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Journal of Cardiac Critical Care TSS

Article in Press

Original Article *Cardiac Critical Care*

Soluble Urokinase Plasminogen Activated Receptor in Type 2 Diabetes Mellitus Patients Undergoing Coronary Artery Bypass Grafting: A Prospective Interventional Cohort Study

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Received: 14 October 2024
Accepted: 16 November 2024
EPub Ahead of Print: 18 December 2024
Published:

DOI
10.25259/JCCC_48_2024

Quick Response Code:

ABSTRACT

Objectives: Elevated levels of soluble urokinase plasminogen activator receptor (suPAR) increase mortality in various systemic diseases. This has been shown amply in recent literature. The primary aim of the study was to investigate that whether this increase in suPAR levels have same results in type 2 diabetes mellitus (T2DM) patients undergoing coronary artery bypass grafting (CABG). We also aimed to observe the duration of mechanical ventilation and length of stay in the intensive care unit in these patients as our secondary aim.

Materials and Methods: Blood samples of adult patients having T2DM admitted for elective on-pump CABG surgery were collected after induction of anesthesia before skin incision (T1) and 48 h post-cardiopulmonary bypass (CPB) (T2) from the year 2022 to 2023. The study was conducted on 196 patients of either sex of age at least 18 years with T2DM with the American Society of Anesthesiologists status III to IV. Patients were randomly divided into 2 groups with alternative allocation. Patients of the study group (n = 96) were measured suPAR, high-sensitivity C-reactive protein (hsCRP), and blood sugar, while patients of the control group (n = 100) were measured hsCRP and blood sugar only. Threshold suPAR levels for predicting mortality in the immediate post-operative period were assessed through receiver operating characteristic curves and optimal values decided using Youden's Index.

Results: There was a significant rise in suPAR and hs-CRP levels before the start of surgery and 48 h post-CPB ($P < 0.001$).

Conclusion: In patients with T2DM undergoing on-pump CABG, increased pre-bypass, and especially 48-h post-CPB, levels of suPAR and hsCRP predict more mortality.

Keywords: Soluble urokinase plasminogen activator receptor, High-sensitivity C-reactive protein, Inflammation, Cardiovascular disease

INTRODUCTION

The key role of inflammation in atherosclerosis is well known.[1] Inflammatory markers have proven to be supportive for the assessment of risk in cardiovascular disease (CVD). Increased levels of high-sensitivity C-reactive protein (hsCRP) have not only been found to be associated with subclinical inflammation but also with increased cardiovascular risk and Framingham Risk Score for risk stratification.[2] Soluble urokinase plasminogen activator receptor (suPAR)

is a new biomarker of prognostic significance in several clinical settings, including CVD.[2-4] It is bound to uPAR in its membrane and is released with a systemic inflammatory reaction.[5] Since CVDs represent the inflammatory state, newer evidence shows that the pathophysiological pathway of suPAR is more closely associated with atherosclerosis and subclinical organ damage (SOD) than C-reactive protein (CRP). In addition to this, the plasma suPAR levels are more stable than CRP.[6] The suPAR level is increased in patients with CVDs, atherosclerosis,[7] ischemic heart disease,[7-9] type 2 diabetes mellitus (T2DM),[10] poor prognosis,[11-14] and venous thromboembolism.[15] Raised suPAR levels also indicate ischemia at the microcirculatory level and help in risk stratification of patients for coronary artery disease on extracorporeal membrane oxygenation.[16] Anti-inflammatory agents are known to affect suPAR levels but limited literature is available for its guidance in the management of cardiac surgical patients. Therefore, we primarily aimed to assess whether the measurement of suPAR in patients with T2DM undergoing coronary artery bypass grafting (CABG) assists in predicting mortality.

MATERIAL AND METHODS

Study design

Prospective, interventional cohort study.

Ethics review

We obtained informed consent from each patient/legal guardian for those who were eligible to participate in the study and institutional ethics committee approval.

Patients

We evaluated suPAR in patients with T2DM undergoing elective CABG between September 2022 and January 2024. Randomization into the two groups was done by a sealed envelope technique by a neutral operation theater personnel not knowing about the study; thus the study was blinded. Patients of the study group S (suPAR group) (n = 96) were measured suPAR, hsCRP, and blood sugar, while patients of the control group C (control non-suPAR group) (n = 100) were measured hsCRP and blood sugar only [Flow chart 1].

Sample size

As per feasibility, limited time for study, available resources, and expected number of cases meeting the inclusion and exclusion criteria, we propose a possible sample size for our study to be = 196 (52) (in the reference study, mean standard deviation (SD) of 2012 red blood cells (RBC), fresh frozen plasma (FFP) and platelet concentrate in U/T with reference and margin of error 3 and 95%, confidence level 95%, minimum sample size required was 190, so for our study, 196 subjects were included).

Inclusion criteria

All CABG patients undergoing corrective open heart surgery on cardiopulmonary bypass (CPB) within the proposed study period were chosen. Patients of at least 18 years of age or older, known cases of T2DM, American Society of Anaesthesiologists (ASA) physical status III to IV were included in this study.

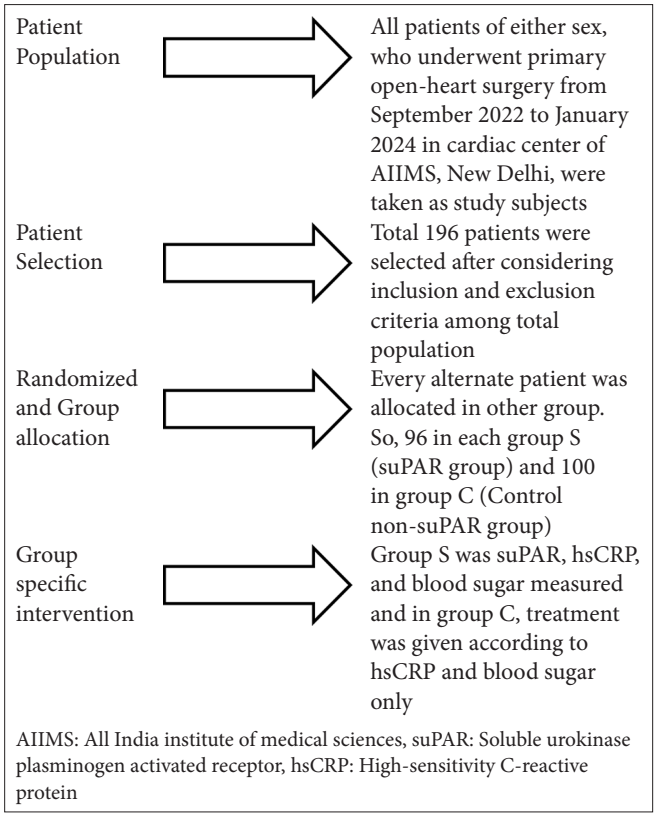
Exclusion criteria

Patients below 18 years of age, patients undergoing another procedure along with CABG, redo cardiac surgery, off-pump CABG, alcohol or other abuse, sepsis, and refusal of consent for participation were excluded.

Data collection

We recorded the demographic and clinical variables: Age, sex, and comorbidities. Laboratory tests, including hsCRP and suPAR were recorded before surgery after induction of anesthesia (T_1) and 48 h post-CPB (T_2).

The primary outcome measure was to evaluate whether the measurement of suPAR levels is associated with a reduction of



Flow chart 1: Cohort flow diagram.

mortality in patients with T2DM undergoing CABG surgery. We also recorded the duration of mechanical ventilation and length of intensive care unit (ICU) stay as secondary outcome measures. Blood sugar was also recorded along with the above parameters. In the control group, we recorded the same demographic, clinical variables, and laboratory parameters as stated above, except suPAR [Table 1].

The number of hours the patient remained intubated after shifting to the ICU was the duration of mechanical ventilation. The number of hours between the date of surgery and ICU discharge was the length of ICU stay.

Measurement of plasma suPAR levels

One mL of whole blood was drawn in an EDTA or heparin anticoagulant and centrifuged at ×3,000 g for 10 min. Plasma samples were transferred and stored in separate marked tubes. Plasma was loaded in the cassette and inserted in the quick triage (QT) device to obtain the suPAR readings. This QT test was done by a suPARnostic point of care test kit (code A003), which gives prognostic patient triage in approximately 20 min. Each kit contains 25 units and a ready-to-use buffer solution. It does not require a clinical laboratory and can be done in the emergency room. The suPAR value should be within the range of 2–15 ng/mL [Table 2].[16]

Statistical tests

In both the groups, quantitative variables were expressed as mean±SD. Comparison between the groups was done using unpaired *t*-tests and paired *t*-tests. These tests were used within each group at various follow-ups. The Chi-square test was used to compare qualitative variables, which were expressed as frequencies/percentages. Threshold suPAR levels for predicting mortality were assessed through receiver operating characteristic (ROC) curves and optimal values decided using Youden's Index. We considered $P < 0.05$ as statistically significant. IBM Statistical Package for the Social Sciences version 20.0 was used for statistical analysis.

Table 1: List of laboratory parameters recorded in the study group and control group.

Study group	Control group
suPAR	Blood sugar
hsCRP	hsCRP
Blood sugar	

hsCRP: High-sensitive C-reactive protein, suPAR: Soluble urokinase plasminogen-activated receptor

Table 2: suPAR cut-off values and their interpretation.

suPAR level (ng/mL)	Interpretation
<4	Patient can be discharged
4–6	Need to be interpreted in light of patient's history of comorbidities, which may increase them
>6	Alarming sign of risk for unfavorable outcome
>12	Critically ill patients

suPAR: Soluble urokinase plasminogen-activated receptor

Management of anesthesia

Syrup midazolam (0.5 mg/kg) was given to all patients before surgery. Balanced anesthesia technique included etomidate (0.3 mg/kg), fentanyl (1–2 μg/kg), and rocuronium (1 mg/kg) and maintenance with sevoflurane (0.5–3.0%) and a continuous infusion of cisatracurium (0.1 mg/kg/h). Invasive blood pressure monitoring was done by a cannula placed in the right radial artery. Heparinization was done to get an activated clotting time of >480 s. CPB with membrane oxygenation and roller pumps with a non-pulsatile flow and a normothermic bladder temperature (36.5–37.0°C) were used during the surgical procedure. Perfusion was maintained at a pump flow of 2.5 L/min/m^2

Based on the Society of Thoracic Surgeons Practice Guideline Series, blood sugar levels were targeted to be not more than 180 mg/dL.[17] Continuous insulin infusions were used for hyperglycemic management both during the intraoperative period and during the ICU stay.

RESULTS

The study was conducted on 196 patients of either sex of age at least 18 years or older with T2DM with ASA status III to IV. A total of 196 patients were randomly divided into 2 groups. Patients of the study group ($n = 96$) were measured suPAR, hsCRP, and blood sugar, while patients of the control group ($n = 100$) were measured hsCRP and blood sugar only. The majority of patients in both groups belong to the age bracket of 51–70 years, with a mean age of 58.18 ± 9.34 in cases and 59.11 ± 9.89 in controls. Both groups had no significant difference in terms of age ($P = 0.249$). In both groups, the overwhelming majority of patients were males, with no significant difference in the percentages ($P = 0.069$). While 10.42% was the mortality rate in cases, it was 10% in controls. However, there was not any significant difference between the two groups [Table 3].

Furthermore, there was no significant difference in the total duration of ventilation ($P = 0.149$), mean length of ICU stay ($P = 0.410$) [Table 4], and blood sugar levels in both the groups for up to 48 hours post-surgery [Table 5]. Between T1 and T2 levels of suPAR before surgery and 48 h after surgery, there was a significant difference seen at 2-time intervals, signifying an ischemic and inflammatory effect of CPB ($P < 0.001$) [Table 6 and Figure 1]. At time T1, the hsCRP

Table 3: Distribution of patients according to age in both the groups.

Parameters	Case		Control		*P*-value
	n	%	*n*	%	
Age (years)					
<50	19	19.8	18	18.0	0.249
>50	77	80.21	82	82	
Total	96	100	100	100	
Mean±sd	58.18±9.34		59.11±9.89		
Gender					
Male	91	94.79	89	89.00	0.069
Female	5	5.21	11	11.00	
Total	96	100	100	100	
Mortality					
Yes	10	10.42	10	10.00	0.462
No	86	89.58	90	90.00	
Total	96	100	100	100	

sd: Standard deviation, *P*-value: Probability value, *n*: Number of patients

Table 4: Mean duration of mechanical ventilation and length of ICU stay in both the groups.

Parameters	Case	Control	*P*-value
	Mean±sd	Mean±sd	
Total duration of mechanical Ventilation (hrs)	10.15±5.15	10.84±3.56	0.149
Length of ICU stay (hrs)	44.95±20.3	44.42±9.55	0.410

hrs: Hours, sd: Standard deviation, ICU: Intensive care unit, *P*-value: Probability value

Table 5: Blood sugar levels in both the groups.

Blood sugar in (mg/dL)	Case	Control	*P*-value
	Mean±sd	Mean±sd	
Pre-op (S0)	107.58±23.67	103.99±21.02	0.131
Post-op (S1)	176.33±46.46	180.06±45.26	0.285
At 6 hrs (S6)	153.75±51.14	145.35±42.65	0.106
At 12 hrs (S12)	161.75±36.44	160.67±31.94	0.413
At 18 hrs (S18)	170.58±54.81	165.07±49.33	0.230
At 24 hrs (S24)	178.08±49.64	173.87±44.29	0.266
At 30 hrs (S30)	164.58±36.56	169.41±35.75	0.176
At 36 hrs (S36)	137.92±28.12	138.15±28.1	0.477
At 42 hrs (S42)	172.92±37.52	179.19±34.05	0.111
At 48 hrs (S48)	154.42±38.26	152.35±32.41	0.342

Pre-op: Preoperative, Post-op: Post-operative, hrs: hours, S0: Blood sugar level before incision, S1: Blood sugar level after reaching ICU, S6: Blood sugar level 6 h after reaching ICU, S12: Blood sugar level 12 h after reaching ICU, S18: Blood sugar levels 18 h after reaching ICU, S24: Blood sugar Levels 24 h after reaching ICU, S30: Blood sugar levels 30 h after reaching ICU, S36: Blood sugar levels 36 h after reaching ICU, S42: Blood sugar levels 42 h after reaching ICU, S48: Blood sugar level 48 h after reaching ICU, *P*-value: Probability value

Table 6: Mean suPAR values before surgery and 48 h after ICU admission.

suPAR	Case
	Mean±sd (ng/mL)
Before surgery (T1)	4.56±2.74
48 h post-CPB (T2)	8.39±5.1
P-value	<0.001

suPAR: soluble urokinase plasminogen activated receptor, CPB: Cardiopulmonary bypass, sd: Standard deviation, *P*-value: Probability value, ng/mL: Nanogram per milliliter, ICU: Intensive care unit, T1: Before surgery, T2: Post 48 hours after cardiopulmonary bypass termination

Table 7: Distribution of hsCRP values before the surgery in the two groups.

hsCRP (mg/L) - T1	Case		Control		*P*-value
	n	%	*n*	%	
<0.3	49	51.04	66	66.00	0.017
0.3	0	0.00	4	4.00	0.024
0.4	22	22.92	11	11.00	0.013
0.5	13	13.54	5	5.00	0.019
0.6	0	0.00	4	4.00	0.024
0.8	0	0.00	1	1.00	0.163
Total	84	88	91	91	-
mean±sd	0.77	±1.43	0.50	±0.77	0.050

hsCRP: High sensitive C-Reactive protein, *P*-value: Probability value, sd: Standard deviation, mg/L: Milligram per liter, n: Number of patients

Table 8: Distribution of hsCRP values 48 h post-cardiopulmonary bypass in the two groups.

hsCRP (mg/L) - T2	Case		Control		*P*-value
	n	%	*n*	%	
2	0	0.00	1	1.00	0.163
4	0	0.00	1	1.00	0.163
6	0	0.00	4	4.00	0.024
7	0	0.00	1	1.00	0.163
8	28	29.17	9	9.00	<0.001
9	14	14.58	14	14.00	0.454
>10	43	44.79	61	61.00	0.012
Total	85	89	91	91	-
mean±sd	10.09	±2.73	9.93	±2.47	0.335

hsCRP: High sensitive C-reactive protein, *P*-value: Probability value, sd: Standard deviation n: Number of patients, mg/L: Milligram per liter

values of 0.4 and 0.5 were significantly higher in cases, while all the other values were significantly higher in controls. The mean hsCRP at T1 in cases was 0.77 ± 1.43, which was significantly higher than in controls at 0.50 ± 0.77 ($P = 0.050$) [Table 7 and Figure 2a]. At time T2, the hsCRP values were

similar in both groups. However, values of 6 mg/L and >10 mg/L were significantly higher in controls, while the value of 8 mg/L was higher in cases. The mean hsCRP at T2 in cases was 10.09 ± 2.73, which was not significantly different than in controls at 9.93 ± 2.47 (P = 0.335). This shows that hsCRP values increased significantly post-surgery in both groups [Table 8 and Figure 2b].

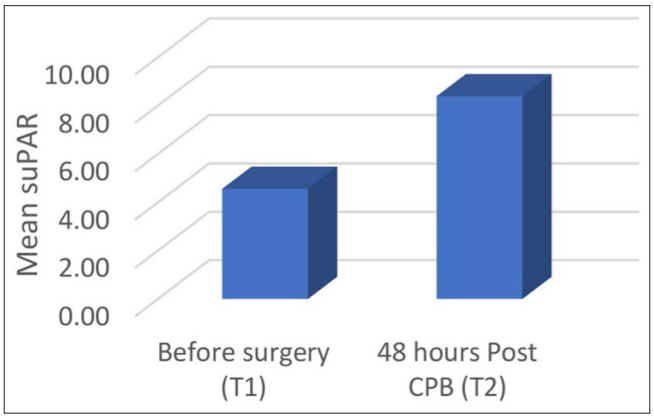


Figure 1: Graphical representation of mean soluble urokinase plasminogen activated receptor values before surgery and 48 h post-cardiopulmonary bypass**.** suPAR: Soluble urokinase plasminogen activated receptor, T1: Before surgery, T2: Post 48 hours after cardiopulmonary bypass termination. CPB: Cardiopulmonary bypass.

Mortality was assessed in the immediate postoperative period. The area under ROC for the parameter suPAR (T1) in predicting mortality is 71%. A threshold of ≥4.9 ng/mL for death yields a sensitivity of 80%, specificity of 74.42%, positive predictive values (PPV) of 26.67%, negative predictive values (NPV) of 96.97%, and accuracy of 75%. The area under ROC for the parameter hsCRP (T1) in predicting mortality is 98.1%. A threshold of ≥1.6 ng/mL for death yields a sensitivity of 100%, specificity of 97.67%, PPV of 83.33%, and accuracy of 97.92%. The area under ROC for the parameter suPAR (T2) in predicting mortality is 96.3%. A threshold of ≥16.25 ng/mL for death yields a sensitivity of 100%, specificity of 91.86%, PPV of 58.82%, and accuracy of 92.71%. The area under ROC for the parameter hsCRP (T2) in predicting mortality is 99.9%. A threshold of ≥ 12.5 for death yields a sensitivity of 100%, specificity of 98.84%, PPV of 90.91%, and accuracy of 98.96% [Table 9 and Figure 3].

DISCUSSION

Detection of a physiological variable that correlates with cellular hypoperfusion and can be used as an appropriate resuscitation measure is challenging.[18] Cardiac biomarkers are similar to an intervention.[19] Lactic dehydrogenase, CK, and Creatine kinase MB (CKMB) have been used in the past

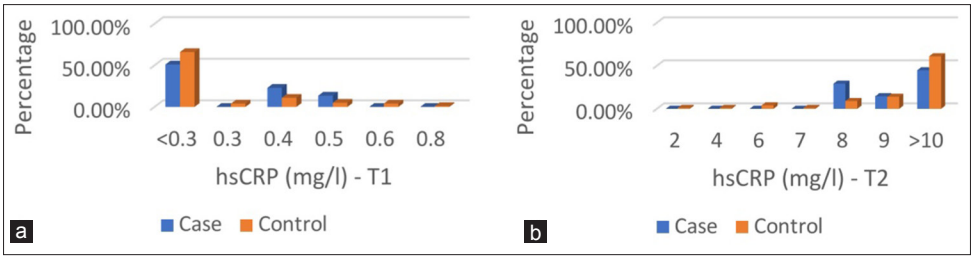


Figure 2: (a) Graphical representation of distribution high senstivity C- reactive protein values before the surgery at time T1 in the two groups. (b) Graphical representation of distribution of high senstivity C-reactive protein values 48 hours post-cardiopulmonary bypass at time T2 in the two.

Table 9: Correlation between suPAR and hsCRP.

Parameters	Threshold value	Mortality		Survived		*P*-value	AUROC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
		n	%	*n*	%							
suPAR (T1)	<4.9	2	20.00	64	74.42	<0.001	0.710	80.00	74.42	26.67	96.97	75.00
	≥4.9	8	80.00	22	25.58							
hsCRP (T1)	<1.6	0	0.00	84	97.67	<0.001	0.981	100.00	97.67	83.33	100.00	97.92
	≥1.6	10	100.00	2	2.33							
suPAR (T2)	<16.25	0	0.00	79	91.86	<0.001	0.963	100.00	91.86	58.82	100.00	92.71
	≥16.25	10	100.00	7	8.14							
hsCRP (T2)	<12.5	0	0.00	85	98.84	<0.001	0.999	100.00	98.84	90.91	100.00	98.96
	≥12.5	10	100.00	1	1.16							

suPAR: Soluble urokinase plasminogen-activated receptor, hsCRP: High sensitivity C-reactive protein, PPV: Positive predictive values, NPV: Negative predictive values, n: Number of patients, T1: Before surgery, T2: Post 48 hours after cardiopulmonary bypass termination, AUROC: Area under receiver operating characterstic curve

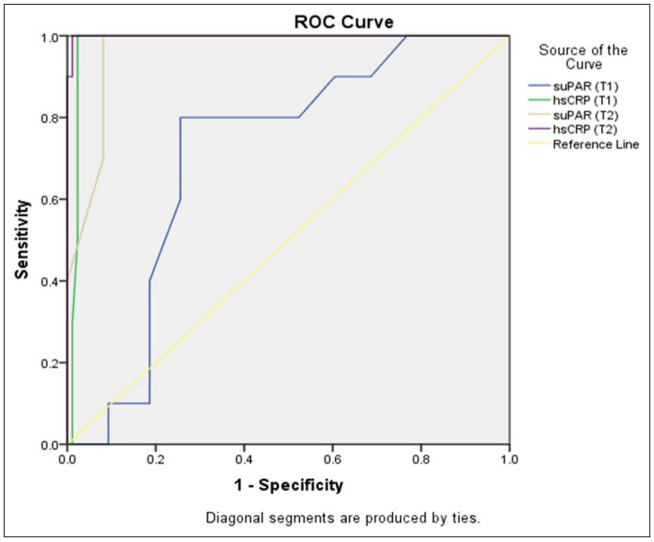


Figure 3: ROC curve for 30-day post-operative mortality predicted from combinations of soluble urokinase plasminogen-activated receptor and high sensitivity C-reactive protein. ROC: Receiver operating characteristics, T1: Before surgery, T2: Post 48 hrs after cardiopulmonary bypass termination.

Table 10: suPAR levels in survived and mortality group.

suPAR	Died	Survived	*P*-value
	Mean±sd	mean±sd	
Before surgery (T1)	5.58±1.24	4.44±2.84	0.108
48 hrs Post-CPB (T2)	18.47±0.99	7.22±3.96	<0.001

suPAR: Soluble urokinase plasminogen-activated receptor, CPB: Cardiopulmonary bypass, hrs: Hours, T1: Before surgery, T2: Post 48 hours after cardiopulmonary bypass termination

but now, troponins are the current standard for diagnosis of myocardial infarction. glycogen phosphorylase isoenzyme BB (GPBB), heart type fatty acid binding protein (HFABP), soluble suppressor of tumorigenicity-2 (sST2), suPAR, and miRNA have proven to be helpful for the diagnosis and treatment of patients suspected of an adverse cardiac event.[20] Both suPAR and hsCRP have shown prognostic significance in CVDs.[11,12,21-23] However, the association between the biomarkers and prognosis after cardiac surgery has not been established.[24]

Since suPAR is known to be raised for more than 24 hours in cardiac surgical patients, we measured its levels in the case group before surgery and 48 hours post-CPB. It was seen that 48 h post-CPB, the suPAR levels increased by almost 3 times in the mortality group as compared to less than twice in the survival group [Table 10]. Sehestedt *et al.* (2011) concluded in their study that raised suPAR levels indicate SOD and cardiovascular injury.[25] Rasmussen *et al.* (2021) concluded that a rise in suPAR and hsCRP levels before a cardiac surgical procedure was associated with increased mortality.[26] Our study aligned with these studies, showing that increased levels of suPAR and hsCRP in the population with T2DM undergoing CABG in the perioperative period indicate an increased risk of mortality in the immediate postoperative period.

AHA states that a biomarker should be synergistic to already known risk factors, helpful in patient management, and should be able to predict possible outcomes.[27] Increased suPAR and hsCRP both predict adverse cardiovascular events.[2,28,29]. suPAR is a stable protein and has lesser circadian fluctuations. It is membrane-bound and gets into the bloodstream after getting cleaved from the urokinase-type plasminogen activator receptor. It is found on the surface of various cells, which include inflammatory and endothelial cells.[6,11,30,31] Its performance also gets enhanced when it is combined with other biomarkers such as procalcitonin and CRP.[32]

In a healthy adult population, women have increased suPAR levels as compared to men and a positive correlation with age in both men and women has been observed.[33-38] Gender-specific physiology may be the cause of increased suPAR levels in women.[39] However, there is a greater annual increase in suPAR levels in men than in women.[40] Studies have shown both positive and negative correlations between basal metabolic index and suPAR levels.[33-35,38] However, body mass index (BMI) >35 kg/m^{-2} is a known chronic inflammatory state that may lead to increased sugar levels.[38] Lifestyle choices such as tobacco smoking, unhealthy diet, levels of HDL cholesterol, sedentary lifestyle, and alcohol intake have also been found to affect sugar levels.[38,40] Furthermore, genetic factors, as well as environmental factors, also affect suPAR levels.[41]

suPAR levels are reduced by anti-inflammatory agents, leading to a reduced risk of adverse cardiovascular outcomes. Hypolipidemic agents like simvastatin cause decrement in suPAR levels in patients with subclinical aortic stenosis. However, there is no established relation between the effects of hypolipidemic drugs and decreased suPAR levels, leading to lesser mortality and reduced adverse cardiovascular events.[42] Corticosteroids reduce both inflammation and suPAR levels in patients with chronic obstructive pulmonary disease.[43] Anakinra, an interleukin (IL)-1 receptor antagonist, has proven efficacy in reducing the acute inflammatory response in acute myocardial Infarction (AMI).[44] Ridker *et al.* have shown a reduced incidence of MI with canakinumab, a monoclonal antibody against IL-1β.[45]Although studies have depicted the effect of anti-inflammatory agents on suPAR levels leading to reduced adverse cardiovascular outcomes, more investigations are required for its use in guiding the treatment of patients with CVD.

CRP is also a protein and it represents acute inflammation. It is also involved in the vascular remodeling process.[37] During

inflammation, the release of proinflammatory cytokines stimulates hepatocytes to produce CRP. Recent data suggest that CRP levels are increased during atherosclerosis.[46] CRP in small ranges of 0.01–10 mg/L can also be traced with modern high-sensitivity assay techniques, which include immunonephelometry, immunoturbidimetry, high-sensitivity enzyme-linked immunosorbent assay, and resonant acoustic profiling.[47] Therefore, lesser grades of inflammation can also be detected with these newer high-sensitivity assay techniques. The hsCRP is one of the most commonly used biomarkers for CVD risk prediction across the world. However, hsCRP is not a reliable marker as its levels are affected by several drugs, infections, inflammation, and external stress stimulus.[48-50]

Raised suPAR levels indicate cardiovascular disorders and more incidence of deaths in the population.[28,29,34,51] The prognostic significance of elevated suPAR levels in cardiac surgical patients and their association with increased postoperative complications is a lesser explored area.[51] Elevated suPAR levels on the 1st day after surgery indicate more duration of ventilation and increased duration of ICU stay.[52] A rise in suPAR levels after the cardiac surgical procedure also depicts an aggravated risk of acute kidney injury.[53] Interestingly, our study was also in consonance with these facts which have been proven by some small number of studies earlier. However, there was no significant change in patient outcome after including suPAR in known risk models. This proves that perioperative mortality is dependent on other factors.

Our study had some considerable limitations, too. The generalizability to other centers and races was limited because the population assessed was mainly Indians, and the surgical procedures were performed at the same cardiac surgical center. Although the literature has shown suPAR to be associated with low ejection fraction, our study was limited to patients with normal ejection fraction only.[54] Post-adverse outcomes such as acute kidney injury and stroke were not recorded. Additional information could have also been obtained by recording the cause of death and following the patients for the long term.

CONCLUSION

suPAR, an important biomarker, reflects systemic inflammation leading to the pathogenesis of CVD. Its increased levels (pre-bypass and especially 48 h post-CPB) were associated with increased mortality in T2DM patients undergoing elective on-pump CABG, thereby reflecting more severe disease. However, it lacks consensus reference ranges, and its assays are non-standardized. To summarize, various circulating forms of suPAR and different methods to control them need to be explored for better outcomes after cardiac surgery. suPAR for prognosis of patients having type 2 diabetes mellitus undergoing CABG needs more prospective studies to have a strong relationship between the two.

Ethical approval

The research/study was approved by the Institutional Review Board at AIIMS, number IECPG-778/December 23, 2021, dated 28th January 2022.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

Financial support and sponsorship

Nil.

Conflicts of interest

Dr.Poonam Malhotra Kapoor and Minati Choudhury are on the Editorial Board of the journal.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

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How to cite this article: Prakash M, Kapoor PM, Mujahid OM, Choudhury M, Malhotra AK, Rajashekar P. Soluble Urokinase Plasminogen Activated Receptor in Type 2 Diabetes Mellitus Patients Undergoing Coronary Artery Bypass Grafting: A Prospective Interventional Cohort Study. J Card Crit Care TSS. doi: 10.25259/JCCC_48_2024