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Original Articles

Pre and postoperative immune status in patients enduring cardiac surgery

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ABSTRACT

Pre and post operative levels and T and B lymphocytes and immunoglobulin (IgG, IgM and IgA) were studied in 120 patients suffering from chronic rheumatic heart disease (RHD) / non-RHD and undergoing open and closed heart surgery (OHS/CHS). A highly significant rise ($p<0.001$) in percentage of active T cells is observed in both RHD ad non RHD groups of patients as compared to controls with no significant difference in the proportion of total T cells. B cells showed highly significant rise ($p<0.001$) only in RHD group. OHS has shown to produce more significant depression in T cell counts than that produced by CHS. No significant change was seen in the percentage of B lymphocytes after OHS as well as CHS. This study revealed highly significant ($p<0.001$) raised levels of IgG, IgM and IgA in study group as compared to controls. Significant post operative fall in the levels of IgG and IgA was recorded after OHS as well as CHS even though the fall was found to be more significant after open cardiac procedure. Levels of IgM did not show any post operative change in both OHS and CHS groups of patients. A study of post operative infections in these patients revealed *Staphylococcus aureus* as a major isolate followed by *Pseudomonas aeruginosa,* Proteus vulgaris. Patients with OHS showed higher post infection rate than in CHS patients.

1. Introduction

Rheumatic heart disease (RHD) is the maximum among cardiovascular disorders in India. Interpretation in experimental animals [1-3] and incidence of circulating anticardiac auto-antibodies in patients among Rheumatic fever (RF) and rheumatic heart disease [3, 4] have a propensity to recommend that immunological mechanism may be involved in the pathogenesis of this disease. As a result of this study, the immunological behavior of RHD patients was well studied and they were screened for assorted immune parameters to elucidate its pathogenicity.

Escalating data has recommended that suppressed humoral and cell mediated immunological response accompany foremost surgical procedures [3, 5-7]. The changes rooted by surgical procedures in peripheral blood lymphocytes counts, understanding lymphocytic population types and functions associate with grade of surgical trauma [8], which is a main foundation of morbidity and mortality. Cardiac surgical procedure in general and open heart surgery (OHS) in particular causes numerous immunological modifications than any other surgical procedures producing major trauma and condition of immune suppression in these patients [3].

The category of host immune response before, during and after surgical stress and trauma plays an imperative role in determining an upshot, endurance and enhancement in patient's health. The information on immune status in cardiac patients is limited consequently this study was undertaken to explore the consequence of trauma caused by cardiac surgery on the immunity of the patient depending on its severity and mortality [9, 29, 30]. The key breakdown of host defense mechanism has been associated with increased post operative infection rate in these patients was also studied and interrelated with the type of surgery experienced by them.

2. Materials and Methods

2.1. Patient details and Control

A battery of 120 patients suffering from diverse cardiovascular diseases aged between 14 58 years was included in this study group who underwent open/closed heart surgery (OHS/CHS). The patients included in this study were grouped into two major categories including RHD and non RHD. This group was made by the consultant cardiovascular surgeons and non RHD patients embody the group of patients not having any previous rheumatic

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history but suffering from diseases such as coronary artery disease, ventral septal defect, atrial septal defect and other congenital heart diseases. The control group of 40 healthy non hospitalized individuals of both sexes and were age and sex matched with subjects. The basic details, clinical diagnosis and surgery types underwent among the 120 subjects are well studied (Table 1). The T and B lymphocytes were enumerated using sheep cell rosetting techniques [10-12]. The venous blood was collected with anticoagulants from patients 3 days prior to surgery whereas post surgical blood samples on 3rd or 4th post operative day right through the study.

2.2. Lymphocyte separation

Blood sample was diluted 1:2 with equal volume of phosphate buffered saline (PBS) pH of 7.2. This sample was undergone for layering on Ficoll-Hypaque density gradient solution. It is then centrifuged for 20 minutes at 2500 rpm. The buffy coat of lymphocytes formed at the interface was removed and washed thrice and suspended in TC 199 medium. Viability of these separated lymphocytes was checked with 1% trypan blue solution and lymphocyte suspension with more than 90-95% viability was used in this investigation. The final concentration of lymphocytes was adjusted to 2000 cells/µl with TC 100 medium. The lymphocyte suspension in this medium was divided into two aliquots. Among them one is used for erythrocyte rosetting technique for T lymphocyte and other used for erythrocyte amboceptor-complement (EAC) rosetting for B lymphocytes.

Table 1. Incidence of cases in cardiac surgery

Clinical diagnosis	No. of patients	OHS	CHS
RHD	89	58	31
Non RHD	31	18	13

2.3. E Rosetting

Washed sheep cells were treated with freshly prepared AEIB (2-amino ethyl isothiouronium bromide) solution to stabilize the rosettes. AEIB treated cells were then suspended in TC-199 medium and mixed with heat inactivated fetal calf serum to prepare 1% cell suspension. Equal volume of lymphocytic suspension and sheep erythrocytes were incubated at 37°C for 10-15 minutes and rosettes subsequently scored as positive, in any cells showing three or more adherent erythrocytes. These T cells were considered as Active T cells. The same aliquot was then incubated overnight at 4°C to calculate Total T cells.

2.4. EAC rosetting

Equal amount of 5% erythrocyte suspension and agglutinating dilution of amboceptor were incubated for 30 minutes at 35°C. Washed cells of erythrocyte and amboceptor conjugate were further incubated with 1:40 diluted human AB serum (a source of complement) for 30 minutes [11]. This mixture thus formed a complex was washed and diluted to give 1% suspension.

2.5. Immunoglobulin estimation

Pre and postoperative estimation of the immunoglobulin levels (IgG, IgA and IgM) in patient's serum was done by immunodiffusion technique based on the principle of Mancini using partigen plates [13]. Statistical analysis was done using paired and unpaired student 't' tests. In case of any post operative complications developed by any patient, the respective increase in the level of immunoglobulins was observed and included in this study.

2.6. Microbiology

In post operative complications, the retrospective analysis of samples like pus swab, endotracheal secretion, sputum, blood and urine were collected and processed microbiologically on blood, McConkey, Sabaroud Dextrose and *Candida* selective agar. The isolates were identified further by various biochemical and selective reactions. The susceptible and resistant strains from the isolates were identified by standard antimicrobial susceptibility testing [14].

3. Results

The values of T (active and total) cells and B cell counts in RHD and non RHD cases were compared with those of control cases (Table 2). Active T cells were found to be significantly raised ($p<0.001$) in both RHD and non RHD group of patients whereas proportion of B cells reached statistically significant rise only in RHD cases ($p<0.001$). Total T cells population was found to remain almost same in both study and control group. The development of Acute Rheumatic Fever (ARF) and RHD is generally accompanied by disturbances in immunological behavior of the person.

A significant post operative depression in proportion of active T cells was seen in both OHS and CHS cases though the fall in percentage was more in OHS ($p<0.01$) than in CHS cases ($p<0.05$) (Table 3). B cell population did not show any striking postoperative change in both OHS and CHS groups. On the other hand, total T cells were shown to be significantly reduced after OHS ($p<0.02$) with no significant change after CHS.

When the same comparison between pre and post operative values was done separately in RHD and non RHD patients it was observed that only Total T cells showed significant post operative fall in their percentages after OHS with no significant change in them after CHS in RHD patients (Table 4). Comparison of levels of IgM, IgG and IgA in RHD, Non RHD cases with that of control cases was performed (Table 5). Results were recorded in mg/dl and expressed as mean ± SD.

A highly significant elevation ($p<0.001$) in serum immunoglobulin levels (IgM, IgG and IgA) of both RHD and Non RHD groups of patients as compared to controls was performed (Table 6). Comparison between pre and post surgical levels of immunoglobulins in patients undergoing OHS/CHS was done (Table 7). Significantly reduced levels of IgG and IgA were observed post surgery compared to their pre surgical levels in both the groups of patients undergoing OHS and CHS. Postoperative fall observed in the percentage of IgG was found to be more significant after OHS ($p<0.001$) than after CHS ($p<0.02$). In post surgical, there is no significant change in the IgM levels of OHS and CHS cases.

Comparison between pre and post surgical levels of immunoglobulins was also done separately in RHD and non-RHD patients. The highly significant postoperative depression was observed in immunoglobulin concentration (IgG, IgM and IgA) of RHD patients underwent open cardiac procedure (Table 8). CHS in RHD patients produced significant postoperative decrease only in IgA levels ($p<0.01$) with no significant change in IgM and IgG levels. Non RHD group of patients showed no significant postoperative change in immunoglobulin concentrations after both cardiac procedures (Table 9).

Due to extensive surgical trauma, active T cells were more depresses in OHS patients, thus making these patients more prone to infections. Higher incidence of post operative infections in patients undergoing OHS (16.56%) was recorded as compared to the patients undergoing CHS (2.40%). *Staphylococcus aureus*

was isolated as a main pathogen responsible for the post operative infections with the isolation rate of 69.69% followed by other pathogens like *Pseudomonas aeruginosa*, *Proteus vulgaris*, *P. mirabilis*, *Streptococcus pneumonia*, *S. pyogens* and *Klebsiella sp*.

Table 2. Percentages of Active T cells, Total T cells and B cells in RHD and Non RHD and contr ol cases

Types of cells	Statistical Analysis	RHD (n=89)	Control (n=40)	Non RHD n=31)
Active T cells	Mean ± S.D.	56.46± 18.59	56.46± 18.59	59.68± 15.09
	p	< 0.001		< 0.001
Total T cells	Mean ± S.D.	79.69± 10.20	79.69± 10.20	< 0.001
	p	Not Significant		Not Significant
B cells	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	29.16± 13.86
	p	< 0.001		Not Significant

Two patients with RHD died after OHS before post operative sample could be collected

Table 3. Pre and Post operative comparison of percentages of T and B cells in patients undergoing OHS/CHS

Types of cells	Statistical Analysis	OHS (n=65)		CHS (n=53)	
		Pre-op	Post-op	Pre-op	Post-op
Active T cells	Mean ± S.D.	56.81± 17.18	50.89 ±16.66	57.86±19.28	49.71 ±19.02
	p	< 0.001		< 0.005	
Total T cells	Mean ± S.D.	80.48 ±09.54	76.33 ±12.09	78.81±10.29	80.78 ±09.27
	p	< 0.02		Not Significant	
B cells	Mean ± S.D.	30.79± 11.32	31.00±11.50	28.42±12.76	26.07±11.31
	p	Not Significant		Not Significant	

Two patients with RHD died after OHS before post operative sample could be collected

Table 4. Comparison between pre and post operative percentages of (Active and Total) T cells and B cells in RHD patients undergoing OHS/CHS.

Types of cells	Statistical Analysis	OHS (n=55)		CHS (n=37)	
		Pre-op	Post-op	Pre-op	Post-op
Active T cells	Mean ± S.D.	56.36±18.33	51.83±16.28	56.93±19.57	49.89±18.93
	p	Not Significant		Not Significant	
Total T cells	Mean ± S.D.	80.44 ±10.29	76.47 ±11.69	78.80±10.28	80.08 ±10.07
	p	< 0.05		Not Significant	
B cells	Mean ± S.D.	30.87± 11.04	32.60±11.52	28.71±12.10	27.74±11.44
	p	Not Significant		Not Significant	

Table 5. Comparison between pre and post operative percentages of (Active and Total) T cells and B cells in Non-RHD patients undergoing OHS/CHS.

Types of cells	Statistical Analysis	OHS (n=16)		CHS (n=11)	
		Pre-op	Post-op	Pre-op	Post-op
Active T cells	Mean ± S.D.	58.52±12.43	47.36±18.31	61.22±18.76	49.08±21.57
	p	Not Significant		Not Significant	
Total T cells	Mean ± S.D.	80.61 ±06.37	75.58 ±14.04	78.84±10.97	83.38 ±05.09
	p	< 0.05		Not Significant	
B cells	Mean ± S.D.	30.50± 12.84	25.12±09.65	27.37±15.71	19.96±08.91
	p	Not Significant		Not Significant	

Table 6. Levels of Immunoglobulin G,M and A in RHD and Non RHD and contr ol cases

Immunoglobulin	Statistical Analysis	RHD (n=89)	Control (n=40)	Non RHD (n=31)
Immunoglobulin G	Mean ± S.D.	2030.35± 850.03	1378.65± 375.27	2066.28± 791.06
	p	< 0.001		< 0.001
Immunoglobulin M	Mean ± S.D.	274.01± 125.27	157.35± 42.95	288.04± 95.74
	p	< 0.001		< 0.001
Immunoglobulin A	Mean ± S.D.	280.88± 81.84	216.30 ± 62.96	298.04± 57.81
	p	< 0.001		< 0.001

Table 7. Comparison of Pre and Post operative levels of Immunoglobulin G, M and A in patients undergoing OHS/CHS

Immunoglobulin	Statistical Analysis	OHS (n=65)		CHS (n=53)	
		Pre-op	Post-op	Pre-op	Post-op
Immunoglobulin G	Mean ± S.D.	2018.52±865.95	1590.59±800.66	2083.71±798.22	1841.65 ±687.93
	p	< 0.001		< 0.02	
Immunoglobulin M	Mean ± S.D.	288.43 ±120.23	265.87±122.38	257.58±166.07	260.85±114.26
	p	Not Significant		Not Significant	
Immunoglobulin A	Mean ± S.D.	273.65±81.62	268.14±80.86	298.00±70.52	275.56±75.25
	p	< 0.01		< 0.01	

Two patients with RHD died after OHS before post operative sample could be collected

Table 8. Comparison between pre and post operative percentages of Immunoglobulin G, M and A in RHD patients undergoing OHS/CHS

Immunoglobulin	Statistical Analysis	OHS (n=55)		CHS (n=37)	
		Pre-op	Post-op	Pre-op	Post-op
Immunoglobulin G	Mean ± S.D.	2004.50±865.64	1589.81±804.49	2090.22±840.04	1834.63±761.69
	p	< 0.001		Not Significant	
Immunoglobulin M	Mean ± S.D.	282.04±127.38	251.01±124.33	258.13±121.50	256.50±115.92
	p	< 0.01		Not Significant	
Immunoglobulin A	Mean ± S.D.	271.18±86.35	268.78±85.37	292.00±75.51	270.27±78.09
	p	< 0.01		< 0.01	

Table 9.: Comparison between pre and post operative percentages of Immunoglobulin G, M and A Non-RHD patients undergoing OHS/CHS

Immunoglobulin	Statistical Analysis	OHS (n=16)		CHS (n=11)	
		Pre-op	Post-op	Pre-op	Post-op
Immunoglobulin G	Mean ± S.D.	2071.10±903.51	1593.50±821.44	2059.85±668.75	1897.36 ±322.13
	p	Not Significant		Not Significant	
Immunoglobulin M	Mean ± S.D.	312.39±88.82	321.57±100.64	255.57±99.97	276.82±113.11
	p	Not Significant		Not Significant	
Immunoglobulin A	Mean ± S.D.	282.92±63.05	265.74±64.29	318.65±45.49	294.91±64.00
	p	Not Significant		Not Significant	

4. Discussion

The presence of circulating anticardiac antibodies in patients of ARF and RHD tend to suggest that immunological mechanism may be involved in the pathogenesis of this disease [4]. A state of enhanced cellular activity to streptococcal membrane and ribonucleic acid proteins existing in patients with RF and RHD suggested a role of cell-mediated immunity in these patients. Thus lymphocytes sensitized to various membrane and extracellular products of streptococci during ARF remain activated in the body resulting into the slow damage of the heart glycoprotein having cross reactivity to streptococcal membrane protein.

This investigation was undertaken to determine if pathogenesis of RHD is reflected the immune status of these patients with alterations in peripheral blood lymphocytes and immunoglobulin levels thus suggesting participation of humoral and cellular immune response in RHD. The comparative analysis in the alterations in RHD and non-RHD cases are well studied. Active T cells are thought to be a better reflection of T cell competence than total T cells [12, 30]. A distinct rise in the percentage of active T cells was seen in patients of RHD/ non-RHD as compared to controls. Thus activation of cell mediated immune response in these lymphocytes in the pathogenesis of heart disease particularly RHD causing damage to the myocardial tissue.

Thus the actual quantification of the active T cells in RHD cases lymphocytic involvement of this disease has been reported [15, 16]. Raised levels of B cells in RHD patients reflect the activated humoral response in them which can be correlated to the anticardiac antibodies production in these patients as demonstrated by previous studies [17]. The present investigation showed the raised levels of B cells only in RHD patients ($p<0.001$) can be further correlated with significant rise in immunoglobulin levels observed in these patients. Induction of post streptococcal rheumatic lesions in RHD was thought to be a result of streptococcal antigen combining with tissue components forming new antigenic determinants to which antibodies are induced.

The activated cellular and humoral immune responses in RHD patients suggest the involvement of immunological mechanism in the pathogenesis of this disease. Our findings of raised immunoglobulin levels in RHD patients are in close agreement with many previous studies [18-21]. Such a rise in the levels of immunoglobulins can also be considered as an immunopathological marker of unbalancing in the immune system during the course of ARF and RHD. A significant post surgical fall in the mean percentage of Active T cells and total T ells in both OHS and CHS patients of this investigation suggested post operative depression in cellular immune competence of these patients.

The active T cells mainly responsible for the cellular defense mechanism were more significantly reduced after open surgical procedure than after CHS. The incidence of acquired defects in host resistance has major implications for the patients in the high incidence of associated infection. Higher incidence of postoperative infections observed after OHS (16.56%) than after CHS (2.4%) in this present study suggested more immune compromised state of OHS patients due to acute surgical trauma as compared to CHS patients. The T cells also showed significant decrease after OHS, which was observed to be non- significant after CHS. This can be explained by traumatisation of lymphocytes in the pumps and particularly by the suction of H/L machine during OHS, which is not required for the closed procedure. On comparing with the previous studies [8], this study also indicates that the use of cardio pulmonary bypass (CPB) in OHS increase the magnitude of postoperative lymphocyte changes.

More than quantification, immunosuppresiveness of lymphocytes was well studied [8, 22] and B cells defects or T cell regulatory mechanisms resulting in a decreased capacity of cell and humoral mediate after OHS. Though no significant post surgical change was observed in B cell counts, significant reduction in post surgical immunoglobulin levels suggest that B cell function and antibody producing capacity might have been impaired post surgery procedures [22]. The results of several studies suggest that denaturation of proteins present in the blood gas interface in the heart lung machine may be responsible for some of the post surgical difficulties [23, 24]. Complications arising from prolonged OHS are directly related to the denaturation of globulins at blood gas interfaces in the oxygenator.

Significant postoperative decrease in immunoglobulin levels following OHS is in comparison with the result was observed [25, 26]. Such post surgical depression in immunoglobulins concentration was thought to be due to immune complex formation during this type of operation. Such depression in serum immunoglobulins after OHS might have caused primarily by sequestration of proteins, protein degradation, aggregate formation and haemodilution and not by defect in immunoglobulin synthesis [27, 29]. Air liquid interface of the oxygenator, CPB aid in OHS may cause denaturation of immunoglobulins or may bring depression of in vitro phagocytic and bactericidal capacity of neutrophils which could be directly related to depletion of immunoglobulins [28, 30].

5. Conclusion

OHS with CPB has major traumatizing effect on the cellular components as well as proteins of the blood due to extensive denaturation of proteins. So the length of CPB may affect the post surgical changes in immunological parameters after OHS and the extent of postoperative suppression may be directly related to the degree of operative trauma. Thus to get exact idea of post surgical immune changes serial measurements of T and B lymphocytes, their responses and functional capacities should be done on successive post surgical days. Further research in contribution of immunosuppression of factors associated with the surgical procedures such as length of CPB, associated blood loss, hypertension and duration and type of anesthesia may be of great value on determining postoperative outcome.

6. References

[1] Cavetti PA. Studies on the pathogenesis of R.F. II Cardiac lesions produced in rats by means of autoantibodies to heart and connective tissues. Arch Pathol. 1947; 4:13 - 15.

[2] Gupta RK, Gupta S. Effect of Streptolysin O on immunological cardiac lesion in rats. Ind J Med Res. 1983; 77:219 - 230.

[3] Gaonkar TA, Gogate A, Chaukar AP. A study of pre and postoperative immune status in patients undergoing Cardiac surgery. The Ind Pract. 1997; 50:597 - 606.

[4] Van De Rijn I. Serial studies on circulating immune complexes in post streptococcal sequelae. Clin Exp Immunol. 1978; 34:318 - 324.

[5] Howard Richard T, Simmons Richard L. Acquired immunologic deficiencies after trauma and surgical procedures. Surg Gynaecol Obstet. 1974; 139:771 - 781.

[6] Lundy J, Ford CM. Surgery, trauma and immune response suppression. Ann Surg. 1983; 197:434 - 438.

[7] Park SK, Brody JI, Wallace HA, Blackmore WS. Immunosuppresive effects of Surgery. Lancet. 1971; 1:53 - 55.

[8] Ryhanen P, Elja H, Hollmen A, Nuttinen L, Raimo P, Erkki S. Changes in peripheral blood, leucocyte count, lymphocyte subpopulations and in vitro transformations after heart valve replacement. J Thor Card Surg. 1979; 7:259 - 266.

[9] Jonathan M, Pietsch JB, Bubenick O. Delayed hypersensitivity: Incidence of acquired failure of host defense in sepsis and trauma. Ann Surg. 1977; 186:241 - 249.

[10] Bianco C, Nussenzweig V, Lay WH, Mendes NF. Binding of sheep RBC to a large population of human lymphocytes. Nature. 1971; 230:531 - 537.

[11] Jondal M, Holm G, Wigzell H. Surface markers on human T and B lymphocytes. J Exp Med. 1972; 136:207 - 215.

[12] Wybran J, Fudenberg HH. How clinically useful T and B cell quantification? Ann Int Med. 1974; 80:765 - 767.

[13] Mancini G, Vaerman j, Carbonara AO, Heremans JF. A single radial immunodiffusion method for the immunological quantification of protein. XI Colloquim on protides of biological fluids. Eds peters H. Elsevier publishing Co. 1964: 370.

[14] Sood S, Kapil A, Das B, Rattan A. A five year study of positive blood cultures: with emphasis on polymicrobial bacteraemia. The Ind Pract. 1997; 50:575 - 580.

[15] Prakash K, Bhatnagar PK. Probable role of streptococcal antigen in patients of RF and RHD. Ind J Med Res. 1987; 86:347 - 350.

[16] Yang LC, Sprey PR, Wittner MK, Fox EN. Streptococcal induced cell mediated immune destruction of cardiac myofibers in vitro. J Exp Med. 1977; 146:344 - 347.

[17] Kaplan MH, Meyesserian M. An immunological cross-reaction between group A streptococci. Lancet. 1962; 1:706 - 710.

[18] Agarwal BV, Gupta RM, Singh VP, Somani PN. Serum Immunoglobulins in RHD. Ind J Med Res. 1975; 63:570 - 575.

[19] Carlisle R, Ogunba EO, Mcfarane H, Onayemi OA, Oyeleye VO. Immunoglobulins and antibody to Loa loa in Nigerians with endomyocardial fibrosis and other heart diseases. Brit Heart J. 1972; 34:678 - 680.

[20] Subbarwal NC, Bhattacharya SK, Singh NK, Sen PC. Serum levels of immunoglobulins in acute RF and RHD. JAPI. 1987; 35:171 - 172.

[21] Velangi SV, Jaskar SP. Pre operative and post operative changes in immunoglobulins levels in open heart surgery. Ind J Med Res. 1981; 73:280 - 283.

[22] Escola J, Salo M, Vijanen MK, Ruskanen O. Impaired B lymphocyte function during open heart surgery: Effect of Anaesthesia and Surgery. Br J Anaesth. 1984; 56:333 - 337.

[23] Parker DJ, Cantrell JW, Karp RB, Stroud RM, Diagerness SB. Changes in serum complement and immunoglobulins following cardiopulmonary bypass surgery. J Surg Res. 1972; 137:714 - 718.

[24] Prutt Kenneth M, Stroud RM, Scott JW. Blood damage in the heart lung machine. Proc Soc Exp Bio Med. 1971; 137:714 - 718.

[25] Hariston P, Manos JP, Graber CHD, Lee WH. Depression of immunologic surveillance by pump oxygenation perfusion. J Surg Res. 1969; 9:587 - 593.

[26] Lozano R, Navarro M, Salinas JC. Intraoperative changes of immunoglobulins and complement fractions during open heart surgery using membrane oxygenators. Cardiovascular Surgery 1980: Bricks W, Ostermeyer J, Schulte HD eds. Berlin Springer verlag. 1981:308.

[27] Ryhanen P, Elja H, Hollmen A, Nuttinen L, Raimo P, Erkki S. Are changes in serum immunoglobulin and complement levels following open heart surgery influences by oxygenator type and parenteral nutrition. Ann Clin Res. 1979; 11:9 - 15.

[28] Kaplan EL, Castaneda AR, Ayoub EM, Quie PG. Effects of cardiopulmonary bypass on the phagocytic and bactericidal capacities of polymorpho nuclear leucocytes. Circulation. 1968; 1:158 - 163.

[29] Xing YJ, Jing SS, Jian S, Wang Y, Ping HC. Effects of radical cholecystectomy on nutritional and immune status in patients with gall bladder carcinoma. W J Gastroentero. 2000; 6:445 - 447.

[30] Whelan RL, Franklin M, Holubar SD, Donahue J, Fowler SD, Munger C, Balli JE, Glass J. Post operative cell mediated immune response is better preexposed after laproscopic vs open colorectal resection in humans. Surg Endoscopy. 2003; 17:972 - 978.