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Post-Cardiac Surgery Leukocytosis: Associations, Predictors, and The Role of Prophylactic Antibiotics

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ABSTRACT

Background: Cardiac surgery has long been recognized to cause an inflammatory response. When an inflammatory reaction is triggered, the white blood cell (WBC) count rises, which is known as leukocytosis.

Aim of the work: To describe the association between post-operative leukocytosis and baseline characteristics, operative characteristics, and postoperative outcomes**.**

Patients and Methods: This was a hospital-based, single-center, observational study, conducted at Prince Sultan Cardiac Center, Najran, KSA, during the period from September 2021 to May 2022. A total of 150 patients who underwent coronary artery bypass graft (CABG) Surgery and/or valve surgery within the Cardiac surgery department during the study period, were enrolled in this study.

Result: The incidence of post-operative leukocytosis was (19.33%). Patients with post-operative leukocytosis were elder than those with no post-operative leukocytosis and associated with a higher proportion of severe obesity (p=0.001), DM (p=0.025), pulmonary diseases (p<0.001), dialysis (p<0.001), smoking (p<0.001), and prior ICU admission (p<0.001). The multivariate analysis showed that the independent significant predictors of post-operative leukocytosis were BMI >37 (OR= 5.79, p=0.014), DM (OR= 13.98, p=0.001), HTN (OR= 0.018, p<0.001), dialysis (OR= 17.26, p=0.012), prior ICU (OR= 9.40, p=0.001), and prior Coronary Angio (OR= 4.35, p=0.018).

Conclusion: The current evidence demonstrated that CBP was associated with a 19% incidence of post-operative leukocytosis. BMI >37, DM, HTN, dialysis, prior ICU, prior coronary angio, and left main disease ≥50% were significant independent predictors of postoperative leukocytosis. Improving process-of-care elements such as antibiotic optimal timing while taking into account patient-specific risk factors reduced the risk of postoperative leukocytosis.

Keywords: *Leukocytosis; WBC; Prophylactic Antibiotics; CBP; SSI.*

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INTRODUCTION

The use of a cardiopulmonary pump (CPB) is still associated with inflammatory responses, despite improvements in anesthetic, perfusion, and surgical methods.[1,2] Cardiac surgery has long been recognized to cause an inflammatory response, which is caused by the exposure of blood to non-physiologic surfaces and happens in situations when CPB is administered.[1,3,4] When an inflammatory reaction is triggered, the white blood cell (WBC) count rises, which is known as leukocytosis.[5,6] Therefore, post-cardiac surgery patients are at risk of infection if they do not receive regular follow-up care. Prior to undergoing cardiac surgery, individuals with a high risk of infection must be identified, and their safety to have surgery must be verified.[7,8] Pre-operative WBC counts are frequently used as a measure of inflammation or infection. Preoperative WBC count has been found to be a predictor of death and significant bleeding in heart surgery patients.[9] In addition, preoperative WBC count may assist in the risk stratification of patients before surgery.[10]

Post-operative prophylaxis of antibiotics in cardiothoracic surgery has been shown to have a significant effect on the prevention of surgical site infections (SSIs) in placebo-controlled studies.[11] Given the serious implications of sternal wound infections, antibiotic prophylaxis has been a routine practice in cardiac surgery since then. Nowadays, there is a lot of discussion about the best antibiotic(s), dosage, and prophylactic duration. Cefazolin and cefuroxime are the most widely prescribed antibiotics in the guidelines.[12–17] General surgical guidelines suggest 24-hour post-operative prophylaxis,[15–17] whereas cardiac surgery-specific recommendations in the United States advocate for

48-hour post-operative prophylaxis.[13,18] According to surveys, adherence to these or similar recommendations is very low.[19–21] The usage of glycopeptides on a regular basis and for a longer period of time are common deviations. In cardiac surgery, there is a broader variety of prevention strategies than in other surgical procedures.[21] This study aimed to describe the association between post-operative leukocytosis and baseline characteristics, operative characteristics, and post-operative outcomes. Moreover, we aimed to report the change in neutrophile and lymphocyte after the administration of ABP. This is crucial for producing hospital-specific epidemiological data on SSIs and assisting in the implementation of SSI prevention strategies in both hospital- and community-based settings.

PATIENTS AND METHODS

Study Design: This descriptive study was conducted over a period of nine months from September 2021 to May 2022, at three centers: Prince Sultan Cardiac Center (Najran, n=29 patients), Mohamed bin Nasser Hospital (Jizan, n= 68 patients), and Prince Faisal Bin Khalid Cardiac Center (Abha, n= 53 patients), KSA. This study was done after taking both the approval of the ethical committee of the hospital and written consent from the patients.

Inclusion and Exclusion Criteria: Included patients were those who had either CABG, valve surgery, or both. Patients who underwent off-pump cardiac surgery, pediatric surgery, heart transplantation, and patients on immunosuppressive medication or active preoperative infections were excluded from the study.

Study Procedures: Patients undergoing cardiac surgery were closely observed by infection-control stuff, who also checked microbiology logs and other medical records in order to look for signs of SSI. The hospital epidemiologist evaluated and verified the data. An additional set of data was gathered from computerized databases in the departments of administration, pharmacy, and laboratory. Patients were required to shower and have their chest hair clipped prior to the operation. Povidone-iodine was administered to the operative site just prior to the surgical incision. Preoperative intravenous antibiotics (cefazolin 1 g and vancomycin 1 g) were given to each patient in the operating room. The second dose of cefazolin was delivered following CBP to ensure adequate serum levels of the antibacterial agent if the intervention lasted more than 6 hours. ABP was indicated to be administered for no more than 48 hours after surgery.

Data Collection: The outcome of interest was the elevated level of WBC count. All enrolled patients will be subjected to:

Collection of demographic data: age, sex, duration of hospital stay (pre and post-operative), type of surgery, body mass index (BMI), comorbidities, smoking, operation class (elective or emergency), blood transfusion, ICU stay time, SSI (superficial or deep).

Post-operative WBC count, in the form of neutrophils count, and lymphocyte count.

History of previous cardiac surgery, internal mammary artery graft, anemia, diabetes mellitus, obesity (BMI >37 kg/m^2), comorbidities (e.g., pulmonary and renal disease), age, gender, previous intensive care unit (ICU) stay, and type of surgery either urgent, emergent, or elective were all collected as risk factors for post-operative leukocytosis. Based on their post-operative WBC count, patients were classified into two groups: less than 11,000 and 11,000 or over. For each of the two WBC count groups, mortality and other unfavorable outcome rates were calculated.

Statistical Analysis: The Statistical Package for Social Science (SPSS) was used to analyze the collected data (IBM SPSS Statistics for Windows, Version 23.0, IBM Corporation, Armonk, New York). Qualitative data were presented as numbers and percentages and compared between groups using the Chi-square test or Fisher exact test. Predictors of post-operative leukocytosis were determined using the univariate and multivariate binary logistic regression and were presented using odds ratio (OR) and 95% confidence interval (CI). A p-value less than 0.05 was considered significant.

RESULTS

Between September 2021 and May 2022, 150 adult patients underwent cardiac surgery, including combined CABG and valve replacement 7 (4.67%), CABG only 84 (56%) patients, and valve replacement procedures 59 (39.33%). The median age of the patients was 55 years (30 to 80), with 60% of the population ≥ 60 years old. Of these patients, 36% were female. The median preoperative stay for all patients was 2 days (0 to 5). The average operative time was five hours. The median overall length of hospital stay was 15 days (8 to 30). The prevalence of post-operative leukocytosis was 29/150 (19.33%).

Difference between patients with post-operative leukocytosis and normal WBCs group

Based on the WBC, we had two groups, the first group had post-operative leukocytosis (n=29 patients with a mean WBC count of 13.29±1.59), and the second group had normal WBCs count (n= 121 patients with a mean WBC count of 6.54±1.98). Patients with post-operative leukocytosis were elder than those with no post-operative leukocytosis (57.96±13.84 vs. 49.90±15.42 years), respectively. Moreover, patients with post-operative leukocytosis were associated with a higher proportion of obesity (BMI >37) than those with no post-operative leukocytosis (41.4% vs. 14.9%, p=0.001), respectively. Regarding the comorbidities, the proportion of DM, pulmonary diseases, dialysis, smoking, and prior ICU admission were significantly ($p<0.05$) higher in the post-operative leukocytosis group. On the other hand, 76% of the patients in the non-post-operative leukocytosis group had HTN, compared to 24.1% in the post-operative leukocytosis group ($p<0.001$). In terms of cardiac history, congestive heart failure, prior CABG, and prior coronary angio were also significantly higher in the post-operative leukocytosis group. Both groups were comparable in terms of single-vessel disease,

multiple vessel disease, and ejection fraction. **Table 1** summarizes the difference between patients with

Predictors of post-operative leukocytosis

Univariate analysis showed a significant association between the occurrence of post-operative leukocytosis and patients age (OR= 1.04, 95% CI: 1.008 – 1.068, p=0.013), BMI >37 (OR= 4.04, 95% CI: 1.65 – 9.86, p= 0.002), DM (OR= 2.80, 95% CI: 1.11 – 7.04, p=0.029), pulmonary diseases (OR= 5.84, 95% CI: 2.14 – 15.92, p=0.001), and dialysis (OR= 17.87, 95% CI: 5.14 – 62.22, p<0.001). The multivariate analysis showed that the independent significant predictors of post-operative leukocytosis were BMI >37 (OR= 5.79, 95% CI: 1.43 – 23.43, p=0.014), DM (OR= 13.98, 95% CI: 2.92 – 66.95, p=0.001), HTN (OR= 0.018, 95% CI: 0.004 – 0.091, p<0.001), dialysis (OR= 17.26, 95% CI: 1.89 – 157.41, p=0.012), prior ICU (OR= 9.40, 95% CI: 2.57 – 34.35, p=0.001), prior coronary angio (OR= 4.35, 95% CI: 1.29 – 14.67, p=0.018), and left main disease ≥50% (OR= 6.46, 95% CI: 1.34 – 31.02, p=0.020). **Table 2**

Adverse events	Post-operative leukocytosis (WBC> 11,000) (n=29)	Normal WBC count (WBC ≤11,000) (n=121)	p-value
In-hospital mortality	5 (17.2%)	0 (0%)	<0.001
Stroke	7 (24.1%)	0 (0%)	<0.001
Low-cardiac output	10 (34.5%)	10 (8.3%)	<0.001
postoperative IABP	10 (34.5%)	10 (8.3%)	<0.001
New atrial fibrillation	10 (34.5%)	10 (8.3%)	<0.001
Mediastinitis	10 (34.5%)	10 (8.3%)	<0.001
Superficial infection	1 (3.4%)	10 (8.3%)	0.332
Deep infection	9 (31.0%)	0 (0%)	<0.001
Leg wound infection	5 (17.2%)	0 (0%)	<0.001
Reintubation	10 (34.5%)	10 (8.3%)	<0.001
Pneumonia	10 (34.5%)	0 (0%)	<0.001
Deep vein thrombosis	5 (17.2%)	0 (0%)	<0.001
Exploration for bleeding	10 (34.5%)	10 (8.3%)	<0.001
Blood transfusion	10 (34.5%)	10 (8.3%)	<0.001
Renal insufficiency	10 (34.5%)	0 (0%)	<0.001
Urinary tract infection	10 (34.5%)	0 (0%)	<0.001
Cardiac arrest	5 (17.2%)	0 (0%)	<0.001
Coma	5 (17.2%)	0 (0%)	<0.001
Myocardial infarction	10 (34.5%)	0 (0%)	<0.001
Septic shock	5 (17.2%)	0 (0%)	<0.001

Table 2: Adverse events

Adverse events

Patients with post-operative leukocytosis were associated with higher proportion of post-operative stroke (24.1% vs. 0%), low-cardiac output (34.5% vs. 8.3%), atrial fibrillation (34.5% vs. 8.3%), mediastinitis (34.5% vs. 8.3%), deep infection (31.0% vs. 0%), leg wound infection (١٧.٢% vs. 0%), reintubation (34.5% vs. 8.3%), pneumonia (34.5% vs. 0%), deep vein thrombosis (17.2% vs. 0%), blood transfusion (34.5% vs. 8.3%), renal insufficiency (34.5% vs. 0%), and urinary tract infection (34.5% vs. 0%). Moreover, the rate of post-operative septic shock, myocardial infarction, coma, and cardiac arrest, was significantly higher in leukocytosis and those without leukocytosis.

patients with post-operative leukocytosis (**Table 3**). Regarding the in-hospital mortality, the rate was significantly higher in patients with post-operative leukocytosis compared with non-leukocytosis group (17.2% vs. 0%), p<0.001.

Variable	Univariate	P-value	Multivariate	P-value
Age	1.04 (1.008 – 1.068)	0.013		
BMI ≥37	4.04 (1.65 – 9.86)	0.002	5.79 (1.43 – 23.43)	0.014
DM	2.80 (1.11 – 7.04)	0.029	13.98 (2.92 – 66.95)	0.001
HTN	0.10 (0.04 – 0.26)	<0.001	0.018 (0.004 – 0.091)	<0.001
Pulmonary disease	5.84 (2.14 – 15.92)	0.001		
Dialysis	17.87 (5.14 – 62.22)	<0.001	17.26 (1.89 – 157.41)	0.012
Prior ICU	14.86 (5.70 – 38.75)	<0.001	9.40 (2.57 – 34.35)	0.001
Congestive heart failure	3.41 (1.46 – 7.96)	0.005		
Prior CABG	4.83 (1.30 – 18.0)	0.019		
Prior Coronary Angio	11.22 (4.47 – 28.20)	<0.001	4.35 (1.29 – 14.67)	0.018
Left main disease ≥50%	9.97 (3.56 – 27.92)	<0.001	6.46 (1.34 – 31.02)	0.020
Emergent	5.84 (2.14 – 15.92)	0.001		
Urgent	0.262 (0.075 – 0.920)	0.037		
CABG/valve	6.29 (1.33 – 29.89)	0.021		

Table 3: Univariate and multivariate analysis for post-operative leukocytosis predictors

Changes in neutrophils and lymphocyte counts

Preoperatively, the proportion of patients with neutrophilia was 6.00%, which increased to 64.67% during operation, and then decreased to 40% on the 1st day post-operative, 13.33% on the 3rd day post-operative, and 13.33% on the 7th day post-operative. Regarding lymphocyte, 13.33% of the patients had lymphocytosis preoperatively, 20% during operation, 24.67% on the 1st day post-operative, 13.33% on the 3rd post-operative, and 13.33% on the 7th day post-operative (**Figure 1**).

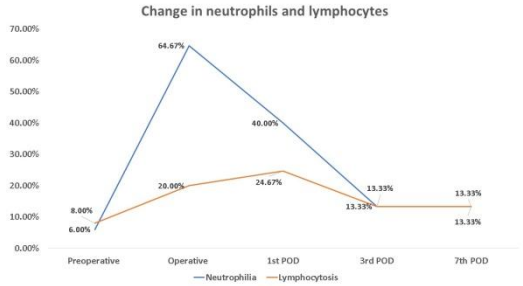

Figure 1: Change in neutrophils and lymphocyte counts

Parameters		Post-operative leukocytosis (WBC> 11,000) (n=29)	Normal WBC count (WBC ≤11,000) (n=121)	p-value
WBC count		13.29±1.59	6.54±1.98	**<0.001**
		Demographics		
Age		57.96±13.84	49.90±15.42	**0.011**
Gender	Male	21 (72.4%)	76 (62.8%)	0.331
	Female	8 (27.6%)	45 (37.2%)	
BMI ≥37		12 (41.4%)	18 (14.9%)	**0.001**
		Co-morbidities		
DM		22 (75.9%)	64 (52.9%)	**0.025**
HTN		7 (24.1%)	92 (76.0%)	**<0.001**
Pulmonary disease		10 (34.5%)	10 (8.3%)	**<0.001**
Dialysis		11 (37.9%)	4 (3.3%)	**<0.001**
Smoking		29 (100%)	51 (42.1%)	**<0.001**
Prior ICU		18 (62.1%)	12 (9.9%)	**<0.001**
Anemia		3 (10.3%)	2 (1.7%)	0.05
		Cardiac history		
Myocardial infarction		10 (34.5%)	30 (24.8%)	0.289
Congestive heart failure		14 (48.3%)	26 (21.5%)	**0.003**
Prior CABG		5 (17.2%)	5 (4.1%)	**0.011**
Prior valve		4 (13.8%)	6 (5.0%)	0.102
Prior Coronary Angio		20 (69.0%)	20 (16.5%)	**<0.001**
		Cardiac anatomy and function		
Left main disease ≥50%		12 (41.4%)	8 (6.6%)	**<0.001**
Single-vessel disease		8 (27.6%)	35 (28.9%)	0.886
Multi-vessel disease		10 (34.5%)	38 (31.4%)	0.750
		Ejection fraction		
<40%		10 (34.5%)	30 (24.8%)	0.289
40%–59%		7 (24.1%)	42 (34.7%)	0.276
≥60%		11 (37.9%)	49 (40.5%)	0.800
		Procedural characteristics		
Emergent		10 (34.5%)	10 (8.3%)	**<0.001**
Urgent		3 (10.3%)	37 (30.6%)	**0.019**
Elective		14 (48.3%)	76 (62.8%)	0.151
CABG		15 (51.7%)	69 (57.0%)	0.606
Valve		10 (34.5%)	49 (40.5%)	0.552
CABG/valve		4 (13.8%)	3 (2.5%)	**0.026**
Duration of ABP ≥ 48Hours		10 (34.5%)	10 (8.3%)	**<0.001**
Duration of surgery >5 Hours		10 (34.5%)	10 (8.3%)	**<0.001**
CBP time ≥100 min		10 (34.5%)	10 (8.3%)	**<0.001**
		On-pump surgery		
Nadir hematocrit <20		3 (10.3%)	17 (14.0%)	0.430
Low cardiac output		7 (24.1%)	23 (19.0%)	0.535
Return to bypass		5 (17.2%)	25 (20.7%)	0.679
		Management RBC transfusions intraoperative		
None		10 (34.5%)	30 (24.8%)	0.289
One		6 (20.7%)	34 (28.1%)	0.418
Two or more		13 (44.8%)	57 (47.1%)	0.825
Use inotropes		16 (55.2%)	54 (44.6%)	0.307
		Postoperative factors		
Poly-transfusion		10 (34.5%)	10 (8.3%)	**<0.001**
Febrile at 72 hours (>37)		10 (34.5%)	10 (8.3%)	**<0.001**
Extubating within 4 hours		13 (44.8%)	47 (38.8%)	0.555
ICU after surgery (≥3 day)		10 (34.5%)	10 (8.3%)	**<0.001**
Total in hospital (≥30 day)		10 (34.5%)	10 (8.3%)	**<0.001**
Hospital mortality		5 (17.2%)	0 (0%)	**<0.001**

Table 1: Difference between patients with post-operative infection and non-infection group.

DISCUSSION

Most major surgeries should have postoperative ABP terminated within 24 hours, according to consensus.[22] However, this clinical approach has not been used in cardiac surgery for a number of reasons, including CBP alterations in the immune system, WBC activation, the reduced capacity to combat infectious organisms, hypothermia, postoperative bleeding risk, and the duration of surgical operations are all risk factors for SSI in cardiac surgery. Cardiothoracic surgeons have always regarded their patients as high-risk; therefore, they utilize antibiotics until chest tubes and central IV lines are removed.[23] ABP may be administered for up to 48 hours following cardiac surgery, according to recent guidelines.[24] Second-generation cephalosporin is the antibiotic of choice for the prevention of SSIs in cardiac surgery because of its low toxicity and high tissue penetration. In terms of cost-benefit, Cefuroxime has a fair price compared to other cephalosporins as well as a favorable spectrum of action, blocking the development of most bacteria found in postoperative surgical sites; consequently, it is highly recommended for ABP use.[25]

In this study, our findings showed that patients with post-operative leukocytosis were associated with older age, a higher proportion of obesity (BMI >37), DM, pulmonary diseases, dialysis, smoking, prior ICU admission, congestive heart failure, prior CABG, and prior coronary angio. Moreover, we found that BMI >37, DM, HTN, dialysis, prior ICU, prior coronary angio, and left main disease ≥50% were significant independent predictors of postoperative leukocytosis. Post-operative leukocytosis was studied by Mahmood et al. for its link to mortality and morbidity. Their findings showed that patients with leukocytosis presented with MI, CHF, COPD, angina, dyspnea, DM, smoking, obesity, and undergoing an emergent procedure. There was no significant difference in the incidence of previous cardiac procedure, history of PVD, incidence of hypertension, alcohol consumption, and gender between the two groups. Regarding the association between leukocytosis and post-operative outcomes, they found that patients with leukocytosis were associated with longer hospitalization, higher risk of sepsis, deep venous thrombosis, pneumonia, acute renal failure, medical complications, and wound disruption.[26]

Post-operative leukocytosis has been linked to a broad range of postoperative complications in a number of different surgical procedures.[27–29] After cardiac surgery, postoperative pneumonia is the most prevalent infection and is a major cause of morbidity and death [30]. Strobel et al. recently used the STS database to construct a risk model for predicting pneumonia following cardiac surgery, concluding that leukocytosis might represent an immunological response to preexisting infections.[31] Various studies have linked leukocytosis to new-onset congestive heart failure, as well as an increased risk of atrial fibrillation, acute cardiovascular events, and ischemic stroke.[32–35] Dacey et al. assessed 11,270 patients who underwent CABG and found that leukocytosis was an independent predictor of death and other unfavorable outcomes.[36] Patients with other established causes of leukocytosis, such as pneumonia, wound infection, SIRS, and sepsis were not excluded from this study. Therefore, the research was unable to establish a causal link between leukocytosis and unfavorable outcomes. It is possible that leukocytosis is a nonspecific sign of some underlying disease that increases the risk of postoperative complications, notwithstanding the high association between leukocytosis and morbidity and death.

ABP helps to reduce the risk of SSIs and leukocytosis after cardiac surgery. Our findings show that extending ABP beyond 48 hours following cardiac surgery is still widely performed and reduces the incidence of SSI. Prophylactic antibiotic treatment should be continued while drains are in place for more than a few days after cardiac surgery, according to some studies.[37,38] It is likely that the antibiotics would protect the wound against a secondary infection that developed in the foreign body and spread to the wound through the bloodstream. Therefore, surgeons prefer to maintain antibiotics if transthoracic devices are left in place after surgery. A survey of 120 UK cardiac surgeons revealed that 28% of them maintained antibiotic treatment even after the removal of all chest drains.[10] A recent review of the evidence suggests that this technique is no longer effective. Cephalothin prophylaxis following heart surgery should only be given for two days, according to Goldmann and colleagues who conducted a randomized trial 20 years ago to establish that a 6-day course of ABP is unnecessary.[39] A large systematic review and meta-analysis included 59 RCTs that found comparable rates in deep sternal wound infections (DSWI) or all other categories of SSIs for antibiotics targeting Gram-positive bacteria vs. Gram-negative bacteria; however, Gram-positive antibiotics were associated with a lower rate of all-cause mortality and post-operative pneumonia. Prophylaxis for 24 hours after surgery was associated with a greater incidence of DSWI, any sternal SSI, and endocarditis in studies comparing various antibiotic regimens for different durations. There was no benefit to post-operative regimens extending longer than 48 hours. When comparing glycopeptides to -lactams, glycopeptides had an advantage when the comparators were given for equal durations, whereas -lactams had an advantage when administered for a longer time than the glycopeptides. High doses of antibiotics did not have a noticeable effect.[40] According to a meta-analysis of single-dose vs. multiple-dose prophylaxis for major surgery, multiple-dose regimens had no effect in reducing SSI in different surgical operations requiring postoperative drainage.[41,42]

We acknowledge that our study has some limitations, including the small sample size, the lack of long-term follow-up, and the single-center setting, which may hinder the generalizability of our findings. Furthermore, the risk variables and outcomes in this study were chosen based on earlier studies' recommendations and existing literature on WBC

count and surgical results; hence, the relevance of these risk factors and outcomes can be questioned.

CONCLUSION

In conclusion, the current evidence shows that CBP is associated with a 19% incidence of post-operative leukocytosis. Patients with leukocytosis tend to be older and associated with a higher proportion of obesity (BMI >37), DM, pulmonary diseases, dialysis, smoking, prior ICU admission, congestive heart failure, prior CABG, and prior coronary angio. BMI >37, DM, HTN, dialysis, prior ICU, prior coronary angio, and left the main disease ≥50% were significant independent predictors of postoperative leukocytosis. Our findings showed that improving process-of-care elements such as antibiotic optimal timing while taking into account patient-specific risk factors reduced the risk of postoperative leukocytosis.

REFERENCES

1. Ascione R, Lloyd CT, Underwood MJ, et al. Inflammatory response after coronary revascularization with or without cardiopulmonary bypass. *Ann Thorac Surg.* 2000;69(4):1198–204.
2. Mazandarani M, Yousefshahi F, Abdollahi M, et al. Comparison of hypertonic saline versus normal saline on cytokine profile during CABG. *Daru*. 2012;20(1):49.
3. Rothenburger M, Trösch F, Markewitz A, et al. Leukocyte activation and phagocytotic activity in cardiac surgery and infection. Cardiovasc Surg. 2002;10(5):470–5.
4. Yousefshahi F, Bashirzadeh M, Abdollahi M, et al. Effect of Hypertonic Saline Infusion versus Normal Saline on Serum NGAL and Cystatin C Levels in Patients Undergoing Coronary Artery Bypass Graft. *J Tehran Heart Cent.* 2013;8(1):21–7.
5. Butler J, Rocker GM, Westaby S. Inflammatory response to cardiopulmonary bypass. *Ann Thorac Surg.* 1993;55(2):552–9.
6. Gasz B, Benkö L, Jancsó G, et al. Comparison of inflammatory response following coronary revascularization with or without cardiopulmonary bypass. *Exp Clin Cardiol.* 2004;9(1):26–30.
7. Gelijns AC, Moskowitz AJ, Acker MA, et al. Management practices and major infections after cardiac surgery. *J Am Coll Cardiol.* 2014;64(4):372–81.
8. Cove ME, Spelman DW, MacLaren G. Infectious complications of cardiac surgery: a clinical review. *J Cardiothorac Vasc Anesth.* 2012;26(6):1094–100.
9. Brown JR, Landis RC, Chaisson K, et al. Preoperative white blood cell count and risk of 30-day readmission after cardiac surgery. *Int J Inflam.* 2013;2013:781024.
10. Mehran R, Pocock SJ, Nikolsky E, et al. A Risk Score to Predict Bleeding in Patients With Acute Coronary Syndromes. *J Am Coll Cardiol* [Internet]. 2010;55(23):2556–66. Available from: https://www.sciencedirect.com/science/article/pii/S073510971001288X
11. Kreter B, Woods M. Antibiotic prophylaxis for cardiothoracic operations. Meta-analysis of thirty years of clinical trials. *J Thorac Cardiovasc Surg.* 1992;104(3):590–9.
12. Bratzler DW, Houck PM. Antimicrobial prophylaxis for surgery: an advisory statement from the National Surgical Infection Prevention Project. *Clin Infect Dis an Off Publ Infect Dis Soc Am.* 2004; 38(12):1706–15.
13. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Art. *J Am Coll Cardiol.* 2004;44(5):e213-310.
14. Engelman R, Shahian D, Shemin R, et al. The Society of Thoracic Surgeons practice guideline series: Antibiotic prophylaxis in cardiac surgery, part II: Antibiotic choice. *Ann Thorac Surg.* 2007;83(4):1569–76.
15. Mangram AJ, Horan TC, Pearson ML, et al. Guideline for prevention of surgical site infection, 1999. Hospital Infection Control Practices Advisory Committee. *Infect Control Hosp Epidemiol.* 1999;20(4):250–80.
16. (UK NCC for W and CH. Surgical site infection: prevention and treatment of surgical site infection. 2008.
17. Network SIG. Antibiotic prophylaxis in surgery: A national clinical guideline. Scottish Intercollegiate Guidelines Network; 2008.
18. Edwards FH, Engelman RM, Houck P, et al. The Society of Thoracic Surgeons Practice Guideline Series: Antibiotic Prophylaxis in Cardiac Surgery, Part I: Duration. Ann Thorac Surg. 2006;81(1):397–404.
19. Alexiou VG, Ierodiakonou V, Peppas G, et al. Antimicrobial prophylaxis in surgery: an international survey. *Surg Infect (Larchmt).* 2010;11(4):343–8.
20. Haydon TP, Presneill JJ, Robertson MS. Antibiotic prophylaxis for cardiac surgery in Australia. *Med J Aust.* 2010;192(3):141–3.
21. Al-Momany NH, Al-Bakri AG, Makahleh ZM, et al. Adherence to international antimicrobial prophylaxis guidelines in cardiac surgery: a Jordanian study demonstrates need for quality improvement. *J Manag Care Pharm.* 2009;15(3):262–71.
22. Torpy JM, Burke AE, Glass RM. Postoperative Infections. JAMA [Internet]. 2010 23;303(24):2544. Available from: https://doi.org/10.1001/jama.303.24.2544

23. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Heal Pharm [Internet]. 2013 Feb 1;70(3):195–283. Available from: https://academic.oup.com/ajhp/article/70/3/195/5112717

24. Tamayo E, Gualis J, Flórez S, Castrodeza J, et al. Comparative study of single-dose and 24-hour multiple-dose antibiotic prophylaxis for cardiac surgery. *J Thorac Cardiovasc Surg*. 2008;136(6):1522–7.

25. Nascimento JWL, Carmona MJC, Strabelli TMV, et al. Perioperative cefuroxime pharmacokinetics in cardiac surgery. *Clinics (Sao Paulo)*. 2007;62(3):257–60.

26. Mahmood E, Knio ZO, Mahmood F, Amir R, Shahul S, Mahmood B, et al. Preoperative asymptomatic leukocytosis and postoperative outcome in cardiac surgery patients. PLoS One [Internet]. 2017 5;12(9): e0182118–e0182118. Available from: https://pubmed.ncbi.nlm.nih.gov/28873411

27. Moghadamyeghaneh Z, Hanna MH, Carmichael JC, et al. Preoperative Leukocytosis in Colorectal Cancer Patients. *J Am Coll Surg*. 2015;221(1):207–14.

28. Sagi HC, Dziadosz D, Mir H, Virani N, Olson C. Obesity, leukocytosis, embolization, and injury severity increase the risk for deep postoperative wound infection after pelvic and acetabular surgery. *J Orthop Trauma*. 2013;27(1):6–10.

29. Bozkurt IH, Aydogdu O, Yonguc T, et al. Predictive Value of Leukocytosis for Infectious Complications After Percutaneous Nephrolithotomy. *Urology*. 2015;86(1): 25–9.

30. Kollef MH, Sharpless L, Vlasnik J, et al. The impact of nosocomial infections on patient outcomes following cardiac surgery. *Chest*. 1997;112(3):666–75.

31. Strobel RJ, Liang Q, Zhang M, et al. A Preoperative Risk Model for Postoperative Pneumonia After Coronary Artery Bypass Grafting. *Ann Thorac Surg*. 2016;102(4):1213–9.

32. Elkind MS V, Sciacca RR, Boden-Albala B, et al. Relative elevation in baseline leukocyte count predicts first cerebral infarction. *Neurology*. 2005;64(12):2121–5.

33. Ridker PM, Buring JE, Shih J, Met al. Prospective study of C-reactive protein and the risk of future cardiovascular events among apparently healthy women. *Circulation*. 1998;98(8):731–3.

34. Rienstra M, Sun JX, Magnani JW, et al. White blood cell count and risk of incident atrial fibrillation (from the Framingham Heart Study). *Am J Cardiol*. 2012;109(4):533–7.

35. Barron H V, Cannon CP, Murphy SA, et al. Association between white blood cell count, epicardial blood flow, myocardial perfusion, and clinical outcomes in the setting of acute myocardial infarction: a thrombolysis in myocardial infarction 10 substudy. *CircIulation*. 2000;102(19):2329–34.

36. Dacey LJ, DeSimone J, Braxton JH, Leavitt BJ, Lahey SJ, Klemperer JD, et al. Preoperative white blood cell count and mortality and morbidity after coronary artery bypass grafting. *Ann Thorac Surg*. 2003;76(3):760–4.

37. Salkind AR, Rao KC. Antibiotic Prophylaxis to Prevent Surgical Site Infections. 2011;585–90.

38. Smith JW, Thoburn R, Arbor A. A study of antibiotic prophylaxis in cardiac surgery. J Thorac Cardiovasc Surg [Internet]. 1969;57(6):757–63. Available from: http://dx.doi.org/10.1016/S0022-5223(19)42646-9

39. Namias N, Harvill S, Ball S, et al. Cost and morbidity associated with antibiotic prophylaxis in the ICU. *J Am Coll Surg*. 1999;188(3):225–30.

40. Lador A, Nasir H, Mansur N, et al. Antibiotic prophylaxis in cardiac surgery: systematic review and meta-analysis. *J Antimicrob Chemother*. 2012;67(3):541–50.

41. Ehrenkranz NJ. Antimicrobial prophylaxis in surgery: mechanisms, misconceptions, and mischief. *Infect Control Hosp Epidemiol*. 1993;14(2):99–106.

42. Taylor KM. SIRS--the systemic inflammatory response syndrome after cardiac operations. *Ann Thorac Surg* [Internet]. 1996;61(6):1607–8. Available from: http://europepmc.org/abstract/MED/8651756