

# 特殊人群结肠镜检查前肠道准备质量的影响因素

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## 摘要

针对老年人、糖尿病、慢性便秘、炎症性肠病、肝硬化、慢性肾脏病等特殊人群结肠镜检查前肠道准备质量的影响因素的相关研究进行综述, 指出通过长时间低纤维饮食、分次剂量方案和肠道准备结束后5小时内结肠镜检查等策略, 可提高老年人的肠道清洁成功率。此外, 尽管对于其他难以进行肠道准备的老年患者, 没有特别推荐的肠道准备方法, 但临床证据表明, 1 L PEG加抗坏血酸制剂与炎症性肠病患者更高的肠道清洁成功率相关。严重肾功能不全(肌酐清除率 < 30 mL/min)的患者应使用等渗高容量PEG溶液进行肠道清洁。目前关于肝硬化患者的肠道准备方案的研究报道还很少。本综述的目的是总结影响特殊人群肠道清洁质量的危险因素的证据, 以及改善这些患者结肠镜检查肠道准备的策略。

## 关键词

结肠镜检查, 肠道准备, 聚乙二醇, 影响因素

# Factors Influencing the Quality of Intestinal Preparation before Colonoscopy in Special Population

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## Abstract

This paper reviews the relevant studies on the factors affecting the quality of intestinal preparation before colonoscopy in the elderly, diabetes, chronic constipation, inflammatory bowel disease, cirrhosis, chronic kidney disease and other special populations, and points out that the success rate of intestinal cleaning in the elderly can be improved through long-term low-fiber diet, graded dose regimen and colonoscopy within 5 hours after the completion of intestinal preparation. In addition, although there is no specifically recommended method of bowel preparation for other difficult-to-perform patients, clinical evidence suggests that 1 L PEG plus ascorbate preparations are associated with higher intestinal cleansing success in patients with inflammatory bowel disease. Patients with severe renal insufficiency (creatinine clearance < 30 mL/min) should be treated with isotonic high-volume PEG solution for intestinal cleansing. At present, there are few studies on intestinal preparation protocols in patients with cirrhosis. The aim of this review was to summarize the evidence on risk factors that affect the quality of bowel cleaning in particular populations, as well as strategies to improve bowel preparation for colonoscopy in these patients.

## Keywords

Colonoscopy, Bowel Preparation, Polyethylene Glycol, Influencing Factor

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## 1. 引言

近年来, 中国结直肠癌的发病率迅速上升, 现已成为癌症相关死亡的第三大原因[1]。早期发现和切除腺瘤性息肉可降低结直肠癌发展的风险。结肠镜检查是目前诊断肠道疾病的金标准, 可以发现早期病变进行诊断和治疗, 可以显著降低结直肠癌的风险[2]。充分的肠道准备对于有效的结肠镜检查至关重要; 不幸的是, 据报道, 在高达 20%~40%的病例中, 结肠镜检查的肠道清洁效果不理想[3]。肠道清洁不良可导致重复结肠镜检查间隔较短[4], 增加医疗保健系统的成本[5], 增加并发症的风险, 延长手术时间, 并增加遗漏病变的可能性[3] [6]。目前, 4 L 聚乙二醇(Polyethylene glycol, PEG)分次剂量方案被广泛使用[7], 因为它具有满意的清洁效果。然而, 许多试验认为[8] [9] [10], 大量摄入液体会降低患者的依从性和耐受性, 同时导致大多数患者对肠道准备产生恐惧。除高剂量 PEG 外, 还有其他肠道清洁方案, 如相对低剂量的 PEG + 辅助制剂、硫酸盐口服溶液(oral sulfate solution, OSS)、镁制剂、口服磷酸钠(oral sodium phosphate, OSP)天然草药及其制剂等[11]。

研究发现, 肠道准备制剂类型、分次给药方案、低纤维饮食、合并症、合并用药、住院情况和年龄等因素都会影响肠道清洁的质量[12]。其中一些变量, 如制剂类型、制备方案和饮食, 是可改变的危险因素。在这方面, 最近的科学研究引入了新的有效的肠道清洁解决方案, 并强调了制定个性化肠道准备方案的重要性。我国成年人在进行结肠镜检查时肠道准备不良的发生率为 24.6% [13], 然而以老年人为研究对象时发现, 肠道准备不良的发生率高达 64.98% [14], 随着年龄增长, 肠道准备不良发生率有所增加。然而关于年龄或合并症等因素是不可改变的危险因素, 不容易干预, 这使得在特定情况下进行干预以提高肠道清洁质量变得更加困难。由于指南并未为具有多种危险因素的患者提供具体建议[11], 本综述的目的

的是总结影响特殊人群肠道清洁质量的危险因素的证据，以及改善这些患者结肠镜检查准备的策略。

## 2. 老年患者

预期寿命的增加导致老年患者成为结肠镜检查的主要人群。除了手术风险外，老年患者肠道准备可能存在肠道清洁效果不佳和其他风险[15]。患者必须经历一段时间的饮食限制、禁食和后来的液体限制，这对于患有糖尿病或慢性肾脏疾病(chronic kidney disease, CKD)的人来说可能很困难[16]。此外，只能通过楼梯、电梯上厕所的老年患者可能无法在家中准备，因此需要住院进行肠道准备或行结肠镜检查的替代检查[16]。尽管关于老年人和高龄人群肠道准备的研究很少，但2016年的一项研究发现，糖尿病、行走困难或进行日常生活活动与65岁以上患者肠道准备不良有关[15] [16]。此外，肠道准备不良是90岁及以上患者结肠镜检查失败的主要原因[16] [17]。肠道准备的副作用包括低血容量、肾功能衰竭和电解质紊乱[18]。由于老年人更有可能有多种合并症和多种用药史，因此准确的肠道准备处方，以及考虑药物潜在的相互作用和副作用对其尤为重要。对于已有慢性肾衰竭的老年患者，所有口服泻药都应谨慎使用，接受透析或患有晚期CKD的患者应咨询肾内科。肾功能衰竭患者应完全避免使用磷酸钠制剂[18]。此外，任何与肠道准备联合使用时可能加重肾功能衰竭的药物，如利尿剂、血管紧张素转换酶抑制剂和血管紧张素II受体拮抗剂，都应避免使用[18]。

目前已经研究了几种肠道准备方案可供使用，其疗效和耐受性各不相同。这些方案包括聚乙二醇 + 抗坏血酸盐(polyethylene glycol plus ascorbate, PEG-ASC) (4 L, 2 L, 和 1 L), 2 L PEG + 柠檬酸盐, 2 L PEG + 比沙可啶, 柠檬酸镁 + 微硫酸镁(magnesium citrate plus picosulphate, MCSP)和硫酸盐口服溶液(OSS) [19]。根据一项前瞻性队列的回顾性分析，在口服1 L PEG-ACS、2 L PEG/PEG-ACS 或 4 L PEG 肠道准备制剂后进行结肠镜检查的65岁以上合并症患者中，有70.3%的患者清洁成功[20]。值得注意的是，老年患者肠道清洁不充分的发生率高于非老年患者(7.0% vs 3.8%,  $P = 0.012$ ) [20]。分次剂量方案，最后结肠镜检查时充分清洁，耐受性评分高，低纤维饮食至少3天，并在肠道准备结束后5小时内进行结肠镜检查( $OR = 2.43, P = 0.003$ ;  $OR = 2.29, P = 0.02$ ;  $OR = 1.29, P < 0.001$ ;  $OR = 2.45, P = 0.001$ ;  $OR = 2.67, P = 0.008$ )是老年人肠道清洁成功的预测因素[20]。老年人1 L PEG-ASC的耐受性评分高于2 L和4 L PEG (7.7 vs 7.2 vs 7.2,  $P = 0.099$ )。有趣的是，与其他制剂相比，1 L PEG-ASC制剂与更高质量的右结肠清洁相关(分别为39.6% vs 17.0% vs 9.4%,  $P < 0.001$ )，因此该方案可能是老年人的首选。在老年人中实现安全和充分的肠道准备的方法应包括明确的指示、提醒电话和对潜在的混杂因素相关患者的病例管理[21]。

## 3. 糖尿病

糖尿病患者胃肠道症状患病率高、结直肠癌的风险增加，对结肠镜检查的需求高于一般人群[22] [23] [24]，可能需要更长的肠道准备时间来确保充分的内镜检查[25]。由于饮食/用药方案的改变、麻醉药物的使用以及糖尿病相关的并发症/合并症，如低血糖、电解质失衡、急性肾功能衰竭和酮症酸中毒，糖尿病患者存在肠道准备不良的风险[26] [27]。糖尿病已被认为是影响肠道准备质量的独立危险因素，它会降低结肠运动[28] [29] [30] [31]。糖尿病患者肠道准备不足的发生率波动在9%~30% [29] [32] [33]，应通过实施多因素策略来降低这一比例。

令人惊讶的是，尽管糖尿病患者是出了名的难以准备，但很少有研究关注在这种情况下的最佳肠道准备管理策略。有研究表明，糖尿病患者结肠镜检查前两天服用300 mL 柠檬酸镁，再加上单剂量4 L PEG，可改善结肠清洁率(从54%提高到70%) [34]。另一项针对糖尿病患者的单盲前瞻性试验发现，在手术前一天将鲁比前列酮(一种用于功能性便秘的局限性氯离子通道激活剂)添加到单次4 L PEG方案中可以改善结肠清洁效果；然而，由于样本量小，差异统计学上不显著[35]。一项针对糖尿病门诊患者的小型

试验研究了 6 L 聚乙二醇肠道清洁策略,但结果并不理想[29]。目前的美国指南不支持上述方案,而是建议糖尿病患者采用不进行调整的分剂量肠道清洁方案[36]。随后的一项欧洲随机、单盲、优势试验比较了传统肠道准备方案与糖尿病特异性准备方案,其中包括 3 天的低纤维饮食、1 天的透明流质饮食和 4 L 分剂量 PEG 方案[36]。后一组给予特殊教育计划,包括饮食、泻药摄入和降糖药调整指导。在常规治疗方案中,肠道清洁不足比糖尿病特异性治疗方案更常见(20% vs 7%; RR = 3.1, 95%CI 1.2~8.0, P = 0.014)。

#### 4. 慢性便秘

最常见的便秘类型是慢性功能性便秘,常发生在经常接受结肠镜检查的妇女和老年人身上,在西方国家的患病率为 2%~27% [37] [38] [39]。便秘已被确定为肠道准备不足的危险因素[11] [40]。目前,欧洲胃肠道内窥镜学会(European Society of Gastrointestinal Endoscopy, ESGE)不推荐对慢性便秘患者进行任何特定的肠道准备[11]。在老年患者中,以排便减少为特征的慢传输型便秘可能导致结肠冲洗和肠道准备不足。这一假设在 2015 年韩国的一项研究中得到证实[41],该研究发现结肠运输时间超过 30 小时与肠道准备不足有关。此外,在 2022 年对 274 名美国慢性便秘患者进行的一项研究中,通过结肠运输试验确定的慢传输型便秘与肠道准备不良风险增加 2 倍以上有关(OR = 2.2, 95%CI 1.1~4.4) [42]。

对于有便秘史的患者,应考虑使用其他肠道清洁辅助制剂[36]。近年来的大量研究表明,慢性便秘患者使用不同的肠道准备方案及辅助制剂效果良好。在 2008 年美国的一项双盲试验中,200 名结直肠癌(CRC)筛查患者在无饮食限制的情况下,随机分配接受 24 g 剂量的鲁比前列酮或安慰剂,然后使用分剂量的聚乙二醇电解质溶液进行肠道准备[43]。与安慰剂相比,使用分剂量的聚乙二醇电解质溶液和鲁比前列酮预处理更有效(P = 0.001)和可耐受(P = 0.003),这很可能是由于腹胀减少(P = 0.049) [43]。在 2015 年意大利的一项随机单盲研究中,400 名便秘患者被随机分配到两组中的一组:分剂量 2 L PEG-柠檬酸盐-西甲硅油 + 2 天比沙可啶或分剂量 4 L PEG [44]。在给药的方便性(P < 0.001)、重复意愿(P < 0.001)和依从性(P = 0.002)方面,2 L PEG-柠檬酸盐-西甲硅油溶液明显更容易接受[44]。在 2016 年,我国的一项随机对照试验[45]中,结肠镜检查前 1 天添加乳果糖联合 4 L 分剂量 PEG 的效果显著优于常规口服 PEG 的肠道准备方案(P < 0.05)。根据 2019 年的一项随机对照试验[46],日本便秘患者的最佳乳果糖剂量为 26 克/天。2016 年,一项随机、双盲、安慰剂对照试验研究了更大范围的亚洲人群[47]。令人惊讶的是,当较低剂量的聚乙二醇与鲁比前列酮联合使用时,没有显著性观察到肠道清洁质量的差异。2021 年, Dang 等[48]对 3 项随机对照试验进行了系统评价和荟萃分析,纳入 225 例慢性便秘患者,其中 47.6%接受磷酸钠治疗,52.4%接受 PEG 治疗。尽管证据质量较低,结肠镜检查前接受磷酸钠治疗的患者比接受 PEG 治疗的患者结肠更清洁(OR = 1.87, 95%CI 1.06~3.32, P = 0.003)。

#### 5. 炎症性肠病

肠道准备不足也与炎症性肠病(Inflammatory bowel disease, IBD)等合并症有关[49]。一项多中心研究证实了这一点,该研究对 211 名接受结肠镜检查的溃疡性结肠炎(ulcerative colitis, UC)成年门诊患者进行了研究,他们接受了 2 L 聚乙二醇加比沙可啶或 4 L 聚乙二醇治疗[50]。低容量 PEG 在 UC 患者的肠道清洁方面并不逊于 4 L PEG (P = NS),但其耐受性(P < 0.0001)和接受度(P < 0.0001)更好。无论何种制剂,分次剂量均与更好的清洁有关。从准备结束到结肠镜检查之间的时间超过 6 小时预示着清洁不良。在 2021 年的前瞻性队列回顾性分析中, Maida 等[51]证明了 1 L PEG-ASC 在 411 例患者中的 45%的有效性和安全性。IBD 患者的清洁成功率(92.9% vs 85.4%, P = 0.02)高于对照组,出现不良事件的患者数量相似(22.2% vs 21.2%, P = 0.821),治疗后出现的不良事件也相似(51% vs 62%, P = 0.821)。此外,IBD 的存在(OR = 2.51, P = 0.019)、较低的年龄(OR = 0.98, P = 0.014)、分次剂量方案(OR = 2.43, P = 0.033)、无糖尿病(OR = 2.85,

$P = 0.015$ )和慢性便秘( $OR = 3.35, P = 0.005$ )都与清肠成功独立相关[51]。

最近有研究发现,内镜下疾病活动可以预测肠道准备不佳,生物治疗已被证明可以保护IBD患者免受其影响。2022年,Kumar等[52]在美国进行的一项研究发现,与轻度或不活跃的疾病相比,中度至重度疾病活动度发生肠道准备不佳的几率更高(aOR 2.7; 95%CI 1.52~4.94),而在整个IBD队列中,生物制剂使用与肠道准备不理想的低发生率相关[aOR, 0.24 (0.09~0.65)]。此外,年龄 > 65岁和单次给药的肠道准备是肠道准备不足的独立预测因素[aOR, 2.99 (1.19~7.54); aOR, 2.37 (1.43~3.95)]。

## 6. 肝硬化

肝硬化预示结肠镜筛查时肠道准备不良[53] [54]。这一发现很可能是由于肝硬化患者肠道运动受到多种因素的影响[55] [56]。在没有肝硬化的情况下,慢性肝病在肠道准备不足的易感性中的作用尚不清楚。

在2016年美国的一项研究中,Anam等[57]将120名肝硬化患者与220名非肝硬化慢性肝病患者进行了比较,第一组患者在肠道准备方面的表现明显更差。肝硬化患者的肠道准备评分低于非肝硬化患者( $P = 0.0027$ ),在肝硬化患者中,48%的患者的肠道准备得分最低,而非肝硬化患者的这一比例为30%。肝硬化患者和非肝硬化患者的息肉检出率没有差异。根据MELD评分评估的肝硬化严重程度并不能预测肠道准备情况恶化。Salso等人研究表明,53名肝硬化患者与52名接受结肠镜筛查的健康受试者相比,肠道准备的失败率和副作用发生率相当[58]。尽管如此,仍有近一半的肝硬化患者(49%)肠道清洁不良。

在2017年,我国的一项回顾性研究中, Lee等[59]比较了两种清肠剂在肝硬化患者中的安全性(2 L PEG-ASC vs 4 L PEG)。与4 L PEG组相比,患者更倾向于使用2 L PEG-ASC。最后,由于两组均成功进行肠道清洁,作者得出结论,在肝硬化患者中使用2 L PEG-ASC进行肠道清洁是一种安全的选择。肝硬化失代偿期患者更容易出现虚弱、认知异常和活动减少。Clayton等[60]发现,121例肝硬化失代偿患者在初始肝移植评估时接受结肠镜检查,患者教育视频并没有改善干预前后的肠道准备。此外,与非腹水患者相比,中度至重度腹水患者结肠镜下肠道准备不足的发生率明显更高[60]。

## 7. 慢性肾脏病

由于存在电解质失衡或肾功能恶化的风险,慢性肾脏病(CKD)患者使用肠道清洁剂时应仔细评估[61]。根据以往的研究[62] [63],PEG在CKD患者中通常是安全的;然而,在某些情况下,结肠镜检查前后应确保足够的饮水量以及监测肾功能,以避免急性肾衰竭[64]。强烈建议有水、电解质紊乱风险的患者选择个体化肠道准备方案[11]。

由于高渗透压和镁毒性以及急性磷酸盐肾病的风险,CKD患者应避免使用镁剂和磷酸钠[11] [65] [66]。此外,由于大容量PEG方案耐受性差,已经提出了低容量PEG (2 L) + 抗坏血酸(PEG-ASC)溶液,以减少患者的过量液体摄入。抗坏血酸因其己糖结构可作为渗透剂,增强PEG的通便作用[67],其令人愉悦的口感使患者更容易吞咽;另一方面,抗坏血酸与肾结石和酸中毒的形成有关,结果相互矛盾[68] [69]。因此,对于许多CKD患者来说,小容量制剂仍然是一个挑战。值得注意的是,ESGE指南不推荐含阿斯巴甜和抗坏血酸的溶液(如2 L和1 L PEG-ASC溶液)用于肾功能不全和肌酐清除率低于30 mL/min的患者。在服用1 L PEG-ASC后,观察到高钠血症的发生率很高,这主要是由于产品的钠含量[11]。Lee等[68]在2016年的一项研究中发现,2 L PEG-ASC是肾功能受损患者结肠镜检查前肠道准备的安全选择。在一个回顾性队列中,GFR为60 mL/min的患者给予4 L PEG或2 L PEG-ASC溶液。2 L PEG-ASC组患者( $n = 61$ )对其耐受性和可接受性的评价高于4 L PEG组( $n = 80$ ) [68]。服用两种制剂后,电解质、血尿素氮或肌酐的变化均无统计学意义。比较两种方案时,7.5%的4 L PEG患者和11.5%的2 L PEG-ASC患者的肌酐水平短暂性升高>30%,但差异无统计学意义[68]。Ohmiya等[70]在日本2021年的一项研究中发

现,使用聚乙二醇电解质溶液加抗坏血酸(PEG-ELS-ASC)进行当日常规肠道准备对 56 名 CKD 患者是安全有效的。

只有回顾性队列研究发现,对于肾功能受损的患者,PEG 比其他制剂更安全[71]。最严重的肾损伤病例报告了使用口服磷酸钠(OSP)行结肠镜检查后几周内可逆的急性肾衰竭,19%的患者需要肾脏替代治疗[72]。此外,在 2006~2007 年期间,美国食品和药物管理局收到了 171 例使用 OSP 引起的肾功能衰竭病例和 10 例使用 PEG 引起的肾功能衰竭病例的报告[72]。2005 年冰岛一项基于人群的回顾性研究发现,活组织检查证实的急性磷酸盐肾病的风险约为每销售 1000 剂 OSP 中有 1 剂[72]。三个比较 OSS 制剂与 4 L PEG 的随机对照试验发现,在疗效、安全性和耐受性方面,分剂量 OSS 并不比分剂量大容量 PEG 差。在肾功能不全的情况下,OSS 的实际数据有限,尽管该制剂在急性肾功能衰竭的发生率上没有显著差异,但欧洲指南仍建议[11]严重肾功能不全(肾小球滤过率 < 30 mL/min)的患者避免使用 OSS。根据 ESGE 指南和目前的证据,严重肾功能不全患者应使用等渗大容量 PEG 溶液,而不是小容量 PEG 或非 PEG 方案。

## 8. 结论

迄今为止,人们已经做出了许多努力来提高结肠镜检查息肉和晚期腺瘤的检出率,从而降低间隔期结直肠癌的风险[73] [74]。其中包括结肠镜检查关键性能质量指标的应用[75],远端附着装置的使用[76] [77],以及提高肠道清洁质量的新型肠道制剂[78]。尽管做出了这些努力,但充分的肠道清洁仍然是高质量结肠镜检查的基本前提,因为它会影响其他质量指标,包括不良反应和盲肠插管率。老年、慢性便秘、糖尿病、IBD、肝硬化、严重肾功能衰竭是结肠镜检查准备失败的主要患者相关预测因素。

在老年人中,包括长期低纤维饮食、分次剂量方案和在准备结束后 5 小时内进行结肠镜检查在内的策略可能会增加清洁成功率。此外,尽管对于其他特殊人群的肠道准备没有特别推荐的方案,但最近的证据表明,1 L PEG-ASC 制剂可能更适合 IBD 患者。根据目前的指南,严重肾功能不全(肌酐清除率低于 30 mL/min)的患者应使用等渗大容量 PEG 溶液,而不建议使用小容量 PEG + 佐剂(例如 1 L/2 L PEG-ASC 和 1 L PEG + 柠檬酸盐)或非 PEG 方案(例如 MCSP 或 OSS)。为了确定对老年人、便秘和肝硬化患者最有效的肠道准备方案,需要更多高质量的前瞻性研究。

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