



Malnutrition-Inflammation Liaison in Predicting AKI following OPCABG in Diabetics: Role of a Novel Monocyte/High-Density Lipoprotein \times Albumin Ratio

Armaanjeet Singh^{1,2} Rohan Magoon^{1,2} Souvik Dey^{1,2} Noopur Bansal^{1,2} Iti Shri^{1,2}
Jasvinder Kaur Kohli^{1,2} Ramesh Chand Kashav^{1,2}

¹ Department of Cardiac Anaesthesia, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS), New Delhi, India

² Department of Cardiac Anaesthesia, Dr. Ram Manohar Lohia Hospital, New Delhi, India

Address for correspondence Souvik Dey, MD, Department of Cardiac Anaesthesia, Atal Bihari Vajpayee Institute of Medical Sciences (ABVIMS) and Dr. Ram Manohar Lohia Hospital, Baba Kharak Singh Marg, New Delhi 110001, India (e-mail: souvik_23march@yahoo.in).

J Card Crit Care 2022;6:17–24.

Abstract

Background Monocyte/high-density lipoprotein ratio (MHR) has been recently proposed as a parsimonious inflammatory marker. Akin to MHR, hypoalbuminemia (a malnutrition marker) has a considerable proinflammatory potential and confers an accentuated risk of postcardiac surgery complications, like acute kidney injury (AKI). The present study evaluated the AKI-predictive value of the preoperative monocyte/high-density lipoprotein \times albumin ratio (MHAR) in diabetic patients undergoing off-pump coronary artery bypass grafting (OPCABG).

Methods The retrospective study conducted at our tertiary cardiac care center included 687 diabetic OPCABG patients. Forty-eight hours postoperative data was evaluated for the occurrence of AKI, as defined by the Acute Kidney Injury Network criteria. The perioperative attributes of the AKI and non-AKI groups were compared to evaluate the predictors of AKI, by employing a regression analysis.

Results A total of 109 patients (15.87%) developed AKI postoperatively. On univariate analysis: age, EuroSCORE II, preoperative congestive heart failure, systemic hypertension, serum albumin, MHR, MHAR, intraoperative packed red blood cell transfusion, postoperative low cardiac output syndrome, and vasoactive-inotropic score (VIS) predicted AKI. AKI subsequent to multivariate analysis, age (odds ratio [OR]: 1.029), EuroSCORE II (OR: 1.264), MHAR (OR: 1.403), and VIS (OR: 1.07) were the independent predictors (*p*-values: 0.020, < 0.001, 0.013, 0.002, respectively). The AKI predictive cutoffs of albumin, MHR, and MHAR were ≤ 2.95 , ≥ 15.25 , and ≥ 4.08 (area under the curve:sensitivity:specificity of 0.761:84.86%:89.62%; 0.754:93.12%:86.68%; 0.798:89.63%:88.34%, respectively). MHAR ≥ 4.08 was also associated with a higher incidence of postoperative atrial fibrillation and major adverse cardiac events.

Conclusion Preoperative elevated MHAR independently predicts AKI following OPCABG in diabetics, implying a malnutrition-inflammation liaison at heart of the matter.

Keywords

- ▶ acute kidney injury
- ▶ diabetes mellitus
- ▶ malnutrition
- ▶ monocyte/high-density lipoprotein ratio (MHR)
- ▶ monocyte/high-density lipoprotein \times albumin ratio (MHAR)
- ▶ inflammation
- ▶ off-pump coronary artery bypass grafting

DOI <https://doi.org/10.1055/s-0042-1750112>
ISSN 2457-0206.

© 2022. Official Publication of The Simulation Society (TSS), accredited by International Society of Cardiovascular Ultrasound (ISCU). All rights reserved.

This is an open access article published by Thieme under the terms of the Creative Commons Attribution-NonDerivative-NonCommercial-License, permitting copying and reproduction so long as the original work is given appropriate credit. Contents may not be used for commercial purposes, or adapted, remixed, transformed or built upon. (<https://creativecommons.org/licenses/by-nc-nd/4.0/>)

Thieme Medical and Scientific Publishers Pvt. Ltd., A-12, 2nd Floor, Sector 2, Noida-201301 UP, India

Highlights

- Monocyte/high-density lipoprotein ratio (MHR) has captivated attention as a parsimonious proinflammatory marker albeit remains underevaluated in cardiac surgery.
- The recent proposition of MHR as a marker of diabetic nephropathy is also noteworthy.
- Preoperative hypoalbuminemia (related to both poor nutritional status and proinflammatory predisposition) demonstrates an independent prognostic importance in cardiac surgical setting.
- We retrospectively discovered a heightened risk of postoperative acute kidney injury (AKI) in off-pump coronary artery bypass grafting (OPCABG) diabetic patients with a preoperative monocyte/high-density lipoprotein \times albumin ratio (MHAR) ≥ 4.08 .
- The former highlights that poor preoperative nutritional and proinflammatory profile potentially liaises to result in an accentuated postoperative cardiac-surgical morbidity.

Introduction

Metabolic inflammation (metaflammation) constitutes a topical research area, particularly in diabetic patients with an underlying coronary artery disease (CAD).^{1–3} This becomes all the more relevant amidst an ever-growing cohort of diabetic CAD.⁴ While the underlying baseline low-grade inflammation can be potentially exaggerated in the perioperative period,^{5,6} the importance of preoperative malnutrition in modulating the postoperative cardiac surgical outcomes can also not be undermined.⁷

Appropriate to the context, hypoalbuminemia, conventionally envisaged as a preoperative marker of malnutrition, has an important proinflammatory potential as well.⁶ Albumin classifies as a negative acute phase reactant⁹ and hence, hypoalbuminemia can significantly contribute to an ongoing inflammatory process. Furthermore, an elevated monocyte/high-density lipoprotein ratio (MHR) has been recently described to be a parsimonious proinflammatory marker of prognostic importance in operative^{10–12} and non-operative CAD settings.^{13–16} The elucidation of coexistence of low serum albumin levels and high MHR in postcoronary artery bypass grafting (CABG) patients with saphenous vein graft disease by Akboga et al, is intriguing.¹⁷ The former provides subtle clues to the communion between poor nutritional status and proinflammatory predisposition.

With regards to the postoperative cardiac surgical complications, cardiac surgery associated-acute kidney injury (CSA-AKI) transpires with an accentuated frequency in diabetics and accounts for a considerable morbidity and mortality.^{18,19} Alongside the recent proposition of MHR as a biomarker of diabetic nephropathy,²⁰ hypoalbuminemia has also been described to be associated with an enhanced risk of CSA-AKI.^{21,22} Therefore, the present study sought to retrospectively evaluate the AKI-predictive value of preoperative monocyte/high-density lipoprotein \times albumin ratio (MHAR) in diabetic patients undergoing off-pump CABG (OPCABG).

The secondary objectives were to compare the incidence of postoperative low cardiac output syndrome (LCOS), major adverse cardiac events (MACE), atrial fibrillation (AF), and sepsis, in the patients demonstrating preoperative MHAR values higher than the AKI-predictive cutoff and those having MHAR values less than the computed cutoff.

Materials and Methods

Following a formal approval from the Institutional Ethics Committee (No.601 (18/2020) IEC/ABVIMS/RMLH), the data of 813 diabetic patients, that is, patients who presented with fasting serum glucose > 126 mg/dL or on treatment with oral hypoglycemic medications/insulin, who had undergone elective OPCABG at our tertiary care referral center from January 2015 to December 2020, was retrospectively collected and evaluated. The patients who underwent emergency surgery, those with preoperative chronic kidney disease, and preoperative critically ill state (patients on mechanical ventilation, intra-aortic balloon pump [IABP], and/or inotropes) were excluded from the study. The patients who had systemic disorders potentially linked to hypoalbuminemia, such as hepatic dysfunction, active malignancy, certain endocrine disorders, for example, hypothyroidism, hyperthyroidism, etc., low hemoglobin (Hb) levels (≤ 10 g/dL), active infection, active or chronic autoimmune disease, lymphoproliferative disease, and patients on long-term treatment with steroids or chemotherapeutic drugs, were also excluded. The patients who required intraoperative cardiopulmonary bypass and/or postoperative IABP support, were excluded from the study. The lack of laboratory data within three preoperative days before was deemed as a study exclusion. After considering the loss to follow-up, the data of 687 patients was accumulated from the hospital archives and electronic database. The patient enrollment is illustrated as a flowchart in **Fig. 1**.

Preoperative patient data including age, sex, body mass index, European System for Cardiac Operative Risk Evaluation (EuroSCORE II), prior myocardial infarction (MI), peripheral vascular disease, hypertension, chronic obstructive pulmonary disease, smoking history, preoperative congestive heart failure (CHF), preoperative drugs (β blockers, statins, angiotensin-converting enzyme inhibitors), left ventricle ejection fraction, and left main disease, history of coronary angiogram within 7 days preoperatively, etc. were noted. The laboratory parameters obtained were: Hb, total leucocyte count, absolute monocyte count (AMC), high-density lipoprotein (HDL), serum creatinine, aspartate transaminase, alanine transaminase, and serum albumin levels. The intraoperative and postoperative parameters namely duration of surgery, number of distal vessel anastomosis, LCOS, vasoactive-inotropic score (VIS), postoperative AF, postoperative sepsis, MACE following surgery, requirement of renal replacement therapy (RRT), postoperative duration of mechanical ventilation (DO-MV), length of intensive care unit stay (LOS-ICU), and length of hospital stay (LOS-H), were also documented.

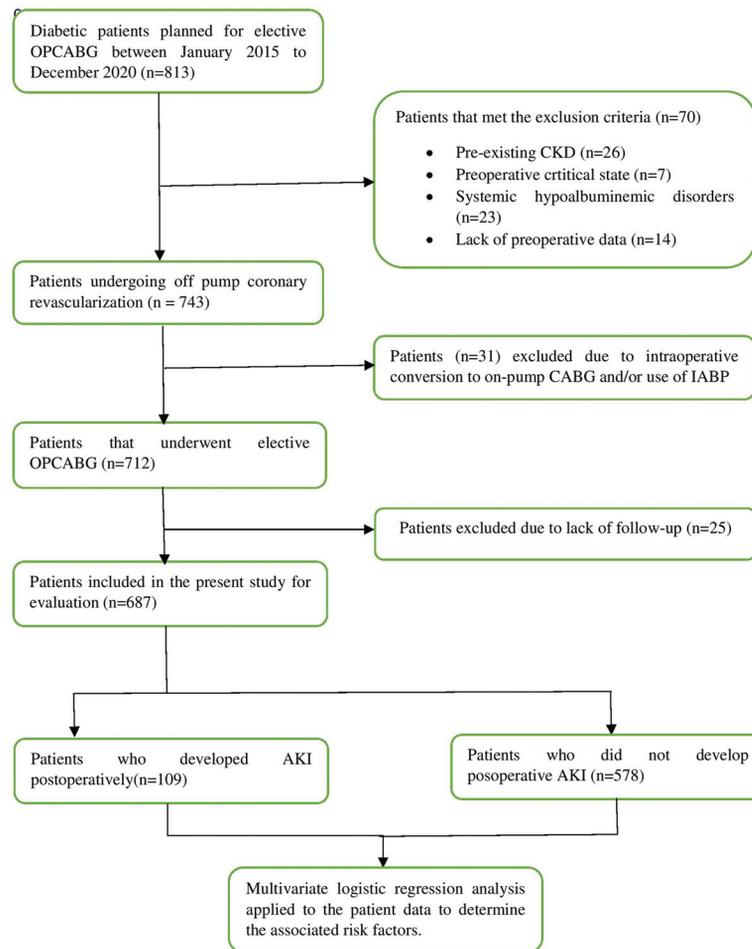


Fig. 1 The flow diagram depicting the patient enrolment methodology. AKI, acute kidney injury; CKD, chronic kidney disease; IABP, intra-aortic balloon pump; OPCABG, off-pump coronary artery bypass grafting.

MHR and MHAR were then calculated as per the following formulae:

- MHR = AMC/HDL
- MHAR = MHR/Albumin

The induction and maintenance of anesthesia, was as per a predefined institutional protocol. Volume-controlled ventilation was employed with oxygen and air in the ratio of 0.6 to result in an end tidal carbon dioxide concentration of 35 mm Hg along with 1.0 minimum alveolar concentration isoflurane. A Swan-Ganz catheter (Edwards Lifesciences, Irvine, California, United States) was inserted in the pulmonary artery (PA) via a 7Fr sheath placed in right internal jugular vein for monitoring PA pressures. The intraoperative bispectral index was maintained between 40 and 60.

After a midline sternotomy, left internal mammary artery and saphenous venous grafts were harvested. Upon administering heparin in a dose of 200 IU/kg of body weight and reaching an activated clotting time of > 300 seconds, the octopus evolution tissue stabilizer (Medtronic, Inc, Minneapolis, Minnesota, United States) was placed to stabilize the diseased coronary artery and inserting the intracoronary shunts. The distal anastomosis was executed with 6–0 or 7–0

prolene sutures, while proximal anastomosis was achieved using 5–0 prolene sutures. Once the coronary anastomosis concluded, protamine dose in a ratio of 1 mg/100 IU heparin was used to reverse the anticoagulation and all the patients were subsequently transferred to cardiac ICU for further management.

With respect to the glucose homeostasis, the glucose levels were evaluated at hourly intervals with arterial blood gas measurements. The perioperative blood glucose levels were regulated with an insulin infusion to the target glucose of 140 to 180 mg/dL.

Analysis of the 48 hours postoperative data was performed to determine the incidence of de novo AKI, defined by the Acute Kidney Injury Network (AKIN) criteria²³ as:

- AKIN stage 1: increased creatinine level > 50% or 0.3 mg/dL from baseline, or urine output < 0.5 mL/kg/h continuing more than 6 hours.
- AKIN stage 2: increased creatinine level by > 100%, or urine output < 0.5 mL/kg/h over 12 hours.
- AKIN stage 3: increased creatinine level by > 200% or serum creatinine level > 4 mg/dL with an acute increase of > 0.5 mg/dL, new-onset RRT, urine output < 0.3 mL/kg/h over 24 hours, or anuria over 12 hours.

The intraoperative and postoperative mean arterial pressure was maintained above 65 mm Hg²⁴ with the assistance of vasopressors and inotropic support, as per the institutional regimen. The corresponding hemodynamic support was quantified as VIS²⁵ wherein, $VIS = \text{Dopamine } (\mu\text{g/kg/min}) + \text{dobutamine } (\mu\text{g/kg/min}) + \text{milrinone } (\mu\text{g/kg/min}) \times 10 + \text{epinephrine } (\mu\text{g/kg/min}) \times 100 + \text{norepinephrine } (\mu\text{g/kg/min}) \times 100 + \text{vasopressin } (\mu\text{g/kg/min}) \times 100 + \text{vasopressin } (\mu\text{g/kg/min}) \times 1000$.

Postoperative MACE was defined by the occurrence of any of the following: cardiac arrest, MI, and/or the need of repeat coronary revascularization.²⁶

Statistical Analysis

The categorical variables of the AKI and non-AKI groups were converted to numerical values and percentages and analyzed using the chi-square test. The continuous variables were denoted as mean \pm standard deviation and evaluated using the unpaired *t*-test. For assessing the correlation among continuous variables, Pearson's correlation analysis was applied. The nonparametric receiver operating characteristic (ROC) curve analysis was used to elucidate the accuracy of all variables in predicting AKI demonstrated by their respective area under the curve (AUC). The precise AKI-predictive cutoff was calculated as the cutoff mark with the maximum [(sensitivity + specificity)/2] ratio, at which there was the highest accuracy of postoperative AKI as an outcome. The sensitivity, specificity, and predictive values were then reported utilizing the created cutoff. The multivariate analysis was performed with binary logistic regression. The statistical software SPSS version 20 (IBM Corp, Armonk, New York, United States) was applied for the analysis. A confidence interval (CI) of 95% with 80% power of study, with a *p*-value of < 0.05 was considered as significant.

Results

The 687 OPCABG patients enrolled in the study comprised of 563 males (81.95%) and 124 females (18.05%). A total of 109 patients (15.87%) developed postoperative AKI. The demographic and perioperative characteristics of these patients, as categorized by the manifestation of postoperative AKI, are shown in **Tables 1** and **2**.

The following variables were found to be significant predictors of postoperative AKI in the univariate analysis: advanced age, a higher logistic EuroSCORE II, elevated MHR, MHAR, and lower preoperative serum albumin concentrations. Patients with AKI were also more likely to have pre-existing comorbidities such as hypertension and CHF. In addition, the packed red blood cell units transfused during surgery, postoperative LCOS, and mean VIS were also associated with the development of postoperative AKI (**Table 3**). The patients with AKI, demonstrated a higher requirement of RRT, DO-MV, LOS-ICU, and LOS-H, in contrast to those without AKI (**Table 2**). Preoperative MHAR was independently associated with postoperative AKI (multivariate logistic analysis; odds ratio [OR]: 1.403; 95% CI: 1.073–1.833; *p*-value: 0.013). Age

(OR: 1.029; 95% CI: 1.005–1.054; *p*-value: 0.020), EuroSCORE II (OR: 1.264; 95% CI: 1.1–1.451; *p*-value: < 0.001), and VIS (OR: 1.074; 95% CI: 1.027–1.123; *p*-value: 0.002) also emerged as independent predictors of postoperative AKI, as outlined in Table 3.

Herein, albumin \leq 2.95, MHR \geq 15.25, and MHAR \geq 4.08 (AUC; 95% CI; sensitivity; specificity: 0.761; 0.698–0.822; 84.86%; 89.62% [*p*-value < 0.001], 0.754; 0.694–0.814; 93.12%; 86.68% [*p*-value = 0.015], and 0.798; 0.74–0.856; 89.63%; 88.34% [*p*-value < 0.001], respectively) were the estimated AKI-predictive cutoffs based on the ROC curve analysis (**Fig. 2**). Interestingly, the study subset who had a preoperative MHAR > 4.08 (the computed AKI predictive cutoff) also demonstrated a higher incidence of postoperative AF and MACE (**Table 4**).

Discussion

The demonstration of an independent AKI-predictive value of MHAR highlights that poor preoperative nutritional status potentially liaises with a prevailing proinflammatory milieu to result in an accentuated postoperative morbidity. As far as AKI (primary outcome under evaluation) is concerned, we discovered an incidence of 15.87% AKI in our diabetic subset undergoing OPCABG. The considerable variation in the reported incidence of 3.5 to 31% of CSA-AKI emanates as a result of the heterogeneity of the diagnostic criteria employed, surgical cohort under evaluation (off-pump or on-pump), design of the study including the exclusion criterion, and the procedure-specific predilection.¹⁹ Despite a homogeneous inclusion of OPCABG patients, the evaluation of an isolated diabetic subset could have attributed an incremental risk for postoperative AKI in our setting. Talking of the factors which independently predicted AKI in the index analysis, EuroSCORE II, in general implies an elevated cardiac surgical risk²⁷ whereas a higher vasopressor-inotropic support (estimated as VIS), has also been linked to morbid postoperative outcomes.²⁸ The other two independent AKI-predictive factors, including advanced age and MHAR in diabetic patients, herald a plausible constellation of inflammaging and metaflammation.²

In the context of a CSA-AKI-predictive value of MHAR outlined in the present study, the literature is replete with the prognostic importance of preoperative MHR^{10–16} and albumin.^{21,22} While substantial research proposes a prognostic role of MHR in nonoperative settings (including cardiac patients),^{13–16} there remains a dearth of studies featuring the role of the former in cardiac surgery. Herein, the findings of the research group led by Saskin et al deserve mention, which highlight the association of an elevated preoperative MHR with postoperative AF in a retrospective analysis of 662 patients undergoing on-pump CABG.¹⁰ They outline a MHR \geq 0.0185 as the AF-predictive cutoff (AUC: 0.835; sensitivity: 84.6%; specificity: 81.0%) whereas a MHR \geq 15.25 (AUC: 0.754; sensitivity: 93.12%; specificity: 86.68%) emerged as the AKI-predictive cutoff in our study. This is explained by the fact that Saskin et al consideration of

Table 1 Comparison of preoperative patient characteristics and laboratory parameters between AKI and non-AKI groups

Parameter	AKI group (n = 109)	Non-AKI group	p-Value
Age (y)	65.72 ± 8.84	62.6 ± 9.30	< 0.001
Female	21 (19.27)	103 (17.82)	0.719
BMI (kg/m ²)	24.25 ± 2.33	23.98 ± 2.00	0.301
Smoking	43 (39.45)	198 (34.26)	0.297
Family history	50 (45.87)	314 (54.33)	0.105
Hypertension	71 (65.14)	304 (52.6)	0.016
Hyperlipidemia	62 (56.88)	302 (52.25)	0.374
Peripheral vascular disease	12 (11.01)	76 (13.15)	0.540
COPD	6 (5.5)	24 (4.15)	0.607
Preop CHF	17 (15.6%)	38 (6.57)	< 0.001
Prior MI	26 (23.85)	167 (28.89)	0.283
LVEF (%)	48.05 ± 7.60	49.45 ± 7.18	0.083
EuroSCORE-II	3.6 ± 1.6	3.0 ± 1.7	< 0.001
Left main disease	37 (33.94)	151 (26.12)	0.093
Preoperative CAG	22 (20.18)	106 (18.33)	0.651
ACE inhibitor use	46 (42.2)	232 (40.14)	0.687
Statin use	53 (48.62)	303 (52.42)	0.467
Beta blocker use	62 (56.88)	352 (60.9)	0.432
Hb (g/dL)	12.02 ± 1.26	12.18 ± 0.70	0.148
TLC (×10 ³ /mm ³)	8.24 ± 1.99	8.07 ± 1.83	0.818
ANC (cells/mm ³)	4137 ± 1306	4041 ± 911	0.242
ALC (cells/mm ³)	3252 ± 887	3364 ± 918	0.260
AMC (cells/mm ³)	543 ± 110	526 ± 109	0.073
HDL (mg/dL)	38.06 ± 6.24	39.72 ± 8.54	0.259
MHR	14.75 ± 4.28	13.8 ± 3.94	0.037
Serum creatinine (mg/dL)	1.11 ± 0.59	0.99 ± 0.36	0.518
Serum albumin (g/dL)	3.34 ± 0.65	3.53 ± 0.61	0.003
MHAR	4.60 ± 1.61	4.08 ± 1.54	< 0.001
AST (IU/L)	56.23 ± 14.59	57.59 ± 15.39	0.404
ALT (IU/L)	55.64 ± 14.46	58.25 ± 15.69	0.235

Abbreviations: ACE, angiotensin-converting enzyme; AKI, acute kidney injury; ALC, absolute lymphocyte count; ALT, alanine aminotransferase; AMC, absolute monocyte count; ANC, absolute neutrophil count; AST, aspartate transaminase; BMI, body mass index; CAG, coronary angiogram; CHF, congestive heart failure; COPD, chronic obstructive pulmonary disease; EuroSCORE-II, European System for Cardiac Operative Risk Evaluation II; Hb, hemoglobin; HDL, high-density lipoprotein; LVEF, left ventricular ejection fraction; MHAR, monocyte/high-density lipoprotein × albumin ratio; MHR, monocyte/high-density lipoprotein ratio; MI, myocardial infarction; TLC, total leucocyte count.

Note: Data are presented as a mean ± standard deviation or number (%). p-Values < 0.05 are italicized.

monocyte cell lineages introduced a divisible factor of 1,000 to obtain the corresponding MHR values.¹⁰

Akin to the study by Saskin et al¹⁰ and another study by Tekkesin et al,¹¹ we also discovered a higher incidence of postoperative AF in our patients having a preoperative MHAR values higher than the computed AKI-predictive cutoff. In addition, MACE transpired with a higher incidence in these patients which is in harmony with the Cetin et al¹³ description of an elevated risk of MACE in patients of acute coronary syndrome with an elevated MHR.

In another evaluation of 145 patients who underwent transcatheter aortic valve implantation by Karahan and Okuyan, the mortality remarkably increased from 4.1 to 76.1% owing to an elevation of MHR above the median value of 13.73.¹² Alongside a 50% mortality risk accentuation for every 1 unit increase in MHR in the study, the ratio correlated positively with C-reactive protein, suggesting a proinflammatory predisposition at the cornerstone of an enhanced mortality.¹² Albeit an underlying CAD being implicated for such an exorbitant mortality association of MHR by Karahan

Table 2 Comparison of perioperative clinical parameters compared between AKI and non-AKI groups

Parameter	AKI group (n = 109)	Non-AKI group (n = 578)	p-Value
Duration of surgery (min)	253.93 ± 30.84	249.83 ± 26.51	0.199
No. of grafts	2.89 ± 0.59	2.86 ± 0.51	0.274
PRBC transfused	1.21 ± 0.77	0.95 ± 0.82	<i>0.002</i>
Mean CVP (mm Hg)	10.40 ± 2.85	9.99 ± 1.91	0.101
Mean VIS	14.72 ± 5.71	12.83 ± 4.72	<i>< 0.001</i>
LCOS	7 (6.42)	9 (1.56)	<i>0.007</i>
Postoperative RRT	9 (8.25)	0 (0.00)	<i>< 0.001</i>
Duration of MV (h)	82.07 ± 48.12	71.19 ± 42.60	<i>0.030</i>
LOS ICU (d)	4.67 ± 2.01	4.22 ± 1.78	<i>0.030</i>
LOS hospital (d)	8.66 ± 1.99	8.06 ± 1.69	<i>0.015</i>

Abbreviations: AKI, acute kidney injury; CVP, central venous pressure; ICU, intensive care unit; LCOS, low cardiac output syndrome; LOS, length of stay; MV, mechanical ventilation; PRBC, packed red blood cell; RRT, renal replacement therapy; VIS, vasoactive-inotropic score.

Note: Data are presented as a mean ± standard deviation or number (%). p-Values < 0.05 are italicized.

and Okuyan, Dolapoglu et al²⁹ failed to discover any association between MHR and morbidity–mortality following CABG. Despite a degree of contradiction in the preliminary reports, the recent description of MHR as a biomarker of diabetic nephropathy by Karatas et al²⁰ supports our finding of an AKI-predictive value of MHAR in diabetic cardiac surgical patients.

The prognostic importance of preoperative hypoalbuminemia can simultaneously not be underemphasized. Specific to literature on coronary revascularization, low albumin levels predict the risk of postoperative AKI, both in diabetics and nondiabetics.^{21,22} Interestingly, the Akboga et al observation of low serum albumin levels in post-CABG patients (with saphenous vein graft disease) demonstrating higher MHR, pinpoints the possible links between the two independent markers of prognostic importance.¹⁷ At the same time,

the depiction of an all-cause mortality predictive value of monocyte/albumin ratio in settings of percutaneous coronary interventions by Zhang et al, is equally noteworthy.³⁰

Delving into the pathophysiology, the incremental value of MHAR over MHR and albumin possibly highlights a perilous liaison of malnutrition and inflammation. MHR derives its prognostic value from the combined proinflammatory potential of monocyte activation and the anti-inflammatory effects of HDL.³¹ This becomes all the more relevant in the light of literature to support an augmented targeted priming of monocytes to an inflammatory state in patients with lipid profile perturbations.³² While MHR can hence be equated with proinflammation, the dual relationship of hypoalbuminemia with malnutrition and inflammation,⁸ is expected to compound the postoperative outcomes furthermore. This is adequately highlighted in the anti-inflammatory,

Table 3 Univariate and multivariate regression analysis of demographic and perioperative parameters for predicting the occurrence of postoperative AKI

Parameter	Univariate analysis			Multivariate analysis		
	OR	95% CI	p-Value	OR	95% CI	p-Value
Age	1.038	1.014–1.061	<i>< 0.001</i>	1.029	1.005–1.054	<i>0.020</i>
Hypertension	1.594	1.388–1.910	<i>0.016</i>	1.297	0.806–2.087	0.295
Preop CHF	1.381	1.206–1.703	<i>< 0.001</i>	1.351	0.745–2.197	0.074
EuroSCORE-II	1.270	1.112–1.450	<i>< 0.001</i>	1.264	1.100–1.451	<i>< 0.001</i>
MHR	1.058	1.007–1.112	<i>0.037</i>	1.171	0.963–1.428	0.120
Serum albumin	0.619	0.448–0.854	<i>0.003</i>	0.351	0.129–0.951	0.085
MHAR	1.493	1.153–1.932	<i>< 0.001</i>	1.403	1.073–1.833	<i>0.013</i>
PRBC transfused	1.214	1.075–1.370	<i>0.002</i>	1.146	0.924–1.282	0.199
VIS	1.083	1.037–1.130	<i>< 0.001</i>	1.074	1.027–1.123	<i>0.002</i>
LCOS	1.809	1.344–2.837	<i>0.007</i>	1.772	0.762–2.703	0.091

Abbreviations: AKI, acute kidney injury; CHF, congestive heart failure; CI, confidence interval; EuroSCORE-II, European System for Cardiac Operative Risk Evaluation II; LCOS, low cardiac output syndrome; MHAR, monocyte/high-density lipoprotein × albumin ratio; MHR, monocyte/high-density lipoprotein ratio; OR, odds ratio; PRBC, packed red blood cell; VIS, vasoactive-inotropic score.

Note: p-Values < 0.05 are italicized.

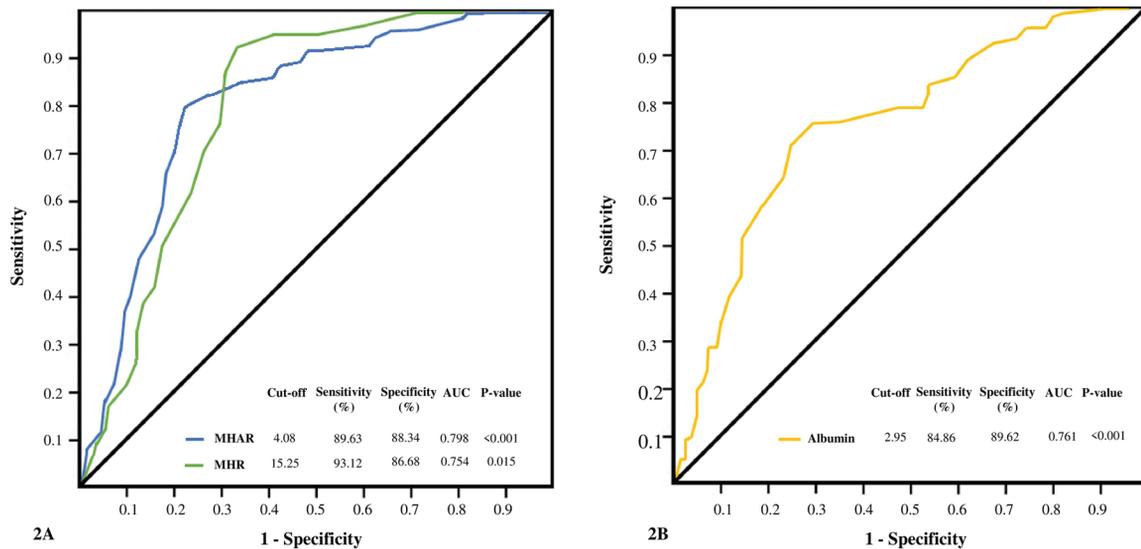


Fig. 2 (A) The AKI-predictive potential of MHR and MHAR assessed in context of AUC under ROC curve delineating the highest AUC of 0.798 for MHAR. The AKI-predictive cutoff values of the parameters have been presented in the lower part of the figure. (B) ROC curve for albumin in terms of AUC delineating the highest AUC of 0.761 for prediction of AKI. The predictive cutoff value of the albumin has been presented in the lower part of the figure. AKI, acute kidney injury; AUC, area under curve; MHAR, monocyte/high-density lipoprotein × albumin ratio; MHR, monocyte/high-density lipoprotein ratio; ROC, receiver operating characteristic.

Table 4 Comparison of postoperative complications between the groups with MHAR ≥ cutoff value and MHAR < cutoff value

Parameter	MHAR ≥ Cutoff	MHAR < Cutoff	p-Value
MACE	14 (2.04)	6 (0.87)	<i>0.016</i>
AF	98 (14.26)	52 (7.57)	<i>< 0.001</i>
LCOS	7 (1.02)	9 (1.31)	0.305
Sepsis	5 (0.73)	8 (1.16)	0.079

Abbreviations: AF, atrial fibrillation; LCOS, low cardiac output syndrome; MACE, major adverse cardiac events; MHAR, monocyte/high-density lipoprotein × albumin ratio.

Note: Data are presented as number (%). p-Values < 0.05 are italicized.

antioxidative stress and osmotic effects of albumin.⁸ The aforementioned explains the synergy behind the independent prognostic role of the novel MHAR highlighted in our multivariate analysis.

Strengths and Limitations

To the best of the authors' knowledge, the present study classifies as a maiden research endeavor of evaluating the AKI-predictive of a novel ratio, MHAR. Moreover, the study included a homogeneous cohort of diabetic patients who are peculiarly predisposed to AKI. The isolated evaluation of OPCABG patients additionally obviates the possible deleterious renal effects of extracorporeal circulatory conduct.^{33,34} However, the study had a few limitations. First, the retrospective study design is prone to residual confounding.³⁵ This is particularly pertinent in the context of CSA-AKI which is essentially multifactorial.^{33,34} Second, the lack of availability of the renal oxygenation monitoring trends (near-infrared spectroscopy based) for all the included cases, is an additional limitation.³⁶ Third, the inclusion of other markers

of malnutrition, frailty, and/or inflammation could have enhanced the lucidity of the study findings.

Conclusion

Preoperative elevation of MHAR independently predicted postoperative AKI in the retrospective evaluation of our diabetic patients undergoing OPCABG. While the novel ratio concocts the nutritional and inflammatory predisposition and can potentially assist risk stratification and individualization^{37,38} of targeted therapy, future prospective studies are warranted to validate the initial encouraging findings across diverse clinical settings.

Conflict of Interest

None declared.

References

- 1 Aravindhan V, Madhumitha H. Meta-inflammation in diabetic coronary artery disease: emerging role of innate and adaptive immune responses. *J Diabetes Res* 2016;2016:6264149

- 2 Prattichizzo F, De Nigris V, Spiga R, et al. Inflammation and metaflammation: the yin and yang of type 2 diabetes. *Ageing Res Rev* 2018;41:1–17
- 3 Hotamisligil GS. Inflammation, metaflammation and immunometabolic disorders. *Nature* 2017;542(7640):177–185
- 4 Jenkins DJA, Dehghan M, Mentz A, et al; PURE Study Investigators. Glycemic index, glycemic load, and cardiovascular disease and mortality. *N Engl J Med* 2021;384(14):1312–1322
- 5 Magoon R, Makhija N. Endothelial glycocalyx and cardiac surgery: newer insights. *J Cardiothorac Vasc Anesth* 2020;34(01):310–311
- 6 Dey S, Kashav R, Kohli JK, et al. Systemic immune-inflammation index predicts poor outcome after elective off-pump CABG: a retrospective, single-center study. *J Cardiothorac Vasc Anesth* 2021;35(08):2397–2404
- 7 Unosawa S, Taoka M, Osaka S, et al. Is malnutrition associated with postoperative complications after cardiac surgery? *J Card Surg* 2019;34(10):908–912
- 8 Don BR, Kaysen G. Serum albumin: relationship to inflammation and nutrition. *Semin Dial* 2004;17(06):432–437
- 9 Jain S, Gautam V, Naseem S. Acute-phase proteins: as diagnostic tool. *J Pharm Bioallied Sci* 2011;3(01):118–127
- 10 Saskin H, Serhan Ozcan K, Yilmaz S. High preoperative monocyte count/high-density lipoprotein ratio is associated with postoperative atrial fibrillation and mortality in coronary artery bypass grafting. *Interact Cardiovasc Thorac Surg* 2017;24(03):395–401
- 11 Tekkesin AI, Hayiroglu MI, Zehir R, et al. The use of monocyte to HDL ratio to predict postoperative atrial fibrillation after aorto-coronary bypass graft surgery. *North Clin Istanbul* 2017;4(02):145–150
- 12 Karahan S, Okuyan E. Monocyte-to-high density lipoprotein cholesterol ratio as a predictor of mortality in patients with transcatheter aortic valve replacement. *Eur Rev Med Pharmacol Sci* 2021;25(16):5153–5162
- 13 Cetin MS, Ozcan Cetin EH, Kalender E, et al. Monocyte to HDL cholesterol ratio predicts coronary artery disease severity and future major cardiovascular adverse events in acute coronary syndrome. *Heart Lung Circ* 2016;25(11):1077–1086
- 14 Korkmaz A, Demir M, Unal S, et al. Monocyte-to-high density lipoprotein ratio (MHR) can predict the significance of angiographically intermediate coronary lesions. *Int J Cardiovasc Acad* 2017;3:16–20
- 15 Ya G, Qiu Z, Tianrong P. Relation of monocyte/high-density lipoprotein cholesterol ratio with coronary artery disease in type 2 diabetes mellitus. *Clin Lab* 2018;64(06):901–906
- 16 Sercelik A, Besnili AF. Increased monocyte to high-density lipoprotein cholesterol ratio is associated with TIMI risk score in patients with ST-segment elevation myocardial infarction. *Rev Port Cardiol (Engl Ed)* 2018;37(03):217–223(Engl Ed)
- 17 Akboga MK, Yayla C, Balci KG, et al. Relationship between serum albumin level and monocyte-to-high-density lipoprotein cholesterol ratio with saphenous vein graft disease in coronary bypass. *Thorac Cardiovasc Surg* 2017;65(04):315–321
- 18 Marcheix B, Vanden Eynden F, Demers P, Bouchard D, Cartier R. Influence of diabetes mellitus on long-term survival in systematic off-pump coronary artery bypass surgery. *Ann Thorac Surg* 2008;86(04):1181–1188
- 19 Ramos KA, Dias CB. Acute kidney injury after cardiac surgery in patients without chronic kidney disease. *Rev Bras Cir Cardiovasc* 2018;33(05):454–461
- 20 Karatas A, Turkmen E, Erdem E, Dugeroglu H, Kaya Y. Monocyte to high-density lipoprotein cholesterol ratio in patients with diabetes mellitus and diabetic nephropathy. *Biomarkers Med* 2018;12(09):953–959
- 21 Aksoy R, Adademir T, Yilmaz E, et al. Is hypoalbuminemia a predictor for acute kidney injury after coronary bypass grafting in diabetes mellitus patients? *Rev Bras Cir Cardiovasc* 2019;34(05):565–571
- 22 Lee EH, Baek SH, Chin JH, et al. Preoperative hypoalbuminemia is a major risk factor for acute kidney injury following off-pump coronary artery bypass surgery. *Intensive Care Med* 2012;38(09):1478–1486
- 23 Mehta RL, Kellum JA, Shah SV, et al; Acute Kidney Injury Network. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. *Crit Care* 2007;11(02):R31
- 24 Antonelli M, Levy M, Andrews PJ, et al. Hemodynamic monitoring in shock and implications for management. International Consensus Conference, Paris, France, 27–28 April 2006. *Intensive Care Med* 2007;33(04):575–590
- 25 Belletti A, Lerose CC, Zangrillo A, Landoni G. Vasoactive-inotropic score: evolution, clinical utility, and pitfalls. *J Cardiothorac Vasc Anesth* 2021;35(10):3067–3077
- 26 Beattie WS, Wijeyesundera DN, Chan MTV, et al; ANZCA Clinical Trials Network for the ENIGMA-II Investigators. Implication of major adverse postoperative events and myocardial injury on disability and survival: a planned subanalysis of the ENIGMA-II trial. *Anesth Analg* 2018;127(05):1118–1126
- 27 Kapoor PM, Magoon R, Rawat RS, et al. Goal-directed therapy improves the outcome of high-risk cardiac patients undergoing off-pump coronary artery bypass. *Ann Card Anaesth* 2017;20(01):83–89
- 28 Magoon R, Makhija N, Das D. Vasoplegic syndrome after cardiac surgery: better the devil you know!. *J Card Surg* 2019;34(12):1679–1680
- 29 Dolapoglu A, Avci E, Kizilgul M. Monocyte count to HDL-cholesterol level ratio on post-operative outcome after coronary bypass surgery. *Tepecik Egit ve Arast HastDergisi* 2018;28:187–190
- 30 Zhang ZL, Guo QQ, Tang JN, et al. Monocyte-to-albumin ratio as a novel predictor of long-term adverse outcomes in patients after percutaneous coronary intervention. *Biosci Rep* 2021;41(07):BSR20210154
- 31 Libby P. Inflammation in atherosclerosis. *Arterioscler Thromb Vasc Biol* 2012;32(09):2045–2051
- 32 Patel VK, Williams H, Li SCH, Fletcher JP, Medbury HJ. Monocyte inflammatory profile is specific for individuals and associated with altered blood lipid levels. *Atherosclerosis* 2017;263:15–23
- 33 Magoon R, Dey S, Walian A, Kashav R. Nitric oxide: renoprotective in cardiac surgery!. *Rev Bras Cir Cardiovasc* 2020;35(04):602–603
- 34 Kapoor PM, Karanjkar A, Magoon R, et al. Effect of goal-directed therapy on post-operative neutrophil gelatinase-associated lipocalin profile in patients undergoing on-pump coronary artery surgery. *Indian J Thorac Cardiovasc Surg* 2019;35(03):445–452
- 35 Magoon R, Jose J. Safeguarding anaesthesia research from spin. *Br J Anaesth* 2020;125(06):e460–e462
- 36 Tholén M, Ricksten SE, Lannemyr L. Renal near-infrared spectroscopy for assessment of renal oxygenation in adults undergoing cardiac surgery: a method validation study. *J Cardiothorac Vasc Anesth* 2020;34(12):3300–3305
- 37 Magoon R. Implications of practice variability: comment. *Anesthesiology* 2020;133(04):943–944
- 38 Magoon R. Precision cardiac anaesthesia: welcome aboard!. *J Cardiothorac Vasc Anesth* 2020;34(09):2551–2552