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◇临床医学◇

肝细胞癌病人介入术后急性严重腹痛发生危险因素及预测模型构建

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摘要: 目的 探讨肝细胞癌(HCC)病人肝动脉插管化疗栓塞(TACE)术后急性严重腹痛发生危险因素。**方法** 回顾性分析2017年1月至2020年9月于焦作市第二人民医院行TACE治疗的HCC病人共178例临床资料,根据TACE术后急性严重腹痛发生情况分为急性严重腹痛组和非急性严重腹痛组,采用单因素和多因素法评价HCC病人TACE术后急性严重腹痛发生风险独立影响因素,并基于此构建预测模型。**结果** 178例病人TACE术后24 h内发生急性严重腹痛28例,发生率为15.73%;急性严重腹痛组初治比例、病灶最大径>5 cm比例、病灶数量≥3个比例、病灶侵犯血管比例、既往TACE术后中重度腹痛史比例及接受载药微球TACE比例分别为75.00%(21/28),64.29%(18/28),75.00%(21/28),46.43%(13/28),28.57%(8/28),60.71%(17/28),显著高于非急性严重腹痛组的57.62%(87/151),39.07%(59/151),50.99%(77/151),25.17%(38/151),11.92%(18/151),33.77%(51/151)(P<0.05);急性严重腹痛组既往TACE治疗史比例为39.29%(11/28),显著少于非急性严重腹痛组的62.25%(94/151)(P<0.05);多因素分析结果显示,肝内多发肿瘤病灶、既往TACE术后腹痛史、既往TACE治疗史及TACE类型均是HCC病人TACE术后急性严重腹痛发生风险独立影响因素(P<0.05);TACE术后急性中重度腹痛发生风险预测模型ROC曲线分析结果显示,AUC=0.81,95%*CI*:(0.75,0.88),最佳截断值为0.49,灵敏度和特异度分别为75.86%,73.10%。**结论** HCC病人TACE术后急性严重腹痛发生风险与肝内多发肿瘤病灶、既往TACE术后腹痛史、既往TACE治疗史及TACE类型独立相关,基于此构建预测模型具有良好预测效能。

关键词: 癌,肝细胞; 肝动脉插管化疗栓塞; 腹痛; 风险; 影响因素

Risk factors for moderate and severe acute abdominal pain in patients with HCC after TACE and predictive model establishment

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Abstract: Objective To investigate the risk factors for moderate and severe acute abdominal pain in patients with HCC after TACE. **Methods** Clinical data of 178 patients with HCC after TACE were retrospectively chosen in the Second People's Hospital of Jiaozuo from January 2017 to September 2020. All patients were grouped according to the incidence of moderate and severe acute abdominal pain after TACE and the independent risk factors for moderate and severe acute abdominal pain after TACE were evaluated by univariate and multivariate methods to establish the predictive model. **Results** Twenty-eight cases in 178 patients had moderate or severe acute abdominal pain within 24 hours after TACE and the incidence rate was 15.73%. The proportion of initial treatment cases, lesions with the maximum diameter of >5 cm,lesions number ≥3, lesions invading blood vessels,the history of moderate and severe abdominal pain after TACE and patients receiving drug loaded microspheres TACE in acute severe abdominal pain group were 75.00%(21/28),

64.29%(18/28),75.00%(21/28),46.43%(13/28),28.57%(8/28),60.71%(17/28),respectively, which were significantly higher than those of the non-acute severe abdominal pain group 57.62%(87/151), 39.07%(59/151), 50.99%(77/151), 25.17%(38/151), 11.92%(18/151), 33.77%(51/151) (P<0.05).The proportion of previous TACE treatment cases in the acute severe abdominal pain group for 39.29%(11/28) was significantly lower than that of non-acute severe abdominal pain group for 62.25%(94/151) (P<0.05). Multivariate analysis showed that multiple intrahepatic tumor lesions, previous history of abdominal pain after TACE, previous TACE treatment history and type of operation were independent risk factors for the occurrence of moderate to severe acute abdominal pain in HCC patients after TACE (P< 0.05). ROC curve analysis of the risk prediction model of acute moderate and severe abdominal pain after TACE showed that AUC was 0.81,95%*CI*:(0.75,0.88), the best cut-off value was 0.49,and the sensitivity and specificity were 75.86% and 73.10%, respectively.**Conclusion** The risk of moderate to severe acute abdominal pain in HCC patients after TACE is independently associated with multiple intrahepatic tumor lesions, previous history of abdominal pain after TACE,previous TACE treatment history and type of operation.

Key words: Carcinoma,hepatocellular; TACE; Abdominal pain; Risk; Influencing factors

肝动脉插管化疗栓塞(TACE)目前已被广泛用于不可切除肝细胞癌(HCC)病人临床治疗,同时对于存在高复发风险肝癌病人术后采用TACE预防性治疗可有效降低复发率,延长生存时间[1]。急性腹痛被认为是TACE术后常见并发症,超过70%病人术后24 h内可见腹痛症状,而严重腹痛比例接近40%,严重影响术后康复进程[2-3]。肝癌病人TACE术后腹痛发生危险因素相关研究较少,有报道认为年龄、性别、病灶最大径及病灶位置可能与TACE术后腹痛发生有关[4]。本研究探讨HCC病人TACE术后急性严重腹痛发生危险因素,现报告如下。

1 资料与方法

1.1 一般资料 纳入2017年1月至2020年9月于焦作市第二人民医院行TACE治疗的HCC病人共178例;纳入标准:①临床确诊HCC;②ECOG评分0~2分;③年龄≥18周岁;④Child Pugh分级A~B级;⑤术前无明显腹痛症状。排除标准:①长期服用止痛药物;②围手术期未预防采用自控镇痛;③术后24 h内出现大出血或肝昏迷。病人及其近亲属签署知情同意书。本研究符合《世界医学协会赫尔辛基宣言》相关要求。

1.2 观察指标 查阅病例记录性别、年龄、疾病状态、病灶数量、病灶最大径、病灶距包膜距离、肿瘤侵犯血管、TACE治疗情况及术后疼痛药物使用情况;肝内多发肿瘤病灶指数量≥3个。术后腹痛程度评价采用NRS评分,其中≥5分判定为严重腹痛[5];记录TACE术后24 h内腹痛发生时间和强度,其中轻度腹痛指疼痛数字评分(NRS)1~2分,中度腹痛指NRS评分3~4分,重度腹痛指NRS评分≥5分[5]。

1.3 统计学方法 选择SPSS 20.0软件处理数据;计数资料比较采用χ^2检验,以例(%)表示;采用logistic回归模型进行多因素分析并构建预测模型;描绘ROC曲线评价模型预测效能;P<0.05为差异有统计学意义。

2 结果

2.1 HCC病人TACE术后急性严重腹痛发生情况分析 178例病人TACE术后24 h内发生急性严重腹痛28例,发生率为15.73%;其中术后30 min内发生4例,术后6~12 h发生18例,术后12~24 h发生6例,占比分别为14.29%,64.29%,21.42%。

2.2 HCC病人TACE术后急性严重腹痛发生危险因素单因素分析 急性严重腹痛组初治比例、病灶最大径>5 cm比例、病灶数量≥3个比例、病灶侵犯血管比例、既往TACE术后中重度腹痛史比例及接受载药微球TACE比例分别为75.00%(21/28),64.29%(18/28),75.00%(21/28),46.43%(13/28),28.57%(8/28),60.71%(17/28),显著高于非急性严重腹痛组的57.62%(87/151),39.07%(59/151),50.99%(77/151),25.17%(38/151),11.92%(18/151),33.77%(51/151)(P<0.05);急性严重腹痛组既往TACE治疗史比例为39.29%(11/28),显著少于非急性严重腹痛组的62.25%(94/151)(P<0.05)。见表1。

2.3 HCC病人TACE术后急性严重腹痛发生危险因素多因素分析 多因素分析结果显示,肝内多发肿瘤病灶、既往TACE术后腹痛史、既往TACE治疗史及TACE类型均是HCC病人TACE术后急性严重腹痛发生风险独立影响因素(P<0.05)。见表2。

2.4 预测模型构建及预测效能ROC曲线分析 基于多因素分析结果建立TACE术后急性中重度腹痛发生风险预测模型。ROC曲线结果显示,上述预测模型曲线下面积为0.81,95%*CI*:(0.75,0.88),最佳截断值为0.49,灵敏度和特异度为75.86%,73.10%。

3 讨论

TACE是HCC治疗常用手段之一,对于症状控制良好病人术后24 h左右即可出院;以急性腹痛为代表TACE术后栓塞综合征发生风险较高,其中腹痛症状如未有效控制往往导致住院时间增加[6]。目前认为TACE术后急性腹痛发生可能与栓塞所致血管痉挛、病灶内部急性缺血坏死、大量炎性介质释

表1 肝细胞癌(HCC)178例肝动脉插管化疗栓塞(TACE)术后急性严重腹痛发生危险因素单因素分析/例

指标	非急性严重腹痛组(*n*=151)	急性严重腹痛组(*n*=28)	χ^2值	*P*值
性别			0.07	0.796
男	24	5		
女	127	23		
疾病状态			3.89	0.048
初治	83	21		
复发	68	7		
病灶距包膜距离			1.01	0.315
0~1 cm	28	3		
>1 cm	123	25		
病灶最大径			6.13	0.013
0~5 cm	92	10		
>5 cm	59	18		
病灶数量			5.50	0.019
1~2个	74	7		
≥3个	77	21		
病灶侵犯血管			5.24	0.022
否	113	15		
是	38	13		
既往TACE治疗史			5.14	0.023
有	94	11		
无	57	17		
既往TACE术后腹痛史			5.28	0.022
无/轻度	133	20		
中重度	18	8		
TACE类型			7.28	0.007
常规TACE	100	11		
载药微球TACE	51	17		
使用栓塞微球			0.02	0.899
是	34	6		
否	117	22		
使用聚乙烯醇颗粒			0.14	0.713
是	20	3		
否	131	25		
术后镇痛药物类型			3.96	0.412
帕瑞昔布钠	20	5		
氟比洛芬	35	7		
地佐辛	58	10		
喷他佐辛	4	0		
无	19	8		

放及个体疼痛阈值差异有关[7]。

本次研究178例病人TACE术后24 h内发生急性严重腹痛28例,发生率为15.73%,且以术后6~12 h腹痛发生比例最高;需要注意本次研究报道急性严重腹痛发生率低于既往研究[8],这一差异可能与以下因素有关:①本次研究中纳入预防性TACE治疗人群,此类病人未见严重腹痛发生,这可能与栓塞剂和化疗药物使用量较少有关。但有研究认为预防性TACE术后急性腹痛发生率更高,这主要因无病灶虹吸效应导致碘化油广泛刺激血管继发痉挛造成,推荐对于此类病人药物注射应尽可能缓慢且控制碘化油用量[9];②研究中病人围手术期均接受预防性镇痛药物使用;有学者研究证实[10],术后自控镇痛可降低行TACE治疗病人急性严重腹痛发生率至10%以内;另有报道提示给予接受TACE治疗病人围手术期积极有效镇痛干预后,95%以上腹痛获得明显改善,均可在术后24 h内出院[11]。

常规TACE采用碘油+化疗药物乳剂可导致药物大量进入血液循环,影响局部治疗效果,加重全身不良反应;而载药微球TACE则能够在一定程度上改善以上问题,通过缓慢释放化疗药物,维持病灶内部药物峰值,降低全身不良反应[12]。有报道显示[13],载药微球TACE相较于常规TACE,病人术后急性腹痛发生率和严重程度均更高。本次研究证实,采用载药微球TACE治疗病人术后急性严重腹痛发生风险更高,笔者认为这主要与载药微球TACE可加快病灶内部肿瘤细胞坏死和加重局部缺血效应有关。

理论上肝脏肿瘤病灶越大或越接近包膜,则病人TACE术后腹痛则越明显[14]。本次研究多因素分析仅证实肝内多发肿瘤病灶是HCC病人TACE术后急性严重腹痛发生风险独立影响因素(*P*<0.05);需要注意本次研究纳入指标为单一病灶最大径,而非全部病灶直径,无法代表肿瘤整体负荷,故可能属于混杂因素,故采用病灶数量代表肿瘤负荷价值更高,同时多个肿瘤病灶诱发急性腹痛风险更高,与以往报道结果相符[15]。HCC病人病灶数量越多、病灶体积越大则栓塞剂用量亦越多,血管栓塞范围越广,病灶在较短时间内缺血坏死所致腹痛反应则越严重。

表2 肝细胞癌(HCC)178例肝动脉插管化疗栓塞(TACE)术后急性严重腹痛发生危险因素多因素分析

指标	*β*值	*SE*值	*Wald* χ^2值	*OR*值	95%*CI*	*P*值
肝内多发肿瘤病灶	1.07	0.44	11.31	4.43	(1.23,9.20)	<0.001
既往TACE术后腹痛史	2.87	0.69	17.88	8.15	(4.22,15.67)	<0.001
既往TACE治疗史	−0.62	0.35	6.16	0.64	(0.47,0.90)	0.020
术式	1.94	0.57	8.90	3.31	(1.94,8.67)	<0.001

本次研究结果显示,既往TACE术后腹痛史和既往TACE治疗史均是HCC病人TACE术后急性严重腹痛发生风险独立影响因素($P<0.05$),这一发现在以往报道中较少涉及;其中既往TACE腹痛史病人腹痛再次发生风险提高7.15倍,这可能与个体疼痛阈值差异、肝脏病理状态及治疗方案有关。同时既往接受TACE治疗发生腹痛风险较低,这与既往研究结果相符[16-21],这一现象发生主要与病人随TACE治疗次数增加、反复接受相同刺激导致疼痛耐受性提高有关。本次研究ROC曲线分析结果显示,预测模型曲线下面积为0.81,95%*CI*:(0.75,0.88),最佳截断值为0.49,灵敏度和特异度分别为75.86%,73.10%,证实这一预测模型具有良好预测准确性、灵敏度及特异度,可辅助指导临床治疗护理方案制定。

综上所述,HCC病人TACE术后急性严重腹痛发生风险与肝内多发肿瘤病灶、既往TACE术后腹痛史、既往TACE治疗史及TACE类型独立相关,基于此构建预测模型具有良好预测效能。但需要注意本次研究属于小样本单中心回顾性报道,无法完全排除混杂因素影响,所得结论有待后续研究进一步确证。

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