

老年人胆囊结石危险因素浅析

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摘要

胆囊结石是全球最常见的胃肠道疾病之一, 极大危害人类的健康。在我国, 成年人群胆结石的患病率为4.2%~21.7%, 平均为11.0%。胆囊结石的患病风险也随着年龄的增长而增加。随着我国老年化进程的发展, 老年人胆囊结石患者比例也逐年增加。本文结合近几年有关老年人胆囊结石的危险因素进行总结分析, 为老年人胆囊结石的临床治疗和预防提供参考。

关键词

胆囊结石, 老年, 危险因素

Analysis of Risk Factors of Gallbladder Stones in the Elderly

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Abstract

Gallbladder stones are one of the most common gastrointestinal diseases in the world, which greatly endanger human health. In my country, the prevalence of gallstones in the adult population is 4.2% to 21.7%, with an average of 11.0%. The risk of gallbladder stones also increases with age. With the development of my country's aging process, the proportion of elderly patients with gallbladder stones has also increased year by year. This article summarizes and analyzes the risk fac-

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tors of gallbladder stones in the elderly in recent years, and provides references for the clinical treatment and prevention of gallbladder stones in the elderly.

Keywords

Gallstone, Elderly, Risk Factors

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1. 引言

胆囊结石是全球最常见的胃肠道疾病之一, 根据结石组成成分的不同分为三类: 37%~86%为胆固醇类结石, 2%~27%胆色素类结石, 4%~16%为混合性结石[1]。胆结石的形成是遗传、环境、代谢和其他危险因素复杂相互作用的结果。其中的一些危险因素可导致胆囊胆汁过饱和, 胆固醇、胆汁脂质分泌增加、促成核因子和胆囊运动障碍。胆囊结石的患病风险也随着年龄的增长而增加[2]。老年人胆囊结石形成原因复杂, 与多种危险因素有关。本文结合近几年有关老年人胆囊结石的危险因素进行总结, 做出如下综述。

2. 代谢综合征与老年人胆囊结石的关系

肥胖和血脂异常与老年人胆囊结石相关。有研究认为肥胖是一种慢性炎症, 与促炎症因子水平的升高有着密切的联系[3]。增加肝脏胆固醇的分泌, 并通过增加胆汁胆固醇的分泌使胆汁过饱和, 从而导致胆囊结石的形成。M. L. Petroni 等人认为肥胖者的胆囊体积增大, 排空反应减弱也是重要原因[4]。血脂异常在老年人中普遍存在。其中体内甘油三酯与高密度脂蛋白水平异常被认为是胆囊结石的危险因素。较高的甘油三酯水平会导致胆囊收缩减少[5], 而高密度脂蛋白能够促进胆固醇向胆管分泌, 降低胆汁中胆固醇的饱和度, 血液中较低水平的高密度脂蛋白不利于肝胆酸的合成, 从而促进结石的形成[6]。血糖升高与老年人胆囊结石也存在一定相关性。高血糖和血糖正常的高胰岛素血症均会抑制胆囊收缩素的功能, 导致胆囊运动减弱[7]。高胰岛素血症也可能是这些观察中的一个关键因素, 因为胰岛素调节钠钾泵, 这可能会对包括胆囊肌细胞在内的平滑肌细胞的离子和渗透稳态产生不利影响。另有研究表明高胰岛素血症大鼠体内具有特异性 FOXO1 蛋白, 可促进胆固醇进入胆汁, 有利于结石的形成[8]。

3. 胃切除术后与老年人胆囊结石的关系

有研究发现病人胃切除术后胆囊结石发生率明显增加[9] [10], 其影响因素较多, 目前大部分研究者认为, 迷走神经损伤、消化道重建导致胆囊收缩功能减退为重要原因, 胃切除手术如胃癌根治术, 难以避免损伤到迷走神经, 支配胆囊运动的迷走神经损伤后会使得影响胆囊收缩神经调节, 导致胆囊出现异常运动, 胆囊排空功能降低。另外胃切除范围、淋巴结清扫范围、手术创伤及术后胆道感染也可能与胆囊结石的形成密切相关。全胃切除患者酸性环境消失, 肠道菌群失衡, 易导致胆道感染, 而胆道感染也是诱发胆囊结石的一重要因素。

4. 骨质疏松症与老年胆囊结石的关系

Sukhontip Klahan 等研究发现老年骨质疏松患者中患胆结石的风险更高[11]。慢性炎症可能在胆囊结

石的发生中起到关键作用,骨桥蛋白是一种促炎症细胞因子,在涉及广泛生物学过程的各种组织中表达。骨桥蛋白参与骨重塑过程,并刺激破骨细胞的粘附、迁移和骨吸收[12]。骨桥蛋白也是胆固醇结石的核心蛋白[13],参与了胆固醇胆石的形成,骨桥蛋白分子结合羟基磷灰石和钙离子,抑制体内胆固醇晶体的成核。

5. 类风湿性关节炎与老年人胆囊结石的关系

有研究发现类风湿性关节炎老年女性患者患胆囊结石的风险增加。但其生物学机制尚不清楚,María Carmen 等人认为可能与慢性炎症和 HDL 代谢有关。炎症情况下,胆囊内脂质循环的内皮功能会减弱,类风湿患者中存在的慢性炎症状态,与脂质谱和胆囊功能有关[14]。Pamuk O N 等人则认为可能与类风湿性关节炎患者胆囊排空功能障碍有关[15]。

6. 肝脏疾病与老年人胆囊结石的关系

6.1. 病毒感染增加老年人胆囊结石风险

慢性 HBV、HCV 感染为老年胆囊结石重要危险因素[16]。老年胆囊结石的更高患病率与乙型肝炎感染的持续时间和严重程度有关。随着乙型肝炎携带者年龄的增长,慢性肝炎可能进展并增加胆石症的风险。有研究表明,乙型肝炎病毒 X 蛋白与载脂蛋白 AI 相互作用,阻碍载脂蛋白 AI 与脂质聚集颗粒的形成,从而导致肝细胞胆固醇积聚[17],并可能促进胆固醇结石形成。也有学者认为,这可能与乙肝病毒感染导致患者有不同程度的肝硬化有关,相关研究表明肝硬化患者胆囊结石的发病率要比正常人高[18]。另有研究发现大于 60 岁的慢性 HBV 老年患者中患胆囊结石风险显著增加[19],有几种机制可以解释老年慢性 HCV 感染患者发生胆囊结石的风险增加[20]。第一,胆囊功能障碍和胆汁成分改变都会影响 HBV 感染患者胆结石的形成。脾功能亢进导致的慢性溶血、高雌激素、胆汁脂质比例发生变化、胆汁盐的低肝脏合成和转运以及非结合胆红素均有助于慢性 HBV 患者胆结石的发生。还有研究发现,胆囊病毒感染可能通过改变胆囊粘膜功能或运动障碍增加胆石形成[21];第二,胆囊的 HCV 直接感染可能在胆结石的形成中起重要作用。胆管损伤是慢性 HCV 感染的组织学特征,已被发现是肝内胆管癌的危险因素[22]。HCV 核心蛋白也能促进人胆管上皮细胞的恶性转化。Loriot18 等发现血清、胆汁和胆囊上皮细胞培养中的 HCV RNA 浓度相同,从胆囊上皮细胞分离的 HCV 颗粒水平支持这一说法。在慢性 HCV 感染患者的胆囊解剖标本中已经检测到 HCV RNA 和 HCV 抗原[23]。第三,无论 HCV 的基因型或肝脏损伤的严重程度如何,内脏肥胖患者的胆固醇胆结石和慢性 HCV 感染的胰岛素抵抗都会增加[24]。胰岛素抵抗的增加可能提供慢性 HCV 感染和胆囊结石之间的联系,可能通过胆汁饱和胆固醇分子数量的增加来所致。

6.2. 肝硬化与老年人胆囊结石患者的关系

肝硬化为老年胆囊结石患者的重要危险因素。有研究表明肝硬化患者胆结石的患病率明显高于对照组,且越到肝硬化晚期胆结石的发病率会较高[25]。其胆结石的主要成分是色素型胆结石[26]。肝硬化导致门脉高压,较高的门脉压力导致胆囊壁长期充血和水肿,最终导致胆囊壁增厚[27]、胆囊收缩力降低[28],这可能为肝硬化患者胆结石发病率增加的主要因素。其次肝硬化患者中代谢功能也发生改变,继发于脾功能亢进和溶血的胆汁中非结合胆红素增加,胆固醇分泌减少,胆汁酸合成和分泌减少[29],载脂蛋白 AI 和载脂蛋白 AII 也分泌减少[30],最终导致结石的形成。

老年人胆囊结石危险因素较多,我们发现了部分老年人胆囊结石的危险因素,但还有很多未知危险因素。掌握老年人胆囊结石的危险因素,有助于老年人群对胆囊结石进行预防,在生活中可尽量减少胆囊的发病因素,以降低胆囊结石的患病率。目前老年人胆囊结石危险因素还有很多未知领域需要探索,

其相关的分子机制也还需进一步研究。

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