·临床研究·

临床及内镜特征联合外周血炎症相关指标的评估在回肠末端病变的病因诊断价值初探

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［摘　要］ **目的：**总结分析回肠末端病变患者临床、内镜特征及临床转归，探究患者临床及内镜特征联合外周血炎症相关指标改变对克罗恩病（Crohn's disease，CD）的诊断价值，为临床诊疗提供有益依据。**方法：**本研究为单中心回顾性研究，纳入2014年1月—2021年6月于南京医科大学第一附属医院行结肠镜检查发现回肠末端病变的患者，收集患者一般信息、病历资料、内镜及病理报告等，统计并分析所纳入患者的临床、内镜特征及病因诊断。根据诊断结果筛选出CD及非特异性回肠末端溃疡患者，比较两组患者在初诊时的临床、内镜特征及外周血炎症相关指标变化。**结果：**共纳入回肠末端病变患者956例，其中93例诊断明确，包括CD、肠结核、良性肿瘤、腺癌等，425例失访，另有438例患者病因诊断不明，诊断不明患者中有293例复查肠镜，其中182例显示病变消失。最终筛选出CD患者22例，非特异性回肠末端溃疡患者73例。与后者相比，CD患者初诊时腹痛发生率更高，且更易表现为回盲瓣受累的内镜特征。血小板、血红蛋白、白蛋白、血小板/淋巴细胞比值、中性粒细胞/淋巴细胞比值等外周血炎症相关指标对于辅助诊断CD有一定价值，5项指标联合诊断价值更高，曲线下面积为0.83。**结论：**回肠末端病变大多数为非特异性良性病变，且预后较好。对于肠镜下首次发现回肠末端病变尤其是溃疡的患者，需关注其临床症状、内镜下特征，同时结合外周血炎症相关指标改变，有助于回肠末端病变的病因诊断。

［关键词］ 回肠末端病变；临床特征；内镜特征；外周血炎症相关指标

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Diagnostic value of clinical and endoscopic features combined with peripheral blood inflammatory markers in etiology of terminal ileum lesions

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［**Abstract**］ **Objective:** To summarize the clinical and endoscopic features, as well as clinical outcomes, of patients with terminal ileum lesions, and to explore the diagnostic value of combining clinical and endoscopic features with changes in peripheral blood inflammatory markers for Crohn's disease（CD）, providing valuable evidence for clinical diagnosis and treatment. **Methods:** This study was a single-center retrospective study, including patients who underwent colonoscopy between January 2014 and June 2021 at the First Affiliated Hospital of Nanjing Medical University, with ileal terminal lesions identified. General information, medical records, endoscopy and pathological reports of the patients were collected, and clinical and endoscopic characteristics and etiological diagnosis were statistically analyzed. The patients with CD and non-specific terminal ileum ulcer were screened, and the clinical and endoscopic characteristics and peripheral blood inflammatory markers of the two groups were compared. **Results:** A total of 956 patients with terminal ileal lesions were included, 93 of whom had a clear diagnosis, including CD, intestinal tuberculosis, benign tumors, adenocarcinoma, etc., 425 were lost to follow-up, and another 438 patients with unknown causes. Among the patients with unknown diagnoses, 293 underwent follow-up colonoscopy, and 182 of them showed disappearance of lesions. Finally, 22 patients with CD and 73 patients with non-specific terminal ileal ulcer were screened out. Compared with the latter, patients with CD have a higher incidence

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of abdominal pain at initial diagnosis and are more likely to show endoscopic features of ileocecal valve involvement. Peripheral blood inflammatory markers such as platelet count, hemoglobin, albumin, platelet/lymphocyte ratio, and neutrophil/lymphocyte ratio, were found to be of certain value in assisting the diagnosis of CD. The combined diagnostic value of the five indicators demonstrated a higher, with an area under the curve of 0.83. **Conclusion:** Most terminal ileal lesions are non-specific benign lesions and have a good prognosis. For patients with terminal ileal lesions, especially ulcers, identified during initial colonoscopy, attention should be paid to their clinical symptoms and endoscopic characteristics, and combined with changes in peripheral blood inflammatory markers, which can assist in the etiological diagnosis of terminal ileum lesions.

[**Key words**] terminal ileum lesion; clinical feature; endoscopic feature; peripheral blood inflammatory marker

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回肠末端是靠近回盲瓣30 cm以内的回肠远端部分，该部位淋巴组织丰富，是小肠疾病的多发部位[1]。近年来随着对结肠镜检查进入回肠末端意识的增强，该处病变的检出率在不断提高[2]。回肠末端病变内镜下表现多样，包括充血糜烂、溃疡、增生、息肉等，病因复杂多样[3-6]。既往研究发现，克罗恩病（Crohn's disease，CD）、肠结核（intestinal tuberculosis，ITB）、淋巴瘤、感染性肠炎、溃疡性结肠炎（ulcerative colitis，UC）、药物性损伤等均可累及回肠末端，其中CD是回肠末端溃疡最常见的病因之一[7-12]。部分CD患者初诊时仅表现为回肠末端溃疡，病理结果亦无特殊，与非特异性回肠末端溃疡（无确切病因，经简单对症治疗后溃疡消失）鉴别诊断较为困难[13-14]。有研究发现，腹痛是回肠末端溃疡最终诊断为CD的危险因素，但其辅助诊断价值尚有争议[15]。CD患者因肠道炎症负荷，常伴随血小板（platelets，PLT）、血小板/淋巴细胞比值（platelet to lymphocyte ratio，PLR）、中性粒细胞/淋巴细胞比值（neutrophil to lymphocyte ratio，NLR）升高，血红蛋白（hemoglobin，HB）、白蛋白（albumin，ALB）降低等变化[16-18]。

回肠末端病变的疾病过程及临床预后如何，是否会发展为CD无法预判，并且其病因诊断较为困难。因此，进一步了解回肠末端病变疾病谱，分析不同病变的临床、内镜特征及外周血炎症相关指标改变对其病因的诊断及治疗方案的制定具有重要的临床价值。因此，本研究旨在总结、分析回肠末端病变患者临床、内镜特征及临床转归，初步探讨临床、内镜特征及外周血炎症相关指标改变对孤立性回肠末端溃疡患者诊断为CD的价值，为临床诊疗提供有益的依据。

1 对象和方法

1.1 对象

本研究是一项单中心回顾性研究，纳入2014年1月—2021年6月于南京医科大学第一附属医院行结肠镜检查并初次发现回肠末端病变的患者956例。纳入标准：①结肠镜检查发现回肠末端病变并取组织活检者；②临床资料完整。排除标准：①患有自身免疫性疾病、炎症性肠病、缺血性肠病、血液系统疾病、恶性肿瘤等；②肠道常见致病菌感染以及合并其他部位感染；③严重心肝肾功能不全；④临床资料不全。炎症性肠病的诊断标准参考《炎症性肠病诊断与治疗的共识意见（2018年·北京）》[19]，ITB、淋巴瘤、良性肿瘤及腺癌等的诊断则结合患者临床、实验室、内镜、组织病理学检查结果确定。本研究将无明确病因诊断的回肠末端病变统称为“不明原因的回肠末端病变”，将病理结果无特殊，且经菌群调节、促进黏膜修复等对症治疗后病变消失的回肠末端溃疡患者称为“非特异性回肠末端溃疡”患者。本研究已通过南京医科大学第一附属医院伦理委员会审核批准（伦理编号：2021-SR-136）。

1.2 方法

从医院电子病历系统收集符合纳入排除标准的患者的一般信息、病历资料、内镜及病理报告等。由2位高年资的消化科医师独立回顾性评估以上患者的内镜及病理报告，并对诊断进行复审。统计并分析所纳入回肠末端病变患者的临床、内镜特征及病因诊断。最终根据诊断结果筛选出CD及非特异性回肠末端溃疡患者。记录2组患者初诊时的PLT、HB、ALB等外周血指标，并计算PLR、NLR。比较2组患者在初诊时的临床、内镜特征及外周血炎症相关指标变化。

1.3 统计学方法

应用SPSS 26.0软件进行统计学分析。计数资料以例数和百分率表示。符合正态分布的连续变量以均数±标准差（$\bar{x} \pm s$）表示，两组间比较采用独立样本t检验；非正态分布资料以中位数（四分位数）

[$M(P_{25},P_{75})$]表示，组间比较采用非参数检验。组间率的比较采用卡方检验。应用Graphpad Prism 8.0绘制受试者工作特征（receiver operating characteristic，ROC）曲线、计算曲线下面积（area under curve，AUC），Medcalc软件计算约登指数、灵敏度、特异度、临界值（cut-off值）。$P<0.05$为差异有统计学意义。

2 结 果

2.1 患者一般情况

本研究最终共纳入956例患者，其中男620例，女336例，男女比例为1.84∶1。患者年龄12~83岁，中位年龄为47岁。吸烟史、既往史、用药史等临床特征详见表1。

2.2 回肠末端病变内镜下表现及疾病谱分布

956例回肠末端病变患者内镜下表现与疾病谱分布详见表2，其中，充血糜烂521例、溃疡323例、增生111例、其他1例（内镜下表现：黏膜苍白，呈脑回样改变）。以上患者中已明确病因诊断者共93例。其中，38例为溃疡患者，分别为CD 20例，ITB 11例，UC 4例，淋巴瘤2例，回肠末端腺癌1例。54例为回肠末端黏膜增生患者，根据病理结果共诊断为淋巴瘤3例、良性肿瘤51例。此外，1例患者病变较为特殊（黏膜苍白，呈脑回样改变），病理示黏膜固有层内可见嗜伊红色无定型物，后确诊为巨球蛋白血症。其余863例回肠末端病变患者中有425例失访，438例患者随访过程中有293例复查肠镜，其中确诊CD 10例，其余病因尚不明确，在本研究中称为“不明原因的回肠末端病变”。

表1 回肠末端病变患者临床特征

Table 1 Clinical characteristics of patients with terminal ileum lesions

Clinical characteristic	Cases	Percentage（%）
Sex		
Male	620	64.8
Female	336	35.2
Age		
<16 years	23	2.4
16–40 years	333	34.8
41–59 years	432	45.2
≥60 years	168	17.6
Smoking history	262	27.0
Medical history		
History of intestinal obstruction	2	0.2
History of perianal disease	8	0.8
History of osteoarthritis or rheumatic disease	23	2.4
History of cerebral infarction or coronary artery disease	14	1.5
History of previous medication		
NSAID	37	3.9
Glucocorticoids	4	0.4

NSAID：Non-steroidal anti-inflammatory drug.

2.3 不明原因回肠末端病变患者的随访

对863例回肠末端病变患者进行为期3年的随访，有425例失访，其余438例中有293例患者复查肠镜，145例未复查（图1）。结果发现，293例复查肠镜患者中，初次肠镜下表现为溃疡性病变、充血糜烂性病变及增生性病变者分别为188例、93例及12例。其中，116例（62%）溃疡性病变患者、59例（63%）充血糜烂性病变患者及7例（58%）增生性病变患者复查时病变已消失，其余111例患者病变仍存在，其中10例溃疡性病变患者随访过程中确诊CD（图1）。

在病变消失的116例溃疡性病变患者中有73例未服用任何药物或仅经菌群调节、促黏膜修复等对症治疗，在本研究中，这73例病变被称为“非特异性回肠末端溃疡”。

2.4 CD与非特异性回肠末端溃疡患者的临床、内镜特征比较

纳入确诊的20例CD中存在孤立性回肠末端病变12例，同时对随访过程中回肠末端病变复查内镜后仍未消失部分患者进行了为期3年的随访，共筛选

表2 纳入研究的回肠末端病变患者内镜下表现与疾病谱分布

Table 2 Endoscopic manifestations and disease spectrum distribution of patients with terminal ileum lesions

Endoscopic findings	Number(*n*)
Congestive erosion	
Ileitis of unknown etiology	521
Ulceration	
Ileal ulceration with known etiology	20
CD	11
ITB	2
Lymphoma	4
UC	1
Adenocarcinoma	285
Ileal ulceration of indeterminate etiology	3
Hyperplasia	
Lymphoma	51
Benign tumor(including polyps)	57
Unknown etiology	1
Others*	
Macroglobulinemia	956
Total	

*Endoscopic findings: mucosal pallor, with gyriform changes and villi disappearance.

出10例CD患者，本研究最终共纳入CD患者22例，非特异性回肠末端溃疡患者73例。两组患者初诊时临床特征见表3。CD组年龄(33.9±12.1)岁，非特异性回肠末端溃疡组年龄(49.3±15.1)岁，CD组初诊年龄显著小于非特异性回肠末端溃疡组($P<0.001$)。两组在性别、吸烟史、腹部手术史、特殊药物使用史等其他人口统计学特征方面均无显著差异。

将22例CD患者与73例非特异性回肠末端溃疡患者按照性别和年龄进行1∶1匹配，比较两组患者在初诊时的临床及内镜特征。结果发现，CD患者腹痛发生率显著高于非特异性回肠末端溃疡患者，且更易表现为纵行溃疡及回盲瓣受累的内镜特征(P均<0.05)。而两组在发热、腹泻、体重下降、消化道出血、肠梗阻病史、肛周病变病史方面差异无统计学意义(表4)。

2.5 外周血炎症相关指标在CD与非特异性回肠末端溃疡患者的诊断价值

比较两组患者初诊时的外周血炎症相关指标，发现CD组的PLT、NLR、PLR显著高于非特异性回肠末端溃疡组(P均< 0.05)，而HB、ALB则减低(P均< 0.05，表5)。此外，ROC曲线分析显示PLT、HB、ALB、NLR、PLR等指标辅助回肠末端溃疡诊断为CD的AUC值分别为0.71、0.76、0.74、0.69、0.75(图2A、B)，最佳临界值分别为231.00×10^9/L、130.21 g/L、37.30 g/L、1.86、168.39，灵敏度分别为63.6%、72.7%、95.5%、72.7%、86.4%，特异度分别为77.3%、77.3%、59.1%、72.7%、63.6%(表6)。上述5项指标联合辅助回肠末端溃疡诊断为CD的AUC值为0.83(图2C)。

3 讨 论

本研究发现，绝大多数回肠末端病变内镜下仅

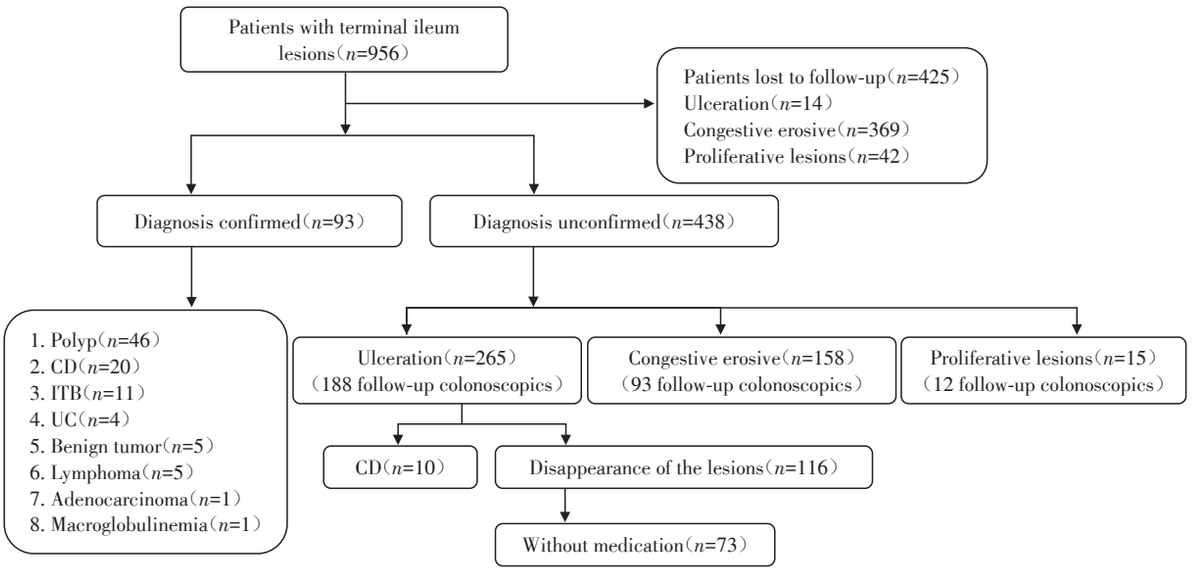


图1 回肠末端病变患者随访结果流程图

Figure 1 Flowchart of follow-up results for patients with terminal ileum lesions

表3 CD与非特异性回肠末端溃疡患者临床特征

Table 3 Clinical characteristics of patients with CD and nonspecific terminal ileum ulcer

Clinical characteristic	CD(n=22)	Nonspecific terminal ileumulceration(n=73)	P
Male/Female	14/8	38/35	0.464
Age(yaers,$\bar{x} \pm s$)	33.9 ± 12.1	49.3 ± 15.1	0.001
Smoking history[n(%)]	5(23)	15(21)	0.775
History of abdominal surgery[n(%)]	4(18)	5(7)	0.205
Medication history[n(%)]			
NSAID	2(9)	5(7)	0.661
Glucocorticoids	3(14)	6(8)	0.428

表4 CD与非特异性回肠末端溃疡患者的临床及内镜特征比较

Table 4 Comparison of clinical and endoscopic features between patients with CD and nonspecific terminal ileum ulcer

[n(%)]

Clinical and endoscopic characteristics	CD(n=22)	Nonspecific terminal ileum ulceration(n=22)	P
Clinical presentation			
Fever	0(0)	0(0)	1.000
Abdominal pain	22(100)	9(41)	<0.001
Diarrhea	7(32)	5(23)	0.736
Weight loss	3(14)	0(0)	0.233
Gastrointestinal bleeding	3(14)	0(0)	0.233
History of intestinal obstruction	0(0)	0(0)	1.000
History of perianal disease	0(0)	0(0)	1.000
Endoscopic findings			
Longitudinal ulcer	5(23)	0(0)	0.049
Intestinal stenosis	0(0)	0(0)	1.000
Ulcer involving the ileocecal valve	19(86)	3(14)	<0.001

表现为充血糜烂，多诊断为不明原因回肠炎，其他如溃疡、增生样病变中仅有少数可根据内镜、实验室、病理结果明确诊断（主要包括CD、ITB，UC、良性肿瘤、淋巴瘤、腺癌）。然而，相当比例的不明原因回肠末端病变患者复查肠镜时病变已消失。这提示，对于内镜下病情较轻，且病理结果无特殊的回肠末端病变患者，临床上可采取对症处理，定期复查，包括复查肠镜。

上述病变中溃疡性病变病因相对复杂，鉴别诊断较为困难，这可能与回肠末端溃疡形成的机制相关[12]。回肠末端溃疡的形成可能与回盲瓣功能异常、炎症、药物、肠道菌群失调等多种因素相关，其病因的诊断对后续治疗、随访具有重要价值[20-21]。病因明确的末端回肠溃疡，如CD所致的溃疡需早期明确诊断、积极治疗，以防严重并发症发生，而非特异性溃疡可通过对症治疗，定期复诊监测病情变化[22-23]。

本研究结果显示，与非特异性回肠末端溃疡患者相比，CD患者腹痛发生率更高，且更易表现为纵行溃疡及回盲瓣受累的内镜特征。此外，CD患者初诊时的HB、ALB显著低于非特异性回肠末端溃疡患者，而PLT、PLR、NLR等则增高，提示CD患者因肠道

表5 CD与非特异性回肠末端溃疡患者外周血炎症相关指标比较

Table 5 Comparison of peripheral blood inflammatory markers in patients with CD and nonspecific terminal ileum ulcer

Variable	CD(n=22)	Nonspecific terminal ileum ulceration(n=22)	P
PLT($\times 10^9$/L,$\bar{x} \pm s$)	286.9 ± 93.61	226.6 ± 57.33	0.014
HB(g/L,$\bar{x} \pm s$)	119.7 ± 16.89	136.1 ± 13.93	0.001
ALB(g/L,$\bar{x} \pm s$)	37.68 ± 4.146	41.42 ± 3.329	0.002
NLR[$M(P_{25},P_{75})$]	2.27(1.75,2.95)	1.74(1.37,2.74)	0.034
PLR($\bar{x} \pm s$)	213.3 ± 109.2	134.1 ± 44.27	0.003

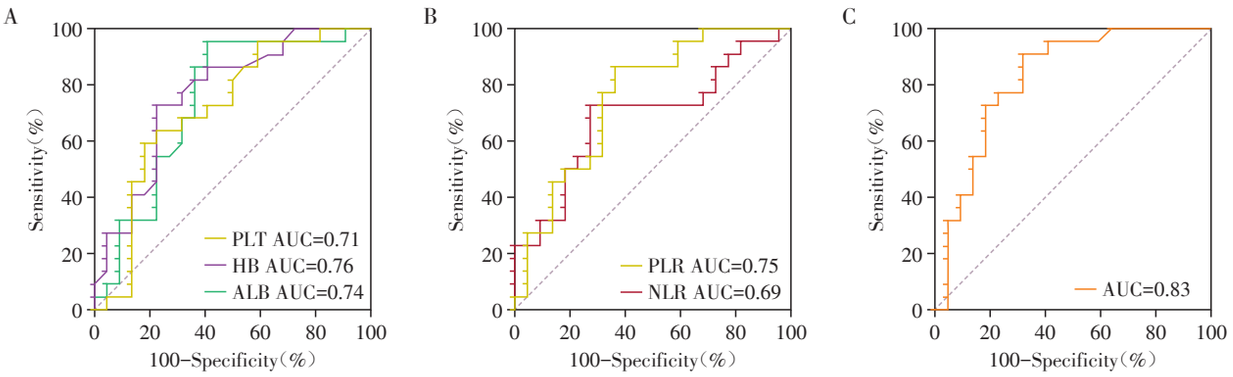
表6　外周血炎症相关指标诊断回肠末端溃疡为CD的效能

Table 6　The efficacy of peripheral blood inflammatory markers in diagnosing terminal ileum ulcer as CD

Variable	AUC	YI	Cut-off	Sensitivity（%）	Specificity（%）
PLT	0.71	0.40	231.00	63.60	77.30
HB	0.76	0.50	130.21	72.70	77.30
ALB	0.74	0.54	37.30	95.50	59.10
NLR	0.69	0.45	1.86	72.70	72.70
PLR	0.75	0.50	168.39	86.40	63.60

炎症负荷重、肠道吸收功能下降等多种因素更易合并贫血及营养不良等临床表现。ROC曲线提示，HB、PLR、NLR、ALB等对CD诊断均具有一定辅助价值，而PLT、HB、ALB、PLR、NLR等5项指标联合诊断回肠末端溃疡为CD的AUC值为0.83，价值更高。

研究表明，成年患者在确诊CD后30年行首次肠切除的累积风险为64%，而儿童患者在确诊CD后5年肠切除的累积风险为34%，可见早期诊断、



A: ROC curve analysis revealed that the AUC values of platelet count (PLT), hemoglobin level (Hb), and albumin level (Alb) for diagnosing terminal ileum lesions as Crohn's disease (CD) were 0.71, 0.76, and 0.74, respectively. B: ROC curve analysis demonstrated that the AUC values of the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) for diagnosing terminal ileum lesions as Crohn's disease (CD) were 0.69 and 0.75, respectively. C: ROC curves illustrating the combined diagnostic performance of platelet count (PLT), hemoglobin level (Hb), albumin level (Alb), neutrophil-to-lymphocyte ratio (NLR), and platelet-to-lymphocyte ratio (PLR) for terminal ileum lesions as Crohn's disease (CD).

图2　外周血指标辅助回肠末端溃疡诊断为CD的ROC曲线

Figure 2　ROC curve of peripheral blood indicators assisting the diagnosis of CD in terminal ileum ulcer

及时治疗、预防及控制并发症的重要性[24]。目前相关研究已提出了早期CD的概念[25]，旨在尽早干预，预防肠道结构的损伤，尽可能保护肠道正常的生理功能。

综上所述，回肠末端病变大多数为非特异性良性病变，预后较好。对于肠镜下首次发现孤立性回肠末端病变尤其是溃疡的患者，需关注其临床症状、内镜下表现及病理结果，同时结合外周血炎症相关指标改变，有助于孤立性回肠末端病变的病因诊断。由于本研究为单中心回顾性研究，且失访率较高，导致样本量较少，存在一定的偏倚，以上结论仍有待大样本、多中心前瞻性研究进一步证实。

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赵小静负责实验设计、数据收集和初步分析，参与论文撰写；张丽数据收集、数据处理和统计分析，协助撰写论文；王璐、王舒、林俊杰和张红杰提供研究思路，指导数据分析；马晶晶负责研究的整体指导和论文的修改完善。

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ZHAO Xiaojing was responsible for experimental design, data collection, and preliminary analysis, and participated in writing the paper; ZHANG Li handled data collection, processing, and statistical analysis, and assisted in writing the paper; WANG Lu, WANG Shu, LIN Junjie, and ZHANG Hongjie provided research ideas and guided data analysis; MA Jingjing provided overall guidance for the research and revised the paper.

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