

· 论著 ·

血清PCT、IL-6及MIP-2水平评估重型颅脑损伤气管切开术后并发肺部感染的价值

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【摘要】目的探讨血清降钙素原(PCT)、白细胞介素-6(IL-6)及巨噬细胞炎性蛋白-2(MIP-2)水平评估重型颅脑损伤气管切开术后并发肺部感染的价值。**方法**2020年5月至2021年10月前瞻性收集145例重型颅脑损伤病人,入院当天行气管切开术,气管切开术前及术后1、3、5 d检测血清PCT、IL-6、MIP-2水平,记录入院1周内肺部感染情况。**结果**入院1周,86例确诊肺部感染,肺部感染发生率为59.31%(86/145)。肺部病人气管切开术后3、5 d血清PCT、IL-6、MIP-2水平明显增高($P<0.05$)。ROC曲线分析显示,气管切开术后3 d血清PCT、IL-6及MIP-2水平增高评估肺部感染的曲线下面积(AUC)为0.907(95% CI 0.848~0.949),灵敏度为96.51%,特异度为76.27%,准确度为88.28%;气管切开术后5 d血清PCT、IL-6及MIP-2水平增高评估肺部感染的AUC为0.898(95% CI 0.837~0.942),灵敏度为94.19%,特异度为74.58%,准确度为86.21%。气管切开术后3、5 d血清PCT、IL-6及MIP-2水平增高评估肺部感染与临床诊断结果一致性的Kappa值分别为0.750、0.706。**结论**重型颅脑损伤气管切开术后发生肺部感染时血清PCT、IL-6、MIP-2水平明显升高,因此,术后监测血清PCT、IL-6、MIP-2水平有助于临床早期诊断肺部感染。

【关键词】重型颅脑损伤;气管切开术;肺部感染;血清;降钙素原;白细胞介素-6;巨噬细胞炎性蛋白-2

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Value of serum levels of PCT, IL-6 and MIP-2 in assessing secondary pulmonary infection in patients with severe traumatic injury after tracheotomy

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【Abstract】 Objective To explore the value of serum levels of procalcitonin (PCT), interleukin-6 (IL-6), and macrophage inflammatory protein-2 (MIP-2) in assessing pulmonary infection in patients with severe traumatic injury (sTBI) after tracheotomy. **Methods** One hundred and fifty-five patients with sTBI were prospectively collected from May 2020 to October 2021. Tracheotomy was performed on the day of admission. Serum PCT, IL-6, and MIP-2 levels were detected before tracheotomy and on days 1, 3, and 5 after tracheotomy, and the pulmonary infection within 1 week of admission was recorded. **Results** Within 1 week of admission, 86 patients were diagnosed with pulmonary infection, and the incidence of pulmonary infection was 59.31% (86/145). The levels of serum PCT, IL-6, and MIP-2 in patients with pulmonary infection significantly increased on days 3 and 5 after tracheotomy ($P<0.05$). ROC curve analysis showed that the area under the curve (AUC) for assessing pulmonary infection using the increased levels of serum PCT, IL-6, and MIP-2 on day 3 after tracheotomy was 0.907 (95% CI 0.848~0.949), with a sensitivity of 96.51%, specificity of 76.27%, and accuracy of 88.28%; the AUC for assessing pulmonary infection using the increased levels of serum PCT, IL-6, and MIP-2 on day 5 after tracheotomy was 0.898 (95% CI 0.837~0.942), with a sensitivity of 94.19%, specificity of 74.58%, and accuracy of 86.21%. The Kappa values for the consistency between the assessment of pulmonary infection using the increased levels of serum PCT, IL-6, and MIP-2 on days 3 and 5 after tracheotomy and the clinical diagnosis results were 0.750 and 0.706, respectively. **Conclusion** When pulmonary infection occurs after tracheotomy in patients with sTBI, the levels of serum PCT, IL-6, and MIP-2 increase significantly. Therefore, monitoring the levels of serum PCT, IL-6, and MIP-2 is helpful for the early clinical diagnosis of pulmonary infection in patients with sTBI after the tracheotomy.

【Key words】 Severe traumatic injury; Tracheotomy; Pulmonary infection; Serum; Procalcitonin; Interleukin-6; Macrophage inflammatory protein-2

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重型颅脑损伤病情发展快且凶险,致残率和病死率较高^[1]。气管切开术是维持重型颅脑损伤病人呼吸道通畅、改善机体缺氧的有效措施,但同时也破坏了机体防御系统,痰液易滞留于肺部滋生微生物,引发肺部感染,影响病人预后^[2,3]。目前,依据临床表

现结合影像学检查诊断肺部感染,但重型颅脑损伤病人早期临床表现不典型,并且影像学表现与症状存在差异,易延误病情^[4]。血清指标检测简便、快捷,在肺部感染评估中的应用也越来越广泛^[5]。白细胞计数和中性粒细胞百分比是临床评估感染的常规指标,但受个体、药物等多种因素影响,在非感染性疾病或组织创伤中水平也会升高^[6]。血清降钙素原(procalcitonin, PCT)是真菌感染、细菌性炎症的特异性指标,大型外科手术后常通过监测其浓度变化评估术后感染风险^[7]。白细胞介素-6(interleukin 6, IL-6)是常见的促炎因子,在感染和炎症发生后,其水平上升早于PCT和C-反应蛋白(creactiveprotein, CRP)等^[8]。巨噬细胞炎性蛋白-2(macrophage inflammatory proteins-2, MIP-2)是作用于中性粒细胞的炎症趋化因子,参与支气管、肺部多种炎症反应^[9]。基于此,本研究观察重型颅脑损伤气管切开术后病人血清PCT、IL-6、MIP-2水平的变化,探讨三者对此类病人并发肺部感染的评估价值,旨在为临床诊治提供参考。

1 资料与方法

1.1 病例选择标准 纳入标准:①符合重型颅脑损伤标准;②生存时间>7 d;③高流量吸氧后病情无好转,伴有呕吐和呼吸困难,经病情评估,短时间内不能清醒,给予气管切开术;④家属均签署本研究知情同意书。排除标准:①入院时已存在肺部感染;②伴有慢性阻塞性肺病等其他肺部疾病;③全身严重多发伤;④合并免疫系统、血液性系统疾病或恶性肿瘤;⑤肝肾等重大器官功能不全。

1.2 研究对象 2020年5月至2021年10月前瞻性收集145例重型颅脑损伤,其中男性80例,女性65例;年龄42~84岁,平均(63.68 ± 10.65)岁;交通事故伤66例,打击伤41例,高空坠落38例。

1.3 肺部感染诊断标准 入院1周内根据临床表现诊断肺部感染,符合以下5项中任意3项即可判定为肺部感染^[10]:①咳嗽、咳脓痰、气促;②伴有发热,白细胞计数升高;③痰培养显示病原菌阳性;④肺部有干湿性啰音;⑤胸部X线检查显示肺部炎性改变。

1.4 血清PCT、IL-6、MIP-2的检测 气管切开术前(T0)及气管切开术后1 d(T1)、3 d(T2)、5 d(T3)采集外周静脉血,分离血清,采用免疫发光测定法检测血清PCT水平,试剂盒购自博锐德生物科技有限公司;采用酶联免疫吸附法检测血清IL-6、MIP-2水平,试剂盒购自武汉博士德生化科技有限公司。血清PCT

水平正常参考范围<0.5 ng/ml;血清IL-6水平正常参考范围<7 pg/ml;血清MIP-2水平正常参考范围在10~30 pg/ml。

1.5 统计学方法 采用SPSS 26.0软件分析;正态分布计量资料以 $\bar{x}\pm s$ 描述,采用独立样本t检验;重复测量资料采用重复测量方差分析和LSD-t检验;计数资料采用 χ^2 检验;采用受试者工作特征(ROC)曲线分析血清PCT、IL-6、MIP-2水平评估病人并发肺部感染的价值;采用Kappa检验评估血清PCT、IL-6、MIP-2水平诊断与临床诊断的一致性,Kappa值0~0.20代表两者一致性差,0.21~0.40代表两者一致性一般,0.41~0.60代表两者具有中等一致性,0.61~0.80代表两者具有高度一致性,0.80~1代表两者几乎完全一致; $P<0.05$ 为差异有统计学意义。

2 结 果

2.1 肺部感染发生率 入院1周,86例确诊肺部感染,肺部感染发生率为59.31%(86/145)。

2.2 并发肺部感染病人的临床特征 与无肺部感染病人相比,并发肺部感染病人的吸烟比例明显增高($P<0.05$),而性别构成、年龄、体质质量指数、合并基础疾病比例、受伤原因、入院GCS评分均无统计学差异($P>0.05$)。见表1。

2.3 并发肺部感染病人血清PCT、IL-6、MIP-2水平变化 气管切开术前、术后1 d,并发肺部感染病人血清PCT、IL-6、MIP-2水平与无肺部感染病人均无统计学差异($P>0.05$);气管切开术后3、5 d,并发肺部感染病人血清PCT、IL-6、MIP-2水平明显增高($P<0.05$)。见表2。

2.4 ROC曲线分析结果 气管切开术后3、5 d血清PCT、IL-6、MIP-2水平增高均对重型颅脑损伤气管切开术后病人并发肺部感染具有一定的诊断价值(图1、表3),但是三者联合诊断价值明显优于单一指标(图1、表3)。

2.5 诊断一致性 气管切开术后3、5 d血清PCT、IL-6及MIP-2水平增高评估肺部感染与临床诊断结果一致性的Kappa值分别为0.750、0.706。

3 讨 论

重型颅脑损伤是常见的外科急症,常因高空作业事故、交通事故等所致,包括脑损伤、头皮损伤、颅内血肿等^[11],常需进行气管切开术以给予生命支持,但气管切开术后易诱发肺部感染,影响术后恢复,甚至危及病人生命安全。本文145例重型颅脑损伤气

表1 重型颅脑损伤气管切开术后并发肺部感染病人的临床特征

Table 1 Clinical features of patients with severe traumatic brain injury complicated with pulmonary infection after tracheotomy

临床特征	肺部感染组(n=86)	无发病感染组(n=59)	统计值	P值
性别(例)			$\chi^2=0.242$	0.623
男	46(53.49%)	34(57.63%)		
女	40(46.51%)	25(42.37%)		
年龄(岁)	63.45±10.42	64.02±10.31	$t=0.325$	0.746
体质量指数(kg/m ²)	23.07±2.04	23.26±2.11	$t=0.543$	0.588
吸烟史(例)	35(40.70%)	14(23.73%)	$\chi^2=4.504$	0.034
合并基础疾病(例)				
高血压	31(36.05%)	19(32.20%)	$\chi^2=0.229$	0.632
糖尿病	28(32.56%)	21(35.59%)	$\chi^2=0.144$	0.704
冠心病	24(27.91%)	13(22.03%)	$\chi^2=0.635$	0.426
受伤原因(例)			$\chi^2=0.960$	0.619
交通事故	37(43.02%)	29(49.15%)		
打击伤	24(27.91%)	17(28.81%)		
高空坠落	25(29.07%)	13(22.03%)		
入院GCS评分(分)	6.46±1.12	6.25±1.14	$t=1.101$	0.273

表2 重型颅脑损伤气管切开术后并发肺部感染病人血清PCT、IL-6、MIP-2水平变化

Table 2 Changes in serum levels of PCT, IL-6, and MIP-2 in patients with severe traumatic brain injury complicated with pulmonary infection after tracheotomy

评估指标	评估时机	肺部感染组	无肺部感染组	统计值	P值
血清PCT(ng/ml)	T0	0.47±0.09	0.45±0.08	$F_{\text{组间}}=10.652$	$P_{\text{组间}}<0.001$
	T1	0.53±0.10	0.44±0.07		
	T2	1.42±0.28*	0.47±0.09		
	T3	1.55±0.19*	0.45±0.08		
血清IL-6(pg/ml)	T0	15.42±2.81	14.71±2.66	$F_{\text{组间}}=24.795$	$P_{\text{组间}}<0.001$
	T1	21.75±4.52	20.65±3.64		
	T2	68.48±10.04*	28.06±5.23		
	T3	75.39±9.84*	22.52±3.40		
血清MIP-2(pg/ml)	T0	30.61±5.67	29.58±5.51	$F_{\text{组间}}=15.635$	$P_{\text{组间}}<0.001$
	T1	40.61±6.70	38.68±6.32		
	T2	79.05±8.14*	45.22±7.16		
	T3	82.85±9.41*	40.70±7.02		

注:与无肺部感染组相应值比,* $P<0.05$;PCT.降钙素原;IL-6.白细胞介素-6;MIP-2.巨噬细胞炎性蛋白-2;T0.气管切开术前;T1.气管切开术后1 d;T2.气管切开术后3 d;T3.气管切开术后5 d

管切开术后肺部感染发生率为26.03%,这与杨欣刚等^[12]报道的24.24%大致相吻合,提示重型颅脑损伤病人气管切开术后肺部感染风险较高。因此,需对这类病人肺部感染情况进行评估,以便临床及时采取干预和管理措施,改善病人预后。

本研究发现,并发肺部感染病人吸烟比例明显

增高,提示吸烟可能对气管切开术后肺部感染有不利影响。有调查显示,长期吸烟病人易诱发肺部慢性炎症,增加易感性,增加术后肺部感染的风险^[13]。

IL-6是响应感染和组织损伤而产生的一个重要细胞因子,在机体免疫防御机制中起着至关重要的作用,在炎症发生后,水平迅速升高,随后诱导PCT、

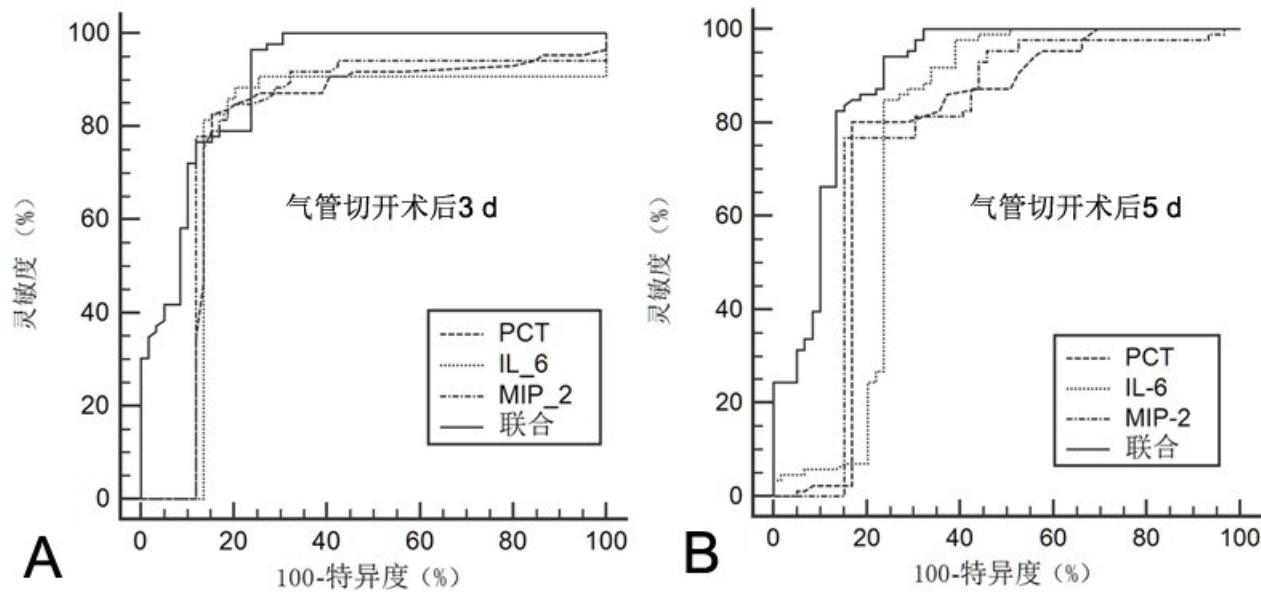


图 1 血清 PCT、IL-6、MIP-2 水平评估重型颅脑损伤气管切开术后并发肺部感染的 ROC 曲线

Figure 1 ROC curves of the serum levels of PCT, IL-6, and MIP-2 for the evaluation of pulmonary infection in patients with severe traumatic brain injury after tracheotomy

表 3 ROC 曲线分析血清 PCT、IL-6、MIP-2 水平评估重型颅脑损伤气管切开术后并发肺部感染的效果

Table 3 ROC curve analysis of the serum levels of PCT, IL-6, and MIP-2 for assessing the pulmonary infection in patients with severe traumatic brain injury after tracheotomy

预测指标	评估时机	截断值	灵敏度	特异度	曲线下面积	95%置信区间	准确率	阳性预测值	阴性预测值
血清 PCT	T2	0.85 ng/ml	82.56%	84.75%	0.792	0.717~0.855	83.45%	88.75%	76.92%
	T3	0.6 ng/ml	80.23%	83.05%	0.767	0.689~0.833	81.38%	87.34%	74.24%
血清 IL-6	T2	50.22 pg/ml	88.37%	79.66%	0.778	0.701~0.842	84.83%	86.36%	82.46%
	T3	32.17 pg/ml	84.88%	76.27%	0.763	0.685~0.830	81.38%	83.91%	77.59%
血清 MIP-2	T2	70.88 pg/ml	77.91%	88.14%	0.807	0.742~0.852	82.07%	90.54%	73.24%
	T3	52.66 pg/ml	76.74%	84.75%	0.774	0.697~0.839	80.00%	88.00%	71.43%
三者联合	T2	——	96.51%	76.27%	0.907	0.848~0.949	88.28%	85.57%	93.75%
	T3	——	94.19%	74.58%	0.898	0.837~0.942	86.21%	84.38%	89.80%

注:PCT. 降钙素原;IL-6. 白细胞介素-6;MIP-2. 巨噬细胞炎性蛋白-2;T2. 气管切开术后 3 d;T3. 气管切开术后 5 d

CRP 等水平升高^[14]。林维强等^[15]报道,胸外术后病人出现肺部感染时,血清 IL-6 水平异常升高,并加重病情,对临床评估肺部感染有一定价值。PCT 在机体内的稳定性较好,正常状态下,血清含量极低,而当机体被细菌感染,细菌菌毛、内毒素等刺激目标细胞产生 PCT,导致其水平明显升高,期间机体释放的 IL-6、TNF- α 等炎性因子可促进 PCT mRNA 的表达,造成血清 PCT 水平进一步升高^[16]。Wang 等^[17]指出,细菌性肺炎病人血清 PCT 水平显著高于健康对照组,可作为肺炎病人早期评估和治疗的生物标志物。MIP-2 是介导炎症反应的关键蛋白,与肺部感染有密切关系,当 MIP-2 水平异常升高,刺激细胞表面黏附分子表达,诱发炎症反应,释放大量白细胞介

素。鲍利改等^[18]指出,MIP-2 在慢性心力衰竭合并肺部感染的病人中异常高表达,影响病人心肌功能和预后,可作为临床病情评估的指标之一。重型颅脑损伤气管切开术后病人发生肺部感染,会加重机体应激反应、炎症反应,导致炎性因子水平升高。肖华等^[19]研究发现,重型颅脑损伤病人并发肺部感染后 3、5 d 血清 PCT、IL-6、CRP 水平明显增高。本研究结果也显示,并发肺部感染病人气管切开术后 3、5 d 血清 PCT、IL-6、MIP-2 水平明显上升;而且 ROC 曲线分析结果显示,气管切开术后 3、5 d 血清 PCT、IL-6、MIP-2 水平增高均对重型颅脑损伤气管切开术后病人并发肺部感染具有一定的诊断价值,但是三者联合诊断价值明显优于单一指标。

由于PCT到达峰值所需时间较长,不利于感染的早期评估,而IL-6在感染发生后2 h即可达高峰,灵敏度高,但在创伤、外科手术等情况下IL-6亦存在不同程度的升高,不具有肺部感染的特异性。MIP-2在机体内有双重作用,不仅介导炎症反应,在感染中起重要作用,还可特异性趋化中性粒细胞,是肺防御的重要介质,此单一指标评估肺部感染有一定局限性。鉴于三个指标特异性和敏感性不同,本研究将三者联合检测,可优势互补,在不降低特异度的情况下提高了灵敏度,显著提高了评估价值。另外,气管切开术后3、5 d血清PCT、IL-6、MIP-2水平评估重型颅脑损伤气管切开术后病人并发肺部感染与临床诊断结果相比,Kappa值分别为0.750、0.706,提示气管切开术后3、5 d血清PCT、IL-6、MIP-2水平评估肺部感染与临床常规诊断具有较高的一致性。

总之,血清PCT、IL-6、MIP-2水平是评估重型颅脑损伤气管切开术后并发肺部感染的有效指标,而且三者联合评估的价值更高。

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