

*Full Length Research Paper*

# Management and prognosis of HIV infected patients with postoperative sepsis

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To investigate the management and prognosis of HIV infected patients with postoperative sepsis, the clinical data of 126 HIV-infected patients aged 20 to 74 years including 114 males and 12 females were retrospectively analyzed. Patients were divided into 3 groups according to the pre-operative level of CD4+ cells: Group A (n = 73), <200 cells/μl; Group B (n = 36): 200 cells/μl ≤ CD4 + cells < 350 cells/μl; Group C (n = 17): ≥350 cells/μl. The operation was carefully performed aiming to reduce the damage to tissues. Antibiotic prophylaxis, treatments with anti-tuberculous, antifungal and anti-retroviral drugs and timely treatment of complications were carried out. In Group A, B and C, postoperative sepsis occurred in 32, 8 and 3 patients, respectively, of whom 4, 1 and 0 died of multiple organ dysfunction syndrome (MODS), respectively. Analysis showed the proportion of patients with sepsis in Group A was significantly higher than that in Group B and Group C, but no significant difference was found between Group B and C. The HIV infected patients with CD4 + cells <200 cells/μl had significantly increased risk for postoperative sepsis. Appropriate peri-operative treatment for HIV-infected patients may achieve favorable outcome.

**Key words:** Acquired immune deficiency syndrome, operative-risk evaluation, complication, sepsis.

## INTRODUCTION

Sepsis is a common complication following serious trauma/burn, shock, infection or major surgery, and is one of systemic inflammation response syndrome (SIRS) in the presence of infectious factors. Furthermore, sepsis can develop into septic shock and multiple organ dysfunction syndrome (MODS), therefore, it has extremely high mortality. Nowadays, although great progresses have been made in the pathogenesis, diagnosis and prevention of sepsis, the incidence and mortality of sepsis are still at a high level. Studies reveal the mortality of sepsis is as high as 28 to 56% (Dellinger et al., 2008; Marshall et al., 1995; Rangel-Frausto et al., 1995; Zhou and Guo, 2008). Once infected with human immunodeficiency virus (HIV), humans will develop compromised immune function. HIV patients with surgical conditions

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require surgical treatment in certain environments. Because of the compromised immune function, HIV infected patients are susceptible to post-operative sepsis of which the clinical manifestations and prognosis are different from those without HIV infected patients. From September 2008 to August 2010, a total of 126 HIV infected patients underwent surgery in the Department of Surgery, Shanghai Public Health Clinical Center Affiliated to Fudan University, among whom sepsis developed in 43 patients. Herein, we reported the management and prognosis of sepsis in these patients.

## PATIENTS AND METHODS

### Clinical data

**Table 1.** Distribution of surgery types in different groups (n).

Surgery	Group A	Group B	Group C
Gastrointestinal surgery	18	11	6
Hepatobiliary surgery	15	4	2
Orthopedic surgery	4	4	3
Urological surgery	5	2	0
Condylomata acuminata removal	10	2	2
Lymphoma removal	7	3	0
Removal of other tumors	6	3	0
Other surgeries	8	7	4
Total	73	36	17

HIV infection which was confirmed by the disease control center; (2) Patients with complete medical record: General examinations and examination of immune function before and after surgery which were carried out in the department of surgery of Shanghai Public Health Clinical Center. The age of these patients ranged 20 to 74 years with a mean age of  $41.21 \pm 12.42$  years. There were 114 males (89.5%) with a mean age of  $41.56 \pm 11.16$  years and 12 females (10.5%) with a mean age of  $39.40 \pm 7.65$  years. The median course of disease from HIV infection was  $10.50 \pm 6.20$  years and the longest course of disease was 20 years. The whole study was approved by the ethics committee of Shanghai Public Health Clinical Center.

#### Type of surgery and peri-operative management

General examinations were carried out, followed by operative-risk evaluation and preparation for surgery. There were 35 gastrointestinal surgeries, 21 hepatobiliary surgeries, 11 orthopedic surgeries, 7 urological surgeries, 14 surgeries for condylomata acuminata, 11 surgeries for lymphoma, 9 surgeries for other tumors, and 19 surgeries for other conditions such as abscess incision and drainage. For patients with abscess in the abdomen, chest or other organs, or with tuberculosis or cryptococcus infection before surgery, symptomatic treatment was carried out, and opportunistic infection was controlled. After surgery, the vital signs were monitored and complications were timely treated. Anti-inflammation, nutrition support, antiretroviral and anti tuberculosis treatments continued.

#### Grouping

According to the number of CD4 + lymphocytes one week before operation detected with flow cytometry, patients were divided into 3 groups: Group A (n = 73):  $<200$  cells/ $\mu$ l; Group B (n = 36):  $200$  cells/ $\mu$ l  $\leq$  CD4+ cells  $<350$  cells / $\mu$ l; Group C (n = 17):  $\geq 350$  cells/ $\mu$ l. The distribution of surgery types are presented in Table 1.

#### Statistical analysis

Statistical analysis was carried out with SPSS version 13.0 statistic software package. After surgery, the patients meeting the criteria for systemic inflammatory response syndrome (SIRS) with infectious factors other than HIV were diagnosed as having sepsis. Patients with dysfunctions of  $\geq 2$  organs were diagnosed with MODS.

Quantitative data were expressed as means  $\pm$  standard deviation and qualitative data were tested with paired t test and chi square test. A value of  $P < 0.05$  was considered statistically significant.

#### RESULTS

Among 126 HIV infected patients, 43 patients developed sepsis after surgery. Sepsis was found in 32, 8 and 3 patients in Group A, B and C, respectively. Four sepsis patients in Group A died of septic shock and MODS, one in Group B died of MODS and none died in Group C. The incidences of sepsis in different groups are presented in Figure 1. The results of routine blood test, liver and kidney function examination and examination of T lymphocyte subset before surgery and 2 weeks after surgery are displayed in Table 2 (5 patients that died were not included). The correlation between CD4+ cells and white blood cells before surgery was analyzed (Figure 2) and the relationship between CD4+ cells and hemoglobin is displayed in Figure 3.

#### DISCUSSION

##### Definition of sepsis in HIV infected patients

If the sepsis is defined as the SIRS in the presence of infectious factors, almost all HIV infected patients undergoing intricate surgery meet these criteria. Similar to general patients, HIV infected patients also have post-operative fever; the body temperature can reach about  $38^{\circ}\text{C}$ , the respiration and heart rate increase and the white blood cell count increase slightly. These changes may return to normal within 3 to 5 days after surgery. HIV is a kind of lentiviruses and HIV infected patients not always develop obvious constitutional symptoms that occur in the infections of common pathogens. Therefore, the sepsis in HIV patients should be SIRS in the presence of infectious factors except for HIV. HIV selectively infects cells with CD4 receptor of which the CD4+ T lymphocytes are the main affected cells. Once infected by HIV, the functions of CD4+ lymphocytes are

impaired or even these cells are destroyed, which are the main causes of immunodeficiency (Liu et al., 2010). When the number of CD4+ cells <200 cells/ $\mu$ l, patients

may develop AIDS. At this period, the immune function of these patients has been significantly compromised and

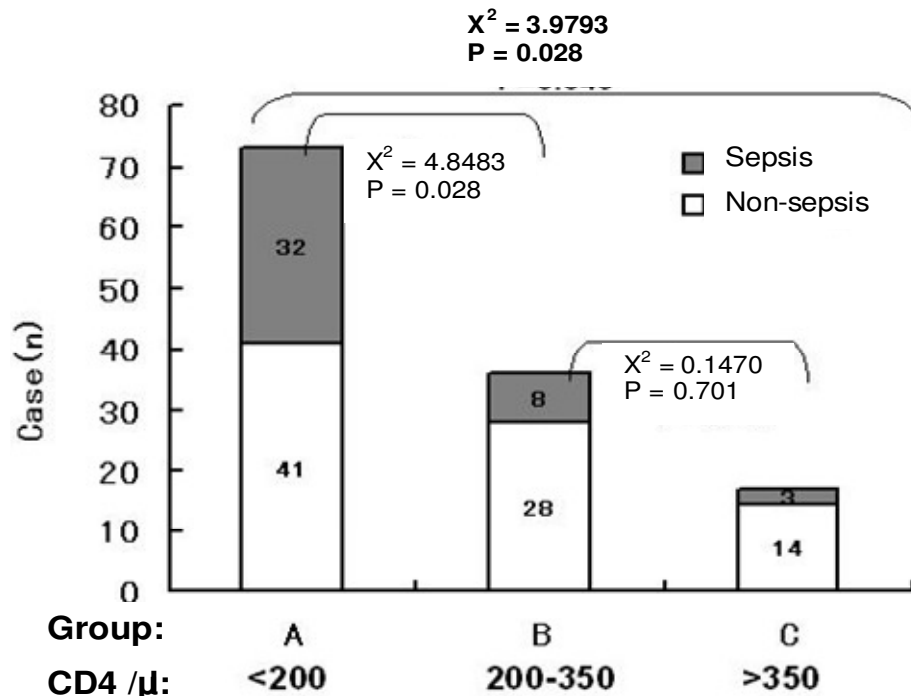


Figure 1. Post-operative sepsis in different groups.

Table 2. Routine blood test, liver and kidney functions before and after surgery in different groups (paired t test) ( $\bar{x} \pm s$ ).

	Before surgery	After surgery	t	P
White blood cell ( $10 \times 10^9$ )	6.28 $\pm$ 2.941	5.89 $\pm$ 3.188	0.718	0.475
Hemoglobin (g/L)	120.61 $\pm$ 21.581	121.27 $\pm$ 16.651	-0.204	0.839
Platelet ( $10 \times 10^9$ )	220.00 $\pm$ 108.001	225.39 $\pm$ 106.661	-0.269	0.789
Total bilirubin ( $\mu$ mol/L)	11.17 $\pm$ 8.614	10.41 $\pm$ 6.199	-0.565	0.574
Albumin (g/L)	38.59 $\pm$ 5.468	38.66 $\pm$ 4.674	-0.167	0.868
Globulin (g/L)	31.91 $\pm$ 5.656	32.07 $\pm$ 6.314	-0.304	0.762
CD4+ cell (cell/ $\mu$ l)	204.61 $\pm$ 122.492	216.76 $\pm$ 115.955	-0.718	0.475
CD8+ cell (cell/ $\mu$ l)	680.26 $\pm$ 324.093	704.03 $\pm$ 329.692	-0.613	0.542

multiple opportunistic infections can be observed in these patients. In addition, infectious complications are also common in these patients. Studies have confirmed HIV positive patients have higher incidence of post-operative sepsis and mortality (Bowley et al., 2007; Karpelowsky et al., 2009; Louis et al., 2007). Depending on patient selection and the kind of operation performed, the perioperative morbidity of these subjects was 9 to 87% (median 33.5%), while postoperative mortality ranged from 0 to 71% (median 8%) (Becker and Erckenbrecht, 2001a).

In the present study, patients were divided into 3 groups according to the number of CD4+ cells. Results

showed the incidence and mortality of sepsis in patients of Group A was significantly higher than that in Group B and Group C, which suggests the CD4+ T lymphocyte count of <200 cells/ $\mu$ l is the main cause of post-operative sepsis. The pathogens of sepsis included Tubercle bacillus, Cryptococcus, cryptosporidium bacteria, *Candida albicans*, etc. Treatment of infections of these pathogens is more difficult than that of common pathogens, and infections of these pathogens have high mortality.

#### Peri-operative treatment

Becker and Erckenbrecht speculated that perioperative morbidity of HIV-infected patients increases with the  
2392 Sci. Res. Essays

stage of their disease and during the postoperative course, HIV-infected patients have to be more often admitted to intensive care unit and kept on artificial

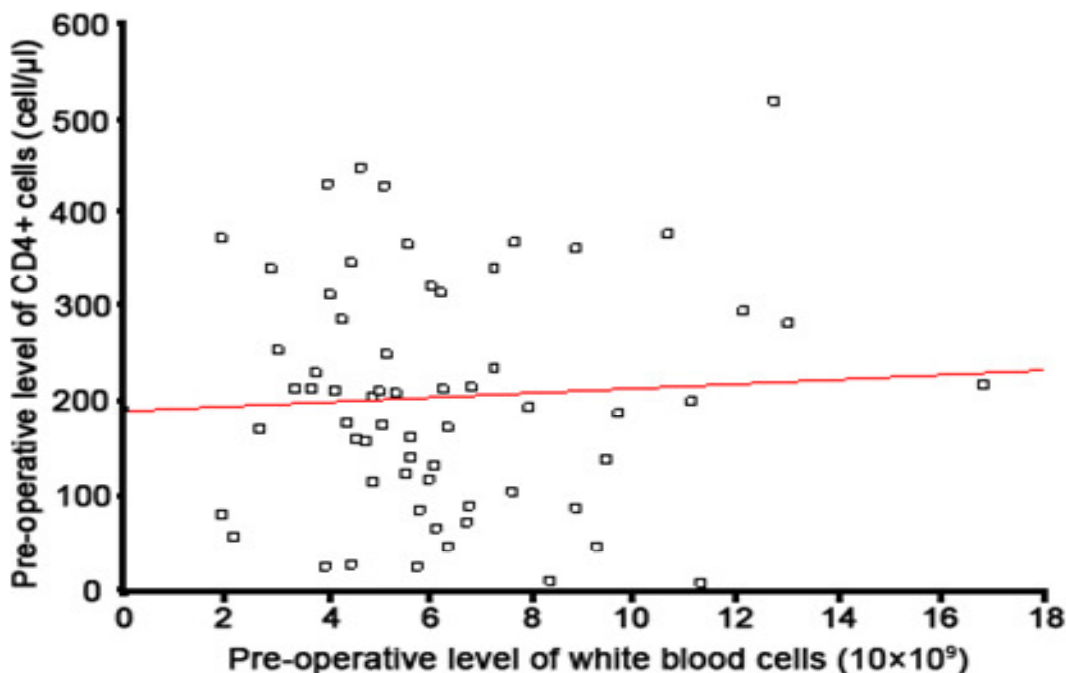


Figure 2. Correlation between CD4+ cells and white blood cells before surgery ( $r = 0.057$ ;  $P = 0.662$ )

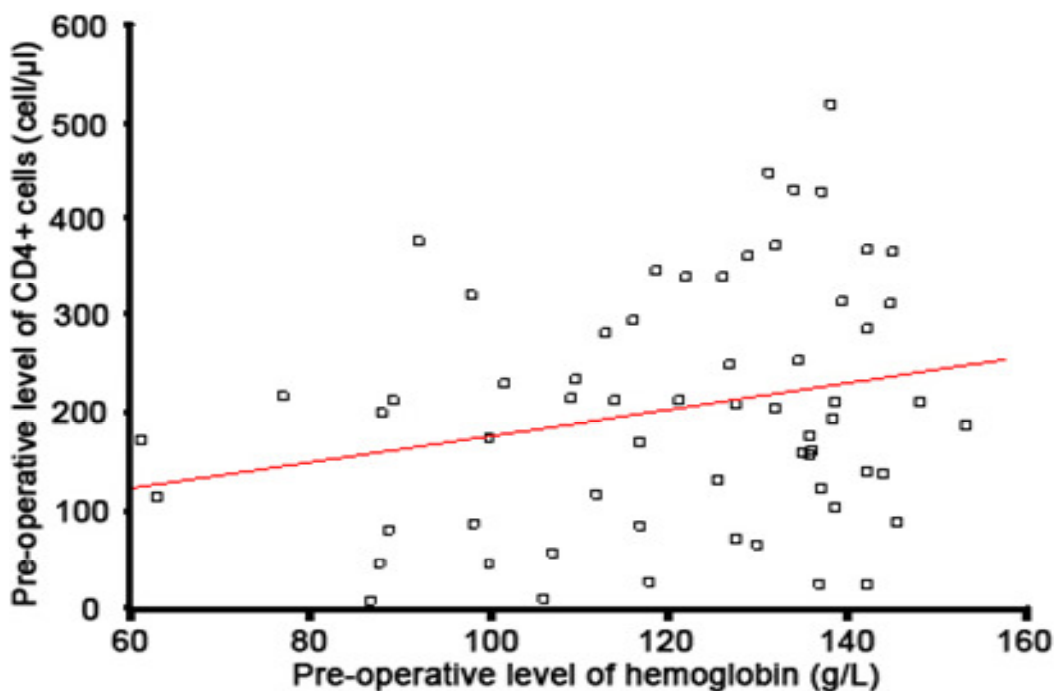


Figure 3. Correlation between CD4+ cells and hemoglobin ( $r = 0.238$ ;  $P = 0.062$ )

respiration unplannedly (Becker and Erckenbrecht, 2001b). Because pulmonary tuberculosis, fungal infection and other opportunistic infections are frequently found in HIV

infected patients (Broder, 2010; Habermann et al., 2008; Liu and Li, 2009), the general conditions of these patients should be improved before surgery. Blood transfusion,

fluid support and anti-infection can be carried out. When CD4+ cell count is <200 cells/ $\mu$ l, sulfamethoxazole and antifungal drugs can be administered to prevent infections of pneumocystis pneumonia and fungal infections. Because postoperative bowel paralysis may last 3 to 5 days after abdominal surgery, antituberculous

drugs may be given intravenously until the gastrointestinal function recovers when oral medication can be performed. Antiretroviral treatment can be discontinued on the day of operation, and continues as soon as possible after surgery. For patients undergoing abdominal surgery, nasogastric catheterization is usually performed. Therefore, the tube should be clamped after medication. The gastric juices can be aspirated when abdominal distension occurs 1 h after medication. In the present study, the anti-viral and anti-antituberculous treatments were not discontinued in the peri-operative period, and disseminated tuberculosis was not observed after surgery. Two weeks after surgery, routine blood test, examinations of liver and kidney functions and detection of cellular immune function were performed. Analysis showed there were no marked differences in the liver and kidney functions and cellular immune function before and after surgery. This finding suggests appropriate peri-operative treatment, timely treatment of complications and nutrition support are beneficial for the post-operative recovery of immune function. The immune function can return to that before surgery within 2 weeks after surgery.

### **Operative risk evaluation**

When the CD4+ cell count is greater than 350 cells/ $\mu$ l, the treatments for HIV infected patients are similar to those in general population and these HIV infected patients have similar indications for surgery to general population. When the CD4+ cell count ranges from 200 to 350 cells/ $\mu$ l, detection of concomitant diseases should be performed. If concomitant diseases are not present, the extent of surgery should be reduced or the vital signs should be kept stable during surgery which may minimize the damage to patients. If concomitant diseases are found, pre-operative risk evaluation is necessary. The surgery program should be based on the control of concomitant diseases. When the CD4+ cell count is lower than 200 cells/ $\mu$ l, the indications for surgery should be carefully evaluated. Under certain conditions, surgery may be the only strategy to save life. However, the risk of surgery and the prognosis should be explained to patients and their relatives before the decision of surgery. In the present study, one patient with CD4+ cell count of 6 cells/ $\mu$ l underwent emergency surgery due to peritonitis in combination with intestinal perforation. The perforated and necrotic intestine was removed and proximal enterostomy was carried out. Although wound infection was observed after surgery, this patient was discharged with favorable wound healing after treatment. For a cryptococcal meningitis patient with CD4+ cell count of 34

cells/ $\mu$ l, sigmoid colostomy was performed due to perianal ulcer. Antifungal and antiretroviral treatments in combination with sterile dressing change were carried out after surgery. When perianal ulcer recovered, sigmoid colostomy closure was performed. The patient was discharged with favorable outcome. A study from Africa Liu et al. 2393

showed although the hospital mortality, hospital stay and severity of sepsis were not related to CD4 counts, the patients with lower level of CD4 cells had higher mortality (Cacala et al., 2006).

In the present study, all the patients aged about 40 years and more males were recruited. About 25% of patients were first diagnosed with HIV infection by HIV antibody test. With the decrease of CD4+ cells, patients develop varied opportunistic infections accompanied by fever, body weight loss, anemia, etc. However, the hemoglobin level and white blood cell count were near normal in some patients although they had decrease of CD4+ cells. Analysis of the correlation between CD4+ cells and hemoglobin or white blood cells showed CD4+ cells were not significantly related to white blood cells and hemoglobin. Therefore, the white blood cells and hemoglobin can not be used to assess the cellular immune function. The operative risk evaluation should include general conditions, the complexity of surgery and the level of CD4 cells.

### **Prognosis of sepsis in HIV infected patients**

The mild infection of wound alone can resolve after timely treatment. For patients with infections of tubercle bacillus or fungus, the surgery should be performed only after these opportunistic infections are controlled unless emergency surgery is necessary. Furthermore, emergency surgery should be performed only after sufficient preventive treatments have been carried out, and antibiotics, anti-fungal drugs can be administered during and after surgery. In the present study, of 43 patients with post-operative sepsis, 5 died among whom 3 died of serious pulmonary infection and 2 died of serious abdominal infection induced septic shock and multiple organ dysfunction syndromes (MODS). The remaining patients with post-operative sepsis recovered after appropriate treatment. Therefore, systematic examination, operative risk evaluation, proper measures to control opportunistic infections and timely surgery to resolve the life-threatening problem or the problems influencing the subsequent treatment are beneficial for improvement of quality of life and survival rate. The application of antiretroviral drugs can keep the HIV infected patients in a stable stage and facilitate the immune reconstruction of these patients which finally prolong the survival time.

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2394        Sci. Res. Essays

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