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Changes in the immune index before and after surgery in urinary malignancy patients with AIDS

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The immune index is an important marker of HIV immune function. Long-term clinical experience revealed that in urinary malignancy patients with AIDS who underwent radical surgery for malignant tumors, the preoperative and postoperative immune indices changed to different degrees, which affected patient prognosis. A total of 48 AIDS patients who underwent radical resection of malignant tumors in the Department of Urology of Beijing You 'an Hospital between 2015 and 2023 were included, including 25 patients with kidney cancer, 12 patients with bladder cancer and 11 patients with prostate cancer. A paired t test was used to study the changes in the immune indices CD4 +T, CD8 +T, CD3 +T and CD4+/CD8 +T cells before and after surgery for different malignant tumors in the urinary tract. The chi-square test was used to study the effects of clinical variables such as age, sex, hypertension status, diabetes status, duration of operation, duration of HIV infection, duration of medication and viral load on preoperative and postoperative immune indices. The area under the ROC curve of the four immune indicators before and after surgery was compared to evaluate the influence of immune indicators on patient prognosis. Survival curves were drawn to study the prognostic risk of immune indicators. The mean CD4 +T, CD8 +T and CD3 +T-cell counts decreased before and after surgery in patients with renal, bladder and prostate cancer, and $P < 0.05$ according to paired t tests indicated statistical significance, while the CD4+/CD8 +T-cell ratio was not significantly different according to paired t tests. Clinical variables such as age, sex, hypertension status, diabetes status, duration of operation, duration of HIV infection, duration of medication and viral load had no statistically significant effects on the preoperative or postoperative immune indices. The area under the ROC curve of the four immune indices was compared, and the results showed that CD8 +T cells [preoperative AUC of 0.678 ($P < 0.05$) and postoperative AUC of 0.702 ($P < 0.05$)] were superior to the other indices. Survival curve analysis revealed that a decrease in CD4 +T, CD8 +T and CD3 +T cells after surgery led to a decrease in the survival rate of patients, but the results were not statistically significant. CD4 +T, CD8 +T and CD3 +T cells decreased before and after surgery in patients with malignant tumors of the urinary system complicated with AIDS, and CD8 +T cells had a statistically significant effect on patient prognosis compared with other immune indices.

Keywords Malignant tumor of the urinary system, AIDS patient, Immune index, Survival prognosis

Patients with malignant tumors of the urinary system combined with AIDS constitute a special group of patients. Radical resection of malignant tumors is needed to improve quality of life and prolong survival time, but it the affects autoimmune function. Therefore, in addition to the tumor pathology, age, underlying diseases, and operation time of patients with common urinary tract tumors, the perioperative evaluation of this group of patients also included additional proprietary indicators, such as duration of infection with AIDS, duration of antiviral drug treatment, and viral load, to fully evaluate the tolerance and survival prognosis of AIDS patients after tumor resection.

The majority of malignant tumor patients undergoing radical surgery have received good education, usually have a high degree of adherence to doctor's orders, can regularly take antiviral drugs after exposure to HIV, and can regularly monitor relevant immune indicators, including CD4 + T, CD8 + T, CD3 + T, and CD4/CD8, in specialized hospitals. The surgery itself is a shock to the patient, and it is usually performed on the premise that the overall benefits of the surgery outweigh the risks of the surgery itself, such as surgical wound pain, dizziness and nausea caused by postoperative anesthesia, postoperative fasting, postoperative fluid replacement, postoperative decreases in the serum ALB and hemoglobin, and electrolyte disturbances. The levels of CD4

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+T cells, CD8 +T cells, CD3 +T cells, and CD4 +T cells/CD8 +T cells, which are specific indicators of AIDS patients, will decrease or increase before and after surgery to different extents. In this study, we collected relevant clinical data, combined with our clinical experience in the treatment of urinary tract tumors in AIDS patients, to assess the impact of surgery on changes in immune indices and the prediction of survival outcomes in these patients.

Materials and methods

Patients

A total of 48 AIDS patients who underwent radical resection of malignant tumors in the Department of Urology of Beijing You 'an Hospital between 2015 and 2023 were enrolled, and all of them were confirmed to have malignant tumors of the urinary system. These patients were able to take antiviral drugs as required before surgery, and regular follow-up was performed to assess relevant indicators after surgery. Patients with urinary malignancies without AIDS, patients who did not receive antiviral drugs, patients who were lost to follow-up after surgery, and patients who did not have preoperative or postoperative immunoassay results were excluded from the study.

This study was performed in accordance with the Helsinki Declaration and approved by the Ethics Review Committee of the included hospital. During follow-up, patients or next to kin were informed of the study in detail, and informed consent was obtained. The project number is YNKTQN20150212.

ART regimen

Of the 48 patients, 46 were sexually transmitted and 2 were blood transmitted. The time after HIV infection is 10 months to 80 months. All patients underwent ART therapy with Bittovir (a triple compound single tablet containing biketitravir 50 mg, emtricitabine 200 mg, tenofovir profol 25 mg, BIC/FTC/TAF).

Laboratory testing

In addition to routine preoperative blood tests and examinations, all patients underwent preoperative and postoperative blood tests for immune indices, including CD4 +T, CD8 +T, CD3 +T, CD4+/CD8 +T (flow cytometry [FC]) and viral load (real-time PCR), within 1 month of the perioperative period.

Follow-Up and study endpoints

One year after surgery, the patient returned to the hospital for follow-up every 3 months, and routine blood sampling, chest X-ray, abdominal color ultrasound, urinary CT, and tumor marker analysis were performed to determine the patient's current prognosis and whether the tumor recurred or metastasized. We considered OS as the endpoint of the study (in months). OS was defined as the time from the date of surgery to the date of death from any cause.

Statistics

A paired t test was used to determine the associations between preoperative and postoperative immune indices of urinary tumors. The chi-square test was used to study the effects of age, sex, hypertension status, diabetes status, operation duration, duration of HIV infection, duration of medication and viral load on preoperative and postoperative immune indices. Kaplan–Meier survival curves were plotted to estimate OS. GraphPad Prism Version 9 (GraphPad Software, La Jolla California USA, www.graphpad.com) was used to generate survival curves, and paired t tests were performed. Statistical analysis and ROC curve mapping were performed using SPSS version 23 (SPSS Inc., Chicago, IL, USA). Our laboratories used FACSCanto-II flowcytometers (BD Biosciences, San Jose, CA), Standardized EuroFlow SOPs for instrument set-up and calibration were used for the instruments, as provided in detail via the EuroFlow website (www.EuroFlow.org).

Results

Immune indices before and after surgery

Paired t tests revealed that the mean values of CD4 +T (P= 0.002, 95% confidence interval 46.39–188.56), CD8 +T (P= 0.026, 95% confidence interval 22.16–325.27) and CD3 +T (P= 0.014, 95% confidence interval 63.64–502.67) decreased in patients with renal cancer combined with AIDS before and after surgery. For patients with bladder cancer combined with AIDS, the mean numbers of CD4 +T cells (P= 0.001, 95% confidence interval 44.05–118.77), CD8 +T cells (P= 0.001, 95% confidence interval 100.77–291.89) and CD3 +T cells (P= 0.000, 95% confidence interval 185.25–425.41) decreased before and after surgery. For patients with prostate cancer combined with AIDS, the mean values of CD4 +T (P= 0.001, 95% confidence interval 59.02–176.97), CD8 +T (P= 0.046, 95% confidence interval 2.16–196.37) and CD3 +T (P= 0.013, 95% confidence interval 47.79–323.11) decreased before and after surgery (Figs. 1, 2 and 3, Table 1). The changes in CD4+/CD8 +T cells were not statistically significant.

As can be seen from the data results in Table 1, postoperative CD4 +T cells, CD8 +T cells and CD3 +T cells decreased compared with those before surgery, which had no relationship with the type of urinary tract tumor, and the P-value was low, indicating significant statistical significance. A wide confidence interval result is associated with not too high a number of cases, but the 95% confidence interval in our results does not contain zero, indicating a significant difference, and the farther from zero the greater the difference. The greater the absolute value of T-value, the greater the difference between the paired sample means. If the absolute value of T is greater than 1.96, the difference between the paired samples is

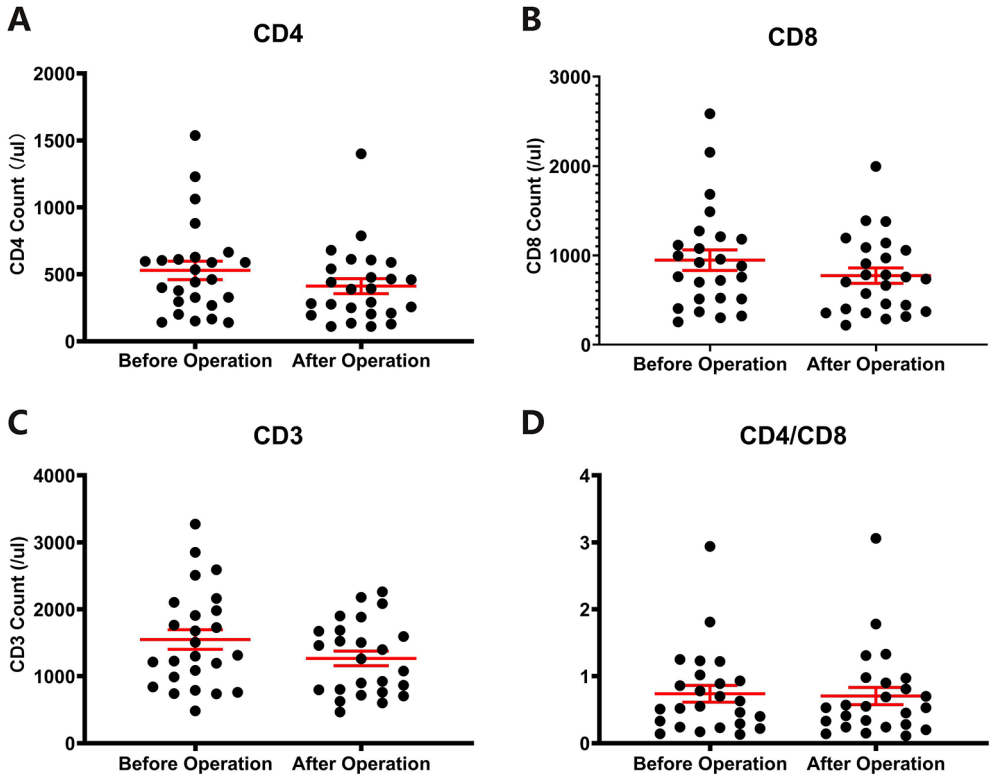

Fig. 1. Immunization index for renal cancer patients before and after operation.

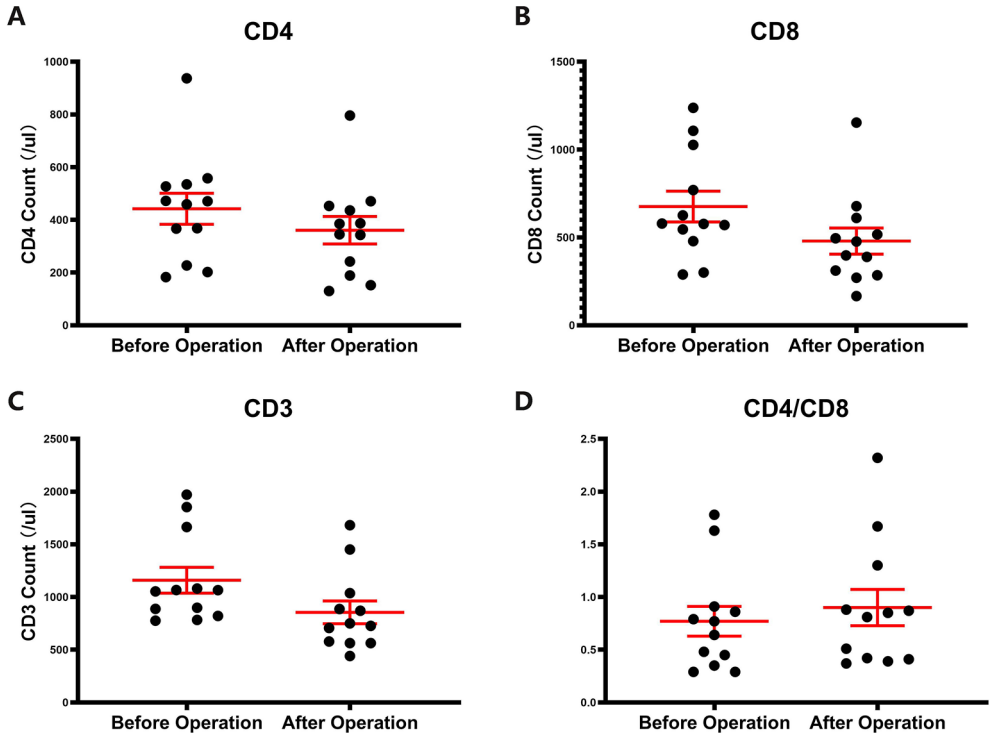

Fig. 2. Immunization index for bladder cancer patients before and after operation.

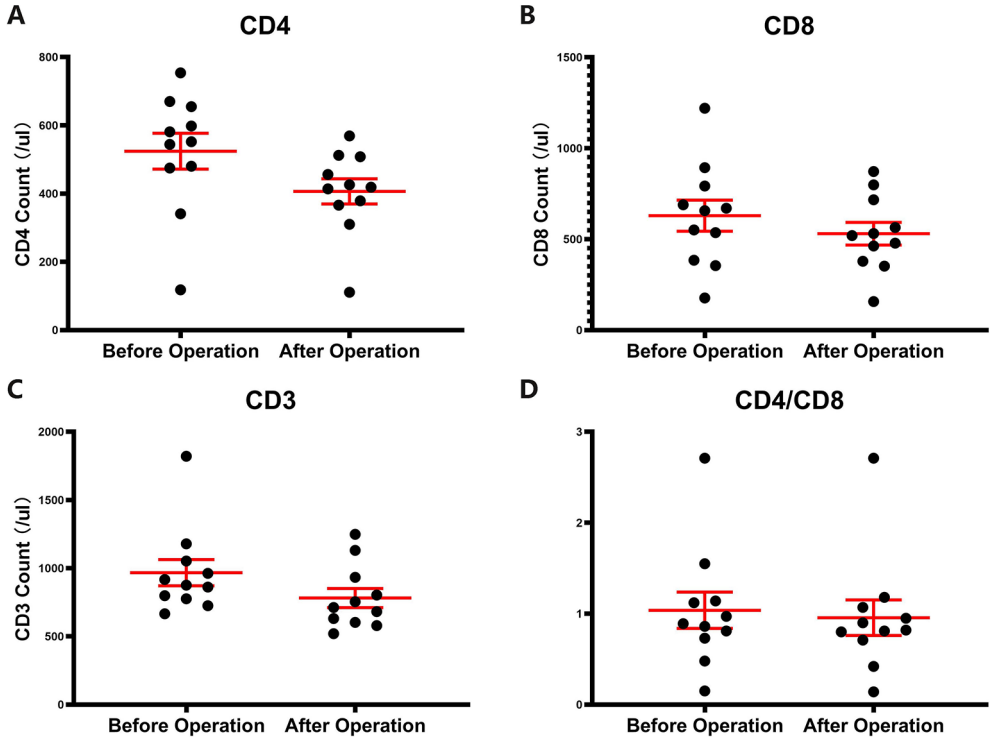

Fig. 3. Immunisation Index for prostate cancer patinents before and after operation.

Group		CD4 + T(%)		CD8 + T(%)		CD3 + T(%)		CD4/CD8	
		Before operation	After operation	Before operation	After operation	Before operation	After operation	Before operation	After operation
RC	*n* = 25	529 ± 69	411 ± 56	946 ± 114	772 ± 86	1548 ± 146	1265 ± 109	0.7380 ± 0.125	0.7040 ± 0.129
	95% confidence interval	46.39–188.56		22.16–325.27		63.64–502.67		− 0.03772- 0.10572	
	T value	3.411		2.366		2.662		0.978	
	P value	0.002		0.026		0.014		0.338	
BC	*n* = 12	442 ± 58	35,260±	675 ± 87	479 ± 74	1159 ± 122	854 ± 108	0.7700 ± 0.141	0.9000 ± 0.172
	95% confidence interval	44.05–118.77		100.77–291.89		185.25–425.41		− 0.23857- − 0.02143	
	T value	4.797		4.522		5.597		− 2.635	
	P value	0.001		0.001		0.000		0.023	
PC	*n* = 11	524 ± 52	406 ± 36	629 ± 85	530 ± 62	966 ± 96	781 ± 70	1.0373 ± 0.199	0.9555 ± 0.195
	95% confidence interval	59.02–176.97		2.16–196.37		47.79–323.11		− 0.05424- 0.21788	
	T value	4.458		2.278		3.002		1.340	
	P value	0.001		0.046		0.013		0.210	

Table 1. Immune indices before and after surgery.

significant. The paired T-test results in Figs. 1, 2 and 3; Table 1 support each other, and more intuitively show the mean difference of preoperative and postoperative immune indicators. In addition to a few points, most of the points in the figure fall near the mean value, which has good statistical significance.

Clinical variables and their effects on preoperative and postoperative immune indices

Among the 48 patients with urinary malignancies complicated with AIDS, there were 25 patients with renal cancer, with a median age of 50 years (30–73), 21 males and 4 females, 4 patients complicated with hypertension and 4 patients with diabetes. The median duration of radical surgery was 156 min (110–200), and the average hospitalization duration was 11 days. There were 12 patients with bladder cancer with a median age of 57 years (30–78), all male, 1 patient with hypertension and 2 patients with diabetes. The median duration of radical surgery was 232 min (180–300), and the average hospitalization duration was 13 days. There were 11 patients

	Renal cancer	Bladder cancer	Prostate cancer
Number of patients	25	12	11
Age (years)	50 (30–73)*	57 (31–78)	67 (52–82)
Gender (M/F)	21/4	12/0	11/0
Duration of surgery (min)	156.4 (110–200)	232.5 (180–300)	265.5 (200–320)
Duration of hospital stay (days)	11.4 (7–14)	13 (9–17)	14.4 (10–20)
Blood transfusion (ml)	0	0	0
Hypertension	4	1	2
Diabetes	4	2	1
Years of infection with AIDS	3.14 (1–7)	1.875 (1–3)	2.5 (1–6)
Time to take antiviral drugs (months)	18.4 (10–80)	22.8 (12–30)	30 (12–72)
HIV virus load(copy/ml)	48,878 (0–514910)	169 (0–1949)	7 (0–40)

Table 2. Patient characteristics, preoperative and intraoperative data. *Data is shown as either medians with ranges or number of patients (n) and percentage (%).

Factor	CD4 + T (%)		CD8 + T (%)		CD3 + T (%)		CD4+/CD8 + T	
	Chi-square test method	*P*-value	Chi-square test method	*P*-value	Chi-square test method	*P*-value	Chi-square test method	*P*-value
Age (> 65/≤ 65)								
	Fisher's exact test	0.621	Fisher's exact test	1.000	Fisher's exact test	1.000	Pearson's chi-squared test	0.653
Sex (Male/Female)								
	Fisher's exact test	0.366	Fisher's exact test	1.000	Fisher's exact test	0.425	Fisher's exact test	0.338
Hypertension status (Yes/No)								
	Fisher's exact test	1.000	Correction for continuity	1.000	Correction for continuity	1.000	Correction for continuity	0.348
Diabetes status (Yes/No)								
	Fisher's exact test	0.562	Fisher's exact test	0.573	Fisher's exact test	0.573	Fisher's exact test	1.000
Duration of operation (< 200 min/≥ 200 min)								
	Fisher's exact test	1.000	Fisher's exact test	1.000	Fisher's exact test	1.000	Pearson's chi-squared test	0.790
Duration of HIV infection (< 2.5Y/≥ 2.5Y)								
	Fisher's exact test	1.000	Fisher's exact test	0.674	Correction for continuity	0.274	Pearson's chi-squared test	0.070
Duration of antiviral drug administration (months) (< 24 M/≥ 24M)								
	Fisher's exact test	1.000	Fisher's exact test	0.360	Fisher's exact test	0.360	Pearson's chi-squared test	0.259
Viral load (copy/ml)(TND/> 40 copy/ml)								
	Fisher's exact test	0.072	Fisher's exact test	0.609	Fisher's exact test	0.124	Pearson's chi-squared test	0.852
Amount of bleeding (< 50 ml/≥ 50 ml)								
	Fisher's exact test	1.000	Fisher's exact test	1.000	Fisher's exact test	1.000	Pearson's chi-squared test	0.658

Table 3. Effects of age, sex, hypertension status, diabetes status, duration of operation, duration of HIV infection, duration of antiviral drug administration, and viral load on the preoperative or postoperative immune indices.

with prostate cancer, with a median age of 67 years (52–82); all were male, 2 had hypertension, and 1 had diabetes. The median duration of radical surgery was 265 min (200–320), and the average hospitalization duration was 14 days. Special infection indicators: The median durations of HIV infection in patients with kidney cancer, bladder cancer and prostate cancer were 3.14 years (1–7), 1.875 years (1–3) and 2.5 years (1–6), respectively. The median duration of antiviral drug use was 18.4 months (10–80), 22.8 months (12–30) and 30 months (12–72). The median viral loads were 48,878 copies/ml (0–514,910), 169 copies/ml (0–1949), and 7 copies/ml (0–40). (Table 2).

In Table 2, we can see that the number of male patients with urinary tract tumors complicated with AIDS is much higher than that of female patients. Although the malignant tumors of the patients are different, there is not much difference in the basic data such as the average age and length of hospital stay, which is one of the reasons why several malignant tumors of the urinary tract are analyzed together. Most of the tumor patients with AIDS have good adherence to medical instructions and can regularly receive antiviral treatment (China accepts anti-HIV drugs for free).

The chi-square test revealed that age, sex, hypertension status, diabetes status, duration of surgery, duration of HIV infection, duration of antiviral drug administration, and viral load had no statistically significant effect on the preoperative or postoperative immune indicators CD4 + T, CD8 + T, CD3 + T or CD4/CD8 + T cells ($P > 0.01$). (Table 3).

All the immunological indicators were examined before and within 1 week after surgery. For patients with non-HIV urinary malignancies, we did not routinely test their immune markers, so we did not set up a control group for patients with non-HIV urinary malignancies. As mentioned in Table 3, for duration of HIV infection (< 2.5Y/≥ 2.5Y), duration of antiviral drug administration (months) (< 24 M/≥ 24 M), as well as preoperative Viral load (copy/ml) (TND/> 40 copy/ml), no statistically significant correlation was found between these specific indicators of AIDS patients and the rise and fall of immune indicators before and after surgery, indicating that surgery itself and malignant tumors had a greater effect on the rise and fall of immune indicators in patients. However, the acceptance of antiviral treatment has a huge impact on the CD4 + T cells of AIDS patients, and efforts to improve the patient's own resistance before surgery and raise the immune index to a higher level will be very helpful to the tolerance of surgery. In 48 patients, viral load results were not reviewed after operation, intraoperative blood transfusion was not performed, and antiviral therapy was not changed after operation.

Survival prognosis

The mean follow-up time was 22.5 (3–87) months. As shown in Fig. 4, the survival rate of the group with decreased CD4 + T, CD8 + T and CD3 + T cells after surgery was worse than that of the group with increased CD4 + T, CD8 + T and CD3 + T cells, but the differences were not statistically significant ($P > 0.01$). The survival rate of patients in the group with decreased CD4+/CD8 + T cell ratio was higher than that in the group with increased CD4+/CD8 + T cell ratio, but the difference was not statistically significant ($P > 0.01$).

The decline of immune indexes after surgery in Fig. 4 represents the overall decline of the patient's resistance and recovery ability, and therefore a relatively poor prognosis. But the impact on prognosis is not only CD4 + T, CD8 + T and so on. Nutritional indicators such as albumin, lymphocyte count, and cholesterol, as well as the presence or absence of underlying disease, tumor recurrence, and tumor pathological stage, can also affect prognosis. Subsequently, the sample size was further increased to further verify whether there was a statistically significant correlation between the rise and fall of immune indicators and the survival of patients.

ROC curve

According to the preoperative ROC curve, the AUC of CD8 + T cells was 0.678, which was greater than that of CD4 + T cells (AUC 0.504), CD3 + T cells (AUC 0.617) and CD4/CD8 + T cell ratio (AUC 0.661), and the differences were statistically significant ($P < 0.05$). The postoperative ROC curve revealed that the AUC of CD8 + T cells was 0.702, which was greater than that of CD4 + T cells (AUC of 0.513), CD3 + T cells (AUC of 0.592) and CD4/CD8 + T cell ratio (AUC of 0.647), and these differences were statistically significant ($P < 0.05$). (Fig. 5)

The optimum critical point is selected according to the maximum Jorden index. The optimum critical point of CD4 + T cells was 382, corresponding to 78.6% sensitivity and 55.9% specificity. The optimal critical point of CD8 + T cells was 1384, corresponding to 71% sensitivity and 97.1% specificity. The optimum critical point value of CD3 + T cells was 541, corresponding to 100% sensitivity and 8.8% specificity. The optimal critical point value of CD4/CD8 + T-cell ratio was 0.975, corresponding to 50% sensitivity and 88.2% specificity.

The ROC curve presented in Fig. 5 provides a more direct comparison of the immune indicators under investigation. By graphically illustrating the relationship between true positive rates and false positive rates, the ROC curve facilitates the evaluation of model performance, threshold selection, AUC calculation, and inter-model comparisons, particularly highlighting the superior performance of CD8 + T cells. In fact, changes in various immune indicators have a certain influence and predictive effect on survival and prognosis. CD8 + T

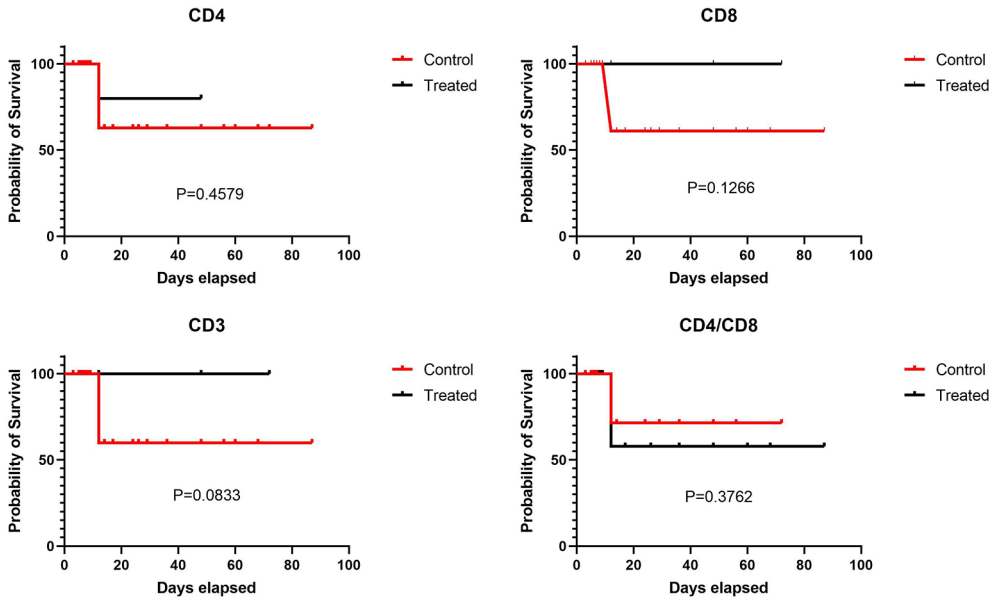

Fig. 4. Survial curves of treated group and control group (Treated group, increased T cells. Control group, decreased T cells.

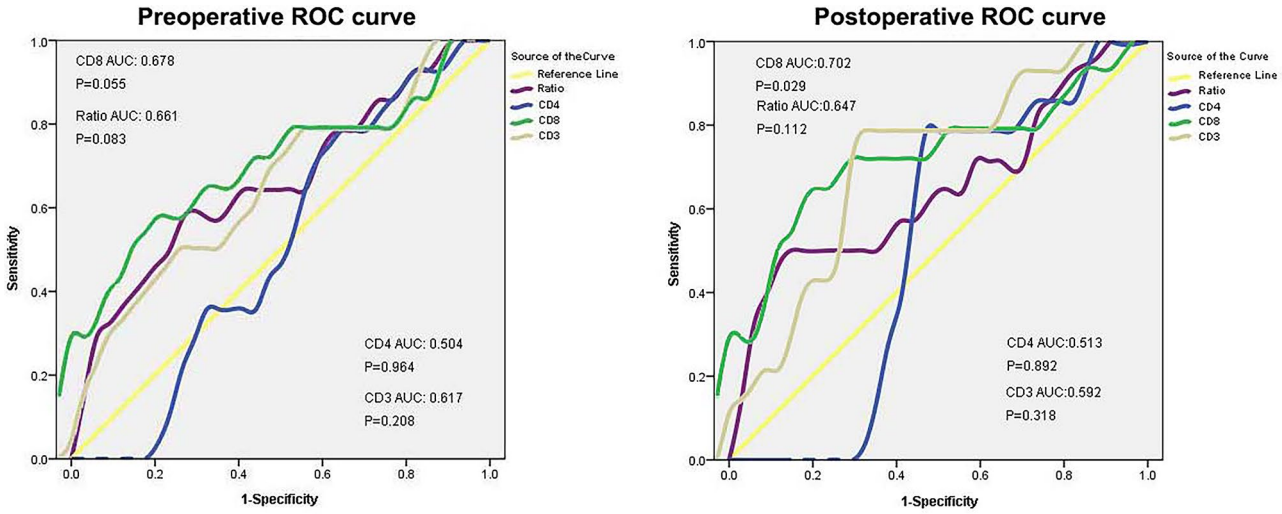

Fig. 5. ROC curve (ROC, receiver operating characteristic. AUC, area under curve.

cells has a higher area under the AUC curve, indicating that it is better associated with prognosis than CD4 + T cells, CD3 + T cells and CD4/CD8 + T cell ratio, which also leads us to pay more attention to changes in CD8 + T cells when detecting patient indicators.

The association between perioperative complications and immune indices

Among 48 HIV-related patients, postoperative hemorrhage occurred in 2 cases, fever in 9 cases, incision infection in 7 cases, gastrointestinal reaction in 11 cases, intestinal obstruction in 1 case, and costoabdominal neuralgia in 4 cases. There was no statistical significance between postoperative immune changes and complications. When the model was included in the Logistic regression model, the comprehensive test result of the model coefficient was $P > 0.05$, and the model was not significant in general.

Discussion

Optimization of antiretroviral therapy (ART) has significantly increased life expectancy for people living with HIV (PLHIV). However, this extended survival has also resulted in a notable rise in the prevalence of comorbidities and non-AIDS-related conditions, including urinary malignancies[1]. The presence of malignancies can impact immune status, particularly when concurrent surgical interventions further compromise immune function. Monitoring dynamic changes in immune markers such as CD4 + T cells and CD8 + T cells counts may assist in refining treatment strategies. For instance, post-operative infection risk assessments can inform decisions regarding the necessity of intensive antimicrobial therapy or immune support measures. Enhanced immune recovery may improve the surveillance of minimal residual lesions and eliminate cancer cells via the cytotoxic activity of T cells. Furthermore, optimal immune function may decrease postoperative infections, thereby reducing complications and indirectly improving patient survival rates. Additionally, the status of the immune system may influence the tumor microenvironment, potentially inhibiting tumor growth and metastasis.

CD4 + T cells, also known as T helper cells, play a crucial role in the proper functioning of the immune system by coordinating immune responses. CD8 + T cells, or cytotoxic T lymphocytes, are primarily responsible for eliminating virus-infected and cancerous cells. HIV predominantly targets CD4 + T cells, resulting in their depletion and consequently impairing immune function, rendering patients susceptible to opportunistic infections and malignancies. Urinary malignancies can also impact the immune system; the presence of malignant tumors may induce immunosuppression, particularly in advanced stages where the tumor microenvironment harbors numerous immunosuppressive cells and factors, further compromising immune responses. Consequently, when a patient is afflicted with both HIV and urinary malignancy, the interaction between these two conditions can exacerbate immune system damage. Considering the effects of surgery, which is inherently traumatic and elicits stress responses in the body, including inflammatory reactions and alterations in immune function, it is pertinent to examine whether the surgical stress leads to more pronounced changes in immune markers, especially the CD4/CD8 + T cell ratio, in HIV patients who already have compromised CD4 + T cells levels.

First, it is essential to consider the baseline CD4 + T cells count in HIV patients. If a patient's CD4 + T cells count is already critically low preoperatively (e.g., below 200 cells/μL), it may decline further post-surgery due to surgical stress and an increased risk of postoperative infections. Although CD8 + T cells levels may be elevated as the body combats the virus, chronically elevated CD8 + T cells levels can contribute to immune exhaustion. Additionally, the status of ART must be evaluated. In patients receiving effective ART with suppressed viral loads, CD4 + T cells levels may stabilize or improve, altering the impact of surgery on immune markers compared to those not on ART. It is crucial to distinguish whether the patient has maintained ART before and after surgery and whether the viral load remains controlled. The type and extent of surgery can also influence changes in immune markers. Major or complex surgeries may elicit a more pronounced stress response, significantly affecting CD4

+T cells and CD8 +T cells levels. For instance, surgeries for urinary system malignancies involving organs such as the kidney and bladder can vary in trauma and immune impact. Postoperative complications, particularly infections, are critical factors. Given that HIV patients have compromised immune function and a higher risk of postoperative infections, these complications can lead to further decreases in CD4 +T cells counts while temporarily elevating CD8 +T cells levels in response to pathogens. Moreover, factors like nutritional status and psychological stress during recovery can indirectly affect immune indices. Adequate nutritional support and psychological care can aid immune recovery, whereas neglecting these aspects may prolong immunosuppression.

Patients with malignant tumors of the urinary system combined with AIDS are a relatively special group in clinical practice, but most of the CD4 +T cells in these patients can be maintained at a relatively normal level rather than at a low level. For such patients, both the indications for surgical resection of malignant tumors and the impact of surgery on autoimmune status should be fully improved before surgery to fully assess whether the immune status of patients can withstand the benefits of surgery. Elevated cancer risks in PLHIV are driven primarily by increased exposure to carcinogens, most notably oncogenic viruses acquired through shared transmission routes, plus acceleration of viral carcinogenesis by HIV-related immunosuppression[2]. The immune system plays a role in preventing the growth of many kinds of tumors by recognizing and destroying tumor cells[3]. However, recent studies have also shown that the immune system may simultaneously promote tumor development by selecting drug-resistant tumor clones, promoting immunosuppression and cell proliferation, and increasing metastasis potential[4], which is also one of the hallmarks of cancer[5,6]. Malignant tumor regulatory viruses can affect the tumor microenvironment by triggering inflammation, changing tumor metabolism, stimulating tumor cell signaling pathways, etc., leading to tumor growth, proliferation and invasion. The higher incidence of malignancy among people living with HIV suggests a more complex relationship between the use of antiretroviral therapy and tumorigenesis[7]. Successful antitumor therapy requires the elimination of all cells with tumor regeneration potential; for example, to prevent HIV- 1 reproduction, all infected cells capable of regenerating new infectious HIV- 1 particles must be eliminated[8,9]. Kidney cancer, bladder cancer and prostate cancer are common urological malignancies, but at the same time, the number of patients with AIDS has greatly decreased, so it is more difficult for us to collect relevant results in this paper. We enrolled a certain number of patients with malignant tumors of the urinary system complicated with AIDS and, through the analysis of their clinical data, monitored the changes in the immune indices of these patients before and after surgery to obtain more information and provide more objective experience for us to refer to when facing the same patients who need surgery in the future.

To comprehensively and accurately assess the immune status of patients, we endeavored to optimize both preoperative and postoperative immune indicators. In addition to the viral load and CD4 +T-cell count of patients, flow cytometry can also detect CD8 +T cells, CD3 +T cells and the CD4+/CD8 +T-cell ratio in patients at our hospital. Regular lymphocyte count monitoring of AIDS patients is conducive to timely understanding of the immune system of patients, and timely adjustment of treatment for patients with low lymphocyte counts is conducive to improving survival. ART constitutes the cornerstone of AIDS management, and the impact of various treatment programs on patients is primarily reflected in viral suppression, immune function recovery, side effect profiles, and quality of life. When selecting a treatment protocol, factors such as patients' viral load, drug resistance, tolerance to side effects, and lifestyle should be carefully considered. To eliminate the influence of different ART regimens on patients' immune indices, all patients were administered the same ART regimen. Surgical interventions significantly affect immune markers and prognosis in HIV patients, particularly those with compromised immune function or uncontrolled viral loads. Preoperative optimization of ART therapy, rigorous postoperative monitoring, and multidisciplinary collaboration can substantially reduce surgical risks and enhance outcomes. Therefore, this study investigated the effects of surgery on various immune indices of AIDS patients and their prognosis to provide a more adequate auxiliary reference for the evaluation of surgical indications and conditions in the future.

In acute HIV infection, the response is suppressed due to significant depletion of CD4 +T cells early after exposure to HIV. Early administration of antiretroviral therapy to control viral progression can prevent CD4 +T-cell killing and salvage an effective CD4 +T-cell response, and peripheral CD4 +T-cell counts are reliable biomarkers for monitoring immunosuppression and recovery from antiretroviral therapy[10]. Widespread access to antiretroviral therapy has greatly improved outcomes for HIV-infected patients and reduced the clinical need for CD4 +T-cell monitoring as the virus continues to be suppressed. However, restoring the CD4/CD8 ratio to normal levels (≥ 1) with antiretroviral therapy is often incomplete and may reflect chronic immune activation that occurs in persistent HIV infection[11]. Previous studies have shown that the infiltration of immune indicators in the tumor microenvironment has prognostic value for various types of cancer, which is similar to our findings in this paper[12]. Our study revealed that increased CD8 +T-cell infiltration in the tumor microenvironment often predicts a good prognosis, which may also explain this phenomenon.

CD8 +T cells play important roles in antitumor immunity, the recognition of tumor-associated antigens and the elimination of tumor cells, and the initial adaptive immune response mainly relies on cytotoxic CD8 +T cells to limit or inhibit the spread of viruses[13]. Studies have shown that an increase in T cells in the tumor microenvironment is associated with a good prognosis in various cancers, such as breast cancer, colorectal cancer, lung cancer and melanoma[14,15]. However, we need to pay close attention to the fact that tumors may develop mechanisms to evade immune surveillance. CD4 +T cells are equally important because they promote the development of CD8 +cytotoxic T cells and memory T cells, helping T cells destroy tumors[4,16]. CD8 +T cells are an important component of the body's adaptive immune response. During viral or intracellular bacterial infections, CD8 +T cells are rapidly activated and differentiated to exert their immune function by producing cytokines[17]. CD8 +T-cell recruitment is very important in the antitumor immune response and is also an important indicator of lesion severity[18,19]. Moreover, CD8 +T cells are an important part of the cellular immune response and play an important role in the control of viral infection. In the Copenhagen cohort, a

CD8 + T-cell count of more than 1500 cells/μL after 10 years of antiretroviral therapy was associated with an 80% increased risk of non-AIDS-related death compared with a CD8 + T-cell count of 500–1500 cells/μL[20]. In another surveillance study, we observed that severe infections were more common in individuals with CD8 + T-cell counts less than 500 cells/μL[21].

Over the past decade, studies of antiretroviral therapy in HIV-infected people have revealed the importance of consistently high CD8 + T-cell counts and low CD4+/CD8 + T-cell ratios. Low CD4/CD8 ratios reflect increased immune activation and are associated with an increased risk of serious non-AIDS events. After acute HIV infection, the CD4+/CD8 + T-cell ratio is quickly disrupted, mainly due to early expansion of the CD8 + T-cell population, followed by a brief progressive decrease in CD4 + T-cell counts. During effective antiretroviral therapy, these trends are only partially reversed in most patients, even with early initiation of antiretroviral therapy[22,23]. Loss of CD4 + T helper cells, persistent viral antigen load, chronic inflammation, etc., are believed to be the causes of CD8 + T-cell cell dysfunction during chronic HIV infection[24]. In addition, low CD4+/CD8 + T-cell ratios in HIV-infected people lead to harmful immune aging and are associated with inflammatory activation, which triggers excessive cancer risk[25]. Low CD4+/CD8 + T-cell ratios are also associated with the risk of non-AIDS outcomes, including older age, CMV coinfection, and low CD4 + T-cell count[26,27], as well as with men and HIV acquisition risk factors (especially men who have sex with men)[28,29]. A low CD4+/CD8 + T-cell ratio predicts the risk of any cancer, independent of factors such as age, sex, CD4 + T-cell count, HIV viral load, chronic hepatitis C virus infection, and smoking history. Therefore, many clinicians now believe that the CD4/CD8 ratio can help monitor HIV, and many researchers now use it as an indicator of efficacy in interventional studies[30]. Studies on antiretroviral therapy for HIV patients have also shown that a low CD4/CD8 ratio also reflects the presence of potential inflammation, oxidative stress, and low control efficiency of CMV, EB virus and other latent viruses[31,32] or hepatitis C virus and other infections[33]. Importantly, HIV patients with low CD4+/CD8 + T-cell ratios exhibit greater inflammatory responses and immune senescence[34]. Studies have shown that the HIV DNA concentration is negatively correlated with the CD4/CD8 ratio[35]. Our study revealed no significant differences in the preoperative or postoperative CD4+/CD8 + T test in patients with kidney cancer, bladder cancer, or prostate cancer.

T lymphocytes with natural killer activity (NKT cells) are CD3 + T cells[36]. CD3 + T-cell downregulation is an important immune escape strategy for lentiviruses because it impairs immune synapse formation and limits T-cell activation, thereby inhibiting the antiviral response and apoptosis. The retention of CD3 + T cells on the cell surface leads to an increase in T-cell activation and cell death[37]. CD3 + T-cell-mediated stimulation of infected T cells increases T-cell activation, envelope surface expression, virion inclusion and infectivity, which is consistent with the involvement of CD3 + T cells in mediating T-cell signaling, T-cell activation and intracellular remodeling[38]. Our study revealed that CD3 + T cells are downregulated before and after surgery, which may be a self-protective effect on the body to minimize the blows and injuries associated with the operation.

In other articles on immune indicators related to similar surgical procedures, we found that in HIV-infected patients with a preoperative CD4 + T-cell count ≤ 200 cells/μL or a CD4+/CD8 + T-cell ratio ≤ 0.15, the incidence of postoperative sepsis was generally greater. The preoperative CD4 + T-cell count or CD4+/CD8 + T-cell ratio can be used as useful indicators of postoperative sepsis in HIV-infected patients undergoing abdominal surgery[39]. The infiltration of CD4 + T cells and CD8 + T cells has important prognostic significance in patients who undergo radical gastrectomy for gastric cancer. For elective thoracoscopic surgery, the levels of CD3 + T cells, CD4 + T cells and CD4+/CD8 + T cells after surgery were significantly lower than those before surgery, and the levels of CD8 + T cells were increased[40]. The levels of CD3 + T cells, CD4 + T cells and CD4+/CD8 + T cells in both groups were lower than those before 24 h and 72 h after thoracoscopic lobectomy and segmental pneumonectomy for non-small cell lung cancer[41]. The above studies show that surgical operations have a certain impact on immune indices, which also confirms our research results.

A retrospective analysis of 352 lung cancer patients treated with minimally invasive surgery by the same surgeon in the thoracic surgery department of a hospital found that the level of t lymphocytes after surgery was lower than that before surgery[42]. Another article included 72 patients with lung cancer, among which 39 patients in the study group received neoadjuvant chemotherapy. The results showed that the primary tumor CD4 + T cells density was significantly decreased after neoadjuvant therapy, and the intratumoral CD4/CD8 T cells ratio was significantly decreased (0.012 and 0.016, respectively). Meanwhile, the author observed that compared with patients who did not receive neoadjuvant chemotherapy, Patients receiving neoadjuvant chemotherapy had a higher percentage of peripheral blood CD4 + T cells, but a lower percentage of peripheral blood CD8 + T cells. These findings suggest that T lymphocyte subsets have potential prognostic significance in the context of neoadjuvant chemotherapy in lung cancer[43]. Changes in Treg frequency in peripheral blood of patients with urothelial bladder cancer before and after tumor resection as assessed by flow cytometry were also analyzed. In pT2-pT4 tumors, reduced postoperative Treg frequency was associated with poorer prognosis: patients with the lowest Treg frequency died first[44]. Chen C et al. studied whether CD4 + CD25 + FOXP3 + and CD8 + CD28- regulatory T cells were reduced in peripheral blood of patients with non-small cell lung cancer who underwent surgery. The study group ($n = 49$), consisting of patients with NSCLC, and the control group ($n = 24$), consisting of age - and sex-matched patients with non-malignant disease, showed a significant decrease in these immune levels after surgery[45].

What are the distinctions in surgical treatment between AIDS patients and ordinary patients? Individuals with HIV/AIDS face a higher risk of post-operative infections due to their compromised immune systems, which may also lead to other complications such as opportunistic infections or drug interactions. Therefore, preoperative assessments are crucial. These include evaluating the patient's HIV status, including viral load, CD4 + T cells and CD8 + T cells counts, stability of these indicators, and whether they are undergoing antiretroviral therapy. If the viral load is high or CD4 + T cells count is low, controlling HIV might be necessary before surgery. Additionally, the patient's overall condition, such as nutritional status and comorbidities like hepatitis or

tuberculosis, can influence surgical risks. Perioperative management is also important, particularly concerning whether antiretroviral therapy needs adjustment. Potential drug interactions, such as those between antiretroviral drugs and anesthetics or antibiotics, should be carefully considered. Postoperative infection prevention is critical and may require more stringent antibiotic use or measures to prevent opportunistic infections, such as pneumocystis pneumonia. During surgery, precautions such as stricter aseptic procedures or minimizing surgery duration to reduce infection risk should be taken. Moreover, the risk of bleeding may be higher due to some antiretroviral drugs affecting clotting function or the patient's reduced platelet count. Postoperative recovery requires close monitoring for signs of infection, wound healing, and nutritional support. Long-term prognostic considerations, such as tumor recurrence, HIV control, and quality of life, must also be addressed. Collaboration with a multidisciplinary team, including specialists from infectious diseases, oncology, urology, etc., is often necessary to develop a comprehensive treatment plan. It is a misconception that HIV patients cannot undergo surgery or that the risk is too high; with advancements in antiretroviral therapy, many HIV patients can receive surgical treatment but require careful evaluation and management. Furthermore, attention should be paid to the patient's psychological state, as they may experience anxiety or depression due to having two serious conditions simultaneously and need psychological support.

Limitations of the study

There is a lack of preoperative and postoperative detection of immune indicators in patients with HIV-negative urinary tract tumors in this article. Further studies in this area will be added in the future to evaluate the results more objectively. The relatively small number of cases is also one of our limitations, so the accuracy of the research results will be insufficient. In the future, we will cooperate with several infectious disease hospitals to further increase the sample size to improve our study.

Conclusion

On the basis of the first-hand clinical data, we obtained a statistical analysis showing that CD4 + T, CD8 + T, and CD3 + T cells were decreased before and after surgery in patients with malignant tumors of the urinary system complicated with AIDS, and CD8 + T cells had a statistically significant effect on patient prognosis. This provides an important reference value for the future operation of urinary malignancies in HIV-infected patients and helps us to have an additional indicator to refer to and evaluate surgical risk and prognosis before surgery. However, the current data are limited, and more clinical data are needed to support our conclusions.

Data availability

The raw data supporting the conclusions of this article will be made available by the author Wenrui Xue, without undue reservation.

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References

1. Ron, R. et al. CD4/CD8 ratio and CD8 + T-cell count as prognostic markers for non-AIDS mortality in people living with HIV. A systematic review and meta-analysis. Front Immunol. ;15:1343124. (2024). https://doi.org/10.3389/fimmu.2024.1343124. Erratum in: Front Immunol. 2024;15:1383117.
2. Engels, E. A. et al. State of the science and future directions for research on HIV and cancer: summary of a joint workshop sponsored by IARC and NCI. *Int. J. Cancer*. **154** (4), 596–606 (2024). Due to the increased.
3. Brito, M. J. et al. CD4(+) and CD8(+) cell populations in HIV-positive women with cervical squamous intra-epithelial lesions and squamous cell carcinoma. *Int. J. Infect. Dis.* **103**, 370–377 (2021).
4. Vonderheide, R. H. The immune revolution: A case for priming, not checkpoint. *Cancer Cell.* **33** (4), 563–569 (2018).
5. Cavallo, F., De Giovanni, C., Nanni, P., Forni, G. & Lollini, P. L. : the immune hallmarks of cancer. Cancer Immunol Immunother, 60(3): 319–326. (2011).
6. Hanahan, D. & Weinberg, R. A. Hallmarks of cancer: the next generation. *Cell* **144** (5), 646–674 (2011).
7. Dandachi, D. & Moron, F. Effects of HIV on the tumor microenvironment. *Adv. Exp. Med. Biol.* **1263**, 45–54 (2020).
8. Jiang, C. et al. Distinct viral reservoirs in individuals with spontaneous control of HIV-1. *Nature* **585** (7824), 261–267 (2020).
9. Sarabia, I., Huang, S.H., Ward, A.R., Jones, R.B.& Bosque, A. The Intact Non-Inducible Latent HIV-1 Reservoir is Established In an In Vitro Primary TCM Cell Model of Latency. *J Virol.* **95**(7), e01297–20 (2021).
10. Le, T. et al. Enhanced CD4 + T-cell recovery with earlier HIV-1 antiretroviral therapy. *N Engl. J. Med.* **368** (3), 218–230 (2013).
11. Francis-Morris, A. et al. Compromised CD4:CD8 ratio recovery in people living with HIV aged over 50 years: an observational study. *HIV Med.* **21** (2), 109–118 (2020).
12. Engelhard, V. H. et al. Immune cell infiltration and tertiary lymphoid structures as determinants of antitumor immunity. *J. Immunol.* **200** (2), 432–442 (2018).
13. Gao, L. et al. Genome-wide expression profiling analysis to identify key genes in the anti-HIV mechanism of CD4(+) and CD8(+) T cells. *J. Med. Virol.* **90** (7), 1199–1209 (2018).
14. Fridman, W. H., Pages, F., Sautes-Fridman, C. & Galon, J. The immune contexture in human tumours: impact on clinical outcome. *Nat. Rev. Cancer*. **12** (4), 298–306 (2012).
15. Reiser, J., Banerjee, A. & Effector Memory, and Dysfunctional CD8(+) T Cell Fates in the Antitumor Immune Response. J Immunol Res, 2016: 8941260. (2016).
16. Vesely, M. D., Kershaw, M. H., Schreiber, R. D. & Smyth, M. J. Natural innate and adaptive immunity to cancer. *Annu. Rev. Immunol.* **29**, 235–271 (2011).
17. Cao, J. et al. Effects of altered Glycolysis levels on $CD8^+$ T cell activation and function. *Cell. Death Dis.* **14** (7), 407 (2023).
18. Scherpereel, A. et al. Defect in recruiting effector memory CD8 + T-cells in malignant pleural effusions compared to normal pleural fluid. *BMC Cancer*. **13**, 324 (2013).
19. Allen, F. et al. CCL3 augments tumor rejection and enhances CD8(+) T cell infiltration through NK and CD103(+) dendritic cell recruitment via IFNgamma. *Oncoimmunology* **7** (3), e1393598 (2018).
20. Helleberg, M. et al. Course and clinical significance of CD8 + T-Cell counts in a large cohort of HIV-Infected individuals. *J. Infect. Dis.* **211** (11), 1726–1734 (2015).

21. Serrano-Villar, S. et al. Predictive value of CD8 + T cell and CD4/CD8 ratio at two years of successful ART in the risk of AIDS and non-AIDS events. *EBioMedicine* **80**, 104072 (2022).
22. Caby, F. CD4+/CD8 + ratio restoration in long-term treated HIV-1-infected individuals. *AIDS* **31** (12), 1685–1695 (2017).
23. Hughes, R. A. et al. Long terms trends in CD4 + cell counts, CD8 + cell counts, and the CD4+: CD8 + ratio. *AIDS* **32** (10), 1361–1367 (2018).
24. Schweneker, M., Favre, D., Martin, J. N., Deeks, S. G. & McCune, J. M. HIV-induced changes in T cell signaling pathways. *J. Immunol.* **180** (10), 6490–6500 (2008).
25. Castilho, J. L. et al. Sudenga S L. CD4/CD8 ratio and cancer risk among adults with HIV. *J. Natl. Cancer Inst.* **114** (6), 854–862 (2022).
26. Sigel, K. et al. Immunological and infectious risk factors for lung cancer in US veterans with HIV: a longitudinal cohort study. *Lancet HIV*. **4** (2), e67–e73 (2017).
27. Triplette, M. et al. A low peripheral blood CD4/CD8 ratio is associated with pulmonary emphysema in HIV. *PLoS One*. **12** (1), e170857 (2017).
28. Combes, J. D. et al. Human papillomavirus antibody response following HAART initiation among MSM. *AIDS* **31** (4), 561–569 (2017).
29. Verboeket, S. O. et al. Human immunodeficiency virus (HIV)-Negative men who have sex with men have higher CD8 + T-Cell counts and lower CD4+/CD8 + T-Cell ratios compared with HIV-Negative heterosexual men. *J. Infect. Dis.* **224** (7), 1187–1197 (2021).
30. Ron, R. et al. CD4/CD8 ratio during human immunodeficiency virus treatment: time for routine monitoring?? *Clin. Infect. Dis.* **76** (9), 1688–1696 (2023).
31. Smith, D. M. et al. Asymptomatic CMV replication during early human immunodeficiency virus (HIV) infection is associated with lower CD4/CD8 ratio during HIV treatment. *Clin. Infect. Dis.* **63** (11), 1517–1524 (2016).
32. Rosado-Sanchez, I. et al. Thymic function impacts the peripheral CD4/CD8 ratio of HIV-Infected subjects. *Clin. Infect. Dis.* **64** (2), 152–158 (2017).
33. Bandera, A. et al. The impact of DAA-mediated HCV eradication on CD4(+) and CD8(+) T lymphocyte trajectories in HIV/HCV coinfected patients: data from the ICONA foundation cohort. *J. Viral Hepat.* **28** (5), 779–786 (2021).
34. Serrano-Villar, S. et al. HIV-infected individuals with low CD4/CD8 ratio despite effective antiretroviral therapy exhibit altered T cell subsets, heightened CD8 + T cell activation, and increased risk of non-AIDS morbidity and mortality. *PLoS Pathog.* **10** (5), e1004078 (2014).
35. Chen, Y. et al. Expression of RNA-m6A-related genes correlates with the HIV latent reservoir level and the CD4 + and CD8 + T cell profiles of patients with AIDS. *Cell. Mol. Biol. (Noisy-le-grand)*. **69** (4), 125–132 (2023).
36. de Almeida, S. M. et al. CD3(+)CD56(+) and CD3(-)CD56(+) lymphocytes in the cerebrospinal fluid of persons with HIV-1 subtypes B and C. *J. Neuroimmunol.* **377**, 578067 (2023).
37. Schmokel, J. et al. Link between primate lentiviral coreceptor usage and Nef function. *Cell. Rep.* **5** (4), 997–1009 (2013).
38. Mesner, D., Hotter, D., Kirchhoff, F. & Jolly, C. Loss of Nef-mediated CD3 down-regulation in the HIV-1 lineage increases viral infectivity and spread. *Proc. Natl. Acad. Sci. U S A*. **117** (13), 7382–7391 (2020).
39. Xia, X. J. et al. Preoperative CD4 count or CD4/CD8 ratio as a useful indicator for postoperative sepsis in HIV-infected patients undergoing abdominal operations. *J. Surg. Res.* **174** (1), e25–e30 (2012).
40. Li, X. et al. Low dose of Methylprednisolone for pain and immune function after thoracic surgery. *Ann. Thorac. Surg.* **113** (4), 1325–1332 (2022).
41. Xu, J., Huang, L., Wang, Y., Guo, D. & Sun, J. A Retrospective Study of Effectiveness of Thoracoscopic Lobectomy and Segmentectomy in Patients with Early-Stage Non-Small-Cell Lung Cancer. Dis Markers, 2022: 6975236. (2022).
42. Hong, Z. et al. Effects of Da Vinci robot versus thoracoscopic surgery on body trauma and lymphocyte subsets in lung cancer patients: A propensity score matching study. *J. Surg. Oncol.* **128** (4), 667–674 (2023).
43. Elicora, A. et al. Prognostic significance of T lymphocyte subgroups (CD4 and CD8) in lung cancer patients after neoadjuvant chemotherapy. *J. Cardiothorac. Surg.* **19** (1), 113 (2024).
44. Jóźwicki, W., Brożyna, A. A., Siekiera, J. & Slominski, A. T. Frequency of CD4 + CD25 + Foxp3 + cells in peripheral blood in relation to urinary bladder cancer malignancy indicators before and after surgical removal. *Oncotarget* **7** (10), 11450–11462 (2016).
45. Chen, C. et al. Changes of CD4 + CD25 + FOXP3 + and CD8 + CD28- regulatory T cells in non-small cell lung cancer patients undergoing surgery. *Int. Immunopharmacol.* **18** (2), 255–261 (2014).

Author contributions

WRX participated in manuscript preparation and writing. YZ provided suggestion and edits. MMZ provided relevant patients data and offered suggestions for revising the article. ZH conceptualized, wrote, and revised manuscript. All authors contributed to the article and approved the submitted version.

Declarations

Competing interests

The authors declare no competing interests.

Additional information

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