

FREQUENCIES OF CD4 LYMPHOCYTES AND IL-4 IN PRE AND POST-OPERATIVE PERIODS AMONG LAPAROSCOPIC VERSUS CONVENTIONAL SURGERY IN IRAQI PATIENTS

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ABSTRACT

Surgery is a technology consisting of a physical intervention on tissues. The present study was conducted to evaluate the effect of conventional and laparoscopic surgery on CD4 lymphocyte expression and IL-4 serum concentration. The CD4 lymphocyte expression and IL-4 serum concentration were evaluated and investigated the IL-4 serum concentration and expression of CD4 in 50 subjects which divided into open surgery group (25) patients and laparoscopic surgery group (25) patients. The count of CD4 lymphocytes, in Conventional Surgery group post-operative was significantly less than that of Laparoscopic Surgery group. Mean serum concentration of IL-4 in Conventional Surgery group post-operative was 34.24 ± 0.6 versus Laparoscopic Surgery group; 47.73 ± 1.84 . The results in the study showed that the reduced degree of T lymphocyte subsets (CD4) by laparoscopic surgery significantly lower than that by open surgery with a rapid postoperative recovery, showing that the immune function inhibition degree by laparoscopic surgery was significantly lower than that by open surgery.

Keywords: Surgery, IL-4, CD4, laparoscopic, conventional

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INTRODUCTION

Surgery is a technology consisting of a physical intervention on tissues ⁽¹⁾. All forms of surgery are considered invasive procedures; so-called "noninvasive surgery" usually refers to an excision that does not penetrate the structure being excised (e.g. laser ablation of the cornea) or to a radio-surgical procedure ⁽²⁾. Minimally invasive surgery is any technique involved in surgery that does not require a large incision. This relatively new approach allows the patient to recuperate faster with less pain ⁽³⁾. Surgical trauma affects both the innate and acquired immunity. The severity of immune disorders is proportional to the extent of surgical trauma and depends on a number of factors, including primarily the basic disease requiring surgical treatment, often coexisting infections and impaired nutritional status ⁽⁴⁾. Postoperative immune suppression particularly a loss of cell-mediated immunity is commonly seen after surgery due to an increased release of immune suppressing hormones such as catecholamine, prostaglandins and cortisol depending on the amount of surgical stress and tissue damage, blood transfusion, hypothermia, dehydration and anesthetics can further attenuate immunity ⁽⁵⁾. As demonstrated by

numerous studies, trauma is associated with an increase in the leukocytes count, but also with a decrease in the number of lymphocytes, both CD4 which can deepen immunosuppression⁽⁶⁾. Cytokines are key modulators of inflammation and play both inflammatory and anti-inflammatory roles⁽⁷⁾. Over past decades, cytokines have gained more attention in the understanding of physiological changes after trauma or surgery. Cytokines participate in acute and chronic inflammation in a complex network of interactions⁽⁸⁾. Cytokine secretion by T-lymphocytes is suppressed after major surgery giving rise to an increased susceptibility to infection with intracellular pathogens such as listeria and mycobacteria. PGE2 is also capable of stimulating Th2 subclass to produce the cytokines IL-4 and IL-10 which inhibit Th1 cytokine production during surgical injury. IL-10 down regulates the major histocompatibility complex (MHC) class II molecules on the surface of monocytes and T cells⁽⁹⁾.

MATERIALS AND METHODS

The current study was carried on 50 patients (18 males, 32 females) age range between 20-60 years from March to August 2018, excluded patients with Parasite, malignancy, regional or local anesthesia, Psychiatric and patients with chronic liver diseases or kidney disorders, 25 patients with conventional open surgery and 25 patients with laparoscopy surgery. Patients were interviewed directly by using an anonymous questionnaire form which covered age, sex, family history of any malignant disease and others. This study was in agreement with ethics of Al-Diwaniya Teaching Hospital and verbal informed consent was obtained from all participants.

Flow Cytometry: CD4 lymphocyte count detection by Flow Cytometry assay kits that have been used in this study are Flow cytometry kit for CD4 Thermo Fisher/ Bioscience™ USA

Serum cytokine assay: Serum concentration of IL-4 was measured by using ELISA Kit (Elabscience USA) following the manufacturer's instructions.

Statistical analysis: The Statistical Package For Social Sciences (SPSS) software program (version 23.0) and Microsoft excel 2016, The measurement data were expressed as mean \pm SD and Chi-square test was used. $P < 0.05$ was regarded as statistically significant.

RESULTS

Table (1): demonstrated that the majority of surgical patients in both studied groups with age interval (46-52) years, statistically there was no significant difference ($P < 0.645$), table (2) shows the demographic profiles of both laparoscopy and conventional surgery regarding the gender, Table (3): shows mean serum concentration of IL-4 in Conventional Surgery group post-operative was 34.24 ± 0.6 versus Laparoscopic Surgery group; 47.73 ± 1.84 and P-value was ($P < 0.008$). Table (4), shows the count of CD4 lymphocytes, in Conventional Surgery group post-operative was significantly less than that of Laparoscopic Surgery group; 38.04 ± 1.16 versus 40.59 ± 1.4 with P-value was ($P < 0.168$). Figure (1) shows the flow cytometry analysis of CD4 expression on lymphocyte cells in laparoscopic surgical patients before taken anesthesia (A) and after surgery

(B) and figure (2), shows the flow cytometry analysis of CD4 expression on lymphocyte cells in conventional surgical patients before taken anesthesia (A) and after surgery (B).

Table 1: Frequency Distribution of patients who subjected to Conventional and Laparoscopic surgery according to age interval

Age Interval	Laparoscopic Surgery group NO (%)	Conventional Surgery group NO.(%)
25-31	5(20)	4(16)
32-38	3(12)	6(24)
39-45	6(24)	5(20)
46-52	7(28)	8(32)
53-60	4(16)	2(8)
Total	25	25
P value	0.645(NS)	0.287(NS)

Table 2: Frequency distribution of patients who subjected to Conventional and Laparoscopic surgery according to gender

Gender	Laparoscopic Surgery group NO.(%)	Conventional Surgery group NO.(%)
Male	8(32)	10(40)
Female	17(68)	15(60)
Total	25	25
P value	0.011(S)	0.157(NS)

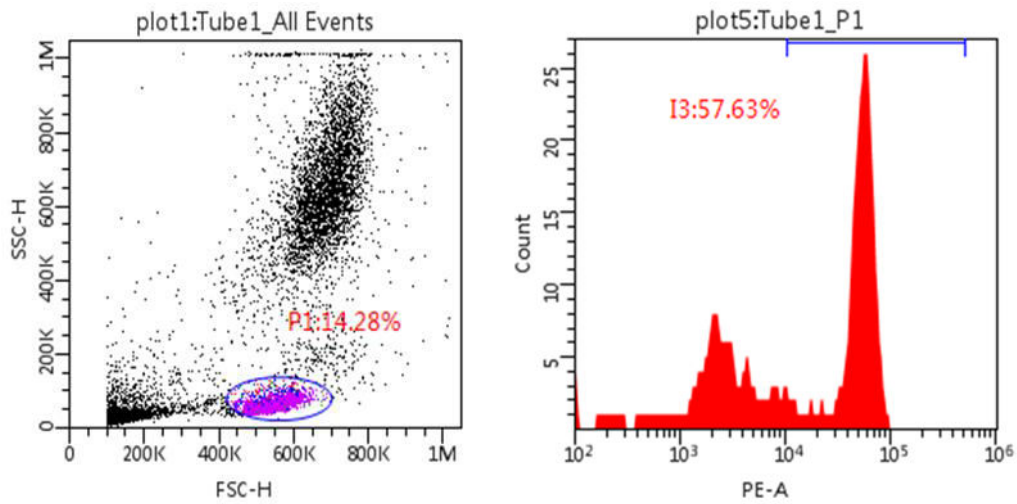
Table 3: Mean Serum concentration of Interleukin -4 in patients who subjected to Conventional and Laparoscopic surgery group before and after surgery

Serum IL4 pg/ml	Laparoscopic Surgery group		Conventional Surgery group		P value
	pre	post	pre	post	
mean±SE	48.77±2.22	47.73±1.84	53.27±1.92	34.24±0.6	0.008
Range	43.35	34.36	44.41	12.85	
Median	45.49	45.66	51.29	33.38	
Inter-quartile range	14.92	13.83	12.55	2.16	

Table 4: The comparison between the study groups pre-operatively and post operatively regarding CD4 expression

CD4 expression	Laparoscopic Surgery group		Conventional Surgery group		P value
	pre	post	pre	post	
Mean ±SE	47.2±1.62	40.59±1.4	49.73±1.38	38.04±1.16	0.168 (NS)
Range	26.67	22.1	22.14	18.83	
Median	48.22	41.14	50.7	38	
Inter-quartile range	13.6	12.21	11.5	9.22	

A



B

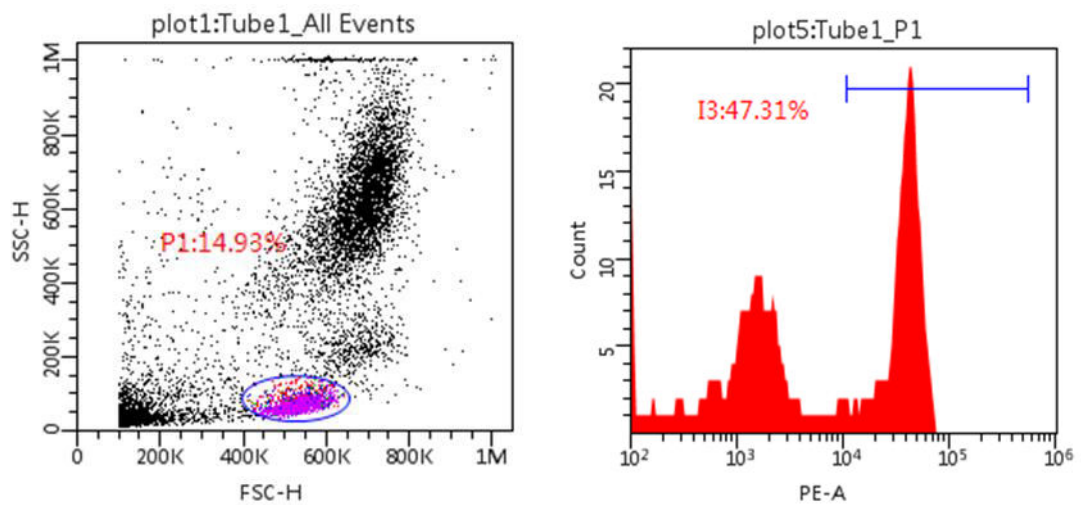
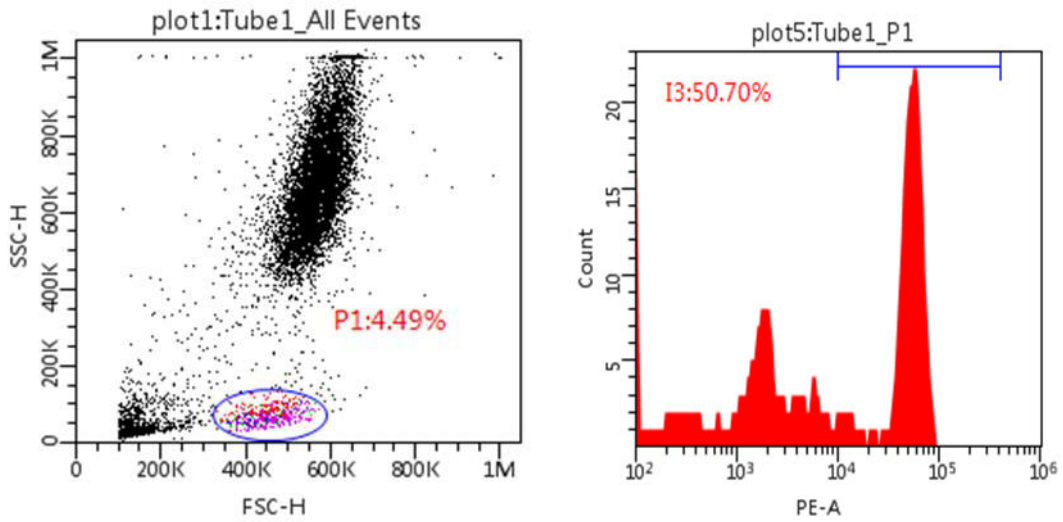


Figure 1: Flow cytometric analysis of CD4 expression on lymphocyte cells in Laparoscopicsurgical patients before taken anaesthesia (A) and after surgery (B)

A



B

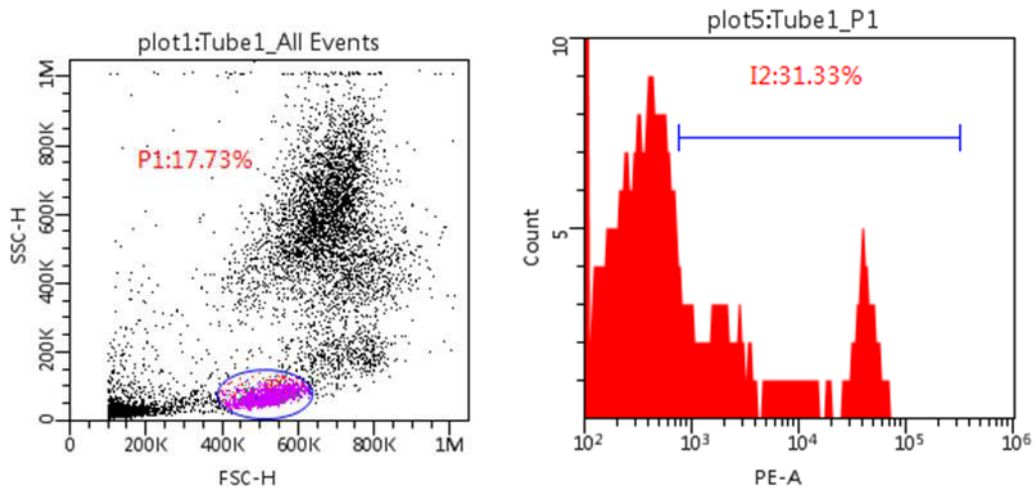


Figure 2: Flow cytometric analysis of CD4 expression on lymphocyte cells inconventional surgical patients before taken anesthesia (A) and after surgery (B)

DISCUSSION

There was no significant association between type of surgery and patients age. These results agreed with Sista et al⁽¹⁰⁾ who concluded that there was no significant difference in age in both Lap. and Con. Disagree, while the Frisch et.al.⁽¹¹⁾ found that there was a statistically difference in age with surgery at $P < 0.001$.

The concept of aging of immune system is recent and controversial. Several suggestions have been proposed to explain the reduced number of some cell types that are involved in adaptive and innate immune response and the most widely accepted explanation is the aging of bone marrow the source of all cells involved in immune system⁽¹²⁾. In agreement with current results, surgery of any kind harm homeostasis and generate various hemodynamic, metabolic and immunologic reactions. Experimental and clinical outcome have demonstrated that surgical trauma is correlated with damaged postoperative immune responses, which could be associated with an impaired generation of proinflammatory cytokines, or with inhibition of cellular responses⁽¹³⁾. The laparoscopic method is associated with less handling and traction of abdominal organs by retractors, no use of tampons on viscera or need for retraction of abdominal wall⁽¹⁴⁾. In this study the mean serum concentration of IL-4 postoperative not affected in Lap. Surgery patients while in Conventional surgery highly decreases. Fujii et al⁽¹⁵⁾ revealed that laparoscopic procedure is followed by stable IL-4, compared with open surgery group, where there is a significant increase of IL-4, suggesting that the laparoscopic approach may be related to better Th1 function, while the open approach clearly leads to activation of Th2 mediated immunity and B cell stimulation. Frank et al⁽¹⁶⁾ studied 20 patients undergoing elective cardiac surgery and concluded that the release of IL-4 was significantly reduced in the immediate postoperative period and reached a minimum in one day.

Also, the current study demonstrated that the CD4 was decreased in both groups after surgery but, in the Lap. group, the CD4+ counts was significantly higher, compared with that of open surgery group. Overall, based on recent data from prospective clinical studies, surgical stress and up-regulation of innate immunity inhibits the stimulation of cellular immune response. In particular, Decker et al⁽¹⁷⁾ in a study evaluating laparoscopic versus open cholecystectomy for symptomatic cholelithiasis, have shown that cell-mediated immunity is down-regulated while antibody-mediated immunity is up-regulated after every surgery, which seems to be obvious via a shift in the Th1/Th2 balance toward Th2 two hours after surgical incision. Huang et al⁽¹⁸⁾ showed the CD4 cell counts were decreased in both groups after surgery but, in the LC group, the CD4 counts was significantly higher. These results are in consistence with Ogawa et al⁽¹⁹⁾ in which the number of CD4 decrease immediately after operation. During the perioperative and postoperative periods, a complex biologic response takes place in response to surgical stress. This response is intended to restore homeostasis as one aspect of host defenses against surgical stress. Thus, it is a very important response for the host, but it is harmful to cellular immunity because it suppresses immunocyte function⁽²⁰⁾.

CONCLUSION

The results in the study showed that the reduced degree of T lymphocyte subsets (CD4) by laparoscopic surgery significantly lower than that by open surgery with a rapid postoperative recovery, which demonstrated that the immune function inhibition degree by laparoscopic surgery was significantly lower than that by open surgery. The production of IL-4, representing Th2 cell function, not affected in Lap. Surgery while in Con. surgery highly decreased in surgical patients.

ETHICAL CLEARANCE

The Research Ethical Committee at scientific research by ethical approval of both environmental and health and higher education and scientific research ministries in Iraq

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

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