

doi: 10.13241/j.cnki.pmb.2017.21.013

# 胆囊切除术后急性胰腺炎患者 314 例的发病特点分析 \*

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**摘要 目的:**研究胆囊切除术后患者发生急性胰腺炎的发病特点。**方法:**回顾性分析 2009 年 10 月至 2013 年 10 月四川大学华西医院诊断为急性胰腺炎且既往行胆囊切除术患者的病因、病情严重程度、临床特征与转归。**结果:**研究共纳入 314 例患者,以高脂血症性胰腺炎占比最高,共 110 例(35%),胆源性胰腺炎和混合性胰腺炎分别为 107 例(32%)、96 例(31%),酒精性仅 7 例(2%)。轻症 215 例,中度 31 例,重度 68 例。高脂血症性胰腺炎患者重症率(36%)、胰腺及胰周坏死率(28%)、持续性器官功能衰竭率(36%)、呼吸衰竭率(41%)、ICU 转入率(26%)均显著高于胆源性组和混合组,差异具有统计学意义( $P < 0.05$ )。**结论:**胆囊切除后的急性胰腺炎以胆源性胰腺炎和高脂血症性胰腺炎居多,其中高脂血症性胰腺炎的病情更严重。

**关键词:**胆囊切除术;胆源性胰腺炎;高脂血症性胰腺炎

中图分类号:R575;R576 文献标识码:A 文章编号:1673-6273(2017)21-4055-04

## Characteristic Analysis of 314 Cases of Patients with Acute Pancreatitis after Cholecystectomy\*

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**ABSTRACT Objective:** To determine the characteristics of patients with acute pancreatitis (AP) after cholecystectomy. **Methods:** The etiology, severity, clinical feature of AP patients with the history of cholecystectomy in West China Hospital from October 2009 to October 2013 were retrospectively analyzed. **Results:** 314 patients were enrolled. The most frequent causes were hyperlipidemic pancreatitis (110, 35%), biliary pancreatitis (107, 32%), alcoholic pancreatitis (7, 2%), and the mixed-causes pancreatitis (96, 31%). 215 cases were mild AP, 31 cases were moderately severe AP, 68 cases were severe AP. The rate of severe AP(36%), pancreatic and peripancreatic necrosis(28%), persistent organ failure(36%), respiratory failure(41%), ICU transferring(26%) in hyperlipidemic pancreatitis were significantly higher than those of the biliary pancreatitis and the mixing-causes pancreatitis. **Conclusion:** Biliary pancreatitis and hyperlipidemic pancreatitis were dominantly prevalent in AP patients with history of cholecystectomy, hyperlipidemic pancreatitis was more severe than that of biliary pancreatitis.

**Key words:** Cholecystectomy; Biliary pancreatitis; Hyperlipidemic pancreatitis

**Chinese Library Classification(CLC): R575.6; R576 Document code: A**

**Article ID:** 1673-6273(2017)21-4055-04

### 前言

急性胰腺炎(acute pancreatitis, AP)是临床常见的急腹症之一,其轻症是一种自限性疾病,但重症可发展为胰腺及胰周坏死、器官功能衰竭甚至死亡<sup>[4]</sup>。胆源性因素是国内 AP 发生的首位病因<sup>[1]</sup>。作为一种胆源性疾病,胆囊切除对于诊断明确的胆源性急性胰腺炎(biliary acute pancreatitis, BAP)治疗和预防有重要作用,通常建议首次发病后,在 AP 病情稳定时即将胆囊切除<sup>[18]</sup>。但关于有胆囊切除术(Cholecystectomy)既往史的 AP 患者的临床研究较为缺乏,本研究通过纳入既往已行胆囊切除术的 AP 患者,并对该患者群体发病时临床特点和临床转归进行总结与分析。

### 1 资料与方法

#### 1.1 病例筛选

纳入标准:(1)确诊为 AP 且发病时间小于 72 小时的患者;(2)年龄 18-85 岁;(3)既往存在胆囊切除病史。排除标准:未达到治疗预期自动出院。

诊断标准:参考 2012 年亚特兰大急性胰腺炎指南修订版,AP 诊断标准如下:(1)腹痛症状;(2)血淀粉酶、脂肪酶升高正常值三倍以上;(3)影像学证据证实胰腺形态改变。满足以上三条中任意 2 条则可诊断为 AP<sup>[3]</sup>。胆源性胰腺炎诊断标准如下:(1)影像学发现胆道结石;(2)在排除慢性肝脏疾病和其它疾病影响的情况下,入院时即出现肝功能异常,且合并总胆红素和直接

\* 基金项目:四川省科技厅支撑计划项目(2015SZ0229)

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(收稿日期:2017-03-06 接受日期:2017-03-28)

胆红素升高,符合一条及以上诊断为胆源性胰腺炎。存在长期饮酒史,并在发病前24 h内饮酒且排除其它诱因下发生AP,诊断为酒精性胰腺炎<sup>[9]</sup>。特发性或归因感染、遗传、外伤等其他少见病因的急性胰腺炎,归为混合性病因胰腺炎。符合急性胰腺炎诊断标准,入院时血浆甘油三酯不小于11.3 mmol/L,或不小于5.65 mmol/L且血浆呈牛奶色,并排除结石、oddi括约肌功能障碍、感染、药物性AP等致病因素,诊断为高脂血症性胰腺炎<sup>[12]</sup>。

严重程度分级标准:参考2012年修订版亚特兰大急性胰腺炎指南推荐标准:不存在器官功能衰竭与局部并发症为轻症急性胰腺炎;有局部并发症和(或)一过性(小于48 h)器官功能衰竭为中度重症急性胰腺炎;存在持续性器官功能衰竭为重症急性胰腺炎。

## 1.2 观察指标

入院时生化指标,临床评分(SIRS评分、APACHEII评分);结局指标包括:并发症(液体积聚和胰腺/胰周坏死)发生率、胰腺/胰周感染及其它部位感染发生率、器官功能衰竭发生率、

住院时长、ICU转入率及病死率。

## 1.3 统计学分析

采用SPSS18.0软件进行统计分析,计量资料用 $\bar{x} \pm s$ 表示,正态分布的计量资料,采用方差分析;非正态分布的计量资料,采用秩和检验,多组间计量资料采用方差分析;计数资料采用例数和百分比表示,采用 $\chi^2$ 检验,以 $P < 0.05$ 为差异具有统计学意义。

## 2 结果

### 2.1 胆囊切除术后患者急性胰腺炎发病的临床特点

纳入的314例患者中,男161例,女153例;平均年龄52岁;轻度215例,中度31例,重度68例;高脂血症、胆源性是主要病因。混合性病因中,有1例为妊娠AP,ERCP术后AP性2例,其余均为特发性;基础疾病中,有心肺基础疾病患者28例,其中17例都为重症AP;合并糖尿病患者67例,脂肪肝患者78例,既往有AP病史106例。

表1 胆囊切除术后患者急性胰腺炎发病的基线情况

Table 1 The baseline information of AP patients with history of Cholecystectomy

Severity	Mild	Moderate-severe	Severe	Total
Cases	(215)	(31)	(68)	(314)
Sex(M/F)	111/104	16/15	34/34	161/153
Age(year)	52±12	51±13	52±12	52±13
Cause(case,%)				
Biliary	77(36%)	8(26%)	16(24%)	101(32%)
Hyperlipidemia	58(27%)	12(39%)	40(59%)	110(35%)
Alcoholic	3(1%)	2(6%)	2(3%)	7(2%)
Mixing-causes	77(36%)	9(29%)	10(15%)	96(31%)
Medical history(case,%)				
Heart and lung	6(3%)	5(16%)	17(25%)	28(9%)
Diabetes	36(17%)	9(29%)	22(32%)	67(21%)
Fatty liver	53(25%)	9(29%)	16(24%)	78(25%)
AP history	67(31%)	14(45%)	25(37%)	106(34%)

### 2.2 不同病因的患者入院时临床特征比较

纳入患者中胆源性AP101例,高脂血症性AP110例,酒精性AP7例,混合性病因AP96例。入院时,胆源性AP患者的年龄、总胆红素(TBIL)、直接胆红素(DBIL)、谷丙转氨酶(ALT)、谷草转氨酶(AST)、血淀粉酶(AMY)和血脂肪酶(LIP)水平明显高于高脂血症性AP和混合性AP,差异具有统计学

意义( $P < 0.05$ )。高脂血症性AP入院时甘油三酯(TG)、胆固醇(CHOL)、随机血糖水平(GLU)和SIRS评分显著高于胆源性、高脂血症性和混合病因性AP,且差异具有统计学意义( $P < 0.05$ )。高脂血症性AP伴随脂肪肝(Fatty liver)和糖尿病(Diabetes)基础疾病所占百分比也显著高于其他三组,且差异具有统计学意义( $P < 0.05$ )。

表2 不同病因组AP患者入院时临床特征比较

Table 2 Comparison of the clinical features of AP patients with different causes on admission

Causes	Biliary	Hyperlipidemia	Alcoholic	Mixing-causes
Cases	101	110	7	96
Age(years)	58±14 <sup>s</sup>	46±9	53±12	54±7
Sex(M/F)	44/67	54/56	7/0	56/40
WBC(×10 <sup>9</sup> /L)	11.62±5.33	13.18±4.73	11.14±2.83	11.76±5.18
HCT	0.41±0.06	0.42±0.06	0.47±0.09	0.42±0.05
TBIL(IU/L)	54.7±36.6 <sup>s</sup>	25.8±24.8	34.4±22.2	21.3±21.2

DBIL(IU/L)	37.7± 31.6 <sup>§</sup>	12.1± 18.9	13± 8.7	9.3± 13.3
ALT(U/L)	255± 224 <sup>§</sup>	65± 115	113± 130	58± 77
AST(U/L)	294± 303 <sup>§</sup>	92± 217	120± 84	64± 98
TG(mmol/L)	1.2± 0.9 <sup>§</sup>	13.6± 9 <sup>§</sup>	4.3± 6.3	1.6± 1.2
CHOL(mmol/L)	3.71± 1.1	7.97± 4.25 <sup>§</sup>	4.89± 1.89	3.99± 1.25
GLU(mmol/L)	8.89± 3.38	12.62± 6.65 <sup>§</sup>	9.11± 1.74	8.58± 3.91
Ca <sup>2+</sup> (mmol/L)	2.13± 0.22	1.99± 0.34	2± 0.36	2.11± 0.22
AMY(U/L)	1325± 1191 <sup>§</sup>	492± 517	683± 366	789± 753
LIP(U/L)	1371± 1445 <sup>§</sup>	694± 824	949± 1031	831± 527
SIRS score	1± 1	2± 1 <sup>§</sup>	1± 1	1± 1
APACHEII score	5± 4	5± 4	5± 3	6± 2
Fatty liver(cases,%)	13(13%)	46(42%) <sup>§</sup>	1(14%)	20(21%)
Diabetes(cases,%)	4(4%)	38(35%) <sup>§</sup>	2(29%)	18(19%)

\*: Biliary AP vs.Hyperlipidemia AP, P<0.05; § : Biliary APvs.Alcoholic AP, P<0.05;

§:Biliary AP vs.mixing-causes AP, P<0.05; § : Hyperlipidemia AP vs.other three causes AP, P<0.05.

### 2.3 中重度 AP 胰腺炎患者的临床转归比较

与胆源性 AP 和混合性 AP 比较, 高脂血症性 AP 具有更高的重症率(36%)、胰腺及胰周坏死率(28%)、持续性器官功能

衰竭率(36%)、呼吸衰竭率(41%)、ICU 转入率(26%)且具有统计学差异(P<0.05)。各组间循环衰竭、肾功能衰竭、感染比较差异均无统计学意义(P>0.05)。

表 3 不同病因组 AP 患者的临床转归比较

Table 3 Comparison of the clinical outcomes between AP patients with different causes

Causes	Biliary	Hyperlipidemia	Alcoholic	Mixing-causes
Cases, %	101(100%)	110(100%)	7(100%)	96(100%)
Mild	77(76%)	58(53%)	3(43%)	77(80%)
Moderate-severe	8(8%)	12(11%)	2(29%)	9(9%)
Severe	16(16%)	40(36%) <sup>§</sup>	2(29%)	10(11%)
Acute fluid collection	15(15%)	29(26%)	3(75%)	12(13%)
Necrosis collection	9(9%)	31(28%) <sup>§</sup>	3(75%)	11(11%)
Transient organ failure	3(3%)	6(5%)	0(0)	2(11%)
Persistent organ failure	16(16%)	40(36%) <sup>§</sup>	2(50%)	9(9%)
Respiratory failure	15(15%)	45(41%) <sup>§</sup>	2(50%)	11(11%)
Circulatory failure	4(4%)	8(7%)	0	4(4%)
Renal failure	4(4%)	12(11%)	1(25%)	4(4%)
Pancreatic infection	10(10%)	11(10%)	1(25%)	5(5%)
Other infection	10(10%)	9(8%)	0(0)	6(6%)
ICU transferring	9(9%)	29(26%) <sup>§</sup>	0(0)	5(5%)
Hospital stay(D)	13± 10	14± 13 <sup>δ</sup>	16± 5	11± 7
Death	6(6%)	8(7%)	0	3(3%)

\*vs. Biliary AP, P<0.05; vs. .Alcoholic AP, P<0.05; §vs. Biliary AP and mixing-causes AP, P<0.05; δvs. mixing-causes AP, P<0.05.

### 3 讨论

胆囊切除术(cholecystectomy)是针对胆源性胰腺炎与其它胆石症的有效治疗手段。对于明确的胆源性急性胰腺炎(Biliary acute pancreatitis, BAP),无论首次发作还是复发,都推荐行胆囊切除术,可有效降低包括 BAP 在内的胆石症复发率<sup>[2,9]</sup>。研究显示 60.9%入院时确诊 BAP 未行胆囊切除即出院的患者在切除胆囊前再次经受了胆石相关性疾病,其中 AP 复发率约 14%(15/110)<sup>[22]</sup>。但 Beat 等曾报道 BAP 中有 13%(17/132) 的患

者有胆囊切除病史,且有胆囊切除史的复发 AP 患者中,ERCP 查见结石率高<sup>[6]</sup>。本研究结果显示既往无论何种原因行胆囊切除术的而发生 AP 患者中,胆源性因素(32%)占约三分之一,且仅 28 例胆源性患者通过 B 超、CT 或核磁共振影像学检查明确胆管结石诊断,11 例患者为 ERCP 明确,而其余患者均通过胆红素水平及肝酶学升高,排除其他因素而诊断。胆道结石和(或)胆泥是胆囊切除术后发生 BAP 的重要因素<sup>[16]</sup>。有研究显示亚洲国家患者的胆道阻塞与肝内胆管结石形成密切相关,其中中国患者胆道结石的 38%来自于肝内胆管<sup>[16]</sup>。切除胆囊可以降低

胆道梗阻风险,但不能完全杜绝,仍然存在胆道结石阻塞或刺激胰胆管诱发AP的风险。胆道微结石和泥沙样结石隐秘的致病途径,影像学难以捕捉<sup>[14]</sup>,且胆囊切除后会出现胆道扩张的继发性改变,只能通过实验室检查和影像学表现联合推测,但仍难以精确把握胆源性病因在这部分AP患者中的具体占比。胆石的形成受遗传因素和环境因素影响<sup>[17]</sup>。胆囊切除后,在患者并未调整自身的生活环境和习惯时,胆石的形成可能并未受到负面影响。其中,由于膳食结构不合理和久坐少运动的生活方式造成的血脂异常、2型糖尿病、肥胖和年龄的增长均会促进胆石症的发病<sup>[11,19]</sup>。而高脂血症的产生与肥胖、2型糖尿病、脂肪肝、代谢综合征等因素密切相关<sup>[8]</sup>。本研究中,有胆石相关疾病史患者中,21%(67/314)有糖尿病,25%(78/314)有脂肪肝。其中,胆源性AP组13%(13/101)有糖尿病,4%(4/101)有脂肪肝,低于高脂血症性AP组42%(42/110)糖尿病和38%(38/110)脂肪肝,而高脂血症性AP(110)略多于胆源性AP(101)。这种现象说明在切除胆囊降低胆石症发病率的前提下,由于患者的饮食和生活习惯未改变,机体处于或将处于糖脂能量代谢紊乱的处境中,相较于胆源性AP,可能更容易促成高脂血症性AP的发生。

近年来,高脂血症性AP的发病呈上升趋势,行病学调查显示1990年至2005年中国广东由于不合理的饮食结构,高脂血症性胰腺炎发病率增长了2.6倍<sup>[7]</sup>。中国北京市流行病学调查显示2006年至2010年,胆源性因素仍是AP的最大病因,但高脂血症性AP增长明显,成为第二病因<sup>[23]</sup>。高脂血症致病机制不明,可能与甘油三酯过多分解产生游离脂肪酸(FFAs)引起脂毒性、胰腺微循环障碍有关<sup>[20]</sup>。高脂血症性AP相较其它病因AP的严重程度仍有争议<sup>[15]</sup>。但近年的临床研究表明高脂血症性AP较其它病因AP有更严重的临床表现。高脂血症性AP的严重程度与肥胖、脂毒性密切相关<sup>[10,13]</sup>。Qiu等回顾性研究表明909例AP中,129例(14.2%)为高脂血症性AP,表现出更高的胰腺坏死率和器官衰竭率,且年龄更小<sup>[12]</sup>。Huang等的回顾性研究表明高脂血症性AP比胆源性AP有更高的重症AP、器官功能不全和死亡率<sup>[7]</sup>。Yin等回顾性研究了2009年至2013年1073例AP后发现高脂血症性AP的病因占比由2009年的13%增长到2013年的25.6%,且急性液体积聚、肾脏功能衰竭和重症胰腺炎在高脂血症性AP中占比更高<sup>[21]</sup>。本研究中,高脂血症性AP病因占比为35%,高于Yin等的研究结果,原因可能是切除胆囊后降低了胆源性AP占比,并有较高比例患者存在糖脂代谢紊乱,从而增加了高脂血症性AP占比。同样,本研究显示相较于胆源性AP,高脂血症性AP也表现出更高的急性液体积聚率、胰腺胰周坏死率、呼吸功能衰竭率和重症率,但死亡率无明显差异。

综上,胆囊切除的患者虽然胆源性AP发病率降低,但肥胖、高脂高糖饮食、久坐等尚未改变仍然会形成胆道结石而引发AP,且高脂血症的形成所需的环境因素与胆石形成密切相关。糖脂代谢紊乱导致的血脂升高会增加高脂血症性AP的风险,高脂血症性AP可能比胆源性AP有更高的重症率、器官功能衰竭率、胰腺坏死率。所以胆囊切除患者既需要处理胆道结石或胆泥的潜在威胁,更重要的是改变自身生活习惯,减少高能量高脂饮食,监测血糖血脂,做到有效预防急性胰腺炎。

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