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全腹平扫CT在胃肠间质瘤靶向治疗疗效评估中的应用价值

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[摘要] 目的 评价全腹平扫CT在胃肠间质瘤(gastrointestinal stromal tumors, GIST)靶向治疗疗效评估中的应用价值。方法 回顾性分析2015年3月—2022年9月河北医科大学第四医院收治的经病理证实、接受靶向治疗且治疗前后影像资料完整的GIST患者53例。参照实体瘤疗效评价标准实体肿瘤反应评估(Response Evaluation Criteria in Solid Tumors, RECIST)1.1选取靶病灶,分别于平扫和静脉期图像测量治疗前后靶病灶的长径及CT衰减值,计算长径之和变化率及平均CT值变化率,观察有无新发病灶、靶病灶有无新发出血及钙化,参照RECIST 1.1及Choi两种标准评估疗效。对比平扫及静脉期疗效评估结果。记录各次检查平扫及增强CT扫描的辐射剂量。结果 平扫与静脉期测量的靶病灶长径之和、长径之和变化率的差异均无统计学意义(P 均 >0.05),且一致性很强[组内相关系数(intraclass correlation coefficient, ICC)值分别为1.000、0.999];两者测量的靶病灶平均CT值变化率的差异有统计学意义($P<0.05$),但一致性较强(ICC值为0.672);治疗后出现3例新发病灶,3例瘤内出血,5例瘤内钙化,均可被平扫识别。参照RECIST1.1标准、Choi标准,平扫与静脉期疗效评估结果一致性均很强,Kappa值分别为1.000($P<0.05$)、0.882($P<0.05$)。平扫较增强扫描辐射剂量降低约70.11%。结论 全腹平扫CT降低了患者的辐射暴露及检查费用,可以较为准确地评估胃肠间质瘤靶向治疗效果,具有一定的临床应用价值。

[关键词] 胃肠道间质肿瘤;多探头的计算机断层扫描;靶向治疗 doi:10.3969/j.issn.1007-3205.2025.05.009

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The application value of whole abdominal plain CT in the assessment of the efficacy of targeted therapy for gastrointestinal stromal tumours

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[Abstract] **Objective** To evaluate the application value of whole abdominal plain CT in the assessment of the efficacy of targeted therapy for gastrointestinal stromal tumors (GIST). **Methods** Fifty-three patients with pathologically confirmed GIST who received targeted therapy and had complete pre-and post-treatment imaging were retrospectively analyzed in the Fourth Hospital of Hebei Medical University from Mar. 2015 to Sept. 2022. The target lesions were selected with reference to the solid tumor efficacy evaluation criteria Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. The length diameters and CT attenuation values of the target lesions before and after treatment were measured on the plain and venous images, respectively, and the rate of change in the sum of the length diameter and that in the mean CT value were

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calculated. Observations were made to determine the presence of new lesions, new hemorrhages in target lesions, and calcifications. Efficacies were evaluated according to both the RECIST1.1 and Choi criteria. The results of the efficacy assessment of the scanning and venous phases were compared. Radiation doses were recorded of each examination for both plain and enhanced CT scans. **Results** The differences between the sum of the length diameters of the target lesions and the change rate of the sum of the length diameters measured in the plain and venous phases were not statistically significant (both $P > 0.05$) and were in good agreement [intra-class correlation coefficient (ICC) values of 1.000 and 0.999, respectively]. The difference in the change rate of the mean CT values of the target lesions measured by both was statistically significant ($P < 0.05$), but the consistency was strong (ICC value of 0.672). Three new lesions, three intratumoral hemorrhages, and five intratumoral calcifications appeared after treatment, all of which could be identified by plain scanning. With reference to the RECIST1.1 criteria and Choi criteria, the consistency in the assessment results of the efficacy of the plain and venous phases was very strong, with Kappa values of 1.000 ($P < 0.05$) and 0.882 ($P < 0.05$), respectively. Radiation dose reduced approximately 70.11% for plain scan compared with enhanced scan. **Conclusion** The whole abdominal plain CT scan reduces the radiation exposure and examination expenses of patients and can evaluate the targeted therapeutic effect of gastrointestinal stromal tumors relatively accurately, which has certain clinical application value.

[Key words] gastrointestinal stromal tumors; multi-detector computed tomography; targeted therapy

胃肠间质瘤(gastrointestinal stromal tumors, GIST)是胃肠道最常见的间叶源性肿瘤,发病率为(10~20)/100万^[1-2],且近年来发病率呈逐年上升趋势^[3]。治疗首选手术切除,但对于难以达到R0切除,手术风险较大或需要多脏器联合切除者,需行术前靶向药物治疗。伊马替尼已在晚期及特殊部位GIST的综合治疗中发挥着重要作用^[4-8]。CT是评估GIST靶向治疗效果的首选影像学方法^[9-12]。中国临床肿瘤学会胃肠间质瘤诊疗指南推荐中、高危及复发转移GIST患者服用靶向药物后每3个月进行一次全腹增强CT随访^[13]。已有学者关注频繁CT检查带来的高辐射剂量及高检查费用问题^[14-15]。因此,在临床工作中存在靶向治疗期间行全腹平扫CT进行随访的情况,但目前尚无应用平扫CT进行胃肠间质瘤靶向治疗疗效评估的研究报道,其应用价值尚不明确。本研究采用实体肿瘤反应评估(Response Evaluation Criteria in Solid Tumors, RECIST)1.1标准^[16]及Choi标准^[17]两种评价标准,对比平扫及增强CT疗效评估结果,评价平扫CT在GIST靶向治疗疗效评估中的准确性及可行性。

1 资料与方法

1.1 资料 回顾性分析2015年3月—2022年9月

河北医科大学第四医院收治的胃肠间质瘤患者病例53例,其中男性34例,女性19例,年龄29~90岁,平均(60.72±10.97)岁;原发肿瘤部位:胃40例、腹腔7例、十二指肠4例、小肠1例、直肠1例;存在远处转移者17例,其中肝转移9例、腹腔转移6例、肝和腹腔均存在转移2例。

本研究经医院伦理委员会审核批准通过。

1.2 纳入标准及排除标准 纳入标准:①内镜活检或经腹穿刺活检证实为胃肠间质瘤患者;②因瘤体较大或发现远处转移而靶向药物治疗者;③于靶向治疗前、后均行全腹增强CT检查且影像资料完整者。排除标准:图像质量差者。

1.3 方法

1.3.1 图像采集方法 患者于检查前禁食4~6h,扫描前口服水500~800mL。采用美国通用电气公司Revolution扫描仪及西门子公司SOMATOM Definition Flash扫描仪,扫描范围:自膈顶至坐骨结节水平。扫描参数为:管电压120kV,自动调节管电流,准直器宽度分别为80cm和128mm×0.6mm,螺距分别为0.992和0.900,层厚、层间距均为5mm,重建层厚分别为1.25mm和1.00mm。平扫结束后经肘静脉注入对比剂(碘浓度300g/L),剂量1.5mL/kg,速率3.0mL/s,于注药后35s及70s后分别进行动脉期及静脉期扫描。

1.3.2 数据处理方法

1.3.2.1 靶病灶选取方法 由两位分别具有3年和17年腹部诊断经验的影像医师独立阅片,参照RECIST1.1标准,选取长径>1 cm、具有良好测量重复性的可测量病灶作为靶病灶,每个器官最多选取2个靶病灶,每例患者最多选取5个靶病灶。2位医师对靶病灶选取意见不一致时经讨论达成一致。记录每例患者靶病灶的数量、位置及层面。

1.3.2.2 靶病灶分析方法 分别分析平扫及静脉期图像,间隔时间约2周,每次仅分析一种,不参考另外一种图像。于5 mm层厚的平扫及静脉期图像上选取靶病灶最大层面,测量治疗前、后靶病灶最长径;沿靶病灶轮廓内缘勾画ROI,勾画时避开胃肠腔内容物、周围脂肪及血管,测量其平扫及静脉期CT衰减;观察有无新发病灶、靶病灶内有无新发出血(平扫65~130 HU)及钙化(平扫≥130 HU)。测量值均取3次测量的平均值。

1.3.2.3 靶病灶疗效评估数据计算方法 ① 分别

计算平扫、静脉期靶病灶长径之和变化率,参照RECIST 1.1标准进行疗效评估。长径之和变化率=(当次检查长径总和-基线检查长径总和)/基线检查长径总和,正值表示增加,负值表示减少。② 分别计算平扫、静脉期靶病灶平均CT值变化率,结合长径之和变化率,参照Choi标准进行疗效评估。平均CT值变化率=(当次检查CT值总和-基线检查CT值总和)/(基线检查CT值总和×靶病灶个数),正值表示增加,负值表示减少。

1.3.2.4 检查辐射剂量 记录各次检查平扫及增强扫描的剂量长度乘积(dose-length product, DLP),计算有效辐射剂量(effective dose, ED), ED = DLP×0.015。

1.4 疗效评估标准 疗效标准分为:完全缓解(complete remission, CR)、部分缓解(partial response, PR)、疾病稳定(stable disease, SD)、疾病进展(progressive disease, PD)。目前常用的评价标准为RECIST1.1标准及Choi标准,见表1。

表1 GIST 靶向治疗影像学评估标准

Table 1 Imaging evaluation criteria for targeted therapy in GIST

疗效	RECIST1.1 标准	Choi 标准
CR	全部病灶消失,无新发病灶	全部病灶消失,无新发病灶
PR	肿瘤长径缩小≥30%	肿瘤长径缩小≥10%;或肿瘤密度(HU)减小≥15%;无新发病灶;非靶病灶无明显进展
SD	不符合CR,PR或PD标准	不符合CR,PR或PD标准;无肿瘤进展引起的症状恶化
PD	肿瘤长径增大≥20%;或出现新发病灶	肿瘤长径增大≥10%,且密度变化不符合PR标准;出现新发病灶;新的瘤内结节或已有瘤内结节体积增大

1.5 观察指标 ①比较同次检查中平扫与静脉期测量的靶病灶长径之和、靶病灶长径之和变化率、靶病灶平均CT值变化率的差异;②将静脉期疗效评估结果作为金标准,计算疗效评估数据分别按照RECIST1.1标准、Choi标准进行评估,比较同一患者在靶向治疗前后的平扫、静脉期疗效评估结果的一致性;③患者有无新发病灶、靶病灶内有无新发出血;④比较同次检查中全腹平扫CT与增强CT的有效辐射剂量的差异。

1.6 统计学方法 应用SPSS 23.0统计软件处理数据。符合正态分布的计量资料,采用t检验;非正态分布的计量资料,采用Wilcoxon检验。配对样本检验差异无统计学意义的数据使用组内相关系数(intraclass correlation coefficient, ICC)评价其一致性,有序变量使用加权Kappa检验分析评价其一致性。ICC或Kappa值<0.2认为无一致性、0.2~0.4为一致性一般、0.4~0.6为一致性中等、0.6~0.8为一致性较强、0.8~1.0一致性很强。P<0.05为差异有统计学意义。

2 结 果

2.1 患者复查及靶病灶选取情况 53例患者中有17例进行了1次复查,16例进行了2次复查,9例进行了3次复查,7例进行了4次复查,2例进行了5次复查,2例进行了6次复查,共计复查126次。53例患者共选取80个靶病灶。

2.2 平扫与静脉期测量结果的比较 平扫与静脉期测量的靶病灶长径之和、靶病灶长径之和变化率的差异均无统计学意义(P均>0.05),且一致性很强(ICC值分别为1.000、0.999)。平扫与静脉期测得的靶病灶平均CT值变化率的差异有统计学意义(Z=7.523, P<0.05),两者一致性较强(ICC值为0.672),见表2。

2.3 平扫与静脉期疗效评估结果的比较 将静脉期疗效评估结果作为金标准,按照RECIST1.1标准进行疗效评估时,平扫与静脉期评估结果一致性很强,Kappa值为1.000(P<0.05),准确度为100%;参照Choi标准进行疗效评估时,平扫与静脉期评估

结果一致性很强, Kappa 值为 0.882 ($P < 0.05$), 见表 3, 准确度为 96.03% (121/126), 其中有 5 次静脉期评效为 PR, 平扫评效为 SD。图 1、2 示 2 例患者靶向治疗后具体评效情况。53 例患者中 3 例随访过程中出现新发病灶, 2 例为肝转移瘤, 1 例为腹壁转移瘤, 因患者未规律随访, 2 例新发肝转移瘤长径分别为 13.2 cm、7.2 cm, 新发腹壁转移瘤长径为 3.6 cm, 3 个新发病灶于平扫及静脉期均可检出。此外, 另有 3 例治疗后新发瘤内出血, 5 例治疗后新发钙化, 出血仅于平扫被识别, 钙化于平扫及静脉期均可被识别, 因范围均较小, 对疗效评估结果均未造成影响。

2.4 辐射剂量 全腹平扫 CT 有效辐射剂量为 8.5

(11.6~6.0)mSv; 全腹增强 CT(平扫+双期扫描)有效辐射剂量为 28.4(34.4~19.2)mSv, 差异有统计学意义 ($P < 0.05$)。平扫较增强检查辐射剂量降低约 70.11%。

表 2 平扫与静脉期测量结果比较

Table 2 Comparison of measurement results between plain scan and venous phase

测量参数	[n=179, M(QR)]		
	靶病灶长径之和 (cm)	靶病灶长径之和变化率	靶病灶平均 CT 值变化率
平扫	8.300(6.680)	-0.303(0.273)	-0.045(0.046)
静脉期	8.300(6.735)	-0.301(0.293)	-0.258(0.388)
Z 值	0.883	0.191	7.523
P 值	0.377	0.849	<0.001
ICC 值	1.000	0.999	0.672

表 3 平扫与静脉期疗效评估结果比较

Table 3 Comparison of efficacy evaluation results between plain scan and venous phase

(n=126, 例数)

RECIST 1.1 标准	静脉期(金标准)			Choi 标准平扫	静脉期(金标准)		
	PR	SD	PD		PR	SD	PD
平扫(预测)							
PR	65	0	0	PR	108	0	0
SD	0	54	0	SD	5	5	0
PD	0	0	7	PD	0	0	8
敏感度	100%				96.03%		
特异度	100%				98.02%		
准确度	100%				96.03%		
Kappa 值	1.000				0.882		
P 值	<0.05				<0.05		

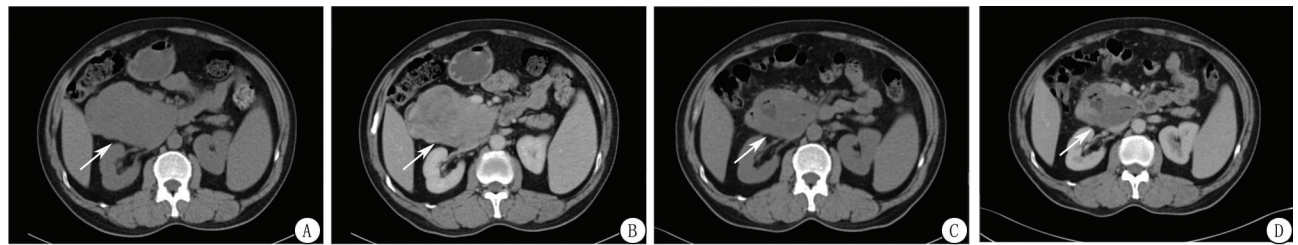


图 1 男, 53 岁, 十二指肠间质瘤(箭头所示为靶病灶)。治疗后靶病灶缩小, 内部出现坏死, 平扫、静脉期长径变化率分别为 29.8%、30.3%, CT 值变化率分别为 29.8%、49.1%。参照 RECIST 1.1 及 Choi 标准, 平扫及静脉期评效均为 PR, 评效一致) A. 治疗前平扫图像; B. 治疗前静脉期图像; C. 治疗后平扫图像; D. 治疗后静脉期图像

Figure 1 The arrow indicates the target lesion. Post-treatment evaluation demonstrated a reduction in lesion size with internal necrosis development. The percentage reductions in the length diameter on the plain and venous phase images were 29.8% and 30.3%, respectively, while the corresponding percentage reductions in CT attenuation values measured 29.8% and 49.1%. According to both RECIST1.1 criteria and Choi criteria, treatment response assessments for both plain and venous phase imaging consistently demonstrated PR, showing concordant evaluation outcomes

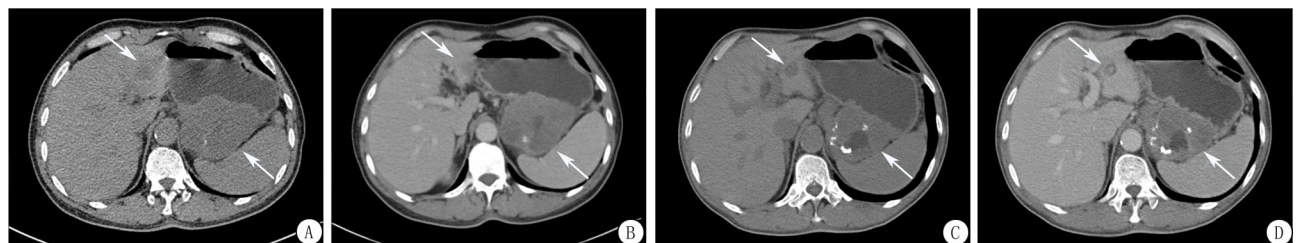


图 2 男, 61 岁, 胃间质瘤伴肝转移(箭头所示为两处靶病灶)。治疗后靶病灶大小变化不明显, 内部出现坏死及新增钙化, 平扫、静脉期靶病灶长径之和变化率分别为 8.8%、6.4%, 平扫平均 CT 值降低 1.6%, 静脉期平均 CT 值增加约 21.9%。参照

RECIST 1.1 及 Choi 标准,平扫及静脉期评效均为 SD,评效一致)

A.治疗前平扫图像;B.治疗前静脉期图像;C.治疗后平扫图像;D.治疗后静脉期图像

Figure 2 The arrow indicates two target lesions. Post-treatment evaluation showed no significant change in lesion size, with internal necrosis and new calcifications observed. The percentage changes in the sum of the length diameters on the plain and venous phase images were 8.8% and 6.4%, respectively. The mean CT attenuation values decreased by 1.6% on plain scans but increased by 21.9% during the venous phase. According to both RECIST 1.1 criteria and Choi criteria, treatment response assessments for both plain and venous phase imaging consistently demonstrated SD, indicating concordant therapeutic efficacy evaluations

3 讨 论

伊马替尼是不可切除、转移或复发的晚期 GIST 患者的一线治疗用药^[18-19],可以显著提高患者的无进展生存期和总生存期,但 40%~50% 的患者在治疗 2 年后产生继发性耐药^[20]。耐药患者需进行调整药物剂量、外科手术或换线治疗^[21]。因此准确评估胃肠间质瘤靶向治疗效果、及时发现病情变化对指导治疗决策具有重要的临床意义。

RECIST1.1 标准是临床常用的实体瘤疗效评价标准,根据靶病灶长径之和的变化判断疗效^[22]。无论原发瘤还是转移瘤,大部分 GIST 多表现为轮廓光滑、边界清楚的软组织肿物^[23-24]。本研究结果显示平扫图像可以准确测量靶病灶的大小,平扫与静脉期测量的靶病灶长径之和、靶病灶长径之和变化率的一致性很强,参照 RECIST1.1 标准,以平扫图像进行疗效评估的准确率达 100%。

不同于细胞毒性药物,靶向药物治疗后肿瘤内可出现囊变、黏液变、出血、坏死等^[25],而肿瘤缩小可不明显,甚至由于肿瘤内部变化导致肿瘤有所增大,另外,GIST 进展也可以表现为肿瘤体积无明显变化但出现瘤内结节^[26],这些情况仅评估肿瘤大小可能会低估疾病进展。因此,Choi 等^[17]结合病灶长径及静脉期 CT 值变化提出了新的 GIST 靶向治疗评效标准,即 Choi 标准。有效的靶向治疗可使肿瘤血供减低,从而使得静脉期 CT 值降低^[27]。本研究结果显示治疗后肿瘤内部成分的变化,也可导致平扫 CT 值的变化,参照 Choi 标准,以平扫图像进行疗效评估的准确率达 96.03%,与静脉期疗效评估一致性很强。本组中出现 5 次平扫与静脉期评效结果不同的情况,均为静脉期评效为 PR,而平扫评效为 SD,分析原因为治疗后肿瘤血供减低显著,而坏死囊变不显著,故平扫 CT 值未见明显降低。

本组中有 3 例患者治疗后肿瘤内新发出血,5 例患者治疗后肿瘤内新发钙化。靶向治疗后肿瘤内出现出血或钙化也被认为是治疗有效的表现,对此平扫图像容易识别,而仅观察静脉期图像会因出血、钙化使肿瘤 CT 值增加而低估治疗效果^[28]。本组

瘤内新发出血及钙化范围较小,尚未对静脉期评效结果造成影响。

RECIST1.1 标准及 Choi 标准均将出现新发病灶视为疾病进展。本组 3 例患者随访中出现新发病灶,但因患者未规律复查,新发病灶长径均 > 3 cm,可被平扫检出。平扫对较小新发病灶的检出能力尚需进一步评价,腹部平扫 CT 对比度有限,影像医师需要更加仔细地观察图像,当无法准确测量或发现可疑新发病灶时应进行增强扫描或 MRI 检查^[29-31]。本研究的局限性:①本研究为回顾性研究,样本量小,基于平扫 CT 值变化判断疗效的诊断阈值有待多中心大样本进一步研究。②腹部平扫 CT 对比度有限,对小新发瘤的诊断价值不明确,后续研究将进行进一步评价。

综上所述,全腹平扫 CT 降低了患者的辐射暴露及检查费用,可以较为准确地评估胃肠间质瘤靶向治疗效果,具有一定的临床应用价值。

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