

急性结石性胆囊炎的治疗现状

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摘要

急性结石性胆囊炎(ACC)是外科常见的急腹症之一, 具有病情进展快、迁延不愈、易反复发作等特征, 延误治疗会引发化脓性感染、胆囊坏疽等严重并发症, 甚至会危及生命。尽管ACC已在临床上进行了很长时间的临床, 但其诊疗仍具有挑战性。本文结合国内外最新研究文献对ACC的诊疗现状进行综述。

关键词

急性结石性胆囊炎, 胆囊炎, 严重程度, 胆囊造口术, 诊断, 治疗

Current Status of Diagnosis and Treatment of Acute Calculous Cholecystiti

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Abstract

Acute cholecystitis is one of the common acute abdomen diseases in surgery. It has the characteristics of rapid progression, incurable disease, and prone to repeated attacks. Delayed treatment can cause severe complications such as suppurative infection, gallbladder gangre, and even life-threatening. Although ACC has been conducting clinical research for a long time, its diagnosis and treatment are still challenging. This article summarises the diagnosis and treatment status of ACC in combination with the latest research literature at home and abroad.

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Keywords

Acute Cholecystitis, Cholecystitis, Severity, Gallbladder Ostomy, Diagnosis, Treatment

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1. 引言

急性结石性胆囊炎(Acute calculous cholecystitis, ACC)是外科常见的急腹症之一[1], 随着生活习惯及饮食结构的改变, ACC 发病率呈上升趋势, 我国成年人胆囊结石发病率达 10%~15% [2]。在 50 岁以下人群中, 女性 ACC 的发病率是男性的三倍[3]。胆囊结石的成因及确切的发病机制仍不清楚, 一般认为与遗传因素、代谢异常、胆囊解剖异常、胆囊功能异常、饮食、生活习惯等因素有关[4] [5] [6] [7] [8]。另外, 患者年龄、性别、药物、雌激素水平、长期口服避孕药、慢性肝病等因素在胆囊结石形成中起着驱动作用[9] [10] [11] [12]。Bove V [13]等文献综述报道, 胆囊血管变异在胆囊结石的形成中发挥重要作用。由于 ACC 病情变化迅速, 不及时治疗会引发胆囊壁坏疽、胆囊穿孔、胆汁性腹膜炎、脓毒症、感染性休克等严重并发症, 甚至会危及生命[14]。ACC 主要治疗方式包括保守治疗、手术治疗, 胆囊造口术。目前腹腔镜胆囊切除术仍然是 ACC 的一线治疗方法[15]。然而, 高龄及病情危重的 ACC 患者行腹腔镜胆囊切除术转开腹率, 术后并发症的发生率及死亡率高, 最佳诊疗方式仍存在争议[16] [17]。本文结合国内外最新研究文献对 ACC 的诊疗现状进行综述。

2. 临床诊断

ACC 发病急, 病情发展速度快, 有些患者体征及临床表现不典型, 疼痛部位不明确, 往往容易被误诊。同时, ACC 的临床表现与急性胰腺炎、阑尾炎、消化性溃疡、急性小肠或结肠疾病、右肾及输尿管结石、右肺及胸膜炎、急性心肌梗死等疾病较为相似[4], 若患者不能得以及时的诊断及干预, 会导致疾病进展, 症状加重, 影响患者预后, 甚至会危及生命[14] [18]。因此, ACC 快速准确诊断至关重要。世界急诊外科学会于 2020 年对(2016 版) ACC 诊断和治疗指南进行更新并建议 ACC 的诊断应基于患者详细的病史、体格检查、实验室检查和影像学检查相结合[19]。

ACC 患者多以右上腹或中上腹部疼痛为首发症状, 通常在进食高脂肪食物后出现右上腹疼痛, 疼痛可持续时间长可长达 6 小时以上, 伴或不伴肩背部放射痛, 可合并有发热, 恶心、呕吐, 厌油等消化道症状[4] [14] [20]。通常出现右上腹压痛、Murphy 征等阳性体征[21]。白细胞、降钙素原和 C 反应蛋白等感染指标可升高。临床实践中, 该指标可作为病情的严重程度及手术难度的预测指标[22] [23]。少数病例可出现肝酶(丙氨酸转氨酶(ALT)、天冬氨酸氨基转移酶(AST)和淀粉酶)的小幅升[24]。影像学检查在 ACC 的诊断中发挥着重要作用。B 超是 ACC 首选影像学检查[19], 具有价格便宜、便于携带、易于使用、电离辐射少等优势[25]。有关研究报道, B 超敏感性和特异性分别为 81%和 83% [10]。ACC 超声检查表现为: ① 胆囊壁增厚(厚度 > 4 mm), 胆囊增大(宽 ≥ 4 cm); ② 存在胆囊结石(伴或不伴颈部嵌顿); ③ 胆囊周围积液, 胆囊周围可见低回声带、胆囊壁“双边征”(低质量证据, 强烈推荐) [26]。有研究显示, CT 与 B 超诊断效率相当, 但是 CT 在复杂性 ACC 诊断效率方面更占优势[27]。横截面成像提供了所有腹部象限更全面的视图, 有利于评估整个腹部, 可以协助鉴别诊断腹部其他疾病[28]。MRCP 和 MRI 诊断

胆结石和胆总管结石的敏感性和特异性优于 US 及 CT, 可显示胆管树, 有助于术前评估与 ACC 相关的并发症, 对人体无射线伤害, 受到病人及临床医生的广泛认可[25] [29]。

3. ACC 的严重程度分级

ACC 的临床诊断可能会低估病情较轻的患者的炎症程度, 而高估病情较严重的患者的手术难度[30]。了解 ACC 的严重程度有助于外科医生预测与病情严重程度有关的并发症风险, 并更加标准化的改善风险及临床结局, 能为适当诊疗方案的选择提供依据[31]。东京指南定义了 ACC 的临床诊断标准和严重程度分级并对它进行了更新修订。严重程度分级见表 1 [21]:

Table 1. Severity grading of acute calculous cholecystitis

表 1. 急性结石性胆囊炎的严重程度分级

ACC 严重程度分级	
I 级(轻度)	ACC 可以定义为健康患者的 ACC, 无器官功能障碍, 胆囊有轻度炎症改变。
II 级(中度)	ACC 与以下内容之一相联系: 白细胞计数升高($>18,000/\text{mm}^3$)、右上腹象限可触及触痛肿块、症状持续时间 >72 小时以及明显的局部炎症(坏疽性胆囊炎、胆囊周围脓肿、肝脓肿、胆汁性腹膜炎和气肿性胆囊炎)。
III 级(重度)	ACC 与器官或系统功能障碍相关, 包括心血管功能障碍、神经功能障碍、呼吸功能障碍($\text{PaO}_2/\text{FiO}_2$ 比值 <300)、肾功能障碍(少尿或肌酐 $>2.0 \text{ mg/dL}$)、肝功能障碍($\text{PT-INR} >1.5$)和血液学功能障碍(血小板计数 $<100,000/\text{mm}^3$)。

4. 治疗

4.1. 保守治疗

所有诊断为 ACC 患者入院后应给予禁食、胃肠减压、解痉、镇痛、抗感染、维持电解质、酸碱平衡等对症支持治疗[4] [26]。整个治疗过程中抗生素是核心[32], 在围术期中 4~5 天的抗生素联合液体电解质治疗对预防病情恶化及缓解症状有重要作用[33]。抗生素的选择取决于患者病情严重程度[21]。抗生素应覆盖革兰氏阳性菌和革兰氏阴性菌、厌氧菌等[33]。2018 年东京指南提供了全面抗生素, 并建议根据病情、药敏实验结果及胆汁培养结果调整抗生素[34]。如患者伴有重要脏器功能障碍、脓毒症, 感染性休克等严重并发症, 应给予器官支持并持续评估生命体征[4]。

现有的文献对保守治疗 ACC 的效益存在相互矛盾的观点[35]。Loozen [36] 等对纳人的 10 项随机对照试验和 14 项非随机研究进行系统评价和汇总分析, 认为保守治疗是治疗轻症 ACC 有效的手段, 随访期间只有 22% 的患者复发以及仅 0.5% 的患者保守治疗无效而死亡。Escartín A [37] 等研究表明, 保守治疗远期 2 年内随访仍有 20% 的复发率, 复发后胆囊炎发作更频繁、病情严重程度高、第二次复发与高并发症的发生和高死亡率有关, 死亡率达到 6%。苏格兰的一项纳入了 47,558 例 ACC 患者的队列研究[25] [29] [38] 表明, 与保守治疗相比手术治疗更安全有效, 早期手术治疗与低死亡率有关, 他们倡导手术治疗作为有效的治疗方法。目前关于保守治疗的研究有限, 无确切证据证实保守治疗替代手术治疗能够获益。笔者认为保守治疗 ACC 不能根本上解决问题, 胆道相关并发症的发生率及复发率高[39], 不应将保守治疗视为确定性诊疗方案。

4.2. 腹腔镜下胆囊切除术

腹腔镜下胆囊切除术(laparoscopic cholecystectomy, LC)是目前治疗 ACC 最有效手段[40]。具有手术创伤小、疼痛少、恢复快、住院时间短、美容效果好等优势[41]。目前 LC 治疗 AAC 最佳手术时机仍存在

争议[30]。90年代初,采用保守治疗后延期行LC是常见的方法。随着医疗器械和技术的改进,早期LC被认为是有效可行的[15]。目前的研究建议,患者评估手术风险后,如果患者病情允许、不存在危及生命的器官功能障碍、循环稳定并且医疗机构能胜任复杂外科手术则应对所有严重等级的ACC(轻度、中度或重度)早期行LC[26][42][43][44][45]。然而,目前早期手术时机的定义比较模糊,多项研究将早期手术时机定义为黄金72h[20][46]。他们指出,发病后72小时内行手术减少术后胆道并发症及中转开腹率,可缩短住院时间,降低死亡率[47]。一项纳入了英格兰43,870例早期行LC手术患者的大型回顾性研究显示,入院后72小时内接受胆囊切除术的患者胆道相关并发症显著降低[48]。最近一项研究[15]报道,24小时内行手术治疗的患者中手术并发症的发生率、手术时间和转化率最低,他们建议最好在24小时内行手术治疗。Bruncel等[49]人将症状出现后3天至7天归类为早期手术,他们的研究显示,症状出现后3日内行手术和4~7天手术患者中转开腹率及手术相关并发症在统计学上无明显差异,超过7天行手术患者胆囊炎的严重程度增加,手术难度高,中转开腹率及手术相关并发症的发生率有增加趋势。WSES指南将入院后7天和症状出现后10天定义为早期手术[19]。胆囊炎症是动态演变的过程,炎症的反复发作、组织瘢痕逐渐增多使后期的手术变得更加困难,这些发现可以用ACC的发病机制来解释。ACC的前2~4天是水肿性胆囊炎的阶段,在此期间,充血和水肿明显。然后,在3~5天时,ACC在坏死期进展,以出血和坏死为主。从7~10天开始,疾病进展到化脓期,也称为化脓性胆囊炎,延误治疗会导致病情进展[50]。有研究建议,如果患者发病时间长或者手术风险高而不能耐受手术者建议保守治疗6周后再行手术治疗。鲍景国等[51]人对保守治疗6周后行手术的治疗方案提出了质疑,他们指出,保守治疗后6~8周炎症尚未完全消退,手术难度大,手术相关并发症的发生率高。最近的一项回顾性研究[52]研究了保守治疗后行LC的手术时机,他们的研究显示,与早期组(4~90天)相比延迟组(90+天)手术时间和术后住院时间显著减少,延迟组失血量,转化率和术后并发症发生率也较低,但差异不大。但是,他们忽略了等待手术期间胆囊炎反复发作、结石落入胆总管引起胆源性胰腺炎等并发症的发生可能以及医疗费用、ACC对患者生活质量的影响等多种因素[39][53]。有研究表明,复发后胆囊炎的严重程度更高,第二次复发导致的死亡率达到6%[53]。综上所述,早期胆囊切除术是ACC患者的首选治疗方法[49]。大多数轻至中度ACC患者能够从中获益[54]。

4.2.1. 治疗决策的选择

研究表明,伴有基础疾病的老年患者及严重程度等级高的ACC与更高的不良事件的发生率和更高的死亡率有关[26][42][55][56]。关于严重程度高、伴有基础疾病的高风险ACC患者治疗策略仍存在争议[32]。有研究显示,表现为胆囊坏疽、化脓等严重胆囊炎患者早期LC是可取的[57],他们还指出,心血管、肾脏等重要脏器衰竭或凝血障碍的患者尽管手术风险高,但通过积极药物支持治疗后脏器功能可能会在短时间内能够改善,这些患者能够受益于早期手术[21][58][59]。Zhang等人[60]研究表明,年龄较大的患者心力衰竭、高血压、慢性阻塞性肺疾病(COPD)和贫血等有增加趋势,LC手术时间更长,失血量更多,肺炎和电解质紊乱更多,他们指出,尽管手术风险高,但通过积极治疗基础病的前提下仍然能从早期手术中受益。根据这些证据,在积极改善基础病的情况下在能够胜任复杂外科手术的医疗机构早期行手术治疗是安全可行的[15]。治疗决策取决于患者病情,术者经验和医疗条件。胆囊炎急性期胆囊水肿明显,组织脆,易出血,大量纤维蛋白渗出,可能会影响手术视野[61],有研究显示,与胆囊炎症消退的ACC患者相比,胆囊炎急性期导致的胆道损伤的发生率是无炎症患者的三倍[62]。但胆囊炎早期胆囊壁组织疏松,胆囊与周围组织没有明显的粘连,胆囊三角区解剖清楚,便于分离[63],通过灵活运用使用吸引器、纱布、电凝钩等能够保持手术视野干净,为LC的顺利进行创造有利条件。随着胆囊炎发病时间延长、胆囊与周围组织粘连严重,胆囊三角解剖不清会增加手术难度及胆道损伤的发生率[52][64],早

期手术避开了胆囊三角粘连致密、瘢痕形成导致的手术困难。另外,局部炎症和手术创伤会诱发代谢紊乱及全身炎症反应[65],发病短时间内争取行 LC 可以有效清除病灶,避免体内炎症反应及应激反应加重[63],降低并发症的发生率、中转开腹率、缩短手术时间、降低手术对患者的打击[66]。因此,建议患者无论病程严重程度如何只要能耐受手术争取早期行 LC [58]。对于无法耐受手术的患者则考虑保守或者穿刺手术治疗[21][54][67]。

4.2.2. 手术难点与应对措施

虽然腹腔镜胆囊切除术目前被认为是一种风险较小的手术,但胆囊炎症重、胆囊与周围组织粘连致密、胆囊三角解剖不清,血管及胆道解剖变异等因素会增加胆道损伤及中转开腹等相关并发症发生的风险[68][69][70][71]。胆道损伤是 LC 最严重的并发症之一,据报道其发病率为 0.3%~0.7% [72]。其他并发症包括胆囊管残端渗漏、因热损伤引起的晚期胆管狭窄、血管损伤等[54]。术前评估患者病情及完善术前相关检查是保证手术安全性的重要环节。年龄、性别,体重指数(BMI),腹部手术史、既往胆囊炎反复发作史、白细胞和 C 反应蛋白水平高,胆囊壁厚(厚度 ≥ 4 mm),胆囊颈部嵌顿结石、胆囊严重程度,calot 三角致密粘连、手术时机等已被证明是困难手术的危险因素[70][71][73]。术前外科医生应评估与手术困难相关的危险因素并完善 MRCP 以了解胆囊三角及胆囊管走行、肝外胆道是否变异以评估手术难易程度。

在手术中,外科医生应尝试实现胆囊三角安全视野窗法(critical view of safety, CVS) [54]。1995 年由 strasberg 等[74]首次提出。具体做法是将胆囊下 1/3 从胆囊床上剥离,清除胆囊三角中的脂肪及纤维组织,暴露胆囊管、胆囊动脉,直至仅看到胆囊管和胆囊动脉两个囊性管到进入胆囊[75]。吲哚菁绿(indocyanine green, ICG)近红外光导航技术是另一种安全有效的方法,可在胆道走行异常或胆道周围炎症严重的情况下降低胆管的损伤风险[72]。有研究者指出,ICG 近红外光导航技术在 LC 中的作用可以扩大到 ACC 患者,这可能有助于提高早期 LC 的安全性[76]。然而,发出的光可能无法穿透腹膜脂肪组织或较厚的瘢痕组织,在重度胆囊炎和体型肥胖的患者中 ICG 近红外光导航技术的识别度受到限制[77]。calot 三角致密粘连,胆囊颈部结石嵌顿、胆道血管解剖变异等因素会影响 CVS 的顺利进行[78][79],这种情况下太执着于实现 CVS 反而会增加血管、胆道、胃肠道损伤等并发症的发生风险[78]。因此,临床上可以结合多种手术方式或者策略,如,逆行式胆囊切除术,后三角入路胆囊切除术,胆囊次全切除术,中转开腹等方法,必要时请示上级医师支援,以达到最佳手术效果及安全性[54]。不同入路行 LC 术治疗效果存在一定差异,术者应灵活选择相应诊疗策略。

正确解剖 calot 三角是手术安全性的关键[80]。吸引器、超声刀、电凝钩是解剖 calot 三角中常用的器械。许多研究比较了超声刀和电凝钩在胆囊切除术中的结局,他们的研究显示,与电凝钩相比,超声刀胆囊切除住院时间,手术时间短,术中术后并发症的发生率低,对镇痛的需求低,术后恢复快[81]。这些结局归因于电凝钩产生的烟雾较多,大量产生的烟雾影响手术视野加之电凝钩热电效应及机械传损伤可能会导致胆道、血管及周围组织损伤[82],而超声刀产生的烟雾较少,热损伤少,能有效解剖粘连致密,纤维化,严重炎症的 calot 三角[83]。此外,超声刀能够凝固直径达 5 mm 的管腔结构,通过凝固胆囊动脉及分支、胆囊管、迷走胆道达到夹闭胆囊管和安全止血的目的,相应减少手术并发症的发生[84][85]。然而,超声刀费用昂贵,一般推荐中度、中度胆囊炎病例中使用,以保证手术安全性。

胆囊切除术后综合征也是目前困扰患者的问题。胆囊或胆囊管残留是胆囊切除术后综合征的原因之一[86]。一般认为,距胆总管 0.3~0.5 cm 处夹闭胆囊管较为合理[87]。随着 LC 的广泛开展,对于胆管损伤的过分强调,使许多术者对此产生了“畏惧”心理,出于安全考虑,他们往往更愿意贴近胆囊壶腹部去离断胆囊管,给远期残余胆囊的发生埋下隐患。笔者结合我中心实施的 LC 术中及术后并发症发生率情况,建议零距离切除胆囊管,即贴近胆总管,可以显著降低残余胆囊,胆囊切除术后综合征等并发症

的发生率, 但有研究表明, 零距离切除可能会导致胆囊管残端缺血挛缩, 以及可吸收生物夹在体内自然吸收过程中压迫胆总管, 从而引起胆漏、胆总管狭窄[88]。笔者认为, 精确把握胆囊管离断位置(零距离切除), 可有效预防远期胆总管狭窄的可能性, 这将考验术者在术中对三管(肝总管、胆总管、胆囊管)的精细解剖及判断夹闭胆囊管的距离提出了更高的要求。目前关于零距离切除的研究很少, 后期还需要高质量的研究来证实零距离切除术的可行性。

4.3. 开腹手术

目前开腹胆囊切除术(Open cholecystectomy, OC)已很少作为首选的术式, 但在因医疗条件受限而尚未开展微创诊疗的基层医疗机构中, 以及因胆囊三角解剖不清、胆囊周围组织粘连严重, 有损伤周围血管、胃肠道和胆道等风险时, 或者在无法进行腹腔镜手术的严峻环境中开腹手术是一种至关重要的挽救方法[89]。因此, 作为外科医师必须掌握这项技术。

4.4. 胆囊引流术

对于无法耐受手术, 且病情进展迅速或保守治疗无效的 ACC 患者, 经皮肝内胆囊引流术(percutaneous transhepatic gallbladder drainage, PT-GBD)被认为是首选疗法[90]。通过排出胆囊中受感染的胆汁或脓液, 并迅速缓解胆囊内压力进一步控制 ACC 患者的炎症和感染状态。据报道, PT-GBD 治疗 ACC 期间技术和临床成功率分别为 95%和 56%~100% [91]。最近 PT-GBD 在高手术风险患者中的效益受到质疑[92], 有研究显示, PT-GBD 与更高并发症的发生率及中转开腹率及更高的复发率及再次入院率有关[91] [93]。相关并发症包括引流管插入部位疼痛、出血、感染、导管移位导管阻塞、胆漏等[94]。尽管 PT-GBD 与高不良事件的发生率有关, 在高危患者中有重要临床意义, 能帮助患者度过急性期, 避免急诊手术带来的风险。PT-GBD 和胆囊切除术之间的最佳时机尚未定论, 一般建议 PT-GBD 术后 8 周内行胆囊切除术[95]。内窥镜作为高危患者的新型替代方案已进入临床中, 虽然尚未与明确的保守治疗进行比较, 但已被证明优于 PT-GBD [39], 因在技术上有一定的挑战性, 对基础设备及技术有一定的要求, 需要熟练的内窥镜医师操作, 在临床上尚待推广[96]。

5. 结语

随着生活水平的提高, ACC 患病率趋于上升趋势, 给患者带来身心伤害, 降低生活质量, 而详细的病史、完整的临床检查、实验室检查和影像学检查是诊断 ACC 的关键。目前 LC 仍然是治疗 ACC 的金标准, 关于国内外 ACC 的诊疗研究成果较多, 但最佳诊疗策略尚未达成共识, 尚处于探索阶段, 还需要进行更高质量的随机对照研究, 为 ACC 的治疗提供新的理论依据。

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