Advances in Clinical Medicine 临床医学进展, 2025, 15(10), 446-453
Published Online October 2025 in Hans. https://www.hanspub.org/journal/acm
https://doi.org/10.12677/acm.2025.15102776

结肠癌治疗的研究进展

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收稿日期：2025年8月26日；录用日期：2025年9月19日；发布日期：2025年9月29日

摘　要

近几年，结肠癌作为全球第三大常见癌症，在治疗领域取得了显著进展，本文将基于2025年发布的研究成果，其中涵盖了手术技术、化疗、靶向治疗、免疫治疗以及个体化治疗等多个方面。本文通过总结结肠癌在治疗方面的进展，目的是为以后的临床研究和未来发展提供参考。

关键词

结肠癌，肿瘤治疗

Research Progress in the Treatment of Colon Cancer

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Received: August 26, 2025; accepted: September 19, 2025; published: September 29, 2025

Abstract

In recent years, colorectal cancer, as the third most common cancer globally, has made significant progress in the field of treatment. This article is based on research findings released in 2025, covering various aspects such as surgical techniques, chemotherapy, targeted therapy, immunotherapy, and personalized treatment. By summarizing the advancements in the treatment of colorectal cancer, the aim is to provide a reference for future clinical research and development.

Keywords

Colon Cancer, Tumor Treatment

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文章引用: 侯文宇, 王强. 结肠癌治疗的研究进展[J]. 临床医学进展, 2025, 15(10): 446-453.
DOI: 10.12677/acm.2025.15102776

1. 引言

本文对结肠癌的多维度治疗进展进行了全面的梳理，涵盖了从传统手术、化疗到前沿的靶向、免疫及个体化治疗。对于临床医生、肿瘤学研究者及医学生而言，该文提供了一个快速了解领域动态的窗口，具有较好的知识普及和参考价值。文章整合了多个不同方向的研究，有助于读者形成对结肠癌综合治疗模式的整体认知。

2. 手术治疗进展

2.1. 腹腔镜与机器人手术

腹腔镜手术已成为结肠癌治疗的标准方法之一，其微创性、恢复快、并发症少等优势已得到广泛认可。自本世纪初以来，机器人平台为腹腔镜手术带来了一种有希望的替代方案，被证明是安全和可行的，特别是在直肠癌手术中[1]-[3]。为了应对这些挑战，机器人手术已经成为腹腔镜手术的一种微创替代方案，提供了一种更精确、侵入性更小的解决方案。机器人手术提供了更高水平的灵活性，这要归功于更灵活的仪器、改进的外科医生人体工程学、更高的机动性(具有近 360˚的运动范围)以及放大的高清视野[4]-[6]。Negrut 等人发表的对 21 项研究(50,771 例)的荟萃分析。2024 年，比较了腹腔镜和机器人手术治疗结肠癌(不包括横结肠)，发现机器人手术与更长的手术时间($p < 0.00001$)、更短的住院时间($p = 0.003$)和更低的中转率($p < 0.00001$)相关[7]。与使用单一部位进行结肠切除术的患者相比，使用 SP 进行结肠切除术的患者伤口长度更短，出血更少，端口使用量更少。使用 SP 平台的机器人结肠切除术具有更好的短期恢复相关结果，需要更少的止痛剂，以及更好的美容效果[8]。机器人技术不仅可以方便术者操作，更可以为患者缩短康复时间，使得手术切口更加美观。然而，机器人手术也有着许多限制，例如：安装机器人手术系统、后续设备的维护与检修需要高额的成本；医生必须经过专业培训的才可以熟练操作；术者缺乏对术区触觉方面的感知。在未来，我们可以着力于人工智能与机器人手术相结合，增加机器人在触觉方面的反馈，逐渐降低技术成本来帮助更多的人。

2.2. 自然腔道标本取出手术(NOSES)

随着医学知识的不断修改和更新，一种侵入性较小的方法——自然开口标本提取手术(Noses)正在世界范围内引起广泛的关注。鼻腔手术采用腹腔镜器械、软性内窥镜或经肛门内窥镜显微手术，通过自然开口取出标本，避免了取材部位的剖腹手术，最大限度地减少了对患者的创伤。近年来，许多机构进行了鼻部手术，发现鼻部手术与更快的肠功能恢复、更少的术后并发症、更少的疼痛、更好的心理和美容效果有关[9]-[14]。经肛门取材手术可能在许多方面有益于老年结直肠病人，如胃肠功能恢复快、与切开相关的并发症发生率低、术后疼痛少、疗效好。美观的效果和更好的生活质量。此外，经肛门取材手术对老年患者的肛门功能和远期疗效也是有保障的[15]。NOSES 虽然可以减轻术后疼痛，减少术后并发症并且可以早期下床活动，但是手术后或通过自然开口取出标本的部位发生腹部感染的可能性仍然是一个有争议的话题[16]也可能会有吻合口瘘、括约肌功能受影响的问题。在未来，可以通过与机器人手术联合减少感染的可能性。

3. 化疗进展

化疗方案优化：2025 年，csco 结直肠癌指南的更新，围手术期新辅助化疗方案：作为精通(PMMR)/微卫星稳定(Mss)状态的最新指南，最新指南引入了在进行根治性手术前进行 2~3 个月新辅助化疗(CAPOX、mFOLFOX6 或 FOLFOXIRI)的 III 类建议，FOXTROT 研究的结果支持了 CAPOX/mFOLFOX6 方案的建议，该研究结果表明，术前 6 周的奥沙利铂－氟嘧啶化疗可以安全地实施，而不会增加围手术期的发病率[17] [18]。

新辅助治疗最新进展：胡华彬等实验的结果表明，氟尿嘧啶、亚叶酸钙和奥沙利铂(MFOLFOX6)或卡培他滨和奥沙利铂(CAPOX)作为新辅助化疗(NAC)与 mFOLFOX6 或 CAPOX 联合治疗并未显著改善局部晚期结肠癌患者的 3 年无病生存率。然而，这种新辅助方法是安全的，并导致相当大比例的 pCR 和降期。NAC 可以被认为是一种可行的治疗选择，除了前期手术的护理标准之外[19]。NAC 的主要缺点是，一些放射学分类错误的低风险肿瘤患者接受了不必要的化疗[20]。

新药：口服呼肠孤病毒重塑结肠癌肠道微生物群并增强抗肿瘤免疫，溶瘤病毒(OV)是一种经过选择或基因工程的治疗剂，专门感染和溶解肿瘤细胞，而不影响正常细胞[21]-[25]。同时也可引起人类上呼吸道和胃肠道的自限性、无症状或轻度感染[26]-[28]。口服呼肠孤病毒抗肿瘤的机制是：呼肠孤病毒 dsRNA 通过 RIG-1 和 MDA5 [29] [30]等 RNA 传感器刺激 TRAIL。TRAIL 然后与表面死亡受体结合，并通过 caspase-3 和 caspase-7 [31] [32]激活细胞凋亡。Won Suk 等的实验证明了口服呼肠孤病毒是一种可行和安全的溶瘤病毒疗法，可以最大限度地提高小鼠结肠癌和黑色素瘤的免疫治疗效果[33]。然而目前尚不了解口服呼肠孤病毒对胃肠癌的肿瘤细胞裂解死亡的作用机制，我们在未来仍然需要进一步研究。

4. 靶向治疗进展

EGFR 通路抑制剂：西妥昔单抗和帕尼单抗仍是 KRAS/NRAS/BRAF 野生型 mCRC 的重要靶向药物。在具有野生型 RAS 的转移性结直肠癌(MCRC)患者中，使用抗 EGFR 抗体，如西妥昔单抗或帕尼单抗，可改善患者的预后。尽管转移性结直肠癌患者对西妥昔单抗或帕尼单抗等抗 EGFR 抗体表现出很高的疗效，但在癌细胞中也观察到了耐药性[34] [35]。西妥昔单抗或帕尼单抗单独或联合化疗的益处仅限于患有野生型 KRAS 和 NRAS (神经母细胞瘤 RAS 病毒癌基因同源)的 mCRC 患者[36]-[41]。EGFR 的缺失降低 LGR5 的表达，EGFR 与 LGR5 相互作用并被西妥昔单抗增强，西妥昔单抗增强 LGR5 靶向 ADCs 的体外效应。西妥昔单抗与 LGR5 ADC 联合使用，与单一药物治疗相比，可以增强肿瘤抑制或肿瘤消退，并延长 RAS 基因突变患者来源的异种移植的存活时间。这些发现支持越来越多的证据表明，ADC 联合疗法可能比单一疗法更有效，并表明西妥昔单抗在治疗 RAS 基因突变的结直肠癌方面有更广泛的临床应用。西妥昔单抗与 8E11-CPT2 联合应用可提高患者来源的结直肠癌异种移植模型的抗肿瘤疗效和生存率。8E11-CPT2 ADC 对 LGR5 表达的 RAS 基因突变结直肠癌具有显著的抗肿瘤作用，与西妥昔单抗联合应用可进一步增强该作用[42]。

VEGF 通路抑制剂：贝伐单抗(Bev)是一种人源化重组免疫球蛋白-1 (IgG1)单抗，具有抗血管内皮生长因子的活性[43]。目前它被用于治疗许多类型的肿瘤，特别是结直肠癌[44]。它的作用是竞争性地抑制肿瘤分泌的血管内皮生长因子，阻止其与邻近内皮细胞上的受体结合[45]。基于阻断血管生成和刺激抗肿瘤免疫反应的协同效应，Bev 和免疫疗法的联合治疗可能会为 MSI-H 肿瘤患者提供显著的治疗益处[46]。周玲等人。强调指出，接受 Bev 治疗的老年患者患严重高血压的风险增加，这可能导致严重的心血管并发症。对于这类患者，建议定期监测血压并尽早开始降压治疗[47]。BEV 呈现出一种独特的不良反应模式，即报告血管、感染性和眼部疾病的可能性很高，但与化疗相比，血液毒性的风险较低[48]。Bev 虽然对结直肠癌的治疗有很多好处，但仍然不可忽略他的并发症，因此希望在未来可以寻求减少贝伐单抗并

发症的方法或者开发出疗效更佳并且副作用更少的药物。

BRAF 抑制剂：BRAF-V600E 突变型 mCRC 的治疗取得进展，恩考芬尼联合西妥昔单抗被推荐用于既往治疗失败的患者。ICIS 治疗 BRAF V600E 突变型 MSS-mCRC，对于 BRAF V600E 突变的 MSS mCRC 患者，如 BRAF V600E 突变的恶性黑色素瘤[49]-[51]中批准的那样，将 MAPK 抑制剂与抗 PD-1 抗体相结合可能是有希望的。在目前的 ICI 治疗时代，具有该突变的 MSI-H CRC 患者在接受 ICI 单一治疗时与未接受 ICI 治疗的患者取得了类似的结果。然而，对于带有 BRAF V600E 的 MSS 亚型，突变可能会加剧免疫抑制环境，导致免疫治疗抵抗。抑制 MAPK 的免疫增强潜力表明它与免疫治疗一样有用。将 BRAF/EGFR 抑制剂与 ICIS 相结合的初步研究显示出了希望[52]。

5. 免疫治疗进展

MSI/dMMR 型结肠癌：在结肠癌中，18.9%~21.3%的 II 期肿瘤和 14.3%~14.4%的 III 期肿瘤存在 dMMR/MSI [53] [54]。Wang 等人的研究表明：Toripalimab (特瑞普利单抗)联合伊立替康和贝伐单抗治疗局部晚期结肠癌或局部进展期直肠癌错配修复缺失或微卫星不稳定性是一种安全有效的方案。特瑞普利单抗联合伊立替康和贝伐单抗具有良好的聚合酶链式反应速率，特瑞普利单抗剂量越大，PCR 率越高。伊立替康和贝伐单抗似乎提高了客观应答率，但不能提高 PCR 率[55]。特瑞普利单抗耐受性良好，无剂量限制性毒性，其所致的 ADR (药品不良反应)可能涉及多个系统，尤其是内分泌系统和皮肤系统，但大多为 1 级或 2 级 ADR，3 级或更高级别的 ADR 发生率相对较低[56]。虽然 ADR 级别较低，但也应该及时预防，积极监测，避免对机体造成不必要的损伤。

6. 个体化治疗与标志物进展

生物标志物驱动的治疗：POLD1 是 DNA 聚合酶 Delta (Pold)的催化亚基，是一种对 DNA 合成和校对至关重要的多域蛋白(125 KDa) [57]。POLD1 突变是癌症生物学的动态设计师，将基因组的不稳定性与免疫逃避交织在一起，同时揭示了新的治疗途径。与肿瘤抑制因子 PBRM1 联合使用，可增强 POLD1 突变肿瘤的 ICI 疗效。在晚期实体肿瘤中，POLD1/PBRM1 联合治疗在升高的 TMB 和 T 细胞允许的微环境的推动下，产生了更高的应答率(70%比单独使用 POLD1 的 40%) [58]。在 MSS 肿瘤中，POLD1 突变通过高 TMB 和克隆性新抗原提高免疫原性，使这些肿瘤对 ICIS 产生反应，从而打破了传统的免疫治疗范式。这些见解将 POLD1 提升为一个潜在的预测生物标记物和创新方法的目标，例如基于新抗原的疫苗或利用复制缺陷的合成致命策略[59]。笔者认为对于肿瘤晚期患者，可以进行全面的基因检测，基于 POLD1/PBRMI 联合治疗以及新抗原疫苗改善患者的预后。

液体活检与动态监测：循环肿瘤 DNA (CtDNA)是一种来源于肿瘤外周血流中发现的游离 DNA (CfDNA)的组成部分，被认为是通过癌细胞的凋亡、坏死和吞噬而释放的。最近的文献表明，ctDNA 是判断原发结直肠癌预后的指标，ctDNA 引导下的 II 期结直肠癌治疗前景看好[60]-[62]。结直肠癌肝转移(CRLM)根治性手术后复发风险仍然很高，通过 Lissa Wullaert 等人在没有(NEO)辅助化疗的可切除 CRLM 患者中进行的研究，证明了手术后可检测到的循环肿瘤负荷对 RFS 的影响。术后 ctDNA 和 CTC 检测是局部治疗后 RFS 缩短的有力预测指标[63]。因此，我们可以根据 CtDNA 和 CTC 的检测能力，动态监测结直肠癌患者病情，不断优化治疗方案，延长 RFS。CtDNA 在结直肠癌方面取得了不错的进展，但在其他癌症方面仍然需要大量的前瞻性数据证明其相关性。

7. 总结与展望

2025 年，结肠癌治疗在手术、化疗、靶向、免疫和个体化治疗方面均取得显著进展。腹腔镜手术和

机器人提高了术者的手术精准度和提升了患者术后的恢复效果及美观；化疗和靶向方案的优化，以及免疫治疗的进步，这些治疗方式均极大地改善了患者的生存期和生活质量。未来，我相信随着更多新技术的发展和进步，结肠癌患者会有更加美好的明天。

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