Acute Increase in Postoperative White Cell Count Predicts Mortality in Isolated Aortic Valve Replacement Patients

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ABSTRACT

Introduction: Inflammatory reaction after cardiac surgery is well documented. In this study, we aimed to investigate association with acute increase in white blood cell count after cardiopulmonary bypass with mortality.
Patients and Methods: We included 35 patients with isolated aortic valve replacement procedure with cardiopulmonary bypass during time phrase June 2009 to July 2013. Blood sampled the day before the operation and on postoperative 24th hour. White blood cell counted and preoperative postoperative difference was calculated.
Results: Total 35 patients were included to study. Four-teen (40%) of them were female. Mean age of patients was 61.14±13.25. Mortality observed patients had two fold increase in mean white blood cell count (preoperative/ postoperative white blood cell count 4.971±1.11/ 8.19±3.47 p=0.03 95% CI 1.88-8.06/3.88-12.50).
Conclusion: Acute increase in white cell count after aortic valve replacement procedure is associated with mortality.
Key Words: Aortic valve; white blood cell count; mortality

İzole Aort Kapak Replasmanı Yapılan Hastalarda Postoperatif Beyaz Küre Artışı Mortalite Belirtecidir

ÖZET

Giriş: Kalp cerrahisi sonrası inflamatuvar reaksiyon iyi dokümante edilmiştir. Bu çalışmada, kardiyopulmoner bypass sonrası beyaz kan hücrelerinde akut artış ile mortalite arasındaki ilişkiyi incelemeyi amaçladık.
Hastalar ve Yöntem: Haziran 2009-Temmuz 2013 arasında kardiyopulmoner bypass eşliğinde izole aort kapak replasmanı uygulanan 35 hasta çalışmaya dahil edildi. Kan örnekleri operasyondan önceki gün ve postoperatif 24. saatte alındı. Beyaz kan hücreleri sayıldı ve operasyon öncesi ve sonrası değerler hesaplandı.
Bulgular: Toplam 35 hasta çalışmaya alındı. On dört tanesi (40%) kadındı. Ortalama yaş 61,14±13,25 idi. Mortalite izlenen hastalarda beyaz kan hücresi sayısında iki kat artış olduğu görüldü (preoperatif-postoperatif beyaz hücre sayıları 4,971±1,11/ 8,19±3,47 p=0,03 95% CI 1,88-8,06/3,88-12,50).
Sonuç: Aort kapak replasmanı sonrası beyaz kan hücrelerinin akut artışı mortalite ile ilişkilidir.
Anahtar Kelimeler: Aort kapak; beyaz kan hücre sayısı; mortalite

INTRODUCTION

Surgery elicits inflammatory reaction in varying degrees. Cardiac surgery particularly cardiopulmonary bypass (CPB) involved cases cause an inflammatory response which is associated with organ dysfunction in some degrees. The inflammatory response is initiated and maintained by activation of the several defense systems caused by contact of blood with non-endothelial surfaces during the course of surgery[1-3]. Several strategies have been explored in order to reduce exaggerated inflammatory reaction to CPB. First strategy was to avoid CPB which ended up off-pump surgery. But in cases when CPB is inevitable a filter is used to capture activated leukocytes from the CPB circuit before entering the patient's circulation.

In this study, we aimed to investigate association with acute increase in white blood cell count after isolated aortic valve replacement with mortality.

PATIENTS and METHODS

We included 40 patients with isolated aortic valve replacement procedure with cardiopulmonary bypass during time phrase June 2009 to July 2013. Redo cases (n=2), patients with endocarditis (n=1) were excluded. Postoperative infectious conditions observed patients were excluded (mediastinitis n=1). Blood sampled the day

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before the operation and on postoperative 24th hour. White blood cell counted and preoperative postoperative difference was calculated. Operative technique and anesthesic agents were standard. Patients who required more than 24 hours of postoperative mechanical ventilation were included in the group of prolonged intubation. Data are presented as absolute numbers and percentages, mean ± standard deviation as appropriate. Relative frequencies were compared using X^2 or Fisher's exact test. Means were compared using Mann-Whitney U-test. A $p<0.05$ was considered to indicate statistical significance. All analyses were performed using SPSS for Windows, version 15. Data were collected retrospectively. Local Ethical Committee approved the study.

RESULTS

Total 35 patients were included to study. Four-teen (40%) of them were female. Mean age of patients was 61.14±13.25. Mortality observed patients had two fold increase in mean white blood cell count (preop/postop white blood cell count 4.971±2.49/ 10.61±3.79 p=0.033 95% CI 1.88-8.06/3.88-12.50). Preoperative, intraoperative and postoperative variables were summarized in (Table 1). Hospital mortality observed in 6 patients. Mortality observed group of patients were older (63.20±4.08) (p=0.120) and had low left ventricular ejection fraction (p>0.150). Prolonged ventilation was observed in 6 patients. Prolonged ventilation was associated with postoperative increase in white blood cell count (p=0.029). Prolonged ICU stay was observed in 8 patients and 3 of them were lost. Prolonged ICU stay was not associated with increased neutrophil count (p=0.491) (Table 3). Postoperative white blood cell count increase and age correlation was weak in mortality observed patients (r=+0.246 p=0.154). Prolonged intensive care unit stay and white blood cell count increase association was also weak (r=0.262 p=0.128). Increase in white blood cell count was adversely associated with left ventricular ejection fraction (r=-0.306 p=0.074). Valve type (biological vs. mechanical) was not associated with increase in white blood cell count (p=0.071).

DISCUSSION

The surgical stress response reflects a combination of endocrinological, immunological, and hematological change occurring after injury/trauma. The degree of the response is proportional to the magnitude of injury and reflects increased demands on organ function[4,5]. In on-pump cardiac surgery inflammatory respond consisted of neuroendocrine and immune responses. Activation of leukocytes and platelets may cause catastrophic results (SIRS). Data recently obtained from an experimental study developed by Okamura et al. showed that ischeima-reperfusion and the resulting inflammatory effects of CPB are determined in the impairment of vascular permeability and viability of organic barriers such as the blood brain barrier[6].

Table 1. Demographic variables

	Variable	Survived	Hospital Mortality Observed	p
Preoperative	Age	59±13.20	63.20±4.08	0.120
	Sex (female)	2 (5.7)	12 (34)	0.694
	Obezity	21 (60)	1 (2.8)	0.119
	Pulmonar Hypertension	12 (34)	1 (2.8)	0.374
	Rythm (non SR)	3 (8.5)	2 (5.7)	0.139
	COPD	5 (14)	0	0.439
	Left Ventricular Ejection Fraction	55.90±6.92	52.0±11.51	0.150
	Preoperative renal insufficiency	1 (2.8)	0	0.143
	DM	3 (8.5)	0	0.620
	HT	10 (28)	0	0.620
	Emergency	1 (2.8)	1 (2.8)	0.269
	Valve (mechanic)	20 (57)	1 (2.8)	0.071
Intraoperative	Aortic Cross Clamp (minutes)	138±46.31	150.0±57.40	0.724
	Total Perfusion Time (minutes)	165.20±46.31	191.60±82.73	0.509
	Prolonged ventilation	2 (5.7)	4 (11)	0.001*
Postoperative	Postoperative renal insufficiency	0	1 (2.8)	0.143
	ICU stay (days)	2.16±0.37	4.86±2.94	0.010*
	Hospital stay (days)	14.03±4.35	20.20±11.63	0.670

COPD: Chronic obstructive pulmonary disease, DM: Diabetes mellitus, HT: Hypertension, ICU: Intensive care unit, SR: Sinus rythm, *Statistically significant

The immediate consequence of this dysfunction is significant change in serum total protein and albumin in relation to their concentration in other body fluids. To reduce the inflammatory response to the CPB several strategies have been explored. One of them was leukocyte filter. Several studies reported better results with filter[7-9]. On the other hand Bechel et al., Emiroglları et al. reported negative results with filter concluding no benefit[10,11]. Also Surer et al. reported leukocyte filter was not beneficial in congenital heart surgery[12]. Second way is off-pump surgery when it is feasible. But procedures involving valves requires CPB. Patients, who experience adequate analgesia, demonstrate decreased levels of pro-inflammatory cytokines and increased lymphocyte activity[13]. Anesthesiologists, in choosing an anesthetic, should carefully consider its clinical impact on the patients' immune function. Volatile anesthetics have a more profound immunosuppressive effect than total intravenous anesthesia (TIVA) and regional anesthetics[14]. In our study we applied standard analgesia and anesthesia. Hirai et al. reported the duration of CPB and cytokinemia, with high IL-6 levels, during this short time frame until just after cardiac surgery might play an important role in the development of the SIRS[15]. In our study CPB time was not statistically significant with mortality (p>0.05) and association was weak (r=0.09 and p=0.957). Brown et al. reported preoperative high white blood cell count is associated with increased risk of 30-day readmission after discharge from cardiac surgery[16]. In our study we did not observed preoperative difference among groups (p>0.05). In our study we detected acute increase in white blood count but we did not detect specific lymphocytic increase (p>0.05) (Table 2). Contrast to our results there are papers advocating specific increase of lymphocyte is associated with mortality[17,18]. In our study we detected statistically significant association with prolonged ventilation and mortality. Laffey et al. reported inflammatory response to surgical stress and CPB cause negative effect on pulmonary system[19]. During CPB patient's apnea may lead to activation of lysosomal enzymes in the pulmonary circulation causing postoperative lung injury[20]. Mechanical ventilation may become a vicious circle by way of increasing inflammatory response and causing lung injury to further requirement of mechanical ventilation. The main pathophysiology is stretch of unrecruited lung units[21].

This is a retrospective clinical study with all its methodological limitations. Although our study design appears to have resulted in well-matched groups regarding almost all variables, unrecognized differences between the groups or in the treatment of the patients might have existed and influenced our results. Type of surgery was unique and can cause a selection bias. However, the fact that routine practice this is a multi surgeon and single center study with a limited number of cases.

Table 2. Blood cell counts

	Variable	Survived	Hospital Mortality Observed	p
Neutrophil count	Preoperative	4.67±1.80	4.97±2.49	0.747
	Postoperative	8.19±3.47	10.61±3.79	0.033*
PLT count	Preoperative	221.93±85.22	215.57.25	0.870
	Postoperative	136.83	108.40	0.192
Lymphocyte Count	Preoperative	2.02±0.787	3.14±3.07	0.085
	Postoperative	1.69±2.64	2.07±3.21	0.774

PLT: Platelet, *Statistically significant

Table 3. Relation between neutrophil count and intensive care unit stay and ventilation period

	Variable	Survived	Hospital Mortality Observed	p
Prolonged ICU stay (mean 2.5±1.42 days)	Preoperative Neutrophil Count	5.82±2.67	5.98±2.79	0.945
	Postoperative Neutrophil Count	8.86±0.83	10.51±3.73	0.491
Prolonged Ventilation	Preoperative Neutrophil Count	4.78±1.77	9.28±4.47	0.634
	Postoperative Neutrophil Count	4.38±2.49	10.46±3.70	0.029*

ICU: Intensive care unit, *Statistically significant

CONCLUSION

As conclusion in this report we had documented acute increase in white blood cell count following isolated aortic valve surgery is associated with increased mortality rate. We advocate that we should refrain from.

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CONFLICT of INTEREST

The authors reported no conflict of interest related to this article.

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