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· 专题研究 ·

胰体尾切除术后胰瘘发生率及其影响因素分析

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摘要

背景与目的: 胰瘘是胰体尾切除 (DP) 术后最常见并发症, 其与患者的预后及转归有着密切的关系。因此, 本研究在探讨 DP 术后胰瘘发生情况及其影响因素, 为制订防治措施提供依据。

方法: 回顾性分析 2015 年 1 月—2021 年 2 月中国人民解放军空军军医大学第二附属医院收治的 99 例因胰腺肿瘤行 DP 术患者的临床资料, 统计患者术后胰瘘的发生率, 对可能导致术后胰瘘发生的相关因素行单因素及多因素 Logistic 回归分析。

结果: 99 例患者 DP 术后生化漏发生率为 34.3% (34/99), B 级胰瘘发生率 18.2% (18/99), C 级胰瘘发生率 1.0% (1/99)。单因素分析结果示, 年龄、手术时间、胰管直径及是否联合脾切与胰瘘发生明显有关 (均 $P < 0.05$), 多因素 Logistic 回归分析结果示, 年龄 < 42 岁 ($OR = 0.955$, 95% $CI = 0.914 \sim 0.998$)、手术时间 ≥ 253 min ($OR = 1.013$, 95% $CI = 1.005 \sim 1.021$) 及联合脾切术 ($OR = 4.152$, 95% $CI = 1.043 \sim 16.535$) 为 DP 术后胰瘘的独立危险因素 (均 $P < 0.05$)。

结论: DP 术后有一定的胰瘘发生率, 年龄、手术时间、联合脾切是 DP 术后胰瘘的独立危险因素。这些危险因素评估对术后胰瘘的风险预测及防范措施的制定提供了一定的依据。

关键词

胰腺切除术; 胰腺肿瘤; 胰腺瘘; 危险因素

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Incidence rate of postoperative pancreatic fistula after distal pancreatectomy and the risk factors

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Abstract

Background and Aims: Pancreatic fistula is the most common complication after distal pancreatectomy (DP), and it is closely related to the patient's prognosis and outcome. Therefore, this study was conducted to investigate the occurrence of postoperative pancreatic fistula after DP and the risk factors, so as to provide a basis for developing the protective measures.

Methods: The clinical data of 99 patients undergoing DP for pancreatic tumors in the Second Affiliated Hospital of Air Force Medical University from January 2015 to February 2021 were retrospectively

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analyzed. The incidence rate postoperative pancreatic fistula was calculated, and relevant factors possibly causing postoperative of pancreatic fistula were determined by univariate and multivariate Logistic regression analysis.

Results: In the 99 patients after DP, the incidence of biochemical leakage was 34.3% (34/99), grade B pancreatic fistula was 18.2% (18/99), and grade C pancreatic fistula was 1.0% (1/99), respectively. The results of univariate analysis showed that age, operative time, pancreatic duct diameter and undergoing combined splenectomy or not were significantly related to postoperative pancreatic fistula (all $P < 0.05$). Multivariate Logistic regression analysis results revealed that age < 42 years ($OR = 0.955$, 95% $CI = 0.914 - 0.998$), operative time ≥ 253 min ($OR = 1.013$, 95% $CI = 1.005 - 1.021$) and combined splenectomy ($OR = 4.152$, 95% $CI = 1.043 - 16.535$) were independent risk factors for postoperative pancreatic fistula after DP (all $P < 0.05$).

Conclusion: There is certain incidence rate of pancreatic fistula after DP. Age, operative time, and synchronous splenectomy are independent risk factors for pancreatic fistula after DP. Assessment of these factors may provide certain basis for predicting the risk of postoperative pancreatic fistula and implementing the prevention measures.

Key words

Pancreatectomy; Pancreatic Neoplasms; Pancreatic Fistula; Risk Factors

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胰腺体尾部肿瘤包括:胰腺囊性肿瘤、胰腺癌、胰腺神经内分泌肿瘤、胰腺转移癌,其中胰腺体尾部癌约占胰腺癌的20%~25%^[1],因发病隐匿、手术切除率低^[2-3]、化疗敏感性差^[4]、恶性程度高^[5]等因素导致其预后较差,目前胰腺癌的发病率呈上升趋势^[6],且5年总体生存率仅为8%^[7]。胰体尾切除术(distal pancreatectomy, DP)是治疗胰腺体尾部肿瘤的标准手术方式^[8-9]。术后胰瘘(postoperative pancreatic fistula, POPF)是DP术后最常见并发症,发生率为20%~30%^[10],常常继发腹腔感染^[11]、出血等严重并发症,术后胰瘘作为术后严重并发症的始动因素,且具有导致并发症呈次联反应的风险,其与患者的预后及转归有着密切的关系。本研究回顾性分析2015年1月—2021年2月中国人民解放军空军军医大学第二附属医院胰腺专业组收治的99例因胰腺肿瘤行DP术患者的临床病理资料,拟讨论DP术后胰瘘发生率及其影响因素,旨在为临床提供一定的理论依据。

1 资料与方法

1.1 一般资料

回顾性分析2015年1月—2021年2月中国人民解放军空军军医大学第二附属医院胰腺专业组收治的99例因胰腺肿瘤行DP术患者的临床资料。纳入标准:(1)经影像学评估诊断为胰腺体尾部肿瘤。包括:胰腺癌、胰腺囊性肿瘤、胰腺神经内分泌肿瘤,胰腺转移癌;(2)经影像学评估无远处转移

且肿瘤可切除。排除标准:(1)合并严重心肺疾病;(2)合并其他慢性脏器功能不全;(3)胰头部肿瘤或需行胰十二指肠切除(PD)或全胰切除;(4)术中发现远处转移,仅行腹腔探查。

1.2 方法

1.2.1 手术治疗 所有纳入病例均行DP术,根据不同肿瘤性质,决定是否联合脾脏切除,如:胰体尾部癌、胰腺囊腺癌、胰腺转移癌,手术过程遵循胰腺体尾部癌的相关标准,同时行标准淋巴结清扫。如浆液性囊腺瘤,经术中冷冻排除恶性病变,行保留脾脏的胰体尾切除术。手术方式包括:腹腔镜、腹腔镜辅助、开腹、达芬奇。胰腺残端闭合方式两种:(1)通过闭合器离断,据胰颈厚度选择合适的钉仓。(2)通过手工缝合,超声刀离断,寻找主胰管,行主胰管“8”字缝合+胰腺残端不可吸收线缝合。

1.2.2 术后引流液淀粉酶检测 术后胰腺残端常规放置腹腔引流管。生长抑素及其类似物术后常规预防使用。术后第1天常规检测血常规、凝血系列、肝肾功电解质。术后第3天测腹腔引流液淀粉酶,各根引流管分别检测,其中以高值为当天引流液淀粉酶值,用于胰瘘诊断。

1.2.3 观察指标 胰体尾切除术后胰瘘发生率情况:生化漏发生率、B级胰瘘发生率、C级胰瘘发生率。胰体尾切除术后B级、C级胰瘘治疗情况。影响胰体尾切除术后胰瘘发生相关因素分析。

1.2.4 评价标准 胰瘘诊断依据国际胰瘘学组(ISGPF)2017年发布标准^[12]。胰瘘是胰腺导管上

皮与其他上皮表面的异常通道，内含源自胰腺富含酶类的液体。诊断标准：术后 ≥ 3 d任意量的引流液中淀粉酶浓度高于本机构正常血清淀粉酶浓度上限的3倍以上。根据临床诊断、治疗策略的改变、及患者转归，将胰瘘严重程度分成3级，并对应相应的治疗策略及临床转归。

1.3 统计学处理

应用SPSS 20.0软件进行分析，计量资料以均数 \pm 标准差($\bar{x} \pm s$)或中位数(四分位数间距)[$M(IQR)$]表示，计数资料采用频数(百分比)[$n(\%)$]表示。单因素分析中计量资料用LSD- t 检验或Mann-Whitney U 检验分析，计数资料分析用 χ^2 或Fisher精确检验。将单因素分析中 $P < 0.10$ 的连续数据通过基于最大Youden指数的受试者工作特征曲线(receiver operating characteristic curve, ROC)寻找最佳界点而获取分组。单因素分析中 $P < 0.05$ 或者被认为有临床意义的变量将被纳入非条件二分类Logistic回归进行多因素分析，结果用比值比(odd ratio, OR)及95%置信区间(confidence interval, CI)表示。 $P < 0.05$ 为差异有统计学意义。

2 结果

2.1 DP术后胰瘘发生率情况

99例患者行DP术后，生化漏发生率为34.3% (34/99)，

B级胰瘘发生率18.2% (18/99)，C级胰瘘发生率1.0% (1/99)。

2.2 DP术后胰瘘治疗情况

18例DP术后B级胰瘘患者中，15例患者经积极保守治疗，均顺利康复。3例患者出现发热，2例患者行超声提示腹腔包裹性积液，1例患者行CT提示胰腺周围包裹性积液，均行B超引导下腹腔穿刺置管引流，后经保守治疗康复出院。1例C级胰瘘患者因腹腔出血经历再次手术，术后经积极治疗顺利康复出院。

2.3 DP术后胰瘘的影响因素分析

单因素分析结果显示，年龄、手术时间、胰管直径及是否联合脾切可能与胰瘘发生有关(均 $P < 0.05$)，而其余的术前、术中及术后资料在两组间差异无统计学意义(均 $P > 0.05$) (表1-3)。通过ROC曲线分析，找到年龄、手术时间及胰管直径最佳界点值分别为42.5岁、252.5 min、0.185 cm，再次行单因素分析，结果仍均有统计学意义(均 $P < 0.05$) (表4)。多因素分析结果表明，年龄 < 42 岁(OR=0.955, 95% CI=0.914~0.998)、手术时间 ≥ 253 min(OR=1.013, 95% CI=1.005~1.021)及联合脾切术(OR=4.152, 95% CI=1.043~16.535)是DP术后胰瘘的独立危险因素(均 $P < 0.05$) (表5)。

表1 胰瘘与无胰瘘患者临床基本特征比较

Table 1 Comparison of the general characteristics between patients with and without pancreatic fistula

因素	胰瘘($n=19$)	无胰瘘($n=80$)	$t/Z/\chi^2$	P
年龄(岁, $\bar{x} \pm s$)	45.63 \pm 14.99	53.73 \pm 14.64	-2.157	0.033
BMI(kg/m^2 , $\bar{x} \pm s$)	23.40 \pm 4.22	22.64 \pm 2.97	0.919	0.360
性别[$n(\%)$]				
女	13(68.4)	43(53.8)	1.345	0.246
男	6(31.6)	37(46.2)		
吸烟史[$n(\%)$]				
有	3(15.8)	13(16.2)	0.284	0.594
无	16(84.2)	67(83.8)		
饮酒史[$n(\%)$]				
有	2(10.5)	7(8.7)	0.427	0.513
无	17(89.5)	73(91.3)		
腹部手术史[$n(\%)$]				
有	5(26.3)	19(23.7)	0.125	0.723
无	14(73.7)	61(76.3)		
糖尿病[$n(\%)$]				
有	1(5.3)	15(18.7)	1.788	0.181
无	18(94.7)	65(81.3)		
心血管病[$n(\%)$]				
有	5(26.3)	17(21.2)	0.000	0.995
无	14(73.7)	63(78.8)		

表2 胰痿与无胰痿患者术前及术后生化指标比较

Table 2 Comparison of pre- and postoperative biochemical parameters between patients with and without pancreatic fistula

因素	胰痿(n=19)	无胰痿(n=80)	t/Z	P
术前				
白细胞($\times 10^9/L$, $M(IQR)$)	6.03(4.58~6.55)	5.98(4.89~6.67)	-0.116	0.908
血红蛋白(g/L, $\bar{x} \pm s$)	130.58 \pm 17.001	133.16 \pm 18.273	-0.561	0.576
血小板($\times 10^9/L$, $\bar{x} \pm s$)	214.53 \pm 72.548	191.61 \pm 67.916	1.305	0.195
天门冬氨酸氨基转移酶[U/L, $M(IQR)$]	22.94(17.00~28.00)	24.63(17.00~28.75)	-0.729	0.466
丙氨酸氨基转移酶[U/L, $M(IQR)$]	24.57(14.00~32.00)	27.34(18.00~30.00)	-1.356	0.175
总蛋白(g/L, $\bar{x} \pm s$)	72.85 \pm 8.688	70.75 \pm 8.431	0.971	0.334
白蛋白(g/L, $\bar{x} \pm s$)	43.79 \pm 3.676	42.35 \pm 5.010	1.174	0.243
癌胚抗原[ng/mL, $M(IQR)$]	2.70(0.95~3.29)	7.32(1.49~3.86)	-1.919	0.055
CA125 [U/mL, $M(IQR)$]	24.10(6.39~22.74)	24.04(7.45~19.38)	-0.080	0.936
CA19-9 [U/mL, $M(IQR)$]	259.97(9.16~29.05)	484.12(7.93~132.38)	-0.191	0.848
术后				
白细胞($\times 10^9/L$, $\bar{x} \pm s$)	15.84 \pm 7.234	15.28 \pm 5.891	0.358	0.721
血红蛋白(g/L, $\bar{x} \pm s$)	113.84 \pm 20.017	114.96 \pm 14.748	-0.277	0.783
血小板($\times 10^9/L$, $\bar{x} \pm s$)	181.52 \pm 63.684	170.95 \pm 80.465	0.534	0.595
天门冬氨酸氨基转移酶[U/L, $M(IQR)$]	82.47(31.00~67.00)	54.48(26.00~47.00)	-1.08	0.280
丙氨酸氨基转移酶[U/L, $M(IQR)$]	57.52(32.00~55.00)	49.70(25.00~52.75)	-1.43	0.154
总蛋白(g/L, $\bar{x} \pm s$)	54.88 \pm 10.389	53.05 \pm 9.308	0.752	0.454
白蛋白(g/L, $\bar{x} \pm s$)	30.03 \pm 6.552	29.95 \pm 5.289	0.060	0.953

表3 胰痿与无胰痿患者手术相关资料比较

Table 3 Comparison of the relevant surgical variables between patients with and without pancreatic fistula

因素	胰痿(n=19)	无胰痿(n=80)	t/Z/ χ^2	P
病灶大小[cm, $M(IQR)$]	5.15(2.90~6.30)	5.52(3.00~6.80)	-0.147	0.883
病灶位置[n(%)]				
体部	12(63.2)	38(47.5)	1.506	0.220
尾部	7(36.8)	42(52.5)		
胰颈厚度(cm, $\bar{x} \pm s$)	1.39 \pm 0.31	1.35 \pm 0.33	0.366	0.716
胰管直径[cm, $M(IQR)$]	0.19(0.14~0.24)	0.24(0.18~0.27)	-2.171	0.030
侵犯血管[n(%)]				
是	10(52.6)	41(51.3)	0.012	0.914
否	9(47.4)	39(48.8)		
手术方式[n(%)]				
达芬奇	2(10.5)	13(16.3)	4.848	0.303
腹腔镜	3(15.8)	8(10.0)		
腹腔镜辅助	9(47.4)	29(36.3)		
开放	5(26.3)	30(37.5)		
联合脾切除[n(%)]				
是	10(52.6)	63(78.8)	5.408	0.020
否	9(47.4)	17(21.3)		
残端闭合方式[n(%)]				
闭合器	7(36.8)	35(43.8)	0.300	0.584
手工缝合	12(63.2)	45(56.3%)		
手术时间(min, $\bar{x} \pm s$)	317.11 \pm 76.40	272.65 \pm 86.14	0.918	0.042
术中出血量[mL, $M(IQR)$]	856.31(150.00~1 500.00)	672.25(200.00~1 000.00)	-0.38	0.704
术后病理[n(%)]				
良性	14(73.7)	39(73.6)	3.837	0.050
恶性	5(26.3)	14(26.4)		

表4 胰瘘与无胰瘘患者年龄、手术时间、胰管直径按最佳界点值分层比较[n (%)]

Table 4 Stratified comparison of age, operative time and pancreatic duct diameter between patients with and without pancreatic fistula [n (%)]

因素	是(n=19)	否(n=80)	χ^2	P
年龄(岁)				
<42	10(52.6)	19(23.7)	6.183	0.013
≥42	9(47.4)	61(76.3)		
手术时间(min)				
<253	3(15.8)	41(51.3)	7.819	0.005
≥253	16(84.2)	39(48.7)		
胰管直径(cm)				
<0.185	10(52.6)	22(27.5)	4.433	0.035
≥0.185	9(47.4)	58(72.5)		

表5 影响术后胰瘘的多因素分析

Table 5 Multivariate analysis of factors for postoperative pancreatic fistula

临床相关因素	B	SE	Wald	OR	95% CI	P
年龄(<42岁)	-0.046	0.022	4.277	0.955	0.914~0.998	0.039
手术时间(≥253 min)	0.013	0.004	9.969	1.013	1.005~1.021	0.002
联合脾切	1.424	0.705	4.077	4.152	1.043~16.535	0.043
胰管直径(<0.185 cm)	-5.536	4.905	1.274	0.004	0.000~59.029	0.259

3 讨论

胰瘘是DP术后常见且严重的并发症,发生率为20%~30%,高于PD术^[13-16]。这往往和术后胰瘘的临床危险因素有着密不可分的关系。因此术后胰瘘的危险因素和减少其发生的有效措施是临床的关注点,本研究对POPF发生可能的相关危险因素进行纵向分析,旨在探索POPF发生的独立危险因素,为临床制定减少其发生的有效措施提供一定的理论依据。

本研究共纳入99例行DP手术的病例,其中临床相关的术后胰瘘(clinically relevant postoperative pancreatic fistula, CR-POPF)发生率为19.2%(19/99),本研究中术后胰瘘的发生率低于部分文献报道^[10]。许多研究表明,众多的患者相关因素(年龄^[17-18]、性别^[19]、体质指数^[20]、糖尿病^[21])及手术相关的因素(胰腺质地^[22-23]、胰腺厚度^[21,24],手术时间^[25-27]、联合脾脏切除^[27]、术中出血量^[27]、淋巴结清扫^[1]、开放手术^[28])被报道为DP术后胰瘘的危险因素。本研究结果表明年龄是术后胰瘘的独立危险因素之一,年龄<42岁患者胰瘘发生风险增大。Yoshioka等^[17]的研究结果显示年龄<65岁是术后胰瘘的独立危险因素。同样,在Eguchi等^[18]的研

究中也提示年龄偏小是术后胰瘘的独立危险因素。本研究及上述研究结果均提示年龄越小,术后胰瘘的发生率越高,究其原因可能与胰腺外分泌功能的年龄依赖性下降有关。然而,我们的研究结果中发生胰瘘的年龄界点(42岁)比Yoshioka等^[17]的年龄界点(65岁)更小,究其原因可能与研究所纳病例年龄分布及样本量有一定的关系。但均提示在临床中行DP手术时,面对年龄更小的患者,需提高警惕,积极采取预防措施以减少胰瘘的发生。

手术时间被认为是DP术后胰瘘发生的重要危险因素,本研究中,手术时间≥253 min组的术后胰瘘发生率为84.2%(16/19),多因素分析结果显示手术时间≥253 min、联合脾切是胰瘘的独立危险因素,与以往研究结果一致;一项包含302例DP患者的回顾性研究^[29]结果显示较长的手术时间(超过480 min)与较高的胰瘘发生率相关;一项纳入2 070例病例的Meta分析认为手术时间延长会增加术后胰瘘的风险^[26]。手术时间的延长归因于各种与手术操作有关的因素,例如肿瘤分期较晚、淋巴结清扫、术中出血量多、联合脾脏切除等;其次,更长的手术时间可能预示着更复杂或更困难的手术。因此,在DP术中,精细、准确的操作有

助于控制手术时间,这将对减少胰瘘的发生有极为重要的意义。

临床相关性胰瘘需要胰腺外科医师快速识别并加以干预,以避免严重并发症的发生。对于DP术后胰瘘的预测一直是胰腺外科医师的关注点,风险识别和风险分层可能会有助于预防术后胰瘘,因此,更为准确的风险预测模型或评分系统的创建是亟需解决的问题。

本研究仍存在一定的局限性。首先,本研究是单中心、回顾性的,因此,可能存在一定的偏倚;其次,研究样本量较少,可能一些临床重要数据未被纳入,因此,可能需要更多多中心、前瞻性随机对照试验研究进一步验证,为临床提供更高级别的循证医学证据。

综上,年龄、手术时间、联合脾切是DP术后胰瘘的独立危险因素。这些危险因素对术后胰瘘的风险预测模型或评分系统的建立提供一定的依据,同时为临床医生筛选出高危胰瘘患者提供一定的帮助,对临床工作有极为重要的指导意义。

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