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结肠癌病理 T 分期、N 分期与肿瘤沉积的相关性

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[摘　要]　**目的：**探讨结肠癌患者肿瘤沉积的发生率与病理T分期、N分期的相关性。**方法：**回顾性分析2017—2018年于徐州医科大学附属医院就诊的经手术病理证实的257例结肠癌患者的临床病理资料。按照第8版AJCC结直肠癌分期指南将患者分为T_2，T_3，T_4期组；N_0，N_+(N_1+N_2)期组；以及肿瘤沉积阳性、阴性组。肿瘤沉积与T分期、N分期的相关性分析采用行×列表卡方检验，组间比较采用卡方分割法。**结果：**T_2，T_3，T_4期分别有2例(5.6%)，30例(14.6%)，10例(66.7%)患者发生肿瘤沉积。不同T分期患者肿瘤沉积的发生率差异有统计学意义(χ^2=31.327，P<0.05)。组间比较T_2期、T_3期结肠癌患者肿瘤沉积的发生率均低于T_4期，差异具有统计学意义(χ^2=21.976，25.606，均P<0.016)；T_2期，T_3期结肠癌患者间肿瘤沉积发生率无明显统计学差异(P=0.141)。N_0，N_+期结肠癌分别有7例(4.2%)，35例(38.0%)例患者出现肿瘤沉积，卡方检验比较差异具有统计学意义(χ^2=49.360，P<0.001)；N_1，N_2期亚组分析结果表明差异无统计学意义(χ^2=3.091，P=0.079)。**结论：**T_4期、N_+期结肠癌患者出现肿瘤沉积的风险更高，肿瘤沉积与T分期、N分期的增高具有相关性。

[关键词]　结肠癌；肿瘤沉积；病理T，N分期；淋巴结

Correlation of pathological T and N staging with tumor deposits in colon cancer

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Abstract　**Objective:** To investigate the association between pathological TN staging and tumor deposits in colon cancer. **Methods:** Pathological data of 257 colon cancer cases from 2017 to 2018 was retrospectively analyzed. According to the 8th edition of the American Joint Committee on Cancer (AJCC) staging manual, all patients were devided into T_2, T_3 and T_4 groups, N_0, N_+(N_1+N_2) groups, tumor deposits positive and negative group. R×C chi-suqare test was performed to analyze the correlations of T and N stage with tumor deposits. Using the chi-square decomposition to further pairwise comparison. **Results:** Of which, 2 cases (5.6%) with tumor deposits positive

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in T_2 group, 30 cases (14.6%) in T_3 group, 10 cases (66.7%) in T_4 group. Chi-square test showed that tumor deposits during three groups were statistically different (χ^2=31.327, P<0.05 respectively). Pairwise comparison showed that the incidence of tumor deposits in T_2 and T_3 groups was lower than those of the T_4 group, the difference with statistical significance (χ^2=21.976, 25.606, respectively and P<0.016, P<0.016 respectively). Nevertheless, there was no significant difference between T_2 and T_3 groups (P=0.141). In the N staging, 7 cases (4.2%) with tumor deposits in N_0 group, 21 cases(22.8%) in N_1 group, 14 cases (15.2%) in N_2 group. Chi-square test showed significant different between N_0 and N_+ groups (χ^2=49.360, P<0.001 respectively). Subgroup analysis was carried by N_+ group, the difference between N_1 and N_2 groups was not statistically significant (χ^2=3.091, P=0.079). **Conclusion:** T_4 and N_+ staging colon cancer patients have the higher risk of tumor deposits than other stages, tumor deposits is associated with elevating pathological T and N staging in colon cancer.

Keywords colon cancer; tumor deposits; pathological T N staging; lymph node

结直肠癌(colorectal cancer，CRC)居全球恶性肿瘤发病率的第3位，恶性肿瘤病死率的第2位[1]。结肠癌患者就诊时多为中晚期，手术联合辅助放化疗后仍有20%~30%的患者发生远处转移[2-3]。因此有必要对预后相关指标进行研究，在术后对患者进行风险分层，制订个性化术后随访及治疗方案。

肿瘤沉积(tumor deposits，TDs)是指结直肠癌原发病灶淋巴引流区域内孤立的肿瘤结节，病理学上结节没有可辨别的淋巴、脉管及神经结构[4]。TDs与结直肠癌的分期、预后密切相关，美国癌症联合委员会(American Joint Committee on Cancer，AJCC)第8版结直肠癌指南将TDs阳性而淋巴结转移阴性的结肠癌患者定义为N1c/III期[3-4]。文献报道病理T分期、N分期、TDs与结肠癌预后相关，但是仍缺乏进一步深入研究[3]。

因此，本文旨在进一步明确结肠癌患者TDs与病理T分期、N分期及其亚组的相关性进行研究。

1 对象与方法

1.1 对象

回顾性收集2017—2018年于徐州医科大学附属医院就诊且行手术治疗的原发性结肠癌患者的临床病理学资料。本研究经徐州医科大学附属医院医学伦理委员会同意。

入组标准：1)手术病理证实为结肠癌；2)术前未进行任何治疗；3)无其他恶性肿瘤及相关治疗史；4)患者病理资料完整。本研究共纳入257例结肠癌患者，其中男151例(58.8%)，女106例(41.2%)，年龄25~88(61.32±12.70)岁。

1.2 术后病理学评估

由2名病理科医生(从事胃肠道肿瘤诊断工作>10年)对患者的术后切片进行复阅，对结果判定不一致的病例由2名医师协商决定。

参照AJCC第8版结直肠癌指南，评估的内容包括：1)有无肿瘤沉积。将没有残存淋巴结构的孤立的结直肠旁癌结节定义为TDs阳性，将周围有淋巴滤泡及被膜下窦等组织定义为TDs阴性(图1)。2)结肠癌T分期。T1期：肿瘤侵犯黏膜下层；T2期：肿瘤侵犯固有肌层；T3期：肿瘤侵犯浆膜下或无腹膜被覆的结肠旁组织；T4期：肿瘤侵透脏层腹膜和/或直接侵犯其他器官或结构(图2)。3)结肠癌N分期。N_1期：1~3枚区域淋巴结转移；N_2期≥4枚区域淋巴结转移。N_1，N_2期归为N_+期，而术后无淋巴结转移归为N_0期。

1.3 统计学处理

采用SPSS 19.0软件进行统计分析。计量资料采用均数±标准差($\bar{x}\pm s$)表示，计数资料采用率(%)表示。行×列卡方检验分析TDs与T分期相关性，P<0.05认为差异有统计学意义。组间比较采用Bonferroni校正，校正后检验水准α=0.016，P<0.016认为组间差异有统计学意义。N分期组间比较采用四格表卡方检验，P<0.05认为差异有统计学意义。

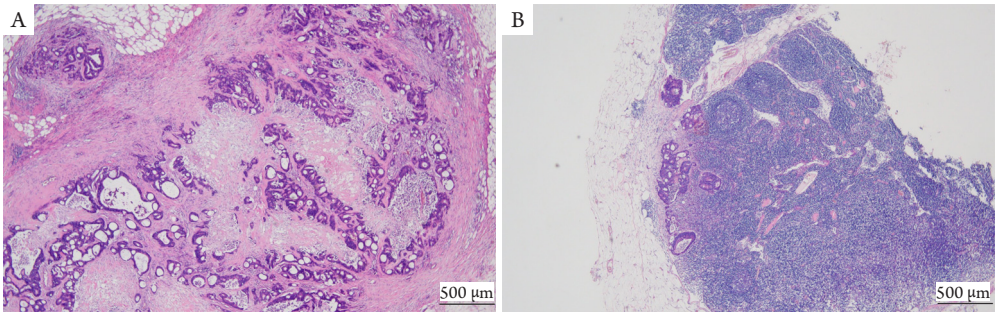

图1 TDs阳性与阴性结果(HE，×40)

Figure 1 Positive and negative results of tumor deposits (HE, ×40)

(A)结肠腺癌，癌结节1枚；(B)结肠腺癌，淋巴结转移，未见癌结节。

(A) Colonic adenocarcinoma, one cancer nodule; (B) Colonic adenocarcinoma, lymph node metastasis, no cancer nodule.

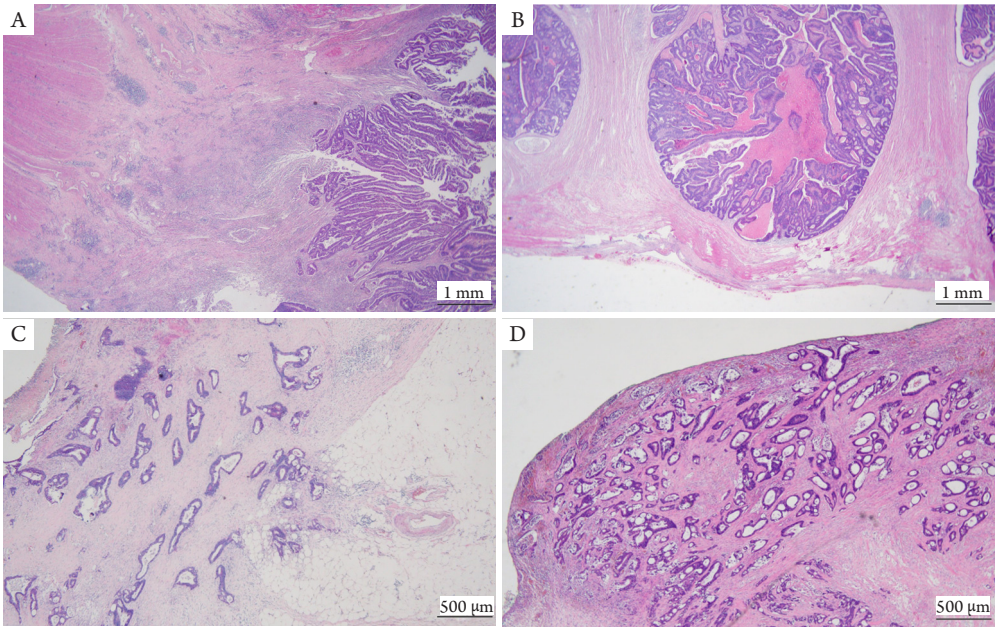

图2 AJCC第8版结直肠癌T分期标准

Figure 2 AJCC 8th edition T staging standard for colorectal cancer

(A)结肠腺癌，肿瘤侵犯黏膜下层(T_1；HE，×20)；(B)结肠腺癌，肿瘤侵犯肌层(T_2；HE，×20)；(C)结肠腺癌，肿瘤侵及浆膜下层(T_3；HE，×40)；(D)结肠腺癌肿瘤累及肠壁浆膜外(T_4；HE，×40)。

(A) Colonic adenocarcinoma, the tumor invaded the submucosa (T_1; HE, ×20); (B) Colonic adenocarcinoma, the tumor invaded the muscular layer (T_2; HE, ×20); (C) Colonic adenocarcinoma, the tumor invaded the serosa (T_3; HE, ×40), (D) Colonic adenocarcinoma, the tumor invaded outside of the serosa (T_4; HE, ×40).

2 结果

2.1 入组患者 TDs 及病理 T，N 分期

TDs阳性组42例(16.3%)，TDs阴性组215例(83.7%)。T_2，T_3，T_4期患者分别为36例(14.0%)，206例(80.2%)和15例(5.8%)。N_0，N_1，N_2期分别为165例(64.2%)，65例(25.3%)和27例(10.5%)。

2.2 TDs 与 T 分期的相关性

TDs在T_2，T_3，T_4期发生率分别为2例(5.6%)，30例(14.6%)，10例(66.7%)。卡方检验对三组结肠癌患者TDs发生率的比较，差异具有统计学意义(χ^2=31.327，P<0.05；表1)。T_2与T_3期、T_2与T_4期、T_3与T_4期组间比较，T_4期出现TDs的风险高于T_2、T_3期(χ^2=21.976，25.606，均P<0.016)，T_2期与T_3期

差异无统计学意义(χ^2=2.167，P=0.141；表2)。

2.3 TDs 与 N 分期相关性

TDs在N_0期、N_+期发生率分别为TDs阳性分别7例(4.2%)，21例(22.8%)，14例(15.2%)，差异具有统计学意义(χ^2=49.360，P<0.001)。N_1，N_2期亚组间比较，差异无统计学意义(χ^2=3.091，P=0.079；表3)。

表1 结肠癌患者TDs与T分期相关性

Table 1 Correlation of pathological T staging with tumor deposits in colon cancer

T分期	n	TDs阴性/[例(%)]	TDs阳性/[例(%)]
T_2	36	34 (94.4)	2 (5.6)
T_3	206	176 (85.4)	30 (14.6)
T_4	15	5 (33.3)	10 (66.7)
χ^2			31.327
P			<0.001

表2 T分期亚组TDs比较

Table 2 Pairwise comparison of Tumor Deposits between T staging

组间比较	TDs阴性/[例(%)]	TDs阳性/[例(%)]	χ^2	P
T_2与T_3			2.167	0.141
T_2	34 (94.4)	2 (5.6)		
T_3	176 (85.4)	30 (14.6)		
T_2与T_4			21.976	<0.001
T_2	34 (94.4)	2 (5.6)		
T_4	5 (33.3)	10 (66.7)		
T_3与T_4			25.606	<0.001
T_3	176 (85.4)	30 (14.6)		
T_4	5 (33.3)	10 (66.7)		

表3 N_0与N_1+N_2以及N_1+N_2亚组间比较结果

Table 3 Comparison of N_0 with N_1+N_2 and N_1+N_2 subgroups

N分期	TDs阴性/[例(%)]	TDs阳性/[例(%)]	χ^2	P
N_0与N_1+N_2			49.360	<0.001
N_0	158 (94.4)	7 (4.2)		
N_1+N_2	57 (62.0)	35 (38.0)		
N_1与N_2			3.091	0.079
N_1	44 (47.8)	21 (22.8)		
N_2	13 (14.2)	14 (15.2)		

3 讨论

结直肠患者中TDs阳性的发生率为10%~29%[2-3,5]。TDs是结直肠癌独立预后危险因素，TDs阳性患者与阴性患者预后存在显著差异[3,6-7]。

有学者[8]研究发现TDs与CD133，CD44高表达有关。王剑峰等[9]的研究结果表明TDs可能与IL-6，IL-7和Foxp3水平有关。其他临床病理学特征如肿瘤分化程度、神经侵犯、合并糖尿病病史也被证实与TDs有关[3,10-11]。因此，积极寻找与TDs相关的危险因素，对患者治疗方案的选择、延长生存期具有重要意义。

本研究发现T_4期患者出现TDs的风险更高，这与Tong等[12]的研究结果是一致的。肿瘤的T分期反映了肿瘤的外侵程度，相对于T_2，T_3期结肠癌患者，T_4期结肠癌侵透脏层腹膜和/或直接侵犯其他器官或结构。而有研究表明[13]TDs与结肠癌侵犯血管有关。因此，我们认为这可能是T_4期结肠癌TDs发生率更高的原因。本研究发现：亚组分析中T_2期、T_3期结肠癌患者TDs的发生率没有明显的统计学差异。有研究[14-15]表明结肠癌疗前影像T分期的准确性达到75.0%~89.7%，因此治疗前影像T分期可能提供更多TDs的相关信息。

淋巴结转移是结肠癌的主要转移方式，是影响患者预后的重要因素[16]。既往研究[2,17]常将TDs与转移淋巴结(lymph node metastasis，LNM)混淆，而二者在起源上存在根本差别。目前研究[18]认为TDs与脉管侵犯、肿瘤组织侵犯淋巴结被膜、神经侵犯以及肿瘤的直接播散有关。本研究表明TDs与LNM具有相关性，这与既往的研究[2,19]结果一致。而N_1，N_2期TDs的发生率差异无统计学意义，不同文献对结肠癌影像学N分期的准确性变化较大，Rollven等[14]的研究表明利用1.5T MR评估结肠癌N分期的准确性高达69%，因此有必要研究疗前影像学N分期、病理N分期与TDs的相关性。

本研究尚存在以下不足：1)T_2，T_4期的病例相对较少；2)每例手术标本肠周淋巴结的取材部位及数量有较大差异；3)没有比较肿瘤分级纳入分析因素。

综上所述，结肠癌T，N分期均与TDs具有相关性，T_4期、N_+期结肠癌患者发生肿瘤沉积的风险更高。T_2，T_3期及N_1，N_2期亚组患者TDs的发生没有明显差异。

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