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Research Article

Risk Assessment System For Postoperative Concurrent Sepsis In HIV-Infected Trauma Patients

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ABSTRACT

Background: Patients with acquired immunodeficiency syndrome (AIDS) are more prone to sepsis after trauma. No systematic evaluation system during the perioperative period is available for the risk assessment of posttraumatic sepsis with AIDS. **Objective:** This study aimed to investigate the risk factors for sepsis in human immunodeficiency virus (HIV) -infected trauma patients during the perioperative period. **Methods:** A retrospective analysis was performed based on the clinical data. A total of 89 HIV-infected trauma patients, who underwent surgical treatment at the Shanghai Public Health Clinical Center from January 2009 to December 2016, were divided into sepsis and non-sepsis groups according to the presence or absence of sepsis. A risk assessment table was designed to evaluate the scores of the two groups. Risk indicators included CD4+ T cell score, surgical grade score, surgical classification score, opportunistic infection score, organ function score, and comprehensive score. **Results**: Sepsis occurred in 18 patients. Statistically significant differences were observed in CD4+ T cell score, surgical grade score, surgical classification score, opportunistic infection score, organ function score, and comprehensive score between sepsis and nonsepsis groups. From ROC curve, the cutoff value of comprehensive score was 8.5, the sensitivity value was 1, the specificity value was 0.92, and the area under the curve was 0.99. **Conclusions**: The risk of sepsis in HIV-infected trauma patients can be predicted through the comprehensive score. Therefore, if the comprehensive score is more than 8.5, relevant response measures are recommended for the prognosis of sepsis in HIV-infected trauma patients.

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INTRODUCTION

Posttraumatic sepsis is a common complication of severe trauma (1, 2). Human immunodeficiency virus (HIV) weakens the human immune system by destroying certain white blood cells called CD4+ cells. The infection-related complications are more likely to occur in HIV-infected patients who need surgery after severe trauma. Sepsis is a systemic inflammatory response syndrome caused by infection. It can further develop into severe sepsis, resulting in septic shock and multiple-organ dysfunction syndrome. Therefore, the mortality rate is extremely high (3, 4). The risk assessment in normal trauma patients includes patients' general condition and difficulty in surgery during the perioperative period. However, no uniform evaluation criteria are available for HIV-infected trauma patients. This study aimed to establish a systematic evaluation system for assessing postoperative sepsis.

MATERIALS AND METHODS

Clinical data and grouping

A total of 89 HIV-infected trauma patients were retrospectively analyzed, including 73 males and 16 females, and treated at the Shanghai Public Health Clinical Center from January 2009 to December 2016. Their average age was 38.8 years. All trauma patients received general emergency treatment in the nearest hospital. The HIV antibody test was positive. Therefore, the patients underwent surgical treatment in the Shanghai Public Health Clinical Center. They were divided into sepsis (18 patients) and non-sepsis groups (71 patients) based on the presence or absence of sepsis after the operation. No patient died during the surgery.

Flow cytometry analysis

Blood was collected in EDTA-coated tubes. Red blood cells were lysed by adding 5 mL of ammonium–chloride–potassium lysing buffer (0.16M NH_4Cl, 10mM $KHCO_3$, 0.13mM EDTA, pH 7.2) for 5 min on ice, followed by washing with phosphate-buffered saline twice. Single-cell suspensions (1×10^6 cells per sample) were incubated with appropriate antibodies for 45 min at 4°C. Then, the cells were washed twice and detected using a FACS Canto II flow cytometer (BD Biosciences, San Jose, CA, USA). Data were analyzed using FlowJo (Tree Star, OR, USA). The following antibodies were purchased from BioLegend (CA, USA): fluorescein isothiocyanate–labeled anti-CD3, PE-labeled anti-CD4, and APC-labeled anti-CD8.

Treatment strategies

Routine preoperative tests were performed after admission, including the peripheral blood CD4+ T cells, by flow cytometry. The five indicators, including numbers of CD4+ T cells, wound classification, surgical grade, opportunistic infection, and organ function, were divided into four grades. Table 1 shows surgical risk scores for HIV-infected patients. The surgical risk was scored using the surgical risk score table. The surgical strategy was adjusted according to the surgical risk score. Surgery types included were as follows: fracture reduction and internal fixation in different parts, anastomosis of urethral rupture for trauma, loosening of intestinal adhesions, closure of bowel fistula, traumatic debridement, and so on. The general situation of patients improved before the operation, and anti-infection treatment was given because of preoperative infection (common bacterial infection, tuberculosis, fungal infection, and so on). The antiretroviral therapy (ART) was performed before and after the operation. Postoperative monitoring of vital signs, detection of various complications, anti-infection treatment, nutritional support, and other treatments were also performed in each group.

Statistical analysis

Descriptive data were expressed as mean ± standard deviation, whereas counting data were expressed as percentage. The differences between the samples were analyzed using the rank-sum analysis. The receiver operating characteristic (ROC) analysis method was used to evaluate the reliability of the risk assessment model so as to establish a risk assessment model for HIV-infected patients.

RESULTS

Of the 89 patients, 18 had sepsis. The CD4+ T lymphocyte count was 293.8 cells/μL in the sepsis group, which was significantly lower than 446.0 cells/μL in the non-sepsis group ($P < 0.05$). Statistically significant differences were found in CD4+ T cell score, surgical grade score, wound classification score, opportunistic infection score, organ function score, and comprehensive score between the two groups ($P < 0.05$). The ROC curve was used to determine the risk score of sepsis. The cutoff value of comprehensive score, sensitivity, and specificity were 8.5, 1, and 0.92, respectively. The area under the ROC curve was 0.99 (95% confidence interval: 0.942–1.015). As shown in Figure 1A, the surgical risk score was used to determine postoperative sepsis. In this study, 89 HIV-infected patients were discharged, and no intraoperatively or postoperative deaths were reported. Figure 1B shows the distribution of scores in the two groups after the operation.

Figure 1. Comprehensive score on the prediction of postoperative sepsis.
(A) ROC analysis of postoperative sepsis risk assessment.
(B) Surgical risk score distribution in the sepsis and non-sepsis groups.

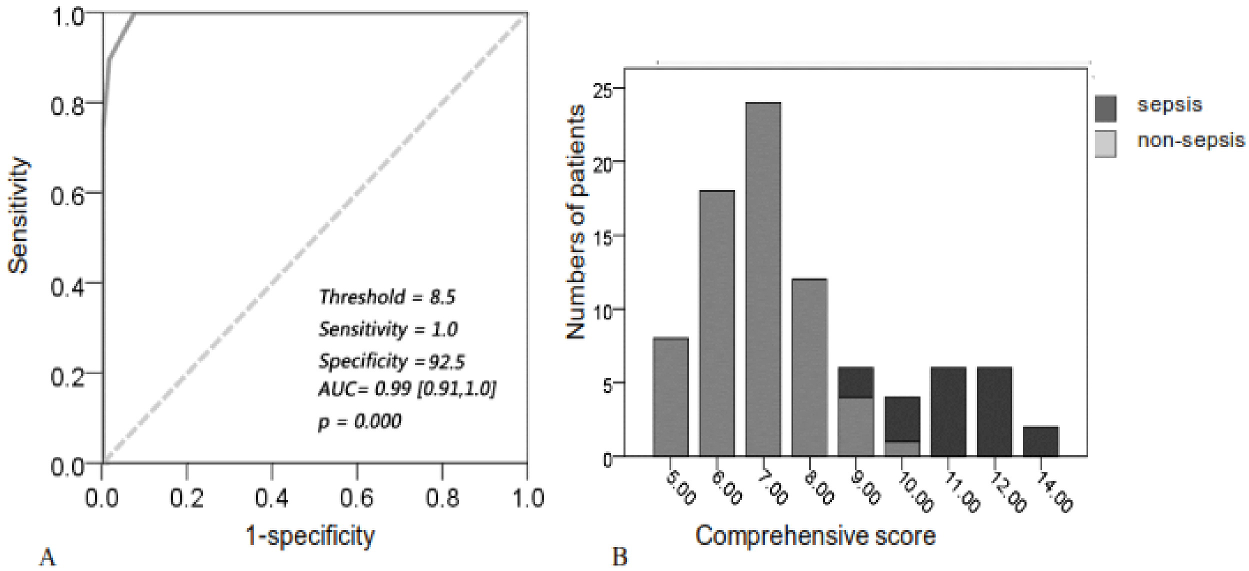

Table 1. Surgical risk scores for HIV-infected patients

Risk scores	1	2	3	4
CD4+ T cells （cells/μL)	＞350	350–200	Between ＞50 and ＜ 200	≤50
Surgical grade	Clean	Clean –polluted	Polluted	Infected
Surgical classification	I	II	III	IV
Opportunistic infection	No	Existed in the past	Mild infection	Serious infection
Organ function	Normal	Abnormal but no symptoms	Mildly abnormal	Seriously abnormal

Table 2. Basic information scores in sepsis and non-sepsis groups

Risk scores	Sepsis	Non-sepsis	Mann–Whitney *U*(standardized) /Fisher's exact test	*P* value
Sex (male/female)	13/5	60/11	–	0.30
Age	38.3 (32.1–44.6)	43.9 (40.1–47.1)	1.61	0.10
CD4+ cells	2.2 (1.77–2.63)	1.5 (1.3–1.6)	3.40	0.00
Surgical classification	2.0 (1.37–2.63)	1.1 (1.0–1.2)	4.04	0.00
Surgical grade	2.7 (2.3–3.1)	2.2 (2.0–2.4)	2.58	0.01
Opportunistic infection	2.4 (2.1–2.8)	1.1 (1.0–1.2)	7.05	0.00
Organ function	1.9 (1.6–2.3)	1.1 (1.0–1.1)	7.18	0.00
Comprehensive score	11.2 (10.2–12.2)	6.9 (6.6–7.2)	4.62	0.00
CD4+ (mean)	293.8 (184.2–403.6)	446.0 (393–9,498.1)	2.85	0.04

DISCUSSION

Design of risk score table for HIV infection

CD4+ T lymphocytes can be selectively violated after HIV infection in the human body. HIV replicates and damages CD4+ T lymphocytes, resulting in immunodeficiency (5-8). Opportunistic infections (such as tuberculosis, fungal infection, pneumocystis carini pneumonia, and so on) may occur simultaneously when the count of CD4+ T lymphocytes is below 200 cells/μL, leading to related organ dysfunction (such as respiratory dysfunction because of tuberculosis or pneumocystis carini pneumonia). Therefore, a reduction in the number of CD4+ T lymphocytes is an important risk factor for surgery (9-13). However, the risk of postoperative trauma surgery is related to microbial contamination during surgical incision, degree of difficulty in surgery, opportunistic infections, and function of the main organs such as heart, liver, and kidney (14, 15). At present, no risk assessment system for HIV infection is available at home and abroad. Therefore, the surgical risk score table was designed in this study, including CD4+ T lymphocytes, surgical grade, surgical classification, opportunistic infection, and major organ function.

The number of CD4+ T lymphocytes in HIV-infected patients was >350 cells/μL. The scoring in the score table was as follows: 1 point, the immune function was not significantly damaged; 2 points, the number of CD4+ T lymphocytes was 350–200 cells/μL; 3 points, the number of CD4+ T lymphocytes was between <200 and >50 cells/μL; 4 points, the number of CD4 + T lymphocytes was ≤50 cells/μL. The surgical grading was as follows: 1, clean; 2, clean–polluted; 3, polluted; and 4, infected. The surgery was classified as follows: 1, simple surgery (I); 2, more complex surgery (II); 3, complex surgery (III); and 4, difficult and complex surgery (IV). Opportunistic infections were divided as follows: 1, no opportunistic infections; 2, past opportunistic infections but not before surgery; 3, mild opportunistic infections before surgery; and 4, serious opportunistic infections before surgery. Preoperative heart, lung, liver, and kidney functions were classified as follows: 1, basic normal; 2, abnormal but no symptoms; 3, mild symptoms; and 4, serious symptoms. This surgical risk score table served as a more comprehensive assessment because it combined the patient's immune status, surgical incision, complexity of surgery, opportunistic infection, and general condition. In this study, the basic information was compared between the two groups. No statistical differences were found in terms of sex ($P = 0.30$) and age ($P = 0.10$) between the two groups, but significant differences were observed in CD4 + T cell count, incision classification, surgical grade, opportunistic infections, and organ function ($P < 0.05$).

Clinical application of surgical risk score table

At present, HIV-infected patients in China are sent to the infectious disease hospital, but HIV-infected trauma patients are usually sent to the nearest hospital. Some trauma patients are not aware of HIV infection before emergency surgery. Doctors in the hospital become panicky once the HIV-infected patients are diagnosed for emergency surgery. In fact, the damage to the immune system can be quickly controlled using ART, resulting in the long-term survival of HIV-infected patients. Currently, about 10 million new patients are diagnosed with HIV infection every year in China, including HIV-infected trauma patients needing emergency treatment (16, 17). The risk of surgery is assessed based on the difficulty in surgery, patient's general condition, and tabulation to determine the treatment program in patients without HIV. However, a large number of studies reported that CD4+ T lymphocyte counts in HIV-infected patients were associated with postoperative infection–related complications (18-20). In this study, significant differences were found in CD4+ T lymphocyte counts between the two groups. However, the issue was how to easily assess the risk of HIV infection based on clinical findings. The scores of CD4+ T lymphocytes, incision classification, surgical grade, opportunistic infection, and organ function were used in this study. Table 2 shows statistically significant differences in these five indicators between the two groups. The risk assessment model based on the total score using the ROC classification method is shown in Figure 1A. The sepsis risk score was 8.5, which was the best set point to assess the sensitivity and specificity of sepsis after surgery. If the total score was less than 8.5 in HIV-infected patients, the possibility of no sepsis was 100%. The score of sepsis was ≥9, and the incidence of sepsis was 92.5%; that is, the specificity of sepsis was 92.5%. The assessment of total score and the probability of occurrence of postoperative sepsis could improve the efficacy of the treatment of sepsis. Most scholars believe that the CD4+ T lymphocyte count ≥200 cells/μL guarantees surgical safety (21, 22). The data on cases of HIV infection in the past were summarized, and the CD4+ T lymphocyte count <50 cells/μL was found to be appropriate for surgery; however, the risk of sepsis was high. Patients with high viral load and CD4+ T lymphocyte count <350 cells/μL should be given antiviral drugs to block viral replication for at least 10 days, thereby reducing the number of viruses in the body and CD4+ T lymphocyte damage and increasing the patient's immunity. However, open reduction and internal fixation surgery should be performed in 3 weeks after injury. General ART should be given immediately after a definite diagnosis and completed in 3 weeks. As HIV-infected patients are often associated with tuberculosis, fungal infection, pneumocystis carini pneumonia, and other opportunistic infections, the general situation of patients should be improved as much as possible by anti-infection, anti-fungal, anti-tuberculosis, and other treatments. Patients with no opportunistic infection should be given fluconazole and sulfamethoxazole to prevent fungal infection and pneumocystis carini pneumonia when the CD4+ T lymphocyte count is <200 cells /μL. HIV-infected patients with multiple-organ dysfunction should be given preoperative treatment to correct their general condition and restore organ function. It may reduce the incidence of sepsis. If the preoperative risk of surgery is fully assessed, HIV-infected patients can be treated effectively to shorten the operation time and simplify the surgical process.

No sepsis occurs in patients when the score is below 9 points according to the surgical risk score table; these patients are not different from normal patients. When the score reaches 9 points or above, a variety of measures should be taken, including performing ART, giving life support, improving vital organ function, shortening the operation time, simplifying the surgical process, and reducing the risk score. For example, open fractures can be first debrided to decrease the incision classification score, intestinal peritonitis with abdominal trauma can be resolved using intestinal fistula and abdominal drainage, and urethral rupture can be resolved using bladder fistula and urinary extravasation. These methods can improve the general condition and reduce surgery risk score for the second phase of surgery. The five indicators from different aspects reflected the patient's immune system, organ function, surgical method, infection related to surgical incision, and difficulty in surgery. These factors can affect the occurrence of postoperative sepsis in patients, or even the prognosis of patients. Preoperative surgical risks should be assessed for a positive response. Especially patients with high scores should be given appropriate treatment during the perioperative period. For example, if the risk assessment score is more than 12, life support treatment should be given as far as possible to improve the organ function and determine the use of simple surgical program to reduce the risk score. When the risk assessment score is more than 15, the risk of surgery is extremely high. In this study, no more than 15 patients died without operation.

CONCLUSIONS

The occurrence of sepsis is related to the CD4+ T cell score, surgical grade score, surgical classification score, opportunistic infection score, organ function score, and comprehensive score. The risk of sepsis in HIV-infected trauma patients can be predicted from the comprehensive score. Therefore, if the comprehensive score is more than 8.5, the relevant response measures are recommended for the prognosis of sepsis in HIV-infected trauma patients.

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