Temporal Changes in Inflammation, Oxidative Stress, Apoptosis, and Endothelial Glycocalyx Degradation in Correlation to Organ Function Assessment Following On-Pump Coronary Artery Bypass Graft Surgery

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ABSTRACT

Background: *A coronary artery bypass graft is a complex procedure that can cause various physiological responses, including inflammation, oxidative stress, apoptosis, and endothelial dysfunction. Nevertheless, the correlation between these responses with organ function after CABG has not yet been established. This study aims to investigate the correlation between inflammation, oxidative stress, apoptosis, endothelial dysfunction markers, and postoperative organ function assessment as evaluated by the Cardiac Surgery Score (CASUS).* ***Methods:*** *A prospective cohort study was conducted on patients undergoing coronary artery bypass graft from two hospitals in Jakarta. IL-6, MDA, caspase-3, and syndecan-1 levels were measured at three points in time: before surgery, on ICU Day-1, and ICU Day-2. Postoperative organ function was assessed on ICU Day 2 by Cardiac Surgery Score (CASUS).* ***Results:*** *Fifty-one patients were included in the study. There was a positive correlation between IL-6 measured before surgery ($r = 0.325$, $p = 0.020$) and at the time of admission to the ICU ($r = 0.374$, $p = 0.007$). Positive correlation was also found between syndecan-1 levels on ICU day 1 ($r = 0.304$, $p = 0.030$) with CASUS. MDA correlated with CASUS on ICU day 2 ($r = 0.392$, $p = 0.004$); meanwhile, no significant association was found between caspase-3 and postoperative organ function assessment.*

***Conclusion**: Interleukin-6 levels pre-surgery and on ICU day 1, syndecan-1 levels on ICU day 1, and MDA levels on ICU day 2 were correlated with CASUS.*

***Keywords**: IL-6, MDA, caspase-3, syndecan-1, cardiac surgery score, coronary artery bypass graft.*

INTRODUCTION

Coronary artery bypass grafting (CABG) is a major surgical procedure that involves bypassing atheromatous blockages in the coronary arteries using harvested venous or arterial conduits, restoring blood flow to the ischemic myocardium, and alleviating angina symptoms. With nearly 400,000 surgeries performed annually, CABG is one of the most common major surgeries. However, the procedure, particularly when utilizing cardiopulmonary bypass (CPB), initiates complex physiological responses, including inflammation, oxidative stress, and reperfusion injury. These reactions can lead to endothelial dysfunction, cell death, and organ failure. CPB, which temporarily substitutes the heart and lungs, exacerbates the inflammatory response by activating immune pathways and causing an imbalance in cytokines.[1,2]

The inflammatory response and oxidative stress are closely linked in CABG surgery. Neutrophils, which are the primary source of reactive oxygen species (ROS), release pro-inflammatory mediators and enzymes that damage endothelial cells.[3,4] This process leads to lipid peroxidation, with malondialdehyde (MDA) serving as a marker of oxidative stress. The high levels of MDA disrupt the integrity of cell membranes, contributing to cellular dysfunction and initiating apoptosis.[4-8] Apoptotic cell death, particularly in endothelial cells, is mediated by caspases such as caspase-3, which is activated during the extrinsic (death receptor) and intrinsic (mitochondrial) apoptotic pathways. Caspase-3 activation plays a crucial role in inducing cell death and amplifying the inflammatory cascade.[9]

Furthermore, CPB causes significant damage to the endothelial glycocalyx, which is vital for vascular health. During surgery, inflammatory cytokines like TNF-α and IL-6 trigger the breakdown of glycocalyx components, including syndecan-1 and heparan sulfate. Syndecan-1, a marker of glycocalyx degradation, has been found to increase significantly following CPB, indicating the extent of endothelial injury. This degradation impairs microvascular perfusion and promotes systemic organ dysfunction. Studies have shown that the levels of syndecan-1 correlate with inflammatory cytokines, including IL-6, and markers of oxidative stress, underscoring the relevance of these factors in the pathophysiology of CABG-related complications.[10-12]

The CASUS (Cardiac Surgery Score) is a scoring system designed to assess organ dysfunction severity in cardiac surgery patients. Despite its limited utilization, it offers a comprehensive evaluation by incorporating parameters including hemodynamic factors, CPB-related procedures, lactate, creatinine, inflammatory cytokines (such as IL-6 and TNF-α), oxidative stress, and endothelial dysfunction. This approach facilitates precise evaluation of organ function and the potential for complications following surgical intervention.[15,16] This study aimed to examine the correlation between inflammation, oxidative stress, apoptosis, endothelial dysfunction, and postoperative organ function assessment, as reflected by the CASUS score, in patients undergoing coronary artery bypass graft surgery.

METHODS

Study, Design, and Setting

A prospective cohort study was conducted on 61 consecutive patients scheduled for on-pump CABG surgery at the Cipto Mangunkusumo General Hospital and Jakarta Heart Center (Jakarta, Indonesia) from April to August 2023. Patients who were unwilling to participate or who underwent cardiac surgery other than isolated CABG were excluded.

Data Collection

Demographic characteristics were collected, including the patient's age, gender, and comorbidities (such as diabetes mellitus,

hypertension, kidney disease, dyslipidemia, stroke, and smoking status), along with clinical characteristics that included BMI, left ventricular ejection fraction, CPB time, AOX time, cardiac output, mean arterial pressure, IL-6, MDA, caspase-3, and syndecan-1. Postoperative organ function was evaluated using the Cardiac Surgery Score (CASUS), which consists of 10 parameters, each scored from 0 to 4. The total score was calculated on ICU Day 2.

Follow-up and determination of organ dysfunction

All patients were prospectively followed throughout their clinical course, starting from hospital admission, preoperative preparation, surgery, and ICU. Organ function was evaluated using CASUS, a validated scoring system for evaluating organ failure in patients undergoing cardiac surgery. IL-6, MDA, Caspase-3, and Syndecan-1 levels were measured at three points in time: before surgery, upon arrival in the ICU (ICU Day-1), and 24 hours postoperatively (ICU Day-2). CASUS was calculated at ICU Day-2 (24 hours postoperatively), using standardized clinical and laboratory parameters. On both ICU Day-1 and Day-2, ten CASUS parameters were evaluated. Each parameter has a score ranging from 0 to 4, and the total CASUS score is calculated by summing the values of all parameters.

Sample Collection and Measurement

Inflammation was defined by measuring plasma levels of interleukin-6 (IL-6), assessed using enzyme-linked immunosorbent assay (ELISA) kits according to the manufacturer's protocol. Oxidative stress was assessed by determining malondialdehyde (MDA) concentration via the Thio barbituric acid reactive substances (TBARS) method, with values expressed in μM. Apoptosis was assessed by measuring caspase-3 with ELISA kits. Endothelial glycocalyx degradation was assessed by measuring syndecan-1 levels with ELISA kits.

Statistical Analysis

All statistical analysis was conducted using STATA version 16.0 (Stata Corp LLC). The correlation between IL6, caspase-3, MDA, and syndecan-1 levels with CASUS was assessed using the Pearson test or the Spearman test if the data were not normally distributed. Additionally, a determinate analysis will evaluate whether the patient's clinical characteristics are associated with the findings.

Ethical Approval

The study was approved by the Ethical Committee (KET-886/UN2.F1/ETIK/PPM.00.02/2022). Before enrollment, the patients were informed about the study protocol, and written informed consent was obtained.

RESULTS

The inclusion and exclusion process of study participants is summarized in **Figure 1**. Out of 61 patients who underwent elective on-pump CABG during the study period, 9 were excluded due to having other cardiac procedures, and 1 patient declined to participate, resulting in a total of 51 patients included in the final analysis.

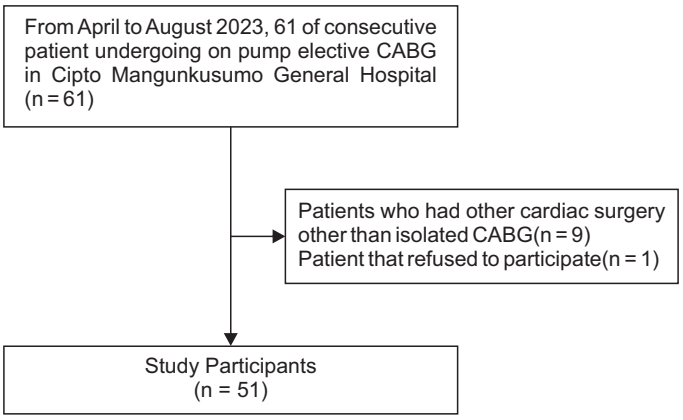

Figure 1. Inclusion and Exclusion of Study Patients

Table 1 presents the clinical and demographic characteristics of the patients. The mean age of the subjects is 60.9 years, and 80.4% of them are male. Patients had multiple comorbidities, with hypertension and type 2 diabetes being the most common comorbidities.

Table 2 presents the correlation between variables including inflammatory markers (IL-6), oxidative stress markers (MDA), apoptosis markers (caspase-3), and endothelial dysfunction markers (syndecan-1) and postoperative organ function as evaluated by the CASUS.

Among all the variables examined, only IL-6, MDA, and syndecan-1 levels demonstrated a statistically significant correlation with CASUS, indicating their temporary changes might be related to the development of organ dysfunction following CABG surgery.

IL-6 levels measured on pre-surgery (r = 0.325) and ICU Day-1 (r = 0.374) were positively correlated with CASUS. This indicates that an increase in IL-6 levels is associated with greater severity of postoperative organ dysfunction.

MDA levels showed a significant correlation with CASUS (r = 0.392). Syndecan-1 levels measured on ICU Day-1 (r = 0.304) also showed

Table 1. Demographic and Clinical Characteristics of CABG Patients

Variables	Total (n = 51)
Age (y), mean (SD)	60.9 (6.7)
Male, n (%)	41 (80.4)
BMI (kg/m^2), mean (SD)	26.5 (4.2)
Comorbidities (n, %)	
Hypertension	34 (66.7)
Diabetes Mellitus	27 (52.9)
Smoking	12 (25.5)
Stroke	7 (13.7)
Dyslipidemia	6 (11.8)
Kidney Disease	5 (9.8)
ACEF score, median (IQR)	1 (0.95-1.13)
EuroSCORE, median (IQR)	1 (0-2)
Cardiac Output	
ICU Day-1 (L/m), median (IQR)	4.4 (3.9-5.0)
ICU Day-2 (L/m), median (IQR)	4.3 (3.7-4.8)
Mean Arterial Pressure	
ICU Day-1 (mmHg), median (IQR)	83 (75-95)
ICU Day-2 (mmHg), median (IQR)	71 (67-78)
CPB time (min), median (IQR)	89 (49-172)
AOX time (min), median (IQR)	
IL-6	
Pre-operation (pg/mL), median (IQR)	2.42 (1.46-3.23)
ICU Day-1 (pg/mL), median (IQR)	137.33 (56.32-276.97)
ICU Day-2 (pg/mL), median (IQR)	103.78 (38.11-243.86)
MDA	
Pre-operation (μM), median (IQR)	3.57 (2.84-4.78)
ICU Day-1 (μM), median (IQR)	3.73 (3.17-4.73)
ICU Day-2 (μM), median (IQR)	3.86 (3.11-4.43)
Caspase-3	
Pre-operation (ng/mL), median (IQR)	0.17 (0.13-0.28)
ICU Day-1 (ng/mL), median (IQR)	0.16 (0.12-0.27)
ICU Day-2 (ng/mL), median (IQR)	0.17 (0.11-0.26)
Syndecan-1	
Pre-operation (ng/mL), median (IQR)	12.7 (10.2-15.3)
ICU Day-1 (ng/mL), median (IQR)	43.7 (30.2-69.7)
ICU Day-2 (ng/mL), median (IQR)	36.1 (16.2-74.1)

IQR: interquartile range, SD: standard deviation

a significant positive correlation with CASUS. These findings suggest that oxidative stress and endothelial dysfunction, reflected by elevated MDA and syndecan-1 levels, are associated with the extent of organ function following CABG surgery.

The immune responses in our patients align with previous studies, indicating that cardiac surgery triggers an unpredictable immune response due to blood exposure to artificial surfaces, shear stress, and surgical trauma. IL-6 levels rise during cardiopulmonary bypass (CPB), reach a plateau by the end of the surgery, and persist for 224 hours postoperatively, with variability among patients.[38] While many studies link CPB to immune responses, limited research explores the impact of CPB duration. Longer CPB time correlates with increased inflammation, oxidative stress, apoptosis, glycocalyx degradation, and elevated biomarkers like IL-6, syndecan-1, and CASUS.[17,18]

IL-6 ICU Day-1 (r = 0.515) and Syndecan-1 ICU Day-2 (r = 0.302) both have a weak association with CPB time, suggesting that the longer CPB time might increase IL-6 and syndecan-1 levels. Meanwhile, organ function evaluated with CASUS showed a significant association with CPB time on ICU Day-1 (r = 0.309) and ICU Day-2 (r = 0.424).

Table 2. Correlation between Inflammatory, Oxidative Stress, Apoptosis, Endothelial Glycocalyx Degradation Markers and Postoperative Organ Function Assessment

Biomarkers	CASUS ICU Day-2
Il-6 pre-surgery	r = 0.325*
Il-6 ICU Day-1	r = 0.374*
Il-6 ICU Day-2	r = 0.248
MDA pre-surgery	r =- 0.113
MDA ICU Day-1	r = -0.050
MDA ICU Day-2	r = 0.392*
Caspase-3 pre-surgery	r =0.131
Caspase-3 ICU Day-1	r = 0.039
Caspase-3 ICU Day-2	r = -0.044
Syndecan-1 pre-surgery	r = 0.070
Syndecan-1 ICU Day-1	r = 0.304*
Syndecan-1 ICU Day-2	r = 0.173

* $p < 0.05$ (Spearman's rank correlation test)

Table 3. Correlation between CPB time and Inflammatory, Oxidative Stress, Apoptosis, Endothelial Glycocalyx Degradation Markers and Postoperative Organ Function Assessment

Parameter	CPB time
Il-6 pre-surgery	r = 0.234
Il-6 ICU Day-1	r = 0.515*
Il-6 ICU Day-2	r = 0.078
MDA pre-surgery	r = 0.176
MDA ICU day-1	r = -0.049
MDA ICU day-2	r = 0.275
Caspase-3 pre-surgery	r = 0.230
Caspase-3 ICU day-1	r = 0.093
Caspase-3 ICU Day-2	r = -0.039
Syndecan-1 pre-surgery	r = 0.062
Syndecan-1 ICU Day-1	r = 0.210
Syndecan-1 ICU Day-2	r = 0.302*
CASUS ICU Day-1	r = 0.309*
CASUS ICU Day-2	r = 0.424*

* $p < 0.05$ (Spearman's rank correlation test)

DISCUSSION

This study aims to deepen the understanding of the correlation between inflammation, oxidative stress, apoptosis markers, and endothelial dysfunction with postoperative organ function assessment in CABG patients. There are significant correlations between inflammatory markers (IL-6), oxidative stress markers (MDA), and endothelial dysfunction markers (syndecan-1) with postoperative organ function assessment based on CASUS. Meanwhile, the apoptosis marker (caspase-3) has no significant association with postoperative organ function assessment based on CASUS.

IL6 and Organ Function Assessment

The elevated levels of IL-6 postoperatively, as observed by Musleh et al,[13] show a significant correlation with the risk of acute renal dysfunction in patients undergoing CABG. Specifically, IL-6 levels greater than 100 pg/ml, measured 12 hours after surgery, were associated with a 1.3-fold increased risk of renal dysfunction ($p < 0.017$). Additionally, Hudetz et al[14] found that IL-6 concentrations were significantly correlated with cognitive function outcomes, with higher IL-6 levels being linked to poorer cognitive performance at 1 week after surgery ($p = 0.04$). These findings further emphasize the role of IL-6 as a predictor of postoperative complications after CABG. Our study aligns with these findings, showing a similar relationship between elevated IL-6 levels post-CABG and the occurrence of organ dysfunction, as indicated by higher CASUS scores.

IL-6 is a key pro-inflammatory cytokine that plays a central role in the systemic inflammatory response following CABG, particularly when CPB is used. Ischemia-reperfusion injury and surgical trauma stimulate the release of IL-6 from activated leukocytes, endothelial cells, and cardiac myocytes. This elevation in IL-6 initiates a cascade of inflammatory responses that can impair organ function.[19,22]

IL-6 promotes endothelial activation and increases vascular permeability, which can lead to interstitial edema, impaired tissue perfusion, and microcirculatory dysfunction.[10] These changes compromise oxygen delivery to vital organs, contributing to the development of organ dysfunction. Furthermore, IL-6 is involved in the pathogenesis of SIRS, a condition that can lead to multiple organ dysfunction syndrome (MODS).[3,10]

Elevated IL-6 levels have also been associated with myocardial depression, renal impairment, and longer durations of mechanical ventilation and hospitalization in post-cardiac surgery patients.[19,20] According to Bauer et al.[19], IL-6 is a reliable predictor of poor in-hospital outcomes following cardiac surgery. These findings are backed by several studies showing significant correlations between IL-6 levels and adverse postoperative events, including endothelial dysfunction, cardiac impairment, and kidney injury.[23,24] Therefore, perioperative measurement and potential modulation of IL-6 may offer a valuable strategy in identifying high-risk patients and improving postoperative outcomes.

MDA and Organ Function Assessment

Dias et al.[6] and Djordjevic et al.[5] have found significant changes in oxidative stress levels following CABG. This study identified an association between MDA and CASUS 24 hours after surgery. This lack of association may be due to a difference in the peak concentration time for this marker compared to the timing of organ dysfunction. Djordjevic et al.[5], found that the peak concentration of MDA occurred 12 hours after surgery, suggesting that MDA requires more time to reach its peak. The levels then decrease over the following 12 hours and stabilize between 24 – 48 hours. This aligns with our study findings, where MDA levels were not associated with ICU Day-1 outcomes because, at that time point (2 hours post-surgery), MDA levels had not yet risen significantly, while other factors such as IL-6 had already increased markedly alongside elevated CASUS scores. However, MDA levels were correlated with CASUS scores on ICU Day-2. From a pathophysiological perspective, MDA tends to decline within 24–48 hours, corresponding with decreasing CASUS scores or an improving clinical condition.

Syndecan-1 and Organ Function Assessment

Cavalcante et al.[25] demonstrated that syndecan-1 is associated with organ dysfunction.

In their study involving 289 patients undergoing cardiac surgery, early postoperative levels of syndecan-1 were significantly related to acute kidney injury (OR 1.42–8.87), which is one of the components of the CASUS score. The diagnostic accuracy of syndecan-1 for predicting severe kidney injury was moderate, with an AUC of 0.77 (95% CI: 0.68–0.85). Additionally, syndecan-1 levels were linearly related to longer ICU stays and prolonged hospitalization.

Similar results were reported by Lin et al., who studied 70 patients undergoing CPB and found that serum syndecan-1 levels a marker of endothelial glycocalyx degradation increased significantly during surgery, peaked in the early postoperative period, and declined after 24 hours. Elevated syndecan-1 levels were related to prolonged ICU length of stay (LOS), indicating that greater glycocalyx shedding reflects a more severe endothelial injury and systemic inflammation. [26]

The degradation of the endothelial glycocalyx during CPB is largely driven by systemic inflammatory responses and ischemia-reperfusion injury. This process activates MMP-9, which cleaves syndecan-1 from the endothelial surface.[4] This shedding disrupts endothelial integrity, increases vascular permeability, and leads to tissue edema and impaired microcirculation factors that contribute to postoperative organ dysfunction.[27,28]

Pesonen et al. further demonstrated that syndecan-1 levels correlate with both pro-inflammatory cytokines (IL-6 and IL-8) and the anti-inflammatory cytokine IL-10, measured preoperatively and 6 hours postoperatively, suggesting that syndecan-1 is not only a marker of endothelial damage but also a surrogate of inflammation severity triggered by CPB.[12]

Apoptosis Association with Organ Function Assessment

In this study, caspase-3, a marker of apoptosis, showed no significant correlation with postoperative organ function up to 24 hours after cardiac surgery. This suggests several possibilities, such as the presence of a caspase-independent apoptosis pathway following the inflammation induced by CABG and the use of CPB, known as caspase-independent cell death (CICD), as discussed in previous research.[34,35] Alternatively, the observed increase in caspase-3 may not be related to its role as an executioner in the apoptosis pathway, but rather to its functions in tissue differentiation, regeneration, neural development, or regulating growth and homeostasis.[36,37] Further studies with different variables are needed to give a better understanding of the relationship between caspase-3 and the apoptosis process during and after CABG surgery.

Association between CPB, Syndecan-1, and IL-6 with Organ Function Assessment

Cardiac surgery triggers an unpredictable immune response, primarily due to blood exposure to artificial surfaces, shear stress from roller pumps, and the trauma caused by the surgical procedure. Puchinger et al[38] reported an increase in IL-6 levels following the initiation of CPB, which came to a plateau by the end of surgery and persisted through the first postoperative day. The study noted a heterogeneous inflammatory response, with significant variation between individuals in IL-6 levels, consistent with earlier studies.[39,40]

While numerous studies have highlighted the association between CPB and immune response, limited research has focused on the specific impact of CPB duration on it. CPB time has a significant correlation with increased inflammation, oxidative stress, apoptosis, and glycocalyx degradation.[17,18] Similarly, CPB time has a significant correlation with IL-6, syndecan-1, and CASUS.

The use of CPB significantly contributes to glycocalyx degradation, endothelial dysfunction, and oxidative stress. The contact of blood with artificial surfaces in the CPB circuit activates inflammatory pathways, leading to the release of pro-inflammatory cytokines like IL-6 and TNF-α. These cytokines trigger endothelial cell activation, causing the breakdown of the glycocalyx, which is essential for maintaining vascular integrity. The degradation of glycocalyx components, such as syndecan-1, further exacerbates endothelial dysfunction, impairing microcirculatory perfusion. Additionally, oxidative stress, induced by reactive oxygen species (ROS) from neutrophil activation, leads

to lipid peroxidation and cellular damage. This cascade of events results in a compromised vascular function and contributes to systemic inflammatory response syndrome (SIRS), increasing the risk of organ dysfunction and post-surgical complications.[10]

Glycocalyx is a thin layer that separates the blood within the lumen from the endothelial cells. It comprises three major components: proteoglycan, glycoprotein, and dissolved components. Proteoglycan is a protein linked by a glycosaminoglycan chain. The other two proteins bound to the cell membrane are syndecan-1 and glypican. These proteins connect to the membrane through membrane-spanning and GPI anchoring. Similarly, glycosaminoglycans are categorized into five types: heparan sulfate, chondroitin sulfate, dermatan sulfate, keratan sulfate, and hyaluronic acid. Glycoprotein is composed of a short branching carbohydrate chain expressed by the endothelial cell to varying degrees depending on activation and cell stimulation.[29,30] Finally, the dissolved component of the glycocalyx is found above the proteoglycan and glycoprotein network, comprised of protein and dissolved proteoglycan. Glycocalyx has an important role in maintaining homeostasis through its four functions: mechanical transduction, vascular permeability, immunology, and hemostasis.[30]

Glycocalyx degradation is indicated by elevated levels of its components in the plasma. The inflammatory response to cardiac surgery and CPB is linked to pro-inflammatory cytokines such as IL-6 and IL-8, as well as markers of glycocalyx degradation, like syndecan-1.[12] An experimental model conducted on pig hearts by Bruegger et al.[32] suggests that the shedding of the endothelial glycocalyx is associated with increased levels of syndecan-1 and heparan sulfate in circulation. This study also correlates CPB time with increased postoperative syndecan-1 and IL-6 levels. Robich et al.[33] also found that longer CPB durations correspond with higher plasma levels of soluble syndecan-1 in 54 patients undergoing cardiac surgery.

Degradation of the glycocalyx leads to alterations in microcirculation due to inadequate vascular oxygen delivery and an increase in nitric oxide at the capillary level. These changes result in decreased functional capillary density within the tissue, particularly in the kidney's medulla, which is highly sensitive to oxygen supply. It is not surprising that the kidneys are typically the first organ to exhibit reduced function following cardiac surgery. Furthermore, various processes contribute to the development of sepsis as a consequence of the inflammatory cascade following cardiac surgery, including neutrophil accumulation, myocardial depression, disturbances in calcium homeostasis, intravascular coagulation, and direct cell damage. Eventually, this will lead to multiple organ dysfunction, which can be evaluated with scoring systems such as SOFA or, in the case of cardiac surgery, the CASUS score.[31]

Left untreated, the inflammatory processes could further progress to SIRS, leading to cell destruction. Since the inflammatory process begins at the start of surgery, organ dysfunction related to the inflammatory cascade and endothelial dysfunction can occur at any time during or after CABG surgery, especially if CPB is used. As demonstrated by Hirai et al.,[3] SIRS lasting more than 12 hours, marked by higher IL-6 levels, indicates a more severe inflammatory process. Accordingly, our study found a significant correlation between IL-6 levels and CPB time. This strongly suggests that longer CPB times will result in severe inflammation as a consequence.

Strengths and Limitations

To date, this is the first study to present details of inflammatory, oxidative stress, apoptosis, and endothelial dysfunction markers in CABG patients, although there are some limitations of this study . Further studies are needed to deepen the understanding of inflammatory, oxidative stress, apoptosis, and endothelial dysfunction markers with postoperative dysfunction, and to determine whether they could be used as predictive factors.

CONCLUSION

We identified a significant relationship between postoperative organ dysfunction, as evaluated by CASUS, and postoperative IL-6, syndecan-1, and MDA. This finding highlights

the effects of the inflammatory process on endothelial dysfunction following on-pump CABG.

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CONFLICT OF INTERESTS

The authors declare no conflict of interest.

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ABBREVIATIONS

ACEF: age, creatinine, ejection fraction, CABG: coronary artery bypass graft, CAD: coronary artery disease, CPB: cardiopulmonary bypass, CASUS: cardiac surgery score, ICU= intensive care unit, LVEF: left ventricular ejection fraction, MDA: malondialdehyde, MMP: metalloproteinase, ROS: reactive oxygen species, SOFA: sequential organ failure assessment, SIRS: systemic inflammatory response syndrome

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