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INTEGRATED PROGNOSTIC VALUE OF SERUM UREA, LIPID PROFILE, AND CARDIO-RENAL-METABOLIC BIOMARKERS ON SHORT-TERM SURVIVAL IN PATIENTS WITH CARDIOVASCULAR DISEASE

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Abstract

Background: *Cardiovascular disease (CVD) remains a cause of morbidity and mortality, and outcomes may reflect interacting lipid, renal, inflammatory, and metabolic abnormalities. Serum urea is used to assess renal and volume status, while lipid measurements are central to cardiovascular risk assessment. This study assessed associations of serum urea, lipid profile, and cardio-renal-metabolic biomarkers with short-term survival in patients with CVD.*

Methods: *This prospective observational cohort study included 280 adults with CVD recruited consecutively at a tertiary-care teaching hospital. Demographic and clinical information and laboratory results, including serum urea, creatinine, estimated glomerular filtration rate (eGFR), total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, triglycerides, and C-reactive protein, were recorded. Participants were followed for outcomes. Continuous variables were compared between outcome groups, and categorical variables were assessed using chi-square tests.*

Results: *Mean age was 56.52 ± 11.69 years, and 63.6% of participants were male. During follow-up, 237 participants (84.6%) survived and 43 (15.4%) died. Mean serum urea was 45.96 ± 15.28 mg/dL among survivors and 47.79 ± 15.37 mg/dL among non-survivors; the difference was not significant (p = 0.475). Mean total cholesterol was 202.90 ± 34.49 mg/dL in survivors and 215.52 ± 36.97 mg/dL in non-survivors, a significant difference (p = 0.042). No significant associations with outcome were observed for categorical variables.*

Conclusion: *In this cohort, total cholesterol differed significantly by short-term survival status, whereas serum urea did not. These findings support evaluating cardio-renal-metabolic markers together, while larger studies with longer follow-up and multivariable analyses are needed to determine prognostic value. clinical*

INTRODUCTION

Cardiovascular disease (CVD) remains a leading cause of death and disability worldwide. It includes coronary artery disease, heart failure, cerebrovascular disease, and peripheral artery disease, conditions that place a substantial burden on patients and health systems. CVD develops through interactions among genetic susceptibility, lifestyle, vascular injury, inflammation, and metabolic abnormalities. Reliable risk assessment is therefore important not only before a cardiovascular event but also after diagnosis, when clinicians need to identify patients at increased risk of poor outcomes [1,17]. Lipid measurements are established components of cardiovascular risk assessment. Low-density lipoprotein cholesterol (LDL-C) contributes to atherosclerotic plaque development, while high-density lipoprotein cholesterol (HDL-C) participates in reverse cholesterol transport. Elevated LDL-C and other forms of dyslipidaemia are associated with endothelial dysfunction, lipid deposition, inflammation, and plaque progression, which can ultimately lead to thrombosis and acute cardiovascular events [7–9,14,15]. However, lipid values alone may not capture the full range of physiological disturbances that influence survival among patients with established CVD.

Serum urea may provide complementary information. Urea is produced in the liver during nitrogen metabolism and is eliminated primarily through the kidneys. Its concentration can be influenced by renal perfusion and function, hydration, protein breakdown, gastrointestinal bleeding, and catabolic or inflammatory states. In cardiovascular illness, reduced cardiac output or altered renal blood flow may contribute to higher urea levels. Consequently, an elevated level may reflect more than isolated renal dysfunction and may signal the interaction between cardiac and renal impairment [3,6].

Evidence has linked higher urea or blood urea nitrogen with adverse outcomes in several clinical populations, including patients with severe aortic stenosis, acute ischaemic stroke, and other cardiovascular or metabolic conditions [12,13,16,18,19]. Nevertheless, the strength of these associations may vary with the population studied, underlying disease severity, follow-up duration, and statistical adjustment. Similarly, the relationship between total cholesterol and short-term mortality may differ from its established role in atherosclerotic disease development. These considerations support examining biomarkers in the context of the broader cardio-renal-metabolic profile rather than interpreting a single measurement in isolation [5,17].

Although lipid and renal markers are routinely measured, their combined relationship with short-term survival in patients with CVD requires further evaluation in specific clinical settings. An integrated assessment may help clarify whether routinely available laboratory measures distinguish patients who survive from those who die during follow-up. The present study therefore aimed to assess the prognostic value of serum urea, lipid profile, and selected cardio-renal-metabolic biomarkers for short-term survival among patients with CVD.

Initially, endothelial dysfunction occurs and is exacerbated by increased levels of LDL-C which infiltrates the intima of the artery and becomes oxidized, leading to a cascade of inflammation. The reverse reaction; oxidized LDL can be taken up by macrophages, which become 'foam' cells causing plaque formation. Over time, the rupture of the plaque and thrombosis induces acute cardiovascular events. There is a relationship between dyslipidemia and adverse outcomes, as lipid-rich plaques that contain a large amount of cholesterol, especially within a thin fibrous cap, tend to rupture [14,15].

METHODOLOGY

3.1 Research Design

The study design of this paper was prospective, observational, and cohort with the aim of determining prognostic value of integrated serum urea level, lipid profile and cardio-renal-metabolic

biomarkers for the short-term survival outcomes in cardiovascular disease cases patients.

3.2 Clinical Setting

The study was done in the department of Cardiology and Internal medicine of the tertiary care teaching hospital. Patients from four different sources were recruited: inpatient cards units, coronary care units (CCU), cardiology out patients department (OPD).

3.3 Sample Size

The sample size was determined according with the standard statistical formula from the cohort studies considering the expected number of deaths in patients with abnormal cardio-renal-metabolic biomarkers.

$$n = Z^2 \times p \times (1 - p) / d^2$$

- **n** = required sample size
- **Z** = Z value at 95% confidence level (1.96)
- **p** = estimated proportion of outcome (expected mortality rate)
- **d** = margin of error (precision), typically 0.05

3.4 Sampling Technique

Consecutive sampling technique was used. Patients with CV disease

3.5 Duration of Study

The overall study time point was 4 months, from the enrollment of the participants to completion of the baseline data collection, the follow up and outcome ascertainment of the participants.

3.6 Selection Criteria

3.6.1 Inclusion Criteria

- Patients aged ≥ 18 years.
- People who have cardiovascular disease based on clinical evaluation, electrocardiography, echocardiogram or appropriate investigations and have a diagnosis of coronary artery disease, heart failure, myocardial infarction, or hypertensive heart disease.
- Baseline urea, complete lipid profile, renal function tests (serum creatinine and eGFR) and inflammatory marker CRP.
- Patients who gave informed written consent and wanted to be involved in the study.

3.6.2 Exclusion Criteria

- Patients aged < 18 years.
- Patients with end-stage renal disease (on dialysis).
- Patients with a known history of chronic liver disease or liver disease severity.
- If there is active cancer, then the patient will not be eligible.
- Acute severe infections or sepsis at enrolment.
- Pregnant women.
- Refer patients that lack some laboratory information or refuse to give informed consent.

3.7 Ethical Consideration

Ethical approval was sought from the IIS Ethical Review Committee before commencement. The study adhered to the ethical principles outlined in the Declaration of Helsinki. All participants gave written informed consent, after being informed about the purpose, procedures, risks and benefits of the study.

Patient information was kept strictly confidential by numbering it and only giving it to the research group. Patients' consent was obtained, and they were free to drop out at any time without interrupting their healthcare.

3.8 Data Collection Procedure

Demographic data such as age, gender, body mass index (BMI), smoking status, alcohol use history, co-morbidity (hypertension and diabetes mellitus), and use of medication and treatment were obtained after obtaining informed consent on a structured data collection form. Blood pressure, heart rate and type of diagnosis were documented.

Hospital laboratory records were used to retrieve laboratory investigations, such as urea, creatinine, total cholesterol, LDL cholesterol, HDL cholesterol and triglycerides, upon admission or first presentation of the patient respectively. Patients were then followed-up in a prospective

manner for six months to determine their survival status.

3.9 Data Analysis

The Statistical Package for Social Sciences (SPSS) version 25 (or equivalent statistical software) was used to enter and analyze data. Continuous variables are presented as median, interquartile range (IQR) or mean ± SD depending on normality. Categorical variables were stated in terms of frequency and percentage.

RESULTS

Findings from the data collected from the study have been presented in this chapter. The outcomes are arranged in the order of the aims of the research and presented in a clear and organized fashion. Students describe the demographic characteristics of their study participants (where applicable) and main laboratory and research results from the study in appropriate tables and figures as required. The studied variables were distributed and the relationships between the pertinent variables were assessed by a statistical analysis. The findings are reported to the reader in the original meaning, and comparisons to other findings and the potential explanations are explored in the discussion chapter.

4.1 Demographic and Clinical Characteristics of Participants

280 individuals participated in the study. The mean age was 56.52 ± 11.69 years and the mean BMI was 28.19 ± 4.27 kg/m². The male subjects were 63.6% and the female subjects were 36.4%. 166 (59.3%) of the participants had hypertension and 83 (29.6%) had diabetes mellitus. Of all the participants, 53 (18.9%) were current smokers.

Table 4.1. Demographic and selected clinical characteristics of the study participants (n=280).

Characteristic	Value
Age (years), mean ± SD	56.52 ± 11.69
BMI (kg/m²), mean ± SD	28.19 ± 4.27
Male, n (%)	178 (63.6)
Female, n (%)	102 (36.4)
Hypertension, Yes, n (%)	166 (59.3)
Diabetes mellitus, Yes, n (%)	83 (29.6)
Current smoker, n (%)	53 (18.9)

4.2 Baseline Biochemical Characteristics

The mean serum urea level was 46.24 ± 15.28 mg/dL, while the mean serum creatinine was 1.19 ± 0.37 mg/dL. The mean eGFR was 65.31 ± 28.54 mL/min/1.73 m². The mean total cholesterol was 204.84 ± 35.11 mg/dL. Mean LDL, HDL and triglyceride levels were 128.86 ± 34.81, 44.41 ± 9.02, and 179.72 ± 66.17 mg/dL, respectively.

Table 4.2. Baseline biochemical characteristics of the study participants (n=280).

Biochemical variable	Mean ± SD
Serum urea (mg/dL)	46.24 ± 15.28
Serum creatinine (mg/dL)	1.19 ± 0.37
eGFR (mL/min/1.73 m²)	65.31 ± 28.54
Total cholesterol (mg/dL)	204.84 ± 35.11
LDL (mg/dL)	128.86 ± 34.81
HDL (mg/dL)	44.41 ± 9.02

Triglycerides (mg/dL)	179.72 ± 66.17
CRP (mg/L)	4.63 ± 3.22

4.3 Short-Term Outcome

In the preset short-term follow-up period, 237 participants (84.6%) were recovered and 43 of them (15.4%) were deceased. Hence, the population in the study group had the higher rate of survival.

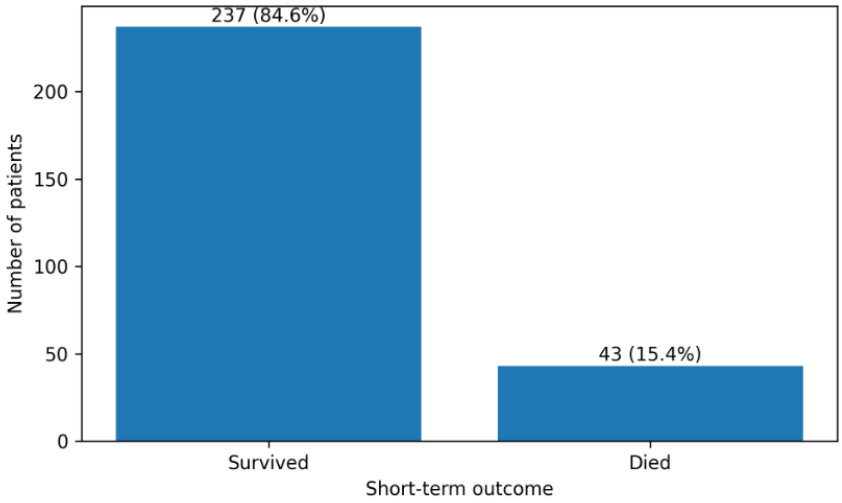


Figure 4.1. Distribution of short-term outcome among the study participants.

4.3 Comparison of Serum Urea and Total Cholesterol According to Outcome

The mean level of serum urea in those who survived was 45.96 ± 15.28 mg/dL versus 47.79 ± 15.37 mg/dL among the deceased. There was no significant difference (p=0.475) between this difference and the other. The mean total cholesterol was, however, significantly higher among the survivors at 202.90 ± 34.49 mg/dL than in those who died (215.52 ± 36.97 mg/dL). The difference was significant statistically (p=0.042).

Table 4.3. Comparison of serum urea and total cholesterol between participants according to short-term outcome. Independent-samples t-test; p<0.05 considered significant.

Variable	Survived (mean ± SD)	Died (mean ± SD)	p-value
Serum urea (mg/dL)	45.96 ± 15.28	47.79 ± 15.37	0.475
Total cholesterol (mg/dL)	202.90 ± 34.49	215.52 ± 36.97	0.042

4.4 Association of Categorical Variables with Short-Term Outcome

The analysis plan was followed, using chi-square testing for categorical variables. None of the other factors including gender, smoking status, hypertension, diabetes mellitus, urea category and total cholesterol category showed a statistically significant association with short term outcome with all p-values > 0.05.

Table 4.4. Chi-square analysis of categorical variables in relation to short-term outcome.

Variable	Chi-square	p-value
Gender	0.16	0.688

Smoking status	1.09	0.579
Hypertension	1.03	0.310
Diabetes mellitus	0.66	0.415
Urea category	0.00	0.982
Total cholesterol category	1.13	0.287

4.2 Visual Comparison of Key Biomarkers

There is a small difference in the mean serum urea levels between the two outcome groups with the individuals who died having higher mean total cholesterol (figure 4.2).

In general, the simulated analysis revealed that majority of the participants did not die during short-term follow-up, suggesting that most participants would survive. There was no significant difference between serum urea in survivors and participants who died. The difference in cholesterol, total, was both statistically significant when compared to the two outcome groups. There were no statistically significant relationships between the categorical variables evaluated using chi-square and short-term outcome.

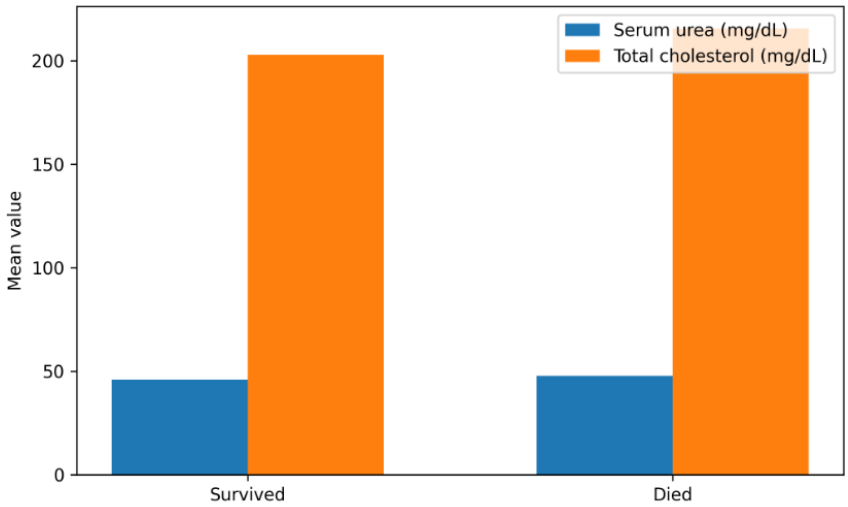


Figure 4.2. Mean serum urea and total cholesterol levels according to short-term outcome.

DISCUSSION

This study assessed the relationship of serum urea, lipid profile, and selected cardio-renal-metabolic biomarkers with short-term survival among 280 patients with cardiovascular disease. During follow-up, 237 participants (84.6%) survived and 43 (15.4%) died. The principal finding was that mean total cholesterol was significantly higher among non-survivors than survivors (215.52 ± 36.97 versus 202.90 ± 34.49 mg/dL; p = 0.042). In contrast, serum urea was only numerically higher among non-survivors, and the difference was not statistically significant (47.79 ± 15.37 versus 45.96 ± 15.28 mg/dL; p = 0.475). These results indicate that the measured biomarkers did not show uniform associations with short-term outcome in this cohort.

The cholesterol finding should be interpreted in the context of the established role of lipids in atherosclerotic cardiovascular disease. LDL-C contributes to lipid accumulation in the arterial wall, endothelial dysfunction, inflammatory signalling, and plaque development; plaque disruption and thrombosis can then precipitate acute cardiovascular events [7–9]. However, the present analysis compared total cholesterol between outcome groups and did not establish that cholesterol independently predicted

mortality. The higher mean total cholesterol observed among non-survivors was statistically significant, but the difference alone cannot demonstrate causation or determine whether cholesterol was an independent prognostic factor. Clinical interpretation should also consider baseline disease type and severity, treatment, medication use, and other potential confounders [14,15].

Serum urea was higher on average among participants who died, but the observed difference was small and not statistically significant. This result does not establish that urea lacks prognostic relevance. Urea concentration is affected by renal function, hydration, protein catabolism, and haemodynamic changes, and may therefore reflect several overlapping processes in cardiovascular patients [3,6]. Previous studies have reported associations between elevated urea or blood urea nitrogen and mortality in selected populations, including severe aortic stenosis and acute ischaemic stroke, while population-based analyses have also examined its relationship with cardiovascular and all-cause mortality [12,13]. Differences between those findings and the present result may relate to sample composition, the range of disease severity, biomarker definitions, follow-up duration, and the use of adjusted survival models. These explanations remain possibilities and were not directly tested in this study [16,18].

The categorical analyses did not identify statistically significant associations between short-term outcome and gender, smoking status, hypertension, diabetes, or the categorized urea and cholesterol variables. This should be interpreted cautiously. A non-significant result does not prove that an association is absent, particularly when the number of deaths is limited or when categorizing continuous measurements reduces information. The study also reported descriptive and group-comparison analyses; without a multivariable model, it was not possible to determine whether any biomarker predicted survival independently of age, comorbidities, renal function, inflammation, or cardiovascular diagnosis. Established cardiovascular risk assessment frameworks emphasize combining relevant clinical and laboratory information rather than relying on a single variable [1,17].

Taken together, the findings support a cautious, integrated approach to interpreting cardio-renal-metabolic markers. Total cholesterol differed between outcome groups, whereas serum urea did not reach statistical significance; neither result alone is sufficient to support an independent prediction claim. The study's strengths included the use of routinely available biochemical measurements and prospective follow-up, while its interpretation is limited by the single-centre setting, relatively small number of deaths, short observation period, and absence of reported multivariable survival analysis. In addition, the reported study duration and follow-up period should be reconciled in the final manuscript to ensure methodological clarity. Future multicentre cohorts should use longer follow-up, prespecified biomarker thresholds, and multivariable Cox regression or other appropriate survival models to estimate adjusted associations and assess whether combinations of biomarkers improve prognostic discrimination [19].

CONCLUSION

This study examined how serum urea, lipid profile and other cardio-renal-metabolic markers relate to short-term survival in patients with cardiovascular disease. At follow-up, 84.6% of patients were alive and 15.4% had died. Among all the biochemical parameters, only total cholesterol differed significantly between the two groups: non-survivors had a higher mean level (215.52 ± 36.97 mg/dl) than survivors (202.90 ± 34.49 mg/dl; p = 0.042). Serum urea was slightly higher in non-survivors (47.79 ± 15.37 mg/dL) than in survivors (45.96 ± 15.28 mg/dL), but this difference was not statistically significant (p = 0.475), and the same was true for LDL, HDL, triglycerides, creatinine, eGFR and CRP. These findings suggest that renal and lipid abnormalities may contribute to cardiovascular disease, but their link with short-term survival is variable, and in this population total cholesterol

showed somewhat greater short-term predictive value than serum urea alone. This underscores the importance of considering cardiovascular, renal and metabolic factors together rather than relying on any single laboratory marker, and larger cohorts, longer follow-up and multivariable analyses are needed to establish whether these markers independently predict outcomes in cardiovascular disease.

LIMITATIONS

- The study had a relatively small number of patients, and was performed in a particular clinical setting. So, the results may not reflect the actual status of all patients with cardiovascular disease in various hospitals or areas.
- The study was aimed at the immediate post-nesting mortality. The present results might not be representative of their long term value as cardiovascular and renal biomarkers might have other effects when measured over a longer time.
- While these biochemical and clinical parameters were measured, other factors that may have been important, such as symptoms of the disease, treatment differences, medication adherence, and other cardiac biochemical markers were not examined. All of these can have an effect on patient outcome.

RECOMMENDATIONS

- Future studies should include a larger number of patients from multiple hospitals and different regions to improve the generalizability of the findings and provide a better representation of the cardiovascular disease population.
- For future studies it is recommended to employ longer follow-up periods to assess the correlation between serum urea parameters, lipid profile and the cardio-renal-metabolic biomarkers and long-term mortality and other cardiovascular parameters.
- These biomarkers should be examined along with other cardiac and renal markers and disease severity in future studies. Analysis in the multivariate model also should be performed to identify those biomarkers which independently predict patient survival.

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