经腹肠道超声对溃疡性结肠炎疾病活动及生物制剂治疗效果的预测价值

摘　　要

溃疡性结肠炎(ulcerative colitis, UC)是一种以反复发作为特征的慢性非特异性疾病，STRIDE-II 共识将黏膜愈合作为 UC 的长期治疗目标，需要长期监测，但内镜检查的患者接受度差，不适合反复进行，经腹肠道超声(transabdominal ultrasound, TAUS)快速、廉价、无需肠道准备，患者接受度高，是用于 UC 密切监测的理想客观检查工具。最近国际研究提示 TAUS 可用于评估 UC 的内镜疾病活动度，但识别内镜活动的 TAUS 参数临界值仍存在争议。此外，探索 TAUS 对 UC 抗炎治疗效果评估作用的纵向研究较少，以内镜检查为疗效判断标准的数据更为缺乏。本研究对 TAUS 参数与 UC 内镜活动进行横向分析，并对 TAUS 参数变化与生物制剂治疗后 UC 内镜结局进行纵向分析，旨在探索 TAUS 在 UC 疾病活动评估及治疗随访中的应用价值。

第一部分 经腹肠道超声参数与溃疡性结肠炎疾病活动的相关性研究

目的：探讨 TAUS 参数与 UC 疾病活动的相关性。

方法：回顾性观察性研究。收集 2022 年 1 月至 2024 年 2 月就诊于河北医科大学第二医院东院消化内科的 108 例次 UC 患者的临床资料。分析肠道超声参数与 Mayo 内镜评分(Mayo endoscopic score，MES)及溃疡性结肠炎内镜严重程度指数(ulcerative colitis endoscopic index of severity，UCEIS)评分的相关性，并应用受试者工作特征 (receiver operator characteristic, ROC)曲线分析计算识别不同程度内镜疾病活动的肠壁厚度(bowel wall thickness, BWT)最佳临界值，同时探索 TAUS 参数与实验室炎症、营养指标的相关性。

结果：

1. 根据 MES、UCEIS 评分将 UC 患者分为缓解期及轻度、中度、重度活动期，BWT 随内镜疾病活动等级增高而增加，其中 MES 1 分与 MES 2 分、MES 2 分与 MES 3 分之间的平均 BWT 差异有统计学意义，UCEIS 评分 0~1 分与 UCEIS 评分 2~4 分、UCEIS 评分 2~4 分与 UCEIS 评分 7~8

分之间的 BWT 差异有统计学意义。

2. ROC 曲线分析显示，BWT 识别 MES=0 分的最佳临界值为 3.45mm(AUC=0.972, 95%CI: 0.944-1.000, *P*＜0.001)，敏感度为 93.88%，特异度达 100%；BWT 识别 UCEIS 评分≤1 分的最佳临界值为 4.45mm(AUC=0.960, 95%CI: 0.924-0.996, *P*＜0.001)，敏感性为 87.21%，特异性为 90.91%。BWT 识别 MES≥2 分、UCEIS 评分≥5 分的最佳临界值均为 4.95mm。BWT 对 UC 内镜活动度的检验效能优于粪便钙卫蛋白。

3. 单因素 Logistic 回归分析显示 BWT、彩色多普勒信号(color doppler signal，CDS)评分、肠壁层次结构、肠系膜脂肪增生与内镜缓解相关。多因素 Logistic 回归分析显示 BWT、CDS 评分是 UCEIS≤1 分的独立预测因素，BWT 是 MES=0 分的唯一独立预测因素。

4. Spearman 秩相关分析显示，BWT、CDS 评分、肠壁层次结构、肠系膜脂肪增生与 MES、UCEIS 评分呈中-强度正相关。BWT、CDS 评分与内镜评分的相关性最强，TAUS 参数与实验室炎症指标呈弱-中度正相关，与实验室营养指标呈中度负相关。

结论：

1. BWT 可准确区分 UC 内镜下不同程度的疾病活动，BWT 预测 MES=0 分的最佳临界值为 3.45mm，预测 UCEIS 评分≤1 分的最佳临界值为 4.45mm，预测 MES≥2 分、UCEIS 评分≥5 分的最佳临界值为 4.95mm。

2. TAUS 参数可以预测内镜活动，BWT、CDS 评分是 UCEIS 评分≤1 分的独立预测因子，BWT 是 MES=0 分的唯一独立预测因子。

3. TAUS 参数与 MES、UCEIS 评分中-强度正相关，与实验室炎症指标呈弱-中度正相关，与实验室营养指标中度负相关。

第二部分 经腹肠道超声对生物制剂治疗溃疡性结肠炎疗效的预测价值

目的：以内镜检查为金标准，探讨 TAUS 对生物制剂治疗 UC 疗效的预测价值，探索治疗早期 TAUS 参数变化。

方法：前瞻性纵向研究。纳入开始生物制剂治疗的 UC 患者，在基线、治疗后第 14±8 周进行内镜、TAUS、实验室检查及临床评估。以 MES 及 UCEIS 评分为标准，将治疗效果分为内镜缓解(MES=0 分或 UCEIS 评分≤1 分)、内镜应答(MES 下降≥1 分或 UCEIS 评分下降≥2 分)、无内镜

应答，分析 TAUS 参数变化与不同内镜结局的关系。此外，在治疗后第 2±1 周、治疗后 6±4 周进行 TAUS 检查，探索生物制剂治疗早期 TAUS 参数的变化趋势。

结果：

1.纳入 45 名开始生物制剂治疗的 UC 患者，39 名患者完成随访并纳入分析。治疗前后 BWT 差值与 MES、UCEIS 评分差值中度正相关。生物制剂治疗后，达到内镜缓解患者 BWT 显著低于未达到者，有内镜应答患者 BWT 下降程度显著大于无内镜应答者。

2. 单因素 Logistic 回归分析显示，CDS 评分等级升高、CDS 评分≤1 分、肠壁层次结构消失、肠系膜脂肪增生与治疗后达到 UCEIS 评分≤1 分相关。CDS 评分等级升高与治疗后达到 MES=0 分相关，所有达 MES=0 分的患者 CDS 评分均≤1 分，且均不存在肠壁层次结构消失、肠系膜脂肪增生、肠系膜淋巴结肿大。治疗后 CDS 评分降低值增大、肠系膜脂肪增生与 MES 下降≥1 分相关，仅肠系膜脂肪增生与 UCEIS 评分下降≥2 分相关。

3.ROC 曲线分析显示，生物制剂治疗 14±8 周时，识别 MES=0 分、UCES 评分≤1 分 BWT 的最佳临界值均为 3.55mm (MES: AUC=0.933, 95%CI: 0.852-1.000, P＜0.001, 灵敏度=100%, 特异度为=81.25%; UCEIS: AUC=0.913, 95%CI: 0.825-1.00, P＜0.001，灵敏度=95.45%，特异度=70.59%)。BWT 下降百分比高于 32.04%可以预测 UCEIS 评分下降≥2 分 (AUC=0.833, 95%CI: 0.700-0.971, P=0.003)，灵敏度为 53.33%，特异度为 100%。BWT 下降百分比高于 23.47%可以预测 MES 下降≥1 分 (AUC=0.871, 95%CI: 0.753-0.989, P=0.002)，灵敏度为 81.25%，特异度为 85.71%。分别以 MES、UCEIS 评分为标准分析，CDS 评分≥1 分可以预测内镜缓解，CDS 评分降低值≥1 分可以预测内镜应答。

4. BWT 在生物制剂治疗第 2±1 周即出现明显的下降，CDS 评分、肠系膜脂肪增生在治疗后第 6±2 周出现明显改善，肠壁层次结构破坏在治疗 14±8 周后出现明显改善。生物制剂治疗第 2±1 周、第 6±2 周时，达到内镜缓解的患者中位 BWT 存在小于未达到者的趋势，达到内镜应答的中位 BWT 下降程度存在大于无应答者的趋势，但差异无统计学意义。

结论：

1. BWT 可以预测生物制剂治疗 UC 后内镜结局。治疗后，BWT 预测 MES=0 分、UCEIS 评分≤1 分的最佳临界值为 3.55mm，BWT 下降百分比大于 23.47%可以预测 MES 下降≥1 分，大于 32.04%可以预测 UCEIS 评分下降≥2 分。

2. 其他 TAUS 参数中，CDS 评分、肠壁层次结构破坏、肠系膜脂肪增生与内镜缓解相关，CDS 评分降低值增大、肠系膜脂肪增生与内镜应答相关。CDS 评分≤1 分可以预测内镜缓解，CDS 评分降低值≥1 分可以预测内镜应答。

3. 生物制剂治疗 UC 早期即可出现超声参数的显著改善，其中 BWT 变化出现最早，发生在治疗后 2±1 周。在生物制剂治疗的早期，达到内镜缓解、内镜应答者的 BWT 改善程度有大于未达到者的趋势。

关键词：超声，溃疡性结肠炎，疾病活动，治疗反应，生物制剂

目　　录

Predictive value of transabdominal ultrasound for disease activity and treatment efficacy of biological agents in ulcerative colitis

ABSTRACT

Ulcerative colitis (UC) is a chronic non-specific disease characterized by recurrent flare-ups, and the STRIDE-II consensus identifies mucosal healing as a long-term therapeutic goal for UC. However, endoscopy is unattractive for frequent monitoring. Transabdominal ultrasound (TAUS) offers an ideal alternative due to its fast, low cost, lack of need for bowel preparation, and acceptability. Recent data showed that TAUS can be used to assess endoscopic disease activity in UC, but the critical values of TAUS parameters for recognizing endoscopic activity remain controversial. However, only a few longitudinal studies have explored the role of TAUS in assessing the efficacy of anti-inflammatory treatments for UC, and the data in comparison with endoscopy are more scarce. This study aimed to explore the value of TAUS in monitoring disease activity and evaluating therapeutic effects by comparing TAUS parameters with UC endoscopic activity in a cross-sectional cohort and comparing TAUS parameter changes with UC endoscopic outcomes in a longitudinal UC cohort under biologic treatments.

The First Part: Correlation between transabdominal ultrasound parameters and ulcerative colitis disease activity

Objective: To investigate the correlation between TAUS parameters and UC disease activity.

Methods: Retrospective study. Clinical data of 108 UC patients who attended the Department of Gastroenterology of the Second Hospital of Hebei Medical University from January 2022 to February 2024 were collected. The correlation between TAUS parameters with Mayo endoscopic score (MES) and ulcerative colitis endoscopic index of severity (UCEIS) was analyzed. Receiver operator characteristic (ROC) curve analysis was applied to calculate the best

cut-off value of bowel wall thickness (BWT) to identify different degrees of endoscopic disease activity. The correlation of TAUS parameters with laboratory inflammatory and nutritional indicators was also explored.

Results:

1. UC patients were categorized into remission and mild, moderate and severe activity according to MES and UCEIS. BWT increased with endoscopic disease activity grade. BWT was statistically different between MES 1 and MES 2 endoscopic activity and between MES 2 and MES 3 endoscopic activity. BWT was statistically different between UCEIS 0-1 and UCEIS 2-4 endoscopic activity and between UCEIS 2-4 and UCEIS 7-8 endoscopic activity

2. ROC curve analysis showed that the best cut-off value of BWT for MES=0 was 3.45mm (AUC=0.972, 95%CI: 0.944-1.000, P<0.001), with a sensitivity of 93.88% and a specificity of 100%; the best cut-off value for BWT to recognize UCEIS ≤ 1 was 4.45mm (AUC=0.960, 95%CI: 0.924-0.996, P<0.001) with 87.21% sensitivity and 90.91% specificity. The most accurate cut-off value of BWT for MES≥2 or UCEIS≥5 was 4.95mm. BWT exhibited better prognostic efficacy compared with fecal calprotectin.

3. Univariable logistic regression showed that BWT, color Doppler signal (CDS) score, wall layer stratification, and fat wrapping were associated with endoscopic remission. Multivariable logistic regression showed that BWT and CDS score were independent predictors for UCEIS≤1, and BWT was the only independent risk factor for MES=0.

4. Spearman correlation analysis showed BWT, CDS score, wall layer stratification, fat wrapping were moderate-strong positively correlated with UCEIS and MES, and the correlation between BWT, CDS score and endoscopic score was the strongest. TAUS parameters were weak-to-moderate positively correlated with laboratory inflammatory markers and moderate-to-strong correlated with laboratory nutritional markers.

Conclusions:

1. BWT can identify the endoscopic severity of UC accurately, BWT＜3.45mm can identify MES=0, ＜4.45mm identify UCEIS≤1, BWT＞4.95mm

can identify MES≥2 and UCEIS≥5.

2. TAUS parameters were strongly correlated with endoscopic activity, with BWT and CDS being independent predictors of UCEIS≤1 and BWT being the only independent predictor of MES=0.

3. TAUS parameters were moderate-strong positively correlated with MES and UCEIS, significantly weak-moderate positively correlated with laboratory markers of inflammation, and moderately negatively correlated with laboratory markers of nutrition.

The Second Part: Predictive value of transabdominal ultrasound for the efficacy of biological agents in the treatment of ulcerative colitis

Objective: To investigate the predictive value of TAUS on the efficacy of biologics in the treatment of UC using endoscopy as the gold standard, and to explore the changes in early TAUS parameters.

Methods: Prospective longitudinal study. UC patients who started biologic therapy were enrolled. All patients underwent endoscopy, TAUS, laboratory examination and clinical assessment at baseline, and at week 14±8 after treatment. The endoscopic outcome was classified as endoscopic remission (MES=0 or UCEIS≤1), endoscopic response (a decrease of MES ≥ 1 point or a decrease of UCEIS≥2 points), and no endoscopic response using MES and UCEIS, and the relationship between the changes in TAUS parameters and different endoscopic outcomes was analyzed. At week 2±1 and week 6±4, TAUS was also performed to explore the trends of TAUS changes in the early stage of biologic treatment.

Results:

1. A total of 45 patients with UC who started biologic therapy were included, and 39 patients completed follow-up and were included in the analysis. Change in BWT was moderately positively correlated with MES and UCEIS. After biologic therapy, BWT was significantly lower in patients who achieved endoscopic remission than those who did not, and BWT decreased significantly more in patients with endoscopic response than in those without endoscopic response.