

胃癌肝转移诊断与综合治疗中国专家共识(2019版)

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【关键词】 胃癌;肝转移瘤;分型;多学科综合治疗

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肝脏是胃癌血行转移最常见的靶器官^[1]。胃癌肝转移的总体发生率约9.9%~18.7%^[2-3],其中同时性胃癌肝转移的比例约73.3%,异时性胃癌肝转移的比例约26.7%^[4]。胃癌根治术后发生肝脏转移的中位间隔时间约14个月,中位生存时间约11个月,5年存活率<20%^[5]。经原发灶、转移灶根治性切除的胃癌肝转移病人5年存活率可提高至23.8%^[6]。

胃癌异质性强、病情进展快,胃癌肝转移预后差,临床诊疗具有挑战性。现代治疗技术和诊疗理念的进展,为胃癌肝转移治疗提供了新的选择,并逐渐形成以多学科综合治疗协作组(multiple disciplinary treatment,MDT)为核心的治疗模式,但具体方案尚存诸多争议。为进一步提高我国胃癌肝转移的诊断和综合治疗水平,中国研究型医院学会消化道肿瘤专业委员会、中国医师协会外科医师分会上消化道外科医师委员会、中国抗癌协会胃癌专业委员会、中华医学会外科学分会胃肠外科学组组织国内相关领域专家进行讨论,制定本专家共识。

本文推荐度评定:高,≥90%;中,75%~<90%;低,50%~<75%。

1 胃癌肝转移病理学特征与诊断

胃癌肝转移灶病理学类型常与胃原发癌灶相同,以腺癌为主,其他少见类型还包括腺鳞癌、髓样癌、肝样腺癌、鳞状细胞癌以及未分化癌。Lauren分型进一步将腺癌分为弥漫型、肠型和混合型^[7]。影响胃癌肝转移预后的因素除胃癌原发灶特征外,肝转移灶的数量和大小也同样重要^[8]。根据肝转移灶出现时间的不同,可将胃癌肝转移分成两类:同时性胃癌肝转移(包括胃癌手术后6个月内出现肝转移灶)和异时性胃癌肝转移(胃癌手术后6个月以上出现肝转移灶)^[9]。

1.1 影像学检查 腹部增强MRI和超声造影是明确肝脏转移瘤的必要手段,肝细胞特异性造影剂在发现肝脏微小转移灶方面具有很高的敏感度^[10-14]。MRI可明确转移灶大小、数目、位置及周围毗邻关系,而术中肝脏超声或超声造影^[15]检查,还可发现术前影像学检查没有发现的转移灶。PET/CT能够显示病人的全身状况,提示肝外转移灶,在术前分期、术后复发与转移的评估方面具有重要意义^[16]。此外,肝转移灶18F-氟代脱氧葡萄糖(18F-FDG)代谢值的改变不仅可在化疗早期阶段(2周)区分有应答病例,还可作为判断病人预后的指标^[17]。

推荐意见:胃癌肝转移病人,如有条件,建议行PET/CT检查,以明确全身是否有扩散转移,使临床分期更加精准。

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1.2 诊断性腹腔镜探查 对于胃癌肝转移病人,诊断性腹腔镜探查联合腹腔灌洗液细胞学检查有助于排除影像学或肉眼不可见的肝转移灶或腹膜播散种植转移^[18-19]。

推荐意见:拟行手术治疗的病人应常规行诊断性腹腔镜探查。

推荐度:高

1.3 病理学检查 对于疑似肝转移的胃癌病人,胃原发灶除常规诊断所需的病理形态学检查外,还应增做免疫组化、分子检测等必要项目,如HER2^[20]、PD1/PD-L1^[21]和MSI/MMR^[22]等。肝转移灶的经皮穿刺活检为诊断转移的金标准,但鉴于穿刺为有创检查,肝穿刺仅应用于病情需要的病人(如胃原发灶存在特殊类型癌、影像学无法确认的转移瘤等)。

1.4 血清学检查 胃癌肝转移病人术前血清肿瘤标记物癌胚抗原(CEA)、CA19-9、CA72-4、CA125、甲胎蛋白(AFP)升高提示复发率高和预后不良^[8,23-29]。胃癌根治术后淋巴细胞单核细胞比值降低与肝转移的发生密切相关,也提示有较高的复发可能^[30]。部分复发的病人血清肿瘤

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标记物指标升高先于影像学诊断2~3个月^[31]。

2 胃癌肝转移临床分型

在严格筛选病人群体前提下^[9, 32-35],切除原发灶和转移灶可将胃癌肝转移病人5年总体存活率提高至20%以上^[6, 8, 36-38]。而现有的胃癌肝转移分型系统,如同时性/异时性分类、日本《胃癌治疗指南》H分型系统,对治疗指导价值有限。因此,综合现有研究^[3, 4, 6, 8, 10, 32-33, 36-66]和专家推荐意见,以原发灶及转移灶的可切除性为基础,本共识提出一种新的胃癌肝转移临床分型体系:C-GCLM分型(Chinese Type for Gastric Cancer Liver Metastasis),以利于临床制定诊疗决策(图1,表1)。

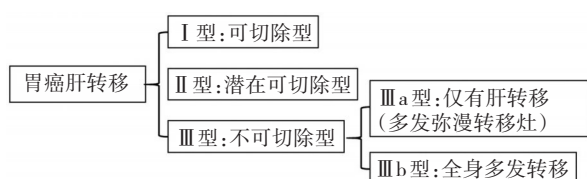


图1 胃癌肝转移临床分型

3 MDT在胃癌肝转移中的价值

MDT模式需贯穿胃癌肝转移病人的诊疗全程^[14, 70]。由MDT专家团队讨论病人的诊断、临床分型、治疗方案选择、疗效评估及随访流程,制定个体化方案^[71]。

(1)对于原发灶和转移灶均可R0切除者,可选择同期切除原发灶和转移灶,根据MDT评估结果决定围手术期系统治疗方案。

(2)对于原发灶或转移灶其一不可切除者,可行术前系统治疗并定期评估,如转化为原发灶、转移灶均可R0切除

者行手术治疗,其一不可切除则再次进入MDT治疗评估流程。

(3)对于原发灶和转移灶均无法切除者,建议行全身化疗为主的综合治疗,治疗期间定期MDT评估。

(4)对于病人一般状况差,不适合积极治疗者,采取最佳支持治疗。

(5)对于合并出血、穿孔、梗阻等情况的病人,根据病人全身情况,可行局部姑息性手术治疗。

(6)对于联合肝外转移等情况复杂的病人,根据MDT讨论结果制定具体计划。

4 胃癌肝转移初次诊疗流程图

胃癌肝转移初次诊疗流程图见图2。

5 不同临床分型胃癌肝转移综合治疗

胃癌肝转移的多学科综合治疗主要包括:系统治疗(全身化疗、靶向治疗和免疫治疗等)、手术切除、局部物理治疗和放射治疗等疗法。

5.1 I型(可切除型) 根据MDT的综合评估,胃原发灶和肝转移灶均可手术切除,可选择直接手术切除或术前系统治疗。术前系统治疗建议联合化疗,HER2阳性者联合靶向治疗^[72],具体方案选择参照相关指南。胃原发灶手术切除标准:胃癌根治术+D2淋巴结清扫。肝转移灶手术切除标准:R0切除。肝转移灶切除范围:(1)局部肝切除术。(2)肝区、段切除术。(3)半肝切除术。(4)联合肝区、段切除术。手术技术方法:开腹、腹腔镜或机器人手术。射频消融(RFA)是继手术切除之后对肝脏转移灶又一有效毁损方法,可辅助手术治疗^[41, 53],也可单独使用^[42, 73-74]。术后推荐完成4~8周期系统治疗,2~3个月进行一次评估。

推荐意见:C-GCLM I型病人行术前系统治疗。

推荐度:高

表1 胃癌肝转移C-GCLM分型

I 型	胃原发灶:浸润深度≤T4a;淋巴结转移D2清扫范围内(不包括 Bulky N2) Bulky N2—肝总动脉、腹腔干、脾动脉周围单个淋巴结直径≥3 cm(可以是融合成团的淋巴结)或≥3枚连续的淋巴结直径≥1.5 cm ^[67-68] 肝转移灶:肝脏转移灶1~3枚,最大病灶直径≤4 cm(或病灶局限于肝脏一叶内),不累及重要血管和胆管 具体情况判断: (1)经肝胆外科专科医师评估转移灶技术上是否可切除 (2)经肝脏储备功能评估是否可耐受肝切除手术
II 型	胃原发灶:胃原发灶浸润深度T4b,或 Bulky N2,或局限的 No.16a2、b1淋巴结肿大 肝转移灶:数量与大小超出 I 型范围,但从外科技术上仍具切除可能性
III 型	胃原发灶: (1)肿瘤外侵严重,与周围正常组织无法分离或包裹重要血管(包括脾动脉) (2)区域淋巴结转移固定、融合成团,或转移淋巴结不在手术可清扫范围内,如肿瘤浸润肠系膜根部或累及腹主动脉旁淋巴结(影像学高度怀疑或活检证实) ^[69] 转移灶: III a 型:弥散型肝转移灶,不伴肝外转移 III b 型:肝转移同时合并一个或多个肝外器官转移,伴或不伴腹膜转移

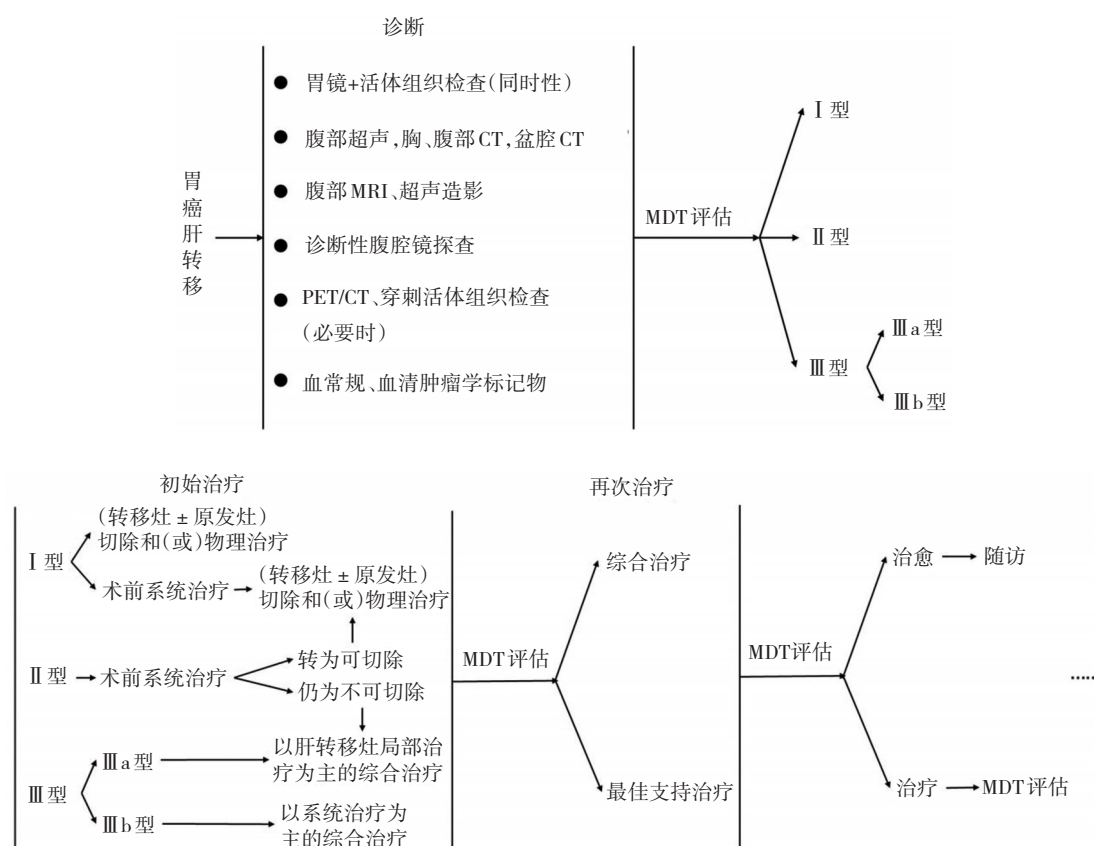


图2 胃癌肝转移初次诊疗流程图

5.2 II型(潜在可切除型) 术前系统治疗也应争取应用联合化疗方案配合靶向治疗,以争取手术机会。另外,肝脏局部化疗方式[肝动脉化疗栓塞术(TACE)^[5,42,75-77]和肝动脉灌注化疗(HAIC)^[78-80]]在提高肝脏局部药物浓度的同时不增加全身毒副反应,可用于术前系统治疗,也可用于术后防止肝内复发。三维适形放射(3D-CRT)治疗可联合化疗应用于胃癌肝转移病人的术前辅助治疗^[18]。立体定向放射治疗(SBRT)和调强放射治疗(IMRT)技术,可处理一些位置特殊(如肝门区、包绕大血管)的转移灶,尤其适用于最大直径<5 cm的寡转移灶。对于一般情况不适宜或拒绝手术的异时性肝转移和(或)肝内复发者,RFA可多次反复使用^[81-83]。微波消融^[84]、经皮冷冻消融术^[85]、质子射线治疗^[86]、钇90玻璃微球^[87]等局部物理疗法也逐步应用到胃癌肝转移的治疗中,并取得了初步成果。局部物理疗法适用于最大直径<3 cm的转移灶,建议单次最多消融5枚。

推荐意见:C-GCLM II型胃癌肝转移病人只有在具备“R0”切除可能时才推荐手术治疗。

推荐度:高

5.3 III型(不可切除型) 对于一般情况较好能够耐受化疗的病人,包含靶向药物在内的系统治疗仍是首选方案。免疫治疗亦有重要作用^[88],包括免疫检查点抑制剂PD-1/PD-L1抗体^[89-90]、嵌合抗原受体T细胞、热休克蛋白gp96等具体疗法。另外,联合TACE或HAIC还可作为一线、二线化疗方案失败病人的补充治疗。部分III型病人可从放射治疗中获益。当出现穿孔、梗阻、出血等并发症时,可行姑息手术以缓解症状。对于肿瘤所致的狭窄、持续性出血,能够安全地施行胃切除时行姑息性胃切除;但存在困难或危险时应行胃空肠吻合等短路手术。

推荐意见:C-GCLM III型病人出现并发症时应即时行手术治疗,除此之外,不建议行减瘤手术,鼓励病人在MDT指导下参加免疫治疗临床试验。

推荐度:高

6 胃癌肝转移随访

随访检查项目及间隔时间见表2。

表2 胃癌肝转移随访检查项目及间隔时间

检查项目	间隔时间
病史、体格检查、营养状况评估、血常规、血生化、肿瘤标记物、腹部超声	1、3、6、9、12、15、18、21、24、30、36、42、48、54、60个月;5年后每年1次
胸、腹部、盆腔增强CT	6、12、18、24、36、48、60个月;5年后必要时
腹部增强MRI、PET/CT、胃镜	重大临床决策时;必要时

《胃癌肝转移诊断与综合治疗中国专家共识(2019版)》编写委员会

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《中国实用外科杂志》2019年第6期重点内容介绍

本期重点选题:腹腔感染

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复杂腹腔感染的外科阶梯治疗(李幼生,黎介寿)

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