

肺癌术后患者血清 ACE2 和 CD40L 水平表达与感染程度及致病菌类属的鉴别价值

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摘要: 目的 探讨肺癌术后感染患者血管紧张素转换酶 2 (ACE2) 和 CD40 配体 (CD40L) 与感染程度的关系及对致病菌类属的鉴别价值, 为临床早期经验用药提供参考。方法 选取民航总医院 2017 年 1 月~2021 年 12 月经手术治疗的肺癌患者 1 186 例作为研究对象。统计术后感染发生情况 (感染率、严重程度、病原菌类型), 比较不同感染程度、不同致病菌类属患者 ACE2 及 CD40L 水平, Spearman 分析 ACE2 及 CD40L 水平与感染程度的相关性, 受试者工作特征 (ROC) 曲线分析 ACE2 和 CD40L 对致病菌类属的鉴别价值。结果 1 186 例肺癌患者术后感染率为 6.75% (80/1 186), 其中轻度感染 26 例, 中度感染 35 例和重度感染 19 例。分离病原菌 93 株, 其中革兰阴性菌 (G^-) 67 株, 革兰阳性菌 (G^+) 26 株; 与肺癌术后未感染患者比较, 术后感染患者血清 ACE2 (73.99 ± 16.18 U/L vs 49.42 ± 10.33 U/L) 和 CD40L (30.91 ± 5.91 μ g/L vs 21.67 ± 5.02 μ g/L) 水平升高, 差异具有统计学意义 ($t=17.833, 14.321$, 均 $P < 0.001$); 随着感染程度加重血清 ACE2 (67.77 ± 7.53 U/L, 74.49 ± 12.57 U/L, 81.60 ± 9.63 U/L) 和 CD40L (28.27 ± 3.76 μ g/L, 31.42 ± 4.83 μ g/L, 33.45 ± 3.41 μ g/L) 水平均呈上升趋势, 差异具有统计学意义 ($F=5.534, 13.746$, 均 $P < 0.001$); 血清 ACE2, CD40L 水平与肺癌患者术后感染程度均呈正相关关系 ($r=0.835, 0.710$, 均 $P < 0.001$); G^- 菌感染患者血清 ACE2 (74.56 ± 5.57 U/L) 及 CD40L 水平 (31.08 ± 2.72 μ g/L) 高于 G^+ 菌感染患者 (68.05 ± 4.76 U/L, 28.33 ± 2.47 μ g/L), 差异具有统计学意义 ($t=2.479, 2.309$, 均 $P < 0.05$); ACE2 (OR=2.627, 95%CI: 1.268 ~ 5.443, $P=0.001$) 和 CD40L (OR=3.628, 95%CI: 1.752 ~ 6.097, $P < 0.001$) 水平升高是肺癌患者术后存在 G^- 感染的独立危险因素; ACE2 联合 CD40L 鉴别肺癌患者术后感染病原菌类型的 AUC, 敏感度和特异度分别为 0.935, 87.50% 和 90.48%。结论 肺癌患者术后 ACE2 和 CD40L 高表达, 且与感染严重程度存在正相关关系, 检测 ACE2 和 CD40L 对鉴别肺癌术后感染病原菌类型有重要价值, 可指导临床早期经验用药。

关键词: 肺癌; 术后感染; 血管紧张素转换酶 2; CD40 配体; 病原菌分布

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Expression of ACE2 and CD40L in Serum of Patients with Lung Cancer after Operation and the Value of Differential Diagnosis between the Degree of Infection and the Genus of Pathogenic Bacteria

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Abstract: Objective To explore the relationship between angiotensin-converting enzyme 2 (ACE2) and CD40 ligand (CD40L) and the degree of infection in patients with postoperative infection of lung cancer and the value of differential diagnosis of pathogenic bacteria, so as to provide reference for early clinical experience in drug use. **Methods** A total of 1 186 patients with lung cancer who underwent surgical treatment from January 2017 to December 2021 were selected, and all of them underwent surgery. The incidence of postoperative infection (infection rate, severity and pathogen type) was counted, and the levels of ACE2 and CD40L in patients with different infection degrees and pathogen types were compared. The correlation between the levels of ACE2 and CD40L and the degree of infection was analyzed, and receiver operating characteristic (ROC) curve was used to analyze the value of ACE2 and CD40L in differentiating pathogen genus of pathogenic bacterias. **Results** The postoperative infection rate of 1 186 lung cancer patients was 6.75% (80/1 186), among with 26 cases of mild infection, 35 cases of moderate infection, and 19 cases of severe infection. 93 strains of pathogenic bacteria were isolated including 67 strains of Gram-negative bacteria (G^-), 26 strains of Gram-positive bacteria (G^+). The serum levels of ACE2 (73.99 ± 16.18 U/L vs 49.42 ± 10.33 U/L) and CD40L (30.91 ± 5.91 μ g/L vs 21.67 ± 5.02 μ g/L) in patients with infection after lung cancer surgery were higher than those

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in patients without infection, the differences were statistically significant($t=17.833, 14.321$, all $P < 0.001$). Serum ACE2 ($67.77 \pm 7.53, 74.49 \pm 12.57$ and 81.60 ± 9.63 U/L) and CD40L ($28.27 \pm 3.76, 31.42 \pm 4.83$ and 33.45 ± 3.41 μ g/L) levels increased with the severity of infection ($F=5.534, 13.746, P < 0.001$). Serum ACE2 and CD40L levels were positively correlated with postoperative infection degree in patients with lung cancer ($r=0.835, 0.710$, all $P < 0.001$). The serum levels of ACE2 (74.56 ± 5.57 U/L) and CD40L (31.08 ± 2.72 μ g/L) in patients with G⁻ infection were higher than those in patients with G⁺ infection (68.05 ± 4.76 U/L), (28.33 ± 2.47 μ g/L), and the severity of infection was more severe than that in patients with G⁺ infection, the differences were statistically significant ($t=2.479, 2.309$, all $P < 0.05$). Elevated levels of ACE2 (OR=2.627, 95% CI: 1.268 ~ 5.443, $P=0.001$) and CD40L (OR=3.628, 95% CI: 1.752 ~ 6.097, $P<0.001$) were independent risk factors for postoperative G⁻ infection in patients with lung cancer. The AUC, sensitivity and specificity of ACE2 and CD40L combined to identify the types of pathogenic bacteria in patients with lung cancer after surgery were 0.935, 87.50% and 90.48%, respectively.

Conclusion Postoperative infection in patients with lung cancer promotes high expression of ACE2 and CD40L, and there was a positive correlation with the severity of infection. Detection of ACE2 and CD40L is of great value in identifying the types of pathogenic bacteria infected after lung cancer surgery, and it can guide early clinical experience and medication.

Keywords: lung cancer; postoperative infection; angiotensin-converting enzyme 2; CD40 ligand; distribution of pathogenic bacteria

肺癌是癌症导致死亡的最主要病因,其发病率、死亡率在我国恶性肿瘤中均为第一位,五年生存率约19.7%^[1]。肺切除术是挽救肺癌患者的重要方案,但由于免疫功能较低、手术应激损伤、呼吸道症状等因素,肺癌患者术后感染风险较高。感染可导致术后康复时间延长、病情恶化、经济负担加重、死亡风险提高,故加强肺癌患者术后感染防控具有重要意义。血管紧张素转换酶2(angiotensin converting enzyme 2, ACE2)及CD40配体(CD40 ligand, CD40L)均在炎症反应^[2-3]中异常表达,其水平变化可反映炎症损伤程度,感染可诱发炎症反应已在临床研究^[4-5]中得到证实,但在不同病原菌感染患者中表达差异尚未明确。基于此,本研究通过分析ACE2和CD40L与肺癌患者术后感染及致病菌类属的关系,为临床早期抗感染治疗提供参考。报告如下。

1 材料与方法

1.1 研究对象 选取民航总医院2017年1月~2021年12月经手术治疗的肺癌患者1186例为研究对象,其中男性675例,女性511例;年龄50~71(60.38 ± 4.53)岁。纳入标准:①符合原发肺癌诊断标准^[6],且经手术病理学检查确诊,均为非小细胞肺癌;②TNM分期为I~IIb期;③均行胸腔镜下肺段切除术;④未经放化疗干预;⑤肝肾功能正常;⑥原发肺癌;⑦术后感染患者为肺部细菌性感染;⑧均知情本研究,签署同意书。排除标准:①全身状况差,不耐受手术;②近6周出现心肌梗死;③并发未控制的心力衰竭或严重室性心律失常;④自身免疫性疾病;⑤年龄>75岁;⑥并发其他肿瘤;⑦术前存在感染;⑧术前经抗感染治疗;⑨肺内双原发或多原发癌。本研究经民航总医院伦理委员会审批通过。

1.2 仪器与试剂 ACE2试剂盒及CD40L试剂盒(上海酶联生物科技有限公司,货号:LZ-H93449, mls_w_E0852), TGL-16G高速离心机(上海圣科仪器设备有限公司),全自动微生物鉴定系统(法国梅里埃生物科技有限公司)。

1.3 方法

1.3.1 ACE2, CD40L检测: 术后1天非抗凝管抽取清晨空腹静脉血4ml,离心提取血清(半径8cm,时间10min,转速3500r/min),酶联免疫法检测ACE2及CD40L水平。操作严格按照试剂盒说明书步骤规范完成。

1.3.2 肺部感染标准^[7]: 至少存在以下两项:①体温<36℃或≥38℃;②白细胞计数≥ 10×10^9 /L;③病原菌检测结果为阳性;④气道分泌物明显增多或出现脓性分泌物。肺部感染严重程度以临床肺部感染评分^[8](clinical pulmonary infection score, CPIS)进行评估,内容包括体温、白细胞计数、氧合情况、X线胸片肺部浸润影、气管分泌物等,最高12分,分值越高表明感染越严重,其中<6分为轻度感染,6~9分为中度感染,>9分为重度感染。

1.3.3 病原菌检测: 采集肺癌术后感染患者清晨深咳痰(若无力咳痰则以纤维支气管镜采集标本),接种于血琼脂平板、麦康凯平板、巧克力色琼脂平板,置于37℃孵育箱48h,以全自动微生物鉴定系统鉴别病原菌。

1.4 统计学分析 通过SPSS22.0处理数据,符合正态分布的计量资料以均数±标准差($\bar{x} \pm s$)表示,感染与未感染、不同病原菌感染的患者ACE2及CD40L水平比较采用独立样本 t 检验,不同感染程度患者ACE2和CD40L水平比较采用单因素方差分析,两两比较以LSD- t 检验;采用Spearman分

析ACE2及CD40L水平与感染程度的相关性;性别、年龄、并发症、吸烟史、慢性阻塞性肺疾病史、肿瘤类型、住院时间、手术方式、手术时间等计数资料以率表示,用 χ^2 检验;等级资料(不同病原菌感染患者感染程度、TNM分期)采用秩和检验,Logistic回归分析感染不同病原菌感染的影响因素,ACE2及CD40L水平对不同病原菌的鉴别价值采用受试者工作特征(receiver operating characteristic curve, ROC)曲线分析,获取AUC,置信区间、敏感度、特异度及截断值,联合预测实施Logistic二元回归拟合,检测标准 $\alpha=0.05$ 。

2 结果

2.1 肺癌术后感染发生率及ACE2和CD40L水

表1 不同感染程度患者ACE2和CD40L水平比较($\bar{x} \pm s$)

项目	轻度($n=26$)	中度($n=35$)	重度($n=19$)	F	P
ACE2(U/L)	67.77 \pm 7.53	74.49 \pm 12.57 ^a	81.60 \pm 9.63 ^{ab}	5.534	0.006
CD40L(μ g/L)	28.27 \pm 3.76	31.42 \pm 4.83 ^a	33.45 \pm 3.41 ^{ab}	13.746	<0.001

注:中度、重度与轻度感染比较,^a $t=2.420, 3.512; 5.408, 4.900$,均 $P<0.05$;与中度感染比较,^b $t=2.144, 2.234$,均 $P<0.05$ 。

2.3 肺癌术后感染患者ACE2及CD40L水平与感染程度的相关性 Spearman相关性分析结果显示,血清ACE2及CD40L水平与肺癌患者术后感染程度均呈正相关($r=0.835, 0.710$,均 $P<0.001$)。

2.4 肺癌术后感染患者病原菌分布情况 见表2。80例术后感染患者共分离病原菌93株,其中G⁻67株(72.04%),G⁺26株(27.96%)。80例术后感染患者中有3例患者同时感染G⁻及G⁺,其余77例患者中56例患者感染G⁻,21例患者感染G⁺。

表2 肺癌术后感染患者病原菌分布情况

病原菌	株数(n)	占比(%)
G ⁻ 菌	肺炎克雷伯菌	24
	25.81	
	鲍曼不动杆菌	18
	19.35	
	大肠埃希菌	11
	11.83	
G ⁺ 菌	铜绿假单胞菌	7
	7.53	
	肠杆菌	4
	4.30	
	其他	3
	3.23	
	金黄色葡萄球菌	14
G ⁺ 菌	15.05	
	表皮葡萄球菌	6
	6.45	
	粪肠球菌	4
G ⁺ 菌	4.30	
	其他	2
G ⁺ 菌	2.15	

2.5 不同病原菌感染患者一般资料比较 见表3。80例剔除3例同时感染G⁻及G⁺的患者。G⁻感染患者血清ACE2和CD40L水平高于G⁺感染患者,感染严重程度较G⁺感染患者更重,差异具有统计

学意义($P<0.05$)。

平比较 1186例肺癌患者中,术后感染80例,感染率为6.75%。肺癌术后感染患者血清ACE2(73.99 \pm 16.18U/L)和CD40L(30.91 \pm 5.91 μ g/L)水平高于未感染患者(49.42 \pm 10.33U/L, 21.67 \pm 5.02 μ g/L),差异有统计学意义($t=17.883, 14.321$,均 $P<0.001$)。

2.2 不同感染程度患者ACE2和CD40L水平比较 见表1。80例肺癌术后感染患者中,轻度感染26例,中度感染35例,重度感染19例。单因素方差分析显示不同感染程度患者血清ACE2及CD40L水平比较差异有统计学意义,两两比较显示随感染程度加重血清ACE2及CD40L水平均呈上升趋势,差异有统计学意义($P<0.05$)。

学意义(均 $P<0.05$)。

2.6 不同病原菌感染多因素分析 见表4。将ACE2及CD40L水平、感染严重程度进行多重共线性检验,发现ACE2及CD40L水平与感染严重程度存在多重共线性(方差膨胀系数 >10),手动移除感染严重程度。以不同病原菌感染类别为因变量(赋值:G⁻=1, G⁺=0),以ACE2和CD40L水平为自变量(赋值:实际值),进行Logistic回归多因素分析,结果显示ACE2及CD40L水平升高是肺癌患者术后存在G⁻感染的独立危险因素($P<0.05$)。

2.7 ACE2和CD40L鉴别肺癌术后感染患者病原菌类型的价值 见表5,图1。以G⁻患者数据作为阳性数据,以G⁺患者数据作为阴性数据,绘制血清ACE2, CD40L水平鉴别不同病原菌感染的ROC曲线,得到AUC值分别为0.848, 0.825,继续Logistic二元回归拟合得到联合鉴别的AUC值0.935最大。

3 讨论

手术切除是早中期肺癌患者的主要治疗方案,但存在术后感染风险。马颖欣等^[9]研究中496例老年肺癌患者术后发生感染117例,术后感染率达23.6%;呼爱鲜^[10]报道中显示730例肺癌患者术后肺部感染82例,术后感染率为11.23%,均明显高于本研究肺癌术后感染率6.75%(80/1186),其原因可能与手术方案、麻醉方式、医疗条件、肿瘤分期等多种因素有关。不同类型病原菌的耐药性及治疗方案均有所差异,探究术后感染病原菌的预警机制对合理给予抗生素有指导作用,是临床加强医

源性感染防控的研究方向。

表 3		不同病原菌感染患者一般资料比较 [n (%)]			
类 别		G ⁻ (n=56)	G ⁺ (n=21)	χ^2	P
性别	男	37 (66.07)	13 (61.90)	0.117	0.733
	女	19 (33.93)	8 (38.10)		
年龄	< 60 岁	25 (44.64)	9 (42.86)	0.020	0.888
	≥ 60 岁	31 (55.36)	12 (57.14)		
吸烟史	有	42 (75.00)	16 (76.19)	0.012	0.914
	无	14 (25.00)	5 (23.81)		
并发症	糖尿病	8 (14.29)	4 (19.05)	0.026	0.608
	高血压	5 (8.93)	2 (9.52)	0.133	0.716
TNM 分期	I 期	27 (48.21)	11 (52.38)	0.242	0.809
	II a 期	21 (37.50)	7 (33.33)		
	II b 期	8 (14.29)	3 (14.29)		
肿瘤类型	鳞癌	45 (80.36)	18 (85.71)	0.835	0.659
	腺癌	9 (16.07)	3 (14.29)		
	其他	2 (3.57)	0 (0.00)		
慢性阻塞性肺疾病史	有	33 (58.93)	11 (52.38)	0.267	0.605
	无	23 (41.07)	10 (47.62)		
手术方式	完全性切除	31 (55.36)	12 (57.14)	0.031	0.985
	不完全性切除	19 (33.93)	7 (33.33)		
	不确定性切除	6 (10.71)	2 (9.52)		
手术时间 (h)	< 3	30 (53.57)	12 (57.14)	0.079	0.779
	≥ 3	26 (46.43)	9 (42.86)		
住院时间 (d)	< 20	15 (26.79)	6 (28.57)	0.025	0.876
	≥ 20	41 (73.21)	15 (71.43)		
ACE2($\bar{x} \pm s$ U/L)		74.56 ± 5.57	68.05 ± 4.76	2.479	0.015
CD40L($\bar{x} \pm s$ μg/L)		31.08 ± 2.72	28.33 ± 2.47	2.309	0.024
感染严重程度	轻度	14 (25.00)	11 (52.38)	2.291	0.022
	中度	26 (46.43)	8 (38.10)		
	重度	16 (28.57)	2 (9.52)		

表 4		不同病原菌感染多因素分析				
项 目	β	SE	Wald χ^2	OR	P	95%CI
ACE2 水平	0.966	0.392	6.071	2.627	0.001	1.268 ~ 5.443
CD40L	1.184	0.426	7.728	3.268	< 0.001	1.752 ~ 6.097

表 5		ACE2 和 CD40L 鉴别肺癌术后感染患者病原菌类型的价值				
项 目	AUC	95%CI	P	截断值	敏感度 (%)	特异度 (%)
ACE2	0.848	0.748 ~ 0.920	< 0.001	> 71.68 U/L	78.57	85.71
CD40L	0.825	0.722 ~ 0.902	< 0.001	> 29.36 μg/L	85.71	71.43
联合检测	0.935	0.854 ~ 0.978	< 0.001		87.50	90.48

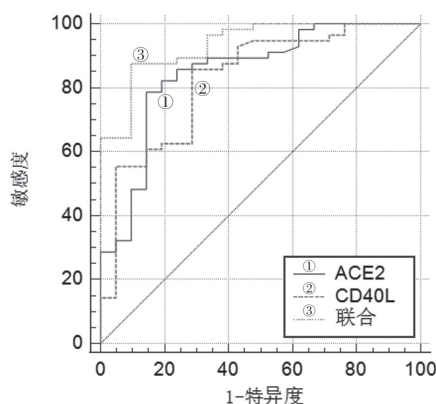


图1 ACE2和CD40L鉴别肺癌术后感染患者病原菌类型的ROC曲线

ACE2是ACE同工酶,但与ACE促使血管紧张素1转换为血管紧张素2的机制相反,ACE2可通过水解血管紧张素舒张血管,具有降低血压、保护心血管作用。ACE2在多种肿瘤疾病中均有异常表达,相关研究^[11]指出ACE2可抑制血管内皮生长因子A/血管内皮生长因子受体2/细胞外信号调节蛋白激酶通路,对乳腺癌血管生成具有抑制作用。另有研究^[12]证实新型冠状病毒肺炎的SARS-CoV-2可通过ACE2受体进入宿主,同时该研究指出肺癌患者ACE2存在高表达,且是肺癌患者感染SARS-CoV-2高易感性的重要因素。本研究发现相较于未感染患者,肺癌术后感染患者ACE2水平更高,与上述研究存在一定相似性。由此推测,肺癌患者术后ACE2水平情况可能与是否发生感染有关。进一步分析发现,ACE2表达与感染严重程度存在正相关关系。分析原因可能在于ACE2具有抗炎作用,肺癌患者术后感染时可激活或增强机体炎症机制,而ACE2可通过介导P38蛋白激酶、细胞外调节蛋白激酶通路抑制炎症因子释放避免炎症反应过度激活,因此,感染后ACE2代偿性高表达以保护机体组织受到炎症损伤,且感染程度越严重,则ACE2代偿性越高越显著^[13-14]。继续Logistic回归多因素分析发现,ACE2水平升高是肺癌患者术后存在G⁻菌感染的独立危险因素,上述推测得到印证,说明肺癌患者术后ACE2水平变化与发生感染有关,且G⁻菌因生成内毒素机体炎症反应更显著。

CD40L是细菌性炎症反应标志物,近年来其与肺炎患儿相关的研究^[15-16]有所增加。CD40L具有促炎作用,可被嗜酸性粒细胞识别,结合平滑肌细胞、血管内皮细胞内的CD40受体可激活核因子- κ B信号通路,增加炎症因子表达,加剧炎症反应。有研究^[17]指出,CD40L-CD40信号转导可激活肺外膜成纤维细胞促炎表型,证实CD40L在肺部炎症反应中具有积极作用。本研究显示肺癌术

后感染患者CD40L水平更高,且感染程度越严重其水平变化越明显,这是由于机体感染诱发免疫应答造成的炎症反应,而CD40L可活化B淋巴细胞、T淋巴细胞表达的跨膜糖蛋白,调节B淋巴细胞、T淋巴细胞相互作用,刺激炎症因子释放,该过程中CD40L水平显著升高^[18-19]。另外,CD40L同样具有抗肿瘤作用,其与自身受体相结合可作用于树突状细胞,活化树突状细胞中具有抗凋亡作用的丝氨酸蛋白酶抑制剂,增强Bcl-2表达,延长树突状细胞生存期,改善肿瘤患者树突状细胞过快自发性凋亡的情况;同时CD40L可通过与CD40相互作用促使特异性T细胞抗肿瘤免疫活化,增强NK抗肿瘤细胞毒反应。上述研究说明CD40L水平变化可能与肺癌患者术后感染有关。

病原菌检测是诊断感染的金标准方式,但由于存在明显滞后性,难以适用于临床早期抗感染治疗,通过预警因子水平变化鉴别致病菌类属是临床抗感染的重要研究方向。本研究证实ACE2及CD40L水平在肺癌术后感染患者体内存在异常表达,且与感染程度存在明显相关性,这是研究二者能否鉴别不同致病菌类属的必要前提;另外,Logistic回归多因素分析表明ACE2及CD40L水平升高是感染G⁻的独立危险因素,ROC曲线进一步证实ACE2及CD40L可用于鉴别G⁻与G⁺感染,其原因可能与G⁻及G⁺感染造成的炎症反应程度不同有关。G⁻菌体细胞壁含有大量高效致炎因子内毒素,可结合受体诱导巨噬细胞、血管平滑肌细胞、内皮细胞分泌炎症介质,加剧炎症反应;同时G⁻感染可通过Toll样受体4参与细胞激活,Toll样受体识别配体后激活下游信号转导通路,启动白介素-1,白介素-6,肿瘤坏死因子- α 等前炎症因子表达,促使炎症反应发生及进展,进而导致ACE2及CD40L异常表达^[20-21]。卢秋维等^[22]研究指出,G⁻感染的患者血清降钙素原、C反应蛋白、脑钠肽等炎症指标均高于G⁺感染患者,表明G⁻感染可造成更严重的炎症反应。另有研究^[23]指出,G⁻主要成分脂多糖可特异性通过Toll样受体激活血小板参与免疫炎症反应,并通过Bcl-xL启动血小板凋亡程序,相较于G⁺危险性更高。因此,通过检测ACE2及CD40L水平鉴别致病菌类属具有较高价值,对指导临床早期抗感染具有积极作用。

综上,ACE2及CD40L水平与肺癌患者术后感染关系密切,其高水平表达表明术后感染更严重,且通过检测ACE2与CD40L水平有助于鉴别G⁻及G⁺感染类型,可指导临床合理使用抗生素,具有重要指导价值。本研究主要分析肺癌患者术后感染ACE2与CD40L水平与不同致病菌类属的关系,而

二者不同水平变化是否对肺癌患者远期预后产生影响, 仍需临床多中心选取病例进一步研究证实。

参考文献:

- [1] 中国肺癌防治联盟, 中华医学会呼吸病学分会肺癌学组, 中国医师协会呼吸医师分会肺癌工作委员会. 肺癌筛查与管理中国专家共识 [J]. 国际呼吸杂志, 2019, 39(21): 1604-1615.
Chinese Alliance Against Lung Cancer, Chinese Medical Association of Respiratory Disease Branch Lung Cancer Study Group, Chinese Medical Doctor Association of Respiratory Doctor Branch Lung Cancer Working Committee. Chinese expert consensus on screening and management of lung cancer[J]. International Journal of Respiration, 2019, 39(21): 1604-1615.
- [2] DA SILVA FILHA R, SERGIO VELOSO BRANT P, E. CORDEIRO T M, et al. Evidence for a role of angiotensin converting enzyme 2 in proteinuria of idiopathic nephrotic syndrome[J]. Bioscience Reports, 2019, 39(1): BSR20181361.
- [3] STEVEN S, DIB M, HAUSDING M, et al. CD40L controls obesity-associated vascular inflammation, oxidative stress, and endothelial dysfunction in high fat diet-treated and db/db mice[J]. Cardiovascular Research, 2018, 114(2): 312-323.
- [4] 马宏境, 黄少祥, 刘彬, 等. 胸腔镜引导下肺癌根治术后感染患者血清急性时相反应蛋白研究 [J]. 中华医院感染学杂志, 2019, 29(11): 1677-1681.
MA Hongjing, HUANG Shaoxiang, LIU Bing, et al. Postoperative infection in patients undergoing thoracoscopy-guided radical resection of lung cancer and acute phase reaction proteins in serum[J]. Chinese Journal of Nosocomiology, 2019, 29(11): 1677-1681.
- [5] 王丽萍, 孙常铭, 张日, 等. 肺癌患者围手术期感染血清炎症因子与 N 末端脑钠肽前体水平变化及临床意义 [J]. 中华医院感染学杂志, 2020, 30(2): 220-223.
WANG Liping, SUN Changming, ZHANG Ri, et al. Changes of serum inflammatory factors and N-terminal pro-brain natriuretic peptide of lung cancer patients with perioperative infection and their clinical significance[J]. Chinese Journal of Nosocomiology, 2020, 30(2): 220-223.
- [6] 支修益, 石远凯, 于金明. 中国原发性肺癌诊疗规范 (2015 年版) [J]. 中华肿瘤杂志, 2015, 37(1): 67-78.
ZHI Xiuyi, SHI Yuankai, YU Jinming. Standards for the diagnosis and treatment of primary lung cancer (2015 version) in China[J]. Chinese Journal of Oncology, 2015, 37(1): 67-78.
- [7] 中华医学会呼吸病学分会. 肺部感染性疾病支气管肺泡灌洗病原体检测中国专家共识 (2017 年版) [J]. 中华结核和呼吸杂志, 2017, 40(8): 578-583.
Chinese Thoracic Society. Consensus of Chinese experts on detection of bronchoalveolar lavage pathogens in pulmonary infectious diseases (2017 Edition)[J]. Chinese Journal of Tuberculosis and Respiratory Diseases, 2017, 40(8): 578-583.
- [8] LUYT C E, CHASTRE J, FAGON J Y. Value of the clinical pulmonary infection score for the identification and management of ventilator-associated pneumonia[J]. Intensive Care Medicine, 2004, 30(5): 844-852.
- [9] 马颖欣, 张国平, 乔安邦, 等. 老年肺癌患者术后发生院内肺部感染的病原菌分布及多重耐药性分析 [J]. 传染病信息, 2020, 33(2): 147-150.
MA Yingxin, ZHANG Guoping, QIAO Anbang, et al. Distribution of pathogenic bacteria and multi-drug resistance in postoperative nosocomial lung infection in senile patients with lung cancer[J]. Infectious Disease Information, 2020, 33(2): 147-150.
- [10] 呼爱鲜. 肺癌患者肺切除术后肺部感染危险因素分析 [J]. 新乡医学院学报, 2022, 39(2): 160-164.
HU Aixian. Risk factors for pulmonary infection in patients with lung cancer after pulmonary resection[J]. Journal of Xinxiang Medical University, 2022, 39(2): 160-164.
- [11] ZHANG Qi, LU Sihong, LI Tianfu, et al. ACE2 inhibits breast cancer angiogenesis via suppressing the VEGFa/VEGFR2/ERK pathway[J]. Journal of Experimental & Clinical Cancer Research, 2019, 38(1): 173.
- [12] SAMAD A, JAFAR T, RAFI J H. Identification of angiotensin-converting enzyme 2 (ACE2) protein as the potential biomarker in SARS-CoV-2 infection-related lung cancer using computational analyses[J]. Genomics, 2020, 112(6): 4912-4923.
- [13] 龚晶婧, 李荣通, 卢卓强, 等. ACE2 小干扰 RNA 对平滑肌细胞 AT1 受体蛋白表达及其下游信号通路的影响 [J]. 中国药理学通报, 2020, 36(3): 354-359.
GONG Jingjing, LI Rongtong, LU Zhuoqiang, et al. Expression of AT1 receptor protein and its downstream signaling pathways in vascular smooth muscle cells after ACE2 siRNA interference[J]. Chinese Pharmacological Bulletin, 2020, 36(3): 354-359.
- [14] OGATA Y, NEMOTO W, YAMAGATA R, et al. Anti-hypersensitive effect of angiotensin (1-7) on streptozotocin-induced diabetic neuropathic pain in mice[J]. European Journal of Pain, 2019, 23(4): 739-749.
- [15] 唐国英, 张连花. 儿童细菌性肺炎患儿血清 CD40L, VCAM-1 表达变化与其疾病严重程度相关关系研究 [J]. 临床肺科杂志, 2019, 24(5): 827-831.
TANG Guoying, ZHANG Lianhua. Study on the relationship between the changes of serum CD40L and VCAM-1 expression and severity of illness in children with bacterial pneumonia in children[J]. Journal of Clinical Pulmonary Medicine, 2019, 24(5): 827-831.
- [16] 全守东, 乐原, 杜振元, 等. 肺炎支原体感染哮喘患儿血清 CD40L 和 VCAM-1 水平及意义 [J]. 中华医院感染学杂志, 2020, 30(22): 3474-3478.
QUAN Shoudong, YUE Yuan, DU Zhenyuan, et al. Significance of serum CD40L and VCAM-1 levels in children with asthma infected by *Mycoplasma pneumoniae*[J]. Chinese Journal of Nosocomiology, 2020, 30(22): 3474-3478.
- [17] PAN Yanyun, YANG Jinxiu, XU Yifei, et al. Yin yang-1 suppresses CD40 ligand-CD40 signaling-mediated anti-inflammatory cytokine interleukin-10 expression in pulmonary adventitial fibroblasts by promoting histone H3 tri-methylation at lysine 27 modification on interleukin-10 promoter[J]. Cell Biology International, 2020, 44(7): 1544-1555.

- 34(3): 189-196.
- [8] MUNNS C F, SHAW N, KIELY M, et al. Global consensus recommendations on prevention and management of nutritional rickets[J]. The Journal of Clinical Endocrinology and Metabolism, 2016, 101(2): 394-415.
- [9] 中华预防医学会儿童保健分会. 中国儿童维生素A、维生素D临床应用专家共识[J]. 中国儿童保健杂志, 2021, 29(1): 110-116.
Society of Child Health, Chinese Preventive Medicine Association. The expert consensus of Vitamin A and Vitamin D application in Clinics [J]. Chinese Journal of Child Health Care, 2021, 29(1): 110-116.
- [10] 卢山, 董辉苒, 任文华, 等. 自动化磁珠法标本制备联合液相色谱串联质谱检测人血清中 25-羟基维生素D的性能评价[J]. 国际检验医学杂志, 2022, 43(10):1234-1237, 1243.
LU Shan, DONG Huiran, REN Wenhua, et al. Performance evaluation of automated magnetic bead-based specimen preparation combined with liquid chromatography-tandem mass spectrometry for the detection of 25-hydroxyvitamin D in human serum [J]. International Journal of Laboratory Medicine, 2022, 43(10): 1234-1237, 1243.
- [11] WANG Danchen, YU Songlin, ZHANG Qi, et al. A robust method for simultaneous measurement of serum 25(OH)D, 1,25(OH)₂D, and 24,25(OH)₂D by liquid chromatography-tandem mass spectrometry with efficient separation of 3-epi analogs, 23R,25(OH)₂D₃, and 4β,25(OH)₂D₃[J]. Journal of Mass Spectrometry, 2022, 57(1): e4792.
- [12] KOWALÓWKA M, GŁÓWKA A K, KARAŻNIEWICZ-ŁADA M, et al. Clinical Significance of analysis of vitamin D status in various diseases [J]. Nutrients, 2020, 12(9):2788.
- [13] 原婷, 李宇丹, 孔琦, 等. 早产儿 25-羟基维生素D水平和围生期相关因素分析[J]. 中国妇幼保健, 2021, 36(15):3574-3577.
YUAN Ting, LI Yudan, KONG Qi, et al. Analysis of 25-(OH)D level in premature and associated factors in perinatal period [J]. Maternal and Child Health Care of China, 2021, 36(15): 3574-3577.
- [14] 黄丽密, 池美珠, 周恩敏, 等. 住院早产儿维生素D水平及相关因素分析[J]. 浙江医学, 2019, 41(7):683-685, 690.
HUANG Limi, CHI Meizhu, ZHOU Enmin, et al. Serum vitamin D level and related factors in hospitalized preterm infants [J]. Zhejiang Medical Journal, 2019, 41(7): 683-685, 690.
- [15] JUNG J H, KIM E A, LEE S Y, et al. Vitamin D status and factors associated with vitamin D deficiency during the first year of Life in preterm infants[J]. Nutrients, 2021, 13(6): 2019.
- [16] OOMS N, VAN DAAL H, BEIJERS A M, et al. Time-course analysis of 3-epi-25-hydroxyvitamin D₃ shows markedly elevated levels in early life, particularly from vitamin D supplementation in preterm infants[J]. Pediatric Research, 2016, 79(4): 647-653.
- [17] AGHAJAFARI F, FIELD C J, RABI D, et al. Plasma 3-epi-25-hydroxycholecalciferol can alter the assessment of vitamin D status using the current reference ranges for pregnant women and their newborns [J]. The Journal of Nutrition, 2016, 146(1): 70-75.
- [18] MYDTSKOV N D, LYKKEDEGN S, FRUEKILDE P B N, et al. S-25-hydroxyvitamin D and C3-epimers in pregnancy and infancy: An odense child cohort study[J]. Clinical biochemistry, 2017, 50(18): 988-996.

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- [18] BAE J, SAMUR M, RICHARDSON P, et al. Selective targeting of multiple myeloma by B cell maturation antigen (BCMA)-specific central memory CD8⁺ cytotoxic T lymphocytes: immunotherapeutic application in vaccination and adoptive immunotherapy[J]. Leukemia, 2019, 33(9): 2208-2226.
- [19] DONG Yuhang, MA Tiejun, ZHANG Xiaoxiao, et al. Incorporation of CD40 ligand or granulocyte-macrophage colony stimulating factor into Hantaan virus (HTNV) virus-like particles significantly enhances the long-term immunity potency against HTNV infection[J]. Journal of Medical Microbiology, 2019, 68(3): 480-492.
- [20] SUN Mengyao, BAI Yang, ZHAO Song, et al. Gram-negative bacteria facilitate tumor progression through TLR4/IL-33 pathway in patients with non-small-cell lung cancer[J]. Oncotarget, 2018, 9(17): 13462-13473.
- [21] SKJESOL A, YURCHENKO M, BÖSL K, et al. The TLR4 adaptor TRAM controls the phagocytosis of Gram-negative bacteria by interacting with the Rab11-family interacting protein 2[J]. PLoS Pathogens, 2019, 15(3): e1007684.
- [22] 卢秋维, 廖美娟, 林雪珍. 5种炎症指标对革兰阴性菌和革兰阳性菌所致脓毒症的早期诊断及鉴别诊断价值比较[J]. 山东医药, 2019, 59(17):79-82.
LU Qiuwei, LIAO Meijuan, LIN Xuezheng. Comparison of five inflammatory markers in early diagnosis and differential diagnosis of sepsis caused by Gram-negative and Gram-positive bacteria[J]. Shandong Medical Journal, 2019, 59(17): 79-82.
- [23] 秦云. 肺炎患者血液PLT、PA/Fig和NGAL联合检测在不同类型病原菌感染鉴别及疗效评估中的价值[J]. 现代检验医学杂志, 2021, 36(5): 83-89.
QIN Yun. Value of combined detection of PLT, PA/Fig and NGAL in the blood of patients with pneumonia in the identification of different types of pathogenic infections and the evaluation of therapeutic effects[J]. Journal of Modern Laboratory Medicine, 2021, 36(5): 83-89.

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