid causes oxidative stress and LDL cholesterol oxidation, resulting in decreased coronary blood flow.[44] As a result, this mechanism supports the correlation between uric acid levels and clinical prognosis in calcification and CCV. Secondly, uric acid causes endothelial dysfunction, which is a precursor to the development of atherosclerosis.[45] The hardening of urate crystals in the walls of coronary blood vessels can cause an inflammatory response, which directly causes injury to the intima of the coronary vessels and, ultimately, activates platelets and the coagulation system.[12] These mechanisms contradict the notion that uric acid is associated with the clinical prognosis of endothelial dysfunction and atherosclerosis. Finally, increased uric acid levels cause thrombotic activity and the activation of chemotaxis proteins, resulting in a severe prognosis with clinical prognoses such as stroke, heart failure, ventricular fibrillation, and death.[46]

Experimental and other studies indicate that uric acid worsens CHD prognosis via oxidative stress, endothelial dysfunction, and inflammation pathways. With a high enough affinity to interfere with nitric oxide, uric acid can activate xanthine oxidase, causing uric acid synthesis, which, in turn, produces oxygen-free radicals.[7] Uric acid also inhibits endothelial proliferation, interfering with nitric oxide production, which aids in coronary vasodilation. Nitric oxide reduction caused by uric acid results in oxidative stress, which causes endothelial dysfunction and a pathological role in CHD.[47] Furthermore, uric acid deposited in plaque stimulates smooth muscle cell proliferation by producing pro-inflammatory, pro-oxidative, and vasoconstrictive substances that cause endothelial dysfunction and the development of CHD.[46]

Urate-lowering therapy research has become a significant focus in improving cardiovascular treatment outcomes. The use of allopurinol, a xanthine inhibitor, can help to lower uric acid levels. A cohort study (n = 65,971) found that allopurinol was associated with a reduction in MACE, defined as a combination of infarction, stroke, and cardiovascular death.[48] Urate-lowering therapy research has become a major focus in improving cardiovascular treatment outcomes.[49] Although recent studies mentioned that some clinical benefits of urate-lowering medication had been demonstrated in small studies, the efficacy of urate-lowering therapy in large-scale trials has yet to be established.[50] Based on the findings of both studies, it is possible to conclude that pharmacology-based therapy has evolved into a modality that can be used to prevent poor CHD prognosis. At the same time, it remains unknown as to whether uric acid is a risk factor for cardiovascular disease. Furthermore, non-pharmacological efforts can be used as a supplement to improve the prevention of poor CHD prognosis associated with increased uric acid.

Several studies have shown that non-pharmacological therapy can be used to reduce uric acid levels. Non-pharmacological interventions to prevent elevated uric acid levels include a low-purine diet, Mediterranean, and vitamin.[51,52] Furthermore, physical activity is associated with decreased uric acid levels.[53] Although various interventions have been recommended, no studies have been conducted to directly prove non-pharmacological interventions as related to the prevention of poor CHD prognosis. As a result, more research is required so that nurses can contribute to efforts to prevent poor CHD prognosis through various non-pharmacological interventions based on strong evidence.

This review highlights that uric acid levels are independently associated with CHD prognosis in the elderly population. First, nurses and other health professionals must assess their patients to determine whether they have elevated uric acid. If this is the case, then techniques for dealing with it should be investigated; these may help with the self-management of healthy living choices. Therefore, collaboration with clinical members of the multidisciplinary team is beneficial.

There are several limitations to this study. First, our scoping review was limited to cohort studies and used a small number of databases. Second, this study did not assess the correlation value. Additional research in the form of a systematic review with meta-analysis is required to complete the identification carried out in this study; adjustment is needed for the use of diuretics and renal functionality because the elderly may have renal function problems as they have diabetes and hypertension more often than the younger population. Furthermore, the reviewed studies have a fairly high risk of bias in quality assessment components, particularly implicit reporting of confounding factors identified and adjusted for in the study, reporting of measurement tools in assessing exposure and reporting follow-up time.

Conclusion

This study contributes to the growing body of evidence that uric acid levels in the elderly are biomarkers or indicators of poor CHD prognosis. The prognosis of clinical outcomes, severity, and mortality with varying prognostic values is included in the prognosis of associated CHD. Based on the studies that have been carried out, 1) Nurses and other healthcare workers should evaluate uric acid levels as a poor prognosis marker; 2) Based on methodological limitations, this study has not provided a synthesis of evidence in the form of the clinical value of the correlation of uric acid levels with CHD prognosis. Further studies are needed in the form of a systematic review with meta-analysis to synthesize the size of the correlation.

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Disclosure

The authors report no conflicts of interests for this work.

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