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胆道支架植入治疗恶性梗阻性黄疸术后并发症的发生因素分析*

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摘要 目的:探讨与分析胆道支架植入治疗恶性梗阻性黄疸术后并发症的发生因素。**方法:**采用回顾性总结研究方法,2015年10月-2019年10月选择在本院重症监护病房(Intensive Care Unit, ICU)诊治的恶性梗阻性黄疸患者112例,所有患者都给予胆道支架植入治疗,记录术后感染并发症发生情况。调查患者的临床资料并进行影响因素分析。**结果:**112例患者术后发生感染并发症18例,发生率为16.1%,其中胆道感染5例,肺部感染4例,切口感染9例。112例患者术后7d的血清介素-6(inter-leukin-6, IL-6)、肿瘤坏死因子- α (tumor necrosis factor- α , TNF- α)、谷草转氨酶(aspartate aminotransferase, AST)、谷丙转氨酶(alanine transaminase, ALT)值低于术前,CD4⁺细胞比例高于术前($P<0.05$),CD8⁺细胞比例在手术前后对比差异无统计学意义($P>0.05$)。Pearson分析显示术后感染与APACHE II评分、住院时间、糖尿病、吸烟、术前IL-6值、术前CD4⁺细胞比例存在相关性($P<0.05$)。Logistic回归分析显示APACHE II评分、住院时间、糖尿病、吸烟、术前IL-6值、术前CD4⁺细胞比例导致患者术后感染发生的主要因素($P<0.05$)。**结论:**胆道支架植入治疗恶性梗阻性黄疸能抑制炎症因子的释放,促进恢复患者的免疫功能,改善患者的肝功能,但伴随有感染并发症的发生,APACHE II评分、住院时间、糖尿病、吸烟、术前IL-6值、术前CD4⁺细胞比例是导致患者术后感染发生的主要因素。

关键词:胆道支架植入;恶性梗阻性黄疸;感染;多因素分析;白介素-6

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Analysis on the Factors of Postoperative Complications of Biliary Stent Implantation for Malignant Obstructive Jaundice*

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ABSTRACT Objective: To explore and analysis the factors of complications after biliary stent implantation in the treatment of malignant obstructive jaundice. **Methods:** From October 2015 to October 2019, Used retrospective research methods, 112 cases of patients with malignant obstructive jaundice who were diagnosed and treated in the Intensive Care Unit (ICU) of our hospital were selected as the research objects. All patients were given biliary tract stent implantation treatment, recorded postoperative infection complications. Investigated the clinical data of patients and analyzed the influencing factors. **Results:** There were 18 cases of postoperative infection complications in the 112 patients that the incidence rate were 16.1%, included 5 cases of biliary tract infection, 4 cases of lung infection, and 9 cases of incision infection. The postoperative 7 d of serum IL-6, TNF- α , AST, and ALT values of 112 patients were lower than that of preoperative, and the ratio of CD4⁺ cells were higher than that of preoperative ($P<0.05$). The ratio of CD8⁺ cells were in the operation ere no statistically significant difference compared between before and after surgery ($P>0.05$). Pearson analysis showed that postoperative infection were correlated with APACHE II score, hospital stay, diabetes, smoking, preoperative IL-6 value and preoperative CD4⁺ cell ratio ($P<0.05$). Logistic regression analysis showed that APACHE II score, length of stay, diabetes, smoking, preoperative IL-6 value, preoperative CD4⁺ cell ratio were the main influence factors of postoperative infection in patients ($P<0.05$). **Conclusion:** Biliary stent implantation in the treatment of malignant obstructive jaundice can inhibit the release of inflammatory factors, promote the recovery of the patient's immune function, and improve the patient's liver function, but it is accompanied by the occurrence of infection complications, APACHE II score, hospital stay, diabetes, smoking, The preoperative IL-6 value and the preoperative CD4⁺ cell ratio are the main factors affect the incidence of postoperative infection in patients.

Key words: Biliary stent implantation; Malignant obstructive jaundice; Infection; Multivariate analysis; Interleukin-6

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前言

恶性梗阻性黄疸(malignant obstructive jaundice, MOJ)是指肝胆胰恶性肿瘤组织压迫效应或转移、浸润肝外胆道,导致胆汁排出受阻的危重疾病^[1]。该病在临床上主要表现为恶心呕吐、皮肤黄染、皮肤瘙痒、腹痛、陶土样大便,可伴有肝肾功能衰竭、胆道感染、胃肠道出血等,具有一定的死亡率,严重影响患者的身心健康^[2,3]。手术为恶性梗阻性黄疸的主要治疗方法,包括经内镜逆行胰胆管造影(Endoscopic retrograd Cholangio-Pancreatography, ERCP)、胆道支架植入术、经皮肝穿刺胆道引流术(Percutaneous transhepatic biliary drainage, PTCD)等,能减轻对于患者的创伤,能提高患者的生存率^[4-6]。其中胆道支架植入术具有很好的微创性,能显著改善患者生活质量^[7,8]。但是任何手术都有一定的创伤,特别是胆道支架植入容易造成水电解质及体内酸碱平衡失调,导致脂肪和脂溶性维生素的吸收障碍,伴有患者体内胆汁的大量流失,易发生术后并发症^[9,10]。感染是胆道支架植入治疗恶性梗阻性黄疸术后的常见并发症,包括胆道感染、肺部感染、切口感染等,严重情况下可造成患者围手术期死亡^[11-13]。本文探讨并分析了胆道支架植入治疗恶性梗阻性黄疸术后并发症的发生因素,以有助于防治早期感染并发症的发生。现总结报道如下。

1 资料与方法

1.1 研究对象

采用回顾性总结研究方法,2015年10月-2019年10月选择在本院重症监护病房(Intensive Care Unit, ICU)诊治的恶性梗阻性黄疸患者112例,其中胰腺癌45例,胆管细胞癌33例,胆囊癌17例,肝癌17例。纳入标准:临床与调查资料完整者;本院伦理委员会批准了此次研究;顺利完成胆道支架植入手术;患者年龄18~65岁,围手术期无死亡情况;急性生理与慢性健康评分(Acute Physiology and Chronic Health Evaluation,

APACHE II)≥12分。排除标准:第二次或多次接受胆道支架植入手术;有严重精神疾患不能合作者;存在胃肠道功能障碍者;临床与调查资料缺乏者;妊娠与哺乳期妇女;住院期间因肿瘤晚期多脏器功能衰竭死亡的患者;胆道支架植入不成功者。

1.2 手术方法

所有患者都给予胆道支架植入治疗,术后禁饮食并卧床休息,应用生长抑素、胰酶抑制物对症治疗,并给予肠内外营养支持。

1.3 观察指标

(1)记录所有患者术后14 d发生的感染并发症情况,包括胆道感染、肺部感染、切口感染等。(2)记录与测定两组患者术前1 d、术后14 d的肝功能、免疫功能和炎症状态,肝功能主要检测指标为血清AST与ALT含量,免疫功能主要检测指标为CD4⁺和CD8⁺值,炎症因子主要检测指标为IL-6和TNF-α。(3)调查所有患者的一般资料,包括APACHE II评分、性别、年龄、体重指数、住院时间、病因、合并疾病、生活行为等。

1.4 统计方法

选择SPSS 19.00软件对本研究所有患者的数据进行分析,计量资料运用“均数±标准差”表示,运用t检验;计数资料采用百分比表示,对比为卡方 χ^2 分析,相关性分析采用Pearson分析,将单因素分析中差异具有统计学意义的自变量进行Logistic回归分析,检验水准为 $\alpha=0.05$ 。

2 结果

2.1 术后感染并发症发生情况

112例患者术后发生感染并发症18例,发生率为16.1%,其中胆道感染5例,肺部感染4例,切口感染9例。

2.2 肝功能、免疫功能和炎症状态变化对比

112例患者术后7 d的血清IL-6、TNF-α、AST、ALT值低于术前,CD4⁺细胞比例高于术前($P<0.05$),CD8⁺细胞比例在手术前后对比差异无统计学意义($P>0.05$),见表1。

表1 112例患者手术前后肝功能、免疫功能和炎症状态变化对比($\bar{x}\pm s$)

Table 1 Comparison of changes in liver function, immune function and inflammatory state of 112 patients before and after surgery ($\bar{x}\pm s$)

Time point	n	IL-6(pg/mL)	TNF-α(ng/L)	AST(U/L)	ALT(U/L)	CD4 ⁺ (%)	CD8 ⁺ (%)
Preoperative	112	30.37±2.78	56.39±3.26	152.49±14.19	142.01±7.88	24.29±3.84	28.11±4.29
7 d postoperatively	112	11.56±1.47*	10.62±2.08*	41.29±2.84*	41.29±4.84*	45.98±8.14*	27.49±5.25

Note: Compared with the preoperative, * $P<0.05$.

2.3 相关性分析

在112例患者中,Pearson分析显示术后感染与APACHE

II评分、住院时间、糖尿病、吸烟、术前IL-6值、术前CD4⁺细胞比例存在相关性($P<0.05$),见表2。

表2 胆道支架植入治疗恶性梗阻性黄疸术后感染并发症与临床资料的相关性(n=112)

Table 2 Correlation between postoperative infection complications and clinical data of biliary stent implantation for malignant obstructive jaundice (n=112)

Index	APACHE II score	length of sta	Diabetes mellitus	Smoking	IL-6 preoperative value	CD4 ⁺ cell ratio before operation
r	0.871	0.535	0.611	0.492	0.549	0.499
P	0.000	0.005	0.001	0.012	0.006	0.011

2.4 影响因素分析

在112例患者中,以术后感染作为因变量,以APACHE II

评分、住院时间、糖尿病、吸烟、术前IL-6值、术前CD4⁺细胞比例作为自变量,Logistic回归分析显示APACHE II评分、住院时

间、糖尿病、吸烟、术前 IL-6 值、术前 CD4⁺ 细胞比例导致患者 术后感染发生的主要影响因素($P<0.05$),见表 3。

表 3 胆道支架植入治疗恶性梗阻性黄疸术后并发症发生的多因素分析($n=112$)

Table 3 Multivariate analysis of complications after biliary stent implantation for malignant obstructive jaundice ($n=112$)

Index	β	SE	Wald	P	OR	95%CI
APACHE II score	1.289	0.564	11.729	0.000	3.628	1.209-10.888
length of sta	1.278	0.553	5.342	0.006	3.568	1.214-10.472
Diabetes mellitus	1.788	0.378	10.564	0.000	2.119	1.093-4.873
Smoking	1.774	0.356	4.678	0.003	2.194	1.098-4.644
IL-6 preoperative value	1.883	0.928	4.114	0.004	6.546	2.444-13.573
CD4 ⁺ cell ratio before operation	1.445	0.876	3.490	0.010	4.294	1.774-23.582

3 讨论

恶性梗阻性黄疸为胰腺癌、胆管细胞癌、胆囊癌、肝癌等压迫、生长及浸润而引起的肝内外胆管阻塞,从而导致肝内胆汁淤积的危重疾病^[14]。由于该病的临床表现不特异,早期难以发现,故大多数患者在就诊时多为晚期,导致预后比较差^[15,16]。手术为恶性梗阻性黄疸的主要治疗方法,也是唯一的根治方法,特别是胆道支架植入具有微创、成功率高等特点^[17]。但是很多患者存在免疫力低下、肠液逆流、肠粘膜屏障损伤等不良因素,胆道支架植入术后患者常因为发生严重感染并发症,最终导致肠源性内毒素入血,从而造成患者预后恢复不良,甚或引起患者围手术期死亡^[18,19]。本研究显示 112 例患者术后发生感染并发症 18 例,发生率为 16.1%,其中胆道感染 5 例,肺部感染 4 例,切口感染 9 例,这与学者肖修林^[20]的研究结果患者术后感染并发症的发生率为 16.5%结果类似,表明胆道支架植入治疗恶性梗阻性黄疸术后感染比较常见。并且主要为胆道感染,从机制上分析其原因可能是恶性梗阻性黄疸可使得机体对各种营养物质吸收不良,导致肠黏膜萎缩^[21],同时患者全身免疫功能下降,胆汁引流受阻、淤积,易致细菌繁殖^[22,23]。

恶性梗阻性黄疸术后过度的促炎反应是导致患者预后变差的重要原因,特别是过度促炎反应后继发的抗炎反应可造成机体免疫功能抑制,使得患者处于一种严重免疫紊乱状态,并且机体的代谢紊乱也会导致机体特异性和非特异性免疫活性细胞功能下降^[24,25]。本研究显示 112 例患者术后 7 d 的血清 IL-6、TNF- α 、AST、ALT 值低于术前,CD4⁺ 细胞比例高于术前,CD8⁺ 细胞比例在手术前后对比差异无统计学意义,学者吴子鑫^[26]等人的研究结果也支持了上述结论。表明胆道支架植入治疗恶性梗阻性黄疸能抑制炎症因子的释放,促进恢复患者的免疫功能,改善患者的肝功能。然而学者陈伟伟^[27]等人报道这一治疗方法虽然对患者的肝功能有所改善,但是临床观察是中发现其改善程度远远达不到理想状态,这也有可能与肿瘤梗阻所在的位置处于肝门有重要关系。

恶性梗阻性黄疸的病理机制是由于胆汁不能排入肠道,体内内毒素增多,胆汁酸盐对肠道内有害细菌的生长失去抑制作用,从而导致肝内外胆管梗阻^[28]。手术治疗虽然可切除恶性病变,但是手术风险比较大,术后容易出现感染并发症^[29]。本研究 Pearson 分析显示术后感染与 APACHE II 评分、住院时间、糖尿

病、吸烟、术前 IL-6 值、术前 CD4⁺ 细胞比例存在相关性;Logistic 回归分析显示 APACHE II 评分、住院时间、糖尿病、吸烟、术前 IL-6 值、术前 CD4⁺ 细胞比例是导致患者术后感染发生的主要影响因素。从机制上分析,APACHE II 评分主要是通过患者生理状态的量化参数进行评分,具有客观性与准确性等特点,可以衡量患者的病情^[30]。住院时间是住院患者预后的重要危险因素,与患者病情的严重程度和预后相关,也是转入高危病房的预测因子^[31]。糖尿病、吸烟可使得患者出现感染易感情况,可表现为机体凝血功能障碍、严重营养不良等^[32]。炎症因子的大量释放表明患者处于过度应激状态,从而降低细胞的免疫反应,不利于患者的康复^[33,34]。本研究也有一定的不足,没有进行长期随访,样本数量也比较少,将在后续研究中进行探讨。

总之,胆道支架植入治疗恶性梗阻性黄疸能抑制炎症因子的释放,促进恢复患者的免疫功能,改善患者的肝功能,但临床需注意患者常伴随有感染并发症的发生,其 APACHE II 评分、住院时间、糖尿病、吸烟、术前 IL-6 值、术前 CD4⁺ 细胞比例是导致患者术后感染发生的主要影响因素。

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