



老年食管癌患者放疗后肺动态顺应性、气道阻力与肺部感染指标的关系*

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【摘要】目的 探究老年食管癌患者放疗后肺动态顺应性(dynamic compliance, Cdyn)和气道阻力(airway resistance, RAW)水平预测肺部感染的效能。**方法** 回顾性选取2017年10月-2022年7月于山西省汾阳医院接受放疗的老年食管癌患者298例,收集临床资料,根据肺部感染情况分为感染组124例和未感染组174例。其中感染组患者根据CURB-65评分评估感染程度又分为轻度感染36例、中度感染58例、重度感染30例。两组患者均检测Cdyn、RAW、感染指标[血清降钙素原(procalcitonin, PCT)、白细胞介素-6(interleukin-6, IL-6)和血管紧张素Ⅱ(angiotensin Ⅱ, Ang Ⅱ)]水平,比较两组患者和不同感染程度患者检测结果差异,采用相关分析评估Cdyn、RAW与PCT、IL-6、Ang Ⅱ水平的相关性,采用受试者工作特征曲线(ROC曲线)评估Cdyn、Raw对感染的预测效能。**结果** 感染组患者Cdyn水平低于未感染组,RAW水平高于未感染组,差异有统计学意义($P<0.05$);感染组中,轻度感染者Cdyn水平高于中度、重度感染者,RAW、PCT、IL-6和Ang Ⅱ水平低于中度、重度感染者;中度感染者Cdyn水平高于重度感染者,RAW、PCT、IL-6和Ang Ⅱ水平低于重度感染者;差异均有统计学意义($P<0.05$);肺部感染患者Cdyn水平与PCT、IL-6、Ang Ⅱ、感染程度负相关($r=-0.501, -0.430, -0.367, -0.484, P<0.05$),RAW与PCT、IL-6、Ang Ⅱ、感染程度正相关($r=0.483, 0.395, 0.374, 0.423, P<0.05$);Cdyn和RAW评估老年食管癌放疗后肺部感染的曲线下面积分别为0.898(95%可信区间:0.857~0.930)、0.823(95%可信区间:0.775~0.865),Cdyn+RAW联合评估时的曲线下面积为0.959(95%可信区间:0.930~0.979),联合评估效能高于单项评估。**结论** 老年食管癌患者放疗后出现肺部感染则Cdyn水平降低,RAW、PCT、IL-6和Ang Ⅱ水平升高,且Cdyn、RAW水平均与PCT、IL-6、Ang Ⅱ相关,应用Cdyn和RAW联合预警患者肺部感染具有良好效能。

【关键词】 老年食管癌 放疗 肺部感染 肺动态顺应性 气道阻力

Relationship Between Dynamic Compliance and Airway Resistance and Infection Indicators in Elderly Patients With Lung Infection After Radiotherapy for Esophageal Cancer TIAN Zhaoxia¹, TIAN Weiwei^{2△}, LI Hongmei¹, XUE Xiaoyan¹, ZHAO Na¹. 1. Fenyang College of Shanxi Medical University, Fenyang 032200, China; 2. Shanxi Fenyang Hospital, Fenyang 032200, China

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【Abstract】 Objective To investigate the performance of using lung dynamic compliance (Cdyn) and airway resistance (RAW) levels to predict lung infection in elderly esophageal cancer patients who have undergone radiotherapy. **Methods** A total of 298 elderly esophageal cancer patients who received radiotherapy at Shanxi Fenyang Hospital between October 2017 and July 2022 were retrospectively enrolled and their clinical data were collected. The patients were divided into an infection group (124 cases) and a non-infection group (174 cases) according to their status of lung infection. Then, in the infection group, CURB-65 score was used to assess the severity of the patients' lung infection and the patients were further divided into subgroups accordingly, with 36 cases in the mild infection subgroup, 58 cases in the moderate infection subgroup, and 30 cases in the severe infection subgroup. The levels of Cdyn, RAW, and infection indicators, including serum procalcitonin (PCT), interleukin-6 (IL-6), and angiotensin Ⅱ (Ang Ⅱ), were measured in both groups of patients and the differences in the findings were compared between the infection and the non-infection groups and among patients with infection of varying degrees of severity. The correlation between Cdyn and RAW and the levels of PCT, IL-6, and Ang Ⅱ was analyzed. Receiver operating characteristic (ROC) curve was used to evaluate the performance of predicting infection with Cdyn and RAW. **Results** The Cdyn level of patients in the infection group was lower than that of patients in the non-infection group, while the RAW level of the infection group was higher than that of the non-infection group ($P<0.05$). Among the infection subgroup, the level of Cdyn of the mild infection subgroup was higher than those of the moderate and severe infection subgroups, while the levels of RAW, PCT, IL-6, and Ang Ⅱ of the mild infection subgroup were lower than those of the moderate severe subgroups. The level of Cdyn of the moderate infection subgroup was higher than that of the severe infection subgroup, while the RAW, PCT, IL-6, and Ang Ⅱ levels of

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the moderate infection subgroup were lower than those of the severe infection subgroup, with all difference being statistically significant ($P < 0.05$). The Cdyn level of patients with lung infection was negatively correlated with PCT, IL-6, and Ang II levels and the severity of infection ($r = -0.501, -0.430, -0.367, \text{ and } -0.484$, respectively, $P < 0.05$), while RAW was positively correlated with PCT, IL-6, and Ang II levels and the severity of infection ($r = 0.483, 0.395, 0.374, \text{ and } 0.423$, respectively, $P < 0.05$). The area under the curve (AUC) of Cdyn and RAW for predicting lung infection in elderly patients with esophageal cancer after radiotherapy were 0.898 (95% confidence interval [CI]: 0.857-0.930) and 0.823 (95% CI: 0.775-0.865), respectively, and the AUC of combined evaluation of Cdyn and RAW was 0.959 (95% CI: 0.930-0.979), which suggested that the predictive performance of combined evaluation was better than evaluation with Cdyn or RAW alone. **Conclusion** When elderly esophageal cancer patients develop lung infection after radiotherapy, their Cdyn level is decreased, while the levels of RAW, PCT, IL-6, and Ang II are increased. In addition, the levels of Cdyn and RAW are correlated with the PCT, IL-6, and Ang II levels. The combined use of Cdyn and RAW shows good performance for predicting lung infection in patients.

【Key words】 Elderly esophageal cancer patients Radiotherapy Lung infection Lung dynamic compliance Airway resistance

食管癌是临床常见消化道恶性肿瘤,好发于50岁以上的中老年人群,在我国发病率高,死亡率在各类癌症中居于第四位,老年患者预后更差^[1]。食管癌早期症状不明显,多数患者确诊时已属中晚期,此时主要治疗手段为放疗、化疗,放疗能够通过放射光线杀死肿瘤细胞,减少肿瘤的复发或转移,延长患者生存时间,改善其预后^[2-3]。但是放疗在杀灭肿瘤细胞的同时也会损伤照射部位的正常细胞,随着治疗的进行或疾病的发展,患者体质与免疫功能下降,容易发生肺部感染^[4]。老年食管癌患者身体机能差、肺功能较弱,出现肺部感染后易出现肺功能减退,而肺功能减退又易使患者反复发生肺部感染,形成恶性循环,增加患者的痛苦、治疗时间和医疗费用支出,影响治疗效果,因此肺部感染是导致患者死亡的重要原因之一^[5-6]。既往研究已关注到了癌症放疗后肺部感染造成的肺功能减退,但多集中于肺通气指标,对于能够反映气流受限情况和肺部氧代谢状态的肺的动态顺应性(dynamic compliance, Cdyn)、气道阻力(airway resistance, RAW)的研究较少^[7]。此外,肺部感染时机体存在炎症应激反应和免疫应答反应,降钙素原(procalcitonin, PCT)、白细胞介素-6(interleukin-6, IL-6)、血管紧张素 II(angiotensin, Ang II)等因子是反映机体炎症应激和免疫调节的重要指标,在肺部感染后存在明显变化^[8],但关于三者与Cdyn、RAW在食管癌放疗后肺部感染中的关系仍缺乏相关研究。基于此,本研究分析老年食管癌放疗后肺部感染患者呼吸指标Cdyn、RAW与感染指标的关系,并分析二者预测感染的效能。

1 对象与方法

1.1 一般资料

回顾性纳入2017年10月-2022年7月在山西省汾阳医

院接受放疗治疗的298例老年食管癌患者,根据肺部感染情况分为感染组124例和未感染组174例。其中感染组患者根据CURB-65评分^[9]评估感染程度分为轻度感染36例、中度感染58例、重度感染30例。纳入标准:参照《食管癌诊疗规范(2018年版)》^[10]诊断标准,经病理学检查确诊;年龄 ≥ 60 岁;均完成1个疗程以上的放疗;肺部感染患者符合第9版《内科学》^[9]中肺部感染的标准;放化疗前无感染;临床资料完整。排除标准:食管鳞癌复发、转移患者;合并其他恶性肿瘤;肝肾功能不全;存在全身感染、贫血、恶病质等严重并发症;合并免疫系统、中枢神经系统、血液系统等系统性的疾病。本研究获山西医科大学汾阳学院伦理委员会批准(2023030)。

1.2 研究方法

1.2.1 资料收集

由专人从医院病历系统调取患者资料,内容包括性别、年龄、体质量指数、病理分期、合并症情况等一般资料以及病原菌鉴定结果、呼吸功能指标、实验室检查指标等。

1.2.2 放疗方案及随访管理

单纯三维适形放疗,照射剂量50~60 Gy/次,5~6次/周。放疗期间每周至少完成1次辅助检查。放疗结束后采用定期复查方式随访,每次随访时进行1次辅助检查。辅助检查包括血常规、肝肾功能、食管钡餐检查、胸片、腹部超声、病原菌检测等。

1.2.3 病原菌鉴定

采集患者痰标本,清晨应用生理盐水漱口,取患者咳深部痰液,放置无菌痰盒内,无菌送检,应用梅里埃VITEK 2 Compact全自动细菌鉴定仪测定患者病原菌情况,严格按照《全国临床检验操作规程》^[11]操作。质控菌株:大肠埃希菌ATCC 25922、铜绿假单胞菌ATCC 9027、

金黄色葡萄球菌ATCC 25923。

1.2.4 检测呼吸功能

采用肺功能检测仪(瑞士Schiller公司)检测患者的呼吸功能指标,检测指标包括Cdyn、RAW。由专业检验人员严格按照仪器和试剂说明书进行操作,检测时患者含口器并平静呼吸至呼气末水平稳定,平静呼气末让患者做浅快呼吸收集呼气流量-体描箱压曲线计算得出RAW,常规麻醉后插入仪器导管测试获得Cdyn。

1.2.5 PCT、IL-6和Ang II检测

抽取两组患者5 mL外周静脉血,高速离心,取血清,采用全自动化学发光仪(美国贝克曼公司)检测PCT水平,采用酶联免疫吸附法(试剂盒购自深圳康兰生物技术有限公司)检测IL-6和Ang II水平。

1.3 统计学方法

数据分析采用SPSS22.0软件,连续正态分布变量以 $\bar{x} \pm s$ 表示,采用多组间比较单因素方差分析,两两比较采用LSD-*t*检验;分类变量以频数及百分数表示,采用 χ^2 检验分析;相关性分析采用Pearson相关分析法和Spearman相关分析法,经受试者工作特征曲线(ROC曲线)评估Cdyn、Raw对感染的预测效能。检验水准为 $\alpha_{\text{双侧}}=0.05$ 。

2 结果

2.1 两组患者一般资料比较

两组患者的一般资料比较差异无统计学意义($P > 0.05$)。见表1。

2.2 两组患者Cdyn和RAW比较

感染组患者Cdyn水平低于未感染组,RAW水平高于未感染组,差异均有统计学意义($P < 0.05$);感染组中,轻度感染者Cdyn水平高于中度、重度感染者,RAW水平低于中度、重度感染者,差异均有统计学意义($P < 0.05$);中度感染者Cdyn水平高于重度感染者,RAW水平低于重度感染者,差异均有统计学意义($P < 0.05$)。见表2。

2.3 两组患者PCT、IL-6和Ang II水平比较

感染组患者PCT、IL-6和Ang II水平均高于未感染组

表 1 两组患者一般资料比较

Table 1 Comparison of general data between the two groups of patients

Indicator	Non-infection group (n=174)	Infection group (n=124)	t/χ^2	P
(Male/female)/case	107/67	82/42	0.670	0.413
Age/yr., $\bar{x} \pm s$	69.21±5.21	68.94±5.07	0.446	0.656
Body mass index/(kg/m ²), $\bar{x} \pm s$	22.85±2.76	22.73±3.01	0.356	0.722
Pathological staging/case (%)			1.923	0.382
II a	43 (24.71)	30 (24.19)		
II b	58 (33.33)	33 (26.61)		
III	73 (41.95)	61 (49.19)		
Complication/case (%)				
Hypertension	55 (31.61)	30 (24.19)	1.953	0.162
Diabetes mellitus	34 (19.54)	36 (29.03)	3.630	0.057
Cardiovascular disease	31 (17.82)	18 (14.52)	0.574	0.449

表 2 感染组与未感染组患者Cdyn、RAW水平比较 ($\bar{x} \pm s$)

Table 2 Comparison of Cdyn and RAW levels between the two groups of patients ($\bar{x} \pm s$)

Group	n	Cdyn/(mL/cmH ₂ O)	RAW/(cmH ₂ O/[L·S])
Non-infection	174	40.61±9.35	16.01±3.50
Infection	124	25.80±5.53 ^a	20.70±3.58 ^a
Mild infection	36	33.27±4.04	16.58±1.45
Moderate infection	58	25.15±3.44 ^b	21.10±1.78 ^b
Severe infection	30	19.48±2.84 ^{b,c}	24.87±2.46 ^{b,c}

Cdyn: lung dynamic compliance; RAW: airway resistance. ^a $P < 0.05$, vs. the non-infection group; ^b $P < 0.05$, vs. the mild infection subgroup; ^c $P < 0.05$, vs. the moderate infection subgroup.

($P < 0.05$);感染组中,PCT、IL-6和Ang II水平比较:轻度<中度<重度($P < 0.05$),两两比较差异均有统计学意义($P < 0.05$)。见表3。

2.4 感染组Cdyn、RAW与PCT、IL-6、Ang II、感染程度的相关性

感染组患者Cdyn水平与PCT、IL-6、Ang II、感染程度负相关($P < 0.05$),RAW与PCT、IL-6、Ang II、感染程度正相关($P < 0.05$)。见表4。

表 3 感染组与未感染组患者PCT、IL-6和Ang II水平比较 ($\bar{x} \pm s$)

Table 3 Comparison of PCT, IL-6, and Ang II levels between the two groups of patients ($\bar{x} \pm s$)

Group	n	PCT/(ng/mL)	IL-6/(ng/mL)	Ang II/(pg/mL)
Non-infection	174	5.97±1.18	7.19±1.12	50.38±11.43
Infection	124	17.60±6.60 ^a	19.17±5.14 ^a	67.21±12.15 ^a
Mild infection	36	10.21±2.05	15.42±2.32	58.01±10.00
Moderate infection	58	17.50±2.06 ^b	18.61±4.19 ^b	67.08±8.92 ^b
Severe infection	30	26.67±4.27 ^{b,c}	24.75±4.57 ^{b,c}	78.50±10.58 ^{b,c}

PCT: procalcitonin; IL-6: interleukin-6; Ang II: angiotensin II. ^a $P < 0.05$, vs. the non-infection group; ^b $P < 0.05$, vs. the mild infection subgroup; ^c $P < 0.05$, vs. the moderate infection subgroup.

表 4 感染组患者Cdyn、RAW与PCT、IL-6、Ang II、感染程度的相关性
Table 4 Correlation of Cdyn and RAW levels of the infection group with PCT, IL-6, and Ang II levels and infection severity

Item		PCT	IL-6	Ang II	Infection severity
Cdyn	<i>r</i>	-0.501	-0.430	-0.367	-0.484
	<i>P</i>	<0.001	<0.001	<0.001	<0.001
RAW	<i>r</i>	0.483	0.395	0.374	0.423
	<i>P</i>	<0.001	<0.001	<0.001	<0.001

Cdyn: lung dynamic compliance; RAW: airway resistance; PCT: procalcitonin; IL-6: interleukin-6; Ang II: angiotensin II.

2.5 Cdyn和RAW评估老年食管癌患者放疗后肺部感染的效能

ROC曲线显示, Cdyn、RAW、Cdyn+RAW在所有老

年食管癌放疗后患者中评估是否肺部感染的曲线下面积 (area under the curve, AUC)分别为0.898、0.823、0.959, 联合评估效能高于单项评估, 见表5及图1。

表 5 Cdyn和RAW评估老年食管癌患者放疗后是否肺部感染的ROC曲线指标

Table 5 ROC curve indicators of Cdyn and RAW for predicting lung infection in elderly patients after radiotherapy for esophageal cancer

Indicator	AUC	Standard error	95% CI	Cut-off value	Sensitivity/%	Specificity/%
Cdyn	0.898	0.0174	0.857 - 0.930	33.36 mL/cmH ₂ O	89.52	75.29
RAW	0.823	0.024	0.775 - 0.865	17.78 cmH ₂ O/(L·S)	77.42	72.99
Combined evaluation	0.959	0.010	0.930 - 0.979	-	93.55	73.56

AUC: area under curve; 95% CI: 95% confidence interval; Cdyn: lung dynamic compliance; RAW: airway resistance.

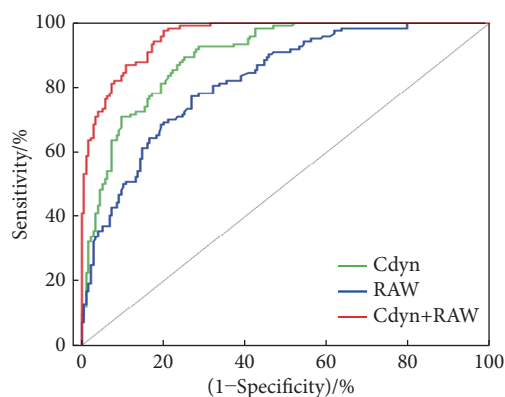


图 1 Cdyn和RAW评估老年食管癌患者放疗后肺部感染的ROC曲线
Fig 1 ROC curves of Cdyn and RAW for predicting lung infection in elderly patients after radiotherapy for esophageal cancer

3 讨论

中晚期食管癌病死率较高, 多数患者死于并发症而非癌症本身^[12]。肺部感染成为了食管癌患者死亡的首要原因^[13], 早期防治食管癌放疗后的肺部感染对延长患者生存时间具有重要意义。

正常情况下, 气道阻力约占肺通气阻力的1/3, 且随着呼吸发生周期性变化。而肺部感染时, 在各种致病因子作用下, 会发生毛细血管损伤、肺泡上皮损伤及气道炎性反应等, 气道顺应性随之降低, 气道阻力随之增大。因

此, 食管癌肺部感染主要体现在肺通气及肺换气功能两方面的双呼吸功能障碍^[14]。Cdyn是人体呼吸周期中气流未阻断时的肺顺应性, 其水平与肺组织弹性和气道压力情况有关^[15]。RAW是气道内单位气体流量所产生的压力差, 反映气道阻塞程度^[16]。本研究显示, 感染组患者Cdyn水平低于未感染组而RAW水平高于未感染组, 且随着感染程度的加深, Cdyn水平不断降低, RAW水平不断升高, 说明老年食管癌放疗后出现肺部感染的患者肺功能受损, 不同感染程度的患者存在不同程度的呼吸功能异常, 提示临床检测Cdyn和RAW水平可为肺部感染诊疗提供有效的参考信息。此外, 食管癌患者出现肺部感染后, 机体的防御功能失衡, 细菌可产生大量内毒素和PCT、IL-6、Ang II等炎症、应激因子, 损伤气道, 影响肺部氧代谢状态^[17-18]。PCT、IL-6和Ang II均是目前临床评估感染、应激、炎症状态时常用的血生化指标, 临床应用价值较高^[19-20]。本研究中, 感染组患者PCT、IL-6和Ang II水平均明显高于未感染组, 且随着感染程度的加深, 三者水平也随之升高, 表明肺部感染后, 老年食管癌患者处于炎症应激的状态, 机体持续生成炎症和应激因子, 且PCT、IL-6和Ang II水平均能够反映患者炎症应激的活跃程度。而相关性分析发现, Cdyn水平与PCT、IL-6、Ang II、感染程度负相关, RAW与PCT、IL-6、Ang II、感染程度正相关, 说明老年食管癌患者放疗后出现肺部感染后,

肺功能状态与炎症应激因子的异常表达存在相关性。可能的机制是肺部感染后,病原菌分泌的大量内毒素和炎症应激因子,促进PCT、IL-6和Ang II的释放,使呼吸道产生炎症损伤,使Cdyn水平降低,RAW水平升高,肺功能受损,对肺部氧化代谢造成不良影响。而肺功能降低又可反过来创造病原菌大量繁殖的有利环境,加重感染,形成恶性循环。因此,密切监测Cdyn、RAW、PCT、IL-6和Ang II水平均可了解食管癌患者放疗后的肺部感染状况。本研究ROC曲线分析显示,Cdyn和RAW均可用于评估老年食管癌放疗后肺部感染的情况,且二者联合评估的效能高于单项评估,提示Cdyn和RAW可作为老年食管癌患者放疗期间肺部感染的预警指标,提醒医师对感染的诊治。

综上所述,老年食管癌患者放疗后出现肺部感染会造成肺功能的下降,体现为Cdyn水平降低、RAW水平升高,还会使机体处于应激状态,体现为PCT、IL-6和Ang II水平的升高,且随着感染程度的加深,肺功能不断降低,应激状态活跃,可检测Cdyn和RAW预警肺部感染,提醒临床医师及时评估患者是否存在肺部感染,以便早期进行肺部感染诊治,提高治疗效果。但本研究样本量不足,且未能评估各指标在诊断肺部感染和肺部感染分级中的效能,有待改进。

* * *

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