Original Research

Analysis of the Efficacy of LNSRH Surgery for Early Cervical Cancer Based on T, B, and NK Lymphocytes

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Abstract

Background: The analysis is based on the level of T, B, NK lymphocytes to evaluate the efficacy of laparoscopic nerve-sparing radical hysterectomy (LNSRH) for early cervical cancer. **Methods**: Selected 30 patients with early cervical cancer who underwent LNSRH surgery in Tianjin Fifth Central Hospital from December 2019 to January 2021 as the cervical cancer group, and 30 healthy female who underwent physical examination in our hospital during the same period were selected as the control group. The expressions of CD_4+, CD_8+, $CD_{20}+$, and $CD_{57}+$ were detected by flow cytometer, female sexual function index (FSFI) and overall assessment scale of cancer treatment function (FACT-G) score were used to evaluate female sexual function and quality of life, and the receiver operating characteristic curve (ROC) was used to analyze the expression predictive value of CD_4+, CD_8+, $CD_{20}+$, and $CD_{57}+$ in LNSRH of early cervical cancer. **Results**: The expression of CD_4+ and $CD_{57}+$ in the cervical cancer group was lower than that in the healthy group,and the expression of CD_8+ and $CD_{20}+$ was higher than that in the healthy group ($p < 0.05$). The expression of preoperative CD_4+ and $CD_{57}+$ was higher for postoperative, and the expression of preoperative CD_8+ and $CD_{20}+$ was lower ($p < 0.05$) for postoperative. The expression of postoperative 1 day CD_4+ and $CD_{57}+$ was higher for at 3 days postoperative, and the expression of postoperative 1 day CD_8+ and $CD_{20}+$ was lower at 3 days postoperative ($p < 0.05$). CD_4+, $CD_{57}+$ expression was positively correlated with FSFI score, and CD_8+, and $CD_{20}+$ expression was negatively correlated with FSFI score, CD_4+, and $CD_{57}+$ expression was positively correlated with FACT-G score, and CD_8+, and $CD_{20}+$ expression was negatively correlated with FACT-G score ($p < 0.05$). ROC analysis of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ expression sensitivity was lower than the four-item combination, the specificity was higher than the four-item combination and the results with significant statistical difference ($p < 0.05$) and the four combined tests have good predictive value for the efficacy of LNSRH for early cervical cancer ($p < 0.05$). **Conclusions**: Cervical cancer patients were mainly cellular immunity and performed low expression of CD_4+, high expression of CD_8+, high expression of $CD_{20}+$, and low expression of $CD_{57}+$. T, B, and NK lymphocytes could be used for immunological detection of cervical cancer.

Keywords: T lymphocytes; B lymphocytes; NK cells; early cervical cancer; laparoscopic extensive hysterectomy with preservation of autonomic nerves

1. Introduction

Cervical cancer, also known as carcinoma of uterine cervix, is a common gynecological malignancy. Human papillomavirus (HPV) is the main risk factor for the cervical cancer, which is mostly caused by smoking, premature sexual life and immune deficiency diseases [1]. Most patients may have no symptoms in the early stage, which is often found through screening. Contact bleeding and abnormal vaginal bleeding may occur in supplementary patients, and other tissues and organs will be invaded in the advanced cervical cancer [2]. Therefore, it is very important to predict early cervical cancer. Some studies have confirmed that patients with cervical cancer have different degrees of abnormal cellular immune function [3]. CD_4+ refers to T lymphocytes with CD_4+ T molecules on the surface. CD_8+ is a leukocyte differentiation antigen and a subgroup of T cells [4]. $CD_{20}+$ expresses and secretes immunoglobulin

of B cells, and plays a regulatory role in the proliferation and differentiation of B cells. $CD_{57}+$ mainly marks natural killer (NK) cells in lymphoid tissue [5]. At present, there are few studies on T lymphocytes, B lymphocytes and NK cells in predicting the effect of laparoscopic nerve-sparing radical hysterectomy (LNSRH) for early cervical cancer.

2. Materials and Methods

2.1 General Information

30 patients with early cervical cancer who underwent (LNSRH) in Tianjin Fifth Central Hospital from December 2019 to January 2021 were selected as the cervical cancer group which age from 31 to 58 (44.51 ± 10.79) years, the body weight from 48 to 75 (61.49 ± 10.81) kg, and 10 cases in stage Ia (TNM stage), 11 cases in stage Ib (TNM stage) and 9 cases in stage IIa (TNM stage). Another 30 healthy female who underwent physical examination in Tianjin Fifth

Central Hospital during the same period were selected as the control group, which age from 32 to 59 (45.49 ± 10.80) years, the body weight was from 46 to 74 (59.99 ± 11.21) kg. There was no significant difference in general data between the two groups ($p > 0.05$).

2.2 Inclusion Criteria

The following inclusion criteria were established for cervical cancer: (1) Meet the diagnostic criteria for cervical cancer in the Expert Consensus On Immunoprophylaxis of Human Papillomavirus-Related Diseases [6]. (2) Patients with available 3-year follow-up data (for non-recurring patients; patients who recurred were included even if they did not complete the three-year follow-up period). (3) It belonged to the early stage of cervical cancer. (4) The clinical data were complete and all patients with cervical cancer were operated on in Tianjin Fifth Central Hospital. (5) Good cognitive function. (6) All subjects signed informed consent and was approved by the ethics committee of Tianjin Fifth Central Hospital.

2.3 Exclusion Criteria

Exclusion criteria were the following: (1) Age <18 years. (2) Used immunosuppressants and enhancers in recent one year. (3) Patients with other malignant tumors. (4) Patients with other infectious and immune diseases. (5) Unable to perform surgery. (6) History of HIV and other conditions downregulating the immune system. (7) Ongoing pregnancy; and (8) History of hysterectomy.

2.4 Operation Method

All patients with cervical cancer performed pulmonary function, liver and kidney function and blood routine examination before operation. The steps of LNSRH were (1) cut off the ligaments around the uterus, (2) unfolded the retroflexion of bladder peritoneum, (3) exposed the rectum to lie on one side, opened the rectal space and separated the inferior abdominal nerve, (4) the uterine artery was cut off at 1 cm from the internal iliac artery and the fallopian tube was freed, (5) fully exposed the paravaginal space, (6) identify paravesical space and separate fascia, (7) dissected the blood vessels of the posterior lobe of the bladder cervical ligament, (8) deep uterine vein and inferior abdominal plexus were separated, (9) vut off paravaginal tissue and uterine branch of inferior abdominal plexus, (10) the rectovaginal space was separated, the uterus was removed, and then the pelvic cavity was cleaned. The equipment was evacuated and the incision was sutured after there was no active bleeding.

2.5 Index Detection

2.5.1 Detection of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$

All patients with cervical cancer were sampled 3 mL of fasting peripheral venous blood in the morning before operation, 1 day and 3 days after operation. Healthy women were sampled 3 mL of fasting peripheral venous blood and then added with CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ antibodies, sealed in a normal temperature incubator, protected from light for 30 min, added with hemolysin (batch number: 2012-1400523 Shanghai MINKE Biotechnology Co., Ltdn, Shanghai, China) 200 μL for each tube, and kept away from light in the conservatory for 15 min until the cells lysed. After the solution was clarified, 1 mL of phosphate-buffered saline (PBS) solution was added and centrifuged (rotating speed 3000 r/min, centrifugation 15 min), serum was separated, and 100 μL of 1% paraformaldehyde solution (batch number: FS-B0287, Shanghai MINKE Biotechnology Co., Ltdn, Shanghai, China) was fixed and determined by flow cytometry. The instrument was BD FACS Calibur flow (FACSVis) cytometry that was purchased from BD, New York, NY, USA.

2.5.2 FSFI and FACT-G Scores

The female sexual function index (FSFI) score was used to evaluate female sexual function (a total score from 2 to 36, a high score indicated that sex life was good), and the overall assessment scale of cancer treatment function (FACT-G) score was used to evaluate the quality of life of patients (from 0 to 108, a high score indicated that the quality of life of patients was good).

2.6 Statistical Analysis

The statistical analyses were performed using the Statistical Package for the Social Sciences version 19.0 (SPSS Inc., Chicago, IL, USA). Levene method was used to test the homogeneity of variance, student's t test (t test) was used to independent sample, analysis of variance (ANOVA), were used in the testing for repeated measurements in comparison between the groups, and chi-square test were used to compare proportion values. Receiver operator characteristics (ROC) curve and Pearson correlation analysis was used to analyze the predictive value of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ on the efficacy of LNSRH in the treatment of early cervical cancer. Statistically significant differences were assumed when $p < 0.05$.

3. Results

3.1 The CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ Expression between the both Groups

The expression of CD_4+ and $CD_{57}+$ in cervical cancer group were lower than that in control group, and the expression of CD_8+ and $CD_{20}+$ were higher than that in control group ($p < 0.05$), as shown in Table 1.

3.2 The CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ Expression in Cervical Cancer Group at Different Time Points

The expression of CD_4+ and $CD_{57}+$ were higher and the expression of CD_8+ and $CD_{20}+$ were lower postoperative than preoperative ($p < 0.05$). Compared with postoperative 1 d, the expression of CD_4+ and $CD_{57}+$ at post-

Table 1. The CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ expression between the two groups ($\bar{x} \pm s$).

Groups	n	CD_4+ (%)	CD_8+ (%)	$CD_{20}+$ (%)	$CD_{57}+$ (%)
Control group	30	35.49 ± 5.22	23.01 ± 3.01	13.03 ± 1.75	15.88 ± 3.01
Cervical cancer group	30	29.87 ± 4.02	28.32 ± 4.03	19.17 ± 3.01	12.18 ± 2.01
t		4.672	5.782	9.659	5.599
p		0.001	0.001	0.001	0.001

Table 2. The CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ expression in cervical cancer group at different time points ($\bar{x} \pm s$).

	n	CD_4+ (%)	CD_8+ (%)	$CD_{20}+$ (%)	$CD_{57}+$ (%)
Preoperative	30	29.65 ± 3.92	28.21 ± 3.81	19.02 ± 2.96	12.32 ± 2.08
Postoperative 1 d	30	30.02 ± 4.01	27.35 ± 3.56	18.68 ± 2.36	12.98 ± 2.21
Postoperative 3 d	30	33.21 ± 4.28	25.26 ± 3.19	16.85 ± 2.01	14.35 ± 2.63
F		3.360	3.252	3.322	3.316
p		0.001	0.001	0.001	0.001

operative 3 d were higher, and the expression of CD_8+ and $CD_{20}+$ were lower at postoperative 3 d ($p < 0.05$), as shown in Table 2 and Fig. 1.

3.3 The FSFI and FACT-G Scores between the Two Groups

The FSFI and FACT-G scores of cervical cancer group were lower than control group ($p < 0.05$). As shown in Table 3.

Table 3. The FSFI and FACT-G scores between the two groups ($\bar{x} \pm s$).

Groups	n	FSFI (Score)	FACT-G (Score)
Control group	30	35.69 ± 4.41	89.68 ± 7.98
Cervical cancer group	30	26.35 ± 3.39	64.21 ± 5.68
t		9.197	14.240
p		0.001	0.001

FSFI, female sexual function index; FACT-G, overall assessment scale of cancer treatment function.

3.4 Correlation between the Expression of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ and FSFI, FACT-G Scores

The expression of CD_4+, $CD_{57}+$ were positively correlated with FSFI score, the expression of CD_8+, $CD_{20}+$ were negatively correlated with FSFI score, the expression of CD_4+, $CD_{57}+$ were positively correlated with FACT-G score, and the expression of CD_8+, $CD_{20}+$ were negatively correlated with FACT-G score ($p < 0.05$), as shown in Table 4.

3.5 Analysis of the Detection Value of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ Expression in LNSRH for Early Cervical Cancer

The sensitivity of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ expression in ROC analysis was lower than that in the four combinations, and the specificity was higher than that in the four combinations, with statistical difference ($p < 0.05$). The four combined tests were better in detecting early post-

Table 4. Correlation between the expression of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ and FSFI, FACT-G scores.

	FSFI	FACT-G
CD_4+	$r = 0.529$	$r = 0.507$
	$p = 0.001$	$p = 0.001$
CD_8+	$r = -0.491$	$r = -0.439$
	$p = 0.002$	$p = 0.003$
$CD_{20}+$	$r = -0.532$	$r = -0.557$
	$p < 0.001$	$p < 0.001$
$CD_{57}+$	$r = 0.532$	$r = 0.557$
	$p < 0.001$	$p < 0.001$

FSFI, female sexual function index; FACT-G, overall assessment scale of cancer treatment function.

operative cervical cancer ($p < 0.05$), as shown in Table 5 and Fig. 2.

4. Discussion

Cervical cancer is a common gynecological tumor, with a high incidence of carcinoma *in situ* at the age of 30–35 and invasive cancer at the age of 45–55 [7]. The disease types are mostly squamous cell carcinoma, adenocarcinoma, adenosquamous carcinoma, clear cell carcinoma, small cell carcinoma, etc. In most cases, cervical cancer is caused by a persistent infection from human papillomavirus (HPV) and developed through a series of precursor dysplastic lesions of the cervical epithelium (i.e., cervical dysplasia) [8]. Human immune dysfunction may lead to cervical cancer. Some studies have shown that the state of the patients immune function can be used to assess the curative effect and prognosis of cervical cancer [9].

The study found that cervical cancer group CD_4+ was low and CD_8+ was high in cervical cancer patients than control group. CD_4+ was high and CD_8+ was low on the postoperative 3 d than postoperative 1 d. CD_4+ expression was positively correlated with FSFI and FACT-G scores, and CD_8+ expression was negatively correlated with FSFI and
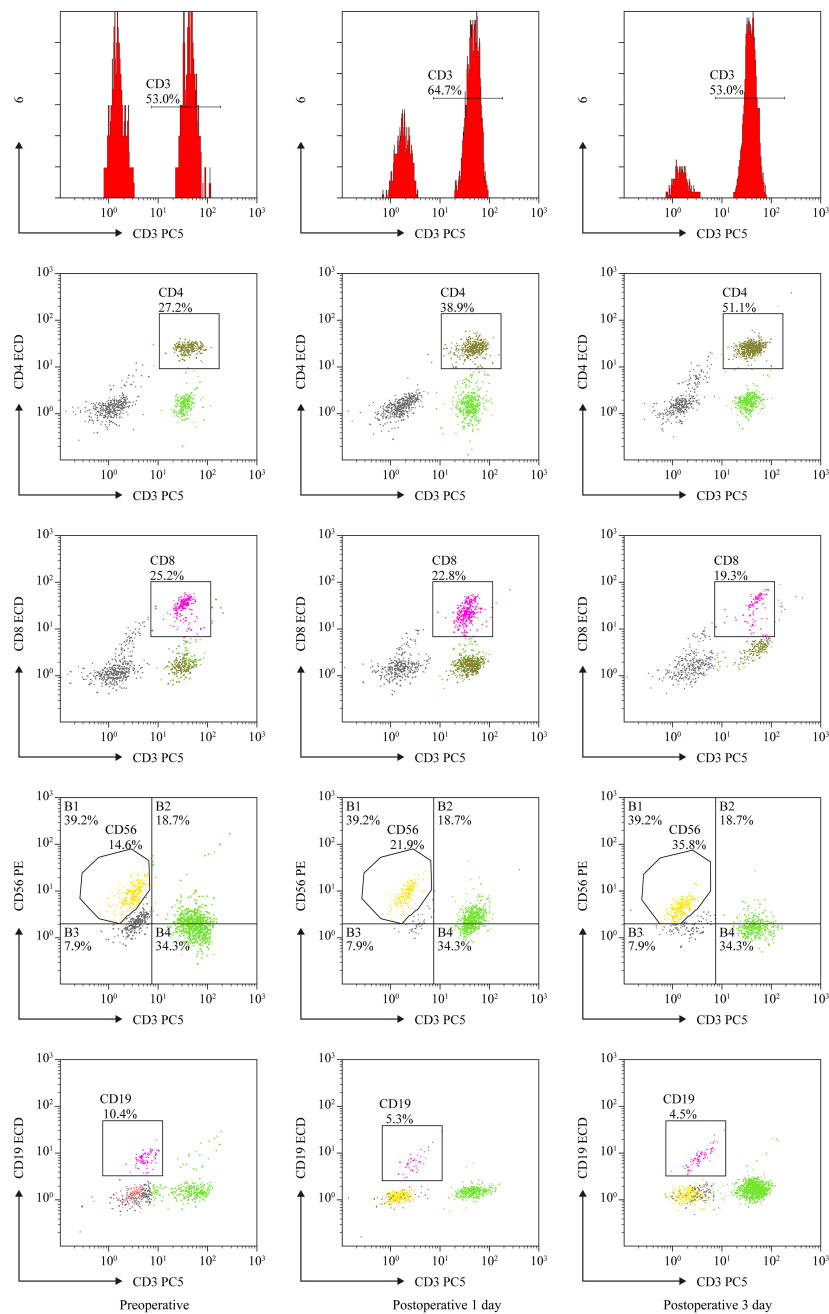
Fig. 1. The CD$_4$+, CD$_8$+, CD$_{20}$+, CD$_{57}$+ expression in cervical cancer group at different time points flow chart.

Table 5. Analysis of the detection value of CD$_4$+, CD$_8$+, CD$_{20}$+, CD$_{57}$+ expression in LNSRH for early cervical cancer.

Index	AUC	p	Sensitivity (%)	Specificity (%)	Accuracy (%)	95% CI
CD$_4$+	0.877	0.001	63.33 (19/30)	56.67 (17/30)	60.00 (36/60)	0.779–0.974
CD$_8$+	0.840	0.001	66.67 (20/30)	60.00 (18/30)	63.33 (38/60)	0.738–0.942
CD$_{20}$+	0.738	0.001	73.33 (22/30)	63.33 (19/30)	68.33 (41/60)	0.614–0.862
CD$_{57}$+	0.783	0.001	70.00 (21/30)	56.67 (17/30)	63.33 (38/60)	0.669–0.896
Four combined detection indexes	0.929	0.001	86.67 (26/30)	53.33 (16/30)	70.00 (42/60)	0.867–0.990

LNSRH, laparoscopic nerve-sparing radical hysterectomy; AUC, area under the curve; CI, confidence interval.

FACT-G scores, CD$_4$+ lymphocytes decreased, resulted in low immune function [10–13]. CD$_8$+ is a kind of cytotoxic T lymphocytes, which can kill human cells infected by viruses and can inhibit antibody synthesis [14,15]. In-
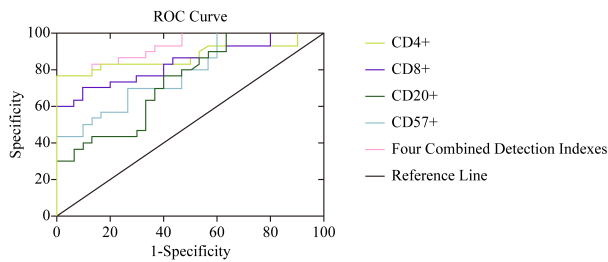
Fig. 2. Detection value of CD_4+, CD_8+, $CD_{20}+$, $CD_{57}+$ expression in LNSRH for early cervical cancer. ROC, receiver operating characteristic curve; LNSRH, laparoscopic nerve-sparing radical hysterectomy.

dicated that lymphocyte immune function decreased with the development of the cervical cancer, but the T lymphocyte immune function improved after LNSRH. Suggested that LNSRH was beneficial to the recovery of cervical cancer patients, and T lymphocytes could be used as a clinical indicator of cervical cancer, which were in line with the previous literature reports. LNSRH could use to laparoscopic technique to preserve nerves on the basis of treatment. LNSRH has been proved to be associated with many benefits in the management of different gynecological cancers, in terms of reduced postoperative morbidity, improved recovery and reduced inpatient stay [16].

The study found $CD_{20}+$ was highly expressed in patients with cervical cancer that compared with control group. Compared with postoperative 1 d, the expression of $CD_{20}+$ was lower on the postoperative 3 d. The expression of $CD_{20}+$ was negatively correlated with FSFI and FACT-G scores, indicated that B lymphocyte $CD_{20}+$ participated in the occurrence and development of cervical cancer, $CD_{20}+$ played a regulatory role in B cell differentiation and proliferation [17] and $CD_{20}+$ was closely related to the cervical cancer which were in line with the previous literature reports [18,19].

NK cells can secrete a variety of cytokines and plays a role in hematopoiesis and immune regulation [20]. $CD_{57}+$ is expressed in neuroendocrine cells, derived tumors, and NK cells mainly marking lymphoid tissues [21]. The study found the expression of $CD_{57}+$ was low in patients with cervical cancer that compared with control group. Compared with the postoperative 1 d, the expression of $CD_{57}+$ was higher on the postoperative 3 d. The expression of $CD_{57}+$ was positively correlated with FSFI and FACT-G scores, indicated that the NK cell immune function decreased with the development of the disease. However, the NK cell immune function gradually improved after LNSRH, suggested that LNSRH was conducive to the recovery of patients with cervical cancer.

The results of the study showed that the sensitivity of CD_4+, CD_8+, $CD_{20}+$, and $CD_{57}+$ in ROC were 63.33%, 66.67%, 73.33%, 70.00%, and 86.67% respec-

tively, and the accuracy was 60.00%, 63.33%, 68.33%, 63.33%, and 70.00% respectively and sensitivity and accuracy both lower than the four combined tests, suggested that CD_4+, CD_8+, $CD_{20}+$, and $CD_{57}+$ had high detection value for early cervical cancer treated with LNSRH which was involved in the occurrence and development of cervical cancer. The CD_4+, CD_8+, $CD_{20}+$, and $CD_{57}+$ of patients after LNSRH were improved, and LNSRH was of high value in the treatment of early cervical cancer.

Among the limitations of the present study, we mention the retrospective design, the relatively small number of patients included. Interestingly, a recent analysis has confirmed that, in female with the International Federation of Gynecology and Obstetrics (FIGO) stage Ib1-IIa2 cervical adenocarcinoma (CA), there were no significant differences between LNSRH and open surgery in terms of disease-free survival and overall survival [22,23]. So, further analyses of larger series are needed to better investigate the effect of LNSRH on the survival rate of early cervical cancer (ECC) patients. The main strengths of the current investigation were: FSFI, FACT-G scores were used to evaluate female sexual function and quality of life, the homogeneous and long-term (3-year) analysis of outcomes. The four combined test have good predictive value for the efficacy of LNSRH for early cervical cancer.

5. Conclusions

In conclusion, our study shows that LNSRH is a feasible, safe and effective procedure that conjugates adequate radicality with an improvement in post-operative functional outcomes. In the present study, we evaluated LNSRH is beneficial to the recovery of cervical cancer patients of life that were investigated. T, B, and NK lymphocytes combined test have good predictive value for the efficacy of LNSRH for early cervical cancer. Our data provide a reliable picture of the everyday clinical scenario in patients affected by early-stage as well as locally advanced cervical cancer. These data may serve as the basis for clinical counselling and future discussions on this relevant topic.

Availability of Data and Materials

All data generated or analysed during this study are included in this published article.

Author Contributions

Conception and design—LH; Administrative support—HZ; Provision of study materials or patients—LH; Data analysis and interpretation—LM; Manuscript writing—All authors; Final approval of manuscript—All authors. All authors read and approved the final manuscript.

Ethics Approval and Consent to Participate

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Conflict of Interest

The authors declare no conflict of interest.

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