

• 专题研究:肿瘤 •

靶向联合免疫方案结合或不结合TACE/放疗在中晚期肝细胞癌转化治疗中的应用

兰 欣, 韩国勇, 吴金道*

南京医科大学第一附属医院肝胆中心, 江苏 南京 210029

[摘要] 目的: 评估靶向联合免疫方案结合或不结合经导管动脉化疗栓塞术(transcatheter arterial chemoembolization, TACE)/放疗对初始不可切除中晚期肝细胞癌(hepatocellular carcinoma, HCC)的有效性及安全性。方法: 回顾性分析20例巴塞罗那临床肝癌(Barcelona clinic liver cancer, BCLC)分期B/C期HCC患者资料, 所有患者均接受靶向联合免疫治疗。19例联合TACE, 其中4例加用放疗。评价指标包括客观缓解率(objective response rate, ORR)、显微镜下切缘阴性(microscopic margin-negative, R0)率及安全性。结果: 总体ORR为55%, 疾病控制率为85%。4例(20%)成功实施R0切除, 术后病理显示2例达到主要病理缓解。3级不良事件发生率为20%, 多为免疫相关性肝损伤, 安全性可控。全组中位随访18.3个月。4例手术患者中, 3例在术后12个月无复发生存。结论: 以靶向联合免疫为核心的多模式方案对中晚期HCC具有显著的降期能力, R0切除率达20%, 病理缓解显著且安全性可控。

[关键词] 肝细胞癌; 转化治疗; 靶向联合免疫; 经导管动脉化疗栓塞术; 放疗

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Application of targeted immunotherapy combined with or without TACE/radiotherapy in the conversion therapy for intermediate-to- advanced hepatocellular carcinoma

LAN Xin, HAN Guoyong, WU Jindao*

Hepatobiliary Center, the First Affiliated Hospital of Nanjing Medical University, Nanjing 210029, China

[Abstract] **Objective:** To evaluate the efficacy and safety of targeted therapy plus immunotherapy $\pm$ transcatheter arterial chemoembolization (TACE)/radiotherapy for conversion therapy in initially unresectable intermediate - to - advanced hepatocellular carcinoma(HCC). **Methods:** We retrospectively analyzed 20 patients with Barcelona clinic liver cancer(BCLC) stage B/C HCC treated with targeted therapy and immunotherapy; 19 received concurrent TACE, and 4 received radiotherapy among them. The evaluation indicators include objective response rate (ORR), microscopic margin-negative (R0) resection rate and safety. **Results:** The overall ORR and the disease control rate were 55% and 85%, respectively. Four patients (20%) successfully underwent R0 resection, with 2 achieving major pathological response. The incidence of grade ≥ 3 adverse events was 20%, primarily immune-related liver injury. At a median follow-up of 18.3 months, 3 of the 4 resected patients remained recurrence-free 12 months post-surgery. **Conclusion:** The multimodal approach centered on targeted combined immunotherapy has a significant ability to downstage advanced HCC. The R0 resection rate is 20%, and the pathological remission is remarkable with controllable safety.

[Key words] hepatocellular carcinoma; conversion therapy; targeted therapy combined with immunotherapy; transcatheter arterial chemoembolization; radiotherapy

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*通信作者(Corresponding author), E-mail: wujindao@njmu.edu.cn(ORCID: 0000-0002-2317-6565)

肝细胞癌(hepatocellular carcinoma, HCC)是我国最常见的恶性肿瘤之一,多数患者初诊时已处于中晚期^[1-3]。常伴有大血管侵犯或肝外转移,大多失去根治性手术机会^[4]。对于这部分初始不可切除的患者,传统姑息治疗生存获益有限^[5]。

“转化治疗”通过抗肿瘤干预促使肿瘤降期、癌栓退缩,将“不可切除肿瘤”转化为“可切除肿瘤”^[6]。经导管动脉化疗栓塞术(transcatheter arterial chemoembolization, TACE)曾是降期治疗的主要手段,但单一TACE转化率不理想^[7]。对于合并门静脉主干/分支癌栓或下腔静脉癌栓的患者,放疗具有较好的局部控制作用,可促使癌栓退缩、降低复发风险^[8-9]。因此,寻找TACE、放疗与全身治疗相联合的更高效方案成为必然趋势。

靶向与免疫治疗的进展为中晚期HCC系统治疗带来突破^[10-11]。多靶点酪氨酸激酶抑制剂(tyrosine kinase inhibitor, TKI)联合程序性死亡受体-1(programmed cell death 1, PD-1)/程序性死亡配体-1(programmed cell death ligand 1, PD-L1)单抗在中晚期HCC中展现出较高客观缓解率(objective response rate, ORR),成为降期治疗的理想选择^[12]。在此基础上,联合TACE或放疗等局部治疗可进一步协同增效^[13-14]。然而,该方案作为术前降期治疗的临床证据尚处积累阶段。尤其是联合TACE及放疗的多模式转化方案,其显微镜下切缘阴性(microscopic margin-negative, R0)率、术后病理缓解程度及远期生存获益仍需更多数据证实^[15]。目前临床依赖改良版实体瘤疗效评价标准(modified response evaluation criteria in solid tumors, mRECIST)进行动态影像评估,但影像学缓解与术后病理缓解的一致性仍缺乏足够数据支持^[16]。

基于此,本研究作为一项初步的临床回顾性探索,分析了20例接受靶向联合免疫(±TACE/放疗)治疗的中晚期HCC患者资料,评估该方案的有效性与安全性,初步探讨mRECIST在指导手术决策中的价值。

1 对象和方法

1.1 对象

回顾性分析2023年9月—2024年9月于南京医科大学第一附属医院肝胆中心接受靶向联合免疫方案结合或不结合局部TACE/放疗转化治疗的中晚期HCC患者的临床资料。本研究经南京医科大学第一附属医院伦理委员会批准(审批号:2021-

SRFA-372),且对患者资料均进行了严格保密与去隐私化处理。

纳入标准:①增强计算机断层扫描(computed tomography, CT)/磁共振成像(magnetic resonance imaging, MRI)确诊HCC(影像不典型者以病理为准);②巴塞罗那临床肝癌(Barcelona clinic liver cancer, BCLC)B/C期;③经多学科协作(multidisciplinary team, MDT)评估无法R0切除,并符合以下任一情况[门静脉主干/分支或下腔静脉癌栓,肝内病灶≥3个或分布超半肝,肝外转移,剩余肝体积不足(正常肝<30%,肝硬化<40%),Child-Pugh A/B级≤7分];④东部肿瘤协作组(Eastern Cooperative Oncology Group, ECOG)体能状态评分0~1分;⑤至少1个mRECIST可测量靶病灶(强化灶≥1.0 cm);⑥连续接受≥2个周期术前治疗;⑦资料完整。排除标准:①既往系统治疗史;②其他恶性肿瘤史(治愈<5年);③长期应用激素或免疫抑制剂;④严重的重要器官功能障碍;⑤活动性感染、乙肝或艾滋阳性;⑥凝血异常或近期出血史;⑦妊娠或哺乳期。

按照预设的纳入标准对所有不可切除患者进行筛选,最终共20例患者成功入组并接受治疗。

1.2 方法

1.2.1 治疗方法

靶向药物:仑伐替尼(体重≥60 kg, 12 mg/d; <60 kg, 8 mg/d;口服)或多纳非尼(0.2 g/次,口服,每日2次)。免疫药物:信迪利单抗/卡瑞利珠单抗/替雷利珠单抗(在治疗周期的第1天通过静脉注射给药200 mg,每3周重复1次)。TACE:在靶免治疗中按需进行。基线肿瘤负荷极高者,可于治疗启动前1周内行首次TACE快速减瘤。后续TACE(间隔4~6周)依据评估决定,存在可治疗的活性强化灶则追加,否则继续靶向联合免疫治疗。放疗:针对合并门静脉主干/分支或下腔静脉癌栓的患者,联合放射治疗。每3周为1个周期,持续至达到可切除标准、疾病进展(progressive disease, PD)或出现不可耐受毒性。每2个周期(6周)行增强CT/MRI评估。末次治疗后4~6周,影像学评估达部分缓解(partial response, PR)且符合手术指征者。

1.2.2 影像学评估

所有患者于治疗前、每2个治疗周期后及术前1周内行上腹部增强CT或MRI。采用mRECIST标准,由两位医师独立评估。评估指标包括肿瘤数目、直径之和、癌栓分级及有无转移,肝脏储备功能即吲哚菁绿15 min滞留率(indocyanine green reten-

tion rate at 15 minutes, ICG-R15)及剩余肝体积。

1.2.3 治疗反应定义

依据 mRECIST 标准, 疗效判定如下: 完全缓解 (complete response, CR), 所有肝内靶病灶动脉期强化完全消失; PR, 靶病灶动脉期强化直径之和较基线减少 $\geq 30\%$; PD, 靶病灶动脉期强化直径之和较研究中的最小值增加 $\geq 20\%$, 或新发病灶; 疾病稳定 (stable disease, SD), 介于 PR 与 PD 之间, 未达到 CR/PR 或 PD 标准。

在整个转化治疗期间, 最佳总缓解 (best overall response, BOR) 定义为自治疗开始至 PD 或因任何原因终止原方案前, 所记录到的最佳疗效评价结果。在此基础上, ORR 定义为基于 BOR 达到 CR 与 PR 的患者比例之和 [$ORR = (CR + PR) / \text{总例数} \times 100\%$]; 疾病控制率 (disease control rate, DCR) 定义为基于 BOR 达到 CR、PR 与 SD 的患者比例之和 [$DCR = (CR + PR + SD) / \text{总例数} \times 100\%$]。

1.2.4 手术及术后处理

转化成功后行 R0 切除需满足: 影像学达 PR/CR; 癌栓退缩至二级分支 (Vp1-Vp2) 或肝静脉分支水平; 未来剩余肝体积 (future liver remnant, FLR)/标准化肝体积 (standardized liver volume, SLV) $\geq 30\%$ (肝硬化 $\geq 40\%$); Child-Pugh A 级; 无手术禁忌证。对于基线伴有肝外寡转移如肺转移、淋巴结转移的患者, 需影像学证实肝外病灶已完全消失 (即 CR), 或可同期/分期行根治性切除 (如淋巴结清扫), 方可实施肝脏转化手术。

手术方式根据肿瘤位置及范围, 采用解剖性肝段/叶切除术或非解剖性局部切除术, 术中确保切缘阴性 (R0 切除)。

术后标本行常规病理检查, 评估指标包括: 肿瘤坏死率 [(坏死区面积/总面积) $\times 100\%$]; 切缘状态, R0 (镜下切缘无肿瘤细胞残留)、R1 (镜下切缘见肿瘤细胞); 淋巴结状态, 有无淋巴结转移及转移数目; 缓解情况, 病理学完全缓解 (pathological complete response, pCR) (肿瘤坏死率 100%), 主要病理缓解 (major pathological response, MPR) (肿瘤坏死率 $\geq 90\%$), 非主要病理缓解 (non-major pathological response, Non-MPR) (肿瘤坏死率 $< 90\%$)。

对于成功实施 R0 切除的患者, 待术后肝功能恢复良好且无严重并发症时, 常规继续采用原靶向联合免疫方案进行术后辅助治疗, 以期降低复发风险。

1.2.5 安全性及随访

依据不良事件通用术语标准 (Common Termi-

nology Criteria for Adverse Events, CTCAE) 5.0 版, 对治疗期间及术后随访期内发生的所有不良事件 (adverse event, AE) 进行分级记录。

术后每 3 个月复查 1 次, 复查项目包括上腹部增强 CT/MRI。肿瘤复发定义为影像学检查出现新发病灶或原有病灶较前增大。随访时间截至 2025 年 12 月 31 日。

1.3 统计学方法

采用 SPSS 26.0 统计学软件进行数据分析。由于本研究属于单中心、小样本的回顾性探索性研究, 样本规模不足以支撑多因素生存回归模型 (如 Cox 模型) 的建立, 故统计分析以描述性统计为主。不符合正态分布的连续变量以中位数 (四分位数) [$M(P_{25}, P_{75})$] 表示, 分类变量以频数 (百分比) [$n(\%)$] 表示。对于亚组极小样本 (如手术亚组 $n=4$) 仅描述其实际频数及事件节点。随访生存情况以实际发生事件进行描述性报告。

2 结果

2.1 基线资料

20 例患者基线资料见表 1。根据治疗反应和手术结局, 将 20 例患者分为 4 组: 成功转化手术的 PR 组、未手术的 PR 组、SD 组和 PD 组 (图 1)。所有疗效评价均基于 BOR。

2.2 新辅助治疗的影像学反应

2.2.1 总体疗效

分析 20 例患者总体治疗过程和靶病灶较基线的最佳变化百分比 (图 2)。其中无 CR 病例, PR 11 例 (55.0%), SD 6 例 (30.0%), PD 3 例 (15.0%)。ORR 为 55.0% (11/20), DCR 为 85.0% (17/20)。在接受治疗后, 靶病灶最大径的中位缩小比例为 33.85% (范围: -60.76%~28.21%)。11 例 PR 患者中, 靶病灶最大径平均缩小 41.45%; 3 例 PD 患者观察到靶病灶增大或出现新发病灶。

2.2.2 典型案例展示

成功转化手术的 PR 代表病例 (图 3): 治疗前基线 MRI 扫描, 提示肝脏巨大原发病灶合并腔静脉有癌栓 (红箭头示); 联合转化治疗后 MRI 复查, 可见原发肿瘤体积明显缩小, 且动脉期强化显著减弱 (黄箭头示), 腔静脉癌栓明显退缩。依据 mRECIST 标准评定为 PR, 患者随后成功实施 R0 切除术。

未手术的 PR 代表病例 (图 3): 治疗前基线增强 CT 扫描, 提示肝内肿瘤伴 (红箭头示) 明确的大血管

表1 20例中晚期HCC患者的基线临床病理资料

Table 1 Baseline clinical and pathological data of 20 patients with advanced HCC

Baseline characteristics	Cases[n(%)]
Age [n(%)]	
<60 years	11 (55.0)
≥60 years	9 (45.0)
Sex[n(%)]	
Male	16 (80.0)
Female	4 (20.0)
Cause of the disease[n(%)]	
Hepatitis B virus	16 (80.0)
Hepatitis C virus	2 (10.0)
Other/unknown	2 (10.0)
Child-Pugh classification[n(%)]	
Grade A (5–6 points)	16 (80.0)
Grade B (7 points)	4 (20.0)
Serum alpha-fetoprotein level[n(%)]	
≥400 ng/mL	11 (55.0)
<400 ng/mL	9 (45.0)
Maximum tumor diameter[cm, M(P ₂₅ , P ₇₅)]	8.45 (7.0, 11.1)
Number of tumors[n(%)]	
<3	8 (40.0)
≥3	12 (60.0)
Cancer emboli in the portal vein or vena cava[n(%)]	
No	16 (80.0)
Yes	4 (20.0)
Extrahepatic metastasis[n(%)]	
Lung metastasis	4 (20.0)
Lymph node metastasis	1 (5.0)
Initial reason for non-resectability[n(%)]	
Invasion of major blood vessels	4 (20.0)
Multiple and diffuse lesions in the liver(≥ 3)	12 (60.0)
Extrahepatic metastasis	5 (25.0)
Insufficient remaining liver volume	4 (20.0)
Treatment plan[n(%)]	
Targeted therapy+immunotherapy	1 (5.0)
Targeted therapy+immunotherapy+TACE	15 (75.0)
Targeted therapy+immunotherapy+TACE+radiotherapy	4 (20.0)
Number of treatment cycles[M(P ₂₅ , P ₇₅)]	5.5 (3.0, 9.0)

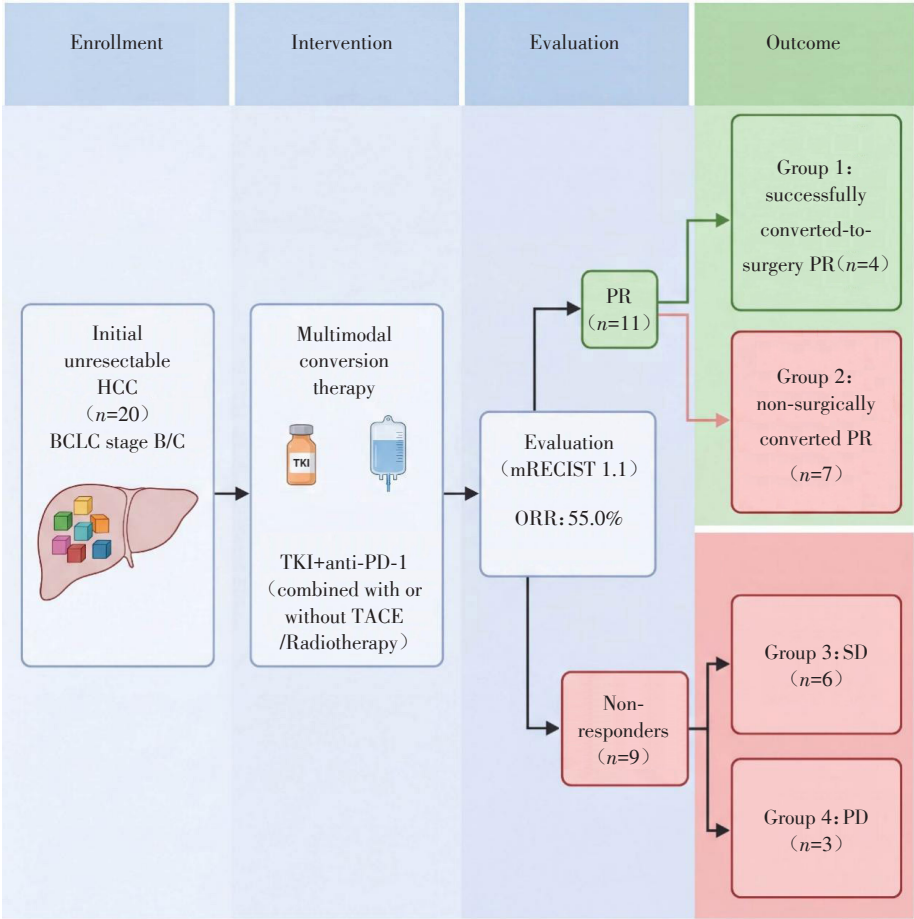
癌栓形成(蓝箭头示);联合转化治疗后CT复查,可见肝内病灶碘油(黄箭头示),且血管癌栓较前出现一定程度的退缩(紫箭头示)。依据mRECIST标准评定为PR但未达手术指针,患者继续维持原方案治疗。

PD代表病例(图3):治疗前基线CT扫描,提示肝脏巨大原发灶(红箭头示)及肺部寡转移灶(绿箭头示);联合治疗后CT复查,尽管肝内靶病灶可见密集

碘油沉积(黄箭头示),但胸部CT肺窗显示双肺出现多发新发转移结节(黑箭头示)。由于出现新发病灶,依据mRECIST标准评定为PD,患者终止术前转化治疗,改行二线方案。

2.3 R0切除情况

全组共有4例(20.0%)患者成功实现R0切除,其中包括3例靶向免疫治疗+TACE方案者及1例靶向免



A total of 20 patients were enrolled and treated with individualized combination regimens. Based on treatment response and surgical outcomes, they were classified into four groups.

图1 患者入组、治疗与结局流程图

Figure 1 Flowchart of patient enrollment, treatment, and outcomes

疫治疗+TACE+放疗方案者。该4例患者在术后均继续接受了原靶向联合免疫方案的辅助治疗(具体干预过程详见图2A)。

4例手术患者术前治疗中位周期数为4.5个(范围:4.0~6.0个),中位手术时间为确诊后4.8个月(范围:4.5~6.0个月)。4例手术患者的基线特征及治疗反应如表2所示。在最终接受手术切除的4例患者中,术后标本病理学评估显示:共2例(50.0%)患者达到了MPR,但均未达到pCR;其余2例(50.0%)患者为Non-MPR。

11例影像学PR患者中,7例未行手术;其中3例因肝储备功能下降或新发重度门静脉高压无法耐受(与TACE及靶向免疫治疗叠加损伤相关);2例因癌栓退缩不足无法R0切除;FLR不足及拒绝手术各1例。部分患者于确诊后7~8个月进展。SD及PD患者:6例SD患者中,5例于数月后进展(SD转PD),靶病灶径线变化-26.80%~8.33%。3例原发耐药患

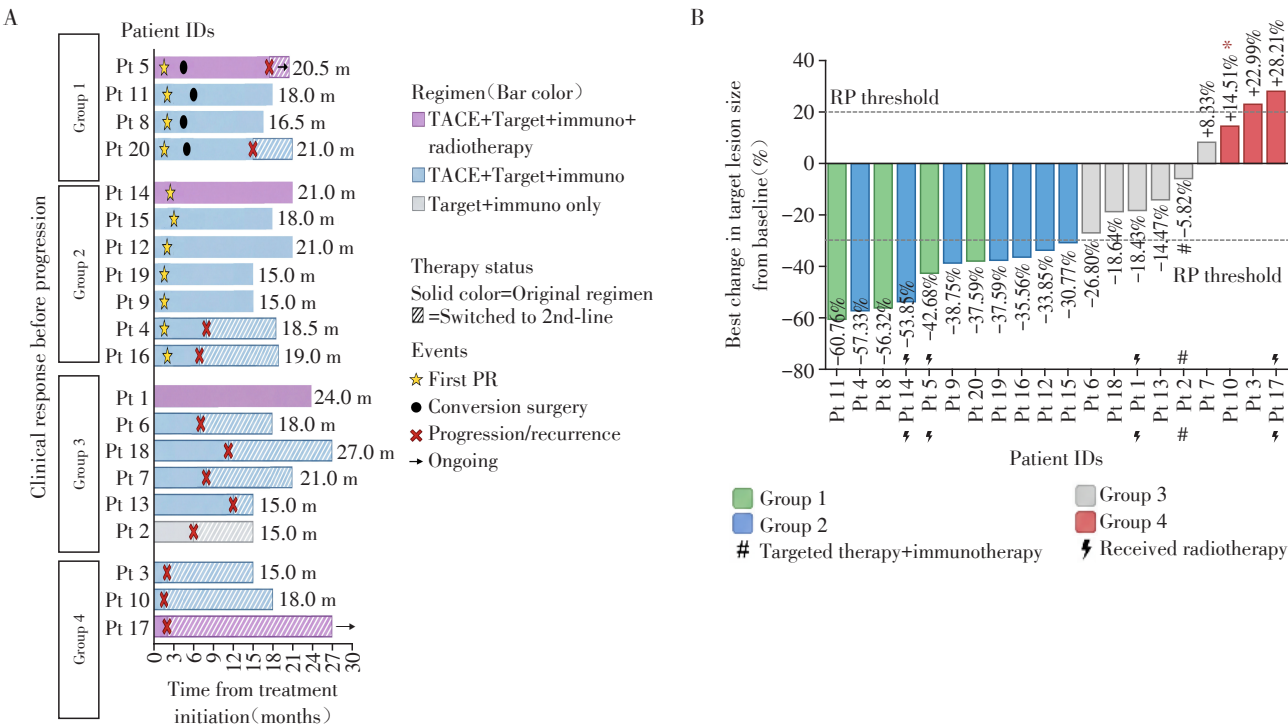
者于治疗6~8周内出现PD(其中1例伴肺转移),均改行二线治疗。

2.4 安全性评价

全组AE以1~2级为主。常见AE包括转氨酶升高(55.0%)、乏力(35.0%)、食欲减退(30.0%)、皮疹(20.0%)及高血压(15.0%)。3级及以上AE发生率为20.0%(4/20),主要为免疫相关性肝损伤(3例)、其中1例免疫相关性肝损伤患者合并严重高血压,另有1例重度腹泻,经对症处理或停药后缓解。手术患者无严重围手术期并发症,全组无治疗相关死亡或因AE失访者。

2.5 随访及生存情况

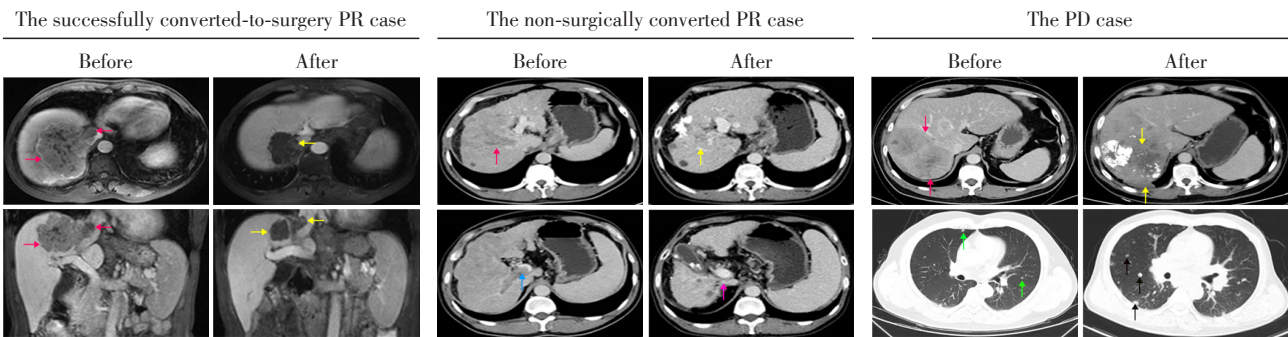
中位随访18.3个月(15.0~27.0个月),本组共12例(60.0%)发生PD或复发。4例手术患者中,有2例出现肿瘤复发(分别发生于确诊后15.0、17.5个月,即术后10.0、13.0个月)。截至术后12个月,共有3例(75%)患者保持无复发状态。



A: Swimmer plot: illustrating the complete clinical course from treatment initiation to last follow-up for each patient. The vertical axis is stratified by best response; bar colors represent the initial treatment regimen. Symbols ★, ●, and ✕ denote first partial response (PR), conversion surgery, and disease progression/recurrence, respectively; diagonal hatching indicates second-line therapy after PD. B: Waterfall plot: showing the best percentage change from baseline in target lesions. Dashed lines indicate the mRECIST thresholds for progressive disease (PD, +20%) and partial response (PR, -30%); colors distinguish clinical subgroups. The symbol ⚡ indicates radiotherapy, and # indicates targeted therapy+immunotherapy alone. The asterisk (*) indicates that patient 10 was classified as PD due to the new pulmonary metastatic lesion. Although target lesion size increased by only 14.51% (did not reach +20%), overall PD was confirmed due to the new pulmonary metastatic lesion. Except where noted, all patients were treated with TACE plus targeted therapy and immunotherapy. Group 1: successfully converted-to-surgery PR; Group 2: non-surgically converted PR; Group 3: SD; Group 4: PD.

图2 20例患者总体治疗过程与靶病灶最佳疗效分析

Figure 2 Overall treatment process of 20 patients and analysis of the best therapeutic effect of the target lesion



Before: pre-treatment imaging; after: post-treatment imaging. Red arrows indicate pre treatment primary liver tumor lesions; yellow arrows indicate post treatment changes of the primary liver tumor lesions; blue arrows indicate pre-treatment vascular tumor thrombus; purple arrows indicate post treatment regression of vascular tumor thrombus; green arrows indicate pre-treatment pulmonary metastases; black arrows indicate post treatment newly developed pulmonary metastases.

图3 靶向联合免疫方案治疗中晚期HCC的典型影像学表现

Figure 3 Typical imaging manifestations of targeted combined immunotherapy in the treatment of advanced HCC

3 讨论

本研究结果表明,以靶向联合免疫治疗为核心

的综合方案在中晚期HCC转化治疗中具有较好的缩瘤能力。全组20例患者中,影像学评估达PR者11例(55.0%),其中4例(20.0%)成功施行R0切

表2 4例手术患者的临床特征及治疗反应

Table 2 Clinical characteristics and treatment responses of 4 surgical patients

Case	Age (years)	Sex	Cause of the disease	Treatment plan	Treatment cycle(n)	Baseline tumor thrombus status
Pt 5	62	Male	HBV	Targeted therapy+immunotherapy+TACE+radiotherapy	4	Caval vein tumor thrombus
Pt 8	51	Male	HBV	Targeted therapy+immunotherapy+TACE	4	No
Pt 11	64	Male	HBV	Targeted therapy+immunotherapy+TACE	6	No
Pt 20	55	Female	HCV	Targeted therapy+immunotherapy+TACE	5	No

Case	Imaging response	Surgical method	Pathological remission	Tumor necrosis rate(%)	Pathological microvascular invasion
Pt 5	PR	Left hemihepatectomy	Non-MPR	84	No
Pt 8	PR	Non-anatomical local resection	MPR	92	No
Pt 11	PR	Non-anatomical local resection	MPR	96	No
Pt 20	PR	Non-anatomical local resection	Non-MPR	73	No

除。值得关注的是,对于伴有大血管侵犯的高危患者,在靶向联合免疫治疗+TACE基础上附加局部放疗,可增强局部控制、实现肿瘤降期^[17-18],本研究中1例此类患者成功转化为R0切除。这提示,放疗等局部强化干预虽不宜作为全人群的常规推荐,但可作为合并大血管侵犯者突破转化瓶颈的有效强化策略^[19]。

R0切除的成功实施只是第1步,术后的病理缓解程度更可能与患者的长期预后密切相关^[20]。在成功手术的4例患者中,2例达到了MPR,且在术后至少12个月内未见复发;相比之下,另2例(坏死率分别为84%、73%)虽也实现了R0切除,但因属于Non-MPR,最终分别于术后13、10个月复发。这一鲜明对比提示在临床实践中,对于Non-MPR的患者,即便手术切缘呈阴性且接受了术后辅助治疗,术后仍需高度警惕早期复发风险,未来应积极探索针对该部分高危人群的更优化的术后辅助治疗策略^[21]。

为尽可能诱导肿瘤深层坏死(争取MPR),把握恰当的手术时机尤为重要^[22]。分析本组成功转化病例的治疗时间线,观察到首次达到PR的时间多在1.5~3.0个月,而最终实施手术的时间则集中在治疗启动后4.5~6.0个月^[23]。这提示临床可能存在一个潜在的“最佳手术窗口期”:即在获得初步影像学PR后,维持原方案额外观察2~3个月^[24]。此举不仅有助于病理学缓解,也能借此验证肿瘤的生物学稳定性,剔除早期继发耐药者^[25]。当然,基线无癌栓或癌栓局限(Vp2)的患者往往更容易、也更早触及这一手术窗口,而大样本队列的准确时间跨度仍有待前瞻性研究予以验证^[26]。目前《晚期肝细胞癌免

疫靶向联合转化序贯外科治疗专家共识(2024版)》指出,转化成功后应在机体状态允许时尽早手术。本研究观察到的4.5~6.0个月时间轴,为这一“尽早”提供了具体的参考时间窗,不仅能兼顾病理缓解,亦能规避长期高强度治疗带来的肝实质不可逆损伤^[27-28]。

然而,在追求深度降期与等待手术窗口的期间,必须警惕强效联合治疗对肝脏造成的隐匿性损伤^[29]。本研究中有7例患者虽达到了影像学PR,却最终未能实施手术,其中3例直接归因于肝脏储备功能下降(降至Child-Pugh B/C级)或新发重度门静脉高压,这与多次TACE造成的局部物理打击以及药物引发的免疫性肝炎叠加密切相关^[30]。这深刻地警示我们,“系统+局部”的高强度转化干预是一把“双刃剑”^[31]。未来的转化治疗策略不能仅着眼于抗肿瘤效能,更需在高效缩瘤与肝脏实质保护之间寻找更精准动态平衡^[32]。

本研究仍存在一定的局限性。首先,本研究为单中心回顾性分析,样本量较小($n=20$),这在很大程度上限制了统计学效能,导致无法通过多因素回归分析剔除潜在的混杂因素,也难以开展严谨的亚组间统计学比较。因此,本研究结论仅代表初步的临床观察结果,其普适性有待大样本、多中心研究进一步验证;其次,回顾性设计不可避免地存在选择偏倚,例如因肝功能恶化或拒绝手术而未能转化的患者被归入“PR未手术”组,可能掩盖了部分临床细节;再者,本研究未能系统采集免疫相关不良反应的长期追踪数据及患者生活质量评分,无法全面评估该强化转化方案的最终获益风险比。

综上,以靶向联合免疫治疗为核心的综合方案

是实现中晚期HCC降期治疗的有效手段。对于早期反应良好的患者,应MDT动态评估肝功能、癌栓退缩及剩余肝体积,抓住转化窗口期积极实施根治性手术,以期获得最佳的长期生存获益。

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Conflicts of Interests:

All authors declare that there are no conflict of interests, including any commercial, financial, or other forms of interests, related to the research, writing, or submission of this article.

作者贡献声明:

兰欣负责研究方案的设计、临床数据的采集与整理、统计学分析以及论文初稿的撰写;韩国勇负责临床诊断指导、手术方案评估、病例复核以及论文主要学术内容的修改;吴金道负责研究课题的整体构思、论文质量把关、经费支持及最终版本的审定校稿。

Author's Contributions:

LAN Xin designed the study protocol, collected and organized the clinical data, performed statistical analysis, and drafted the initial version of the manuscript. HAN Guoyong provided clinical diagnostic guidance, evaluated surgical strategies, reviewed the cases, and revised the core academic content of the paper. WU Jindao conceived the overall research framework, ensured the quality of the manuscript, provided financial support, and critically reviewed and finalized the manuscript.

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