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· 文献综述 ·

内镜逆行胰胆管造影术后胆总管结石复发的相关因素 研究进展

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摘要

胆总管结石是消化系统常见病, 内镜逆行胰胆管造影(ERCP)是目前治疗胆总管结石的重要手段, 但常存在术后结石复发的问題。胆总管结石从清除到复发涉及到复杂的因素, 主要包括既往胆道手术史、胆管扩张、壶腹周围憩室、胆道感染等。笔者就 ERCP 术后胆总管结石复发的相关因素作一综述, 以期为临床预防及治疗提供帮助。

关键词

胆总管结石病; 胰胆管造影术, 内窥镜逆行; 复发; 危险因素
中图分类号: R657.4

Factors for recurrence of choledocholithiasis after endoscopic retrograde cholangiopancreatography: recent progress

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Abstract

Choledocholithiasis is a common disease of the digestive system. Endoscopic retrograde cholangiopancreatography (ERCP) is an important method for the treatment of common bile duct stones, but postoperative stone recurrence is still a major problem. Many complex factors are involved in the process of the recurrence of the common bile duct stones after removal, which mainly include the history of biliary tract surgery, bile duct dilatation, perampullary diverticulum, biliary infection, etc. Here, the authors address the relevant factors for recurrence of common bile duct stones after ERCP, so as to provide help for its prevention and treatment in clinical practice.

Key words

Choledocholithiasis; Cholangiopancreatography, Endoscopic Retrograde; Recurrence; Risk Factors
CLC number: R657.4

胆结石是消化系统常见病、多发病, 在我国胆石病发病率为 3%~11%^[1]。在美国, 胆结石发病率约 15%, 其中 10%~15% 的患者同时伴有胆总管

结石^[2]。目前, 内镜逆行胰胆管造影(ERCP)是治疗胆总管结石的重要方式, 但常存在术后结石复发的问題。胆总管结石复发定义为 ERCP 取石术

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后6个月以上发现的结石^[3]。目前关于胆总管结石复发相关危险因素的研究较多,然而不同的研究得出的结论并不一致。本文针对ERCP术后胆总管结石复发的相关因素作一系统综述。

1 患者因素

1.1 地域、基因、遗传因素

胆结石存在明显的地域分布差异,以欧美国家为高^[1]。已有研究证实ABCB4基因突变是胆结石复发的主要遗传危险因素^[4]。ABCB4基因参与编码肝胆磷脂转运体多耐药蛋白3(MDR3),MDR3损伤导致胆道磷脂酰胆碱水平降低,生成致石性胆汁^[5]。ABCG5/8等位基因与胆总管结石复发有关,其变异基因ABCG8-D19H是目前公认的胆结石形成的遗传危险因素,可有效预测胆囊切除后胆总管结石复发^[6]。

1.2 性别、年龄、生活习惯因素

一般情况下胆结石发病率女性比男性高,然而胆总管结石的男女比例为1:0.89^[2]。且众多研究^[3,7-8]并未发现性别在影响胆管结石复发中的显著作用。Keizman等^[9]比较老年患者(≥80岁)与年轻患者(≤50岁)EST术后胆管结石的复发情况,发现年龄与结石复发存在相关性,老年患者胆管结石复发率(20%)较高,这与老年患者同时合并胆管扩张、壶腹周围十二指肠憩室(PAD)等因素有关。流行病学研究表明,胆结石形成与性别、年龄、脂质代谢、肥胖、运动等因素有关^[2]。血清胆固醇、体质量指数高于正常与胆总管结石复发有显著相关性^[10],因此,控制体质量和血清胆固醇对预防胆总管结石复发具有重要意义。

1.3 患者合并其它疾病

溶血性贫血和甲状腺功能减退是胆总管结石形成和复发的危险因素,应在术后随访的同时并积极治疗原发病,密切关注患者的甲状腺功能^[11-12]。

2 解剖异常因素

2.1 胆管扩张与狭窄

胆管扩张在ERCP术后胆总管结石复发中具有重要作用。Ueno等^[13]通过观察169例胆总管结石患者ERCP术后结石复发情况,发现合并胆管扩张的患者结石复发风险较高,扩张的胆管运动功能减弱,胆汁易于淤积,促进结石形成。在对体外冲击波治疗困难胆管结石患者的随访中发现,胆管直径

扩张是复发性结石形成的危险因素^[14]。Jeon等^[15]探索老年患者胆管直径恢复情况与胆总管结石复发关系,发现非复发组胆管直径恢复程度明显大于复发组,胆管直径恢复状况与结石复发呈反比关系,可见,胆管扩张是胆总管结石复发的高危因素。但目前胆管扩张直径与胆总管结石复发的关系尚无定论, Kim等^[16]发现胆管直径≥13 mm的患者更容易复发结石,而Nzenza等^[17]认为胆管直径≥12 mm是胆总管结石复发的危险因素。

胆管狭窄与胆管结石复发有显著的相关性, Jakobs等^[18]探索激光碎石术后胆管结石复发的相关因素,平均随访1.7年,80例患者中有11例(15.5%)复发胆管结石,胆管狭窄是胆管结石复发的危险因素。胆管狭窄患者胆汁易于淤积、排泄不畅,导致胆管结石反复发作。

2.2 壶腹周围憩室

十二指肠憩室是十二指肠局部向外膨出形成的袋状突出,大多数十二指肠憩室位于十二指肠乳头2 cm内,称为PAD。PAD是后天获得性病变,在40岁以下的患者中很少见,但随着年龄的增长,PAD发生率增加,PAD在一般人群中的患病率约为20%^[19]。PAD可机械压迫末梢胆管,导致胆总管压力增加,干扰胆汁的正常流动,从而增加胆总管结石复发的可能性。另外,食物残渣及消化液易滞留于PAD,对十二指肠乳头形成反复炎症刺激,造成乳头口狭窄。研究^[8,20]显示PAD的存在与ERCP术后胆总管结石复发有关。笔者所在的ERCP中心研究发现PAD与胆总管结石的形成密切相关,尤其在胆囊切除术后,PAD可能是胆总管结石发生和复发的重要危险因素^[21]。

PAD可能引起胆管扩张,研究^[22]表明,胆管直径与PAD大小有关,胆总管结石复发与PAD类型有关。Kim等^[22]将PAD分为3种类型(I型:主乳头位于憩室内;II型:主乳头位于憩室边缘;III型:主乳头位于憩室外),与II、III型PAD相比,I型PAD患者胆管结石复发风险更高。也有报道^[16]十二指肠大乳头位于憩室内或憩室边缘的患者更容易复发胆管结石。

2.3 胆总管成角

正常胆总管近于直线走行,部分患者可因既往胆道手术史等原因导致胆总管受到牵拉,致使胆总管弯曲成角。Yoo等^[3]认为胆总管成角(<145°)与ERCP术后胆总管结石复发有关。Zhang等^[23]研究发现末梢胆管成角(<135°)是ERCP术后结石复发的独立危险因素,胆总管成角

可导致胆汁淤滞,促进结石形成和复发。

2.4 胃肠结构改变

Li等^[24]应用ERCP治疗毕II式术后胆总管结石患者,长期随访(中位随访时间22.5个月)发现胆管结石复发率为12.2%(6/49),其中,女性及既往机械碎石史是胆总管结石复发的危险因素,胃肠结构改变是胆总管结石发生和复发的重要因素。迷走神经损伤、胃切除范围、胃肠重建方式和淋巴结清扫等与胃肠结构改变后胆管结石高发有关^[25]。

2.5 胆囊切除状态

对于同时患有胆总管结石和胆囊结石的患者,经ERCP清除胆总管结石后,应尽早行腹腔镜下胆囊切除术以预防胆囊炎、胰腺炎和胆总管结石复发^[26]。然而,在胆囊切除术后的患者中仍可观察到胆总管结石复发。Yoo等^[3]回顾性研究发现,胆囊切除术后胆总管结石患者在ERCP治疗后的结石复发率为18.5%(115/622),对于胆囊切除术后患者,胆汁淤滞在胆管内易于形成结石。韩国的一项研究^[27]发现,清除胆管结石后预防性行胆囊切除术似乎并不能降低胆总管结石复发率。另外,幼年时行胆囊切除术可导致胆总管代偿性扩张,是胆总管结石形成的后天危险因素^[28]。

3 ERCP 因素

ERCP现已成为治疗胆总管结石的重要方式,常通过内镜下括约肌切开(EST)、内镜下乳头球囊扩张(EPBD)、内镜下胆道支架置入及内镜下机械碎石(EML)治疗胆总管结石。

3.1 EST与EPBD

对EST术后患者长期随访发现,EST是胆总管结石复发的危险因素^[29],EST破坏了Oddi括约肌功能,导致十二指肠液反流入胆道,胆道环境的改变易于结石长期复发。Kojima等^[30]研究发现EPBD术后结石复发率低于EST术后,EPBD术后可保留Oddi括约肌功能,改善远期预后,降低结石复发率。与单纯EST相比,小切口EST联合EPBD在治疗胆总管结石成功率方面无明显差异,但术后结石复发率明显降低,最小尺寸的十二指肠乳头切口可以预防胆管结石复发^[10]。但是, Kim等^[31]的研究发现EST联合内镜下乳头大球囊扩张术后胆总管结石的复发率与单纯EST组相当。

3.2 胆道支架

Kaneko等^[32]回顾性分析78例胆总管结石患者

进行的107例内镜下胆道支架置入术,发现18%的患者在去除塑料支架时有支架-结石复合体(stent-stone complex, SSC)形成,多因素分析发现,塑料支架的长期(≥ 301 d)放置和支架植入期间胆管扩张是形成SSC的独立因素,长时间保留支架可诱导细菌增殖,为结石形成提供条件。

3.3 EML

对于ERCP难以清除的胆总管巨大结石(>1.5 cm),常需要进行EML后取出。Konstantakis等^[33]通过随访495例经历过ERCP治疗的胆总管结石患者,发现67例(13.5%)患者胆总管结石复发,其中22例(32.8%)患者复发2次,ERCP术后胆总管结石复发与患者第1次ERCP取石时是否应用EML、胆总管直径、结石大小等相关。EML可能导致胆管残留微小结石碎块且无法通过胆道造影检测到,这些微结石再次形成结石的核心,成为胆总管结石复发的隐患^[7]。

3.4 十二指肠乳头狭窄

Tanaka等^[34]通过评估EST治疗胆总管结石的疗效,发现胆总管结石复发率为12.3%,其中EST术后致乳头口狭窄患者全部复发胆管结石,十二指肠乳头口狭窄是胆管结石复发的潜在危险因素。EST术后出现十二指肠乳头口狭窄可能是由于括约肌切开时凝血电流过大或者乳头切开不充分所致^[35]。狭窄的十二指肠乳头导致胆汁排泄不畅,易于结石复发。

另外,ERCP术后患者出现多次胆总管结石复发的情况也很常见,在第1次结石复发后,出现第2次复发的风险增加,因此,建议术后常规随访^[36]。胆总管结石复发是ERCP术后的常见问题,我们应慎重考虑ERCP在患者中的不利作用^[17]。

4 胆道感染因素

细菌学和形态学研究结果证实细菌感染与棕色色素结石的形成密切相关,扫描电子显微镜显示84.2%的胆管结石中存在细菌^[37]。细菌可产生 β -葡萄糖醛酸酶导致胆红素二葡萄糖苷酸的去结合,引起胆红素钙沉淀,有助于胆泥和结石形成^[38]。HBV、HCV感染可导致肝细胞受损,胆汁分泌异常致理化性质改变、胆汁淤积,同时胆管系统免疫损伤,引起胆管系统慢性炎症改变^[39-40]。另外,寄生虫感染可破坏胆管上皮,导致胆管慢性炎症,促进胆总管结石形成,华支睾吸虫、蛔虫和血吸虫感染与胆管结石的形成有关^[41]。

5 小 结

ERCP术后胆总管结石复发是多种相关因素影响下的共同结果。应重视Oddi括约肌的保护，Oddi括约肌可维持正常的胆道压力，既能控制胰液和胆汁的排泄，又能防止十二指肠液反流。EST术后，肠道菌群逆行进入胆道，破坏了胆道菌群平衡，因此应谨慎选择EST。其次，积极随访、控制胆道感染、促进胆汁排泄在降低ERCP术后胆总管结石复发方面具有重要作用。

总结ERCP术后胆总管结石复发的相关危险因素，将有助于临床医生在工作中对胆石病患者选择合理的治疗方案，最大化降低胆总管结石复发风险。

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