

# 艾滋病患者血清sCD14、CGRP、FOXO3水平表达与疾病分期和免疫功能的相关性研究

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**摘要:** **目的** 分析艾滋病(AIDS)患者血清可溶性白细胞分化抗原14(sCD14)、神经元降钙素基因相关肽(CGRP)、叉头转录因子O亚型3(FOXO3)水平与疾病分期和免疫功能的关系。**方法** 选取2021年1月~2024年1月石家庄市第五医院和石家庄市妇幼保健院收治的175例AIDS患者及175例健康体检者为研究对象, 分别纳入AIDS组和对照组, 采用酶联免疫吸附法(ELISA)检测两组受试者血清sCD14、CGRP和FOXO3表达水平。采用Spearman法和Pearson法分析sCD14、CGRP、FOXO3水平与疾病分期和免疫功能的相关性, 采用多因素Logistic分析AIDS患者预后不良的影响因素, 采用受试者工作特征(ROC)曲线预测sCD14、CGRP和FOXO3水平对AIDS患者预后不良的预测价值。**结果** 与对照组比较, AIDS组患者血清sCD14( $5.12 \pm 1.25 \mu\text{g/ml}$  vs  $2.83 \pm 0.46 \mu\text{g/ml}$ )、 $\text{CD8}^+$ ( $476.88 \pm 51.38$ 个/ $\mu\text{l}$  vs  $396.57 \pm 35.42$ 个/ $\mu\text{l}$ )水平显著升高; CGRP( $42.38 \pm 14.69$  pg/ml vs  $76.53 \pm 18.54$  pg/ml)、FOXO3( $5.81 \pm 1.34$  ng/ml vs  $8.02 \pm 1.07$  ng/ml)、 $\text{CD4}^+$ ( $271.18 \pm 68.54$ 个/ $\mu\text{l}$  vs  $728.69 \pm 88.49$ 个/ $\mu\text{l}$ )水平及 $\text{CD4}^+/\text{CD8}^+$ ( $0.57 \pm 0.12$  vs  $1.20 \pm 0.15$ )比值显著降低, 差异具有统计学意义( $t=17.049 \sim 54.072$ , 均 $P<0.05$ )。AIDS组患者血清sCD14、 $\text{CD8}^+$ 水平在急性期组、无症状期组、艾滋病期组依次升高, CGRP、FOXO3、 $\text{CD4}^+$ 水平及 $\text{CD4}^+/\text{CD8}^+$ 比值依次下降, 差异具有统计学意义( $F=25.322 \sim 125.502$ , 均 $P<0.05$ )。sCD14与 $\text{CD4}^+$ 、 $\text{CD4}^+/\text{CD8}^+$ 呈负相关, 与 $\text{CD8}^+$ 、疾病分期呈正相关; CGRP、FOXO3与 $\text{CD4}^+$ 、 $\text{CD4}^+/\text{CD8}^+$ 呈正相关, 与 $\text{CD8}^+$ 、疾病分期呈负相关, 差异具有统计学意义( $r=-0.746 \sim 0.759$ , 均 $P<0.05$ )。sCD14、CGRP、FOXO3水平与生殖器疱疹、淋巴瘤及HIV载量有关, 差异具有统计学意义( $t/F=2.381 \sim 39.190$ , 均 $P<0.05$ )。预后不良组患者血清sCD14、 $\text{CD8}^+$ 水平及HIV载量高人数占比显著高于预后良好组, CGRP、FOXO3、 $\text{CD4}^+$ 水平及 $\text{CD4}^+/\text{CD8}^+$ 比值显著低于预后良好组, 差异具有统计学意义( $t=5.071 \sim 10.577$ , 均 $P<0.05$ )。sCD14、 $\text{CD8}^+$ 及HIV载量高为AIDS患者预后不良的危险因素, CGRP、FOXO3、 $\text{CD4}^+$ 及 $\text{CD4}^+/\text{CD8}^+$ 为AIDS患者预后不良的保护因素, 差异具有统计学意义(Wald  $\chi^2=6.349 \sim 18.825$ , 均 $P<0.05$ )。sCD14、CGRP、FOXO3水平联合预测AIDS患者预后不良的AUC高于各项单独预测的AUC, 差异具有统计学意义( $Z=3.757, 3.836, 3.353$ , 均 $P<0.05$ )。**结论** sCD14在AIDS患者血清中上调表达, CGRP、FOXO3下调表达, 与疾病分期和免疫功能关系密切, 三者联合预测AIDS患者预后不良价值较高。

**关键词:** 艾滋病; 可溶性白细胞分化抗原14; 神经元降钙素基因相关肽; 叉头转录因子O亚型3; 疾病分期; 免疫功能

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## Study on the Correlation between the Expression Levels of Serum sCD14, CGRP and FOXO3 in AIDS Patients and Disease Stage and Immune Function

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**Abstract: Objective** To investigate the relationship between the levels of serum soluble cluster of differentiation antigen 14 (sCD14), calcitonin gene related peptide (CGRP), forkhead box transcription protein 3 (FOXO3) with disease stage and immune function in acquired immune deficiency syndromes (AIDS) patients. **Methods** 175 AIDS patients admitted to and 175 healthy individuals under going physical examinations in Shijiazhuang Fifth Hospital and Shijiazhuang Maternal and Child Health Hospital from January 2021 to January 2024 were enrolled as the AIDS group and the control group, respectively. The enzyme-linked immunosorbent assay (ELISA) method was applied to detect the expression levels of sCD14, CGRP and FOXO3 in the serum of both groups. Spearman and Pearson correlation analyses were applied to analyze the correlation between sCD14, CGRP, FOXO3

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levels with disease stage and immune function. Multivariate Logistic regression was used to analyze the factors influencing poor prognosis in patients with AIDS. Receiver operating characteristic (ROC) curve was applied to predict the predictive value of sCD14, CGRP and FOXO3 levels for poor prognosis in AIDS patients. **Results** Compared with the control group, the levels of serum sCD14 ( $5.12 \pm 1.25 \mu\text{g/ml}$  vs  $2.83 \pm 0.46 \mu\text{g/ml}$ ), and  $\text{CD8}^+$  ( $476.88 \pm 51.38 \text{ cells}/\mu\text{l}$  vs  $396.57 \pm 35.42 \text{ cells}/\mu\text{l}$ ) were significantly increased, while the levels of CGRP ( $42.38 \pm 14.69 \text{ pg/ml}$  vs  $76.53 \pm 18.54 \text{ pg/ml}$ ), FOXO3 ( $5.81 \pm 1.34 \text{ ng/ml}$  vs  $8.02 \pm 1.07 \text{ ng/ml}$ ),  $\text{CD4}^+$  ( $271.18 \pm 68.54 \text{ cells}/\mu\text{l}$  vs  $728.69 \pm 88.49 \text{ cells}/\mu\text{l}$ ) and the ratio of  $\text{CD4}^+/\text{CD8}^+$  ( $0.57 \pm 0.12$  vs  $1.20 \pm 0.15$ ) were significantly decreased ( $t=17.049\sim 54.072$ , all  $P<0.05$ ) in the AIDS group. The serum levels of sCD14 and  $\text{CD8}^+$  in AIDS group progressively increased across the acute phase, asymptomatic phase and AIDS phase, while the levels of CGRP, FOXO3,  $\text{CD4}^+$  and the ratio of  $\text{CD4}^+/\text{CD8}^+$  progressively decreased, with statistically significant differences ( $F=25.322\sim 125.502$ , all  $P<0.05$ ). The sCD14 was negatively correlated with  $\text{CD4}^+$  and  $\text{CD4}^+/\text{CD8}^+$ , and positively correlated with  $\text{CD8}^+$  and disease stage. CGRP and FOXO3 were positively correlated with  $\text{CD4}^+$  and  $\text{CD4}^+/\text{CD8}^+$ , and negatively correlated with  $\text{CD8}^+$  and disease stage, with statistically significant differences ( $r=-0.746\sim 0.759$ , all  $P<0.05$ ). The levels of sCD14, CGRP, and FOXO3 were significantly associated with genital herpes, lymphoma, and HIV viral load ( $t/F = 2.381\sim 39.190$ , all  $P<0.05$ ). The levels of serum sCD14,  $\text{CD8}^+$  and HIV viral load in the poor prognosis group were significantly higher than those in the favorable prognosis group. Conversely, the levels of CGRP, FOXO3,  $\text{CD4}^+$  and the  $\text{CD4}^+/\text{CD8}^+$  ratio were significantly lower in the poor prognosis group than those in the favorable prognosis group, with statistically ( $t=5.071\sim 10.577$ , all  $P<0.05$ ). Elevated sCD14,  $\text{CD8}^+$  and HIV viral load were risk factors, while CGRP, FOXO3,  $\text{CD4}^+$  and  $\text{CD4}^+/\text{CD8}^+$  ratio were protective factors for poor prognosis in AIDS patients, with statistical significances (Wald  $\chi^2 = 6.349\sim 18.825$ , all  $P<0.05$ ). The combined AUC for predicting poor prognosis in AIDS patients using sCD14, CGRP, and FOXO3 levels was higher than the AUC for predicting poor prognosis using sCD14, CGRP, or FOXO3 alone significant differences ( $Z=3.757, 3.836, 3.353$ , all  $P<0.05$ ). **Conclusions** sCD14 is upregulated in the serum of AIDS patients, while CGRP and FOXO3 are downregulated, these markers are closely related to disease stage and immune function, and their combined use demonstrates high predictive value for poor prognosis in AIDS patients.

**Keywords:** acquired immune deficiency syndrome; soluble cluster of differentiation antigen 14; calcitonin gene related peptide; forkhead box transcription factor O3; disease staging; immune function

艾滋病全称为获得性免疫缺陷综合征(acquired immune deficiency syndrome, AIDS),是由人类免疫缺陷病毒(human immunodeficiency virus, HIV)引起的严重的传染性疾病,其主要特征是白细胞分化抗原 $4^+$ (cluster differentiation,  $\text{CD4}^+$ ) T淋巴细胞数量显著减少和免疫功能严重受损<sup>[1-2]</sup>。尽管高效抗逆转录病毒疗法(HAART)已取得较高的临床应用价值,但HIV死亡等不良临床结局仍与疾病分期、免疫失调和炎症加剧密切相关<sup>[3-4]</sup>。因此,寻找与AIDS患者疾病分期和免疫功能关系密切的血清标志物,对于评估AIDS患者的疾病进展及改善预后具有重要意义。近年来,免疫调节在HIV感染中的作用备受关注。可溶性白细胞分化抗原14(soluble cluster of differentiation antigen 14, sCD14)作为单核细胞和巨噬细胞激活的标志物,在HIV感染中显著升高,并与免疫激活和炎症反应密切相关<sup>[5]</sup>。神经元降钙素基因相关肽(calcitonin gene related peptide, CGRP)是一种重要的神经肽,能够调节免疫细胞活性,已有研究表明CGRP不仅通过环磷酸腺苷(cAMP)-蛋白激酶(PKA)途径抑制T细胞中的HIV-1传播,还可通过调节抗原呈递进一步降低HIV-1感染风险<sup>[6]</sup>。叉头转录因子O亚型3(forkhead box transcription factor O3, FOXO3)

属于叉头蛋白家族的关键转录因子,能够通过影响T细胞的分化和活化调节免疫细胞功能,FOXO3缺失可能导致免疫功能减弱,从而增加感染和自身免疫疾病风险<sup>[7]</sup>。基于sCD14、CGRP、FOXO3在HIV中的关键作用,本研究对艾滋病患者血清sCD14、CGRP、FOXO3水平表达与疾病分期和免疫功能的相关性进行探讨分析,现报道如下。

## 1 材料与方法

1.1 研究对象 选取2021年1月~2024年1月石家庄市第五医院和石家庄市妇幼保健院收治的175例AIDS患者及175例体检健康者为研究对象,分别纳入AIDS组和对照组。纳入标准:①符合AIDS的诊断标准<sup>[8]</sup>;②HIV抗体确认试验阳性;③年龄 $\geq 18$ 岁;④配合预后随访者。排除标准:①妊娠期和哺乳期;②凝血功能障碍者;③合并其它脏器病变、感染、心脑血管、自身免疫病等疾病史;④近期接受影响免疫功能的药物治疗者。AIDS组男性89例,女性86例,年龄 $18\sim 52(35.73 \pm 10.36)$ 岁;对照组男性87例,女性88例,年龄 $18\sim 55(36.11 \pm 10.58)$ 岁。AIDS组和对照组性别、年龄比较,差异无统计学意义( $\chi^2/t=0.046, 0.339$ ,均 $P>0.05$ )。受试者均签署知情同意书,本研究通过石家庄市第五医院医学伦理委员会批准(NO. 202304-2)。

1.2 仪器与试剂 Sorvall Legend X1/X1R型离心机[赛默飞世尔科技(中国)有限公司]; BioTek ELx800型多功能酶标仪(美国BioTek公司); FACSCalibur流式细胞仪(美国BD公司); sCD14(货号: CB10933-Hu)、CGRP(货号: CB10796-Hu)、FOXO3(货号: CB17199-Hu)酶联免疫吸附法(ELISA)检测试剂盒(上海科艾博生物技术有限公司); HIV病毒载量试剂盒(批号: 488964, 美国Abbott公司)。

### 1.3 方法

1.3.1 血液样本采集及sCD14、CGRP、FOXO3指标检测: 采集AIDS组(入组当日)和对照组(体检当日)外周静脉血5ml, 室温静置30min, 4 000r/min离心15min, 分装上层血清, 储存于-80℃冰箱备用。采用ELISA法检测sCD14、CGRP、FOXO3水平, 具体操作严格按照试剂说明书进行。

1.3.2 T淋巴细胞群的检测: FACSCalibur流式细胞仪检测AIDS组和对照组外周血T细胞亚群CD4<sup>+</sup>、CD8<sup>+</sup>T淋巴细胞计数, 计算CD4<sup>+</sup>/CD8<sup>+</sup>比值。

1.3.3 AIDS分期标准: 根据《中国艾滋病诊疗指南(2018版)》<sup>[8]</sup>中的分期标准, 将175例AIDS患者分为急性期组( $n=35$ )、无症状期组( $n=58$ )和艾滋病期组

( $n=82$ )。

1.3.4 预后分组: 对AIDS患者自出院第一日起进行预后6个月的随访, 根据随访结果, 临床症状较入组前有所好转的纳入预后良好组( $n=104$ ), 临床症状较入组前有所加重或死亡者纳入预后不良组( $n=71$ )。

1.4 统计学分析 数据处理采用SPSS27.0软件, 计量资料均符合正态分布, 以均数±标准差( $\bar{x} \pm s$ )表示, 采用独立样本 $t$ 检验, 多组间比较采用单因素方差分析及SNK- $q$ 检验。计数资料以 $n(\%)$ 表示, 两组间比较采用 $\chi^2$ 检验。采用Spearman法和Pearson法分析sCD14、CGRP、FOXO3水平与疾病分期和免疫功能的相关性, 采用多因素Logistic分析AIDS患者预后不良的影响因素, 采用ROC曲线分析sCD14、CGRP、FOXO3水平对AIDS患者预后不良的预测价值。 $P < 0.05$ 为差异具有统计学意义。

## 2 结果

2.1 AIDS组和对照组血清sCD14、CGRP、FOXO3水平及T淋巴细胞群的比较 见表1。AIDS组患者血清sCD14、CD8<sup>+</sup>水平显著高于对照组, CGRP、FOXO3、CD4<sup>+</sup>水平及CD4<sup>+</sup>/CD8<sup>+</sup>比值显著低于对照组, 差异具有统计学意义(均 $P < 0.05$ )。

表1 AIDS组和对照组血清sCD14、CGRP、FOXO3水平及T淋巴细胞群的比较( $\bar{x} \pm s$ )

项目	AIDS组 ( $n=175$ )	对照组 ( $n=175$ )	$t$ 值	$P$ 值
sCD14 ( $\mu\text{g/ml}$ )	5.12±1.25	2.83±0.46	22.744	< 0.001
CGRP ( $\text{pg/ml}$ )	42.38±14.69	76.53±18.54	19.098	< 0.001
FOXO3 ( $\text{ng/ml}$ )	5.81±1.34	8.02±1.07	17.049	< 0.001
CD4 <sup>+</sup> (个/ $\mu\text{l}$ )	271.18±68.54	728.69±88.49	54.072	< 0.001
CD8 <sup>+</sup> (个/ $\mu\text{l}$ )	476.88±51.38	396.57±35.42	17.024	< 0.001
CD4 <sup>+</sup> /CD8 <sup>+</sup>	0.57±0.12	1.20±0.15	43.386	< 0.001

2.2 不同疾病分期血清sCD14、CGRP、FOXO3水平及T淋巴细胞群的比较 见表2。AIDS组患者血清sCD14、CD8<sup>+</sup>水平在急性期组、无症状期组、

艾滋病期依次升高, CGRP、FOXO3、CD4<sup>+</sup>水平及CD4<sup>+</sup>/CD8<sup>+</sup>比值依次下降, 差异具有统计学意义(均 $P < 0.05$ )。

表2 不同疾病分期血清sCD14、CGRP、FOXO3水平及T淋巴细胞群的比较( $\bar{x} \pm s$ )

项目	急性期组 ( $n=35$ )	无症状期组 ( $n=58$ )	艾滋病期组 ( $n=82$ )	$F$ 值	$P$ 值
sCD14 ( $\mu\text{g/ml}$ )	3.24±0.85	4.85±1.23 <sup>a</sup>	6.12±1.33 <sup>ab</sup>	71.056	< 0.001
CGRP ( $\text{pg/ml}$ )	64.38±15.64	44.59±14.27 <sup>a</sup>	31.43±8.72 <sup>ab</sup>	89.206	< 0.001
FOXO3 ( $\text{ng/ml}$ )	7.72±1.36	6.18±1.25 <sup>a</sup>	4.74±1.11 <sup>ab</sup>	78.401	< 0.001
CD4 <sup>+</sup> (个/ $\mu\text{l}$ )	354.59±51.64	295.31±46.53 <sup>a</sup>	218.52±40.33 <sup>ab</sup>	125.502	< 0.001
CD8 <sup>+</sup> (个/ $\mu\text{l}$ )	435.12±41.61	471.83±44.72 <sup>a</sup>	498.27±45.39 <sup>ab</sup>	25.322	< 0.001
CD4 <sup>+</sup> /CD8 <sup>+</sup>	0.81±0.15	0.63±0.13 <sup>a</sup>	0.44±0.10 <sup>ab</sup>	122.042	< 0.001

注:<sup>a</sup>与急性期组比较,  $t_{\text{无症状期组}}=8.752, 10.618, 8.411, 8.735, 5.458, 9.790$ ;  $t_{\text{艾滋病期组}}=16.597, 18.742, 17.253, 21.255, 9.952, 21.333$ , 均 $P < 0.05$ ;  
<sup>b</sup>与无症状期组比较,  $t=8.613, 8.809, 9.811, 14.116, 4.904, 12.892$ , 均 $P < 0.05$ 。

2.3 AIDS组sCD14、CGRP、FOXO3水平与疾病分期及T淋巴细胞群的相关性 见表3。相关性分析

结果显示, sCD14与CD4<sup>+</sup>、CD4<sup>+</sup>/CD8<sup>+</sup>呈负相关, 与CD8<sup>+</sup>、疾病分期呈正相关, CGRP、FOXO3与CD4<sup>+</sup>、

CD4<sup>+</sup>/CD8<sup>+</sup>呈正相关,与CD8<sup>+</sup>、疾病分期呈负相关, 差异具有统计学意义(均P<0.05)。

表3 AIDS组sCD14、CGRP、FOXO3水平与疾病分期及T淋巴细胞群的相关性

项目	sCD14		CGRP		FOXO3	
	r	P	r	P	r	P
CD4 <sup>+</sup>	-0.675	< 0.001	0.724	< 0.001	0.669	< 0.001
CD8 <sup>+</sup>	0.716	< 0.001	-0.657	< 0.001	-0.733	< 0.001
CD4 <sup>+</sup> /CD8 <sup>+</sup>	-0.746	< 0.001	0.759	< 0.001	0.648	< 0.001
疾病分期	0.752	< 0.001	-0.728	< 0.001	-0.694	< 0.001

2.4 AIDS患者sCD14、CGRP、FOXO3水平与病理特征的关系 见表4。病理特征分析结果显示, sCD14、CGRP、FOXO3水平与AIDS患者年龄、性别、传播途径等无关,差异无统计学意义(均P>0.05),与生殖器疱疹、淋巴瘤及HIV载量有关,差异具有统计学意义(均P<0.05)。

表4 AIDS患者sCD14、CGRP、FOXO3水平与病理特征的关系(̄x±s)

类别	n	sCD14 (μg/ml)	t/F	P	CGRP (pg/ml)	t/F	P	FOXO3 (ng/ml)	t/F	P	
年龄(岁)	≥ 30	93	5.14 ± 1.12	0.241	0.810	41.35 ± 12.42	1.226	0.222	5.77 ± 1.32	0.396	0.693
	< 30	82	5.10 ± 1.07			43.68 ± 12.69			5.85 ± 1.35		
性别	男	89	5.15 ± 1.20	0.404	0.687	43.66 ± 12.53	1.392	0.166	5.69 ± 1.28	1.231	0.220
	女	86	5.08 ± 1.09			41.06 ± 12.17			5.93 ± 1.30		
生殖器疱疹	有	51	5.56 ± 1.18	3.296	< 0.001	38.38 ± 11.45	2.658	0.009	5.43 ± 1.19	2.554	0.012
	无	124	4.94 ± 1.11			44.03 ± 13.28			5.96 ± 1.27		
传播途径	血液传播	46	5.16 ± 1.31	0.281	0.779	40.45 ± 11.52	1.276	0.204	5.85 ± 1.23	0.288	0.774
	性传播	129	5.10 ± 1.22			43.07 ± 12.11			5.79 ± 1.21		
淋巴瘤	有	33	5.57 ± 1.26	2.381	0.018	37.63 ± 10.62	2.525	0.012	5.17 ± 1.18	3.077	0.002
	无	142	5.02 ± 1.18			43.49 ± 12.30			5.96 ± 1.36		
HIV载量	低 (< 10 <sup>3</sup> copies/ml)	44	4.29 ± 1.20	12.876	< 0.001	52.18 ± 14.46	23.022	< 0.001	7.11 ± 1.43	39.190	< 0.001
	中 (10 <sup>3</sup> ~ 10 <sup>5</sup> copies/ml)	51	5.06 ± 1.37			43.32 ± 13.25			5.96 ± 1.31		
	高 (> 10 <sup>5</sup> copies/ml)	80	5.64 ± 1.56			36.38 ± 10.64			4.99 ± 1.18		

2.5 不同预后分组sCD14、CGRP、FOXO3水平及T淋巴细胞群的比较 见表5。预后不良组生殖器疱疹及淋巴瘤的人数占比与预后良好组比较差异无统计学意义(均P>0.05),预后不良组患者血清sCD14、CD8<sup>+</sup>水平及HIV载量高人数占比显著高于预后良好组,CGRP、FOXO3、CD4<sup>+</sup>水平及CD4<sup>+</sup>/CD8<sup>+</sup>比值显著低于预后良好组,差异具有统计学意义(均P<0.05)。

表5 不同预后分组sCD14、CGRP、FOXO3水平及T淋巴细胞群的比较 [n(%), ̄x±s]

类别	预后良好组 (n=104)	预后不良组 (n=71)	t/χ <sup>2</sup>	P	
sCD14 (μg/ml)	4.35 ± 1.14	6.26 ± 1.22	10.577	< 0.001	
CGRP (pg/ml)	47.96 ± 12.67	34.21 ± 8.52	7.990	< 0.001	
FOXO3 (ng/ml)	6.52 ± 1.12	4.77 ± 1.03	10.482	< 0.001	
CD4 <sup>+</sup> (个/μl)	294.25 ± 43.55	237.38 ± 40.36	8.736	< 0.001	
CD8 <sup>+</sup> (个/μl)	460.39 ± 45.38	496.10 ± 46.27	5.071	< 0.001	
CD4 <sup>+</sup> /CD8 <sup>+</sup>	0.64 ± 0.13	0.48 ± 0.11	8.498	< 0.001	
生殖器疱疹	有	25 (49.02)	26 (50.98)	3.234	0.072
	无	79 (63.71)	45 (36.29)		
淋巴瘤	有	15 (45.45)	18 (54.55)	3.294	0.070
	无	89 (62.68)	53 (37.32)		
HIV载量	低	32 (72.73)	12 (27.27)	10.780	0.005
	中	35 (68.63)	16 (31.37)		
	高	37 (46.25)	43 (53.75)		

2.6 AIDS患者预后不良的影响因素分析 见表6。以AIDS患者预后状况为因变量, sCD14、CGRP、FOXO3、CD4<sup>+</sup>、CD8<sup>+</sup>、CD4<sup>+</sup>/CD8<sup>+</sup>比值及HIV载量为自变量进行多因素Logistic分析, 结果显示

sCD14、CD8<sup>+</sup>及HIV载量为AIDS患者预后不良的危险因素, CGRP、FOXO3、CD4<sup>+</sup>及CD4<sup>+</sup>/CD8<sup>+</sup>为AIDS患者预后不良的保护因素, 差异具有统计学意义(均 $P<0.05$ )。

表6 AIDS患者预后不良的影响因素分析

因素	自变量赋值	$\beta$	SE	Wald $\chi^2$	OR	95%CI	P值
sCD14	连续变量	1.210	0.296	16.698	3.352	1.876 ~ 5.988	< 0.001
CGRP	连续变量	-0.837	0.246	11.577	0.433	0.267 ~ 0.701	0.001
FOXO3	连续变量	-0.846	0.273	9.610	0.429	0.251 ~ 0.733	0.002
CD4 <sup>+</sup>	连续变量	-0.675	0.268	6.349	0.509	0.301 ~ 0.861	0.011
CD8 <sup>+</sup>	连续变量	0.931	0.274	11.545	2.537	1.483 ~ 4.341	0.001
CD4 <sup>+</sup> /CD8 <sup>+</sup>	连续变量	-0.658	0.260	6.401	0.518	0.311 ~ 0.862	0.011
HIV载量	低=0, 中、高=1	1.158	0.267	18.825	3.185	1.887 ~ 5.375	< 0.001

2.7 sCD14、CGRP、FOXO3水平预测AIDS患者预后不良的价值 见表7, 图1。ROC曲线分析显示, sCD14、CGRP、FOXO3水平联合预测AIDS患

者预后不良的AUC为0.959, 高于各项单独预测的AUC, 差异具有统计学意义( $Z=3.757, 3.836, 3.353$ , 均 $P<0.05$ )。

表7 sCD14、CGRP、FOXO3水平预测AIDS患者预后不良的价值分析

项目	AUC	95%CI	敏感度(%)	特异度(%)	截断值	约登指数
sCD14	0.838	0.781 ~ 0.896	81.70	70.20	4.92 $\mu$ g/ml	0.519
CGRP	0.832	0.779 ~ 0.897	83.10	60.60	37.07pg/ml	0.437
FOXO3	0.848	0.790 ~ 0.906	84.50	67.30	5.24ng/ml	0.518
联合预测	0.959	0.933 ~ 0.986	93.00	88.50		0.815

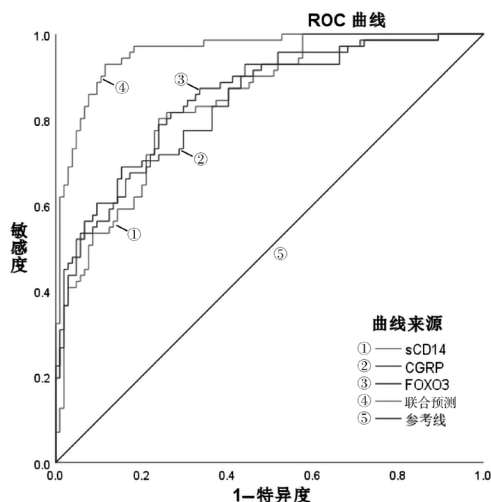


图1 sCD14、CGRP、FOXO3水平预测AIDS患者预后不良的ROC曲线

### 3 讨论

AIDS是一种对人体免疫系统极具攻击性的传染性疾病, 早期可能会出现类似流感的症状, 潜伏期结束后, HIV大量破坏CD4<sup>+</sup>T淋巴细胞等免疫系统, 导致免疫系统被严重破坏, 丧失免疫功能<sup>[9]</sup>。有研究统计截至2020年, 有68万与AIDS相关的死亡, 截至2022年, 全球约有3 900万人感染HIV<sup>[10]</sup>。因此, 寻找与AIDS患者疾病分期及免疫细胞群相关的血清标志

物对于降低治疗难度, 延缓病情发展至关重要。

sCD14是革兰氏阴性菌外膜的主要组分脂多糖的细胞受体, 其水平与IL-1、IL-6、IL-8和TNF- $\alpha$ 的释放及免疫功能有关<sup>[11]</sup>。研究发现与HIV阴性组相比, HIV阳性组患者血清sCD14水平显著升高, 与老年患者的生命年限密切相关<sup>[12]</sup>。本研究结果显示, AIDS组患者血清sCD14水平显著高于健康组, 提示sCD14与HIV感染有关, 推测sCD14表达水平升高与HIV感染后病毒通过与宿主细胞相互作用, 导致免疫系统激活和炎症反应加剧有关<sup>[12]</sup>。猪尾猕猴感染猴免疫缺陷病毒(simian immunodeficiency virus, SIV)后血浆sCD14水平从SIV感染前期至急性SIV感染期显著增加, 经抗逆转录病毒治疗后血浆中sCD14水平显著降低<sup>[13]</sup>。本研究中, AIDS患者在急性期组、无症状期组、艾滋病期组依次升高, 且与CD4<sup>+</sup>、CD4<sup>+</sup>/CD8<sup>+</sup>呈负相关, 与CD8<sup>+</sup>、疾病分期呈正相关, 提示sCD14水平与AIDS患者的免疫功能及疾病分期有关, 与上述前人研究结果一致。

CGRP参与免疫调节, CGRP缺失会导致机体炎症反应<sup>[14-15]</sup>。原发性HIV感染患者血清CGRP水平显著降低, CGRP水平与CD4<sup>+</sup>细胞计数呈正相关, 与病毒载量呈负相关, 可作为评估HIV患者疾病活动的指标<sup>[16]</sup>。本研究结果显示, AIDS组患者血

清CGRP水平显著低于对照组,在急性期组、无症状期组、艾滋病期组依次下降,并与CD4<sup>+</sup>、CD4<sup>+</sup>/CD8<sup>+</sup>呈正相关,与CD8<sup>+</sup>、疾病分期呈负相关,提示CGRP低表达可能与AIDS患者病情加剧恶化有关,且在一定程度上反映了AIDS患者免疫能力的高低,推测在HIV早期,CGRP能够抑制过度的炎症反应,减少免疫系统的过度激活,从而延缓CD4<sup>+</sup>T细胞的耗竭,随着疾病的进展,HIV病毒持续复制,导致免疫系统逐渐衰竭,CGRP水平异常降低可能进一步加剧CD4<sup>+</sup>T细胞的减少,同时影响CD8<sup>+</sup>T细胞的功能<sup>[16]</sup>。

FOXO3具有抗应激、提高免疫系统对病原体的长期记忆等多种细胞功能<sup>[7,17]</sup>。FOXO3缺陷抑制滤泡辅助性T细胞(T<sub>fh</sub>s)分化,调节FOXO3活性有助于增强或预防抗体介导的免疫反应<sup>[18]</sup>。采用FOXO3激动剂治疗的小鼠,其肿瘤微环境中CD8<sup>+</sup>T细胞和NK细胞的浸润水平显著提高<sup>[19]</sup>。本研究结果显示,AIDS组患者血清FOXO3水平显著低于健康组,在急性期组、无症状期组、艾滋病期组依次下降,与CD4<sup>+</sup>、CD4<sup>+</sup>/CD8<sup>+</sup>呈正相关,与CD8<sup>+</sup>、疾病分期呈负相关,提示FOXO3低表达与AIDS患者病情恶化及免疫功能降低有关,推测FOXO3表达水平的降低与HIV感染导致免疫系统功能失调有关,HIV可以通过磷脂酰肌醇3-激酶/蛋白激酶B(PI3K/AKT)信号通路显著降低巨噬细胞中FOXO3的磷酸化水平,促进巨噬细胞凋亡相关基因的表达,从而抑制免疫细胞功能<sup>[20]</sup>。

此外,本研究在进一步分析AIDS患者sCD14、CGRP、FOXO3水平与病理特征的关系中发现,sCD14、CGRP、FOXO3水平与AIDS患者生殖器疱疹、淋巴瘤及HIV载量有关,且sCD14及HIV载量高为AIDS患者预后不良的危险因素,CGRP、FOXO3为AIDS患者预后不良的保护因素,提示监测这些标志物的变化有助于评估AIDS患者的病情及预后。sCD14、CGRP、FOXO3水平联合预测AIDS患者预后不良的AUC高于各项单独预测的AUC,提示三者联合预测AIDS患者预后不良的临床价值更高,结合临床实际,当sCD14 > 4.92 μg/ml、CGRP < 37.07 pg/ml、FOXO3 < 5.24 ng/ml时,应及时采取干预措施改善患者预后。

综上所述,sCD14在AIDS患者血清中上调表达,CGRP、FOXO3下调表达,sCD14、CGRP、FOXO3与疾病分期和免疫功能关系密切,三者联合预测AIDS患者预后不良价值较高。

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