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· 临床研究 ·

外周血炎症指标与口腔鳞状细胞癌患者术后复发转移相关性研究

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【摘要】 目的 探讨手术前后中性粒细胞-淋巴细胞比值(neutrophil-to-lymphocyte ratio, NLR)、血小板-淋巴细胞比值(platelet-to-lymphocyte ratio, PLR)、淋巴细胞-单核细胞比值(lymphocyte-to-monocyte ratio, LMR)、全身免疫炎症指数(systemic immune-inflammation index, SII)、系统性炎症反应指数(systemic inflammation response index, SIRI)等外周血炎症指标与口腔鳞状细胞癌(oral squamous cell carcinoma, OSCC)患者术后复发转移的相关性,为临床评估 OSCC 患者的预后提供参考。**方法** 本研究通过医院伦理委员会批准,并获得患者知情同意。对行 OSCC 根治术的 160 例原发性 OSCC 患者,收集其术前最后一次和术后 1 个月血常规,根据是否术前淋巴结转移、分化程度、临床 T 分期以及是否术后复发转移分组,分析 OSCC 患者 NLR、PLR、LMR、SII、SIRI 等外周血炎症指标与以上临床病理指标、术后复发转移的关系。**结果** 160 例 OSCC 患者,术前淋巴结转移和无转移组的术前 SII 差异有统计学意义($P < 0.05$);术前 NLR、SII、SIRI 在不同分化程度组间差异有统计学意义($P < 0.05$);不同临床 T 分期组的术前 SIRI 指标差异有统计学意义($P < 0.05$)。术前 NLR、PLR、SII、SIRI 在术后复发转移组和无复发转移组间的差异有统计学意义($P < 0.05$),术后外周血炎症指标与术后复发转移无关。单因素 Cox 分析显示:术前外周血炎症指标中,术前 NLR、PLR、SII、SIRI 是影响 OSCC 患者复发转移的影响因素;多因素 Cox 分析结果显示:术前外周血炎症指标中,只有术前 NLR 是影响患者复发转移的独立危险因素。**结论** 外周血炎症指标中,术前 NLR 是 OSCC 患者术后复发转移的独立危险因素,有一定的预测价值。

【关键词】 口腔鳞状细胞癌; 中性粒细胞-淋巴细胞比值; 血小板-淋巴细胞比值; 全身免疫炎症指数; 系统性炎症反应指数; 临床 T 分期; 术前淋巴结转移; 预后; 复发转移

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Correlation of multiple inflammatory indices in peripheral blood with postoperative recurrence and metastasis in oral squamous cell carcinoma patients GUHAIERNISHA · Kaihereman¹, WULAN · Jinensi¹, YAO Zhitao^{1,2}.

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【Abstract】 Objective To investigate the associations of multiple immunoinflammatory markers in peripheral blood before and after operation, such as the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), lymphocyte-to-monocyte ratio (LMR), systemic immune-inflammation index (SII) and systemic inflammatory response index (SIRI), with postoperative recurrence and metastasis in oral squamous cell carcinoma (OSCC) patients, to provide a reference for predicting the prognosis of OSCC patients. **Methods** This study was approved by the hospital ethics commit-

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tee, and informed consent was obtained from the patients. A total of 160 patients with primary OSCC who underwent radical surgery were grouped according to preoperative lymph node metastasis, degree of differentiation, clinical T stage, and postoperative recurrence and metastasis. The last preoperative and 1-month postoperative routine blood test results of all the patients were collected to analyze the relationship between peripheral blood inflammatory indicators, including the NLR, PLR, LMR, SII, and SIRI, before and after surgery. The above clinicopathological indicators and postoperative recurrence and metastasis were evaluated in OSCC patients. **Results** Among the 160 patients, there was a significant difference in the preoperative SII between the preoperative lymph node metastasis group and the no metastasis group ($P < 0.05$); the preoperative NLR, LMR, SII and SIRI were significantly different among the different differentiation degree groups ($P < 0.05$); and the preoperative SIRI in the different clinical T stage groups were significantly different ($P < 0.05$). The preoperative NLR, SII and SIRI were significantly different between the postoperative recurrence and metastasis group and the no recurrence and metastasis group ($P < 0.05$). Postoperative peripheral blood inflammatory markers were not associated with postoperative metastasis and recurrence. Univariate Cox analysis revealed that among the preoperative peripheral blood inflammatory indicators, the preoperative NLR, PLR, SII and SIRI were the factors influencing recurrence and metastasis in OSCC patients. Multivariate Cox analysis revealed that the preoperative NLR was the only independent risk factor for recurrence and metastasis in OSCC patients among the preoperative peripheral blood inflammatory indicators. **Conclusion** Among the peripheral blood inflammatory indicators, the preoperative NLR is an independent risk factor for postoperative recurrence and metastasis in OSCC patients and has certain predictive value.

【Key words】 oral squamous cell carcinoma; neutrophil-to-lymphocyte ratio; platelet-to-lymphocyte ratio; systemic immune-inflammation index; systemic inflammation response index; clinical T stage; preoperative lymph node metastasis; prognosis; recurrence and metastasis

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口腔鳞状细胞癌(oral squamous cell carcinoma, OSCC)是头颈部常见的恶性肿瘤亚型,尽管进行了根治性手术治疗和放化疗,OSCC患者的复发和转移率仍然较高^[1-2]。OSCC每年新发病例超过50万例,约2/3伴有肿瘤的局部浸润和区域淋巴结转移^[3]。OSCC患者的5年总生存期近几十年来没有明显改善,仍然相对较低^[4]。尽管影像学技术已经发展了几十年,但仍不能准确检测出OSCC转移及复发^[5]。目前,肿瘤进展或复发的预测主要依赖于经典的病理学参数,如肿瘤大小、浸润深度、浸润范围和淋巴结状态等^[6]。免疫系统对肿瘤的侵袭和转移至关重要,位于肿瘤微环境(tumor microenvironment, TME)的炎症因子是可以影响肿瘤形成、发展和转移过程的关键因素之一,肿瘤相关中性粒细胞(numor-associated neutrophils, TANs)被视为癌症进展过程中的关键生物标志物之一^[7]。大量研究提示局部免疫反应和全身炎症反应与各种类型肿瘤的进展和预后之间存在一定的联系,如:中性粒细胞-淋巴细胞比值(neutrophil-to-lymphocyte ratio, NLR)、淋巴细胞-单核细胞比值(lymphocyte-to-

monocyte ratio, LMR)和血小板-淋巴细胞比值(platelet-to-lymphocyte ratio, PLR),较高的NLR和PLR与肿瘤复发和预后较差相关^[8-9]。近年研究证实,血液检测中的炎症指标与OSCC的复发、远处转移及预后有明显的相关性^[10-11],表明血液检测中的免疫炎症指标在OSCC的诊断、治疗和预后中具有重要的临床意义。然而,免疫炎症指标与OSCC治疗和预后的相关研究在国内外报道较少。为了明确外周血NLR、PLR、LMR、全身免疫炎症指数(systemic immune-inflammation index, SII)、全身炎症反应指数(systemic inflammation response index, SIRI)等相关参数与OSCC患者复发转移的关系,为临床预测OSCC的复发转移提供参考,本研究对160例经手术治疗的OSCC患者的NLR、MLR、PLR、SII和SIRI的表达进行分析,报告如下。

1 资料和方法

本研究已通过新疆医科大学第一附属医院伦理委员会批准(批号:K202311-02),并获得患者知情同意。

1.1 临床资料

本研究选取2018年1月1日至2023年1月1日于新疆医科大学第一附属医院口腔颌面外科首次接受根治性手术、随访且资料完整的160例OSCC患者作为研究对象。

患者临床病理资料包括:性别、年龄、组织学分化程度、术前是否淋巴结转移、临床T分期;术前(术前最后一次)及术后(术后1个月)NLR、PLR、LMR、SII、SIRI。

纳入标准:①现病史、既往病史、个人及家族史等临床资料齐全;②相关治疗及检查均在本院进行;③肿瘤的病变源于口腔,其病理学上的诊断结果是鳞状细胞癌;④在首次被诊断和接受根治性手术之前,患者并没有进行肿瘤的治疗;⑤无合并对炎症指标的精确度产生影响的血液系统疾病和自身免疫性疾病;⑥身体其他部位无肿瘤合并。

排除标准:①入院前接受过手术、化疗或放疗等治疗的患者;②合并血液病、风湿等自身免疫性疾病或其他影响炎症指标准确性的相关疾病;③患者的临床数据和血细胞计数结果不完整;④患有OSCC以外的肿瘤或存在继发性口腔恶性肿瘤的患者;⑤围手术期死亡的患者。

1.2 随访

手术治疗结束后,研究对象定期接受门诊和电话随访。随访内容包括患者的生存状况、术后相关治疗情况、有无复发、复发部位以及后续治疗情况等。随访的起点为手术日期,终点为复发日期。前两年每3个月随访1次,第3年至第5年每6个月随访1次,5年后每年随访1次。最后一次随访时间为2023年6月9日,预后指标采用无病生存期(disease-free survival, DFS):是指从行根治手术日期开始,至第一次肿瘤复发或转移,研究结束时依然未出现复发转移的患者为随访结束日期。

1.3 分组

160例OSCC患者按照不同性别、有无术前淋巴结转移、分化程度和临床T分期进行分组,并且对不同组间术前外周血炎症指标进行分析;160例OSCC患者按照随访终点有无出现复发转移分为2组,对不同组间外周血炎症指标进行分析。

1.4 统计学分析

将收集的临床资料信息及检查结果录入Excel表格中,采用SPSS25.0软件进行数据统计分析,以 $\alpha=0.05$ 作为组间比较的检验水准。计量资料用

Shapiro-Wilk行正态性检验,符合正态分布计量资料用均数 $\pm$ 标准差描述,不符合正态分布计量资料用中位数(25分位、75分位描述),分类资料用例数和百分数(%)表示。符合正态分布计量资料2组间比较,采用两独立样本 t 检验分析。不符合正态分布计量资料2组间比较,采用Mann-Whitney U 检验分析。计数资料组间比较,采用卡方检验。

采用Cox回归模型单因素、多因素分析影响患者生存率的危险因素,自变量为已用单因素分析评估过的有统计学意义的因素,结果用校正后的优势比(Hazard ratio, HR)和与之相应的95%可信区间(confidence interval, CI)表示。采用Kaplan-Meier法进行单因素生存分析,计算出中位生存时间及生存率。生存曲线用Graphpad Prism7.0软件绘制。

2 结果

160例OSCC患者中,男性90例,女性70例,男女比例1.3:1;年龄35~86岁,平均年龄(59.88 ± 11.40)岁;舌78例、口底15例、牙龈38例、硬腭1例、磨牙后区6例、颊黏膜22例;其中术前淋巴结转移为53例,无淋巴结转移107例;临床T1~T2为110例、T3~T4 50例;高分化72例、中分化为68例、低分化20例。160例患者至随访终点出现术后复发转移的患者51例,其中男性29例、女性22例,原位复发27例,颈部淋巴结转移18例,远处转移6例;高分化12例、中分化为24例、低分化15例。

160例患者不同性别组的LMR和SIRI差异有统计学意义($P < 0.05$),具体体现为男性的LMR指标显著低于女性,男性的SIRI指标显著高于女性;术前淋巴结转移和无转移组的SII差异有统计学意义($P < 0.05$),为伴淋巴结转移的患者SII指标更高;不同分化程度组NLR、SII、SIRI指标差异有统计学意义($P < 0.05$),具体表现为分化程度高的患者术前NLR、SII、SIRI指标均显著低于分化程度低的患者;不同临床T分期组的SIRI指标差异有统计学意义($P < 0.05$),临床T分期高SIRI指标值更高(表1)。

160例观察对象有无复发转移2组间术前的NLR、PLR、SII、SIRI差异均有统计学意义($P < 0.05$),复发转移组显著高于未复发转移组(表2)。

经单因素Cox分析,术前NLR、术前PLR、术前SII、术前SIRI、术前淋巴结转移、分化程度和临床T分期均为影响患者复发转移的影响因素($P <$

表1 OSCC患者术前外周血炎症指标与临床病理指标的相关性分析

Table 1 Correlation analysis between preoperative peripheral blood inflammatory indices and clinicopathological indices in OSCC patients

Indicator	Preoperative NLR	Preoperative PLR	Preoperative LMR	Preoperative SII	Preoperative SIRI
Sex					
Male (<i>n</i> = 90)	2.54 ± 0.28	141.79 ± 10.63	3.66 ± 0.30	603.88 ± 74.59	1.35 ± 0.18
Female (<i>n</i> = 70)	2.52 ± 0.49	138.46 ± 13.64	4.49 ± 0.45	581.15 ± 93.69	1.05 ± 0.15
<i>Z</i>	2.057	0.229	9.168	0.025	9.168
<i>P</i>	0.151	0.633	0.002	0.873	0.002
Preoperative lymph node metastasis					
N0 (<i>n</i> = 107)	2.39 ± 0.32	138.04 ± 10.93	4.13 ± 0.34	555.49 ± 65.27	1.12 ± 0.13
N1+ (<i>n</i> = 53)	2.83 ± 0.46	144.97 ± 12.71	3.79 ± 0.41	671.53 ± 115.62	1.40 ± 0.26
<i>Z</i>	0.451	0.113	1.806	4.063	2.821
<i>P</i>	0.502	0.737	0.179	0.044	0.093
Degree of differentiation					
High (<i>n</i> = 72)	2.08 ± 0.24	131.81 ± 11.01	4.17 ± 0.46	484.63 ± 57.61	1.08 ± 0.17
Medium (<i>n</i> = 68)	2.51 ± 0.45	140.91 ± 12.69	4.01 ± 0.36	597.43 ± 92.36	1.19 ± 0.18
Low (<i>n</i> = 20)	4.21 ± 0.83	169.08 ± 30.97	3.52 ± 0.44	975.50 ± 206.06	1.76 ± 0.33
<i>Z</i>	11.424	2.300	1.022	12.229	11.859
<i>P</i>	0.003	0.317	0.600	0.002	0.003
Clinical T stage					
T1 (<i>n</i> = 37)	2.58 ± 0.78	138.48 ± 17.72	4.02 ± 0.45	571.06 ± 135.61	1.12 ± 0.23
T2 (<i>n</i> = 73)	2.31 ± 0.31	134.68 ± 11.19	4.11 ± 0.36	539.48 ± 70.41	1.13 ± 0.15
T3 (<i>n</i> = 25)	2.87 ± 0.68	147.36 ± 27.21	3.98 ± 0.96	674.43 ± 164.38	1.38 ± 0.29
T4 (<i>n</i> = 25)	2.78 ± 0.55	152.55 ± 20.57	3.80 ± 0.69	706.27 ± 170.51	1.48 ± 0.42
<i>Z</i>	2.698	1.314	2.073	3.338	8.813
<i>P</i>	0.441	0.726	0.557	0.342	0.032

OSCC: oral squamous cell carcinoma. NLR: neutrophil-to-lymphocyte ratio. LMR: lymphocyte-to-monocyte ratio. PLR: platelet-to-lymphocyte ratio. SII: systemic immune-inflammation index. SIRI: systemic inflammation response index. N0: No lymph node metastasis. N1+: with lymph node metastasis

表2 OSCC患者术前术后外周血炎症指标与术后复发转移的相关性分析

Table 2 Correlation analysis between preoperative and postoperative peripheral blood inflammatory indices and postoperative recurrence and metastasis in OSCC patients

Indicator	Norecurrence and no metastasis group	Recurrence and metastasis group	<i>t/χ²/Z</i>	<i>P</i>
<i>n</i>	109	51		
Sex			0.011*	0.915
Male	61 (56.0)	29 (56.9)		
Female	48 (44.0)	22 (43.1)		
Age/years	59.642 ± 11.775	60.373 ± 10.656	-0.377#	0.707
Preoperative NLR	1.695 (1.352, 2.232)	3.527 (2.333, 4.987)	-7.157 [△]	< 0.001
Preoperative PLR	124.896 (95.014, 156.911)	156.034 (122.414, 189.266)	-3.620 [△]	< 0.001
Preoperative LMR	3.865 (2.871, 4.822)	3.511 (2.949, 4.676)	-1.033	0.302
Preoperative SII	386.814 (294.531, 541.393)	775.491 (569.806, 1129.286)	-6.659 [△]	< 0.001
Preoperative SIRI	0.822 (0.622, 1.273)	1.529 (1.015, 2.201)	-5.062 [△]	< 0.001
Postoperative NLR	1.601 (1.139, 2.487)	1.939 (1.139, 2.712)	-0.879 [△]	0.380
Postoperative PLR	143.511 (109.667, 190.675)	154.144 (121.019, 201.031)	-1.038 [△]	0.299
Postoperative LMR	3.573 (2.787, 4.820)	3.290 (2.534, 5.447)	-0.026	0.980
Postoperative SII	404.107 (280.535, 605.388)	475.546 (293.026, 733.661)	-0.709 [△]	0.479
Postoperative SIRI	0.771 (0.538, 1.179)	0.883 (0.529, 1.363)	-0.346 [△]	0.729

OSCC: oral squamous cell carcinoma. NLR: neutrophil-to-lymphocyte ratio. LMR: lymphocyte-to-monocyte ratio. PLR: platelet-to-lymphocyte ratio. SII: systemic immune-inflammation index. SIRI: systemic inflammation response index. *: chi-square test. #: *t*-test. [△]: *U*-test

表3 OSCC患者复发转移的单因素Cox分析
Table 3 Univariate Cox analysis of recurrence and metastasis in OSCC patients

Variable	<i>B</i>	<i>SE</i>	<i>Wald</i>	<i>P</i>	<i>HR</i>	95% <i>CI</i>	
						Lower limit	Upper limit
Sex	-0.037	0.283	0.017	0.897	0.964	0.553	1.679
Age	0.020	0.013	2.556	0.110	1.020	0.995	1.046
Preoperative NLR	0.289	0.040	51.947	< 0.001	1.335	1.234	1.444
Preoperative PLR	0.006	0.002	8.232	0.004	1.006	1.002	1.011
Preoperative LMR	-0.098	0.094	1.097	0.295	0.907	0.754	1.089
Preoperative SII	0.002	0.000	40.495	< 0.001	1.002	1.001	1.002
Preoperative SIRI	0.518	0.121	18.253	< 0.001	1.679	1.324	2.129
Preoperative lymph node metastasis	0.888	0.283	9.866	0.002	2.429	1.396	4.227
Degree of differentiation			20.811	< 0.001			
High	Reference						
Medium	0.929	0.354	6.882	0.009	2.533	1.265	5.071
Low	1.771	0.388	20.778	< 0.001	5.874	2.743	12.576
Clinical T stage			16.690	0.001			
T1	Reference						
T2	0.246	0.449	0.299	0.584	1.279	0.530	3.084
T3	1.249	0.478	6.827	0.009	3.485	1.366	8.892
T4	1.366	0.459	8.859	0.003	3.920	1.594	9.636

OSCC: oral squamous cell carcinoma. NLR: neutrophil-to-lymphocyte ratio. LMR: lymphocyte-to-monocyte ratio. PLR: platelet-to-lymphocyte ratio. SII: systemic immune-inflammation index. SIRI: systemic inflammation response index

0.05),而其余指标均不是影响患者复发转移的影响因素($P > 0.05$)(表3)。

为了进一步检验单因素Cox分析有统计学意义的7个指标与患者复发转移率之间的相关性,进一步进行多因素Cox回归模型分析,将术前NLR、

术前PLR、术前SII、术前SIRI、术前淋巴结转移、分化程度和临床T分期共7个观察指标作为自变量,进行多因素Cox回归分析。

多因素Cox回归结果(表4)显示,术前NLR、术前淋巴结转移和临床T分期3个指标与患者复发

表4 OSCC患者复发转移的多因素Cox分析
Table 4 Multifactorial Cox analysis of recurrence and metastasis in OSCC patients

Variable	<i>B</i>	<i>SE</i>	<i>Wald</i>	<i>P</i>	<i>HR</i>	95% <i>CI</i>	
						Lower limit	Upper limit
Preoperative NLR	0.319	0.119	7.179	0.007	1.376	1.089	1.738
Preoperative PLR	-0.004	0.004	1.161	0.281	0.996	0.988	1.004
Preoperative SII	0.001	0.001	1.115	0.291	1.001	0.999	1.003
Preoperative SIRI	-0.397	0.321	1.536	0.215	0.672	0.358	1.260
Preoperative lymph node metastasis	0.790	0.319	6.128	0.013	2.202	1.179	4.115
Degree of differentiation			3.119	0.210			
High	Reference						
Medium	0.589	0.374	2.478	0.115	1.802	0.866	3.752
Low	0.740	0.462	2.565	0.109	2.096	0.847	5.182
Clinical T stage			9.978	0.019			
T1	Reference						
T2	0.911	0.559	2.655	0.103	2.487	0.831	7.437
T3	1.729	0.576	9.017	0.003	5.636	1.823	17.425
T4	1.291	0.580	4.955	0.026	3.636	1.167	11.334

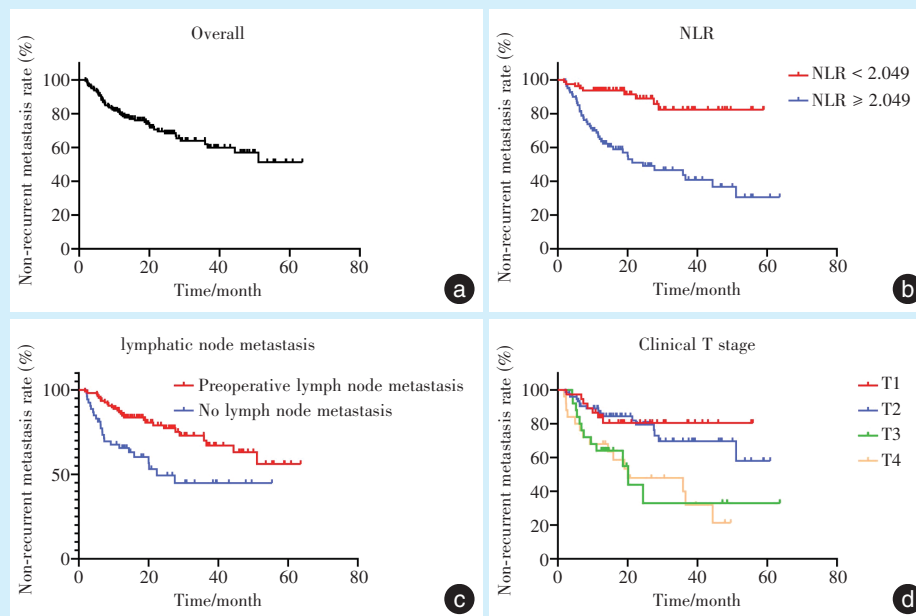
OSCC: oral squamous cell carcinoma. NLR: neutrophil-to-lymphocyte ratio. LMR: lymphocyte-to-monocyte ratio. PLR: platelet-to-lymphocyte ratio. SII: systemic immune-inflammation index. SIRI: systemic inflammation response index

转移存在显著相关关系($P < 0.05$),而且均是影响患者复发的独立危险因素($HR > 1$)。术前NLR越高、伴术前淋巴结转移、临床T分期越高患者的复发转移率越高。而术前PLR、术前SII、术前SIRI、分化程度均不是影响患者复发转移的独立影响因素($P > 0.05$)。

计算得出160例观察对象的NLR指标的中位数为2.049,为了进一步得到NLR低组和NLR高组复发转移率的差异,将160例观察对象根据NLR分为NLR低组($NLR < 2.049$)和NLR高组($NLR \geq 2.049$)。为了得到3个独立影响因素与患者复发转移率及未复发转移生存时间之间的关系,选择

Kaplan-Meier生存分析法进一步分析,计算出整体未复发转移时间中位数为42.9个月。其中,满足术后1年纳入标准患者未复发转移率为79.1%;满足术后3年纳入标准患者未复发转移率为61.9%;满足术后5年纳入标准患者未复发转移率为51.3%。

NLR不同等级、有无术前淋巴结转移、临床T分期对患者复发转移率具有明显影响($P < 0.05$)。且 $NLR \geq 2.049$ 组的未复发转移生存时间和未复发转移率均显著低于 $NLR < 2.049$ 组;伴术前淋巴结转移组的未复发转移生存时间和未复发转移率均较低;临床T分期越高,患者的未复发转移生存时间和未复发转移率越低(图1)。



a: overall survival curve, the overall nonrecurrent metastasis rate was 79.1% at 1 year, 61.9% at 3 years, and 51.3% at 5 years. b: survival curves of the group with a high NLR and the group with a low NLR. There was a significant difference in the prognosis between the group with a high NLR and the group with a low NLR. The lower the NLR was the greater the rate of nonrecurrent metastasis in patients with OSCC, and the better the prognosis. c: the group with preoperative lymph node metastasis group versus the group without lymph

node metastasis. There were differences between the two groups, and the prognosis of the group without lymph node metastasis was better than that of the group with lymph node metastasis. d: survival curves for patients with different tumor stages, the lower the clinical T stage was, the greater the rate of nonrecurrent metastasis, and the better the prognosis. OSCC: oral squamous cell carcinoma. NLR: neutrophil-to-lymphocyte ratio

Figure 1 Survival curves of independent risk factors affecting OSCC recurrence and metastasis

图1 影响OSCC复发转移的独立影响因素的生存曲线

3 讨论

OSCC是头颈部最常见的恶性肿瘤,占口腔癌的90%以上^[12]。近年来手术技术、放疗和抗癌药物的进步改善了OSCC患者的肿瘤预后和生存率,但OSCC的广泛手术切除不可避免地会导致一些口腔功能障碍。研究表明,OSCC患者的预后因素包括TNM分期、原发肿瘤分化程度、侵袭方式、侵袭深度、血管侵袭、淋巴结转移程度和肿瘤进展,

如囊外扩散(extracapsular spread, ECS)^[13-15]。此外细胞介导与肿瘤的发展、生长和转移密切相关^[16]。中性粒细胞、淋巴细胞、单核细胞和血小板等炎性细胞会上调细胞因子并产生炎性介质,这些介质与肿瘤微环境中的肿瘤细胞和其他基质细胞相互作用,促进肿瘤的形成、发展、侵袭和转移^[17-18]。中性粒细胞会产生血管内皮生长因子和白细胞介素8(interleukin-8, IL-8)等血管生成细胞因子,以及基

质金属蛋白9(matrix metalloproteinase-9, MMP-9)(明胶酶B),后者会介导肿瘤细胞的血管生成状态。中性粒细胞明胶酶相关脂褐素与侵袭深度和肿瘤分化有关。除中性粒细胞外,肿瘤相关巨噬细胞和其他白血病细胞通过基质金属蛋白2(matrix metalloproteinase-2, MMP-2)诱导细胞外基质重塑,这与肿瘤的侵袭转移行为有关^[19]。血小板参与恶性肿瘤转移等多个步骤导致不良预后^[20-21]。血小板源性微粒(platelet microparticle, PMP)在OSCC患者血浆中的水平升高,增加了OSCC的促凝活性,并随着肿瘤最大径及肿瘤TNM分期的增加而升高,在淋巴结转移患者中更高^[22]。许多实体肿瘤呈免疫细胞浸润,向周围组织和血流释放炎性细胞因子,导致全身性炎症^[23]。全身炎症和促炎症过程与癌症患者的不良预后有关,并经常与癌症相关的恶病质有关^[24]。Park等^[25]在69例OSCC患者的研究中发现,低LMR,高NLR、PLR与病理分期显著相关,低LMR和高NLR与肿瘤的大小以及临床分期相关,而高PLR与淋巴结转移相关。本研究结果显示,术前淋巴结转移组SII明显高于无转移组;分化程度越高,术前NLR、SII、SIRI越低;临床T分期越高,术前SIRI越高。术前多种炎症指标与高复发转移风险有关,术后炎症指标与复发转移风险无显著相关性。相对于未复发转移组,复发转移组术前NLR、SII、SIRI、术前淋巴结转移率高于未复发转移组,LMR低于未复发转移组。2组患者术后外周血NLR、PLR、LMR、SII、SIRI进行对比,差异均无统计学意义。多因素Cox分析结果显示:外周血炎症指标中只有术前NLR是影响患者复发转移的独立危险因素,可影响患者的预后。

综上,本研究结果显示术前NLR水平、临床T分期、术前淋巴结转移和OSCC的预后相关,是OSCC术后患者预后的重要预测因子。本研究提供了一种基于临床特征和外周血炎症指标预测OSCC预后的思路,与传统的TNM分期等一系列转移复发危险因素相比,NLR容易获取,检测方便,较易应用到临床实践中,结合其他预后指标可帮助提高评估准确性,对OSCC的预后判断有一定的参考价值,也可应用到OSCC患者随访,有助于对手术后复发转移风险高的OSCC患者采取个性化的辅助治疗。

本研究为回顾性研究,存在一定的局限性:样本量较少,随访时间不够长,未能收集OSCC患者

的病理浸润深度、TNM分期等病理学数据,C反应蛋白、转化生长因子- β 1、降钙素等其他临床中非常规检测的一些炎症指标,以及随访期间血常规结果和总生存期等随访信息;分析干扰因素较多,结果可能出现偏倚。需要补充的是每项外周血炎症指标数值是动态的,随着身体状态而发生变化,此研究分析了根治性手术前后的炎症指标与OSCC复发转移的关系;然而,在治疗过程或随访中,哪种标志物对预后更有价值值得进一步探讨。

【Author contributions】 Guhaiernisha·KHRM processed the research, collected, analyzed the data, and wrote the article. Wulan·JES analyzed the data and reviewed the article. Yao ZT designed the study and reviewed the article. All authors read and approved the final manuscript as submitted.

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