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·指南与共识·

结直肠癌肝转移诊断和综合治疗指南（2025版）

中国医师协会外科医师分会；中华医学会外科分会胃肠外科学组；中华医学会外科分会结直肠外科学组；中国抗癌协会大肠癌专业委员会；中国医师协会结直肠肿瘤专业委员会；中国临床肿瘤学会结直肠癌专家委员会；中国医师协会外科医师分会结直肠外科医师委员会；中国医师协会肛肠医师分会肿瘤转移委员会；中华医学会肿瘤学分会结直肠肿瘤学组；中国医疗保健国际交流促进会转移肿瘤治疗学分会；中国医疗保健国际交流促进会结直肠病分会

摘　要　为进一步规范和提升我国结直肠癌肝转移的诊疗水平，《结直肠癌肝转移诊断和综合治疗指南（2025版）》在以往版本基础上，结合近年来国内外研究进展和临床经验，进行了系统更新。新版指南在优化诊断流程、加强多学科团队协作的基础上，全面升级了治疗策略，涵盖可达到无疾病证据状态（NED）患者的外科手术、辅助与新辅助治疗，及无法达到NED状态患者的综合治疗方案；同时拓展了基因检测内容，引入多种局部毁损新技术，强调规范随访与长期管理，力求实现治疗个体化、精准化，最终改善患者预后。指南旨在为全国医疗机构在结直肠癌肝转移的临床实践中提供循证、实用的参考依据。

关键词　结直肠肿瘤；肿瘤转移；诊疗准则
中图分类号：R735.3

Chinese guidelines for the diagnosis and comprehensive treatment of colorectal liver metastases (2025 edition)

Chinese Society of Surgeons, Chinese Medical Doctor Association; Gastrointestinal Surgery Group, Chinese Society of Surgery, Chinese Medical Association; Colorectal Surgery Group, Chinese Society of Surgery, Chinese Medical Association; Colorectal Cancer Committee, Chinese Anti-Cancer Association; Colorectal Oncology Committee, Chinese Medical Doctor Association; Expert Committee on Colorectal Cancer, Chinese Society of Clinical Oncology; Colorectal Surgery Committee, Chinese Society of Surgeons, Chinese Medical Doctor Association; Tumor Metastasis Committee, Coloproctology Society, Chinese Medical Doctor Association; Colorectal Oncology Group, Chinese Society of Oncology, Chinese Medical Association; Division of Metastatic Tumor Therapy, China International Exchange and Promotive Association for Medical and Health Care; Division of Colorectal Diseases, China International Exchange and Promotive Association for Medical and Health Care

Abstract　To further standardize and improve the management of colorectal liver metastases (CRLM) in China, the *Chinese guidelines for the diagnosis and comprehensive treatment of colorectal cancer liver metastases (2025 edition)* have been systematically updated based on previous versions and the latest international and domestic evidence. The updated guideline refines diagnostic pathways, strengthens multidisciplinary

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team collaboration, and comprehensively upgrades therapeutic strategies−including surgical resection, neoadjuvant and adjuvant treatments for patients eligible for no evidence of disease (NED) status, and systemic therapy for those who are not. It also expands the scope of genetic testing, incorporates innovative local ablative therapies, and emphasizes standardized follow-up and long-term management. The guideline aims to promote individualized and precision-based treatment, ultimately improving clinical outcomes and patient survival. It serves as a practical, evidence-based reference for healthcare providers managing CRLM across China.

Key words Colorectal Neoplasms; Neoplasm Metastasis; Practice Guideline

CLC number: R735.3

肝脏是结直肠癌血行转移最主要的靶器官，结直肠癌肝转移（colorectal cancer liver metastases）是结直肠癌治疗的重点和难点之一[1-2]。约有15%~25%结直肠癌患者在确诊时即合并有肝转移，而另15%~25%的患者在结直肠癌原发灶根治术后发生肝转移，其中绝大多数（80%~90%）的肝转移灶初始无法获得根治性切除[3]。肝转移也是结直肠癌患者最主要的死亡原因[4-5]，未经治疗的肝转移患者的中位生存期仅6.9个月，无法切除患者的5年生存率低于5%[6]，而肝转移灶能完全切除[或可以达到无疾病证据（no evidence of disease，NED）状态]患者的中位生存期达35~60个月，5年总体生存率可达40%~57%[7-11]。研究表明，有一部分最初肝转移灶无法根除的患者经治疗后可以转化为可切除或达到NED状态。因此，通过多学科团队（multidisciplinary team，MDT）对结直肠癌肝转移患者进行全面地评估，个性化地制定治疗目标，开展相应的综合治疗，以预防结直肠癌肝转移的发生、提高肝转移灶手术切除率和5年生存率[12-13]。

为了提高我国结直肠癌肝转移的诊断和综合治疗水平，受卫生部临床重点学科项目资助（2008—2010年），中华医学会外科分会胃肠外科学组和结直肠外科学组、中国抗癌协会大肠癌专业委员会自2008年起联合编写了《结直肠癌肝转移诊断和综合治疗指南》（草案），以指导我国结直肠癌肝转移的诊断和治疗，并于2010年、2013年先后进行了两次修订。2016年、2018年、2020年、2023年联合中国医师协会外科医师分会结直肠外科医师委员会、中国医疗保健国际交流促进会转移肿瘤治疗学分会和结直肠病分会、中国临床肿瘤学会结直肠癌专家委员会、中国医师协会结直肠肿瘤专业委员会、中国医师协会肛肠医师分会肿瘤转移委员会、中华医学会肿瘤学分会结直肠肿瘤学组、中国医师协会外科医师分会等多次共同修订了《指南》。2025年再次共同总结国内外先进经验和最新进展修订本《指南》。（本文中出现的推荐级别、循证医学证据分类的界定，详见附录1；本《指南》对结直肠癌肝转移的诊断、预防、外科手术和其他综合治疗提出的建议，请各地医院根据实际情况予以应用，诊疗流程详见附录2）。

1 结直肠癌肝转移的诊断与随访

1.1 结直肠癌肝转移的定义

按照国际共识，同时性肝转移（synchronous liver metastases）是指结直肠癌确诊前或确诊时发现的肝转移；而结直肠癌根治术后发生的肝转移称为异时性肝转移（metachronous liver metastases）[14]。本指南为便于诊疗策略的制定，将按照“结直肠癌确诊时合并肝转移”和“结直肠癌根治术后发生肝转移”两方面阐述。

1.2 结直肠癌确诊时肝转移的诊断常规

对已确诊结直肠癌的患者，除血清CEA、CA19-9等肿瘤标志物检查、病理分期评估外，应常规进行肝脏超声和腹部CT增强等影像检查筛查及诊断肝脏转移瘤。对于超声或CT影像高度怀疑但不能确诊的患者可加行血清甲胎蛋白、肝脏超声造影和肝脏MRI增强检查[15-16]（1a类证据，A级推荐），肝脏细胞特异性造影剂增强MRI检查对于发现<1 cm的微小病灶准确率更高，有条件时可考虑（2a类证据，B级推荐）。PET/CT或PET/MRI检查不作为常规推荐，可在病情需要时酌情应用[17-18]（2a类证据，B级推荐）。

肝脏病灶的经皮针刺活检仅限于病情需要时应用[19]。

结直肠癌手术中必须常规探查肝脏以进一步排除肝转移的可能[20]，对可疑的肝脏结节可行术中超声检查，必要时考虑同步切除或术中活检[6]（3a 类证据，B 级推荐）。

1.3　结直肠癌根治术后肝转移的监测

结直肠癌根治术后，应对患者定期随访[21-23]，了解有无肝转移或其他远处转移的发生。(1) 每 3~6 个月进行 1 次病史询问、体格检查、肝脏超声检查和检测血清 CEA、CA19-9 等适当的肿瘤标志物，持续 2 年，以后每 6 个月 1 次直至满 5 年[24]（1a 类证据，A 级推荐），5 年后每年 1 次。(2) Ⅱ期和Ⅲ期的结直肠癌患者，建议每年进行 1 次胸/腹/盆腔 CT 增强检查，共 3~5 年[25]（1b 类证据，A 级推荐），以后每 1~2 年 1 次。对于超声或 CT 影像高度怀疑肝转移瘤但不能确诊的患者应加行肝脏 MRI 等检查，并建议在随访过程中保持影像检查方法的一致性。PET/CT 检查不作常规推荐。(3) 术后 1 年内应进行电子结肠镜的检查，若发现异常，需在 1 年内复查[26]；如无异常则推荐术后第 3 年复查，以后每 5 年 1 次。如果患者发病年龄<50 岁或确诊 Lynch 综合征则应适当增加电子结肠镜的检查频率。对于结直肠癌原发灶切除术前因梗阻等原因未完成全结肠镜检查的患者，应在术后 3~6 个月内完成首次电子结肠镜检查[26]（1a 类证据，A 级推荐）。

1.4　结直肠癌肝转移灶达到 NED 后的随访

结直肠癌肝转移灶达到 NED 后，对患者也应进行密切的随访，了解有无肝转移复发或出现其他远处转移的可能。(1) 建议术后 2 年内每 3 个月随访血清 CEA、CA19-9 和其他适当的肿瘤标志物，以后第 3~5 年内每 6 个月随访 1 次（1a 类证据，A 级推荐），5 年后每年 1 次。(2) 术后 2 年内每 3 个月进行 1 次腹/盆腔 CT 增强检查或肝脏 MRI 增强检查，必要时肝脏细胞特异性造影剂增强 MRI 检查。以后每 6~12 个月进行 1 次，共 5 年[25]（1a 类证据，A 级推荐），5 年后每年 1 次。不推荐常规 PET/CT 或 PET/MRI 检查。(3) 其他随访内容和频次参照结直肠癌原发灶根治术后的随访进行。

1.5　结直肠癌及其肝转移的相关基因检测

1.5.1　错配修复基因（MMR）/微卫星不稳定性（MSI）检测　推荐结直肠癌患者均进行检测[27-30]（1a 类证据，A 级推荐），以便更精准地制定治疗策略，尤其是对免疫检查点抑制剂的应用至关重要。采用 PCR+毛细管电泳法比较肿瘤组织与正常组织中微卫星序列长度的差异检测微卫星状态，是 MSI 检测的金标准[31-32]。免疫组化检测 MMR 的蛋白表达（包括 MLH1、MSH2、MSH6 和 PMS2），因简便快捷已成为目前最常用的检测方式，可达到与 PCR 检测 90%~95% 以上的一致率[33]。另外，经过验证合格的二代测序法（next-generation sequencing，NGS）也可用于 MSI 检测。

1.5.2　RAS 检测　推荐所有结直肠癌肝转移的患者均进行 KRAS 第 2、3、4 外显子以及 NRAS 第 2、3、4 外显子的检测[34-36]。RAS 基因是否突变不仅具有预后意义[37-39]，更是预测抗 EGFR 治疗有效性的重要生物标志物[40-41]（1a 类证据，A 级推荐）。尤其强调具体突变位点的检测，如 KRAS G12C 或 G12D 等突变还有助于后线治疗对新型靶向药物的选择[42-43]。

1.5.3　BRAF 检测　推荐结直肠癌肝转移患者进行 $BRAF^{V600E}$ 突变检测[44-45]，作为预后的评估指标[46-48]（1b 类证据，A 级推荐）以及疗效预测因子，以指导治疗方案选择。

1.5.4　HER2 检测　在标准治疗失败的转移性结直肠癌患者中抗 HER2 治疗逐渐受到重视，建议转移性结直肠癌患者进行 HER2 检测[49]，为晚期患者后线治疗的临床决策提供依据（2b 类证据，B 级推荐）。另外，HER2 过表达或扩增提示患者可能对抗 EGFR 单抗治疗反应不佳。

1.5.5　其他　NGS 检测肿瘤突变负荷[50]、DNA 聚合酶 epsilon 和 delta 1（POLE/POLD1）[51]、神经营养因子受体酪氨酸激酶（NTRK）融合基因[52]、转染原癌基因（RET）重排、间质表皮转化因子（c-Met）等，均可作为潜在的预测免疫检查点抑制剂治疗或靶向药物治疗疗效的生物标志物[53-54]。结直肠癌原发灶和肝转移灶的基因状态大多无差别[55-57]，对于无法获取肿瘤组织进行检测时可考虑液态活检技术[58]（2b 类证据，B 级推荐）。有研究发现基于循环肿瘤 DNA（ctDNA）指导的微小残留病灶（minimum residual disease，MRD）评估可有效提示结直肠癌患者接受治疗后的治愈情况，因此 MRD 有助于判断预后和制定下一步治疗策略，目前还在不断完善中，仍需要更多循证医学证据[53,59-60]。

2 结直肠癌肝转移的预防

2.1 结直肠癌原发灶根治性切除术

根治性手术切除结直肠癌病灶是迄今为止结直肠癌最有效的治愈方法，也是预防肝转移发生的重要环节。(1) 结肠癌根治性手术范围包括肿瘤全部及其两端足够肠段和周围可能被浸润的组织和器官以及相关系膜、主要供应血管和淋巴引流区，具体手术方式依照肿瘤部位不同而异，但均应遵循完整结肠系膜切除（complete mesocolic excision，CME）原则。(2) 直肠癌根治性手术范围应包括肿瘤全部及其两端足够肠段、周围可能被浸润的组织和器官以及相关的肠系膜和淋巴结。直肠中下段的肿瘤应遵循全直肠系膜切除（total mesorectal excision，TME）原则。(3) 术中发现存在切除范围外的可疑转移淋巴结，应进行术中活检或切除。

2.2 结直肠癌确诊时无肝转移(及其他远处转移)的新辅助治疗

术前通过新辅助治疗控制未被影像学检测到的微小转移灶，可以最大程度地减少根治性手术后的远处转移[61]。

2.2.1 中低位直肠癌的新辅助治疗(注:高位直肠癌，即肿瘤下缘距肛缘10 cm以上者,其新辅助治疗参照结肠癌)

(1) 对于dMMR/MSI-H患者，现有研究[62-64]表明：免疫检查点抑制剂治疗后效果较好，大多可以免除手术或/和放化疗，仅需观察等待。目前数据显示短期结果理想，长期结果有待观察。(2) 对于pMMR/MSS/MSI-L患者，术前诊断为T3期及以上或任何T、淋巴结阳性的直肠癌，在不伴有明显出血、梗阻症状、无穿孔以及其他远处转移等情况时，应用放化疗或放疗或化疗[65-66]。另外，已有多项研究[67-69]发现，新辅助放化疗或放疗联合/序贯免疫检查点抑制剂治疗，可获得更好的病理客观缓解，且安全性不受影响。局部进展期直肠癌还可实施全程新辅助治疗（total neoadjuvant treatment，TNT）[70]，将直肠癌术后辅助化疗也提至术前应用，即术前进行新辅助化疗和同步放化疗，可获得更高的完全缓解率，有助于器官保留，还可以降低远处转移发生，改善长期生存[71-74]（1a类证据，A级推荐）。(3) 肝动脉和肿瘤区域动脉联合灌注化疗，对于术前分期III期，且不伴有出血、梗阻症状或无穿孔的患者，在有条件的单位可考虑应用。5-氟尿嘧啶（5-FU）（或其前体药物）并可联合奥沙利铂，经肝动脉、肿瘤区域动脉分别灌注，化疗后7~10 d施行根治性切除术。目前的临床研究表明该方案虽不能明显降期，但对III期结直肠癌患者有预防肝转移的作用[75]，建议在有条件的单位开展，不作为常规推荐。

2.2.2 结肠癌的新辅助治疗

pMMR/MSS/MSI-L的结肠癌的新辅助治疗尚无明确的循证医学证据，对于术前判断为III期的患者可考虑肝动脉和肿瘤区域动脉联合灌注化疗，以减少肝转移的发生[75]，不作为常规推荐。有研究发现，dMMR/MSI-H的结肠癌患者，应用免疫检查点抑制剂新辅助治疗可获得较为理想的病理客观缓解，从而改善生存。

2.3 无转移结直肠癌患者术中门静脉化疗、腹腔化疗

对于该治疗方案的探讨目前有了一些令人鼓舞的数据[76]，如能联合术后辅助化疗，将可以减少肝转移的发生。但这一结果仍需进一步临床研究证实，故不作为常规手段推荐，临床研究可关注。

2.4 无转移结直肠癌患者根治术后的辅助治疗

对于III期结肠癌，术后辅助化疗能延长5年无病生存率及总生存率[77]。因此，III期结肠癌患者在手术治疗后应进行3~6个月的辅助化疗，可选择的治疗方案有：FOLFOX、CapeOX、5-FU/LV或卡培他滨单药（1a类证据，A级推荐）。

pMMR/MSS/MSI-L的II期患者如不存在复发转移高危因素（T4、组织分化差、肿瘤周围淋巴管神经侵犯、肠梗阻或T3伴有局部穿孔、切缘不确定或阳性、淋巴结活检数量少于12枚），术后两药联合的辅助化疗在许多临床研究中获益不显著，故建议接受临床观察和随访[78]（1b类证据，A级推荐），或建议5-FU单药治疗。但对于高危II期患者应予以辅助化疗，方案参照III期患者[79-80]（2a类证据，B级推荐）。

dMMR/MSI-H的II期患者无论是否存在高危因素均可接受临床观察和随访，但T4患者是否需辅助化疗目前尚有争议[81]。dMMR/MSI-H的II/III期患者，术后是否使用免疫检查点抑制剂作为辅助治疗仍存在争议。

T3及以上和任何T、淋巴结阳性的中低位直肠癌患者如术前没有进行放化疗，术后辅助化疗或放化疗能提高3年无病生存率及降低局部复发

率[82]，但对于能否减少直肠癌肝转移方面研究有限，和辅助治疗的结合方式也需更多临床试验验证。术前接受过放疗或联合放化疗的患者，术后也应接受辅助治疗，但尚无充分的循证医学证据。

总而言之，结直肠癌肝转移最有效的预防方式就是规范化治疗结直肠癌。

3　MDT 在结直肠癌肝转移诊治中的作用

对于肿瘤性疾病，MDT 治疗模式是有效的手段[83]，因此建议结直肠癌肝转移的患者均进入 MDT 治疗模式[84–85]（1a 类证据，A 级推荐）。结直肠癌的 MDT 以患者为中心，成员应包括结直肠外科/胃肠外科、肝脏外科、肿瘤内科、放疗科、放射介入科、放射和超声影像科、病理科及其他相关专业有一定资质的医生[86]。MDT 治疗模式可以减少个体医生做出的不完善决策[87]，其重要作用还包括：(1) 更精准的基因分子分型；(2) 更精确的疾病分期；(3) 减少治疗混乱和延误；(4) 更个性化的评估体系和治疗；(5) 更好的治疗衔接；(6) 更高的生活质量；(7) 最佳的临床和生存获益；(8) 最优的卫生经济学[88–89]。

MDT 根据患者的体力状况、年龄、器官功能、合并症和肿瘤的分子病理特征等进行评估，针对不同的治疗目标，给予患者最合理的检查和最恰当的综合治疗方案[90]（1a 类证据，A 级推荐）。

3.1　患者全身状况较差的处理

患者全身状况较差，不适合进行高强度治疗时，建议单药（或联合靶向药物）、减量的两药方案或最佳支持治疗，以提高生活质量并尽量延长生存时间。如全身情况好转，可以再进行高强度治疗。

3.2　适合高强度治疗患者的治疗策略

3.2.1　可切除肝转移灶　这类患者治疗目的是获得治愈[91]。应该围绕手术治疗进行相应的新辅助和/或辅助治疗，以降低手术后复发的风险。肝转移灶是否可以 R_0 切除的判断应由肝外科、肿瘤外科、影像科专家联合进行。肝转移灶可以 R_0 切除，但手术切除难度较大时也应积极联合其他肿瘤局部毁损手段（如射频消融或/和立体定向放疗等），以达到 NED 状态[92]。

3.2.2　初始不可切除但有望转化者　这类患者的治疗目的主要是最大程度地缩小瘤体或增加残肝体积，应采用最积极的综合治疗，即转化治疗。对于 dMMR/MSI-H 患者：排除禁忌证后，应首选免疫检查点抑制剂治疗，包括单药或两药治疗[93–95]。对于 pMMR/MSS/MSI-L 患者：(1) 结直肠癌确诊时合并无法达到 NED 的肝转移：① 结直肠癌原发灶存在出血、梗阻症状或穿孔时，应先行切除结直肠癌原发病灶，继而进行系统性化疗[或加用肝动脉灌注化疗（HAIC）]，并可联合应用分子靶向药物治疗（1b 类证据，A 级推荐）。治疗后每 6~8 周进行肝脏超声检查和 CT 增强检查并依据 RECIST 标准予以评估。临床重大决策时建议 MRI 增强检查。如果肝转移灶转变成可切除或有望 NED 时，适当时机予以手术治疗和/或其他肿瘤局部毁损手段；如果肝转移灶仍不能达到 NED，则继续进行综合治疗。② 结直肠癌原发灶无出血、梗阻症状及无穿孔时可以行系统性化疗（或加用 HAIC），并可联用分子靶向治疗（1c 类证据，B 级推荐）。每 6~8 周评估 1 次，如果转移灶转化成可切除或有望 NED 时，即手术治疗（一期同步切除或分阶段切除原发病灶和肝转移灶）或手术联合其他肿瘤局部毁损手段；如果肝转移灶仍不能达到 NED，则视具体情况手术切除结直肠癌原发病灶，术后继续对肝转移灶进行综合治疗。此类患者也可选择先行切除结直肠癌的原发病灶，继而进一步治疗，具体方案同上。③ 局部晚期直肠癌合并同时性肝转移，需兼顾直肠癌局部治疗和全身治疗，可长程同步放化疗序贯化疗或联合免疫检查点抑制剂治疗，也可短程放疗联合化疗或联合免疫检查点抑制剂治疗，现有研究结果更倾向于选择后者[96–97]。(2) 结直肠癌根治术后发生的无法达到 NED 的肝转移：① 采用 5-FU/LV（或卡培他滨）联合奥沙利铂或/和伊立替康的两药或三药方案作为一线化疗，并可加用分子靶向治疗，或联用 HAIC[98]（1b 类证据，A 级推荐）。对 5-FU 类药物不耐受的患者可考虑使用雷替曲塞（2b 类证据，B 级推荐）。② 在肝转移发生前 12 个月内使用过奥沙利铂为基础的化疗作为辅助治疗的患者，应采用 FOLFIRI 方案[99]；化疗结束后 12 个月以上发生肝转移，仍可采用 FOLFOX 或 CapeOX 化疗方案，并可加用分子靶向药物治疗，或联用 HAIC（3a 类证据，B 级推荐）。治疗后每 6~8 周检查肝脏超声、CT 增强检查予以评估，临床重大决策时建议 MRI 增强检查。肝转移灶转为可切除或可以达到 NED 的患者，即应接受肝转移

灶切除手术或手术联合其他肿瘤局部毁损手段，术后再予以辅助化疗；如果肝转移灶仍不能达到NED，则应继续进行综合治疗。

3.2.3 始终无法切除或达到NED者 这类患者以控制疾病进展为目的进行治疗，应该采用较为积极的联合治疗。对于结直肠癌原发灶无出血、梗阻症状及无穿孔时合并始终无法达到NED的肝转移灶的患者是否应该切除原发灶目前仍有争议[100-101]。因此，需要MDT综合考虑肿瘤和患者情况，进行个体化决策，是否切除原发灶。

总之，正如多项真实世界研究所证实，多次MDT评估不仅对全身治疗有反应的结直肠癌肝转移患者有价值，而且对最初认为永远无法手术切除的患者也有价值[100,102]。

4 结直肠癌肝转移灶的手术及其他毁损治疗

4.1 手术治疗

手术完全切除肝转移灶仍是目前能治愈结直肠癌肝转移的最佳方法[103-106]，故符合条件的患者均应在适当的时候接受手术治疗。部分最初肝转移灶无法切除的患者经治疗后转化为可切除病灶时也应适时接受手术治疗。

4.1.1 手术适应证和禁忌证 (1)适应证：是否适合手术切除的标准一直在演变，但主要应从以下三个方面来判断（2a类证据，B级推荐）：①结直肠癌原发灶能够或已经根治性切除；②根据肝脏解剖学基础和病灶范围，肝转移灶可完全（R_0）切除，且要求保留足够的功能性肝组织（肝脏残留容积≥30%~40%），采用三维CT、吲哚菁绿、3D数字成像技术等有助于评估残肝体积[107-109]；③患者全身状况允许，没有不可切除或毁损的肝外转移病变，或仅为肺部结节性病灶，但不影响肝转移灶切除决策。随着技术的进步，肝转移灶的大小、数目、部位等已不再是影响判断结直肠癌肝转移患者是否适宜手术的单一决定因素。另外，当前的文献资料已经将切缘不足1 cm[110]、可切除的肝门淋巴结转移[111-112]、可切除的肝外转移病灶（包括肺、腹腔）[113]等也纳入了适宜手术切除的范畴（4类证据，C级推荐）。(2)禁忌证[6,111,114]（3a类证据，B级推荐）：①结直肠癌原发灶不能取得根治性切除；②出现不适合局部处理的肝外转移；③预计术后残余肝脏容积不够；④患者全身状况不能耐受手术。

4.1.2 结直肠癌确诊时合并肝转移的手术治疗 (1)结直肠癌原发灶和肝转移灶一期同步切除：在结直肠癌原发灶切除难度较小、肝转移灶小且多位于周边或局限于半肝，肝切除量低于60%，肝门部淋巴结、腹腔或其他远处转移均可手术切除的患者可建议一期同步切除[115-116]。有研究认为一期同步切除肝转移灶和原发结直肠癌病灶手术的并发症发生率和死亡率可能高于二期分阶段手术[117-118]，故患者的选择上应较为慎重，尤其是需要在两切口下完成的同步手术。急诊手术由于缺少完备的术前检查资料和较高的感染发生机会，不推荐原发结直肠癌和肝脏转移病灶一期同步切除[119]（2c类证据，B级推荐）。(2)结直肠癌原发灶和肝转移灶二期分阶段切除：术前评估不能满足一期同步切除条件的患者，可以先手术切除结直肠癌原发病灶，二期分阶段切除肝转移灶，时机选择在结直肠癌根治术后4~6周；若在肝转移灶手术前进行系统性治疗，肝转移灶的切除可延至原发灶切除后3个月内进行。可根治的复发性结直肠癌伴有可切除肝转移灶的治疗按结直肠癌确诊时合并肝转移处理，但倾向于进行二期分阶段切除肝转移灶。不可切除的结直肠癌肝转移经转化治疗转化为可切除后，倾向于进行二期分阶段切除结直肠癌原发灶和肝转移灶[100]。先切除肝转移灶、再切除结直肠原发灶的“肝优先模式”（liver first approach）也已开展应用，其手术的并发症发生率、死亡率和5年生存率均与传统模式的二期分阶段切除相同[120-121]（3b类证据，B级推荐）。

4.1.3 结直肠癌根治术后发生肝转移的手术治疗 既往结直肠原发灶为根治性切除且不伴有原发灶复发，肝转移灶能完全切除且肝切除量低于70%（无肝硬化者），应予以手术切除肝转移灶，也可考虑先行新辅助治疗（3b类证据，B级推荐）。诊断结直肠癌根治术后发生肝转移应当有两项以上的影像学检查依据，包括肝脏超声或超声造影、CT及MRI增强等，必要时可结合PET/CT或PET/MRI检查以确定病变的范围和有无肝外转移，从而避免不必要的手术治疗[122]。

4.1.4 肝转移灶手术方式的选择(3b类证据,B级推荐) (1)肝转移灶切除后至少保留3根肝静脉中的1根且残肝容积≥40%（同时性肝切除）或≥30%（异时性肝切除）。转移灶的手术切除应符合R_0原

则，切缘至少>1 mm[123-124]。(2) 如是局限于左半或右半肝的较大肝转移灶且无肝硬化者，可行规则的半肝切除。(3) 肝转移手术时采用术中超声或超声造影检查，有助于发现术前影像学检查未能诊断的肝转移病灶。肝脏微创手术切除比例逐渐增多，显示出更好的短期结局。而且，使用人工智能影像进行肝脏手术精准规划应用也日益增多。(4) 应用门静脉选择性的栓塞（PVE）或结扎（PVL）可以使肝转移灶切除术后预期剩余肝脏代偿性增大，增加手术切除的可能。此方法被用于预计手术切除后剩余肝脏体积不足 30% 的肝转移患者。对于那些剩余肝脏体积在 30%~40%，并且接受了强烈化疗而有肝实质损伤的患者，同样也可从中得益[125]（4 类证据，C 级推荐）。联合肝脏离断和门静脉结扎的二步肝切除术（associating liver partition and portal vein ligation for staged hepatectomy，ALPPS）可使残留肝脏的体积在较短时间内明显增大而获得更多Ⅱ期肝切除的机会，但此手术复杂，并发症发生率及死亡率均高于传统肝切除，故建议在严格选择的患者中由经验丰富的肝脏外科医师实施手术[126]。放射性同时门静脉和肝静脉栓塞（radiological simultaneous portohepatic vein embolization，RASPE），又称肝静脉剥夺术[127]（liver venous deprivation，LVD），对比单纯门静脉栓塞和联合肝脏离断和 ALPPS[128]，不仅可使残余肝迅速增生，而且并发症发生率和死亡率低于 ALPPS[129]，具有操作简捷、创伤小、安全等优点，但仍需更多研究进一步评价，临床研究可关注。放射性微球选择性内放射治疗（selective internal radiotherapy，SIRT）是兼具控制肿瘤和增大残余肝体积的临床治疗手段。研究综述显示，钇-90 SIRT 用于单侧肝叶 SIRT 后 1~9 个月，对侧肝叶平均增大 29%~57%，肿瘤控制良好，有利于随后的肝转移切除手术[130-131]。(5) 对于经过肝切除、局部消融治疗、系统性化疗、介入治疗、分子靶向治疗、免疫检查点抑制剂治疗等多种方法的联合或序贯治疗仍无法达到 NED 但仍局限于肝转移的患者，如对全身化疗有反应，肝移植联合全身治疗，显著提高总体生存率，可酌情谨慎选择[132-134]。

4.1.5 肝转移灶切除术后复发和肝外转移灶的切除　在全身状况和肝脏条件允许的情况下，对于可切除的肝转移灶术后的复发病灶，经 MDT 讨论后，可再次选择手术切除或其他局部治疗，文献报道显示其手术并发症发生率和死亡率并不高于第 1 次肝转移灶的切除，而且可获得相同的术后生存率[102,135]（3b 类证据，B 级推荐）。同样，在患者全身状况允许时，如果肺[136]和腹腔[137]等的肝外转移病灶可完全切除，也应进行同步或分阶段切除（3b 类证据，B 级推荐）。

4.2 可以达到 NED 状态的肿瘤局部毁损治疗

除了手术切除肝转移灶外，有些治疗手段（如射频消融、微波消融和放射治疗）也能使病灶发生彻底毁损，所以对于手术切除难度较大的个别肝转移灶应积极联合此类手段，以使更多的患者有机会达到 NED 状态，提高 5 年生存率[138]。

射频消融高效破坏肝转移灶肿瘤细胞，使用方便，安全性好，具有创伤小、可重复等优势[139-141]。可作为肝病灶手术切除的重要补充，达到 NED 状态。建议应用时选择肝转移灶最大直径<3 cm 且 1 次消融最多 5 枚。但局部复发率偏高，不作为可切除病灶的首选推荐。也有研究表明，肝转移灶较小的患者，消融治疗和手术切除的长期生存相当。此外，对于一般情况不适宜或不愿意接受手术治疗的可切除结直肠癌肝转移患者也可以考虑射频消融治疗，但应注意避免肝外热损伤、针道转移、感染和消融不彻底等问题。

微波消融可处理直径<5 cm 的肝转移灶，也可处理贴近重要血管的肝转移灶[141]。快速高温消融使肿瘤周边微血管凝固，减少卫星灶残留风险，显著降低大病灶复发率。微波消融深部肝转移灶，也可作为手术切除主要肝转移灶的重要补充。

对于转移灶数目≤3 个，肿瘤最大直径≤6 cm 的肝内转移灶，立体定向放射治疗（SBRT）可以取得较好的局部控制率。对于直径≤3 cm 的肝寡转移灶，SBRT 可取得媲美于射频消融的局部控制率；对于直径>3 cm 的肝转移灶，SBRT 疗效优于射频消融，是首选的非手术局部治疗手段[142-143]。

5 可达到 NED 状态结直肠癌肝转移的新辅助及辅助治疗

5.1 新辅助治疗

对可达到 NED 的结直肠癌肝转移患者可考虑进行新辅助治疗，主要基于以下几方面原因：(1) 新辅助化疗提供了“窗口期”，观察有无新的无法切除的转移灶的出现，减少没有必要的手术。(2) 新

辅助治疗可增加R_0手术的机会，增加术后残余肝脏的体积。(3) 新辅助化疗可作为评价化疗方案敏感性的依据，指导术后化疗方案的选择。(4) 新辅助化疗的疗效，可作为患者预后评估的一个指标。(5) 新辅助化疗结合辅助化疗，可能改善接受治愈性手术患者的预后。

新辅助治疗在应用时也应关注如下情况的发生：(1) 化疗可能会造成肝脏损伤：如与奥沙利铂治疗相关的肝窦阻塞综合征[144]；与伊立替康治疗相关的脂肪变性和脂肪性肝炎等[145]，这些损害均可能增加肝切除术后并发症的发生[146-147]。(2) 影像学检查消失的转移灶术中仍应积极探查[148-149]，例如术中超声造影等[150]，若病灶有残存，应积极切除；若病灶消失而无法精确定位者应慎重考虑是否切除[151-152]。(3) 转移灶进展致使无法达到NED。

5.1.1 结直肠癌确诊时合并肝转移的新辅助治疗

在原发灶无出血、梗阻症状或无穿孔时，除肝转移灶在技术上切除容易且不存在不良预后因素的患者[如临床危险评分（clinical risk score，CRS）<3]外，可考虑应用新辅助治疗[153-156]（2a类证据，B级推荐），尤其是肝转移灶体积较大、转移灶数量较多或存在原发灶淋巴结可疑转移的患者。对于dMMR/MSI-H的患者，免疫检查点抑制剂应作为首选的新辅助治疗[157]。对于pMMR/MSS/MSI-L的患者，系统性化疗的方案包括FOLFOX、FOLFIRI、CapeOX或FOLFOXIRI[157-159]，可否联合分子靶向治疗目前仍有争议，同时也可以考虑联合HAIC[160-163]。为减少化疗对肝脏手术的不利影响，新辅助化疗原则上不超过6个周期[79,164-166]（1a证据，A级推荐），一般建议2~3个月内完成并进行手术[167-168]。

5.1.2 结直肠癌根治术后发生的肝转移的新辅助治疗

对于dMMR/MSI-H的患者，免疫检查点抑制剂应作为首选的新辅助治疗。对于pMMR/MSS/MSI-L的原发灶切除术后未接受过化疗的患者，或者发现肝转移12个月前已完成化疗的患者，可采用新辅助治疗（方法同上），时间2~3个月[164,169]（2a证据，B级推荐）。而肝转移发现前12个月内接受过化疗的患者，一般认为新辅助化疗作用可能较为有限，宜直接切除肝转移灶，继而术后辅助治疗[170]（2a类证据，B级推荐）。也可考虑更换化疗方案进行新辅助化疗[149,162]，或术前联合HAIC。

5.2 肝转移灶切除术后的辅助治疗

建议肝转移灶完全切除的患者接受术后辅助化疗[171-172]，特别是没有进行过术前化疗及辅助化疗的患者，多数推荐手术前后的化疗时间总长不超过6个月（2c类证据，B级推荐）。对于术前接受过HAIC且有效的患者，术后也可考虑同时联合HAIC[173-176]。经过术前化疗（包括联合分子靶向药物）证实有效的方案，术后如无禁忌应该作为首选的辅助治疗方案。

6 无法达到NED状态结直肠癌肝转移的综合治疗

对于无法达到NED的结直肠癌肝转移的综合治疗包括系统性化疗和介入化疗、分子靶向治疗、免疫检查点抑制剂治疗以及针对肝脏病灶的局部治疗如消融治疗、无水酒精注射、放射治疗等，治疗方案的选择应基于对患者治疗前的精确评估。

部分初诊无法达到NED的肝转移患者，经过系统的综合治疗后，即转化治疗，可转为适宜手术切除[177-178]或达到NED。其术后5年生存率与初始肝转移灶手术切除的患者相似[179-180]，此类患者应当采取较为积极的诱导方案，应用有效的强烈化疗，并考虑联合HAIC及分子靶向药物治疗。

对于肝转移灶始终无法达到NED的患者，综合治疗也可明显延长中位生存期，控制疾病快速进展，明显改善生存质量[181-184]。因此，积极的综合治疗对于适合强烈治疗的晚期结直肠癌肝转移患者同样意义重大。

6.1 dMMR/MSI-H患者

相较于标准化疗±靶向治疗，一线应用免疫检查点抑制剂帕博利珠单抗等PD-1单抗或纳武利尤单抗PD-1单抗联合伊匹木单抗CTLA-4单抗免疫检查点抑制剂治疗可明显提高疾病控制率和转化切除率[185-186]，应作为首选。

多项研究[187-190]表明，单药或两药免疫检查点抑制剂治疗用于二线及三线治疗显示出令人鼓舞的效果。对于未使用过该类治疗的dMMR/MSI-H患者可以优先选择免疫检查点抑制剂。

6.2 pMMR/MSS/MSI-L患者

6.2.1 系统性化疗和HAIC

化疗开始前应充分评估患者的身体状况和肿瘤分期，事先规划好患者的后续治疗和预计有严重化疗毒性反应时剂量和

方案的调整。开始治疗时必须考虑患者的分类（详见“3 MDT 在结直肠癌肝转移诊治中的作用”节）、化疗的安全性以及将来手术或/和局部病灶毁损治疗的可能性。

⑴ 初始化疗：① 对于肝转移灶有潜在 NED 可能的患者进行转化治疗至关重要。转移灶出现的早期退缩（early tumor shrinkage，ETS）更是预后的重要指标之一[191-193]。5-FU/LV（或卡培他滨）联合奥沙利铂或/和伊立替康的化疗方案具有较高的转化切除率（1b 类证据，A 级推荐），应该作为首选的化疗方案。化疗联合分子靶向药物可以进一步提高转化率[194-195]（1b 类证据，A 级推荐）。现有的研究数据显示，化疗联合贝伐珠单抗有良好的疾病控制率和转化切除率[196]，而 RAS 野生型患者还可以采用化疗联合西妥昔单抗治疗[197-198]（1b 类证据，A 级推荐）。有数据[179,197,199]提示，对于 RAS 野生型的结直肠癌肝转移患者，抗 EGFR 治疗的疗效与肿瘤部位存在相关性。原发灶位于左半结肠（脾曲至直肠）肝转移患者使用抗 EGFR 单抗在客观缓解率和总生存上优于抗 VEGF 单抗，而原发灶位于右半结肠（回盲部至脾曲）肝转移患者，抗 EGFR 单抗在客观反应率上优于抗 VEGF 单抗，但总体生存不如抗 VEGF 单抗。以 FOLFOXIRI 为代表的三药化疗方案也有较高的切除转化率[200-202]，在分子靶向药物无法使用且综合患者年龄、体能状况及肝功能状态等因素均适宜的情况下应该作为首选，但该方案的不良反应较多，应予以关注。目前三药化疗方案联合贝伐珠单抗的研究有了较好的临床数据[202-205]，可在选择性的患者中谨慎地应用[182,201,204]（2b 类证据，B 级推荐）。还有研究发现三药化疗联合抗 EGFR 单抗比单纯三药化疗有更高的客观缓解率，能潜在提高 R_0 切除率，改善总体生存[199-200]（2b 类证据，B 级推荐）。也有研究发现三药化疗联合抗 EGFR 单抗，与两药化疗联合抗 EGFR 单抗，并没有显著改善客观缓解率，也没有提高转化切除率或长期生存，且相关毒性增加。BRAF 的状态是重要的预后指标，$BRAF^{V600E}$ 突变的结直肠癌肝转移患者大多预后较差，有数据提示对该类患者化疗联合抗 EGFR 治疗的获益比较有限[206]。因此对 $BRAF^{V600E}$ 突变的结直肠癌肝转移患者，初始治疗采用三药化疗联合抗 VEGF 单抗，或者 BRAF 抑制剂+抗 EGFR 单抗 ± MEK 抑制剂，或者 BRAF 抑制剂+伊立替康+抗 EGFR 单抗。② 对于肝转移灶始终无法达到 NED 的患者，5-FU/LV（或卡培他滨）联合奥沙利铂或伊立替康的化疗方案是首选，也可以联合分子靶向药物治疗[172,182,207]（2b 类证据，B 级推荐）。含奥沙利铂和伊立替康的三药化疗尽管有较高的反应率，但毒性也较大，是否应在此类患者中应用尚不明确。

⑵ 诱导化疗后病情缓解或稳定，但肝转移灶仍无法 R_0 切除：可考虑进入维持治疗（如采用毒性较低的 5-FU/LV 或卡培他滨单药，均可联合贝伐珠单抗）[208-212]或单独使用贝伐珠单抗[213]或暂停化疗，以降低持续高强度联合化疗的毒性反应[213-214]。

⑶ 初始化疗病情进展后的化疗选择：① FOLFOX（或 CapeOX）方案 ± 分子靶向治疗，如果病情进展后可以考虑改用 FOLFIRI（或 mXELIRI[215]）方案；FOLFIRI 方案 ± 分子靶向治疗，如果病情进展可考虑改用 FOLFOX（或 CapeOX）方案，仍可考虑与分子靶向药物的联合[216-218]；二线方案也可选用曲氟尿苷替匹嘧啶联合贝伐珠单抗。如果病情第二次进展，可以使用曲氟尿苷替匹嘧啶 ± 贝伐珠单抗[219-220]或瑞戈非尼[221]或呋喹替尼[222]或西妥昔单抗[223-224]（未用过此类药者，仅限 RAS 野生型）或最佳支持治疗[61]（2a 类证据，B 级推荐）。② 5-FU/LV 联合分子靶向治疗后如果病情进展，应改用 FOLFOX、FOLFIRI 或 CapeOX（均可联合分子靶向治疗），病情再次进展时推荐瑞戈非尼或呋喹替尼或曲氟尿苷替匹嘧啶 ± 贝伐珠单抗或进行最佳支持治疗[225]（3b 类证据，B 级推荐）。③ 对于三线失败后的治疗目前尚无标准方案。据文献报道联合抗 $BRAF^{V600E}$（既往未使用过该方案的伊立替康+抗 EGFR+BRAF 抑制剂，或抗 EGFR+BRAF 抑制剂 ± MEK 抑制剂）的治疗方案[44-45,226-228]、抗 HER2 治疗（HER2 阳性患者）[229-232]、KRAS G12C 抑制剂 + 西妥昔单抗（KRAS G12C 突变患者）都能起到一定作用，但考虑到上述药物的适应证和可及性问题，仅建议在临床研究中谨慎使用，不作常规推荐。

⑷ 肝转移为主的肿瘤负荷较大且药物治疗效果不明显的患者，或者难治性患者或者不能耐受系统治疗的患者：可在适当时机联合应用 HAIC、肝动脉化疗栓塞（TACE）、药物洗脱微球动脉化疗栓塞（DEB-TACE）、钇-90 SIRT 等，有助于延长疾病无进展时间和总体生存期[233-239]，但是单独应用这些治疗并不比全身化疗更具优势。

6.2.2 局部毁损治疗 对于无法手术切除的肝转移灶，应根据其位置、治疗目标、治疗相关并发症及患者自身情况，在系统性化疗基础上选择适当的局部毁损工具以加强局部病灶的控制，具体应由MDT进行决策并结合患者意愿。其他治疗方法包括无水酒精瘤内注射、局部放射性粒子植入和中医中药治疗等，仅可作为综合治疗的一部分，不推荐单独使用。

附录1 本指南采用的推荐级别

推荐分级	证据水平	证据
A	1a	RCT的系统综述
	1b	单项RCT(95% *CI*较窄)
	1c	全或无,必须满足以下要求: (1)传统方法治疗全部致残或治疗失败,新方法治疗后,有部分患者存活或治愈; (2)传统方法治疗许多患者死亡或治疗失败,新方法治疗后,无一死亡或治疗失败
B	2a	队列研究的系统综述
	2b	单项队列研究(包括质量较差的RCT)(如随访率<80%)
	2c	结局研究
	3a	病例对照研究的系统综述
	3b	单项病例对照研究
C	4	系列病例分析及质量较差的病例对照研究
D	5	没有分析评价的专家意见

附录2 诊疗流程

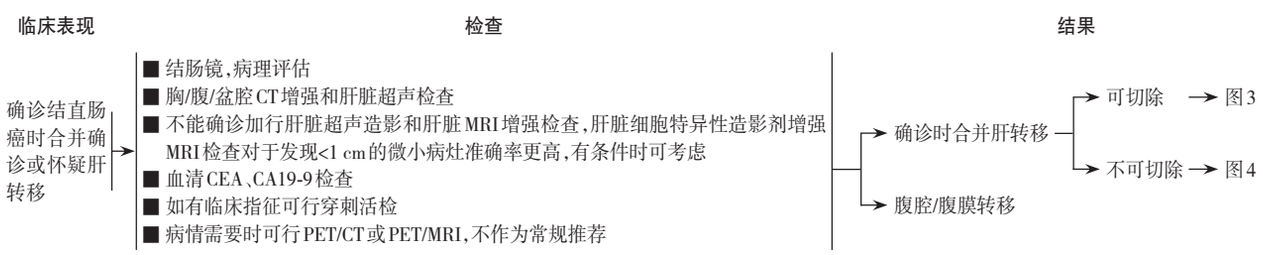

图1 结直肠癌确诊时肝转移的诊断

Figure 1 The diagnosis of liver metastasis at the time of colorectal cancer diagnosis

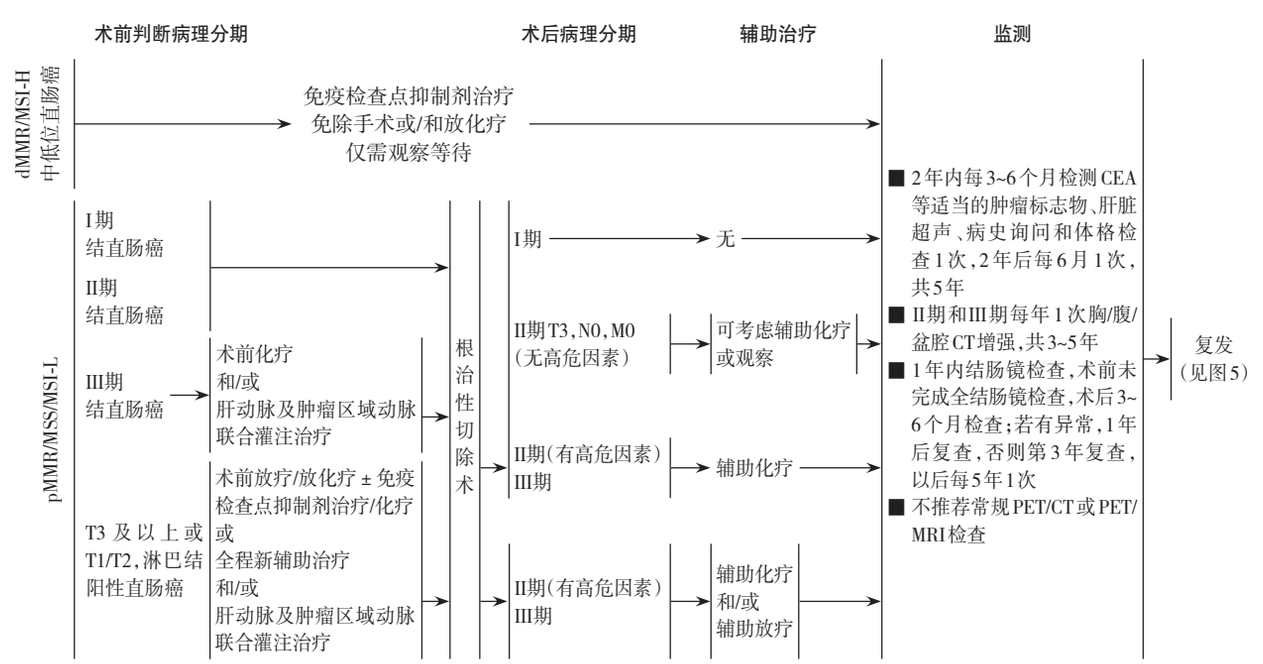

图2 结直肠癌肝转移的预防

Figure 2 Prevention of liver metastasis in colorectal cancer

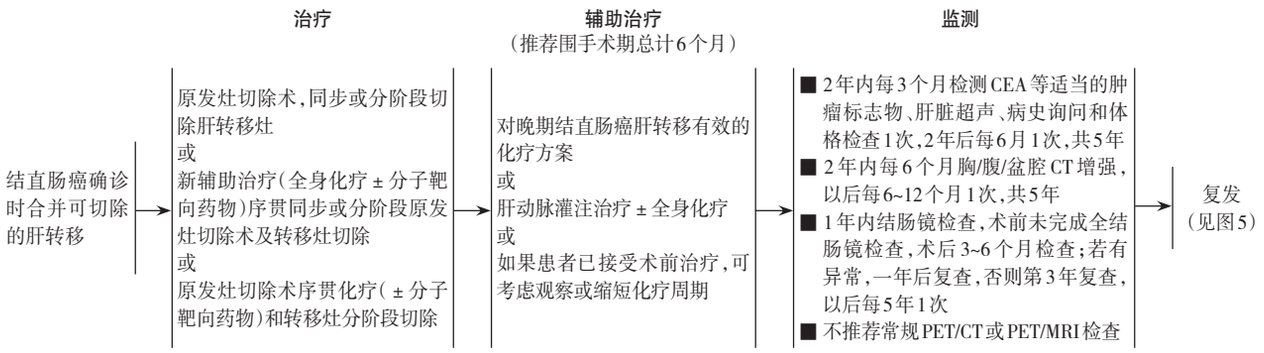

图3　结直肠癌确诊时合并可切除肝转移的治疗

Figure 3　The treatment of colorectal cancer with resectable liver metastases at the time of diagnosis

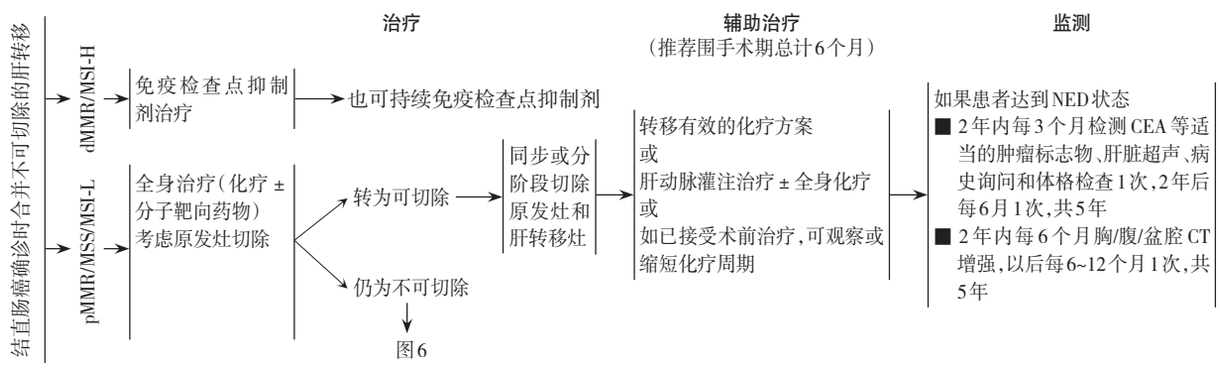

图4　结直肠癌确诊时合并不可切除肝转移的治疗

Figure 4　The treatment of colorectal cancer with unresectable liver metastasis at the time of diagnosis

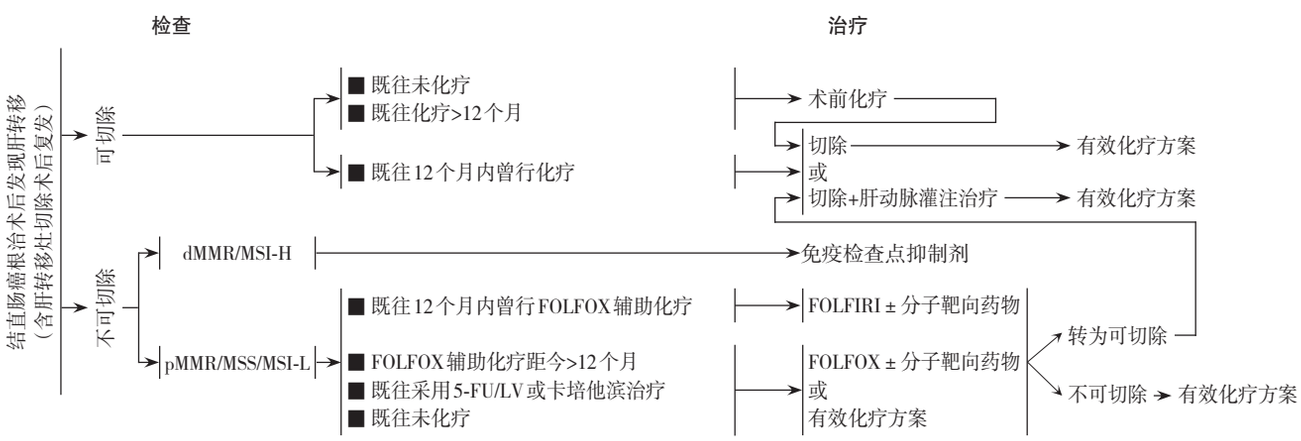

图5　结直肠癌根治术后发现肝转移的治疗

Figure 5　The treatment of liver metastasis after radical resection of colorectal cancer

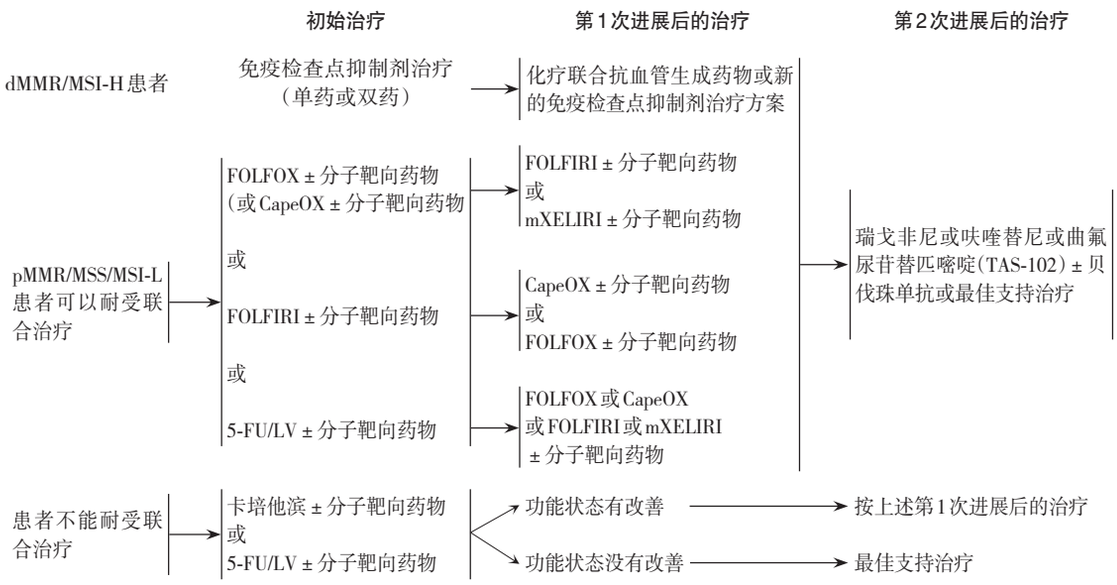

图 6　不可切除结直肠癌肝转移的治疗

Figure 6　Treatment of liver metastases from unresectable colorectal cancer

《结直肠癌肝转移诊断和综合治疗指南（2025 版）》修订专家名单（按姓氏拼音排序）

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