Cardiovasc Surg Int 2020;7(1):8-13
http://dx.doi.org/DOI: 10.5606/e-cvsi.2020.760
www.e-cvsi.org

Cardiovascular Surgery and Interventions

Original Article Open Access

Effects of systemic inflammatory response on coronary artery bypass grafting

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Received: September 10, 2016 ***Accepted:*** November 08, 2016 ***Published online:*** May 18, 2017

ABSTRACT

Objectives: In this study, we aimed to investigate the effects of systemic inflammatory response syndrome (SIRS) on postoperative results of coronary artery bypass grafting (CABG).

Patients and methods: Between April 2016 and April 2018, a total of 287 patients (203 males, 84 females; mean age 62.5 years; range, 21 to 89 years) who underwent CABG were retrospectively analyzed. Data were collected from the medical records. The diagnosis of SIRS was made according to the criteria used by Boehme.

Results: In total, 83.9% of the patients had postoperative SIRS. Univariate analysis revealed that the predictive factors of SIRS were age, preoperative EuroSCORE, on-pump surgery, and preoperative low hemoglobin levels. However, age was detected as the only predictive factor in the multivariate analysis. The diagnosis of SIRS did not affect hospital mortality, neurological complications or length of hospital stay, whereas it prolonged the weaning period and length of intensive care unit stay.

Conclusion: Our study results show that SIRS has no significant effect on mortality and neurological complications in CABG patients. On the other hand, special attention should be given to the inflammatory response, as it prolongs the weaning period and length of intensive care unit stay.

Keywords: Cardiopulmonary bypass, coronary artery bypass grafting, systemic inflammatory response syndrome.

Coronary artery bypass grafting (CABG) is the conventional therapy of coronary artery disease. This procedure became widespread after Gibbon started to use cardiopulmonary bypass (CPB) machines in 1953.[1] Blood contact with non-endothelial surface triggers systemic inflammation through the secretion of mediators. Systemic inflammation during and after cardiac surgery, more particularly in CABG procedures, is related to the secretion of a large number of mediators and to the activation of certain natural defense mechanisms.[1]

Inflammation is one of the basic parameters that affects postoperative results.[2] The magnitude of the inflammatory reaction varies, although the persistence of any degree of inflammation may be considered potentially harmful to the cardiac patient.[3] In addition, systemic inflammatory response syndrome (SIRS) can lead to pulmonary, renal, gastrointestinal, myocardial, and central nervous system dysfunction as well as coagulopathy, vasoconstriction, increased interstitial fluid, fever, leukocytosis, hemolysis, and an increased susceptibility to infections.[3,4] When CPB is avoided (e.g., off-pump CABG [OPCAB]), however, evidence suggests that activation of inflammation still occurs, but is slightly delayed with respect to on-pump bypass.[4] In the present study, we aimed to evaluate the effects of SIRS on the postoperative results of CABG.

PATIENTS AND METHODS

Between April 2016 and April 2018, a total of 287 patients (203 males, 84 females; mean age 62.5 years; range, 21 to 89 years who underwent CABG were retrospectively analyzed. Medical data including pre-, intra-, and postoperative data of the patients

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Citation:
Yeşilkaya N, Gökalp O, İner H, Beşir Y, Durmaz H, Gökkurt Y, et al. Effects of systemic inflammatory response on coronary artery bypass grafting. Cardiovasc Surg Int 2020;7(1):8-13.

were obtained from the hospital archive department. Patients who underwent emergent surgery or who had concomitant peripheral artery intervention, valve repair/replacement or carotid endarterectomy were excluded. A written informed consent was obtained from each patient. The study protocol was approved by the Izmir Katip Çelebi University Faculty of Medicine Ethics Commitee of Retrospective Studies. The study was conducted in accordance with the principles of the Declaration of Helsinki.

The patients were divided into two groups according to the SIRS status: the SIRS-positive group (n=241) and SIRS-negative group (n=46). The two groups were compared in terms of pre-, intra, and postoperative parameters. The diagnosis of SIRS was made according to the criteria used by Boehme.[5] According to these criteria, at least two of the followings were required: fever >38°C or <36°C, heart rate >90 bpm, respiratory rate >20 bpm or partial pressure of carbon dioxide (pCO_2) <32 mmHg, leucocyte $>12\times10^3/\mu L^{-1}$ or $<4\times10^3/\mu L^{-1}$.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max) or number and frequency. Categorical data were compared using the Pearson's chi-square and Fisher's exact tests. The Mann-Whitney U test was used for the comparison of the study groups. The correlation between SIRS and demographic and clinical characteristics of the patients was analyzed using univariate and multivariate regression analyses. A *p* value of <0.05 was considered statistically significant.

RESULTS

In terms of preoperative parameters, the mean age and EuroSCORE were higher and the mean preoperative hemoglobin levels were lower in the SIRS group (p<0.001 and p=0.009, respectively). However, there were no statistically significant differences in the other preoperative parameters (Table 1).

Table 1
Pre- and intraoperative data

	SIRS+ (n=241)			SIRS- (n=46)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Age (year)			64.5±15.9			52.3±16.3	<0.001
Gender							0.114
Female	75	31.1		9	19.6		
Diabetes mellitus	81	33.6		11	23.9		0.197
COPD	13	5.4		2	4.3		0.999
Smoking	100	41.5		21	45.7		0.601
Chronic renal failure	8	3.3		3	6.5		0.392
Hypertension	141	58.5		21	45.7		0.107
Redo surgery	2	0.8		1	2.2		0.410
EuroSCORE			4.1±2.3			2.8±2.4	0.001
Ejection fraction			48.5±11.9			49.7±11.2	0.542
Preoperative hemoglobin			12.3±1.6			13.0±1.8	0.009
Body surface area			1.8±0.2			1.8±0.2	0.177
On-pump surgery	199	82.6		28	60.9		0.001
Intraaortic balloon pump	34	14.1		1	2.2		0.026
CBP time (min)			83.8±31.4			77.4±46.1	0.054
Cross-clamp time (min)			44.3±18.9			43.0±34.0	0.099

SIRS: Systemic inflammatory response syndrome; SD: Standard deviation; COPD: Chronic obstructive pulmonary disease; CPB: Cardiopulmonary bypass.

Table 2
Postoperative data

	SIRS+ (n=241)			SIRS- (n=46)			
	n	%	Mean±SD	n	%	Mean±SD	*p*
Drainage (mL)			585.4±420.8			512.0±238.3	0.510
Blood transfusion (IU)			2.6±2.8			2±1.2	0.791
Revision surgery	25	10.4		5	10.9		0.999
Weaning (h)			13.7±9.4			9.2±3.8	<0.001
ICU length of stay (day)			3.4±2.8			2.5±1.1	0.004
Hospital stay (days)			7.4±4.0			7.6±3.8	0.388
Mortality	22	9.2		2	4.3		0.390
Neurologic complications	6	2.5		0	0		0.594

SIRS: Systemic inflammatory response syndrome; SD: Standard deviation; ICU: Intensive care unit.

In terms of intraoperative data, the use of on-pump surgery and intra-aortic balloon pump (IABP) was statistically significantly higher in the SIRS group (p=0.001 and p=0.026, respectively). On the other hand, there were no statistically significant differences in the cross-clamp and CPB time (Table 1).

In terms of postoperative data, the length of intensive care unit stay and the weaning period were statistically longer in the SIRS group (p<0.001 and p=0.004, respectively). However, there were no statistically significant differences in the incidence of postoperative neurological complications and mortality rates between the groups (Table 2).

Table 3
Univariate logistic regression analysis for predictors of SIRS

	B	SE	Wald	*p*
Age	0.043	0.010	19.105	<0.001
Gender	-0.619	0.397	2.434	0.119
Diabetes mellitus	0.477	0.372	1.646	0.200
COPD	0.227	0.777	0.085	0.771
Smoking	-0.169	0.324	0.274	0.601
Chronic renal failure	-0.709	0.697	1.035	0.309
Hypertension	0.518	0.324	2.562	0.109
Redo surgery	-0.972	1.235	0.620	0.431
EuroSCORE	0.265	0.077	11.858	0.001
Ejection fraction	-0.008	0.014	0.359	0.549
Preoperative hemoglobin	-0.243	0.100	5.871	0.015
Body Surface Area	-0.963	0.860	1.256	0.262
Off-pump CABG	-1.051	0.350	8.997	0.003
On-pump CABG	1.114	0.347	10.329	0.001
CPB time (min)	0.007	0.007	0.939	0.332
Cross-clamp time (min)	0.003	0.010	0.096	0.757

SIRS: systemic inflammatory response syndrome; *B*: Unstandardized beta; SE: Standard error; COPD: Chronic obstructive pulmonary disease; CABG: Coronary artery bypass grafting; CPB: Cardiopulmonary bypass.

Table 4
Multivariate logistic regression analysis for predictors of SIRS

	B	SE	Wald	*p*
Age	0.032	0.012	6.899	0.009
EuroSCORE	0.087	0.091	0.911	0.340
Preoperative hemoglobin	-0.093	0.103	0.818	0.366
Off-pump CABG	0.505	1.199	0.177	0.674
On-pump CABG	1.485	1.180	1.583	0.208
Constant	-0.563	1.912	0.087	0.768

SIRS: systemic inflammatory response syndrome; *B*: Unstandardized beta; SE: Standard error; CABG: Coronary artery bypass grafting.

Table 5
Univariate regression analysis

Dependent variable	Independent variable	*B*	SE	Wald	*p*
Mortality	SIRS	0.802	0.757	1.123	0.289
Neurologic complication		17.535	5926.129	0.000	0.998

B: Unstandardized beta; SE: Standard error; SIRS: Systemic inflammatory response syndrome.

Table 6
Single linear regression analysis

Dependent variable	Independent variable	*B*	SE	β	t	*p*
Weaning period (h)		4.500	1.449	0.190	3.105	0.002
Hospital stay (day)	SIRS	-0.265	0.651	-0.026	-0.408	0.684
ICU stay (day)		0.975	0.423	0.135	2.306	0.022

B: Unstandardized beta; SE: Standard error; SIRS: Systemic inflammatory response syndrome; ICU: Intensive care unit.

Univariate regression analysis was carried out to identify possible variables for SIRS. The analysis revealed that age, EuroSCORE, preoperative low hemoglobin level, and on-pump surgery positively affected SIRS (p<0.001, p=0.001, p=0.015, and p=0.001, respectively). On the contrary, off-pump CABG adversely affected SIRS (p=0.003). The remaining variables were not found to be significant predictors of SIRS (Table 3). Factors which were statistically significant in the univariate analysis were included in the multivariate analysis. Accordingly, age was the only factor which had a significant effect on SIRS prediction (p=0.009) (Table 4). A regression analysis was performed to identify whether SIRS had an effect on the postoperative results, and SIRS was found to have no significant effect on neurological complications or mortality (p=0.998 and p=0.289, respectively) (Table 5). A single linear regression analysis revealed that the length of ICU stay and the weaning period were longer in the patients with SIRS (p=0.022 and p=0.002, respectively) (Table 6).

DISCUSSION

As one of the most common operations, particularly after the introduction of CBP machine, CABG surgery is subject to much interest, as it may lead to prolonged weaning times, increased renal dysfunction, stroke, deep sternal infections, and death.[6] These results are thought to be related to systemic inflammation, which is most probably caused by CBP machines.[7,8] Nevertheless, systemic inflammation which occurs after CABG procedures is affected by many factors other than CPB machines. Tissue damage, endotoxemia, and contact of blood with non-endothelial surfaces are the main known triggers of SIRS.[9,10]

There are two major ways to investigate SIRS both in cardiac surgery and other fields. One is through the use of laboratory parameters such as tumor necrosis factor or interleukins. The other way is with clinical criteria such as hypotension, hyperthermia, leukocytosis.[5,11] Unfortunately, according to the global studies, the number of patients who develop SIRS after cardiac surgery cannot be neglected. In the study of Sasse et al.,[12] the postoperative SIRS ratio was 39% among the patients undergoing cardiac surgery, including pediatric cases. In another study, MacCallum et al.[13] reported that the postoperative SIRS ratio was 96.2% using clinical parameters for patients in an adult cardiothoracic ICU.[13] We used the same method in our study and the postoperative SIRS ratio was found to be 83.9%.

Although previous studies have investigated the risk factors of SIRS in many settings, only a few have evaluated the risk factors of SIRS after CABG procedures. However, as a major factor affecting postoperative outcomes of patients undergoing CABG, many studies regarding the causes of SIRS and related precautions for its avoidance SIRS are expected. One of these studies was by Ferraris et al.,[14] which revealed a relation between the intraoperative blood use and SIRS. According to their study, intraoperative blood use led to negative changes in the immune system and induced SIRS. The authors also reported that other factors which caused SIRS were low preoperative functional capacity, liver dysfunction, chronic obstructive pulmonary disease, male sex, preoperative steroid therapy, preoperative dialysis history, and age above 74 years. In another study, Sinning et al.[15] investigated the postoperative effects of SIRS on patients undergoing transaortic valve implantation. Their results showed that risk factors for SIRS were the amount of contrast agents used, major bleeding, major vascular trauma, and blood transfusion. In a similar study by Lindmann et al.,[16] 747 patients who underwent aortic valve implantation or transaortic valve implantation were included to investigate the relationship between SIRS and mortality. The authors found that the predictors of SIRS were high preoperative hemoglobin and leucocyte count, cerebrovascular disease, and preoperative dialysis history. Another study examining SIRS in pediatric patients undergoing cardiac surgery in the postoperative period revealed that predictors of SIRS were age, low weight, CPB time, and cross-clamp time.[9] In a study by Güvener et al.,[17] 246 pediatric patients were retrospectively evaluated to identify the effects of SIRS on the postoperative results. The study revealed that predictors of SIRS were CPB time, low weight (<10 kg), and right-to-left shunt before surgery. In the present study, preoperative EuroSCORE, on-pump CABG, and IABP use were found to be SIRS predictors. In contrary to aforementioned studies, CPB time was not found to be among the SIRS predictors. Another factor different from other studies was hemoglobin level, as such we found that low hemoglobin levels, but not high hemoglobin levels, were the predictor of SIRS.

Although it is well-known that SIRS is one of the main reasons for adverse postoperative outcomes after cardiac interventions, only a few studies have addressed into this problem. In one of these studies made by Sinning et al.,[15] 152 patients who underwent transcatheter aortic valve implantation (TAVI) were evaluated to question the effects of SIRS on the postoperative results. According to this study, SIRS affected early postoperative results and postoperative first-year mortality rates; however, it had no effect on postoperative stroke. Güvener et al.[17] also evaluated the effects of SIRS on postoperative results of pediatric cardiac operations and SIRS was found to be a strong predictor of postoperative mortality. As mentioned above, Lindmann et al.[16] evaluated 747 patients undergoing postoperative TAVI in terms of SIRS predictors. Clinical parameters were used in their study and the patients with SIRS had a longer ICU length of stay, more frequent ICU admission, longer hospitalization period, and higher acute renal failure incidence. The authors also found that SIRS had no significant effect on postoperative stroke and mortality in the early postoperative period. Subgroup analysis revealed that SIRS was a predictor of mortality in cardiac patients with diabetes in the postoperative period. In another study, Soares et al.[9] evaluated 101 patients who underwent open heart surgery. It was shown that SIRS prolonged the weaning period and the length of ICU and hospital stay. The authors also reported that SIRS had no significant effect on mortality. Our results are consistent with previous studies. According to the present study, SIRS prolonged the weaning period and the length of ICU stay; however, it did not increase neurological outcomes or mortality.

The main limitations of the present study are its retrospective design and the evaluation of clinical parameters only, but not proinflammatory markers. Nevertheless, our study is one of the rare studies which address into the relationship between SIRS and CABG.

In conclusion, the relationship between SIRS and CABG outcomes is still an obscure subject to be elucidated. In our study, mean age and EuroSCORE were higher and preoperative hemoglobin levels were lower in patients with SIRS. On-pump surgery and IABP use were also significantly higher in the SIRS group, while the length of ICU stay and the weaning period were significantly longer in the SIRS group. Based on these results, we can speculate that age is the only factor which has a significant effect on SIRS prediction. Although SIRS seems not to have an evident effect on neurological complications or mortality, it may prolong the length of ICU stay and the weaning period. Further prospective, large-scale, randomized-controlled studies are needed to confirm these findings.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

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