

# 胰十二指肠切除术后急性胰腺炎的现状与发展

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收稿日期: 2023年12月8日; 录用日期: 2024年1月2日; 发布日期: 2024年1月10日

## 摘要

目的: 总结胰十二指肠切除术后急性胰腺炎的研究现状及发展, 旨在探讨胰十二指肠切除术后急性胰腺炎是增加术后并发症发生率及严重程度的预测因子, 以及为预防胰十二指肠切除术后急性胰腺炎提供思路。方法: 检索胰十二指肠切除术后急性胰腺炎的相关文献, 并作一综述。结果: 目前国内外均有使用血清淀粉酶、血清脂肪酶、C反应蛋白及引流液淀粉酶等指标早期预测胰瘘、腹腔感染、腹腔出血、胃排空延迟、胰腺坏死等胰十二指肠切除术后并发症的研究, 但术后胰腺炎对术后并发症影响的研究较少。结论: 术后急性胰腺炎是一个单独的并发症, 具有单独的临床结果, 部分术后胰腺炎在术后早期表现为炎症过程, 但有时也会导致坏死性胰腺炎或其他更严重的临床结局, 提前预防并尽早地诊断术后胰腺炎以防增加术后并发症发生率及严重程度具有一定的临床意义及研究价值。

## 关键词

胰十二指肠切除术, 术后急性胰腺炎, 术后并发症

# Current Status and Development of Acute Pancreatitis after Pancreaticoduodenectomy

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Received: Dec. 8<sup>th</sup>, 2023; accepted: Jan. 2<sup>nd</sup>, 2024; published: Jan. 10<sup>th</sup>, 2024

## Abstract

**Objective:** To summarize the research status and development of acute pancreatitis after pancreaticoduodenectomy, and to explore the role of acute pancreatitis after pancreaticoduodenectomy as a predictor of increasing incidence and severity of postoperative complications, and to provide

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**ideas for prevention of acute pancreatitis after pancreaticoduodenectomy. Methods: The literature on acute pancreatitis after pancreaticoduodenectomy was searched and reviewed. Results: At present, there are studies at home and abroad that use serum amylase, serum lipase, C-reactive protein and drainage fluid amylase to predict early complications after pancreaticoduodenectomy such as pancreatic fistula, abdominal infection, abdominal hemorrhage, delayed gastric emptying, pancreatic necrosis, etc., but there are few studies on the effect of postoperative pancreatitis on postoperative complications. Conclusion: Postoperative acute pancreatitis is a separate complication with a separate clinical outcome. Part of postoperative pancreatitis is characterized by an inflammatory process in the early postoperative period, but sometimes it can also lead to necrotizing pancreatitis or other more serious clinical outcomes. It is of certain clinical significance and research value to prevent and diagnose postoperative pancreatitis as early as possible to avoid increasing the incidence and severity of postoperative complications.**

## Keywords

**Pancreaticoduodenectomy, Postoperative Acute Pancreatitis, Postoperative Complications**

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## 1. 引言

尽管手术技术和围手术期管理有所提高, 但胰十二指肠切除术(Pancreaticoduodenectomy, PD)术后并发症的发生率仍然很高[1] [2] [3]。近年来, 胰腺切除术后急性胰腺炎(postpancreatectomy acute pancreatitis, PPAP)已被认为是一种独立的并发症[4] [5] [6]。目前有研究表明, 术后早期残余胰腺的炎症反应可能是导致进一步并发症, 特别是术后胰瘘(particularly postoperative pancreatic fistula, POPF)发展的诱因[7] [8] [9] [10]。在没有 POPF 的情况下, PPAP 也可能导致其他全身严重并发症[5] [11], 这些情况会导致患者住院天数延长、延缓患者术后康复及增加患者经济负担。Miroslav Ryska 等[6]对 2007~2011 年间 160 例因胰腺头部导管腺癌接受 PD 治疗的患者术后临床过程观察中发现当诊断出 PPAP 后尽快进行手术治疗, 效果是显著的。因此, PPAP 的早期预测及提前干预, 是降低胰腺术后患者并发症发生率及严重程度、改善患者预后的重要手段。本文将对胰十二指肠切除术后急性胰腺炎的定义、病因、预后及预防的现有研究作一综述。

## 2. PPAP 定义的发展

急性胰腺炎(acute pancreatitis, AP)的传统定义是使用亚特兰大分类[12], 诊断需要出现以下 3 个特征中的 2 个: 1) 典型腹痛; 2) 血清胰酶水平大于正常上限(ULN)的 3 倍; 3) 影像学表现与 AP 一致。术后情况下, 根据急性胰腺炎的标准进行诊断是困难的, 第一, 腹痛是腹部大手术后的症状, 与手术相关的腹痛与 PPAP 相关腹痛无法鉴别; 第二, 在术后早期很少进行腹部影像学检查, 这可能限制了术后正常表现与 AP 的区分。Sean P. McGuire [13]对 415 例患者进行了术后血清淀粉酶浓度测定。术后血清高淀粉酶血症(23%)和术后急性胰腺炎(18%)患者的主要发病率较高( $P < 0.001$ )。血清淀粉酶正常的患者术后发生胰瘘的可能性(5%)更低( $P < 0.001$ )。第一个 PPAP 的标准化定义是 Connor [4]提出的, 术后前 2 d 尿胰蛋白酶原  $2 > 50 \mu\text{g/L}$  作为术后急性胰腺炎的诊断标准; 他还提出可通过术后第 2 天 C 反应蛋白是否  $> 180 \text{mg/L}$  预测术后急性胰腺炎的严重程度, 近些年多项报道根据 Connor 的诊断标准进行回顾性的研究。目

前结合影像学表现诊断 PPAP 的研究[8] [14] [15]指出, 由于淀粉酶灵敏度不佳, Connor 仅依赖淀粉酶证据可能高估 PPAP 的发生率。同时 Andrianello 等[11]发现, C 反应蛋白并不能对其临床严重性进行有效分级。2022 年, 国际胰腺外科研究小组(International Study Group for Pancreatic Surgery, ISGPS)发布的 PPAP 定义为: 在胰腺切除术后 < 3 d 出现的残余胰腺的急性炎症状态。诊断依据如下: 1) 术后 48 h 内, 血清淀粉酶持续高于正常参考值。2) 出现临床相关特征, 如腹痛、发热、炎症因子升高等。3) 影像学检查见残余胰腺弥漫性或局限性间质实质水肿、胰周脂肪炎性改变、胰周积液、胰腺周围和实质坏死等[16] [17]。ISGPS 将 PPAP 的严重程度分为 A、B、C 3 个等级, 若仅有术后淀粉酶水平升高, 无其他临床或影像学指征改变, 定义为胰腺术后高淀粉酶血症(postoperative hyperamylasemia, POH)。A 级 PPAP 为单纯 POH; B 级 PPAP 除生化及影像学改变外, 出现病情加重, 需改变临床治疗方案, 包括药物支持治疗(抗炎、营养支持等), 内镜或介入治疗等; C 级 PPAP 指出现持续性器官衰竭等严重并发症, 需重症监护、再次手术治疗甚至死亡[18]。Juanita N. Chui [19]对国际胰腺外科研究小组(ISGPS)定义胰腺切除术后急性胰腺炎的临床验证中第一个将最近发表的国际共识诊断和分级标准应用于临床数据。

### 3. PPAP 的发生机制

Martin Loos 等[15]在分析 2015 年至 2019 年 641 例胰腺部分切除术后患者中有 12 例患者确诊为 PPAP, 其中作者发现 PPAP 患者的胰腺在术中手术刀横断率高于无 PPAP 的患者, 柔软的胰腺有更高的组织炎症和术后第一天血清淀粉酶升高的风险, 故作者提出, PPAP 发生的诱因有手术损伤、胰腺结构、血供改变及吻合口的狭窄。在 ISGPS 规定中将 PPAP 被定义为部分胰腺切除后胰腺残余的急性炎症, 发生在术后早期(手术后三天内), 甚至会进展到全身。

#### 3.1. 与胰腺本身解剖相关

PPAP 的病理生理学尚未阐明, 但越来越多的证据表明, 胰腺残肢大切除后发生的缺血炎症反应取决于其活的腺泡细胞成分[19]。与非手术情况下的急性胰腺炎类似, 术后胰腺炎的临床表现被认为是在从炎症到坏死的严重程度范围内发生的。在此研究中, 观察到腺泡评分与术后急性胰腺炎呈正相关, 为 PPAP 严重程度的等级取决于腺泡细胞密度的观点提供了证据。Gemelli Pancreatic Center [17]在探讨 ISGPS 定义的 PPAP 的临床意义的研究中, 胰腺质地柔软( $P = 0.01$ )和胰管直径 < 3 mm ( $P = 0.01$ )被认为是 PPAP 发病的危险因素, 而胰管直径 3 mm 是唯一显著影响 PPAP 病程加重的特征( $P = 0.01$ )。这与 POPF 的临床研究结论相似, 但深入的机制尚不清楚。

#### 3.2. 与胰腺的供血有关

在 PD 患者中, 由于胰腺缺血, 胰颈分裂后可能出现两种情况。上述吻合的中断可能导致胰背动脉右侧剩余胰颈的分水岭区缺血。另一种情况是, 如果胰腺背动脉的起源异常, 它的分裂可能会中断与胰腺体和胰腺尾的吻合, 导致整个胰腺残肢缺血。胰腺对动脉和静脉缺血都非常敏感, 重要的是, 梗死不是胰腺坏死的先决条件[20]。短暂的低灌注足以引起与急性胰腺炎相关的级联变化。此外, 手术过程中对门静脉、肠系膜上静脉、脾静脉等血管的提拉, 在处理出血或联合血管切除时甚至需短暂阻断血流, 这种反复且短暂的缺血再灌注会导致腺泡损伤, 进而激活细胞内蛋白激酶并最终导致急性胰腺炎[20]。Ikenaga Naoki [21]在对 153 例 PD 后和 166 例远端胰腺切除术后患者资料分析中, PD 术后 PPAP 发生率为 63.4%, DP 术后 PPAP 发生率为 65.7%, 发生率无显著差异。

#### 3.3. 与胰腺基本状态有关

Ráty Sari 等[22]研究中发现, 术后发生急性胰腺炎的独立预后因素是冠状动脉病变( $OR = 16, P = 0.05$ ),

原因是潜在的长期缺血可能造成胰腺慢性损伤。Koichi Fujita 等[23]在评估 ERCP 术后胰腺炎的危险因素的多中心研究中发现, 一部分因胰头肿物常压迫胆管、胰管造成梗阻的患者术前需行内镜逆行胰胆管造影并置入支架以减黄, 治疗过程中会对胰腺造成损伤, 同样会诱发急性胰腺炎。行 PD 手术的患者病理并非都是恶性肿瘤, 有研究报道[5] [11] [18] [24], 这部分非恶性肿瘤患者 PD 术后 PPAP 发生率较恶性肿瘤术后负担更重, PPAP 发生率更高, 是 PPAP 的危险因素。

#### 4. PPAP 术后结局

目前的研究已证实 PPAP 是独立于 POPF 的术后并发症[4], 且 PPAP 是 POPF 的独立危险因素[5] [11] [14] [21] [25] [26], Vonlanthen 等[27]回顾性研究中, 可以观察到胰腺手术后出现任何并发症的患者的费用比没有并发症的患者增加了 3 倍, 值得注意的是, 无论是否是 PPAP 引起的, C 型 POPF 是最严重的并发症之一, 这些患者的住院时间明显长于没有 PF 的患者。近期作者[5] [10]提出 PPAP 是术中胰腺残端缺血损伤引起的胰腺吻合口局部炎症过程, 其临床表现可引起全身淀粉酶浓度升高, 从而导致吻合口愈合受损, 最终导致吻合口漏。但相反, Raty 等[22]研究中, 患者术后 CT 检查 4 例出现 PPAP 的患者并无 POPF 迹象; Bannone 等[28]发现合并 POPF 与否, PPAP 的患者术后均会出现严重并发症。值得注意的是因坏死性 PPAP 的部分需行全胰切除术的患者并未合并 POPF [18] [29]。Bonsdorff 等[26]的研究中, 508 例患者中, 没有发生 PPAP 的患者术后并发症(出血、DGE、胆瘘等)发生率、病死率低于发生 PPAP 的患者。显然, 除了胰肠吻合术的技术因素外, 其他尚未明确的因素也可能导致胰肠吻合术中胰酶的渗漏, 从而引起术后胰瘘。现在已知的引起胰瘘的其他疾病就是 PPAP, 即胰腺组织坏死导致胰酶泄漏。与胰腺炎类似, 发生在胰腺断端局部的炎症过程中胰肠吻合区淀粉酶浓度升高, 导致吻合区愈合受损。所以部分 PPAP 应被认为是 POPF 发生过程中的促进因素, PPAP 也是 POPF 的独立危险因素, 应将 PPAP 当作独立并发症进行管理。

除了 POPF, 也有报道发现, PPAP 会增加其他并发症的发生率及严重程度, 比如胃排空延迟、胆瘘、术后出血及腹腔感染[5] [14] [21] [25] [26] [28] [30], 这无疑会延迟患者 PD 术后康复, 也有研究指出 PPAP 患者术后介入治疗及再次手术的可能性增大, 导致患者住院费用及术后负担增大[17] [18] [31]。

#### 5. PPAP 的预防

目前很少见针对 PPAP 防治相关研究, 在临床上也无统一的防治策略。从术前角度, Bannone 等[5] [28]在回顾性分析中发现接受新辅助治疗者出现术后急性胰腺炎的比例明显下降, 是 PPAP 的保护因素。从术中角度, Alp Demirag 等[32]研究中发现, 采用硬膜外麻醉可以通过阻滞交感神经增加胰腺灌注, 进而减少胰腺组织损伤的发生。对于 PD 病人, Bannone [5]研究中提出术中限制性补液, 即输液量  $< 3 \text{ mL}/(\text{kg}\cdot\text{h})$  更易出现 POH 及 PPAP。与常规输液[ $8.3 \text{ mL}/(\text{kg}\cdot\text{h})$ ]相比, 加快补液速度[ $12 \text{ mL}/(\text{kg}\cdot\text{h})$ ]有助于降低 POPF、PPAP 及其他严重并发症发生率[33]。Chen 等[18]的研究中提出, 采用胰管内支架行胰管-空肠端侧吻合, 减少不必要的胰腺缝合及暴力操作, 注意保护残余胰腺组织及胰周血管, 并由经验丰富的术者实施手术, 有助于预防 PPAP 发生。从术后角度, 定期监测病人血清炎症因子和淀粉酶、脂肪酶水平, 关注病人病情变化[34]。早期(7 天以内)行 CT 检查, 如患者病情变化, 及时影像学检查, 观察病人胰腺炎症范围 and 有无其他潜在腹腔问题[10]。对患者术后使用生长抑素类似物现有争议, 有学者认为可能与其会收缩血管、减少胰腺血供[35] [36]。但当 PPAP 患者在术后管理、药物作用、介入引流效果不佳时, 应根据外科大夫的经验判断考虑行全胰切除术[18] [37]。

#### 6. 总结

PPAP 已被认为是除 POPF 以外独立的并发症, 应被视为术后并发症来管理。PPAP 已经被国际胰腺

外科研究小组(ISGPS)进行定义及分级。经过大量研究证实, PPAP 可以导致术后并发症发生率及严重程度升高, 但对 PPAP 的发生机制及防治策略未统一, 这对改善病人预后及减轻患者术后住院费用有极大的重要性。目前 PPAP 患者产生的术后负担在相关研究中, 保守治疗被推荐为首选, 但我们仍需对 PPAP 高度重视, 研究出对 PPAP 患者合理的管理方案。

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