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# 结肠癌患者中医证型分布与营养标志物的关系

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[摘　要]　**目的：**探讨结肠癌患者术前中医证型分布与营养标志物之间的相关性，为结肠癌患者进行全面的中医辨证治疗提供新思路。**方法：**收集2012年6月至2015年12月江南大学附属医院胃肠肿瘤外科首次入院的结肠癌患者150例，收集其临床资料，进行中医证型判定及其分布情况统计，收集的患者均定期随访，分析术前中医证型与白蛋白(albumin，ALB)、预后营养指数(prognostic nutritional index，PNI)、控制营养状况(controlling nutritional status，CONUT)评分间的相关性。**结果：**结肠癌患者中医证型分布占比由高到低依次为湿热郁毒证(31.33%)、瘀毒内结证(22.00%)、肝肾阴虚证(18.67%)、气血两亏证(14.67%)、脾肾阳虚证(6.67%)、无证型(6.67%)；在5年存活率方面，气血两亏证(63.63%)、瘀毒内结证(66.67%)的存活率最低；中医证型与营养标志物的相关性统计中，瘀毒内结证的ALB水平低于脾肾阳虚证($P$<0.05)、显著低于湿热郁毒证、肝肾阴虚证、无证型($P$<0.01)；气血两亏证的ALB水平低于脾肾阳虚证、无证型($P$<0.05)，显著低于湿热郁毒证、肝肾阴虚证($P$<0.01)。瘀毒内结证与气血两亏证两组的PNI低于脾肾阳虚证($P$<0.05)，显著低于湿热郁毒证、肝肾阴虚证、无证型($P$<0.01)。**结论：**瘀毒内结证及气血亏虚证的患者更易于出现较低水平的ALB、PNI，低ALB值及低PNI值合并瘀毒内结证及气血亏虚证的患者生存率有下降的趋势。

[关键词]　结肠癌；营养标志物；中医证型

# Relationship of the distribution of traditional Chinese medicine syndrome type and nutritional markers of colon cancer patients

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**Abstract**　**Objective:** To investigate the correlation between the distribution of preoperative traditional Chinese

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medicine (TCM) syndrome type and nutritional markers of colon cancer patients, and to provide a new way for comprehensive TCM syndrome differentiation and treatment in colon cancer patients. **Methods:** A total of 150 colon cancer patients were selected, who were first admitted to the Gastrointestinal Tumor Surgery Department of the Affiliated Hospital of Jiangnan University from June 2012 to December 2015. The clinical data were collected, and the TCM syndrome types were determined and their distribution statistics were made. The collected patients were followed up regularly, and the correlation between preoperative TCM syndrome type and albumin (ALB), prognostic nutritional index (PNI), controlling nutritional status (CONUT) scores was analyzed. **Results:** The distribution proportion of TCM syndrome types of colon cancer patients from high to low was the syndrome of damp heat stagnation toxin (31.33%), the syndrome of internal stagnation of blood stasis and toxin (22.00%), the syndrome of liver and kidney yin deficiency (18.67%), the syndrome of qi and blood deficiency (14.67%), the syndrome of spleen and kidney yang deficiency (6.67%), and undocumented discernible type (6.67%). According to the statistics of 5-year survival rate, the survival rates of the syndrome of qi and blood deficiency (63.63%), and the syndrome of internal stagnation of blood stasis and toxin (66.67%) were the lowest. In the correlation statistics between TCM syndrome types and nutritional markers, the level of ALB in the syndrome of internal stagnation of blood stasis and toxin was lower than that in the syndrome of spleen and kidney yang deficiency ($P$<0.05), which was significantly lower than that in the syndrome of damp heat stagnation toxin, the syndrome of liver and kidney yin deficiency, and undocumented discernible type ($P$<0.01). The level of ALB in the syndrome of qi and blood deficiency was lower than that in the syndrome of spleen and kidney yang deficiency and undocumented discernible type ($P$<0.05), which was significantly lower than that in the syndrome of damp heat stagnation toxin and the syndrome of liver and kidney yin deficiency ($P$<0.01). The value of PNI in the 2 groups of the syndrome of internal stagnation of blood stasis and toxin and the syndrome of qi and blood deficiency were lower than that in the syndrome of spleen and kidney yang deficiency ($P$<0.05), which was significantly lower than that in the syndrome of damp heat stagnation toxin, the syndrome of liver and kidney yin deficiency, and undocumented discernible type ($P$<0.01). **Conclusion:** Patients with the syndrome of internal stagnation of blood stasis and toxin and the syndrome of qi and blood deficiency are more likely to have lower levels of ALB and PNI, and the survival rate of patients with low ALB value and low PNI value combined with the syndrome of internal stagnation of blood stasis and toxin and the syndrome of qi and blood deficiency demonstrates a downward trend.

**Keywords** colon cancer; nutritional markers; traditional Chinese medicine syndrome type

结肠癌是常见的消化道恶性肿瘤，根据流行病学统计数据[1]，我国结肠癌的发病率位居恶性肿瘤发病率第4位，病死率居第5位。研究[2-3]显示：肿瘤的发生、发展、转移等与机体的炎性反应和免疫状态存在一定的关联。代表营养状态和炎症反应的实验室指标已被应用于临床治疗来优化恶性肿瘤的分期及风险分层。营养标志物白蛋白(albumin，ALB)、预后营养指数(prognostic nutritional index，PNI)、控制营养状况(controlling nutritional status，CONUT)评分除了能够反映机体营养状况及免疫状态外，在胃肠道恶性肿瘤患者的远期预后方面也具有独立的评估价值，低ALB水平、低PNI、CUNUT高评分提示消化道恶性肿瘤患者的预后不佳[4-6]。中医证型是进行中医诊治的基础，对患者的诊疗预后具有一定的指导性。本研究拟分析结肠癌患者术前中医证型分布与ALB、PNI、CONUT评分的关联性，以期为临床更全面地辨证治疗结肠癌患者，改善其生存提供新的思路。

## 1 对象与方法

### 1.1 对象

收集2012年6月至2015年12月在江南大学附

属医院胃肠肿瘤外科初治的结肠癌患者，均根据2012年国际抗癌联盟第7版进行分期。纳入标准：1)初诊时组织病理学确诊为结肠癌；2)无严重的心、肺、肾疾病；3)接受了根治性手术。排除标准：1)合并其他原发肿瘤；2)未行手术治疗，无明确病理学资料，缺乏术前1周的血清生化实验室数据；3)术前有急性或慢性的炎症性病变或感染；4)合并肠梗阻或穿孔。本研究获得了江南大学附属医院医学伦理委员会审核批准(审批号：LS2020009)。

### 1.2 方法

使用本院检验科SYSMEX血细胞分析仪检测患者术前1周内血常规，Roche cobas C702生化仪检测肝功能，收集患者的实验室数据(淋巴细胞、ALB、胆固醇)、年龄、性别、TNM分期等临床资料。PNI计算公式：PNI=血清ALB值(g/L)+5×外周血淋巴细胞绝对值($\times10^9$/L)。CONUT评分标准见表1。

### 1.3 中医证型分型标准

依据《恶性肿瘤中医诊疗指南》[7]将结肠癌分为5个主要证型。1)湿热郁毒证。主症：便中带血或黏液脓血便，里急后重，肛门灼热，或大便干稀不调。次症：发热，恶心，胸闷，口干，小便短黄。舌质红，苔黄腻，脉滑数。2)瘀毒内结证。主症：腹部拒按，腹部可触及肿块、或局部胀闷、走窜、疼痛，里急后重。次症：面色晦暗或肌肤甲错，皮肤瘀斑，腹胀嗳气，舌质紫暗或有瘀点、瘀斑，脉涩。3)气血两亏证。主症：面色苍白或萎黄无华，口唇、爪甲颜色淡，短气懒言，四肢倦怠。次症：自汗少寐，手足发麻，便溏或脱肛，舌质淡或胖，边有齿痕，苔薄白，脉细弱无力。4)肝肾阴虚证。主症：腹痛隐隐，或腹内结块，便秘，大便带血，头晕耳鸣，腰膝酸软，五心烦热，盗汗遗精。次症：形瘦纳差，口咽干燥，月经不调，舌质红，少苔，脉弦细数。5)脾肾阳虚证。主症：腹痛喜温喜按，或腹内结块，下利清谷或五更泄泻或大便带血，四肢不温。次症：面色白，少气无力，畏寒肢冷，腰膝酸软，舌淡胖，有齿痕，脉沉细无力。以上若具备3个主症加舌脉，或2个主症加1个次症加舌脉即可诊断。但对于无明显症状或不属于上述5种证型的患者辨证为无证型。

### 1.4 随访

采用门诊复查、住院、电话等方法进行生存随访，进展随访项目包括全身物理检查、肿瘤标志物、头胸腹盆CT或MRI。术后3年内每3个月复查，3年以上每6个月复查。此后每年进行1次，随访截至2020年12月。

### 1.5 统计学处理

采用SPSS 23.0统计学软件进行数据分析。计数资料以例(%)表示，采用$\chi^2$检验统计；计量资料以均数±标准差($\bar{x}\pm s$)表示，采用$t$检验。$P<0.05$为差异有统计学意义。

**表1 CONUT评分标准**

**Table 1 Standard of CONUT scoring**

| 检测指标 | 正常 | 轻度 | 中度 | 重度 |
|---|---|---|---|---|
| 血清ALB | | | | |
| 范围/(g·L$^{-1}$) | ≥35.0 | 30.0~34.9 | 25.0~29.9 | <25.0 |
| 得分 | 0 | 2 | 4 | 6 |
| 总淋巴细胞数 | | | | |
| 范围/mm$^3$ | ≥1 600 | 1 200~1 599 | 800~1 199 | <800 |
| 得分 | 0 | 1 | 2 | 3 |
| 总胆固醇 | | | | |
| 范围/(mg·dL$^{-1}$) | >180 | 140~179 | 100~139 | <100 |
| 得分 | 0 | 1 | 2 | 3 |
| CONUT评分 | 0~1 | 2~4 | 5~8 | 9~12 |

## 2 结果

### 2.1 中医证型分布情况

在150例结肠癌患者中，中医证型占比从高到低依次为湿热郁毒证(31.33%)、瘀毒内结证(22.00%)、肝肾阴虚证(18.67%)、气血两亏证(14.67%)、脾肾阳虚证(6.67%)、无证型(6.67%)。在5年存活率方面，气血两亏证(63.63%)、瘀毒内结证(66.67%)的存活率最低(表2)。

**表2 150例结肠癌患者的中医证型分布情况**

**Table 2 Distribution of TCM syndromes in 150 patients with colon cancer**

| 辨证分型 | 例数(%) | 存活率/% |
|---|---|---|
| 湿热郁毒证 | 47 (31.33) | 74.46 |
| 瘀毒内结证 | 33 (22.00) | 66.67 |
| 气血两亏证 | 22 (14.67) | 63.63 |
| 肝肾阴虚证 | 28 (18.67) | 78.57 |
| 脾肾阳虚证 | 10 (6.67) | 70.00 |
| 无证型 | 10 (6.67) | 80.00 |

### 2.2 患者中医证型与临床特征的关系

共收治符合标准的结肠癌患者150例，其中男76例，女74例，年龄19~89(中位数66)岁。所有患者均未中断随访，随访时间为2~101(中位数72)个月，根据2012年国际抗癌联盟第7版分期标准：I期10例，II期57例，III期57例，IV期26例。患者的中医证型分布与年龄、性别、T分期、N分期、临床分期均无统计学意义($P$>0.05，表3)。

### 2.3 中医证型与营养标志物的相关性分析

瘀毒内结证患者的ALB水平低于脾肾阳虚证($P$<0.05)，显著低于湿热郁毒证、肝肾阴虚证、无证型($P$<0.01)；气血两亏证低于脾肾阳虚证、无证型($P$<0.05)，显著低于湿热郁毒证、肝肾阴虚证($P$<0.01)；瘀毒内结证与气血两亏证ALB水平差异无统计学意义。瘀毒内结证与气血两亏证的PNI均低于脾肾阳虚证(均$P$<0.05)、均显著低于湿热郁毒证、肝肾阴虚证、无证型(均$P$<0.01)；瘀毒内结证与气血两亏证的PNI差异无统计学意义。中医证型与CONUT评分之间的差异无统计学意义($P$>0.05，表4)。

**表3 150例结肠癌患者中医证型与临床特征的关系**

**Table 3 Relationship between TCM syndromes and clinical characteristics of 150 patients with colon cancer**

| 临床特征 | 湿热郁毒证($n$=47)/[例(%)] | 瘀毒内结证($n$=33)/[例(%)] | 气血两亏证($n$=22)/[例(%)] | 肝肾阴虚证($n$=28)/[例(%)] | 脾肾阳虚证($n$=10)/[例(%)] | 无证型($n$=10)/[例(%)] | $P$ |
|---|---|---|---|---|---|---|---|
| 年龄/岁 | | | | | | | 0.83 |
| >66 | 20 (13.3) | 17 (11.3) | 13 (8.7) | 13 (8.7) | 4 (2.7) | 5 (3.3) | |
| ≤66 | 27 (18.0) | 16 (10.7) | 9 (6.0) | 15 (10.0) | 6 (4.0) | 5 (3.3) | |
| 性别 | | | | | | | 0.082 |
| 男 | 22 (14.7) | 16 (10.7) | 8 (5.4) | 15 (10.0) | 9 (6.0) | 6 (4.0) | |
| 女 | 25 (16.6) | 17 (11.3) | 14 (9.3) | 13 (8.7) | 1 (0.7) | 4 (2.6) | |
| T分期 | | | | | | | 0.57 |
| T1~2 | 4 (2.6) | 3 (2.0) | 0 (0.0) | 3 (2.0) | 1 (0.7) | 2 (1.3) | |
| T3 | 6 (4.0) | 1 (0.7) | 1 (0.7) | 2 (1.3) | 1 (0.7) | 1 (0.7) | |
| T4 | 37 (24.7) | 29 (19.3) | 21 (14.0) | 23 (15.4) | 8 (5.3) | 7 (4.6) | |
| N分期 | | | | | | | 0.90 |
| N0 | 21 (14.0) | 16 (10.7) | 11 (7.3) | 14 (9.3) | 7 (4.7) | 5 (3.3) | |
| N1 | 16 (10.6) | 12 (8.0) | 7 (4.7) | 10 (6.7) | 3 (2.0) | 2 (1.3) | |
| N2 | 10 (6.7) | 5 (3.3) | 4 (2.7) | 4 (2.7) | 0 (0.0) | 3 (2.0) | |
| 临床分期 | | | | | | | 0.45 |
| I | 3 (2.0) | 1 (0.7) | 0 (0.0) | 3 (2.0) | 1 (0.7) | 2 (1.3) | |
| II | 17 (11.3) | 11 (7.3) | 10 (6.7) | 10 (6.7) | 5 (3.3) | 3 (2.0) | |
| III | 23 (15.3) | 12 (8.0) | 7 (4.7) | 10 (6.7) | 2 (1.3) | 4 (2.7) | |
| IV | 4 (2.7) | 9 (6.0) | 5 (3.3) | 5 (3.3) | 2 (1.3) | 1 (0.7) | |

**表4 6组中医证型与营养标志物的关系**

**Table 4 Relationship of TCM syndromes in six groups and nutritional markers**

| 营养指标物 | 湿热郁毒证 ($n$=47) | 瘀毒内结证 ($n$=33) | 气血两亏证 ($n$=22) | 肝肾阴虚证 ($n$=28) | 脾肾阳虚证 ($n$=10) | 无证型 ($n$=10) |
|---|---|---|---|---|---|---|
| ALB | 41.62 ± 5.72$^{**\#\#}$ | 35.64 ± 4.83 | 36.22 ± 3.98 | 40.81 ± 4.50$^{**\#\#}$ | 40.66 ± 6.80$^{*\#}$ | 40.19 ± 3.87$^{**\#}$ |
| PNI | 50.47 ± 6.42$^{**\#\#}$ | 42.45 ± 6.44 | 42.51 ± 4.60 | 49.01 ± 6.16$^{**\#\#}$ | 47.63 ± 7.50$^{*\#}$ | 49.49 ± 6.24$^{**\#\#}$ |
| CONUT评分 | 2.00 ± 1.86 | 2.85 ± 2.29 | 3.00 ± 2.20 | 1.89 ± 1.31 | 2.27 ± 2.45 | 1.60 ± 1.74 |

与瘀毒内结证组比较，$^{*}P$<0.05，$^{**}P$<0.01；与气血两亏证组比较，$^{\#}P$<0.05，$^{\#\#}P$<0.01。

Compared with the syndrome of internal stagnation of blood stasis and toxin, $^{*}P$<0.05, $^{**}P$<0.01; Compared with the syndrome of qi and blood deficiency, $^{\#}P$<0.05, $^{\#\#}P$<0.01.

## 3 讨论

关于肠癌的最早记载被认为是出现在《黄帝内经》中，《灵枢·五变》有：“黄帝曰：人之善病肠中积聚者，何以候之？少俞答曰：皮肤薄而不泽，肉不坚而掉泽，如此，则肠胃恶，恶则邪气留止……大聚乃起。”因此古代医家多数认为：结肠癌的产生内因为正气亏虚，外为邪毒外侵，正气虚，卫外失司，易邪毒入侵，正邪交争，正虚邪实，则邪毒留滞于肠，郁结发为此病，早期邪实以湿热、瘀毒多见，晚期正虚则以气血两虚、肝肾阴虚、脾肾阳虚多见。现代医家也多共识[8-10]：结肠癌的病因病机概括为正气亏虚为本，热、毒、瘀、痰为标，本虚标实，早期邪实为主，晚期正虚为主或正虚夹邪，治疗当注重扶正固本。结肠癌的辨证分型目前没有统一标准，结肠癌的证型主要为湿热蕴结证、瘀毒内结证、气滞血瘀证、脾胃虚弱证、脾肾阳虚证、气血两虚证、肝肾阴虚证等[11-13]。在本研究150例患者中，中医证型中以实证稍多，占53.3%，实证中又以湿热郁毒证多见，虚证则以肝肾阴虚证稍多见。结肠癌病机为本虚标实，本研究所选择的病例均为初诊病例，尚未行手术及辅助治疗，多数患者正气损耗不大，正是邪正相争之时，故实证稍多见。且本研究病例均处江南地带，该区域多湿多雨，日久可化湿热之邪，阻滞肠腑，故湿热郁毒证较多见。王馨[14]研究200例结肠癌患者中医证型，发现其虚证以肝肾阴虚多见，实证以湿热郁毒证为主，这与本研究的结果相似。

目前将结肠癌的中医证型分布与营养相关因素做关联分析的报道并不多见。梁艳彬等[15]曾分析了140例大肠癌患者中医证型分布与营养风险状况的关系，ALB正常患者居多，中医证型与营养风险具有一定相关性，以肝肾阴虚证、气血两虚证为多见。王威[16]探讨155例结肠癌患者脾虚证相关影响因素时发现III、IV期结肠癌患者脾虚证与ALB、血红蛋白、功能状态(performance status，PS)评分呈负相关。在本研究中，我们选择了ALB、PNI、CONUT评分这3个能够反映患者营养状态的观察指标。血清ALB是反映全身营养状态的常用指标，而营养状态差通常与肿瘤预后不良相关[17]，同时低ALB血症也可以反映全身炎症状况[18]。PNI最初被用于消化道肿瘤患者围手术期营养状态的评估和手术风险的预测，是由2项参数组成的简易指标，指标结合外周血白蛋白及淋巴细胞计数，能较好提示机体免疫状态及营养状况，其中淋巴细胞是人体的重要免疫细胞之一，能介导及调控细胞免疫，发挥机体的抗肿瘤作用[19]。PNI低于45或40通常被定义为中度或重度营养不良。多项研究[6,20-21]表明：低PNI的大肠癌患者预后往往更差，因此PNI被认为能够独立于传统TNM分期和肿瘤标志物以外，对消化道恶性肿瘤的短期并发症及远期预后具有评估价值。CONUT评分是一种较新的评估免疫营养状态的指标，通过计算血清ALB、淋巴细胞计数及胆固醇浓度而得。纳入胆固醇水平是CONUT评分与其他营养标志物的主要区别，胆固醇为细胞膜的重要组成部分，参与了多种与肿瘤发生、发展及免疫应答相关的信号通路[22-23]。有研究[24]表明CONUT评分能独立预测多种恶性肿瘤的预后。

本研究中患者中医证型分布与营养标志物的分析显示：瘀毒内结证、气血两亏证患者中ALB水平、PNI低于其余4证患者，差异有统计学意义。结合6组患者5年存活率的统计，仍以瘀毒内结组及气血亏虚组为最低，这与ALB、PNI低水平提示结肠癌患者预后不佳是一致的。由此我们可以认

为瘀毒内结证及气血亏虚证的患者更易出现ALB水平及PNI降低，低ALB水平、低PNI合并瘀毒内结证及气血亏虚证的患者有生存率降低的趋势。此两证，一为实证，一为虚证，与以往文献[15-16]结果中虚证患者易出现营养状态不佳不同，本研究出现了实证患者的营养指标降低。瘀毒内结多由于脾胃功能失调，水湿内停，日久化为郁毒，留滞经脉，导致血流运行不畅，瘀毒阻滞，为实证，此证型大多邪气旺盛，可加重患者自身的炎症反应，而大量炎症因子的产生又可抑制免疫[25]，故瘀毒内结证患者的ALB、PNI低值比例较其余4组高。“脾主运化”是中医传统理论对人体消化功能的一个高度概括，脾胃虚弱则运化无权，气血生化乏源，久之气血亏虚。PNI是反映营养及免疫状况的有效指标，气血亏虚组患者的ALB、PNI低值比例高，与其“脾失健运”，即消化功能的减弱是一致的。因此，我们建议瘀毒内结证及气血亏虚证患者在传统辨证治疗的同时，均要加强健脾，恢复其脾胃功能，脾胃健旺，则摄纳有权；同时加强营养干预，通过营养支持来改善营养状态，进而提高免疫功能，减轻炎症反应；这三者结合，贯彻治疗始终，既可提高患者生存质量，又有望延长其生存期。

本研究尚存在不足：1)为单中心的数据分析，样本数量偏少，不能全面地代表结肠癌患者的情况，未来课题组希望能开展多中心、大样本的前瞻性研究以进一步验证结肠癌中医证型分布与营养因素的关系；2)中医证型的判定带有主观性的影响；3)为回顾性研究，具有一定的局限性。

将营养标志物和结肠癌患者的中医证型相关联并综合分析，将免疫营养生物标志物应用到中医临床的诊疗中，目前国内尚无报道。瘀毒内结证与气血亏虚证更易获得ALB、PNI低值且生存率降低，提示我们应制订更有针对性的治疗方案，使患者从中收益。

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