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胰十二指肠切除患者术后腹腔感染的危险因素 和病原学特征及药敏试验分析*

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摘要 目的:探讨胰十二指肠切除患者术后腹腔感染的危险因素,并对其进行病原学特征及药敏试验分析。**方法:**回顾性分析 2016 年 1 月到 2018 年 12 月期间在中国人民解放军联勤保障部队第 967 医院接受胰十二指肠切除术治疗的 60 例患者的临床资料,分析术后腹腔感染的危险因素。根据细菌培养结果和药敏试验情况对术后腹腔感染患者的病原菌分布情况及其耐药性进行分析。**结果:**单因素分析显示术中输血量、肺部感染、胆瘘、胰瘘均与腹腔感染的发生有关($P<0.05$)。多因素 Logistic 回归分析显示,术中输血量 ≥ 1000 mL、肺部感染、胆瘘、胰瘘均是胰十二指肠切除患者术后发生腹腔感染的危险因素($P<0.05$)。20 例术后腹腔感染患者的腹腔引流液中共培养出 54 株菌株,其中革兰阳性菌 23 株(42.59%)、革兰阴性菌 28 株(51.85%)、真菌 3 株(5.56%),主要革兰阳性菌(粪肠球菌、屎肠球菌、表皮葡萄球菌)对环丙沙星、红霉素敏感率低,均低于 17.00%,对利奈唑胺、万古霉素敏感率高,均为 100.00%,主要革兰阴性菌(大肠埃希菌、肺炎克雷伯菌、阴沟肠杆菌)对头孢他啶、头孢唑林和哌拉西林的敏感率较低,均低于或等于 25.00%,对庆大霉素、亚胺培南的敏感率较高,均高于或等于 80.00%。**结论:**术中输血量过多以及发生了肺部感染、胆瘘、胰瘘均是胰十二指肠切除患者术后发生腹腔感染的危险因素,临床上应根据药敏试验结果针对性地使用抗菌药物。

关键词:胰十二指肠切除术;腹腔感染;危险因素;病原学特征;药敏试验

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Risk Factors, Etiological Characteristics and Drug Sensitivity Test Analysis of Postoperative Abdominal Infection in Patients with Pancreaticoduodenectomy*

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ABSTRACT Objective: To investigate the risk factors of abdominal infection after pancreaticoduodenectomy and analyze its etiological characteristics and drug sensitivity test. **Methods:** The clinical data of 60 cases undergoing pancreaticoduodenectomy in the 967th Hospital of the PLA Joint Logistics Support Force from January 2016 to December 2018 were retrospectively analyzed, the risk factors for postoperative abdominal infection were analyzed. The distribution and drug resistance of pathogenic bacteria in patients with postoperative abdominal infection were analyzed according to the results of bacterial culture and drug sensitivity test. **Results:** Univariate analysis showed that intraoperative blood transfusion, pulmonary infection, biliary fistula and pancreatic fistula were all related to the occurrence of abdominal infection ($P<0.05$). Multivariate Logistic regression analysis showed that intraoperative blood transfusion greater than 1000 mL, pulmonary infection, biliary fistula and pancreatic fistula were risk factors for abdominal infection after pancreaticoduodenectomy ($P<0.05$). A total of 54 strains were cultured in the peritoneal drainage fluid of 20 patients with postoperative abdominal infection. Among them, 23 strains (42.59%), 28 strains (51.85%) and 3 strains (5.56%) were Gram-positive bacteria. The main Gram-positive bacteria (*Enterococcus faecalis*, *Staphylococcus epidermidis*) were less sensitive to ciprofloxacin and erythromycin, all were below 17.00%, the sensitivity rates to linezolid and vancomycin were 100.00%. The main Gram-negative bacteria (*Escherichia coli*, *Klebsiella pneumoniae* and *Enterobacter cloacae*) less sensitive to ceftazidime, cefazolin and piperacillin, all were below or equal to 25.00%, the susceptibility rates to gentamicin and imipenem were higher, all were higher or equal to 80.00%. **Conclusion:** Excessive blood transfusion during operation and occurrence of pulmonary infection, biliary fistula and pancreatic fistula are risk factors for abdominal infection after pancreaticoduodenectomy. Antibiotics should be use targetedly in clinic according to the results of drug sensitivity test.

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前言

胰十二指肠切除术是治疗慢性胰腺炎、胰腺外伤、胰头癌、胆总管中下段恶性肿瘤的常用手术方法,尤其适用于符合手术适应证的胰腺癌患者^[1,2]。近年随着医学技术的发展,胰十二指肠切除术的病死率已经有所降低,但该术式操作复杂、手术时间长、手术创伤大,易造成腹腔感染、胰瘘、胆瘘、肺部感染、胃排空延迟等手术并发症,严重影响患者的术后康复^[3-5]。腹腔感染是指患者在术后出现发热、腹痛、腹胀等症状,并可引发全身炎症反应综合征,若未能得到及时的治疗,可导致脓毒性休克、多器官功能不全综合征等疾病,危及患者的生命^[6,7]。病原菌检测及药敏试验分析是了解病原菌分布情况及其耐药性的主要方法,在得出结果后可针对性地选取合适的抗菌药物进行治疗,提高临床疗效^[8-10]。为进一步降低我院胰十二指肠切除患者术后腹腔感染概率及方便进行针对性治疗,本研究分析了胰十二指肠切除患者术后腹腔感染的危险因素和病原学特征及耐药性,以期为我院防治胰十二指肠切除患者术后腹腔感染提供参考,现将研究结果整理报道如下。

1 资料与方法

1.1 一般资料

回顾性分析于2016年1月到2018年12月期间在中国人民解放军联勤保障部队第967医院接受胰十二指肠切除术治疗的60例患者的临床资料,纳入标准:①均符合胰十二指肠切除术的适应证;②临床资料齐全;③患者及其家属对本研究知情同意。排除标准:①在术前接受了放化疗或免疫治疗者;②存在精神障碍者;③合并有急性或慢性感染性疾病者。60例患者中男性33例,女性27例,年龄38-65岁,平均年龄 (53.36 ± 4.67) 岁,疾病类型:胰腺癌28例,壶腹部癌10例,十二指肠癌8例,胆管癌6例,慢性胰腺炎6例,胰腺外伤2例。

1.2 腹腔感染的诊断标准

患者在术后符合以下诊断标准中的任何一条即可认定为发生了腹腔感染:①患者在术后出现发热、白细胞计数增多(大于 $10 \times 10^9/L$)等全身感染症状,并出现腹痛、腹胀、明显腹膜炎体征;②B超、CT等影像学检查显示腹腔内存在脓肿、脓性渗出等感染灶;③腹腔引流液是脓性液体,并且细菌学培养结果显示为阳性^[11]。

1.3 资料收集和病原菌检测

收集患者的临床资料,整理好一般人口学特征(性别、年龄)、手术情况(术前减黄、手术时间、术中输血量)、病理学检查结果、术后并发症情况(肺部感染、胆瘘、胰瘘、胃排空延迟)等资料,并根据腹腔感染的诊断标准判断胰十二指肠切除术后出现腹腔感染的病例数,收集术后出现腹腔感染的患者的腹腔引流液进行细菌培养,采用全自动微生物分析仪(法国生物梅里埃公司,型号:Vitek 2 Compact)进行细菌鉴定,采用纸片扩散法进行药敏试验。

1.4 统计学方法

采用SPSS20.0进行统计分析,以率表示计数资料,进行 χ^2 检验,采用多因素Logistic回归分析术后发生腹腔感染的危险因素,检验水准 $\alpha=0.05$ 。

2 结果

2.1 胰十二指肠切除患者术后腹腔感染的单因素分析

60例胰十二指肠切除患者在术后共有20例(33.33%)出现腹腔感染,单因素分析结果显示,年龄、性别、手术时间、术前减黄、病理学检查结果、胃排空延迟与胰十二指肠切除患者术后发生腹腔感染无关($P>0.05$),术中输血量、肺部感染、胆瘘、胰瘘是胰十二指肠切除患者术后发生腹腔感染的影响因素($P<0.05$),见表1。

表1 胰十二指肠切除患者术后腹腔感染的单因素分析[n(%)]
Table 1 Univariate analysis of abdominal infection after pancreaticoduodenectomy[n(%)]

Indexes	n	Abdominal infection		χ^2	P	
		Positive	Negative			
Age(years old)	≥ 50	34	12(35.29)	22(64.71)	0.136	0.713
	<50	26	8(30.77)	18(69.23)		
Gender	Male	33	13 (39.39)	20(60.61)	1.212	0.271
	Female	27	7(25.93)	20(74.07)		
Intraoperative blood transfusion(mL)	≥ 1000	18	11(61.11)	7(38.89)	8.929	0.003
	<1000	42	9(21.43)	33(78.57)		
Operative time(h)	≥ 8	15	8(53.33)	7(46.67)	3.600	0.058
	<8	45	12(26.67)	33(73.33)		
Preoperative reduction of jaundice	Yes	26	9(34.62)	17(65.38)	0.034	0.854
	No	34	11(32.35)	23(67.65)		

表 1 胰十二指肠切除患者术后腹腔感染的单因素分析[n(%)](续表)

Table 1 Univariate analysis of abdominal infection after pancreaticoduodenectomy[n(%)]

Indexes		n	Abdominal infection		χ^2	P
			Positive	Negative		
Pathological examination results	Malignant	52	18(34.62)	34(65.38)	0.018	0.893
	Benign	8	2(25.00)	6(75.00)		
Pulmonary infection	Yes	10	7(70.00)	3(30.00)	5.415	0.020
	No	50	13(26.00)	37(74.00)		
Biliary fistula	Yes	8	6(75.00)	2(25.00)	5.210	0.022
	No	52	14(26.92)	38(73.08)		
Pancreatic fistula	Yes	12	8(66.67)	4(33.33)	5.742	0.017
	No	48	12(25.00)	36(75.00)		
Delayed gastric emptying	Yes	5	2(40.00)	3(60.00)	0.027	0.869
	No	55	18(32.73)	37(67.27)		

2.2 胰十二指肠切除患者术后腹腔感染的多因素 Logistic 回归分析

以术后是否发生腹腔感染为因变量(是=1,否=0),单因素分析中的术中输血量、肺部感染、胆瘘、胰瘘等指标为自变量,

纳入多因素 Logistic 回归模型中。结果显示,术中输血量 ≥ 1000 mL、肺部感染、胆瘘、胰瘘均是胰十二指肠切除患者术后发生腹腔感染的危险因素($P<0.05$),见表 2。

表 2 胰十二指肠切除患者术后腹腔感染的多因素 Logistic 回归分析

Table 2 Multivariate Logistic regression analysis of abdominal infection after pancreaticoduodenectomy

Risk factors	Regression coefficient	Standard error	Wald χ^2	P	OR	95%CI
Intraoperative blood transfusion ≥ 1000 mL	0.964	0.423	5.194	0.023	2.622	1.144-6.008
Pulmonary infection	1.212	0.526	5.309	0.021	3.360	1.198-9.421
Biliary fistula	1.034	0.521	3.939	0.047	2.812	1.013-7.808
Pancreatic fistula	1.365	0.548	6.204	0.013	3.916	1.338-11.462

2.3 胰十二指肠切除患者术后腹腔感染的病原菌分析

20 例术后腹腔感染患者的腹腔引流液中共培养出 54 株菌株,其中革兰阳性菌 23 株(42.59%)、革兰阴性菌 28 株(51.85%)、真菌 3 株(5.56%),排名前 6 的菌株分别为大肠埃希菌、粪肠球菌、肺炎克雷伯菌、屎肠球菌、表皮葡萄球菌和阴沟肠杆菌。见表 3。

2.4 胰十二指肠切除患者术后腹腔感染主要革兰阳性菌药敏试验分析

主要革兰阳性菌(粪肠球菌、屎肠球菌、表皮葡萄球菌)对环丙沙星、红霉素敏感率低,均低于 17.00%,对利奈唑胺、万古霉素敏感率高,均为 100.00%,此外表皮葡萄球菌对利福平、喹奴普丁/达福普汀的敏感率也为 100.00%。见表 4。

2.5 胰十二指肠切除患者术后腹腔感染主要革兰阴性菌药敏试验分析

主要革兰阴性菌(大肠埃希菌、肺炎克雷伯菌、阴沟肠杆菌)对头孢他啶、头孢唑林和哌拉西林的敏感率较低,均低于或等于 25.00%,对庆大霉素、亚胺培南的敏感率较高,均高于或等于 80.00%。见表 5。

表 3 胰十二指肠切除患者术后腹腔感染的病原菌分析[n(%)]

Table 3 Pathogenic bacteria analysis of abdominal infection after pancreaticoduodenectomy[n(%)]

Strain types	Name of strain	n
Gram-positive bacteria(n=23)	<i>Enterococcus faecalis</i>	8(14.81)
	<i>Enterococcus faecium</i>	7(12.96)
	<i>Staphylococcus epidermidis</i>	6(11.11)
	<i>Staphylococcus aureus</i>	2(3.70)
Gram-negative bacteria(n=28)	<i>Escherichia coli</i>	10(18.52)
	<i>Klebsiella pneumoniae</i>	8(14.81)
	<i>Enterobacter cloacae</i>	5(9.26)
	<i>Pseudomonas aeruginosa</i>	2(3.70)
	<i>Acinetobacter citri</i>	2(3.70)
	<i>Xanthomonas maltophilia</i>	1(1.85)
Fungus(n=3) White fungus		3(5.56)

表 4 胰十二指肠切除患者术后腹腔感染主要革兰阳性菌药敏试验分析[n(%)]

Table 4 Drug susceptibility test of major Gram-positive bacteria in abdominal infection after pancreaticoduodenectomy[n(%)]

Antibacterial drugs	<i>Enterococcus faecalis</i> (n=8)	<i>Enterococcus faecium</i> (n=7)	<i>Staphylococcus epidermidis</i> (n=6)
Ciprofloxacin	1(12.50)	1(14.29)	1(16.67)
Gentamicin	4(50.00)	2(28.57)	3(50.00)
Levofloxacin	5(62.50)	1(14.29)	3(50.00)
Linezolid	8(100.00)	7(100.00)	6(100.00)
Rifampicin	2(25.00)	1(14.29)	6(100.00)
Quinoputin/Dafoputin	1(12.50)	5(71.43)	6(100.00)
Tetracycline	1(12.50)	2(28.57)	5(83.33)
Vancomycin	8(100.00)	7(100.00)	6(100.00)
Erythromycin	0(0.00)	0(0.00)	1(16.67)

表 5 胰十二指肠切除患者术后腹腔感染主要革兰阴性菌药敏试验分析[n(%)]

Table 5 Drug susceptibility test of major Gram-negative bacteria in abdominal infection after pancreaticoduodenectomy[n(%)]

Antibacterial drugs	<i>Escherichia coli</i> (n=10)	<i>Klebsiella pneumoniae</i> (n=8)	<i>Enterobacter cloacae</i> (n=5)
Ampicillin/Sulbactam	1(10.00)	4(50.00)	1(20.00)
Amikacin	9(90.00)	7(87.50)	5(100.00)
Ceftazidime	2(20.00)	2(25.00)	1(20.00)
Cefazolin	1(10.00)	2(25.00)	1(20.00)
Ciprofloxacin	4(40.00)	5(62.50)	4(80.00)
Gentamicin	8(80.00)	7(87.50)	4(80.00)
Imipenem	10(100.00)	8(100.00)	5(100.00)
Piperacillin/Tazobactam	7(70.00)	7(87.50)	4(80.00)
Piperacillin	2(20.00)	2(25.00)	1(20.00)
Gatifloxacin	6(60.00)	7(87.50)	4(80.00)

3 讨论

胰十二指肠切除术需要将胰头部、胃幽门窦部、十二指肠和胆总管下段切除,并且在切除相应部位后还需要消化道重建,手术操作较为复杂,导致手术时间较长,同时该术式对患者造成的创伤也较大,患者术中出血量多,易导致多种术后并发症^[12,13]。相关研究报道显示^[14,15],胰十二指肠切除术患者术后并发腹腔感染的概率为 20.00%-38.50%,在本研究中 60 例胰十二指肠切除患者在术后共有 20 例(33.33%)出现腹腔感染,发生率较高。为进一步降低我院胰十二指肠切除患者在术后腹腔感染的概率,本研究进行了腹腔感染的危险因素分析,并进行了药敏试验,以更好的防治腹腔感染。

本研究结果显示,术中输血量、肺部感染、胆瘘、胰瘘均是胰十二指肠切除患者术后发生腹腔感染的影响因素,并且均为危险因素,提示术中输血量、肺部感染、胆瘘、胰瘘均与患者术后是否发生腹腔感染密切相关。分析其中原因,术中输血量较大可影响 T 淋巴细胞、自然杀伤细胞的活性,同时会影响巨噬细胞和单核细胞的功能,导致机体的免疫功能受到一定的影响,进而增加了腹腔感染的概率^[16,17]。肺部感染是胰十二指肠切除术的常见并发症,并发肺部感染的患者免疫力通常较低,且

呼吸道存在炎症浸润,随着淋巴循环系统和血液的传播,相关炎症因子也随之传播到全身各处,引发炎症反应综合征,导致腹腔内渗出液增多,刺激手术创口,增加腹腔感染的概率^[18-20]。胆瘘和胰瘘是指胆汁、胰液通过非生理途径外流的现象,是胰十二指肠切除术的常见并发症,胆汁外流进入腹腔后会引发腹膜炎,增加腹腔内的脓液和渗出液,容易引起脓液在腹腔内积聚,从而导致腹腔脓肿发生,进而引起腹腔感染^[21-23]。而胰液外漏时,胰液中的胰酶会腐蚀周围的组织,若引流不畅,胰液和组织腐蚀形成的脓液聚集在腹腔内,引发腹腔感染,甚至可能导致感染性休克^[24,25]。本研究结果还显示,20 例术后腹腔感染患者的腹腔引流液中共培养出 54 株菌株,感染菌株中的主要种类为革兰阴性菌和革兰阳性菌。药敏试验结果显示,主要革兰阳性菌(粪肠球菌、屎肠球菌、表皮葡萄球菌)对环丙沙星、红霉素敏感率低,均低于 17.00%,对利奈唑胺、万古霉素敏感率高,均为 100.00%,此外表皮葡萄球菌对利福平、喹奴普汀/达福普汀的敏感率也为 100.00%。主要革兰阴性菌(大肠埃希菌、肺炎克雷伯菌、阴沟肠杆菌)对头孢他啶、头孢唑林和哌拉西林的敏感率较低,均低于或等于 25.00%,对庆大霉素、亚胺培南的敏感率较高,均高于或等于 80.00%。这提示部分病原菌对一些抗菌药敏已经产生了较强的耐药性,导致药物敏感率较低,这

可能是由于临床上滥用抗菌药物所致^[26-28],因此在临床治疗时,应减少盲目使用广谱抗菌药物的频率,在前期使用广谱抗菌药物后,后期应根据药敏试验结果来进行针对性的治疗^[29,30]。

综上所述,胰十二指肠切除患者术后腹腔感染的危险因素主要有术中输血量过多以及发生了肺部感染、胆瘘、胰瘘,临床上在进行胰十二指肠切除术时应注意精细化操作,减少术中出血量,同时降低肺部感染、胆瘘、胰瘘等并发症的发生,从而减少腹部感染发生的概率。此外,腹部感染患者的主要感染菌株为大肠埃希菌、粪肠球菌、肺炎克雷伯菌、屎肠球菌、表皮葡萄球菌和阴沟肠杆菌,临床上应根据药敏试验结果针对性地使用抗菌药物。

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