

EASL 胆石症预防、诊断和治疗临床实践指南[☆]

欧洲肝脏研究协会（European Association for the Study of Liver, EASL）*

引言

胆囊结石或胆石症是欧洲和其他发达国家主要的公共卫生问题，受累人群比例高达 20%。胆石症也是欧洲国家患者因消化系统疾病住院的最常见病因^[1]。近几十年来，胆石症患者的跨学科照护有了很大的进步，归功于对疾病病理生理学机制的深入认知和临床内窥镜及手术操作技术的显著提升，但这个常见疾病的一级预防仍处于萌芽阶段。

欧洲肝脏研究学会（European Association for the Study of Liver, EASL）胆石症预防、诊断和治疗临床实践指南（Clinical Practice Guidelines, CPG）旨在为下列问题提供推荐：

1. 胆石症的预防
2. 胆囊结石的诊断
3. 胆囊结石的内科治疗
4. 胆囊结石的外科治疗
5. 胆管结石的诊断
6. 胆管结石的内镜治疗和外科治疗
7. 肝内胆管结石的诊断和治疗
8. 妊娠期胆石症的治疗

EASL 胆石症 CPG 规范了胆石症患者管理中的预防、诊断和治疗方法（包括内科、内镜和外科），介绍了一系列得到普遍认可的胆石症预防、诊断和治疗方法，希望能给医师和其他专业医疗工作者、患者及其他相关人士在临床决策时提供帮助。

指南的制订基于从 PubMed 和 Cochrane 数据库中检索得到的证据，截至 2015 年 9 月前。参照推荐等级评估制定与评价（Grading of Recommendations Assessment Development and Evaluation, GRADE），根据支持证据的

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强度对指南中的证据和推荐意见进行分级^[2-5]。本指南对研究中的偏倚风险（方法学的质量）、证据的直接性、异质性、疗效估计的精准和发表偏倚等都做了考虑。每项推荐意见都标出了支持证据的等级。证据分级如下：（A）高质量证据：进一步研究非常不可能改变该效应估计结果可信度（随机试验或升两级的观察性研究）；（B）中等质量证据：进一步研究有可能严重影响该效应估计结果的可信度，并可能改变该估计结果（降级的随机试验或升级的观察性研究）；（C）低质量证据：进一步研究非常有可能严重影响该效应估计结果的可信度，并很可能改变该估计结果（观察性研究或降两级的随机试验）；（D）极低质量证据：任何效应估计结果都很不确定（病例系列 / 病例报道，降级的观察性研究，降三级的随机试验）。推荐意见的强度基于总体证据质量和对预期获益及风险的评估。强推荐是指：决定推荐意见强度的不同因素都具确定性，如遵循推荐意见，相关人群中的绝大部分或所有个体都可从中获益；弱推荐是指：决定推荐意见强度的不同因素存在不确定性。

胆石症的预防

一级预防

胆囊胆固醇结石和胆色素结石均源于遗传、环境、局部、全身和代谢紊乱之间的复杂相互作用^[6]。在西方人群，胆囊胆固醇结石占有所有胆囊结石的 90%~95%。黑色胆色素结石是慢性溶血性疾病或肝硬化患者的主要结石类型，但大部分黑色胆色素结石患者并不合并这两种疾病。胆囊胆固醇结石和黑色胆色素结石几乎都是在胆囊中形成的，而棕色胆色素结石主要在大胆管中形成。在西方人群中，棕色胆色素结石通常见于胆囊切除术后和硬化性胆管炎患者的胆管，而在东方人群，棕色胆色素结石的发生与慢性感染性胆管炎相关^[7]。胆泥并非胆囊结石形成的原因，随胆汁淤积和胆汁肝肠循环减弱而发生，但胆汁淤积本身即可促进胆囊结石形成。鉴于胆石症是西方国家最

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常见且医疗支出最大的消化系统疾病^[8]，需要在一般人群中进行一级非药物预防^[9]。一些风险因素与胆囊胆固醇结石、胆色素结石和混合型结石相关，对于其中的非遗传性风险因素，可采取一般或特殊一级预防措施。

生活方式

胆石症可以预防吗？

健康的生活方式和饮食、规律的体育活动、保持理想体重，可能预防胆囊胆固醇结石和症状性胆石症（**低质量证据；弱推荐**）

注释：生活方式作用于代谢综合征（肥胖、糖尿病和胰岛素抵抗）的一个或多个因素，从而影响胆囊胆固醇结石的发病机制^[10-16]。肥胖易于形成胆囊结石^[17]并增加了症状性胆囊结石的风险，从而增加胆囊切除风险^[18-28]。因此，身体质量指数（body mass index, BMI）增加是胆结石形成的确定风险因素^[6,20,26,29]，BMI增高本身同时也是引起症状性胆囊结石的风险因素，特别是女性^[30]。有研究报告，症状性胆囊结石的风险随BMI、腰围以及血清甘油三酯水平增加而升高^[31]。

其他与肥胖相关的促进胆囊胆固醇结石形成的因素包括：胆囊淤积^[32-35]、胰岛素抵抗、血脂紊乱[高密度脂蛋白（high density lipoproteins, HDL）减少^[31]和高甘油三酯血症]，久坐的生活方式^[30,36]，激素替代治疗^[30]和快餐摄入^[30]。在探索血脂及其与胆石症和肥胖的关系时，前瞻性队列研究^[31,37,38]较病例对照研究^[28,39,40]和横断面研究^[19,41-43]更具价值。因此，在一般人群中恰当的生活方式干预应着重于超重和肥胖个体理想体重的维持和减重^[30]。胰岛素抵抗和2型糖尿病也与胆囊胆固醇结石强烈相关且独立于肥胖^[44]。这些疾病状态代表了预防胆石症的其他目标方式。

体育活动

问卷调查发现体育活动似乎能预防胆石症的形成^[36,45-48]，使症状性胆囊结石的风险下降约30%^[36,45,49-51]。最近一项前瞻性队列研究[欧洲诺福克癌症前瞻性调查（European prospective investigation into cancer, EPIC）]使用了经过验证的针对能量消耗和心肺适应性的问卷^[52]，研究中，年龄为40~74岁的25 639名志愿者被分到体育活动量依次增加的四个组中，随访超过14年以观察症状性胆囊结石的情况。随访5年和14年，分别记录到135例（简单型）和290例（复杂型）新发症状性胆囊结石，68%的

病例为女性。体育活动量最大的一组（相当于久坐型职业者每天运动1 h，或久站型职业者每天运动30 min，或重体力劳动者不进行额外体育活动），男性和女性人群的症状性胆囊结石风险均降低70%；特别是在观察5年后便显示出可能的因果效应。体育活动对胆石症形成及相关并发症的潜在有益作用受病理机制支持。高胰岛素血症促进肝脏对胆固醇的摄取^[53]，增加胆汁胆固醇分泌^[54]并减少胆汁酸分泌（二者均能诱发胆固醇过饱和和致石性胆汁）^[55]。相反，规律的体育活动降低胰岛素水平^[56]，减轻胰岛素抵抗^[57]、甘油三酯血症^[58]和脂肪酸依赖性的胆囊黏蛋白分泌过多^[59]。而且在进行体育活动时，血清HDL-胆固醇水平增加^[60,61]，标志着肝脏胆固醇逆向转运增加^[62]。值得注意的是，HDL-胆固醇是胆汁酸的前体^[63]，参与降低胆汁胆固醇的饱和度，HDL-胆固醇水平也的确与胆石症的发病率呈负相关^[41]。体育活动的另外一个作用涉及促胃肠动力作用^[64]和胆囊收缩素依赖性的胆囊收缩^[65]。鉴于体育活动对心血管健康的整体有益作用在对胆石症形成的保护作用之上^[29]，因此应对一般人群反复强调维持理想体重和定期进行体育活动的重要性^[45]。

饮食

开展基于大样本人群的长期、前瞻性的流行病学研究来确定膳食组分的预防价值存在困难，原因是难以估计营养素的准确含量和摄入模式。但高纤维、高钙饮食可减少胆汁中的疏水性胆汁酸，而规律的进食模式可增加规律的胆囊排空，从而减轻胆囊淤积^[45]。二者都对胆固醇胆石症有预防作用。典型的西方高热量饮食（包括红肉摄取^[48]）增加了患胆石症的可能性^[66]。因此减少总卡路里的摄入可能有效^[67]。

水果和蔬菜^[68]对胆石症的发生可能具有预防作用，但素食的获益数据仍有争议。尽管较低BMI^[69]和常规食用植物油和维生素C都可能产生保护作用^[46,70]，但在不同人群中开展的研究显示，素食对胆囊结石可能有预防作用^[71-75]，或没有预防作用^[47,76]。

多不饱和脂肪和单不饱和脂肪^[77]，特别是食用坚果^[77,78]可能预防胆石症。可作为健康饮食的一部分。

有关咖啡摄入的数据存在矛盾：一些流行病学研究报道，摄入咖啡因（来源：咖啡、红茶和含咖啡因的软饮）——特别是咖啡，有保护作用^[79-84]，但并非所有研究都得出了这个结果^[47]。地理因素、文化因素和咖啡的饮用方式或许能解释结果的不一致^[47]。除可能作用于肝脏中胆固醇的分泌和肠道的运动外，人们对咖啡因或饮用咖啡的其他作用机制仍知之甚少。

尽管有前瞻性流行病学研究报告，酒精摄入对胆结石的形成有预防作用^[31,78,79]，多因素分析提示，丹麦人群中症状性胆囊结石患者的酒精摄入量低于无症状的胆囊结石患者^[30]。但由于研究结果存在争议^[72,81-83,85,86]，加之酒精对整体健康的不利影响，故不推荐通过饮酒来预防胆结石。

定期补充维生素 C 或经常食用富含维生素的膳食可能对胆囊结石的形成有预防作用。事实上，胆固醇转变为胆汁酸需要 7 α -羟基化且肝细胞中含有适当数量的维生素 C^[87,88]。因而，人体维生素 C 缺乏可能增加胆囊胆固醇结石形成的风险^[70]。在胆结石患者中，补充维生素 C (500 mg, 每日 4 次) 能改变胆汁酸的成分，增加磷脂含量，已证明能通过延长胆汁胆固醇的结晶时间而发挥保护作用^[89]。此外，观察性研究发现维生素 C 摄入减少与胆结石/胆囊疾病^[48,70,90]或胆囊切除^[91]风险之间存在一定联系。在德国的一项基于人群的观察性研究中 (2129 例受试者，年龄 18~65 岁)，定期服用维生素 C (n=232) 的患者和不服用维生素 C 的患者 (n=1897) 超声检测胆结石患病率分别为 4.7% 和 8.2%^[92]。

一般人群的胆结石预防

对于一般人群，是否建议通过药物治疗预防胆结石？

在一般人群中不建议通过药物预防胆结石（**极低质量证据；弱推荐**）

注释：在一般人群中没有应用熊去氧胆酸 (ursodeoxycholic acid, UDCA) 预防胆结石的指征，高危人群除外 (参见“高危人群胆结石的一级预防”部分)。与之相似，妊娠期胆结石可以是一过性的，因此当前也没有足够的证据支持妊娠期女性使用 UDCA 或补充 Ω -3 脂肪酸来预防胆结石或胆泥^[93]。

他汀类药物单独应用或与 UDCA 联合应用对胆结石的预防效果存在争议。两项基于人群的病例对照研究评估了他汀类药物的应用。结果显示常规使用他汀类药物的患者胆结石和胆囊切除的风险均降低^[94,95]，该趋势在另外一项评估他汀类药物应用超过十年的研究 (护士健康研究) 中得到了证实^[96]。一项病例对照研究证实了他汀类药物对胆囊切除风险的预防效果^[97]。尽管这些结果看似很有前景，但洛伐他汀^[98-101]、普伐他汀单药^[102-106]或联合 UDCA^[107]、辛伐他汀单药^[103,108-112]或联合 UDCA^[113,114]以及氟伐他汀^[115]对胆汁胆固醇

的饱和度、胆汁的脂质构成、胆固醇结晶、胆囊结石形成和结石溶解的预防效果很弱，且有时无法得到验证。最近一项纳入了 6 项研究 (4 项病例对照研究，1 项队列研究和 1 项横断面研究) 共 622 868 例受试者的荟萃分析显示，与不使用他汀类药物相比，正在使用他汀类药物的人群胆囊切除风险降低，且这种保护效应在中等量和大量使用他汀类药物时 (即 1-4 次) 较小量使用他汀类药物时更为明显^[116]。芬兰的一项病例对照研究对 272 例使用他汀类药物的患者和年龄、性别匹配的 272 例不使用他汀类药物的患者进行了研究，探索使用他汀类药物对复杂型胆结石胆囊外科手术的影响。使用他汀类药物的患者在胆囊切除术后的预后并不比不使用他汀类药物的患者差，他汀类药物治疗与腹腔镜胆囊切除术手术时间更短相关^[117]。不过到目前为止，仍需要更好的对照研究来证实这些发现，不提倡使用他汀类药物预防胆结石^[118,119]。

依折麦布是选择性胆固醇吸收抑制剂，作用于肠道的尼曼匹克 C1 样蛋白 1 (Niemann-Pick C1-like 1, NPC1L1)。结石饮食饲养的小鼠研究显示，依折麦布对胆汁的脂质成分、小肠胆固醇的吸收和胆汁胆固醇的分泌和饱和、结晶聚集、胆囊结石形成、胆汁流出、胆囊的运动功能和胆囊脂肪变性均可产生有益的影响^[120-123]。结石饮食饲养的仓鼠模型研究中，依折麦布可防止胆汁胆固醇的增加和胆固醇在肝内的蓄积^[124]。依折麦布这些作用的转化价值在一项针对胆囊胆固醇结石患者的先导性试验中得到了证实：依折麦布降低胆汁胆固醇的饱和度，阻止胆固醇形成结晶^[120]。然而，在一项小型的回顾性病例对照研究中，依折麦布似乎没有对胆结石的患病率产生影响^[125]。最近，丹麦的一项纳入了 67 385 例受试者的大型研究显示，NPC1L1 基因变异——模拟了依折麦布单药治疗的作用——的确与血清低密度脂蛋白 (low-density lipoprotein, LDL) 胆固醇浓度的剂量依赖性下降以及缺血性血管疾病的风险下降相关。然而，症状性胆结石的累积发病率增加 (样本量为 3886 例)^[126]。在人类 (小肠和肝脏表达 NPC1L1) 中，存在遗传性 NPC1L1 活性下降导致肠细胞对肠道胆固醇的摄取以及肝细胞对胆汁胆固醇的摄取率下降的可能性。后者可能增加了胆结石的风险。不过，在随访时间最短为 2.5 年的 IMPROVE-IT 试验中，胆囊相关不良事件与依折麦布治疗无关 (研究对比了依折麦布联合他汀类药物治疗与他汀类药物单独治疗的患者)^[127]。总体而言，这些数据提示，使用依折麦布预防胆囊胆固醇结石还需要进一步的探索^[118,119,128,129]。当患者存在代谢异常和高心血管风险时，联合降脂药物治疗时 (他汀类/依折麦布)，有性别特异的胆囊结石风险

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时（女性高于男性）以及考虑依折麦布治疗的总疗程时，需要客观地看待这种治疗方法。

最后，使用阿司匹林预防胆结石目前尚未得到认可^[6]。

高危人群的胆结石一级预防

快速减重

肥胖患者何时可使用熊去氧胆酸预防胆结石？

在导致快速减重的情况下（如，极低热量饮食、减重手术），可推荐短期应用熊去氧胆酸（至少 500 mg/d，至体重稳定）（中等质量证据；弱推荐）

注释：BMI 增加和女性都是胆囊结石生长的明确危险因素^[6,20,26,29]。BMI 增加也是症状性胆结石的致病危险因素^[30]。肥胖影响绝大部分胆囊结石形成的病理机制，包括胆汁胆固醇过饱和、胆固醇结晶倾向增加、结石聚集和胆囊排空受损^[6,26,130-134]。然而，在实施减重计划导致体重快速下降时（ > 1.5 kg/周）^[131,135-137]，胆结石的风险同样显著增加，直到约 2 年后体重稳定时才下降^[138,139]。体重循环也是胆囊结石形成的弱独立危险因素^[48,82,132,140]。相反，肥胖人群以适中的速度（最多 1.5 kg/周）逐渐减轻体重^[136,141,142]能减少过多的胆固醇从头生物合成和胆汁排泄，降低胆囊结石形成的风险。近来一项研究对 171 例患者进行了多变量分析，报道与减重术后胆囊结石形成相关的因素有体重下降过快、胆囊排空比例进行性下降、夜间空腹时间延长、热量和纤维摄入减少^[143]。

快速减重可通过极低热量饮食（即每日饮食中所含热量 < 800 千卡^[139,144-147]）或减重手术，如 Roux-en-Y 胃旁路术（Roux-en-Y gastric bypass, RYGB）^[81,131,137-139,148-152] 实现。尽管快速减重后新形成的胆囊结石大部分都无症状，但单纯型和复杂型胆结石以及胆囊切除的风险仍然有所增加，且极低热量饮食的风险是低热量饮食的 3 倍^[139]。如近期的对照研究所示，极低热量饮食中适当的脂肪含量（至少 7 g/d）或能改善胆囊的运动，降低症状性胆结石的风险^[139,153,154]。快速减重的患者更可能出现症状性胆结石，胃旁路手术后的发病率达 28%~71%^[27,150,151,155,156]。手术 3 年后，高达 1/3 的患者有胆囊切除术指征^[27,150]。在减重手术，特别是胃旁路术或袖状胃减容术后，体重下降超过原体重的 25%，发生胆结石的风险增加达 48%^[157-162]。在术后采取低热量饮食的肥胖患者中观察到了相同的趋势^[137]。

在采取极低热量饮食或接受减重手术以快速减重且未实施胆囊切除术的肥胖患者中，在快速减重后使

用有溶石作用的疏水性 UDCA 可预防胆囊胆固醇结石的形成。然而，必须考虑长期治疗的成本和患者的依从性^[137,138,148-151,163]。有学者对 13 项有关 UDCA 在减重期间的保护作用的随机对照试验（randomized control trial, RCT）进行了荟萃分析，共涉及 1791 例患者，1217 例随机接受 UDCA 治疗，574 例随机接受安慰剂治疗。该分析确认，节食期间或行减重手术后应用 UDCA（300~1200 mg/d）能预防胆囊结石的形成^[164]。UDCA 的剂量（500~600 mg/d）应低于溶石治疗时的剂量，并持续应用至体重稳定^[150]。事实上，体重一旦稳定后，发生结石的风险就会下降，因此减重期间的疗效最佳^[150]。一项决策树分析显示，使用 UDCA 预防胆囊结石可降低成本^[165]。UDCA 已成为肥胖患者在采取极低热量饮食时或接受胃旁路手术后预防胆固醇胆结石的标准治疗。接受垂直束带胃成形术或可调式胃束带术治疗的患者被随机分组接受安慰剂或 UDCA 500 mg/d 治疗，12 个月和 24 个月时胆囊结石形成的发生率在安慰剂组分别为 22% 和 30%，在 UDCA 组分别为 3% 和 8%。胆囊切除率在安慰剂组和 UDCA 组分别为 12% 和 5%^[138]。在 Wudel 等的研究中^[151]，胃旁路术后 12 个月内 71% 的患者发生胆囊结石，41% 为症状性胆囊结石，其中 67% 的患者接受了胆囊切除术。与安慰剂相比，UDCA 能有效预防胆囊结石形成，但依从性不佳是导致治疗结局较差的主要问题。需要进一步研究以验证联合干预措施（如节食联合 UDCA）是否能改善减重期间的胆囊结石预防^[143,166]。

鱼油（n-3）多不饱和脂肪酸对胆汁结晶的有益作用在一项随机双盲安慰剂对照试验中得到了确认，该研究纳入了采取低卡路里饮食（1200 千卡/天）、快速减重的肥胖女性，并与 UDCA（1200 mg/d）进行了比较^[93]。

按照既往研究^[137,138,147,148,151]中采用的剂量（即 300~1200 mg/d）应用时，预期 UDCA 不会产生严重的副作用。Sugerman 等^[150]注意到一些应用 UDCA 治疗的患者因“呕吐或皮疹”而退出试验，但在安慰剂组也观察到相似的比例。Schiffman 等^[147]报道，UDCA 组便秘、头痛、腹泻、头晕和上呼吸道感染等不良事件发生率为 16%~30%，与安慰剂组相似，与 UDCA 剂量无关。

没有使用阿司匹林预防胆结石复发的适应证^[167]。

是否应该在肥胖人群行减重手术快速减重的同时行预防性胆囊切除术？

减重手术时无常规行预防性胆囊切除术的适应证（极低质量证据；弱推荐）

注释：减重手术后，胆囊结石相关的并发症一般在7~18个月内出现^[168-172]。接受RYGB而保留胆囊的患者中位随访3年，约20%出现症状型胆囊结石，需要行胆囊切除术。估计的5年无胆囊疾病生存率低(77.4%)^[173]。理论上，预防性胆囊切除术的另一个优点是能预防将来发生胆管结石，因RYGB术后解剖结构发生改变，很难通过内窥镜治疗移除。根据这些估计，曾推荐RYGB同时行预防性胆囊切除术，理论依据是不增加中转开放式手术的比例，也不增加手术时间或住院时间^[173]。然而，进一步的研究提示RYGB后大部分患者可保持无症状^[156,157,160,168,169,174-178]、不需要进一步干预。因此，腹腔镜旁路手术术中不再常规同时行(预防性)胆囊切除术^[168,169,174-176,179]。

本质上，胆囊切除术是在症状性胆石症或胆囊有异常表现时(如慢性胆囊炎、肿瘤样病变)^[152,171,173,180,181]才进行的。尽管在症状性胆石症患者中，RYGB术后的胆囊切除术变得更加困难，而且内镜下逆行胰胆管造影(endoscopic retrograde cholangiopancreatography, ERCP)可能因解剖原因而不再适用，但即便存在这个事实，这个假设仍然成立^[182]。

RYGB术后患者最具成本效益的胆囊管理策略还存在一些不确定性，近来一个建立在美国医疗系统背景上的决策模型被开发出来^[183]。模型比较了三种可能的选择：预防性同时行胆囊切除术，行RYGB且保留胆囊(术后使用或不使用UDCA治疗)，以及仅对超声发现有胆囊结石的患者行择期胆囊切除术。最具成本效益的策略为行RYGB且保留胆囊——前提是术后出现胆囊结石并发症的风险较小^[180]且不使用UDCA治疗。RYGB术后使用UDCA治疗可能过于昂贵，在这种情况下，同时行胆囊切除术就变得更加经济。应用UDCA的另外一个限制是每日服药的依从性不稳定，依从率在40%到85%之间^[150,151,158,168,172]。

长期应用生长抑素或类似物治疗

应用生长抑素或类似物治疗时是否可使用熊去氧胆酸一级预防胆石症?

对于长期应用生长抑素或类似物治疗的患者，可考虑同时应用熊去氧胆酸治疗，以预防胆囊胆固醇结石的形成**(低质量证据；弱推荐)**

注释：需要生长抑素或各种类似物长期治疗的患者(如神经内分泌肿瘤患者)表现为肠通过时间延长、餐后缩胆囊素(cholecystokinin, CCK)释放良好但胆囊排空

严重受损^[184]，以及胆汁中出现多种致结石性改变^[185-188]。尽管胆石症发生率高，但不常发展为症状性疾病或需要急性期手术^[189]。推荐对这类患者进行密切随访，关注胆石症的变化，也许可考虑同时使用UDCA治疗^[186,187,190]。

全肠道外营养

全肠道外营养支持时是否应对胆石症进行一级预防?

接受全肠道外营养支持的患者胆泥形成风险增加，但无法做出预防推荐**(极低质量证据；弱推荐)**

注释：胆泥形成常见于胆囊淤积增加和/或胆汁成分同时改变时，如空腹时间延长[特别是全肠道外营养(total parenteral nutrition, TPN)支持时]^[191]。由于胆囊动力学和胆汁成分的改变都是一过性的，在恢复经口饮食后，胆泥和小的结石可能会消失(如每日三餐并补充足够的脂肪以促进胆囊排空和胆泥清除)^[192-196]。TPN患者只要有可能就应该转换为肠内营养支持。有关在TPN时使用CCK(每日补充外源性CCK或快速输注大剂量晶体氨基酸)对胆囊的刺激数据结论不一^[92,193,197-199]。一项研究中，2例接受长期TPN的患儿应用豆油/中链甘油三酯/橄榄油/鱼油混合乳剂后，分别在3个月和2个月时出现了胆囊结石消失和结石尺寸缩小，这2例患儿还持续应用UDCA 15 mg/kg/d治疗^[200]。这些研究的整体结果虽然可信，但受到了病例数太少的限制。此外，在TPN中断后有胆泥的患者没有应用UDCA进行预防性治疗的指征^[190]。使用富含 Ω -3脂肪酸的TPN有可能增加胆汁磷脂酰胆碱中的 Ω -3脂肪酸含量，降低胆汁胆固醇的过饱和^[201]，相关机制还包括胆汁黏蛋白的抑制^[202]。

激素治疗

激素替代治疗时是否有通过药物或手术预防胆结石的指征?

处方激素替代治疗的医师应知晓此时胆石症的风险增加。目前尚无激素替代治疗期间通过药物或手术预防胆石症的指征**(极低质量证据；弱推荐)**

注释：激素治疗广泛用于控制更年期症状，也用于老年女性心血管疾病、骨质疏松和痴呆的管理和预防。近

Clinical Practice Guidelines

来的一项 Cochrane 荟萃分析^[203]比较了激素治疗与安慰剂治疗 3~7 年的疗效，给药途径有口服、经皮、皮下或经鼻内给药（单纯雌激素以及联合或不联合持续给予孕激素）。该分析纳入了 23 项随机双盲研究，涉及 42 830 名年龄在 26~91 岁的女性，主要来自心脏和雌激素-孕酮替代研究（Heart and Estrogen-progestin Replacement Study, HERS）1998 和妇女健康倡议（Women's Health Initiative, WHI）1998 研究，结果显示：包括患有心血管疾病的绝经后女性在内，仅使用雌激素 [绝对风险从 26/1000 增至 45/1000, 95% 可信区间 (confidence interval, CI): 36~57/1000] 和联合持续治疗（绝对风险从 27/1000 增至 47/1000, 95% CI: 38~60/1000）的人群，胆囊疾病风险显著升高^[204,205]。激素治疗组的风险增加从治疗第一年就开始。因此推荐医师在处方各种类型的持续激素治疗以控制更年期症状时，应加以注意。经仔细评估潜在的严重健康危害，应只针对具有心血管疾病、静脉血栓栓塞或乳腺癌低危风险的患者给予治疗。胆囊疾病的风险已然明确，但目前尚无随机试验对药物预防胆石症进行研究。

胆管结石复发的预防

是否有有效预防胆管结石复发的策略？

对于胆管结石复发的药物预防，无法做出一般推荐（**极低质量证据；弱推荐**）

注释：经内镜下括约肌切开取石治疗后，5%~20% 的胆管结石患者会复发^[206-211]，通常可通过内镜治疗移除。当前缺乏经过验证的预防措施。药物二级预防的获益不一致，UDCA 的潜在作用^[212]也未在随机对照试验中得到验证^[212,213]。

编码磷脂酰胆碱易位酶 ABCB4 的基因发生突变的患者有发生低磷脂相关胆石症（low phospholipid-associated cholelithiasis, LPAC）的单基因倾向。由于胆汁磷脂浓度下降，患者在 40 岁前发生肝内胆管和胆囊的胆固醇结石，胆囊切除术后胆道症状反复发作^[214-217]。该病的诊断基于病史、临床表现和影像学。通过 ERCP 采集十二指肠或肝内的胆汁并行显微镜检寻找结晶和小结石（及进行化学分析），有助于这类患者的管理。一级亲属的胆石症和胆管结石反复发作家族史能够提供诊断线索^[218]，因此通过 ABCB4 基因的序列分析进行基因检测可能提供更多的信息，但并非诊断 LPAC 所必需。LPAC 患者在年轻时即开始 UDCA 预防性治疗或长期治疗（15 mg/kg/d）以预

防结石的出现或复发以及相关并发症，大部分患者都能获益^[216]。

胆囊结石的诊断

胆绞痛

何时应怀疑症状性胆囊结石？

胆囊结石的特征性症状为右上腹或上腹部剧烈疼痛伴阵发性加剧，持续至少 15~30 min，并向右侧背部或肩部放射，镇痛药物可缓解疼痛，应通过病史和体格检查确定（**极低质量证据；弱推荐**）

注释：西方人群中 10%~20% 存在胆囊结石，其发病率随年龄增加，女性发病率更高。约 80% 的胆囊结石患者无症状。无症状性胆囊结石的自然史提示，大部分患者可能终身不出现症状。出现症状的患者比例为 1%~4%/年，20% 的患者在诊断后 20 年内出现症状^[219-222]。首次胆绞痛发作后，并发症发生率为 1%~3%/年，在无症状患者中并发症的发生率为 0.1%~0.3%^[219,223]。

仅有 3 种症状与胆石症显著相关：胆绞痛 [比值比 (odds ratio, OR)=2.6; 95% CI: 2.4~2.9]、放射痛 (OR=2.8; 95% CI: 2.2~3.7) 和镇痛药有效 (OR=2.0; 95% CI: 1.6~2.5)^[224]。尽管胆区疼痛的阳性似然比为 1.34，但对胆道症状的阳性预测值很低 (0.25)^[225]。可出现恶心和呕吐。疼痛剧烈 (0~10 分疼痛视觉模拟评分的强度高于 5 分)、突然发作或在稳定前持续加重。这是由于胆囊结石或胆泥急性且通常一过性地阻塞胆囊管后胆囊扩张所致。大部分疼痛可自行消退。疼痛周期不规律，约在餐后 1 h 后发作，出现在傍晚或深夜，患者可从睡眠中痛醒，疼痛持续超过 1 h 等都高度提示胆源性疼痛^[226,227]。持续超过 5 h 最常提示急性胆囊炎。超过半数的患者在出现胆囊结石并发病之前都发生过至少一次“预警性”的胆绞痛^[228,229]。

超过 50% 的患者在首次胆源性疼痛发作后疼痛再次发作^[219,223,230]。常见消化不良、烧心、腹胀、肠胀气等症状。这些症状并非胆石症的特征性症状，也可发生于无胆囊结石的个体，可能提示功能性消化不良、胃食管反流病、肠易激综合征或心脏疾病等。如果发生于胆囊结石患者，在胆囊切除术后通常持续存在^[226,231-233]。在对胆源性腹痛进行鉴别诊断时还应考虑其他导致上腹疼痛的原因。

实验室检查对简单型症状性胆囊结石的诊断没有帮助，因为在大部分患者中检查结果正常。

影像学

哪种影像学方法最适合诊断胆囊结石？

对于近期有胆源性腹痛病史的患者，应行腹部超声检查（**高质量证据；强推荐**）

临床高度怀疑胆囊结石而腹部超声检查阴性时，可行超声内镜 [或磁共振成像（magnetic resonance imaging, MRI）] 检查（**低质量证据；弱推荐**）

注释：上腹部疼痛患者的影像学检查应选择腹部超声。腹部超声检测胆囊结石的准确性超过 95%^[234-236]。腹部疼痛不典型的老年患者、感染灶不明的免疫功能低下患者或疑似腹部感染灶的菌血症患者也可进行腹部超声检查，判断是否存在（复杂型）胆囊结石。

腹部超声检查时，胆结石表现为强回声灶伴远端低回声影。可通过活动性鉴别结石和息肉，应在不同体位（仰卧位、左侧卧位或直立位）进行检查以证实。通过超声也可检测到胆泥，呈泥沙样的小强回声灶^[237]。

超声内镜（endoscopic ultrasound, EUS）在胆源性腹痛但腹部超声表现正常的患者中检测胆石症的灵敏度高达 94%~98%^[238]。难以解释的急性和急性复发性胰腺炎可由胆泥引起，该检查可能对这些患者带来额外帮助^[239-242]。当超声检查结果不确定时，推荐进行磁共振成像检查^[243,244]。计算机断层扫描（computed tomography, CT）对胆囊结石的诊断帮助不大。

急性胆囊炎

诊断急性胆囊炎的检查方法有哪些？

如患者出现发热伴右上腹剧烈疼痛持续数小时，触诊时右上腹有压痛（墨菲氏征），应怀疑急性胆囊炎（**中等质量证据；强推荐**）

临床高度怀疑急性胆囊炎时，可行 CT 检查（**极低质量证据；弱推荐**）

注释：急性胆囊炎是胆石症最常见的并发症，见于约 10% 的症状性胆囊结石患者^[245]。胆囊壁的急性炎症通常是由于胆囊管被结石阻塞所致。在急诊室就诊的急性腹部症状患者中，3%~9% 存在急性胆囊炎，这些患者中约 45%~80% 报告曾有过胆源性腹痛发作^[223,229]。急性胆囊炎时，腹痛剧烈并逐渐加重，持续数小时（通常超

过 5 小时），向肩胛间区或右肩部放射，伴发热，通常还伴恶心和呕吐。腹部右（不是左）上象限疼痛伴压痛（墨菲氏征）对诊断急性胆囊炎具高度特异性和敏感性^[246]。患者常常伴有发热和炎症指标升高 [白细胞计数、C 反应蛋白（C-reactive protein, CRP）]。为评估急性胆囊炎的严重程度，可能需要检测血尿素氮、肌酐、白蛋白和进行动脉血气分析，以指导进一步的监测和治疗决策^[247]。

腹部超声可准确检测胆囊结石、胆囊肿大、胆囊壁增厚（> 4 mm）、胆囊周围积液和超声墨菲氏征（探头直接从胆囊上压过时疼痛加重）。急性胆囊炎时超声检测结石的灵敏性下降^[243]，但结合胆囊结石和超声墨菲氏征或胆囊壁增厚，诊断急性胆囊炎的阳性预测值分别为 92% 和 95%^[248]。

尽管 CT 在急性胆囊炎中的应用价值还有待评估，但其可准确形象地展现肿大的胆囊和增厚的胆囊壁，可以发现急性胆囊炎的合并症，如胆囊壁气肿、脓肿形成和穿孔^[249,250]。因此 CT 常被用于急诊手术前的检查。

放射性同位素胆道闪烁显像（Radioisotope cholescintigraphy, Tc-HIDA 扫描）可检测胆囊管梗阻，表现为静脉注射示踪剂后胆囊无法充盈。其诊断急性胆囊炎的灵敏度高^[250-252]，但无法显示胆结石，并且存在电离辐射，使超声成为欧洲首选的影像学检测方法^[244]。尽管近来的荟萃分析显示，腹部超声（83%；95% CI：74%~89%）、MRI（81%；95% CI：69%~90%）、和胆道闪烁显像（90%；95% CI：86%~93%）相比，三种方法的特异性无显著差异^[250]，但后两者不太适合急诊应用。

胆石症的药物治疗

胆汁酸溶石治疗

可以口服胆汁酸溶石治疗吗？

不推荐单独应用胆汁酸溶石或联合体外震波碎石治疗胆囊结石（**中等质量证据；强推荐**）

注释：尽管对 UDCA 溶石治疗研究的荟萃分析^[253]显示，其在胆囊功能良好的小型非钙化结石患者中的治疗成功率良好（治疗 6 个月以上，63% 的患者结石消失），但由于长期复发率高（5 年复发率为 25%~64%，10 年复发率为 49%~80%），因而对后续症状和合并症的预防无效^[254-265]。来自随机对照试验、系统性回顾和队列研究的证据显示，体外震波碎石术（extracorporeal shock wave

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lithotripsy, ESWL) 与单用 UDCA 进行胆汁酸溶石治疗的治愈率均较低, 仅有 55% 经仔细选择的病例维持无结石状态^[266]。

大部分胆囊结石复发为症状性, 1/3 的患者在平均 3 年后不得进行胆囊切除术^[267]。使用 UDCA 治疗 3 个月, 仅 26% 的患者持续不出现绞痛症状, 而安慰剂组为 33%, UDCA 治疗后约 2% 的患者出现胆囊结石并发症, 这与未服药人群并发症的年发生率相似^[253,264,265,268-272]。

日本的一项队列分析结果显示, 溶石治疗能独立降低胆源性腹痛或急性胆囊炎的风险^[273], 但这一结果在随后的一项荷兰研究中并未得到验证, 后者发现在症状明显、等待行胆囊切除术的患者中, UDCA 治疗并不能减轻胆囊症状^[268]。

胆绞痛的治疗

胆绞痛患者如何治疗?

应使用非甾体抗炎药 (如双氯芬酸、吲哚美辛) 治疗胆绞痛 (**中等质量证据; 弱推荐**)

此外, 也可对症给予解痉药 (如丁基东莨菪碱), 症状严重时还可使用阿片类药物 (如丁丙诺啡) (**低质量证据; 强推荐**)

注释: 在治疗急性胆绞痛时, 医师必须区分立即药物镇痛治疗和对因治疗 (即胆囊切除术)。根据唯一一项试验的结果, 在诊断胆绞痛 24 h 内早期行腹腔镜胆囊切除术可去除病因且降低在等待胆囊切除手术期间的发病率^[274], 但在等待时间较短的情况时, 是否推荐该方法还需进一步的 RCT 证实^[275]。

胆绞痛镇痛治疗时常联合镇痛药及解痉药。非甾体抗炎药 (nonsteroidal anti-inflammatory drug, NSAID) 如双氯芬酸 (如 50~75 mg 肌肉注射)、酮洛芬 (如 200 mg 静脉注射) 或吲哚美辛 (如 50 mg 静脉注射或 2×75 mg 栓剂) 对胆绞痛有镇痛作用^[276-278]。近期的 RCT 研究表明, 使用这些 NSAID 可降低胆绞痛期间发展为急性胆囊炎的风险^[278-280]。与其他药物相比, NSAID 的镇痛作用较解痉药更强^[278]。应用时需考虑 NSAID 过敏史/严重变态反应史等禁忌证, 以及肾功能损伤、消化道并发症等情况。在个别病例中, 镇痛作用较弱的安乃近^[281] 和扑热息痛等即可镇痛。此外, 由于胆囊结石引起的胆绞痛也可通过硝酸甘油成功治疗^[282]。

症状严重时, 可给予镇痛作用更强的阿片类药物, 但在 RCT 研究中, 阿片类药物和 NSAID 并无差异^[278]。最适合的药物可能是丁丙诺啡, 因其对胆总管括约肌的收缩作用弱于吗啡^[283-285]。不同药物 (如 NSAID 联合阿片) 联合应用的疗效尚未得到充分评估。

抗生素

抗生素在急性胆囊炎时是否普遍适用?

对于轻度急性胆囊炎, 即无胆管炎、菌血症/脓毒症、脓肿或穿孔时, 始终不推荐使用抗生素 (**极低质量证据; 弱推荐**)

注释: 急性胆囊炎的初始治疗目标为患者的一般支持, 包括补充液体和电解质以及纠正代谢紊乱。急性胆囊炎的抗生素治疗通常是经验性的。然而, 未发现症状严重程度、胆囊情况或胆囊培养物阳性与术后应用抗生素之间有任何相关性^[286]。近来的一项小型随机对照试验显示, 轻度急性胆囊炎患者接受静脉阿莫西林/克拉维酸或联合环丙沙星和甲硝唑治疗, 并不能改善其住院期间的早期预后^[287]。免疫功能不全的复杂型胆囊炎 (急性胆管炎、菌血症/脓毒症、穿孔、脓肿) 患者通常需要进行抗生素治疗。初始治疗应覆盖肠杆菌科致病菌, 特别是大肠杆菌。在临床情况严重时有必要覆盖厌氧菌, 特别是拟杆菌属^[288]。在前瞻性系列研究中, 入院时年龄 ≥ 70 岁, 合并糖尿病、胆囊肿大与保守治疗失败相关, 随访 24 h 和 48 h 时持续白细胞升高和心动过速是需要行胆囊切除术的预测因素^[289]。

胆石症的手术治疗

症状性胆结石患者

症状性胆结石的治疗选择是什么?

胆囊切除术为症状性胆结石的首选治疗方式 (**中等质量证据; 强推荐**)

注释: 根据症状发作的强度和次数, 症状性胆石症应行胆囊切除术, 因为约半数患者会出现胆绞痛复发^[268]。发生急性胆囊炎、胆源性胰腺炎、梗阻性黄疸和胆管炎等并发症的风险为每年 0.5%~3%^[219,221,230,290,291]。手术治

疗的替代方法包括使用 UDCA 进行胆汁酸溶石治疗和 ESWL，但这些治疗的治愈率低、胆结石复发率高、且内科治疗后无法预防症状和并发症，因而不被推荐。UDCA 的治愈率仅为 27%，ESWL 在精心挑选的患者中治愈率仅为 55%，且结石完全溶解后或 ESWL 后 4 年内胆囊结石的复发率超过 40%。此外，不论是否接受 UDCA 治疗，约 30% 的患者在 3 个月内出现症状，UDCA 治疗后并发症的年发生率约为 2%，这与不使用 UDCA 治疗患者的并发症年发生率相似^[190,253,264,265,268,292]。胆囊切除术可预防胆囊结石的并发症，但如果近 5 年未出现胆绞痛或仅出现过 1 次胆绞痛发作（1 年内再次出现胆绞痛的几率约为 50%），不需要行胆囊切除术^[221]。虽然胆绞痛复发并不增加胆囊切除术相关并发症的发生率，但很难预测哪些患者会出现急性胆囊炎、胰腺炎、梗阻性黄疸和胆管炎等并发症，所有这些并发症均会增加中转开放式手术的风险，延长胆囊切除术后的住院时间。胆囊切除术后每 3~4 例患者中有 1 例会持续存在腹部症状^[231,232,293-297]；鉴于症状常常不具特异性，胆囊切除术的治疗决策必须个体化，从而避免过度手术。

无症状性胆囊结石患者的手术适应证

无症状的胆结石患者需要手术治疗吗？

对于无症状性胆囊结石患者，不推荐胆囊切除治疗
(**极低质量证据；弱推荐**)

注释：目前没有 RCT 对胆囊切除术在无症状患者中的获益进行评估。在无症状性胆石症的临床过程方面，既没有全面的临床观察，也没有对前瞻性研究的详细分析，能够证明胆囊切除术在无症状性胆石症患者中的疗效。每年约 0.7%~2.5% 的无症状性胆囊结石患者出现胆囊结石相关症状。急性胆囊炎、急性胰腺炎、梗阻性黄疸或胆管炎等并发症的年发生率为 0.1%~0.3%^[219,221]。对于无症状的胆囊结石患者，开放式或腹腔镜胆囊切除术不能增加患者的预期寿命，因为手术的风险（死亡率和发病率）超过了并发症的可能性^[223,298]。不仅如此，无症状胆囊结石患者若出现症状或并发症时才接受治疗，而不是预防性行胆囊切除术或进行溶石治疗，成本花费更低（参见推荐意见：“可以口服胆汁酸溶石治疗吗？”）^[299]。在胆囊癌流行率低的西方国家^[300]，无症状性胆石症患者的确有轻微的胆囊癌风险，但仍然极低，无法证明对其治疗的合理性^[301,302]。糖尿病患者也无需进行预防性治疗^[303,304]。

例外情况

伴瓷样胆囊的患者是否有胆囊切除术的指征？

对伴瓷样胆囊的无症状患者，可行胆囊切除术
(**极低质量证据；弱推荐**)

注释：伴瓷样胆囊的患者若不行预防性胆囊切除，发生胆囊癌的患者比例较高。根据早期的研究（早期瓷样胆囊的诊断主要依靠腹部 X 线检查）显示，所有伴瓷样胆囊的患者中，发生胆囊癌的比例高达 20%^[305]。但这种关联性在所有的病例系列研究中均未得到确认^[306]，且瓷样胆囊和胆囊癌之间的因果关系也未确立^[307]。还需要对囊壁均匀钙化（发生癌症的比例非常低）和斑点样钙化（发生癌症的比例为 7%）加以鉴别^[308]。囊壁均匀钙化的患者或可避免行胆囊切除术^[304]。目前主要通过超声诊断瓷样胆囊，筛选出的患者人群不同于早期研究。手术前推荐行 CT 检查进行确认。

几项研究注意到胆囊癌和胆石症存在相关性^[309-312]。但鉴于胆囊切除术的并发症包括胆管损伤（参见“胆管损伤”章节），预防性胆囊切除术在这个患者群体中的获益有很大的不确定性。根据其它额外风险因素，需 67~769 例胆囊切除术以预防 1 例胆囊肿瘤^[313]。

胆囊息肉是否有手术指征？

无论症状如何，胆囊息肉直径 ≥ 1 cm，伴或不伴胆结石，均应行胆囊切除术（**中等质量证据；强推荐**）。伴无症状性胆囊结石且胆囊息肉直径为 6~10 mm 的患者，以及息肉生长的患者亦应考虑行胆囊切除术（**极低质量证据；弱推荐**）。

伴原发性硬化性胆管炎的无症状患者，无论息肉大小，可推荐行胆囊切除术（**低质量证据；弱推荐**）

伴无症状性胆囊结石且胆囊息肉直径 ≤ 5 mm 的患者，无胆囊切除术指征（**中等质量证据；强推荐**）

注释：胆囊息肉在一般人群中的患病率为 1%~7%^[314-318]。胆囊息肉患者中，腺瘤（被认为是癌前病变）的流行率 $< 5\%$ ^[315,319]。在几项大型研究中，息肉直径 ≥ 1 cm 明显增加发生腺瘤的可能性。超过 50% 直径 ≥ 1 cm 的息肉可能发生癌变^[315,316,320-323]，因而患者应行胆囊切除术。

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考虑到胆囊切除术的相关并发症（参见“胆管损伤”部分），对于无症状性胆囊结石且胆囊息肉尺寸为6~10 mm的患者，预防性胆囊切除术的获益存在很大的不确定性。一篇基于10项观察性研究的系统性回顾指出，息肉生长的速度可能并不是预测肿瘤性息肉的良好指标^[324]。该综述还指出，尽管绝大部分中等大小的息肉（6~10 mm）都表现为良性的自然进程^[325]，但有部分恶性肿瘤性息肉直径<1 cm（但≥5 mm）。超声内镜较经皮超声能更精准地显示胆囊息肉（87%~97% vs. 52%~76%）^[326,327]，因此，超声内镜可能有助于对经皮超声检查时发现的直径为6~10 mm的胆囊息肉进行疑似胆囊癌的鉴别。

在原发性硬化性胆管炎（primary sclerosing cholangitis, PSC）患者中，胆囊的肿块样病变常为恶性，上皮内瘤样病变的发生率高^[328-330]，因此PSC患者在出现胆囊息肉或其他肿块样病变时，即便病灶<1 cm，行胆囊切除术也是合理的。

对于直径>18~20 mm的息肉，由于存在显著的恶性风险，应首先考虑行开放式胆囊切除术^[319,323,331,332]。尽管没有高质量的证据，但对于直径为6~10 mm的未摘除的息肉，可通过超声（适用于非肥胖患者）或超声内镜随访，开始每3~6个月随访1次，如果息肉大小未见增加，随后可每年随访1次^[316,323]。对于一般检查偶然发现的无症状且直径≤5 mm的息肉，不随访似乎也是合理的。超声检查时，可通过改变患者体位鉴别胆囊息肉和胆囊结石。出现一个以上息肉更倾向于诊断胆固醇息肉而非腺瘤。彩色多普勒超声检查偶尔可发现息肉基底部血管^[333]，为腺瘤的典型特征。

进行其他手术时是否推荐行胆囊切除术？

无症状性胆石症患者在包括减重手术的腹部手术期间以及肾脏、肺或胰腺移植期间，不推荐常规行胆囊切除术（**极低质量证据；弱推荐**）

症状性胆石症患者，在心脏移植或肺移植术后早期应尽可能推迟行胆囊切除术（**极低质量证据；弱推荐**）

注释：在吸收不良型或限制吸收型肥胖手术后，胆结石出现症状或发生并发症的风险为10%~15%^[157,172]。考虑到如果患者出现胆结石相关症状，后续将接受一个大手术，并且事实上并没有证据证明在腹部大型手术同时

行胆囊切除术会导致并发症增加^[171]，因而对于接受腹部大型手术的无症状性胆结石患者或可考虑行预防性胆囊切除术，但并非广泛推荐。

在心脏、肺、肾脏和胰腺移植术后2年内，无症状性胆石症的发病率和并发症发生率升高。预防性胆囊切除术可以降低死亡率，且经计算在心脏移植后的无症状性胆结石患者中具有成本效益^[334,335]，但在接受肾移植或肺移植的患者中则未见成本效益^[334]。由于在心脏或肺移植术前或术后即刻行胆囊切除术会显著增加死亡率，将手术推迟至移植后尽可能长的时间更为可取^[336-339]。相反，实体器官移植患者治疗胆结石的风险与普通人群相当^[340]。

遗传性球形红细胞增多症或镰状细胞病患者是否应行预防性胆囊切除术？

对于伴有遗传性球形红细胞增多症或镰状细胞病的无症状性胆石症患者，在行脾切除术时应考虑同时行胆囊切除术。对伴有镰状细胞病的无症状性胆石症患者，在进行其他腹部手术的同时行预防性胆囊切除术的另外一个原因是避免在发生镰状细胞危象时无法明确诊断（**极低质量证据；弱推荐**）

注释：遗传性球形红细胞增多症属于一组具有异质性的遗传性贫血，以外周血涂片球形红细胞增多为特征。常见并发症包括溶血事件、再生障碍性危象和胆色素性（胆红素盐）胆石症（最常见的结局）^[341,342]。遗传性球形红细胞增多症患者的胆结石患病率随年龄升高，10岁的患者为5%，50岁以上患者为40%~50%，Gilbert综合征患者的风险升高4~5倍。脾切除术是重要的治疗方法，可使大部分遗传性球形红细胞增多症患者得以治愈，预防溶血导致的胆石症。事实上，针对这个特殊的患者人群，需要采取预防性措施，以避免在脾切除术前发生胆结石相关并发症。对于无症状性胆结石患者，建议在行脾切除术同时^[342]行预防性（腹腔镜）胆囊切除术^[157,343]。

镰状细胞病患者形成胆色素结石的风险较高。早期识别镰状细胞病，采取合适的措施预防镰状细胞危象，可预防溶血和感染。对于伴有镰状细胞病的无症状性胆结石患者，建议在因其他原因进行腹部手术时行预防性胆囊切除术，以避免在发生镰状细胞危象时无法明确诊断^[157,343]。

术前检查

在行择期胆囊切除术前哪些检查是必需的？

腹部超声可以确诊胆囊结石（**中等质量证据；强烈推荐**），无需其他常规检查。在个别特定病例可行肝脏生化检查（**极低质量证据；弱推荐**）

注释：计划进行胆囊切除术的患者术前准备工作包括体格检查、腹部超声、实验室检查和其他影像学检查。术前应至少进行一次腹部超声检查以确认胆囊结石；如果已经做过超声检查，进行手术之前无需重复操作。不推荐计划行胆囊切除术的患者常规行食管胃十二指肠镜（esophago-gastro-duodenoscopy, EGD）检查。尽管内镜检查的诊断灵敏度高，但一项对包括了12项队列研究涉及6317例患者的荟萃分析报告，其作为防止手术的工具价值有限，因此仅应选择性地考虑术前进行EGD检查^[344]。

尽管术前常常进行常规心电图（electrocardiogram, ECG）检查，但仅有2%的麻醉医师表示他们会因为ECG的结果调整术前管理方案^[345]。有心脏风险的患者术前应考虑行ECG检查，但对无风险因素和计划进行低危手术（如胆囊切除术）的患者不应作为常规推荐^[346]。

两项随机研究和一项综述对接受或未接受胸部X线检查的无症状患者进行了对比，未发现在延迟手术或取消手术方面存在任何差异^[347-349]。可得出结论，对于年轻患者，可能不需要行ECG和胸部X线检查，对于老年患者或术后并发症风险较高的部分病例，可安排行这两项检查^[350,351]。

包括白细胞计数在内的实验室检查可能对评估术后结局有帮助，特别是对有并发症（如感染）的患者，或用于因急性胆囊炎实施手术时判断白细胞增多的变化情况^[352]。由于腹腔镜胆囊切除术的输血风险为0.7%（如中转开放式手术略高于此数值），因此甚至术前常规评估血红蛋白和血细胞容积均非强制性^[352,353]。计划实施外科手术前，常需要筛查血小板计数、国际标准化比值和部分凝血活酶时间。术前要求评估凝血因子，但并不推荐行凝血试验（除非患者病史中有发生出血的特殊风险因素）^[350]，不过对于所有患者，都必须充分采集出血病史。

肝生化学检查，如胆红素、丙氨酸氨基转移酶（alanine aminotransferase, ALT）、天冬氨酸氨基转移酶（aspartate aminotransferase, AST）、谷氨酰转肽酶（ γ -glutamyl transpeptidase, γ -GT）和碱性磷酸酶（alkaline

phosphatase, AP）可用于预测存在胆管梗阻或其他肝脏疾病^[353-356]，但目前并无证据显示需要强制性进行这些检查。胆总管（common bile duct, CBD）无扩张、无生化学改变时不太可能诊断胆总管结石^[355,357]。对这部分患者，无需进行术前EUS或磁共振胰胆管造影（magnetic resonance cholangiopancreatography, MRCP）或术中胆管造影。

胆囊切除术术式

胆囊切除术应常规行开放式手术还是腹腔镜手术？

对包括急性结石性胆囊炎在内的症状性胆囊结石，腹腔镜胆囊切除术是标准治疗方法（**高质量证据；强烈推荐**）

注释：腹腔镜胆囊切除术已成为全球范围内的标准干预手段。现今，超过93%的胆囊切除术都从腹腔镜手术开始。腹腔镜中转开放式腹胆囊切除术的比例为4%~8%^[358-361]。一次荟萃分析^[362]纳入了比较两种术式的RCT研究^[363,364-397]，结果显示，两者的并发症发生率相同，但腹腔镜胆囊切除术的平均住院时间缩短3天，恢复期缩短3周。反映在成本分析上则表现为腹腔镜手术与开放式手术相比住院治疗的成本下降了18%^[398]。即使是与历史数据比较，当前的并发症发生率（胆漏0.4%~1.5%、伤口感染1.3%~1.8%、胰腺炎0.3%、出血0.2%~1.4%）也都低于开放式胆囊切除术^[358,361]。1996年的一项大型荟萃分析^[399]仍然提示腹腔镜胆囊切除术有更高的胆管损伤趋势。如今，胆囊切除术后的主要胆管损伤率较低（0.2%~0.4%），与手术路径是开放式或是腹腔镜无关^[361,362,400,401]。同样也是荟萃分析证实，“小切口”胆囊切除术与腹腔镜胆囊切除术同样有效，可作为有价值的替代方案^[362]。

RCT结果显示，急性胆囊炎患者也可接受腹腔镜手术^[402-404]。但急性期行腹腔镜胆囊切除术的手术时间、风险和中转开放式手术率均高于急性胆囊炎消失后的择期胆囊切除术。

如果高度疑似（晚期）胆囊癌，应实施开放式胆囊切除术而非腹腔镜胆囊切除术。如存在Mirizzi综合征（若在术前诊断），其本身并不是腹腔镜手术的禁忌证。但需要特别注意在II型Mirizzi综合征（胆囊肝管瘘）时，医师应做好中转开放式手术的准备^[405,406]。

肝硬化患者应行开放式胆囊切除术还是腹腔镜胆囊切除术？

在伴 Child-Pugh 评分 A 或 B 级的肝硬化患者中，对症状性胆囊结石应首选腹腔镜胆囊切除术（**中等质量证据；强推荐**）

注释：对于合并 Child-Pugh 评分 A 或 B 级的肝硬化患者，腹腔镜胆囊切除术的并发症风险低于开放式胆囊切除术，因此是首选方案^[407]。但对于 Child-Pugh 评分 C 级的患者，不论是行腹腔镜还是开放式胆囊切除术，并发症发生率均较高^[408]，绝大部分系列研究都报告，术前终末期肝病评分（Model for End-Stage Liver Disease, MELD）> 13 的患者具有更高的患病率和中转开放式手术率^[409,410]。存在胆囊切除术的强禁忌证时，如终末期肝病和症状严重的胆囊结石，一项小型回顾性系列研究报告可在内镜下放置胆囊十二指肠支架^[411]。

对于症状性胆囊结石患者，是否有方法可替代腹腔镜胆囊切除术？

小切口开放式胆囊切除术（切口 < 8 cm）可作为腹腔镜胆囊切除的替代手术方式（**高质量证据；强推荐**）

注释：有 RCT 对腹腔镜胆囊切除术和小切口开放式胆囊切除术（切口 < 8 cm）进行了对比，发现这两种术式在并发症比例、住院时间和恢复期方面都无差异^[362,366,412-422]，因此小切口开放式胆囊切除术是腹腔镜胆囊切除术合适的替代选择。

腹腔镜胆囊切除术

操作孔的数量和大小

实施腹腔镜胆囊切除术时操作孔的数量和孔径如何选择？

当前腹腔镜胆囊切除术应采用四孔法，其中 2 孔孔径至少为 10 mm，另外 2 孔孔径至少为 5 mm（**极低质量证据；弱推荐**）

注释：小切口开放式胆囊切除术或单孔腹腔镜胆囊切除术与标准腹腔镜胆囊切除术相比，临床获益还存在相

当大的不确定性^[423,424]，其安全性也还需要确立，因此不作为常规推荐^[423-425]。

预防性使用抗生素

择期腹腔镜胆囊切除术前必须常规预防性使用抗生素吗？

择期腹腔镜胆囊切除术前，无须常规使用抗生素预防感染（**极低质量证据；弱推荐**）

注释：一项对 RCT 的系统回顾显示，预防性使用抗生素或不使用抗生素，手术部位感染或腹腔外感染的发生率无显著差异，两种并发症的发生率约为 3% 和 1.4%^[426]。一项 RCT 显示，即使在术中发生胆囊穿孔的患者也无需使用抗生素预防感染^[427]。

术中胆管造影

在胆总管结石风险较低的患者中，行胆囊切除术时必须常规或选择性行术中胆管造影吗？

胆总管结石风险较低的患者行胆囊切除术时，无须常规或选择性行术中胆管造影（**低质量证据；弱推荐**）

注释：一些 RCT 对常规或选择性行术中胆管造影与未行胆管造影进行了比较，对这些 RCT 的系统回顾显示，两者在胆管损伤患者比例（胆管损伤率在行胆管造影者和未行胆管造影者中分别为 0% 和 0.2%）、CBD 残留结石的患者比例或死亡风险方面均无显著差异^[428]。在开放式胆囊切除术时代，常规接受胆管造影的患者发生并发症的比例高于未行胆管造影的患者^[428]，手术时间也更长^[428]（由于增加了操作，这一点在意料之中）。由于常规胆管造影之后未见显著获益，反而延长手术时间，因此目前无证据支持在胆囊切除术中推荐常规行胆管造影。然而，一篇回顾性数据库综述显示，接受术中胆管造影的患者胆管损伤发生率低于未接受术中胆管造影的患者^[429]。因此，在是否常规行术中胆管造影这个问题上还有很大的不确定性。在近来发表的一项 RCT 中，有 CBD 结石中危风险的症状性胆囊结石患者被随机分组，一组立即行胆囊切除术并在术中行胆管造影，另一组术前行 EUS，之后若有必要再行 ERCP，随后进行腹腔镜胆囊切除术并在术中行胆管造影。立即行胆囊切除术的患者住院时间更短、CBD 探查更少，两组的患病率或生活质量无差异^[430]。但两组

检测到的 CBD 结石患者比例均仅有约 20%，可能与纳入标准的中危人群定义（氨基转移酶为 2 倍正常值上限，并且有至少一项其他肝脏生化学检查异常）中的胆管结石特异性相对较低相关。另外，当今很多外科医师进行中胆管造影的经验有限。

术中结石丢失

若胆囊结石掉入腹腔且无法寻回，这样的患者是否具备中转开放式手术的指征？

术中结石丢失不是中转开放式手术的原因（**极低质量证据；弱推荐**）

注释：腹腔镜胆囊切除术中，因胆囊穿孔导致结石掉入腹腔的发生率为 4%~19%^[431-433]。如果结石未能寻回，0%~15% 的患者可能会发生疼痛、切口部位脓肿、腹腔内脓肿、内瘘（如结肠瘘）、外瘘（腹腔内脓肿自发引流至体外）或伤口窦道等结果^[431-433]。因此，应通过腹腔冲洗，尝试各种方法来寻回结石。然而如果无法寻回结石，无须仅出于寻回结石的目的而中转开放式手术。

当日手术

腹腔镜胆囊切除当日手术是否安全？

在无系统性疾病的患者中，当日手术的安全性可能与住院手术相同（**中等质量证据；弱推荐**）

注释：一篇对 RCT 研究进行的系统性综述报告，就腹腔镜胆囊切除术而言，当日手术的安全性似乎和住院手术一样^[434]，当日手术在以患者为导向的结局方面，如恢复正常活动或早日恢复工作等似乎并无改善，但当日手术能显著节省费用，从而能更好地利用有限的医疗资源。

胆囊切除时机

非复杂性胆绞痛

非复杂性胆绞痛患者应何时行腹腔镜胆囊切除术？

非复杂性胆绞痛患者应尽早行胆囊切除术（**低质量证据；弱推荐**）

注释：非复杂性胆绞痛患者推迟手术的主要原因是没有及时列入等待名单，也就是说，并没有医学原因导致适合麻醉的非复杂性胆绞痛患者推迟手术。另一方面，推迟手术使患者暴露于出现胆囊结石并发症的风险。根据一项存在高偏倚风险的研究得出的证据^[274]，早期行腹腔镜胆囊切除术（胆绞痛诊断后 24 h 内）降低择期腹腔镜胆囊切除术等待期间（平均等待 4 个月）的发病率、住院时间和手术时间。因此，早期行腹腔镜胆囊切除术更可取。

急性胆囊炎

急性胆囊炎患者应如何治疗？

急性胆囊炎患者应由经验丰富的外科医师早期实施腹腔镜胆囊切除术（最好在入院 72 h 之内）（**高质量证据；强推荐**）

注释：急性胆囊炎是胆囊结石最常见的并发症。一篇对 RCT 的系统性综述显示，症状发作后 1 周内早期手术与症状消失至少 6 周后的延期手术相比，早期腹腔镜胆囊切除术缩短总住院时间约 4 天^[435]。与延期手术相比，早期腹腔镜胆囊切除术不增加严重并发症的发生率，分别为 5.0% 和 6.5%^[435]。急性胆囊炎行早期或延期腹腔镜胆囊切除术的中转开放式手术率均为 20% 左右^[435]，这个比例远高于非复杂性胆绞痛行择期手术。在麻醉问题或外科问题解决之后就应立即实施手术，原因是手术实施越早，中转开放式手术率越低、住院时间也越短^[436]。急性胆囊炎患者也可行保守治疗，不常规行胆囊切除术。但如果只行保守治疗而不常规行胆囊切除术，超过 1/3 的患者会出现并发症或因胆源性疼痛急诊入院。30% 的患者最终需行胆囊切除术^[437,438]。如果由于诊断较晚或其他医学原因（手术高危风险）而导致患者无法在 1 周内接受早期择期手术^[439]，则在未来 6 周内都不应实施胆囊切除术。证据源于一项 RCT，在诊断后第 7~45 天内实施腹腔镜胆囊切除术的发病率约为早期手术或间隔 6 周后手术的 2~3 倍^[440]。

10%~30% 的急性胆囊炎患者会发生胆囊坏疽、积液或穿孔等严重并发症^[403,441,442]。此时，术前 CT 扫描也许能提供有用的信息。胆囊与胃肠道之间形成瘘管的发生率在所有胆囊结石患者中不足 1%。胆肠瘘的临床表现为上行性胆管炎或胆汁酸消失综合征。约 60% 的胆囊十二指肠瘘没有症状。如果有较大的结石通过瘘管，可导致

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胆石性肠梗阻^[443]。无手术史或内镜操作史的患者出现胆道积气可提示存在瘘管，MRI、MRCP和ERCP进一步检查或可确诊。

胆囊结石和胆管结石并存的患者

在内镜移除胆管结石后，胆囊结石患者何时应行胆囊切除术？

对于同时患有胆囊结石和胆管结石的患者，应在ERCP后72 h内早期对胆管结石行腹腔镜胆囊切除术（**中等质量证据；强推荐**）

注释：一项随机试验评估了在内镜括约肌切开术后实施腹腔镜胆囊切除术的时机，结果显示，与延期手术（6~8周后）相比，在ERCP后72 h内行腹腔镜胆囊切除术，胆道事件复发率显著降低，中转开放式手术率、手术时间或外科并发症无差异^[444]。不推荐同一天内分别进行ERCP和胆囊切除术，因为这可能会影响并发症的管理。没有研究对间隔2~4周和间隔6~8周进行比较。

老年患者和麻醉高风险患者的胆囊切除术

老年患者和麻醉高风险的患者应行胆囊切除术吗？

老年患者和存在麻醉高风险的患者，若合并胆囊结石并发症（如急性胆囊炎、胆石性胰腺炎或梗阻性黄疸），只要一般状况允许手术，就应行胆囊切除术（**低质量证据；弱推荐**）。不能仅因生理年龄的因素而不进行腹腔镜胆囊切除术（**极低质量证据；弱推荐**）

注释：在老年症状性胆石症患者中，只要可能就应实施胆囊切除术。尽管在胆源性胰腺炎患者中，可将胆囊切除术推迟到内镜括约肌切开术之后，但一篇对RCT的系统性综述的证据显示，延期胆囊切除术与更高的死亡率、胆源性疼痛复发、黄疸或胆管炎有关，且需要进一步检查^[445]。然而，这项系统性综述纳入的针对老年患者的试验，大部分已排除了不适合手术的患者。一项研究仅纳入了高危患者——根据下列标准中的一项或几项：年龄超过70岁；心脏风险指数高（戈德曼心脏风险指数

>13）；慢性肺病；肝硬化（Child-Pugh评分B或C级）；神经功能缺陷或关节病伴活动严重受限；BMI > 30 kg/m²。该研究发现高危患者中常规胆囊切除术与延期胆囊切除术的获益比较与低危患者中相似^[445]。

重度急性胆囊炎患者或胆道系统解剖困难的患者，胆囊大部切除术（腹腔镜或开放式）或先行经皮胆囊造口术后再行胆囊切除术，都可作为治疗选择^[446,447]。尤其是经皮胆囊造口术可作为高危急性胆囊炎患者的替代治疗方法^[448,449]。Chang等^[450]报告在中位时间23±16天后拔除引流管，12%的患者出现胆囊炎或胆管炎复发，不过其他研究报告的发生率更高^[451]。由于缺乏相关RCT，目前尚未确定有手术高风险的急性胆囊炎患者是否需要接受限期胆囊切除术治疗。鉴于在经皮胆囊造口术后身体情况得到改善的患者若不进行限期外科治疗，其情况在随访期间可能发生恶化^[437]，因此仍应考虑行胆囊切除术。

内镜下胆囊引流可潜在作为急性胆囊炎的替代引流方法。一项系统性综述显示，经内镜鼻胆管引流术（endoscopic nasogallbladder drainage, ENGBD）和经十二指肠乳头支架胆囊引流术的技术成功率分别为81%和96%、临床成功率分别为75%和88%、不良事件发生率分别为3.6%和6.3%^[452]。

腹腔镜胆囊切除术的年龄限制尚未确定。一些研究显示，年龄超过75~80岁的患者也可安全实施腹腔镜胆囊切除术^[453,454]，而其他研究显示65~70岁以上的患者中转开放式胆囊切除手术率、并发症比例和住院时间均较高^[455,456]。

最后，一项小型随机试验显示，在存在胆囊切除高危风险的老年急性胆囊炎患者中，ERCP联合括约肌切开术治疗优于保守治疗^[457]。

胆管损伤

胆管损伤的诊断

如何在术后诊断胆管损伤？

当患者处于住院密切观察时，术后怀疑出现胆管损伤的患者，应立即接受实验室检查（白细胞、胆红素、肝酶）和影像学检查（腹部超声、增强CT、磁共振胰胆管造影），以确定是否存在胆汁漏出和/或腹腔积液（**低质量证据；弱推荐**）

注释：胆管损伤的定义为胆道系统出现的任意损伤（包括胆汁漏出），对患者产生不利影响。危险因素包括胆囊管结石嵌顿、Mirizzi 综合征、胆囊壶腹结石嵌顿、炎症改变或肝内胆管解剖异常^[458]。胆管损伤是可能导致严重后果的并发症，患者 1 年和 2 年的死亡率显著高于无胆管损伤的患者^[429,459]。MRCP、对比增强 CT、ERCP 和 / 或经皮肝穿胆管造影都可用于胆管损伤的诊断和分类^[460-464]。在胆管损伤经验欠缺的医院，如果有条件应选择 MRCP 作为诊断工具。钆塞酸二钠增强的 MRCP 发现胆汁漏出的灵敏度为 76%~100%，特异性高达 100%^[465-468]，或可用于胆汁漏出的非侵入性检测。随后再行 ERCP，至少 90% 的胆管损伤的性质可被确定^[469,470]。

在胆囊切除术期间，仅能识别约 40% 的损伤。而术中胆管造影可使 70% 的胆管损伤得到早期识别^[469,470]。自引入腹腔镜胆囊切除术后，文献中报告的胆管损伤数量较开放式手术时代增加^[471]。一项研究针对瑞典胆结石手术和 ERCP 登记系统（Swedish Registry for Gallstone Surgery and ERCP, GallRiks）中超过 50 000 例未经选择患者的研究显示，2005~2010 年间接接受胆囊切除的患者中 1.5% 发生了胆管损伤，但其中仅有 1/5（0.3%）的病例为胆管部分或完全横断^[429]。文献报告腹腔镜胆囊切除术后的胆管损伤发病率为 0.04%~1.5%^[362,472-481]。而在开放式胆囊切除术后的发病率为 0%~0.5%^[459,473,480,482,483]。然而，一项纳入腹腔镜手术与开放式手术 RCT 的系统性综述显示，两种类型胆囊切除术后的胆管损伤发病率无显著差异（两组均为 0.2%）^[480]。因此，胆管损伤的真实发病率尚不清楚，可能由于对偏僻的漏报所致^[480]。可能的影响因素包括学习曲线效应、对安全性的考量不够严格和解剖学变异^[458,475,477,478,481,484]。

目前，新型腹腔镜技术（单孔，微型腹腔镜，NOTES）与传统腹腔镜胆囊切除术之间胆管损伤发病率的比较，资料尚不充分。

胆管损伤的治疗

术中发现胆管损伤，应采取哪种治疗措施？

如有外科专家在场，可对术中确认的 A、B 或 C 型胆管病变（见表 1）直接实施手术修复；若为 D 型胆管损伤，须经专家会诊，并建议行单纯肝下引流和转诊治疗，在 6~8 周后行重建手术，常伴肝管空肠吻合术（**低质量证据；弱推荐**）

术后发现胆管损伤，应采取哪种治疗措施？

术后 A、B 或 C 型胆管损伤患者，应行内镜治疗；术后 D 型损伤患者，推荐晚期手术治疗（**低质量证据；弱推荐**）

注释：胆管损伤的正确诊断和分型对治疗的选择有重要意义。由于文献中采取的胆管损伤分型系统各不相同，因而这些数据的比较十分复杂^[458,484-488]。阿姆斯特丹分类法^[486]是常用方法（表 1），因为这种分型方法直接与治疗相关联。在对损伤进行分型后，应将患者转至具备多学科专家团队的专科医院。

表1. 胆管损伤的分型

A: 胆囊管或异位胆管胆漏
B: CBD胆漏，伴或不伴狭窄
C: CBD狭窄，无胆漏
D: CBD完全横断，伴或不伴组织缺损

CBD, 胆总管

在术中发现胆管损伤时，若有外科专家在场，A 型损伤可予以缝合，B、C 或 D 型损伤可做一期修复。否则务必行单纯肝下引流并将患者转入专科中心。

术后确诊胆管损伤，需转至专科中心。初始治疗包括脓毒症治疗和肝下引流。不建议行早期（诊断性）腹腔镜或开放式手术。A、B 或 C 型损伤可通过内镜下经十二指肠乳头置入支架并扩张（C 型）。D 型损伤建议在 6~8 周后进行外科重建。

另外，胆管损伤的外科修复时机仍存争议，包括在胆囊切除术时行一期修复，早期修复（胆囊切除术后，但在约 6 周内）和延期修复（6 周以后）。一项法国的回顾性研究显示，一期修复与早期修复或延期修复相比，死亡率（分别为 3%，2% 和 1%）、发病率（分别为 39%，29% 和 14%）和需要干预（大部分为进一步外科干预）的手术失败率（分别为 64%，43% 和 8%）均较高^[489]。应注意在这项研究中，一期修复组中 40%、早期修复组中 50%、延期修复组中 100% 的患者在三级转诊医院接受治疗，可能造成上述显著差异。直接修复（胆管端端吻合术修复）是一期修复和早期修复的常用方法，而 Roux-en-Y 肝管空肠吻合术是延期修复的常用外科治疗术式^[489]。另外一项成本效益研究表明：在所观察的病例系列中，由专业外科医师进行早期胆管修复较延期修复更具成本效益，而非专业医师进行一期修复最不具有成本效益^[490]。

Clinical Practice Guidelines

肝管空肠吻合术的长期满意率为70%^[491,492]。局部感染或脓毒症是早期外科重建效果不佳的独立风险因素^[493]。胆囊切除术期间出现胆管损伤的患者1年后的死亡率高于未出现胆管损伤的患者(4% vs. 1%)，总风险比为1.92(95% CI: 1.24~2.97)^[429]。

胆管修复后的健康相关生活质量报道不一，一些研究报告接受外科重建的患者具有相似的生活质量，而其他一些研究则报告发生胆管损伤的患者在接受纠正手术后若干年，生活质量较未发生胆管损伤的患者差^[494]。

胆囊切除术后持续出现胆道症状

如何处理胆囊切除术后的持续性症状?

对胆囊切除术后持续伴胆道症状的患者，应考虑采用超声内镜检查或磁共振胰胆管造影，以进行术后诊断性评估(**低质量证据；弱推荐**)

对胆囊切除术后伴有腹痛，但无影像学或实验室检查显著异常的患者，不支持进行内镜括约肌切开术(**中等质量证据；强推荐**)

注释：部分患者在行胆囊切除术后症状可能持续或重新出现。事实上，10%~40%的患者在胆囊切除术后持续有主诉，有时在症状出现前经历一个短暂的无症状间期^[495,496]。过去曾用的“胆囊切除术后综合征”一词现在已被更特异的病因取代。重要的是，应排除胆管结石的存在。在由*ABCB4*基因突变导致的LPAC综合征的罕见亚组患者中，胆囊切除术后重新出现症状是由于肝内出现胆泥和小结石或胆管结石复发所致(参见“胆管结石复发的预防”章节)^[216]。

在一项RCT中^[497]，118例胆囊切除术后出现腹痛的患者接受了筛查，其中12例患者十二指肠胆汁显微镜检查发现结晶。使用UDCA治疗几个月后，胆源性腹痛显著改善或消退。此研究为小结石病是胆囊切除术后腹痛的可能病因提供了证据。该病可通过对ERCP获取的十二指肠胆汁或肝内胆汁进行显微镜检查确诊^[498]。

由于胆石症症状相对并不典型，因此应考虑其他可能的既存因素，如功能性消化不良、肠易激综合征、(十二指肠-)胃-食管反流和(罕见)Oddi括约肌功能障碍^[496]。一项大型RCT显示，胆囊切除术后伴腹痛并接受ERCP测压的患者，括约肌切开术与假手术相比并不能改善因疼痛导致的失能^[499]。因此，这些发现不支持对这些患者实施内镜括约肌切开术。

胆管结石的诊断

病史和体格检查

什么时候应排查胆总管结石?

对于伴黄疸、急性胆管炎或急性胰腺炎的患者应排查胆总管结石(**高质量证据；强推荐**)

注释：CBD结石可见于3%~16%(依赖于年龄)的胆囊结石患者^[500-507]。可因胆囊结石迁移所致(继发结石)，也可在胆管原位产生(罕见)，如在CBD扩张伴淤积的病例中(原发结石)。与胆囊结石相反，CBD结石患者中仅有5%~12%的病例无症状^[508]。无症状性CBD结石的自然病程尚不清楚，似乎比症状性CBD结石更缓和。在一个样本量较小的患者系列中，CBD结石在随访5年后仍无症状^[509]。

症状性CBD结石的常见表现为由于CBD扩张后部分或完全梗阻所导致的急性胆源性腹痛。疼痛位于右上腹或上腹部，持续30 min以上，可长达数小时，与体位无关。难以与胆囊结石所致的腹痛相鉴别。小结石自发进入十二指肠^[510]或回到扩张的胆管，可能使疼痛缓解。特别是Oddi括约肌小结石嵌顿可能导致远端梗阻并诱发急性胰腺炎。较大结石常引起近端梗阻。胆管梗阻后常出现黄疸和胆管炎等并发症。

实验室诊断和影像学检查

胆总管结石的诊断是否应包括实验室检查?

疑似胆总管结石患者的评估通常包括血清肝脏生化学检查(**低质量证据；弱推荐**)

注释：症状性CBD结石患者的肝脏生化学检查常有改变。疑似CBD结石的初始评估包括：血清胆红素、ALT、AST、 γ -GT和AP水平^[511,512]。尤其在胆管梗阻后的最初72 h内，血清氨基转移酶水平会显著升高，如果梗阻持续，则AP和胆红素水平随后逐渐缓慢升高^[513]。如果在疼痛发作后的最初24 h内肝脏生化学检查正常，并且超声未发现CBD扩张，则存在CBD结石的可能性极小^[355,357]。相反，胆红素、AP或 γ -GT异常的阳性预测值仅有25%~50%^[357,512,514,515]。这几项胆汁淤积性肝脏生化学检查指标的血清水平随胆管梗阻的持续时间和严重程度逐步升高。一项研究显示，血清胆红素在1.7

mg/dl (29 μ mol/L) 及以上时预测 CBD 结石的特异性为 60%，而截断值为 4 mg/dl (68 μ mol/L) 时，特异性升高至 75%；但仅有 1/3 或更少的 CBD 结石病患者会出现如此显著的高胆红素血症^[512,514]。

应使用哪种影像学方法检测 CBD 结石？

怀疑有 CBD 结石时，腹部超声应为首选的影像学方法（**低质量证据；弱推荐**）。胆囊结石、胆总管扩张、急性胆囊炎和高胆红素血症是胆总管结石的强预测因素（**高质量证据；强推荐**）

对于胆总管结石可能性中等的患者，应通过内镜超声检查（或磁共振胰胆管造影）进一步评估（**中等质量证据；强推荐**）

注释：腹部超声检测 CBD 扩张灵敏度高，但仅为 CBD 结石的间接征象。事实上，扩张的 CBD 中可直接看到结石。超声诊断 CBD 结石的灵敏度低于胆囊结石^[516,517]，但对于经验丰富的操作者，其诊断灵敏度也可高达 80%^[518]。超声检查证实有胆管结石、CBD 扩张、急性胆管炎征象和黄疸是 CBD 结石的最佳预测因素^[516]。如果超声检查结果呈阴性，不能排除 CBD 结石，但如果肝脏生化检查也正常，则 CBD 结石的可能性极小。

对于 CBD 结石可能性中等且腹部超声检查无法明确结论时，EUS 是有价值的替代方法。EUS 和 MRCP 检测 > 5 mm 的 CBD 结石的准确性相似，但 EUS 较 MRCP 更具成本效益^[519-527]。近期一项系统性综述显示^[528]，EUS 的灵敏度为 95%，特异性为 97%，而 MRCP 的灵敏度为 93%，特异性为 96%。

CT 成像检测 CBD 扩张的灵敏度较高^[529,530]，同时还可评估其他导致上腹痛和胆结石并发症的可能病因，但有很大的辐射。ERCP 检测 CBD 结石的灵敏度极高^[520,530,531]，但该操作有辐射暴露，仅推荐作为 CBD 结石可能性大且计划同时行内镜治疗患者的首选诊断方法。

急性胆管炎的诊断

如何诊断急性胆管炎？

对于有发热、寒战病史，且伴腹痛和 / 或黄疸的患者，应进行白细胞计数、C 反应蛋白和肝脏生化检查，同时将腹部超声作为初始评估方法（**中等质量证据；强推荐**）

注释：急性胆管炎可通过夏科氏三联征来诊断，即右上腹痛、有压痛，高热、通常伴寒战，以及黄疸。夏科氏三联征的特异性高但灵敏度低^[532]。少数患者可能仅出现腹痛症状，某些患者可能没有腹痛，尤其是老年患者。急性胆管炎患者中 60%~70% 可出现黄疸，90% 伴有发热^[532-536]。

急性胆管炎的生化表现为白细胞增多伴核左移、血清 CRP 浓度升高。氨基转移酶活性和胆汁淤积指标通常在疼痛发作后的最初几小时内升高。腹部超声检查时常见 CBD 扩张，但对诊断 CBD 结石不够灵敏，且在急性炎症时通过超声检查远端胆管更为困难。当前已有足够证据证实，对于此时梗阻性黄疸患者 CBD 结石的检测，EUS 优于 MRCP^[522,524] 和 CT^[524]。

急性胆源性胰腺炎的诊断

如何诊断急性胆源性胰腺炎？

急性胆源性胰腺炎的诊断基于：胆囊结石和 / 或胆总管结石患者出现上腹痛且胰腺、肝脏生化检查异常（**中等质量证据；强推荐**）

对于急性胆源性胰腺炎伴可疑胆管结石的患者，通过内镜超声（或磁共振胰胆管造影）排除胆管结石，或可预防性行内镜逆行胰胆管造影的潜在风险（**低质量证据；弱推荐**）

注释：在 4%~8% 的胆囊结石患者中，结石迁移到主要胆管进入十二指肠或嵌顿在 Oddi 括约肌时会导致急性胰腺炎^[537,538]。对急性胰腺炎的详细讨论超出了本指南的范围，推荐读者参考当前国际胰腺协会（International Association of Pancreatology, IAP）的急性胰腺炎指南^[539]。

胆结石迁移，即便是小结石迁移之前，常伴一段时间的胆管梗阻^[540]。50% 的病例没有预警性疼痛^[228,229]。生化检查提示高脂肪酶血症或高淀粉酶血症（高于 3 倍正常上限值），氨基转移酶活性升高和胆汁淤积性指标、白细胞增多和 CRP 浓度升高。在没有酗酒或既存肝脏生化检查异常的情况下，ALT 活性 > 150 U/ml 提示胰腺炎为胆源性，阳性预测值超过 85%^[541-544]。在特发性急性胰腺炎患者中，经 ERCP 采集十二指肠或肝内胆汁，显微镜检查可见胆汁结晶，提示病因为胆源性^[241,242,498,545]。

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超声通常是首先实施的检查方法。胰腺炎或梗阻性黄疸患者的胆囊结石比急性胆囊炎或单纯性胆石病患者数量更多，体积更小^[240]。超声检查常可发现 CBD 扩张，但在急性胰腺炎时检测胆结石不够准确。当胆源性病因不清或考虑 ERCP 时，可实施 EUS 或 MRCP^[356]。

在胆源性胰腺炎患者中，MRCP 检测胆管结石相当准确^[546,547]，但可能会漏掉小的结石。EUS 检测 < 5 mm 的结石（即通常导致急性胰腺炎的结石）优于其他所有方法。其灵敏度高达 100%，特异性为 95%，诊断 CBD 结石的准确性达 97%^[548]。对于病情轻微且计划行腹腔镜胆囊切除术的患者，除非伴有胆管结石（应首先通过 MRCP 或 EUS 确认），否则没有 ERCP 和括约肌切开术指征^[521]。

胆管结石的内镜治疗和外科治疗

无并发症的胆管结石的治疗

胆管结石的推荐治疗方法是什么？

胆管结石的推荐治疗为内镜括约肌切开术及结石移除（**中等质量证据；弱推荐**）。若术者经验丰富，术中内镜逆行胰胆管造影或腹腔镜胆管探查联合胆囊切除为替代疗法（**中等质量证据；强推荐**）。

当标准取石治疗失败时，可实施体外震波、液电或激光碎石术（**低质量证据；弱推荐**）。当患者解剖结构发生改变时（如既往 Roux-en-Y 吻合术、减重手术），可考虑经皮或内镜（球囊内镜辅助）治疗（**低质量证据；弱推荐**）。如果内镜治疗失败，应实施胆囊切除联合胆管探查或术中内镜逆行胰胆管造影（**低质量证据；弱推荐**）。

注释：CBD 结石是症状性胆囊结石患者中相对常见的现象（流行率 3%~16%）。尽管很多病例的结石可自发通过 CBD 进入小肠，但存在发生胆源性腹痛以及黄疸、胆管炎和胰腺炎等并发症的显著风险。因此，普遍的共识是症状性 CBD 结石应予以治疗。无症状性 CBD 结石的自然病程较为缓和。尽管如此，超过 25% 的患者在随访中似乎发生（通常是严重的）并发症^[509,504,549]。选择何种治疗取决于诊断时间（在胆囊切除术前、术中或术后）和当地的专业水平^[550,551]。近几十年来，内镜治疗（括约肌切开后取石）在胆管结石中的应用有很大拓展。虽然如此，ERCP 有并发症（特别是胰腺炎）风险，同时，内镜医师的经验和数量近年来也引起了极大争议。每年至少进行 100 次操作与更好的临床结局相关，患者年龄与并发症风险无关^[552]。

使用大尺寸球囊（12~20 mm）进行内镜下乳头球囊扩张治疗有利于大结石的取出^[553,554]。一项纳入 6 项 RCT，涉及 835 例患者的荟萃分析显示，该方法的整体并发症发生率和穿孔风险都较低，且 ERCP 术后胰腺炎、感染或出血的发生率无差异。

对于同时患有胆囊结石和 CBD 结石的患者，术前 ERCP 和腹腔镜胆囊切除术是目前首选的治疗方式，尽管有证据显示，在胆囊切除术中行 ERCP 与分别进行两项操作相比，能降低 ERCP 相关的胰腺炎风险、缩短住院时间，并具有成本效益^[549,556-558]。根据近期荟萃分析结果，如果内镜治疗失败，可选择腹腔镜或开放式胆囊切除术联合经胆管取石或 CBD 探查或术中 ERCP，其结石清除率、患病率和死亡率堪比初始内镜治疗^[559,560]。在高危病例中（参见推荐：“在外科胆管探查时一次性闭合优于 T 管引流吗？”），放置 T 管仍是最安全的选择^[561,562]。

近几十年来，开放式 CBD 探查的手术经验急剧减少，且具备腹腔镜 CBD 探查经验的外科医师数量也有限。因此目前多数国家都将内镜取石作为首选。然而，括约肌切开术的时机仍有争议。两项试验（一项在胆结石性胰腺炎患者中开展）提示，初始胆囊切除术（及术后 ERCP）与初始内镜评估 CBD 继以胆囊切除相比，内镜操作更少、住院时间更短，且不增加患病率^[430,563]。

在术中或术后检出胆管结石时的最佳治疗形式是什么？

若在术中检出胆管结石，胆管探查、经胆囊结石移除或内镜清除结石都是可选治疗方案（**中等质量证据；弱推荐**）。若在术后检出胆管结石，推荐行内镜括约肌切开和结石移除（**低质量证据；弱推荐**）。

注释：当在术中检测到胆管结石时，如果外科医师有丰富的经胆囊取石经验，可尝试进行该项操作。该方法安全、成功率约为 75%。腹腔镜取石的成功率较高，但并发症发生率也相对高，非专科中心不可开展^[564-566]。在术后诊断胆管结石时，内镜括约肌切开和结石移除为常用治疗方法。

在外科胆管探查时一次性闭合优于 T 管引流吗？

对须接受外科胆管探查且结石复发风险较低的患者，一次性闭合可能优于 T 管引流（**低质量证据；弱推荐**）。

注释：有 RCT 比较了一次性闭合和 T 管引流，针对这些试验的系统性综述和荟萃分析显示，在低风险病例的开放式或腹腔镜 CBD 探查术后，T 管引流与一次性闭合相比，手术时间和住院时间延长，且无任何获益证据^[561,567]。在高危病例中——包括胆管结石复发、急性胆囊炎或多发性胆管结石而 ERCP 治疗失败，放置 T 管或 CBD 十二指肠吻合术等替代手术为安全的选择^[561,562]。

胆囊结石患者经内镜取出胆管结石后，应何时进行胆囊切除术？

对于同时存在胆囊结石和胆管结石的患者，早期腹腔镜胆囊切除术应在术前胆总管结石 ERCP 后 72 h 内实施（**中等质量证据；强推荐**）

注释：参见“胆囊结石和胆管结石并存的患者”部分。

急性胆管炎的治疗

急性胆管炎患者应如何治疗？

胆管炎的治疗包括立即使用广谱抗生素和胆道减压（**中等质量证据；强推荐**）

胆道减压的时机取决于胆管炎的严重程度和抗生素等内科治疗的效果，并且最好在 24 h 内实施；重度胆管炎患者对液体复苏和静脉抗生素治疗无应答时，应考虑紧急胆道减压（**低质量证据；弱推荐**）

伴括约肌切开的内镜治疗是胆道减压的首选方法；当存在括约肌切开禁忌证时，应后期实施胆道支架置入伴结石移除（**低质量证据；弱推荐**）

在内镜减压失败或有内镜治疗禁忌证时，经皮胆管引流为可选治疗（**低质量证据；弱推荐**）

注释：胆管炎是胆囊结石的严重并发症，有很高的发病率和死亡率，尤其在老年人群中^[568]。一线治疗应包括一般支持治疗，其中应包括充分的静脉补液和静脉抗生素——对于有脓毒症的患者，需要在入院后 1 小时内给药^[569]。鉴于受感染的胆汁中含有多种微生物，应使用广谱抗生素。抗生素的覆盖范围取决于胆管炎的严重程

度和当地的抗菌药耐药模式。急性胆管炎患者的胆汁中通常能培养出肠道革兰氏阴性菌，尤其是大肠杆菌属和克雷白杆菌属的一些菌种。然而，由于胆道仪器的使用增加以及人群中抗生素的频繁应用，微生物谱在近几十年来发生了变化。胆汁培养常见多种微生物。厌氧菌常与需氧菌一起从胆汁中分离，而非单独分离，常见于既往曾有胆管仪器操作史和临床病情更严重的病例。胆汁培养与相关血液培养的结果有明显差异^[570]。胆管炎患者胆汁培养的阳性率为 80%~100%，而血液培养的阳性率仅为 20%~60%。血液培养时，少见链球菌属和肠球菌属细菌，罕见厌氧菌。抗生素治疗的主要目标之一是控制菌血症和脓毒症。胆道梗阻时，大部分抗生素（除喹诺酮外）都无法或不能很好地排泄到胆汁中。在获得胆汁培养和血液培养结果前，应考虑采用覆盖需氧革兰氏阴性菌和厌氧菌的抗生素进行经验性治疗。抗生素治疗的疗程取决于就诊时临床状况的严重程度、血液培养是否阳性以及胆汁引流后的恢复情况。

大部分胆管炎患者对初始的广谱抗生素保守治疗都有满意的应答。尽管这些患者可进行选择性胆道减压和结石移除，但所有胆管炎患者应尽早（最好在 24 h 内）进行胆道减压，因为高达 20% 患者的病情会呈进行性发展并严重恶化^[571]。对液体复苏和静脉抗生素无应答的重度胆管炎患者，应考虑紧急胆道减压。已发表了定义胆管炎严重程度的共识标准^[572]。

胆道减压可通过 ERCP、经皮引流或外科手术实现。回顾性试验和前瞻性随机试验均证实，内镜治疗急性胆管炎的效果优于外科治疗^[269,573]。一项非随机研究在老年胆管炎患者中比较了经皮肝穿刺胆道引流术与 ERCP，结果显示，内镜引流引起的发病率和死亡率显著降低^[574]。因此，ERCP 目前作为因胆结石导致的急性胆管炎的治疗选择。在无法实施 ERCP 或专家操作失败、须避免外科手术时，应考虑经皮肝穿刺胆道引流。胆道置管后应在注射对比剂前抽吸胆汁，以免增加胆道压力和引起菌血症。抽吸的胆汁应送培养。对于病情稳定的患者，最初操作时可进行括约肌切开伴结石移除。即使未发现胆管结石，内镜括约肌切开减压也能使患者更快康复、住院时间缩短^[575]。如果患者有显著的凝血障碍，结石大且多发，或病情不稳定，置入鼻胆管引流或胆管支架是首选的初始治疗。这些情况下，鼻胆管引流和胆管支架的疗效相同^[576]。但应优先选择胆管支架，因为胆管支架置入的舒适度更高，且不易脱位^[576,577]。待患者从急性发作期恢复后可进行结石移除。

Clinical Practice Guidelines

急性胆源性胰腺炎的治疗

哪些急性胆源性胰腺炎患者应进行内镜逆行胰胆管造影？

对于疑似同时存在急性胆管炎的胆源性胰腺炎患者，应启动抗生素治疗，并实施伴括约肌切开和结石移除的内镜逆行胰胆管造影，治疗时机取决于胆管炎的严重程度，但最好在 24 h 内（**高质量证据；强推荐**）

内镜逆行胰胆管造影也可能适用于伴有胆源性胰腺炎和梗阻性胆管炎的患者（**低质量证据；弱推荐**）

早期内镜逆行胰胆管造影可能不适用于伴有预期重度胆源性胰腺炎但不伴胆管炎或梗阻性胆管的患者（**低质量证据；弱推荐**）

早期内镜逆行胰胆管造影不适用于伴有预期轻度胆源性胰腺炎但不伴胆管炎或梗阻性胆管的患者（**中等质量证据；强推荐**）

在无胆管炎的可疑胆源性胰腺炎患者中，超声内镜（或磁共振胰胆管造影）若未发现结石，可能避免不必要的内镜逆行胰胆管造影（**低质量证据；弱推荐**）

注释：对急性胰腺炎的详细讨论超出了本指南的范畴，但指南中提到了内镜治疗的相关内容。读者可参考 IAP 急性胰腺炎指南 2013^[539]。本指南的建议与 IAP/ 美国胰腺协会（American Pancreatic Association, APA）的建议一致。

如果怀疑同时并发胆管炎，最好在 24 h 内进行内镜干预^[538,578-580]。重度胆管炎患者对液体复苏和静脉抗生素治疗无应答时，应考虑实施紧急 ERCP。ERCP 在预测不伴胆汁淤积 / 胆管炎的重度胰腺炎患者中的作用尚有争议。一项针对 7 项 RCT 共计 757 例患者的荟萃分析显示，不管预测的胰腺炎严重程度如何，均不支持在不伴胆管炎或胆道梗阻的胆源性胰腺炎患者中应用 ERCP^[581]。然而，该荟萃分析中纳入的预测会发生重度胰腺炎患者的数量太少，不足以得出确切结论。此荟萃分析支持在伴有胆道梗阻但不伴胆管炎的患者中应用 ERCP。需要注意的是，在胆源性胰腺炎的早期阶段，根据肝脏生化学、腹部超声或 CT 来预测胆管结石是非常不可靠的。因为除胆管结石外，胰腺周围水肿也可引起胆道梗阻^[356]。尽管如此，入院后 48 h 内的实验室参数变化可在一定程度

上预测临床病程和持续存在的胆管结石，后者与急性胰腺炎的严重程度和不良预后有关^[582,583]。要注意在怀疑存在胆道梗阻而不伴胆管炎时可能会考虑实施 ERCP，MRCP 或 EUS 可预防一定比例的（起负面作用的）ERCP 操作。虽然 MRCP 是非侵入性、对术者依赖性小的操作，但与 EUS 相比，其检测小 CBD 结石（< 5 mm）的灵敏度较低^[519,522-524,531,547,584-614]。实际上，胆源性胰腺炎患者通常可见这样的小结石^[241,615]。

胆源性胰腺炎合并胆道梗阻但不伴胆管炎的患者，EUS、MRCP 和 ERCP 的最佳实施时机尚不明确（IAP 胰腺炎指南 2013）。一项事后分析研究中，荟萃分析^[581]发现 ERCP 的实施时间对死亡率无显著影响。对于不伴胆管炎或胆道梗阻的轻度胆源性胰腺炎患者，ERCP 并非必需^[538,578,581,616,617]。小的胆管结石常自发通过，实验室参数随之恢复正常，因此胆囊切除术前不必常规实施 ERCP^[618,619]。

急性胆源性胰腺炎后实施胆囊切除术的最佳时机是什么？

对于急性轻度胆源性胰腺炎患者，住院期间行胆囊切除术为首选治疗（**高质量证据；强推荐**）

注释：对于急性轻度胆源性胰腺炎患者，为避免胆囊结石相关并发症的复发，早期腹腔镜胆囊切除术优于常规等待手术^[620,621]。尽管腹腔镜胆囊切除术一般在急性症状缓解、血清淀粉酶活性恢复至接近正常水平后实施，近期 RCT 证实，在同一住院期间实施腹腔镜胆囊切除术不仅可缩短住院时间^[622]，还可使胆结石相关并发症的复发率（胰腺炎、胆囊炎、需 ERCP 的 CBD 结石、胆绞痛的复发）从 17% 降低为 5%^[621]。由于存在预期重度胰腺炎的风险，在极早期进行手术尚存有疑虑^[623]。等待 72 h 以确定胰腺炎为轻度，并在有指征时进行 MRCP、EUS 或 ERCP 等进一步检查和治疗^[624]，或可解决预期重度胰腺炎的隐患。

重度急性胆源性胰腺炎患者的胆囊切除术时机尚无定论，由于缺乏相关 RCT 研究，目前无法对此作出明确推荐^[624]。在开放式胆囊切除方面，观察性研究显示，早期手术（入院后 6 周内）会增加并发症发生率（包括增加感染性胰周积液的风险）并延长住院时间^[625,626]。延期腹腔镜胆囊切除或可降低转开放式手术的比例，因为重度胰腺炎相关的炎症和积液可能在等待期间逐渐平息或变成边界清晰的假性囊肿。延期腹腔镜胆囊切除术的缺点是可能导致胆源性症状复发和住院时间延长^[627]。尽管

如此，对于重度胆源性胰腺炎伴胰周积液的患者，应将胆囊切除术推迟至积液吸收后，如果积液持续存在，则应推迟至胰腺炎发作后至少 6 周。

肝内胆管结石的诊断与治疗

肝内胆管结石的首选诊断方法是什么？

对可疑肝内胆管结石，腹部超声为首选诊断方法，磁共振胰胆管造影为次选方法（**极低质量证据；弱推荐**）

注释：典型的肝内胆管结石（肝石病）发生于胆管狭窄时，见于胆管损伤之后、原发或继发性硬化性胆管炎患者，或化脓性胆管炎（“东方型胆管炎”）复发的患者^[628-631]。上行性胆管炎是肝内胆管结石的常见急性并发症，其慢性并发症包括继发性胆汁性肝硬化、肝段或肝小叶萎缩、肝脓肿和胆管癌。

腹部超声因其非侵入性操作、可发现被非钙化的肝内胆管结石梗阻的胆管，而优于诊断性 ERCP。MRCP 在诊断肝内胆管结石方面也优于 ERCP（灵敏度为 97% vs. 59%），能可靠地检测胆管狭窄（特异性为 97%，灵敏度为 93%）以及梗阻近端的病变和胆管以外的病变^[606,632-634]。尽管 CT 通常不能直接显示结石，但胆管的扩张和狭窄以及肝内脓肿都可显示^[632]。

无症状性肝内胆管结石应该治疗吗？

无症状性肝内胆管结石不一定必须治疗。症状性肝内胆管结石的治疗决策应根据患者情况个体化制订，应通过多学科讨论共同确定（**极低质量证据；弱推荐**）

注释：无症状性肝内胆管结石患者在 15 年的病程中，仅 11.5% 的患者在平均 3.4 年后出现症状^[633]。最常见的症状为绞痛、黄疸和发热，由胆管炎或肝脓肿所致，少数情况下由胆管癌所致^[633]。因此，采取观望策略是合理的。多学科治疗计划有益于症状性结石患者。为安排后续的治疗方案，ERCP 和经皮肝胆管造影都非常重要。对于单侧结石病的患者，应考虑手术切除，尤其当胆道狭窄和 / 或小叶萎缩同时存在时^[635,636]。部分肝脏切除的结石清除率在 80% 以上，复发率低于内镜治疗^[637-639]。

肝内胆管结石的其他治疗方法包括经口胆管镜碎石术（peroral cholangioscopic lithotripsy, POCSL）或经皮肝穿刺胆管镜碎石术（percutaneous transhepatic cholangioscopic lithotripsy, PTCSL），对弥漫分布的肝内胆管结石可能有帮助^[632,636,640-643]。在一个使用 POCSL 治疗肝内胆管结石的病例系列中，结石的完全取出率为 64%^[644]。PTCSL 的结石完全清除率更高（80%~85%）^[645-647]。长期随访中 POCSL 和 PTCSL 的结石复发率均较高（22%~50%），限制了二者的应用。

因 ABCB4 突变导致 LPAC 综合征的患者（参见“胆管结石复发的预防”章节）容易发生肝内胆管结石（单发或并发胆管结石和胆囊结石）^[216]。胆囊切除的指征为出现症状性胆囊结石或胆泥^[216]。症状性肝内胆管扩张并填满结石，可能为胆管引流或部分肝切除的指征。伴有终末期肝病的 LPAC 患者可能需要肝移植。

妊娠期胆石症的治疗

妊娠期间胆囊结石的治疗

妊娠期症状性胆囊结石应如何治疗？

如果存在紧急适应证，无论处于妊娠何期，均可实施腹腔镜胆囊切除术（**低质量证据；弱推荐**）

胆管结石清除后无症状的胆囊和胆管结石患者，应接受产后胆囊切除术（**极低质量证据；弱推荐**）

注释：妊娠妇女中胆泥或胆囊结石的发病率均为 5%，但一项纳入 3254 名妊娠妇女的大型前瞻性研究显示，出现胆泥或胆囊结石的妇女中仅 1.2% 出现胆源性疼痛^[648]。值得注意的是，随机性的干预措施——增加孕期的体育运动量（每周代谢当量 - 小时：第一孕期从 15.7 增加至 18.6，第三孕期从 10.2 增加至 12.1）并未减少妊娠期胆泥或胆囊结石的发生率^[649]。胆泥与妊娠期胆囊排空功能减弱有关，但并非干预的指征。胆泥或胆囊结石的妊娠妇女并非 UDCA 治疗的适应证。无症状的妊娠期胆囊结石患者不予治疗，但其中很多患者在妊娠后 1 年内必须进行胆囊切除术^[650]。

妊娠并非胆囊切除术的一般禁忌证^[651-653]。事实上，胆囊切除术为第二常见的产前非外科手术^[654]。对有症状的妊娠期胆囊结石患者进行外科治疗得到了一些研究支持，研究表明，在第一孕期、第二孕期和第三孕期症状复发的发生率分别为 92%、64% 和 44%^[655,656]，23%~39%

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的患者发生胰胆管并发症^[657,658]。基于6项研究共310例患者的研究数据，有症状的胆石症患者接受保守治疗或外科治疗，两者的早产或胎儿死亡率无显著差异^[655]。第二孕期是实施胆囊切除术最安全的孕期。现有数据和经验表明，第一孕期如出现紧急适应证，也有可能安全实施腹腔镜胆囊切除术^[658-660]。在第三孕期，由于腹腔空间有限以及诱发分娩的风险，手术适应证更加受限。腹腔内压力应维持在低于12~15 mm Hg，且在手术期间应对胎儿情况进行密切监测^[661,662]。

妊娠期间胆管结石的治疗

妊娠期的症状性胆管结石如何治疗？

妊娠期间的症状性胆管结石应通过资深内镜医师实施的内镜括约肌切开和结石取出术进行治疗（**低质量证据；弱推荐**）。在采取辐射暴露最小化措施的情况下，X线检查并非禁忌证（**极低质量证据；弱推荐**）

注释：一些研究已证实 ERCP 在妊娠期间的安全性^[663-666]。由于妊娠是 ERCP 术后发生胰腺炎的独立危险因素^[666,667]，该检查应由经验丰富的内科医师实施。胆管造影术期间的辐射暴露量估计为2~10 rads，胎儿辐射剂量不等^[656,668]。应尽可能限制透视的次数和剂量，且不应进行有额外辐射暴露的硬拷贝X射线摄像。可通过超声成像引导或抽吸胆汁确认胆道置管成功，以减少辐射^[669,670]。妊娠期患者在 ERCP 期间一般取左侧卧位，以尽量减轻对主动脉和腔静脉的压迫。在内镜括约肌切开术期间，不可将子宫置于括约肌切开器和接地板之间。

未来的前景

根据 CPG 专家组成员的意见，未来应对以下研究领域予以支持，以进一步改善胆石症的预防和治疗：

- 胆石症一级预防的策略研究
- 脂肪性肝病患者胆石症发病机制的研究
- 将遗传性和外源性成石危险因素贯彻到新的预防策略中
- 无症状或症状轻微的胆囊结石接受腹腔镜胆囊切除术的成本效益分析

- 胆囊切除术长期结局的护理研究和手术频率的地区差异
- 胆石症替代治疗的研究，尤其是手术高风险患者的替代治疗
- 无症状性胆囊结石或胆囊胆泥患者发生胆绞痛和并发症（尤其是胆囊癌）风险的研究
- 胆总管结石和肝内胆管结石复发的发病机制和预防
- 胆汁微生物和胆管炎症的研究

利益冲突

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