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Immune biomarkers for predicting postoperative pneumonia following hip fracture surgery

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ABSTRACT

Objective: Abnormalities of lymphocyte subsets have been observed in patients with pneumonia. This study investigated the diagnostic efficiency of lymphocyte subsets in the detection of early-stage postoperative pneumonia (POP) among older patients undergoing hip fracture surgery.

Methods: A total of 576 patients with hip fracture were recruited and analyzed for lymphocyte subsets on the first postoperative day.

Results: The incidence of POP was 10.6% (61/576) from March 2016 to December 2023. The area under the curve for the percentage of CD8+ HLA-DR+ T cells was higher than that of CD4+ T and CD4+ CD45RA+ T cells. A high percentage of CD8+ HLA-DR+ T cells was significantly associated with an increased occurrence of POP. The positive findings remained significant after adjusting for confounding factors. Among the multiple complications, patients with diabetes tended to have higher percentages of CD8+ HLA-DR+ T cells.

Conclusions: The percentage of CD8+ HLA-DR+ T cells had a good predictive value for detecting early-stage POP. Multi-center prospective studies with larger sample sizes are needed to verify this finding.

TWEETABLE ABSTARCT

HLA-DR expression in CD8+ T cells is a potential biomarker for the early identification of POP.

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KEYWORDS
Hip fractures; pneumonia; lymphocyte subsets; biomarkers; T cells

1. Introduction

Hip fracture is a common fracture type encountered in clinical practice and has a high incidence in the older population [1]. With the aging of the population, the number of hip fractures [1,124,060] in 2018 is projected to double by 2050 [2], placing a heavy burden on the healthcare system. Surgical intervention is the primary treatment for hip fractures, and it aims to restore hip joint function, improve the quality of life, and reduce the risk of various complications caused by long-term bed rest [3]. Timely surgical intervention is crucial for optimal outcomes because delayed surgery is correlated with higher mortality rates [4]. Among the complications arising from hip fracture surgery, postoperative pneumonia (POP) is particularly prevalent. POP not only prolongs the length of hospital stay and increases medical costs but may also lead to a significant increase in mortality [5,6]. Therefore, the early detection of POP is crucial for appropriate preventive measures, enabling timely screening of high-risk groups and improving postoperative prognosis.

During the initial inflammatory stage after fracture injury, specific cell-mediated immune functions remove necrotitissues, promote angiogenesis and initiate repair [7]. Impaired perioperative immune function may be associated with worse short- and long-term prognosis after major surgical interventions [8]. A significant reduction in TNF-α, IL-2, IFN-γ and lymphoproliferation was observed immediately after surgery, indicating impaired cell-mediated immunity. Lymphocytes, including T lymphocytes (CD4+ T and CD8+ T cells), B cells, and NK cells, are crucial for immune function [9]. Among lymphocytes, T cells are the main cells of cellular immunity. T lymphocyte depletion showed negative effects on fracture healing [10]. Aging further compromises the function of T lymphocyte [11], as CD28 expression on T cells declines, while human leukocyte antigen – DR (HLA-DR) and CD45RO expression increases, reducing resistance to infection [12]. Abnormalities of T lymphocyte subsets have been observed in patients with pneumonia [13,14]. For example, peripheral blood T lymphocyte counts had good predictive value for the development of pneumonia after transplantation, as documented by their area under the curve (AUC) value of 0.792 [15].

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Article highlights

- Predicting postoperative pneumonia during hip fracture surgery is timely and relevant.
- The aging process is characterized by the decline in the immune function of the innate and adaptive systems. Reduced immune system function decreases resistance to infection and increases the risk of disease. The analysis of immune biomarkers is an interesting approach.
- Lymphocytes, including T lymphocytes (CD4+ T and CD8+ T cells), B lymphocytes, and NK cells, are crucial for immune function.
- Few studies have investigated the association between lymphocyte subsets and the risk of postoperative pneumonia.
- Patients with POP had a lower percentage of CD4+ CD45RA+ T cells and exhibited higher T cell activation (CD8+ HLA-DR+).
- The percentages of CD4+ CD45RA+ T or CD8+ HLA-DR+ T cells exhibited good performance in the detection of early-stage POP.
- Individuals with higher percentages of CD8+ HLA-DR+ T cells had a significantly higher risk of postoperative pneumonia.
- Among the multiple complications, patients with diabetes tended to have higher CD8+ HLA-DR+ T percentages.

However, few studies have explored the association between T lymphocyte subsets and the risk of POP among older patients following hip fracture surgery.

Therefore, in this study, we elucidated the postoperative immunological characteristics of patients and evaluate the performance of these indicators in predicting the incidence of POP following hip fracture surgery. Identifying high-risk patients early is crucial for reducing the incidence of postoperative pneumonia, improving patient prognosis, and reducing social and economic burden.

2. Materials and methods

2.1. Patients

This retrospective study was conducted at the trauma center of Wujin Hospital of Traditional Chinese Medical between March 2016 and December 2023. The study included patients aged ≥60 years who sustained acute hip fractures and subsequently underwent orthopedic surgical treatment. Hip fractures were confirmed by X-ray or computed tomography. The exclusion criteria were as follows: (1) patients with old fractures (injury to surgery time greater than 3 weeks); (2) long-term use of immunosuppressive agents; (3) preoperative pneumonia, respiratory tract inflammation, or cancer; (4) incomplete data; and (5) patients with a history of conservative treatment, revision surgery, or reoperation. The study protocol was approved by the institutional review board of Wujin Hospital of Traditional Chinese Medical (ID: IL-2024001). Written informed consent was obtained from all participants before inclusion in the study.

2.2. Data collection

Demographic data, including age, sex, and major comorbidities, were recorded. Major comorbidities included chronic obstructive pulmonary disease (COPD), hypertension, coronary heart disease, type 2 diabetes, prior stroke, and chronic renal failure. Laboratory indicators included white blood cell count (WBC) and biochemical analyses (serum albumin [ALB], creatinine [Cr], and alanine aminotransferase [ALT]). Laboratory measurements and chest examinations (X-ray or computed tomography) were performed within 24 h of hospital admission. The fracture and treatment details were also recorded, including fracture type, the American Society of Anesthesiologists (ASA) Physical Status score, and surgical method.

2.3. Outcome assessment

POP was diagnosed according to the American Thoracic Society guidelines for healthcare-associated pneumonia [16]. The criteria included (1) the presence of new and/or progressive and persistent respiratory symptoms, such as cough; (2) fever or hypothermia; (3) lung consolidation and auscultatory crackles; (4) $WBC > 10 \times 10^9$ cells/L or $WBC < 4 \times 10^9$ cells/L; and (5) new infiltrations observed on chest X-ray or computed tomography. Diagnosis required meeting criteria 1–4 in conjunction with criterion 5 within 24 h postoperatively until discharge.

2.4. Flow cytometry

Peripheral blood (2 mL) was collected from the participants on the first postoperative day, before developing POP. First, empty flow cytometry tubes were prepared. Second, CD45, CD3, CD4, CD8, CD45RA, CD28, and human leukocyte antigen – DR (HLA-DR) antibodies (BD Biosciences) were added. Then, 100 µL of well-mixed whole blood was added to each tube and incubated for 15 min. Subsequently, red blood cell lysis was performed. The cells were washed twice, resuspended in 20 µL phosphate-buffered saline, collected using a BD FACSCanto flow cytometer (BD Biosciences), and analyzed using the FACS DIVA software (BD Biosciences) (Figure 1).

2.5. Statistical analysis

Categorical variables were expressed as number (percentage) and the chi-square test was performed for categorical variables. The Kolmogorov-Smirnov test is used to test whether the variables conformed to normal distribution. For normally distributed continuous variables, the mean and standard deviation (SD) were calculated and compared using the t-test. If the data did not conform to normal distribution (indicated as median (interquartile range)), the Mann-Whitney u test was used to compare differences. Univariate or multivariable logistic regression analysis was performed to evaluate the strength of the associations between immunological indicators and the occurrence of POP based on odds ratios and 95% confidence intervals. The predictive value of these indicators was assessed based on their sensitivity and specificity using receiver operating characteristic curve analysis. Statistical significance was set at $p < 0.05$. All data analyses were performed using SPSS version 25.0 (SPSS, Inc., Chicago, IL, USA) and GraphPad Prism version 6 (GraphPad Software, San Diego, CA, USA).

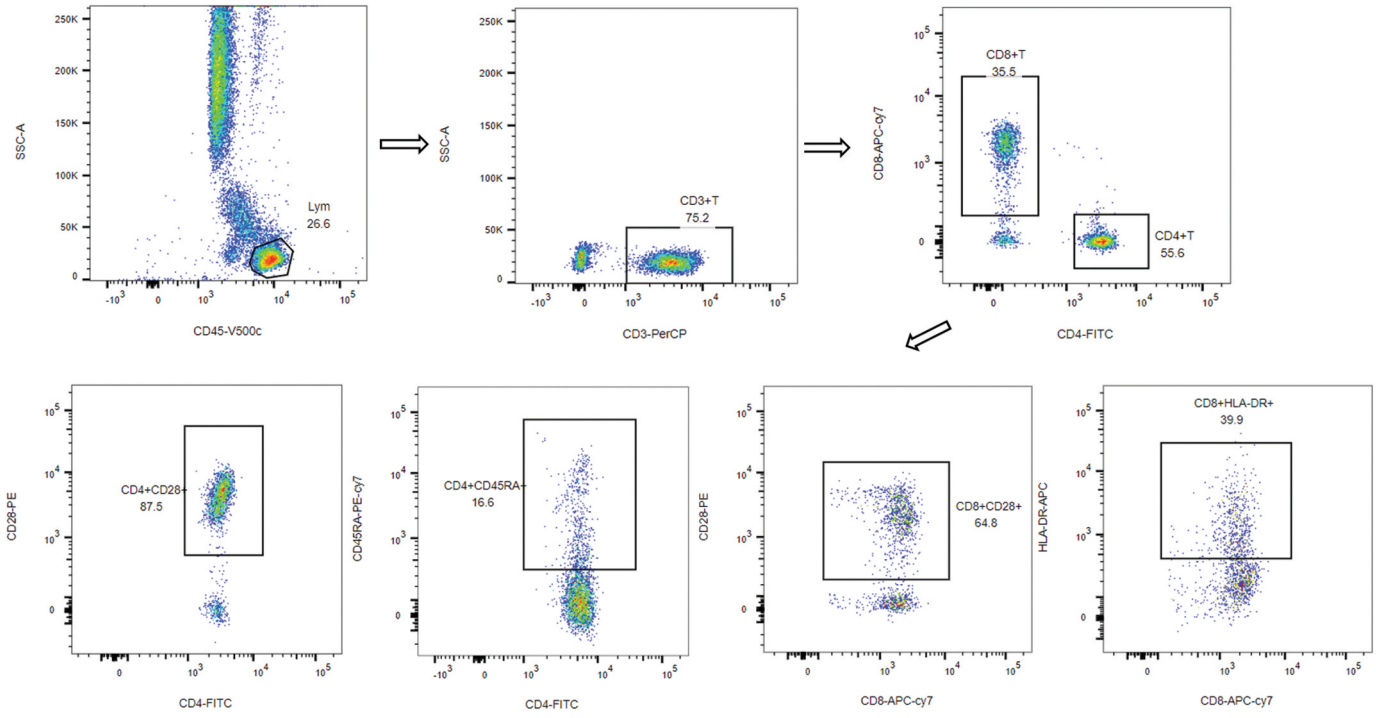

Figure 1. Phenotype analysis of T cell subsets.

3. Results

3.1. Clinical and demographic characteristics of the participants

Table 1 presents the baseline characteristics of 637 older patients diagnosed with hip fractures, among whom 61 (9.58%) experienced POP. The flowchart of the patient screening process is presented in Figure 2. Only four of the continuous variables met a normal distribution, and they were age, WBC, percentage of CD4 +T cells, and percentage of CD8 +T cells. No significant associations were found between the non-POP and POP groups concerning age, sex distribution, and surgical method ($p > 0.05$). The mean age was 81.53 ± 7.42 years in the non-POP group and 80.44 ± 8.05 years in the POP group. No significant difference was found in age between the two groups ($p > 0.05$). In total, 286 men (49.7%) were included in the non-POP group, whereas 37 men (60.7%) were included in the POP group. No significant difference was observed in the sex ratio between the two groups ($p > 0.05$). Furthermore, the POP group differed from the non-POP group in several clinical characteristics, especially in stroke, ASA score, some fracture types, operative time, and lymphocyte subsets ($p < 0.05$).

As shown in Table 2, patients with POP had a higher WBC count and lower ALB levels. No statistical differences were observed in ALT and creatinine between the POP and non-POP groups. Furthermore, the percentages of CD4+ T and CD4 + CD45RA+ T cells were significantly lower in patients who had POP than in those who did not. The expression of the costimulatory marker CD28 on T cells did not differ significantly between the two groups. Notably, patients with POP exhibited higher levels of T cell activation (CD8+ HLA-DR+).

3.2. Clinical efficacy of single-stage POP detection after hip fractures

The Youden index of CD4+ T cells (%) was 0.389, which was higher than that of single parameter (Table 2). We observed that CD8+ HLA-DR+ T percentages presented an AUC of 0.712, which was superior to ALB, CD4+ T, and CD4+ CD45RA+ T percentages. This result indicates that it has a relatively good predictive ability for early POP after hip fracture surgery. The optimal cutoff values for ALB levels, CD4+ CD45RA+ T cell percentages, and CD8+ HLA-DR+ T cell percentages were 38.45 g/L, 26.2%, and 36.21%, respectively. A cutoff value of 36.21% can distinguish between POP (>36.21%) and non-POP (≤36.21%). At this threshold, the percentage of CD8+ HLA-DR + T cells exhibited a sensitivity of 78.7% and a specificity of 58.6%.The percentages of CD8+ HLA-DR+ T and CD4+ CD45RA+ T cells were selected as predictive model markers based on their sensitivity and specificity. Subsequently, we established a predictive model for distinguishing the POP group from the non-POP group as follows:

$$P = 1/[1 + e - (-0.081 \times CD4 + CD45RA + \text{T percentage} + 0.100 \times CD8 + HLA - DR + \text{T percentage} - 3.340)]$$

The AUC value (0.794) of the prediction model was higher than that of single CD4+ CD45RA+ T (0.696) and CD8+ HLA-DR+ T (0.712) cell percentages. The combination of multiple clinical parameters could more accurately predict the occurrence of POP. The Youden index of each parameter reflects its comprehensive performance in distinguishing between POP and non-POP groups.

Table 1. The clinical characteristics of the POP group and non-POP groups.

Variables	Non-POP (*N* = 576)	POP (*N* = 61)	P value
Age, years	81.53 ± 7.42	80.44 ± 8.05	0.283
Male, n(%)	286 (49.7)	37 (60.7)	0.102
Comorbidities			
Hypertension, n(%)	296 (51.4)	36 (59.0)	0.257
Diabetes, n(%)	125 (21.7)	16 (26.2)	0.418
Coronary artery disease, n(%)	93 (16.1)	12 (19.7)	0.480
Stroke, n(%)	106 (18.4)	19 (31.1)	**0.017**
COPD, n(%)	41 (7.1)	8 (13.1)	0.095
Renal insufficiency, n(%)	29 (5.0)	6 (9.8)	0.118
ASA classification			**0.001**
I-II, n(%)	266 (46.2)	14 (23.0)	
III-IV, n(%)	310 (53.8)	47 (77.0)	
Fracture type			0.107
Femoral neck fracture, n(%)	302 (52.4)	24 (39.3)	
Intertrochanteric fracture, n(%)	249 (43.2)	35 (57.4)	
Subtrochanteric fracture, n(%)	25 (4.3)	2 (3.3)	
Surgery method			0.480
Total Hip Arthroplasty, n(%)	78 (13.5)	5 (8.2)	
Hemiarthroplasty, n(%)	133 (23.1)	14 (23.0)	
Intramedullary fixation, n(%)	365 (63.4)	42 (68.9)	
Surgical duration, min	83.0(61.0,141.8)	97.0(73.5,140.0)	**0.005**
Laboratory parameters			
WBC (10^9/L)	8.21 ± 2.84	9.13 ± 2.50	**0.015**
ALT (U/L)	23.0(17.0,31.0)	28.0(15.5,43.0)	0.385
ALB (g/L)	39.8(36.3,43.4)	36.1(30.4,41.4)	**<0.001**
Cr (μmol/L)	69.0(56.0,81.0)	66.0(37.0,114.0)	0.884
Lymphocyte subsets			
CD4+T cells (%)	38.04 ± 6.31	33.29 ± 9.48	**<0.001**
CD8+T cells (%)	30.93 ± 6.93	32.00 ± 7.49	0.258
CD4+CD45RA+ (%)	38.4(30.4,46.4)	31.5(19.9,38.1)	**<0.001**
CD8+HLA-DR cell (%)	34.1(29.6,40.1)	39.5(36.5,51.5)	**<0.001**
CD4+CD28+T cell (%)	90.2(87.0,93.0)	89.2(82.9,95.4)	0.203
CD8+CD28+T cell (%)	51.0(39.1,63.8)	50.5(38.2,57.6)	0.196

*Bold values indicate significant difference.
Continuous variables were expressed as mean±standard deviation or median [Q1, Q3].
Abbreviation: POP, postoperative pneumonia; COPD,chronic obstructive pulmonary disease; ASA, the American Society of Anesthesiologists; WBC, white blood cell; ALT, glutamic pyruvic transaminase; Cr, creatinine; ALB, albumin.

3.3. Multivariate analysis between the POP and non-POP groups

When assessing the above three biomarkers using the optimal cutoff value, lower ALB levels, lower CD4+ CD45RA+ T percentages, and higher CD8+ HLA-DR+ T percentages were significantly associated with an increased incidence of POP (Table 3). Furthermore, the positive correlation remained strong when the above three biomarkers were assessed as continuous variables. The association between elevated CD8+ HLA-DR+ T percentage and a higher incidence of POP was also visually illustrated after adjusting for ASA classification, surgical duration, stroke, diabetes and WBC. The percentage of CD8+HLA-DR + T cells greater than 36.21% was associated with a higher incidence of POP. Albumin, CD4+, CD45RA+ T, and CD8+ HLA-DR+ T exhibited some predictive value for POP following hip fracture surgery. Changes in the levels of these indicators at specific cutoff times can significantly affect the risk of POP.

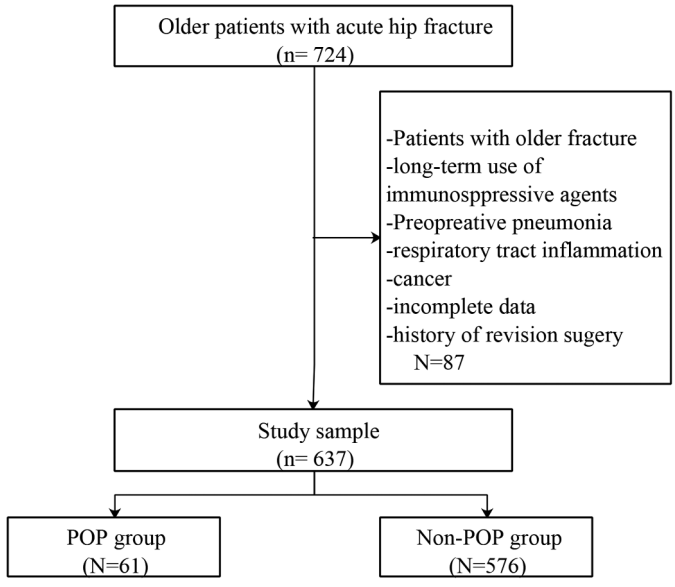

Figure 2. Flow diagram for selection of the study population.

3.4. Postoperative CD45RA and HLA-DR expression in T cells and their clinical features

No significant differences were observed between age, sex, and hypertension about CD4+ CD45RA+ T and CD8+ HLA-DR+ T percentages (Table 4). After surgery, patients with kidney problems had lower percentages of CD4+ CD45RA+ T cells, whereas those with diabetes had higher levels of CD8+ HLA-DR+ T cells.

Table 2. Clinical efficacy of clinical parameters in early POP after hip fracture surgery.

Variables	AUC (95%CI)	cutoff	Sensitivity	Specificity	Youden index
WBC (10^9/L)	0.595(0.526,0.664)	8.05	73.7	47.2	0.210
Albumin (g/L)	0.681(0.600,0.761)	38.45	70.5	60.2	0.307
CD4+T (%)	0.660(0.569,0.751)	33.88	63.9	75.0	0.389
CD4+CD45RA+T (%)	0.696(0.626,0.766)	26.2	55.8	85.2	0.295
CD8+HLA-DR+T (%)	0.712(0.646,0.779)	36.21	78.7	58.6	0.372
Combined	0.794(0.737,0.851)				

Abbreviation: POP, Postoperative Pneumonia; AUC, area under the curve; CI, confidence interval.

Table 3. Univariate and multivariate analyses of risk factors associated with POP.

		Univariate analysis		Multivariate analysis*	
Variables	Group	OR (95%CI)	*P*	OR (95%CI)	*P*
ALB	Continuous	0.864(0.823,0.908)	**<0.001**	0.865(0.822,0.910)	**<0.001**
	Best cutoff				
	<38.45	1 (Reference)			
	≥38.45	0.276(0.155,0.491)	**<0.001**	0.252(0.139,0.458)	**<0.001**
CD4+CD45RA+T	Continuous	0.919(0.892,0.947)	**<0.001**	0.918(0.891,0.946)	**<0.001**
	Best cutoff				
	<26.2	1 (Reference)			
	≥26.2	0.218(0.125,0.380)	**<0.001**	0.206(0.115,0.368)	**<0.001**
CD8+HLA-DR+T	Continuous	1.108(1.072,1.144)	**<0.001**	1.110(1.072,1.147)	**<0.001**
	Best cutoff				
	<36.21	1 (Reference)			
	≥36.21	5.206(2.759,9.823)	**<0.001**	4.810(2.522,9.172)	**<0.001**

*Adjusted for ASA classification, surgical duration, stoke, WBC, diabetes.
Bold values indicate significant difference.
Abbreviation: ALB, albumin; POP, Postoperative Pneumonia; OR, odds ratios; CI, confidence interval.

Table 4. Preoperative immunological parameters and clinical features.

Variables	CD4+CD45RA+T,%	P	CD8+HLA-DR+T,%	P
Sex		0.821		0.116
Male	37.46(29.41,45.64)		36.74(30.90,41.89)	
Female	37.36(29.28,45.76)		34.54(29.91,40.23)	
Age		0.430		0.826
<75 years	37.52(30.66,46.59)		35.13(30.35,40.38)	
≥75 years	37.34(28.42,45.02)		34.91(29.57,41.06)	
Hypertension		0.620		0.557
No	37.00(29.51,45.31)		34.90(29.75,40.43)	
Yes	38.15(28.84,46.14)		35.34(30.25,40.83)	
Diabetes mellitus		0.686		**0.017**
No	37.49(29.43,45.72)		34.48(29.43,40.14)	
Yes	36.45(28.73,45.84)		36.18(31.21,41.66)	
Renal insufficiency		**<0.001**		0.162
No	37.71(30.07,46.10)		34.97(29.86,40.48)	
Yes	28.06(23.76,41.04)		36.50(30.64,42.97)	

4. Discussion

In this study, the percentages of CD4+ CD45RA+ T and CD8+ HLA-DR+ T cell differed significantly between patients who developed POP and those who did not. Notably, CD8+ HLA-DR+ T cell percentages showed better AUC values in for predicting the incidence of POP. Multivariate analysis revealed that the percentage of CD8+ HLA-DR+ T cell was independently associated with POP. By measuring the postoperative levels of these immune biomarkers, patients at high risk of POP can be identified in advance. Notably, significant differences were observed in the percentage of CD8+ HLA-DR+ T cell between patients with diabetes mellitus and those without. Therefore, in clinical practice, more attention should be paid to the immune status of patients with hip fracture and diabetes to actively prevent the occurrence of POP.

Postoperative inflammatory complications may be influenced by both patient factors (such as age, comorbidity, and gender) and surgical factors (including technical skill, anesthetic agent, blood loss, and operating time). However, there is limited data to support the use of these variables as predictors in routine clinical practice. Many recent studies have used the level of laboratory indicators upon admission to predict the occurrence of POP. However, the predictive efficacy is limited, with an AUC value mostly below 0.7. These indicators include partial oxygen pressure [17], oxygen levels [18], and neutrophil-to-lymphocyte ratio [19]. In addition to these preoperative markers, postoperative immune responses also play a critical role. After surgery, an excessive innate immune response or a failure of the adaptive immune response can lead to systemic inflammatory response syndrome, infections (e.g., at the surgical site, in the chest, or urinary tract), and even sepsis [20]. This initial inflammatory storm may signal a prolonged immunosuppressive state later on, thereby increasing the risk of nosocomial infections. Therefore, identifying an exaggerated immune response on postoperative day 1 might serve as an early warning indicator [20].

Lymphocytes are the backbone of adaptive immunity, and T cells in particular can be subdivided into functional (CD4+/CD8+ CD28+), activation (CD4+/CD8+ HLA-DR+), and naïve subsets (CD4+CD45RA). Among them, CD45RA+ naïve T cells are regarded as markers of lymphocyte potential [21]. CD45RA expression on CD4+ T was negatively correlated with IFN-γ-producing ability of CD4+ T cells [22], which reflects T cell functionality [23]. CD4+CD45RA+T cells decreased immediately after operation [24]. The loss of naïve CD4+ CD45RA+ T cells also occurred in the peripheral blood of patients with COVID-19 pneumonia [25]. Moris et al. enrolled 248 patients to assess immunological changes before and after surgery. They found that patients with fewer preoperative CD4+ naïve T cells or higher proportions of CD4+T_{EM} or CD8+ T_{EMRA} were associated with an increased risk of any postoperative complications [26]. This suggests that patients with POP experience impaired T-cell function, reducing their ability to respond to infections and tumors. In this study, patients with POP exhibited reduced percentages of CD4+ T cells and CD4+ CD45RA+ T cells, which were in accordance with the finding of previous studies. Moreover, Liu et al. found that ALB levels were significantly positively correlated with the percentage of CD45RA + CD4+ T cell, which supports the key role of protein intake in maintaining healthy immunity by increasing both the number and potential of lymphocytes. Protein intake should be increased after hip fracture surgery to increase lymphocyte potential, enhance T-cell function, and maintain host immunity.

Surgical stress enhances early lymphocyte activation, as indicated by increased CD4+CD69+ and CD8+CD69+ T cells [27]. T cell activation occurs in three key phases: Signal 1, triggered by antigen binding to T cell receptors; Signal 2, mediated by costimulatory interactions (e.g., CD28 binding to B7 molecules); and Signal 3, driven by cytokine signaling (e.g., IL-2). In the absence of CD28 signaling, T cells may enter an anergic state, leading to a compromised immune response. The postoperative phenotypes (CD8+CD28-) was significantly associated with postoperative infection after elective surgery [26]. However, we found no significant difference in CD28 expression in T cells between patients with and without POP in this study. The differences in results between the two studies can be attributed to population heterogeneity, differences in sampling time, sample size variation, and different types of surgery. Our result is consistent with observations in patients with *Chlamydia pneumoniae* infection in the older population, in whom no significant differences were observed in the percentage of CD8+ CD28+ cells between IgG positivity and weakly positive individuals [28]. HLA-DR, a class II major histocompatibility complex antigen, is expressed on activated T cells during immune responses. The increased expression of HLA-DR on T cells contributes to the persistence of chronic inflammation and is correlated with disease severity. Elevated CD8+ HLA-DR+ T cell percentages are linked to unfavorable outcomes in COVID-19 pneumonia [29]. CD4 + hLA-DR + T cells, but not CD8+, increased over time after adult spinal deformity surgery [30]. In this study, higher CD8 + HLA-DR+ T percentages were observed in patients with POP and showed good performance in predicting the occurrence of POP. CD8+ HLA-DR+ T percentages have high sensitivity and insufficient specificity. Therefore, it is necessary to combine this approach with other indicators to improve diagnostic accuracy.

Some comorbidities are more common in patients with postoperative pneumonia [31]. A study by Yu et al. [32], which involved patients undergoing surgical treatment for hip fractures, found hypertension as the most prevalent comorbidity at 52.0% (59.0% in our study), followed by 23.6% with type 2 diabetes (26.2% in our study). Brunetti et al. [33] reported an increased risk of pneumonia among patients with type 2 diabetes in a meta-analysis involving 14,538,968 patients. Diabetes has several mechanisms that can increase the risk of infection, including highly altered immune cell function, bacterial proliferation, and changes in vascular permeability and endothelial cells, which have been attributed to an increase in the incidence of POP after an array of surgeries [34]. The subgroup analysis revealed that patients with diabetes mellitus tended to have higher CD8+ HLA-DR+ T cell percentages. The peripheral blood of patients with type 2 diabetes and obesity also has a higher level of activated T lymphocytes (CD3+ HLA-DR+), indicating the increased activity of T-cell immunity [35]. Type 2 diabetes with high CD8+ HLA-DR+ T cell percentages may have a significantly higher risk of POP.

5. Limitations

Although our study provides valuable insights, several limitations warrant consideration. First, this was a single-center study with a medium sample size. Therefore, selection bias cannot be avoided. Second, the potential influence of comorbidities on immune function must be explored further. Third, in patients exposed to surgical stress, peripheral blood lymphocyte counts and function were suppressed until at least 2 weeks postoperatively [24]. Future investigations should explore the postoperative dynamic time course of lymphocyte subset percentages. Fourth, other factors that may affect the occurrence of POP were not considered in this study, such as preoperative mobility status, nutritional status, method of anesthesia during surgery, history of chronic lung disease and ventilation management [36]. Fifth, notably, this study mainly analyzed data from older patients with hip fracture; thus, other fracture types and age groups should be investigated in future studies to validate these findings. Finally, this study may not fully exclude early subclinical infections.

6. Conclusion

In conclusion, our study found a notable association between CD8+ HLA-DR+ T cell percentages and POP risk in geriatric patients undergoing hip fracture surgery. Further prospective studies with larger sample sizes are needed to verify the predictive abilities of these biomarkers, thereby improving the prognosis of patients undergoing hip fracture surgery and reducing the incidence of POP.

Authors' contributions

Zemin Wu: design, statistical analysis and write the draft manuscript.
Bing Li and Wenke Zhu managed the co-ordination.
Jingjing Shang and Jiapei Yao participated in the design, managed the data collection and participated in the analysis.
Yong Huang participated in the design and analysis.
Jiansong Yin and Xindie Zhou took an active part in the discussion and interpretation of the findings.
All authors read and approved the final manuscript.

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Disclosure statement

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Writing disclosure

No writing assistance was utilized in the production of this manuscript.

Ethics approval

The study protocol have obtained the approval of the institutional review board of Wujin Hospital of Traditional Chinese Medicine (IRB: IL-2024001) and followed the principles outlined in the Declaration of Helsinki for all human. Written informed consent was obtained from all participants before admission.

The authors state that they have obtained appropriate institutional review board approval (Wujin Hospital of Traditional Chinese Medicine (IRB: IL-2024001) and/or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

Data availability statement

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

AI-based tools and technologies

No AI-based tools and technologies were utilized in the production of this manuscript.

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