论著·临床医学

幼年特发性关节炎不同亚型的超声表型特征及其疾病活动度评估的差异化策略探索:一项横断面研究

牟芳婷[1*],邱 敏[2*],尹春梅[1],唐 毅[1],杨春江[1],唐雪梅[3],陈镜宇[1],肖 欢[1] [1]重庆医科大学附属儿童医院超声科,儿童少年健康与疾病国家临床医学研究中心,儿童发育疾病研究教育部重点实验室,儿童代谢与炎症性疾病重庆市重点实验室,重庆;[2]重庆佑佑宝贝妇儿医院超声科,重庆;[3]重庆医科大学附属儿童医院风湿免疫科,重庆

[**摘要**] **目的** 幼年特发性关节炎(juvenile idiopathic arthritis,JIA)各亚型异质性显著,传统评估对亚临床滑膜炎识别不足。肌肉骨骼超声可敏感显示滑膜增厚、关节积液及异常血流信号,但不同亚型的超声表型特征尚缺乏系统比较。本研究旨在明确JIA不同亚型的特征性关节受累模式,为JIA的个体化超声评估提供依据。**方法** 采用横断面研究设计方案,纳入重庆医科大学附属儿童医院2023年11月至2024年10月收治的261例JIA患儿(女135例,占51.7%;年龄中位数9.0岁,病程中位数为21.5个月),涵盖多关节型(pJIA,77例)、全身型(sJIA,67例)、少关节型(oJIA,48例)、附着点炎相关关节炎(ERA,36例)及未分类型(uJIA,33例)5种亚型。按标准化方案对68个外周关节行超声检查,依据国际风湿病结局评价定义及儿童关节炎与风湿病研究联盟半定量评分体系评估灰阶(grayscale,GS)及能量多普勒(power doppler,PD)超声信号。由2名对临床资料设盲的肌骨超声医师独立完成检查与评分;另从40例患儿中随机抽取GS、PD静态图像各75幅,由2名医师独立评分以评价观察者间一致性。疾病活动度采用JADAS27评分评估(活动期JADAS27>1)。在主体横断面研究中,以亚型及超声评分为分组/预测变量,以关节超声阳性率、GS/PD评分及JADAS27定义的疾病活动状态为结局指标。采用层次聚类分析受累模式,χ^2检验筛选亚型间差异关节,Spearman相关分析评价超声评分与JADAS27的相关性,ROC曲线评价诊断效能。设置一个小样本(n=37)纵向随访评价治疗前后变化。**结果** ①评分体系观察者间一致性优:GS评分ICC=0.87(95%*CI*:0.78~0.95),PD评分ICC=0.85(95%*CI*:0.78~0.91)。共评估17 748个关节,检出滑膜炎829个(4.7%),PD阳性525个(3.0%)。②各亚型呈可区分受累模式:多关节型(polyarticular JIA,pJIA)广泛关节受累[(6.2±10.0)个/例],手部小关节突出(近端指间32.5%、掌指19.5%);全身型(sJIA)以大关节为主[(3.1±4.3个/例)],肩关节受累率19.4%,阳性者81.3%为sJIA;少关节型(oJIA)受累最少[(0.9±1.4个/例)],以膝为主(18.8%);附着点炎相关关节炎(enthesitis-related arthritis,ERA)为(1.5±1.3)个/例。肩、肘、腕、掌指、近端指间、远端指间关节亚型间差异有统计学意义(校正P<0.05)。手-腕关节特征提示pJIA的AUC为0.61;肩关节阳性提示sJIA特异度达0.99。③PD评分与JADAS27相关性(r=0.54,P<0.001)强于GS评分(r=0.48,P<0.001),pJIA中相关系数最高(r=0.71,P<0.001)。PD评分对活动期判别效能中等(AUC=0.67,95%*CI*:0.61~0.75,P<0.001),最佳截断值≥1.0,敏感度51%、特异度82%;pJIA中AUC=0.73,sJIA与oJIA均为0.71,ERA中无统计学意义(P=0.33)。④纵向随访PD可反映治疗效果:平均4.4个月的纵向随访中,32例活动期患儿的JADAS27评分由8.0(4.0,15.3)分降至3.5(1.0,8.1)分(P<0.001,SRM=−0.74);PD评分由

[**基金项目**] 重庆医科大学未来医学青年创新团队项目(W0114);重庆市自然科学基金(重庆市科学技术局)项目(CSTB2023NSCQ-MSX0660)

* 同等贡献者

[**通信作者**] 肖 欢,E-mail:huan106689210@163.com

2097-0927/Copyright © 2026,陆军军医大学(第三军医大学)。这篇开放获取文章遵循CC BY许可协议(https://creativecommons.org/licenses/by/4.0/)

引用格式:牟芳婷,邱敏,尹春梅,等. 幼年特发性关节炎不同亚型的超声表型特征及其疾病活动度评估的差异化策略探索:一项横断面研究[J]. 陆军军医大学学报,2026,48(18):2633-2644. DOI:10.16016/j.2097-0927.202606012.

Citation:Mou F T,Qiu M,Yin C M,*et al*. Ultrasonographic phenotypes of different juvenile idiopathic arthritis subtypes and differentiated strategies for disease activity assessment:a cross-sectional study[J]. J Army Med Univ,2026,48(18):2633-2644. DOI:10.16016/j.2097-0927.202606012.

1.0(0,3.0)分降至0(0,1.0)分(P=0.003,SRM=-0.25),GS评分变化无统计学意义(P=0.67)。**结论** JIA不同亚型呈现可区分的超声表型特征:肩关节阳性高度指向sJIA,腕/MCP/PIP阳性倾向pJIA,oJIA与ERA几乎不累及肩及手部小关节。PD评分可敏感反映疾病活动度与治疗反应,但其诊断效能存在亚型差异:在pJIA中与疾病活动度相关性最强,而在sJIA与ERA中相对较弱,需结合全身炎症指标综合判断。

[**关键词**] 幼年特发性关节炎;超声检查;滑膜炎;疾病严重程度指数;试验预测值;多普勒超声
[**中图法分类号**] R181.23;R445.2;R726.843 [**文献标志码**] A

Ultrasonographic phenotypes of different juvenile idiopathic arthritis subtypes and differentiated strategies for disease activity assessment: a cross-sectional study

Mou Fangting[1], Qiu Min[2], Yin Chunmei[1], Tang Yi[1], Yang Chunjiang[1], Tang Xuemei[3], Chen Jingyu[1], Xiao Huan[1]
[1]Department of Ultrasonography, [3]Department of Rheumatology and Immunology, National Clinical Research Center for Children and Adolescents' Health and Diseases, Key Laboratory of Ministry of Education for Child Development and Disorders, Chongqing Key Laboratory of Pediatric Metabolism and Inflammatory Diseases, Children's Hospital of Chongqing Medical University, Chongqing; [2]Department of Ultrasonography, Chongqing YouYou BaoBei Women's and Children's Hospital, Chongqing, China

[**Abstract**] **Objective** Juvenile idiopathic arthritis (JIA) encompasses highly heterogeneous subtypes, and conventional clinical assessment often fails to detect subclinical synovitis. Musculoskeletal ultrasound can sensitively depict synovial hypertrophy, joint effusion and abnormal blood flow signals, yet the ultrasound phenotypes of different subtypes have not been systematically compared. This study aims to clarify the characteristic joint involvement patterns of different JIA subtypes, providing evidence for individualized ultrasonographic assessment in JIA. **Methods** A cross-sectional study was conducted on 261 children with JIA (135 girls, 51.7%; median age 9.0 years; median disease duration 21.5 months) admitted to the Children′s Hospital of Chongqing Medical University between November 2023 and October 2024, encompassing 5 subtypes: polyarticular JIA (pJIA, n=77), systemic JIA (sJIA, n=67), oligoarticular JIA (oJIA, n=48), enthesitis-related arthritis (ERA, n=36), and undifferentiated JIA (uJIA, n=33). Ultrasonography was performed on 68 peripheral joints according to a standardized protocol. Grayscale (GS) synovitis and power Doppler (PD) signals were assessed using the Outcome Measures in Rheumatology definitions and the semiquantitative scoring system proposed by the Childhood Arthritis and Rheumatology Research Alliance. Examinations and scoring were independently completed by 2 musculoskeletal ultrasound physicians blinded to clinical data. Additionally, 75 GS and 75 PD static images were randomly selected from 40 children for independent scoring by 2 physicians to evaluate interobserver agreement. Disease activity was evaluated using the JADAS27 score (active disease defined as JADAS27 >1). In the main cross-sectional analysis, JIA subtype and ultrasound scores served as grouping/predictor variables, while joint-level ultrasound positivity rate, GS/PD scores, and disease activity state defined by JADAS27 served as outcome measures. Hierarchical clustering analysis was carried out to analyze involvement patterns, *Chi*-square test to identify joints with significant differences across subtypes, Spearman correlation analysis to evaluate the correlations between ultrasound scores and JADAS27, and ROC curve analysis to assess diagnostic performance. A small-sample longitudinal follow-up subset (square test to identify joints with significant differences across subtypes, Spearman correlation analysis to evaluate the correlations between ultrasound scores and JADAS27, and ROC curve analysis to assess diagnostic performance. A small-sample longitudinal follow$n$=37) was included to evaluate the changes before and after treatment. **Results** ①The interobserver agreement of the scoring

system was excellent, with intraclass correlation coefficients of 0.87 (95%*CI*: 0.78 to 0.95) for GS scores and 0.85 (95%*CI*: 0.78 to 0.91) for PD scores. A total of 17 748 joints were evaluated, with synovitis detected in 829 joints (4.7%) and PD positivity in 525 joints (3.0%). ② Distinct patterns of joint involvement were observed across subtypes: pJIA showed extensive polyarticular involvement (6.2±10.0 joints per case), with prominent small-joint involvement in the hands (proximal interphalangeal 32.5%, metacarpophalangeal 19.5%); sJIA predominantly involved large joints (3.1±4.3 joints per case), with shoulder involvement in 19.4% of patients (81.3% of those with shoulder involvement had sJIA); oJIA had the fewest involved joints (0.9±1.4 per case), predominantly the knee (18.8%); ERA had a mean of 1.5±1.3 involved joints per case. Significant differences across subtypes were found in the shoulder, elbow, wrist, metacarpophalangeal, proximal interphalangeal, and distal interphalangeal joint (adjusted $P<0.05$). The hand-wrist joint feature (positivity in wrist/MCP/PIP) yielded an AUC value of 0.61 for identifying pJIA; shoulder joint positivity showed a specificity of 0.99 for sJIA. PD scores were correlated more strongly with JADAS27 score ($r=0.54$, $P<0.001$) than GS scores ($r=0.48$, $P<0.001$), with the highest correlation coefficient observed in pJIA ($r=0.71$, $P<0.001$). ③ PD scores demonstrated moderate diagnostic performance for discriminating active disease (AUC=0.67, 95%*CI*: 0.61 to 0.75, $P<0.001$), with an optimal cutoff of ≥1.0, a sensitivity of 51% and a specificity of 82%; the AUC value was 0.73 in pJIA, 0.71 in both sJIA and oJIA, and not statistically significant in ERA ($P=0.33$). ④ Longitudinal follow-up showed that PD scores could reflect treatment response. During a mean follow-up of 4.4 months in 32 patients with active disease at baseline, the JADAS27 score was decreased from 8.0 (4.0, 15.3) to 3.5 (1.0, 8.1) ($P<0.001$, SRM=−0.74); PD scores were decreased from 1.0 (0, 3.0) to 0 (0, 1.0) ($P=0.003$, SRM=−0.25), whereas GS scores showed no significant change ($P=0.67$). **Conclusion** Distinct ultrasonographic phenotypes are identified across JIA subtypes: shoulder positivity strongly points to sJIA, wrist/MCP/PIP positivity tends to pJIA, while oJIA and ERA rarely involve the shoulder or small joints of the hands. The PD score can sensitively reflect disease activity and treatment response, but its diagnostic performance varies among subtypes: strongest correlation with disease activity in pJIA, whereas relatively weak in sJIA and ERA, requiring comprehensive assessment in considering systemic inflammatory indicators.

[**Key words**] juvenile idiopathic arthritis; ultrasonography; synovitis; severity of illness index; predictive value of tests; Doppler ultrasonography

Mou Fangting and Qiu Min contributed equally to the article. Supported by the Project for Youth Innovation Group in Future Medicine of Chongqing Medical University (W0114), and the Natural Science Foundation of Chongqing (Chongqing Science and Technology Bureau) (CSTB2023NSCQ-MSX0660).
Corresponding author: Xiao Huan, E-mail: huan106689210@163.com

幼年特发性关节炎(juvenile idiopathic arthritis,JIA)是儿童最常见的慢性炎性关节病,以16岁前发病、病因未明、持续6周以上的关节炎为特征,全球患病人数超过200万[1-2]。按国际风湿病学会联盟(international league of associations for rheumatology,ILAR)分类标准可分为7个亚型,各亚型在发病机制、关节受累模式、治疗反应及预后方面存在显著异质性[3-4]。故准确识别不同亚型的关节受累特征对精准诊断与个体化治疗具有重要意义。然而,传统评估主要依赖关节查体与实验室指标,存在观察者间差异较大、对亚临床及深部关节炎症识别不足等局限[5-6],难以满足JIA精细化管理需求。

肌肉骨骼超声(musculoskeletal ultrasound,MSUS)具备无创、可重复、实时动态等优势,能敏感显示滑膜增生、关节积液及异常血流信号,发现临床查体难以察觉的亚临床炎症,已成为JIA评估的重要影像学手段[7-9]。近年来,国际风湿病结局评价(outcome measures in rheumatology,OMERACT)儿科超声工作组与儿童关节炎和风湿病研究联盟(childhood arthritis and rheumatology research alliance,CARRA)相继建立了适用于儿童的滑膜炎标准定义与半定量评分体系,为超声在JIA中的定量化应用奠定了基础[10-13]。

然而,现有研究多为小样本,评估关节数量有限,对不同亚型超声表型的系统比较尚不充分,标准化评分体系在较大样本中的可靠性及其与疾病活动度的关系亦有待验证[14-18]。基于此,本研究对261例JIA患儿的68个外周关节进行系统超声评估,旨在明确不同亚型的特征性关节受累模式、验证标准化超声评分体系的观察者间可靠性,并分析超声评分与疾病活动度的相关性,以期为JIA患儿的个体化超声评估提供依据。

1 资料与方法

1.1 研究对象

本研究采用横断面研究设计方案,分组变量为JIA亚型及超声半定量评分;主要结局指标为各关节超声阳性率、PD/GS评分,以及由JADAS27评分定义的疾病活动状态(活动期*vs*缓解期);次要结局指标为JADAS27连续变量及其亚组分项(AJC、PhGA、ESR)。同时,在主体横断面设计中嵌套一个小样本(n=37)前瞻性纵向随访。研究对象为2023年11月至2024年10月在重庆医科大学附属儿童医院收治的JIA患儿。纳入标准:①年龄1~16岁;②符合ILAR JIA分类标准;③临床资料完整。排除标准:①合并其他风湿性疾病或感染性关节病;②不能配合超声检查;③近4周内接受关节腔内注射治疗;④入组前近4周内接受大剂量糖皮质激素冲击治疗者。对于全身型JIA(systemic JIA,sJIA),无论就诊时是否存在活动性关节炎表现,凡符合ILAR分类标准者均纳入,最终纳入261例JIA患儿。患儿监护人均知情同意。研究经重庆医科大学附属儿童医院伦理委员会批准[伦理审查(科研)2023-490],并在国家医学研究登记备案信息系统备案(MR-50-25-012842)。

1.2 临床资料采集与疾病活动度评估

所有临床检查均由1名具有10年小儿风湿病专科经验的医师完成,对68个外周关节进行系统评估。疾病活动度采用JADAS27评分(Juvenile Arthritis Disease Activity Score-27)[20],包括活动关节计数(active joint count,AJC)、医师总体评估(physician global assessment,PhGA)、患者/家长总体评估(patient/parent global assessment,PtGA)和红细胞沉降率(erythrocyte sedimentation rate,ESR)。同时收集年龄、性别、JIA亚型、病程、类风湿因子(rheumatoid factor,RF)、抗核抗体(antinuclear antibody,ANA)及用药情况。全部亚型均采用统一的JADAS27阈值区分疾病活动期与缓解期:JADAS27>1为活动期,≤1为缓解期(临床非活动);后续ROC分析中活动/缓解的界定即基于此统一标准。

1.3 超声检查、灰阶与能量多普勒评分及一致性评价

采用GE Logiq 11和Logiq e超声仪,配备7~18 MHz高频线阵探头。检查由2名具有10年以上儿童肌肉骨骼超声经验、且对临床资料不知情的医师独立完成,同时采集灰阶(grayscale,GS)和能量多普勒(power doppler,PD)超声图像。PD参数设置为脉冲重复频率0.4~0.6 kHz、低壁滤波,彩色增益调至刚好消除背景噪声(即骨皮质表面及深部无杂散信号),以提高低速血流的检出敏感性。为评价超声评分的观察者间一致性,由上述2名肌骨超声医师对随机抽取的150幅静态图像(源自40例患儿,GS、PD各75幅,覆盖全部关节类型及不同病变严重程度,且GS、PD均含0~3级)进行独立盲法评分,计算组内相关系数(intraclass correlation coefficient,ICC)及95%置信区间。ICC判定标准为:0.75~1.00为优,0.60~0.74为良好,0.40~0.59为中等,<0.40为差[23]。结果显示,GS和PD超声信号评分的观察者间一致性均较高,ICC分别为0.87(95%*CI*:0.78~0.95)和0.85(95%*CI*:0.78~0.91),各关节ICC介于0.85~0.93之间。

每例患儿均按标准化方案系统评估双侧68个外周关节,涵盖肩、肘、腕、掌指(metacarpophalangeal,MCP)、近端指间(proximal interphalangeal,PIP)、远端指间(distal interphalangeal,DIP)、髋、膝、踝(含距舟及距下关节)、跖趾(metatarsophalangeal,MTP)及趾间关节,扫查切面与图像采集均参照Vega-Fernandez等[21]和Sande等[22]的标准化方案。各关节依据OMERACT标准化定义[11]识别GS及PD超声信号,并按CARRA半定量评分体系[21]分级:每个关节经多个标准化切面扫查,逐切面将GS(综合滑膜增生与积液的灰阶滑膜炎等级)与PD信号分别评为0~3分,取各切面评分的平均值作为该关节的GS、PD评分。患者层面的GS、PD分别为68个关节相应评分之和(各0~204分),总超声评分为二者之和,理论范围0~408分。单个关节的超声阳性定义为任一切面GS≥2或PD≥1。所有患儿均在一次中完成68个外周关节评估,未使用镇静、未分次完成;因配合度不足未能完成全部关节评估者不予纳入。

1.4 统计学分析

采用IBM SPSS Statistics 26.0与Python 3.8进行统计分析。经正态性检验,符合正态分布的连续变量以$\bar{x}\pm s$表示,非正态分布数据以$M(P_{25},P_{75})$表示,计数资料以频数(%)表示。连续变量的亚型间比较采用Kruskal-Wallis H检验,计数资料(含关节受累率)比较采用χ^2检验,必要时辅以Fisher确切概率法,对亚型间多个关节(组)受累率的比较以Benjamini-Hochberg法进行错误发现率(false discovery rate,FDR)校正。关节受累模式采用层次聚类分析(各关节检出率经Z值标准化)。超声评分与JADAS27的相关性采用Spearman秩相关分析,诊断效能采用受试者工作特征(receiver operating characteristic,ROC)曲线评价。纵向随访资料的治疗前后比较为探索性分析;为避免基线缓解者稀释治疗反应,疗效评价限于基线处于疾病活动期(JADAS27>1)的随访患儿,组内前后差异采用配对Wilcoxon符号秩检验,并以标准化反应均值(standardized response mean,SRM)评价变化幅度,SRM≥0.20、≥0.50、≥0.80分别代表小、中、大效应。P<0.05为差异有统计学意义。

2 结果

2.1 一般资料

共纳入261例JIA患儿,其中女135例(51.7%),年龄中位数为9.0(5.0~12.0)岁,病程中位数为21.5(12.0~39.0)月。各亚型分布为:多关节型(polyarticular JIA,pJIA)77例(29.5%)、全身型(systemic JIA,sJIA)67例(25.7%)、少关节型(oligoarticular JIA,oJIA)48例(18.4%)、附着点炎相关关节炎(enthesitis-related arthritis,ERA)36例(13.8%)及未分类型(undifferentiated JIA,uJIA)33例(12.6%)。RF阳性20例(7.7%),ANA阳性45例(17.2%)。196例(75.1%)处于疾病活动期;220例(84.3%)接受改善病情抗风湿药(disease-modifying antirheumatic drugs,DMARDs)治疗,146例(55.9%)接受生物制剂治疗(表1)。

2.2 不同JIA亚型的关节受累模式差异显著

共评估17 748个关节(261×68关节)。超声检出滑膜炎829处(4.7%),其中PD阳性525处(3.0%)。不同JIA亚型在受累关节数、受累部位及分布方面差异显著(图1、表2)。pJIA表现为广泛多关节受累[(6.2±10.0)个/例],51.9%存在至少一对对称关节受累;手部小关节受累突出,PIP、MCP关节超声阳性率分别为32.5%和19.5%,肘、膝、腕等大关节亦较高受累(分别为39.0%、32.5%、31.2%)。sJIA主要累及大关节[(3.1±4.3)个/例],以踝、腕受累率相对较高(均为29.9%),肩关节为19.4%。oJIA受累关节最少[(0.9±1.4)个/例],呈选择性大关节受累,膝关节受累最常见(18.8%),其次为踝关节(16.7%)。ERA受累(1.5±1.3)个/例,膝关节超声阳性率相对较高(22.2%),其次为PIP关节(19.4%),MCP关节未检出阳性。uJIA受累相对分散,以膝关节相对多见(21.2%)。

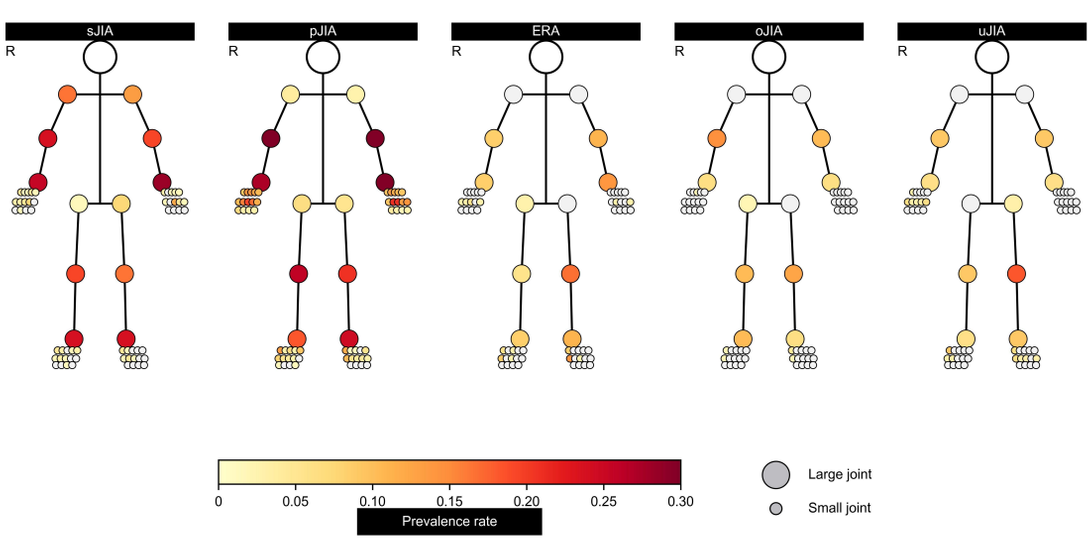


图1 不同JIA亚型的关节受累分布

Figure 1 Distribution of joint involvement across different JIA subtypes

表1 JIA患儿基线人口学及临床特征[例(%),$M(P_{25},P_{75})$,$\bar{x}\pm s$]

Table 1 Baseline demographic and clinical characteristics of children with JIA [n(%),$M(P_{25},P_{75})$,$\bar{x}\pm s$]

Items	Total (n=261)	Follow-up subcohort at baseline (n=37)	Follow-up subcohort at endpoint (n=37)	P
Demographics				
Female	135.00 (51.72)	18.00 (48.65)		
Age/years	9.00 (5.00,12.00)	7.00 (4.00,12.00)		
Disease characteristics				
Disease duration/months	21.50 (12.00,39.00)	17.00 (12.00,36.00)	18.00 (11.00,39.00)	
Follow-up interval/months			4.40±2.40	
JIA subtype				
sJIA	67.00 (25.67)	9.00 (24.32)		
pJIA	77.00 (29.50)	13.00 (35.14)		
oJIA	48.00 (18.39)	9.00 (24.32)		
ERA	36.00 (13.79)	1.00 (2.70)		
uJIA	33.00 (12.64)	5.00 (13.51)		
Laboratory indicators				
ANA positive	45.00 (17.24)	6.00 (16.22)		
RF positive	20.00 (7.66)	5.00 (13.51)		
ESR/(mm/h)	3.00 (2.00,5.00)	3.00 (2.00,5.70)	3.00 (2.00,4.00)	0.43
CRP/(mg/L)	0 (0,1.65)	0 (0,1.12)	0 (0,0)	0.03
Treatment				
NSAIDs	103.00 (39.46)	21.00 (56.76)	19.00 (51.35)	
DMARDs	220.00 (84.29)	36.00 (97.30)	35.00 (94.60)	
Biologics	146.00 (55.94)	22.00 (59.46)	22.00 (59.46)	
Disease activity				
Active	196.00 (75.10)	32.00 (86.49)	25.00 (67.57)	
Remission	65.00 (24.90)	5.00 (13.51)	12.00 (32.43)	
AJC	1.00 (0,3.00)	2.00 (0,4.00)	0 (0,2.00)	<0.01
JADAS27	4.20 (2.00,9.00)	7.20 (2.30,14.00)	3.00 (1.00,8.10)	<0.01
PhGA	2.00 (1.00,4.00)	3.00 (2.00,4.00)	2.00 (1.00,3.00)	0.01
PtGA	1.00 (0,3.00)	2.00 (1.00,3.00)	1.00 (0,2.00)	0.02

JIA: juvenile idiopathic arthritis; sJIA: systemic JIA; pJIA: polyarticular JIA; oJIA: oligoarticular JIA; ERA: enthesitis-related arthritis; uJIA: undifferentiated JIA; ANA: antinuclear antibody; RF: rheumatoid factor; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; NSAIDs: non-steroidal anti-inflammatory drugs; DMARDs: disease-modifying antirheumatic drugs; AJC: active joint count; JADAS27: Juvenile Arthritis Disease Activity Score-27; PhGA: physician global assessment; PtGA: patient/parent global assessment

对各亚型的关节检出率进行Z值标准化后行层次聚类,共识别出4类特征性关节簇(图2):簇1为常见受累关节(膝、踝、腕),簇2为pJIA特征性关节(PIP、MCP),簇3为sJIA偏好关节(肩、肘、髋),簇4为少见受累关节(足部小关节及DIP)。其中,pJIA的PIP、MCP关节簇Z值明显升高(>2.0),sJIA的肩关节Z值达1.8。

2.3 特征关节受累对JIA亚型具有提示价值

经FDR校正后,肩、肘、腕、MCP、PIP及DIP关节组在五亚型间的受累率差异有统计学意义(校正P<0.05),而髋、膝、踝、MTP、PTP、DTP等关节组差异无统计学意义。其中,pJIA的肘(39.0%)、PIP(32.5%)、腕(31.2%)及MCP(19.5%)受累率相对较高,sJIA的肩关节受累率(19.4%)显著高于其他亚型(其余亚型均≤3.9%)。指向性分析显示,肩关节阳性者中81.3%为sJIA(相对倍数12.55),MCP、PIP阳性者亦较多指向pJIA(分别为62.5%、52.1%);oJIA、ERA与uJIA则未见稳定的特征关节。探索性ROC分析中,基于指向性更强的手-腕关节特征,以“腕、MCP、PIP任一关节阳性”提示pJIA的曲线下面积(area under the curve,AUC)

表2 不同JIA亚型关节受累模式比较[例(%),$\bar{x}\pm s$]

Table 2 Comparison of joint involvement patterns among different JIA subtypes [n(%), $\bar{x}\pm s$]

Parameter	pJIA (n=77)	sJIA (n=67)	oJIA (n=48)	ERA (n=36)	P
Overall joint involvement					
No. of involved joints	6.2±10.0	3.1±4.3	0.9±1.4	1.5±1.3	<0.001
Specific joint involvement					
PIP	32.5	19.4	0	19.4	<0.001
MCP	19.5	10.4	2.1	0	0.002
Elbow	39.0	25.4	14.6	13.9	0.005
Knee	32.5	25.4	18.8	22.2	0.351
Ankle	27.3	29.9	16.7	13.9	0.159
Wrist	31.2	29.9	6.2	13.9	0.003
Shoulder	3.9	19.4	0	0	<0.001
Distribution pattern					
Symmetric involvement	51.9	46.3	14.6	19.4	<0.001

PIP: proximal interphalangeal; MCP: metacarpophalangeal

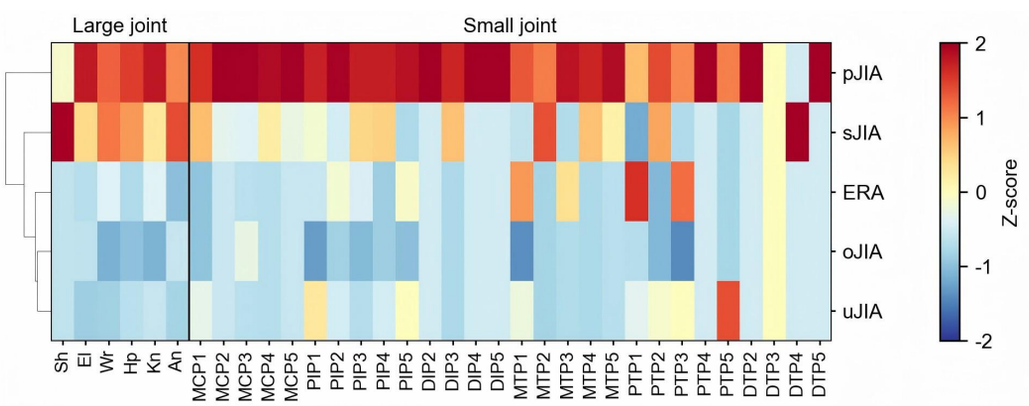


图2 不同JIA亚型各关节组的超声受累率

Figure 2 Ultrasound involvement rates of joint groups in different JIA subtypes

为0.61(敏感度0.48、特异度0.73);肩关节阳性提示sJIA的AUC为0.59(敏感度0.19、特异度0.99,图3)。

2.4 PD评分与疾病活动度的相关性强于GS评分

JIA患儿超声评分与多项临床指标存在显著相关性。与GS评分相比,PD评分与JADAS27(r=0.54,P<0.001)、PhGA(r=0.50,P<0.001)和AJC(r=0.47,P<0.001)的相关性更强。分亚型分析显示,PD评分与JADAS27的相关性在pJIA中最强(r=0.71,P<0.001),其次为sJIA(r=0.55,P<0.001),在ERA中相对较弱(r=0.39,P=0.04)。总体上,PD评分在各亚型中的临床相关性均优于GS评分(图4)。

ROC曲线分析结果显示,在GS、PD及总超声评分中,PD评分对活动期与缓解期的判别效能相对最高(AUC=0.67,P<0.001,图5)。分亚型分析表明,PD评分在pJIA中的诊断效能最高(AUC=0.73),其次为sJIA(AUC=0.71)和oJIA(AUC=0.71),而在ERA中的诊断价值无统计学意义(AUC=0.61,P=0.33)。PD评分最佳截断值为≥1.0,对应敏感度51%,特异度82%。

2.5 PD评分可反映治疗后疾病活动变化

37例完成随访的JIA患儿随访间隔为4.4±2.4个月,其中32例基线处于疾病活动期。治疗后,这32例患儿的临床指标明显改善:JADAS27由8.0(4.0,15.3)分降至3.5(1.0,8.1)分(P<0.001,SRM=−0.74),AJC由3.0(0.8,4.5)个降至1.0(0,2.3)个(P=0.001,SRM=−0.63),CRP由0(0,10.3) mg/L降至0 mg/L(P=0.002)。超声参数的改善幅度小于临床指标。

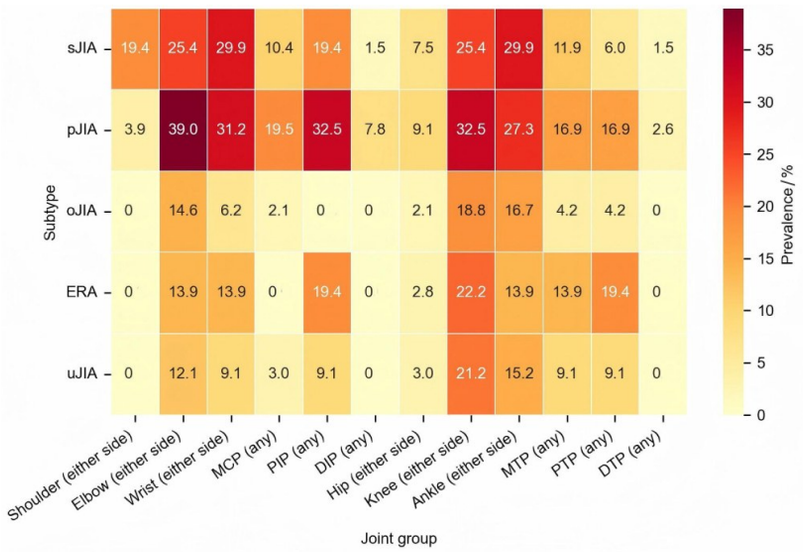
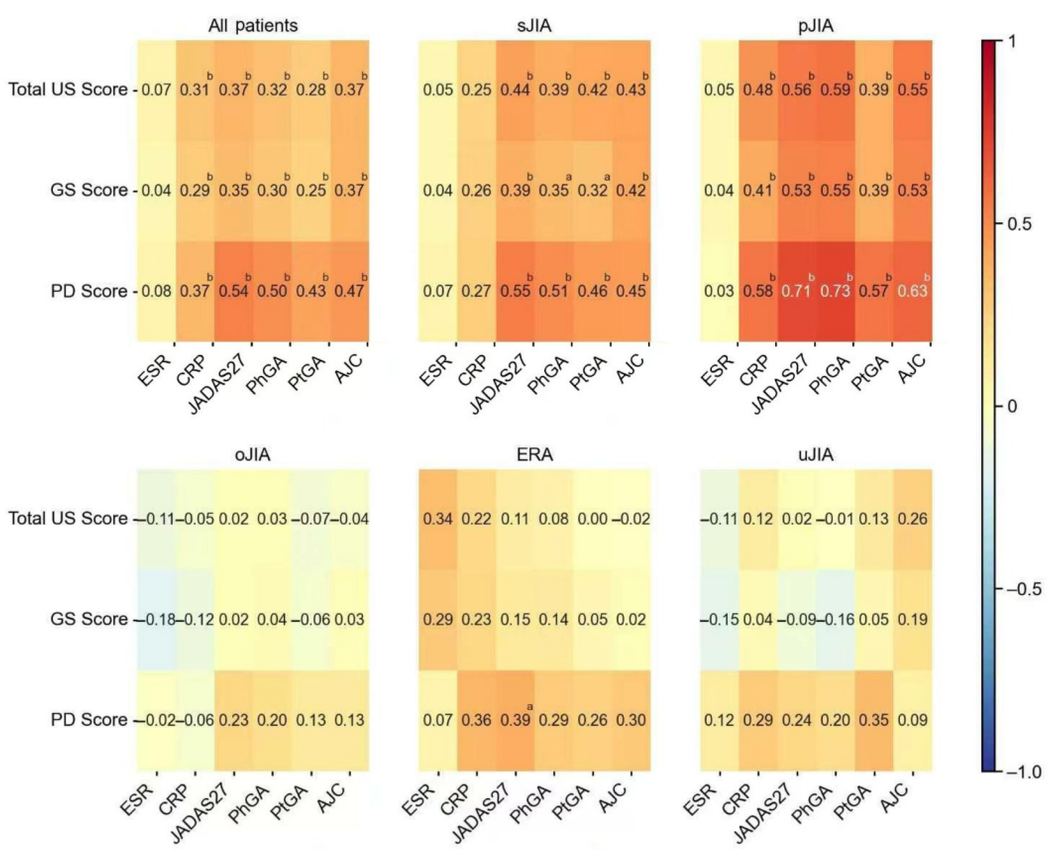


图3 不同JIA亚型各关节组的超声受累率

Figure 3 Ultrasound involvement rates of joint groups in different JIA subtypes



a:P<0.05, b:P<0.01

图4 不同JIA亚型超声评分与临床指标的相关性

Figure 4 Correlation between ultrasound scores and clinical indicators in different JIA subtypes

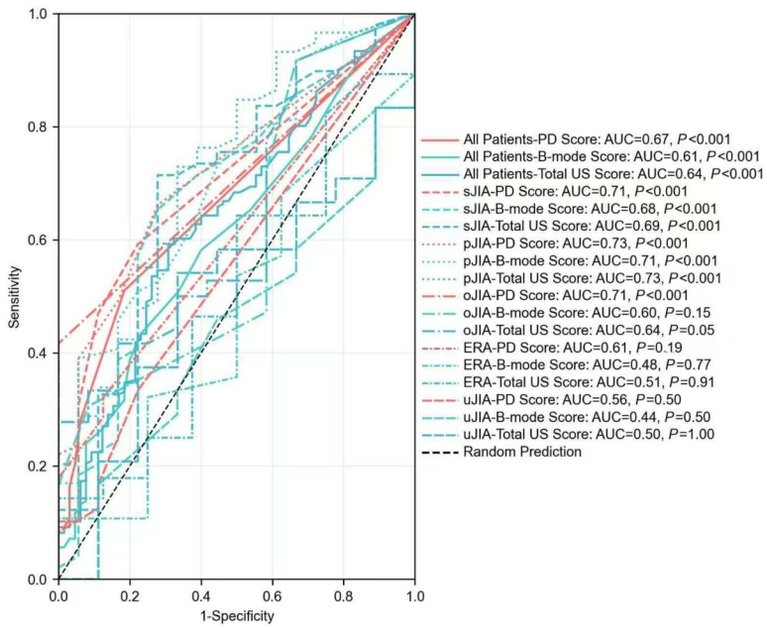


图5 不同JIA亚型超声评分对活动期疾病的诊断效能

Figure 5 Diagnostic performance of ultrasound scores for active disease in different JIA subtypes

PD评分由1.0(0,3.0)分降至0(0,1.0)分(P=0.003,SRM=−0.25);GS评分由5.5(3.8,9.5)分降至5.0(2.0,11.3)分(P=0.67,SRM=-0.16),总超声评分由6.0(5.0,12.3)分降至5.5(2.0,11.3)分(P=0.08,SRM=−0.20),二者均仅呈下降趋势,无统计学意义。PD评分的变化存在明显个体差异:17例(53.1%)下降、2例(6.3%)升高、13例(40.6%)无变化。

3 讨论

本研究在较大样本中系统评估了261例JIA患儿的68个外周关节。结果表明,标准化超声评分体系具有良好的观察者间可靠性,这与近期以全身MRI为参照的效度验证研究相互印证[13,24],为超声在JIA中的定量应用提供了方法学保障。在此基础上,本研究最值得关注的发现是:不同JIA亚型呈现出可区分的特征性关节受累模式,使超声的作用从单纯的炎症探测延伸至亚型判别的辅助。同时,超声评分(尤其是PD评分)与疾病活动度的相关性及其纵向变化,均随亚型而异。超声在JIA中的应用因而不宜采用统一模式,而应依据亚型特点实施差异化策略,为JIA的精细化诊断与管理提供影像学支撑。

3.1 特征关节受累模式的亚型判别价值

不同JIA亚型呈现出可区分的特征性关节受累模式,使超声的作用从单纯的炎症探测延伸至亚型判别的辅助。既往超声多用于确认已知关节的炎症,而本研究提示,特定关节的受累与否可为亚型判别提供方向性线索,这与近期研究关于JIA存在特征性关节分布、其信息价值超越单纯关节计数的观点相印证[25-26]。

具体而言,对临床怀疑sJIA或pJIA的患儿,或体格检查发现肩关节、手部小关节(MCP、PIP)异常者,可优先扫查上述关节:肩关节阳性对sJIA指向性强(本队列阳性者81.3%为sJIA),MCP、PIP阳性则支持pJIA。更具鉴别意义的是排除线索,oJIA、ERA几乎不累及肩关节及手部小关节(两者肩关节受累率均≤3.9%,ERA的MCP受累率为0),故这些关节一旦阳性,可基本排除oJIA与ERA。此外,pJIA特有的对称性受累(51.9%,显著高于oJIA的14.6%)及肘关节高受累率(39.0%),亦有助于区分多关节型与少关节型[6]。该策略具有“高特异度、低敏感度”的特点,以肩关节为例,其阳性对sJIA特异度达0.99、敏感度仅0.19,故超声阳性可提示、阴性不能排除,不能替代基于ILAR标准的临床分型,其确切效能亦有待多中心前瞻性研究验证。

3.2 PD评分反映疾病活动度的敏感性优势

本研究中,PD评分与疾病活动度的相关性整体强于GS评分。这一差异有其病理基础:活动性滑膜炎以血管翳形成和滑膜新生血管增生为特征,滑膜内低

速血流增多,而PD信号正是这一活动性血管生成过程的影像学体现,故与即时炎症活动耦合紧密[27-28];相比之下,GS所示的滑膜增厚在炎症控制后仍可因纤维化和滑膜残余增生而持续存在,与即时活动度的对应相对滞后[29]。这从机制上解释了PD较GS更敏感地反映疾病活动度与治疗反应。不过,ROC分析显示PD评分对活动期与缓解期的整体判别效能仅为中等(AUC=0.67),对应敏感度亦不高(51%),提示PD评分虽是相对最优的影像学活动度指标,却不宜单独作为活动、缓解的判别工具,仍应与JADAS27等临床指标联合应用。

3.3 超声评分临床意义的亚型差异及其机制

超声评分与疾病活动度的相关性存在显著的亚型差异,以pJIA最强(r=0.71)、sJIA次之(r=0.55)、ERA较弱(r=0.39),这与各亚型的免疫发病机制及疾病特点相关。pJIA属抗原驱动、以T淋巴细胞(Th1/Th17)介导的适应性免疫为主的自身免疫性疾病,关节滑膜是其主要炎症靶位、且受累关节数多,故外周关节超声评分能较好反映其整体疾病活动[30]。oJIA虽同属适应性免疫机制,但其受累关节数少(本研究平均仅0.9个/例)、疾病负担轻,超声评分的动态范围有限,与JADAS27的相关性较弱(r=0.23),超声更适合用于其局部关节炎症的直接评估而非整体活动度的定量。sJIA则本质上是以IL-1、IL-6等驱动的固有免疫激活和全身炎症为主的自身炎症性疾病,关节炎并非其必发或主导表现[4,31];本研究纳入全部sJIA患儿,其中95.5%(64/67)可检出超声滑膜炎,提示即便在以全身症状为主导的sJIA中亚临床关节受累亦相当普遍,仅4.5%完全阴性,但其疾病活动更多由全身炎症成分决定[32],单纯外周关节超声难以充分反映。至于ERA,其病变常累及附着点及中轴关节,外周关节超声仅能反映其部分病变,故相关性最弱。因此,超声(尤其PD)评估在pJIA中可作为整体活动度监测的可靠手段,在oJIA中宜侧重局部关节评估,而在sJIA与ERA中则须结合全身炎症指标或附着点、中轴评估综合判断。

3.4 PD评分对治疗反应的监测价值

纵向随访结果进一步凸显了PD评分的价值。经治疗后,PD是唯一显著下降的超声指标(SRM=-0.25),而GS及总超声评分仅呈非显著下降趋势,说明PD能更敏感地反映治疗后炎症活动的消退,可作为疗效监测的主要影像学指标。GS与总评分随访中未见显著下降,则提示影像学缓解可滞后于临床缓解,即临床缓解状态下仍可存在持续的亚临床滑膜炎。结合既往前瞻性研究中临床缓解期PD阳性者复发风险升高的证据[33-34],对临床缓解但PD持续阳性的患儿,减停药决策应更为审慎。由此,超声与临床评估的不一致不应简单视为治疗失败,而应结合亚型、随访时程与个体病程综合解读。

综上,本研究通过对261例JIA患儿68个外周关节的系统超声评估,揭示了不同亚型间可区分的特征性关节受累模式,明确了肩、手部小关节等特征关节对亚型的指向与排除价值,为超声辅助JIA亚型判别提供了新的依据;同时证实PD评分是反映疾病活动度与治疗反应的敏感指标,且其临床意义因亚型而异。研究表明,超声在JIA中的价值已不限于发现关节炎症,更可延伸至辅助亚型判别与个体化活动度监测;其评估不应采用统一模式,而应依据亚型特点有的放矢。本研究亦存在一定局限:作为观察性、以横断面评估为核心的真实世界研究,未设健康对照或干预设计,且多数患儿评估时已接受治疗,故所示为治疗状态下的表型,其诊断效能与对亚型的判别价值仍需多中心、前瞻性研究进一步验证;对ERA、sJIA等复杂亚型,未来应整合外周关节超声、附着点超声及MRI等多模态手段,构建更全面的评估体系[35-36]。

利益冲突 本文所有作者声明不存在利益冲突

参考文献:

[1] Petty R, Southwood T, Manners P, *et al*. International League of Associations for Rheumatology classification of juvenile idiopathic arthritis: second revision, Edmonton, 2001[J]. J Rheumatol, 2004, 31(2): 390-392.

[2] Thierry S, Fautrel B, Lemelle I, *et al*. Prevalence and incidence of juvenile idiopathic arthritis: a systematic review [J]. Joint Bone Spine, 2014;81(2):112-117.DOI:10.1016/j.jbspin.2013.09.003.

[3] Ravelli A, Consolaro A, Horneff G, *et al*. Treating juvenile idiopathic arthritis to target: recommendations of an international task force[J]. Ann Rheum Dis, 2018;77(6):819-828. DOI:10.1136/annrheumdis-2018-213030.

[4] Martini A, Lovell D J, Albani S, *et al*. Juvenile idiopathic arthritis[J]. Nat Rev Dis Primers, 2022, 8: 5. DOI:10.1038/s41572-021-00332-8. DOI:10.1038/s41572-021-00332-8.

[5] Mehta S P, Kendall K M, Reasor C M. Virtual assessments of knee and wrist joint range motion have comparable reliability with face-to-face assessments [J]. Musculoskeletal Care,

2021;19(2):208-216. DOI:10.1002/msc.1525.

[6] Consolaro A, Giancane G, Alongi A, *et al*. Phenotypic variability and disparities in treatment and outcomes of childhood arthritis throughout the world: an observational cohort study[J]. Lancet Child Adolesc Heal, 2019, 3(4): 255-263. DOI:10.1016/S2352-4642(19)30027-6.

[7] Magni-Manzoni S, Epis O, Ravelli A, *et al*. Comparison of clinical versus ultrasound-determined synovitis in juvenile idiopathic arthritis[J]. Arthritis Rheum, 2009, 61(11): 1497-1504. DOI:10.1002/art.24823.

[8] Hemke R, Herregods N, Jaremko J L, *et al*. Imaging of juvenile idiopathic arthritis[J]. Radiologic Clin N Am, 2024, 62(5): 889-902. DOI:10.1016/j.rcl.2024.02.009.

[9] Collado P, Jousse-Joulin S, Alcalde M, *et al*. Is ultrasound a validated imaging tool for the diagnosis and management of synovitis in juvenile idiopathic arthritis? A systematic literature review[J]. Arthritis Care Res, 2012, 64(7): 1011-1019. DOI:10.1002/acr.21644.

[10] Collado P, Naredo E, Calvo C, *et al*. Assessment of the joint recesses and tendon sheaths in healthy children by high-resolution B-mode and power Doppler sonography[J]. Clin Exp Rheumatol, 2007, 25(6): 915-921.

[11] Roth J, Ravagnani V, Backhaus M, *et al*. Preliminary definitions for the sonographic features of synovitis in children[J]. Arthritis Care Res, 2017, 69(8): 1217-1223. DOI:10.1002/acr.23130.

[12] Collado P, Martire M V, Lanni S, *et al*. OMERACT International Consensus for Ultrasound Definitions of Tenosynovitis in Juvenile Idiopathic Arthritis: Systematic Literature Review and Delphi Process[J]. Arthrit Care Res, 2023, 75(11): 2277-2284. DOI:10.1002/acr.25159.

[13] Rossi-Semerano L, Breton S, Semerano L, *et al*. Application of the OMERACT synovitis ultrasound scoring system in juvenile idiopathic arthritis: a multicenter reliability exercise[J]. Rheumatology (Oxford), 2021, 60(8): 3579-3587. DOI:10.1093/rheumatology/keaa804.

[14] El Naggar T E, Nasef S I, Elshahaly M H, *et al*. Role of musculoskeletal ultrasonography in the assessment of disease activity in juvenile idiopathic arthritis children[J]. Egypt Rheumatologist, 2024, 46(3): 125-129. DOI: 10.1016/j.ejr.2024.04.004.

[15] Collado P, Naredo E, Calvo C, *et al*. Reduced joint assessment vs comprehensive assessment for ultrasound detection of synovitis in juvenile idiopathic arthritis[J]. Rheumatology, 2013, 52(8): 1477-1484. DOI: 10.1093/rheumatology/ket148.

[16] Vega-Fernandez P, Oberle E J, Henrickson M, *et al*. Musculoskeletal ultrasound and the assessment of disease activity in juvenile idiopathic arthritis[J]. Arthritis Care Res, 2023, 75(8): 1815-1820. DOI:10.1002/acr.25073.

[17] Snipaitiene A, Slegeryte A, Uktveris R, *et al*. The importance of ultrasound examination in care of juvenile idiopathic arthritis patients: 9 months follow-up study[J]. Front Pediatr, 2024, 12: 1414384. DOI: 10.3389/fped.2024.1414384.

[18] Shoop-Worrall S J W, MacIntyre V G, Ciurtin C, *et al*. Overlap of international league of associations for rheumatology and preliminary pediatric rheumatology international trials organization classification criteria for nonsystemic juvenile idiopathic arthritis in an established UK multicentre inception cohort[J]. Arthritis Care Res, 2024, 76(6): 831-840. DOI:10.1002/acr.25296.

[19] Grimes D A, Schulz K F. An overview of clinical research: the lay of the land[J]. Lancet, 2002, 359(9300): 57-61. DOI:10.1016/S0140-6736(02)07283-5.

[20] Consolaro A, Ruperto N, Bazso A, *et al*. Development and validation of a composite disease activity score for juvenile idiopathic arthritis[J]. Arthritis Rheum, 2009, 61(5): 658-666. DOI:10.1002/art.24516.

[21] Vega-Fernandez P, Ting T V, Oberle E J, *et al*. Musculoskeletal ultrasound in childhood arthritis limited examination: a comprehensive, reliable, time-efficient assessment of synovitis[J]. Arthritis Care Res, 2023, 75(2): 401-409. DOI:10.1002/acr.24759.

[22] Sande N K, Bøyesen P, Aga A B, *et al*. Development and reliability of a novel ultrasonographic joint-specific scoring system for synovitis with reference atlas for patients with juvenile idiopathic arthritis[J]. RMD Open, 2021, 7(2): e001581. DOI:10.1136/rmdopen-2021-001581.

[23] Koo T K, Li M Y. A guideline of selecting and reporting intraclass correlation coefficients for reliability research[J]. J Chiropr Med, 2016, 15(2): 155-163. DOI: 10.1016/j.jcm.2016.02.012.

[24] Sande N K, Kirkhus E, Lilleby V, *et al*. Validity of an ultrasonographic joint-specific scoring system in juvenile idiopathic arthritis: a cross-sectional study comparing ultrasound findings of synovitis with whole-body magnetic resonance imaging and clinical assessment[J]. RMD Open, 2024, 10(1): e003965. DOI: 10.1136/rmdopen-2023-003965.

[25] Borocco C, Anselmi F, Rossi-Semerano L. Contribution of ultrasound in current practice for managing juvenile

idiopathic arthritis[J]. J Clin Med, 2022, 12(1): 91. DOI: 10.3390/jcm12010091.

[26] Eng S W M, Aeschlimann F A, van Veenendaal M, *et al*. Patterns of joint involvement in juvenile idiopathic arthritis and prediction of disease course: a prospective study with multilayer non-negative matrix factorization[J]. PLoS Med, 2019, 16(2): e1002750. DOI: 10.1371/journal.pmed.1002750.

[27] Walther M, Harms H, Krenn V, *et al*. Correlation of power Doppler sonography with vascularity of the synovial tissue of the knee joint in patients with osteoarthritis and rheumatoid arthritis[J]. Arthritis Rheum, 2001, 44(2): 331-338. DOI: 10.1002/1529-0131(200102)44: 2<331:: aid-anr50>3.0.co;2-0.

[28] Walther M, Harms H, Krenn V, *et al*. Synovial tissue of the hip at power Doppler US: correlation between vascularity and power Doppler US signal[J]. Radiology, 2002, 225(1): 225-231. DOI:10.1148/radiol.2251011272.

[29] Naredo E, Bonilla G, Gamero F, *et al*. Assessment of inflammatory activity in rheumatoid arthritis: a comparative study of clinical evaluation with grey scale and power Doppler ultrasonography[J]. Ann Rheum Dis, 2005, 64(3): 375-381. DOI:10.1136/ard.2004.023929.

[30] Macaubas C, Nguyen K, Milojevic D, *et al*. Oligoarticular and polyarticular JIA: epidemiology and pathogenesis[J]. Nat Rev Rheumatol, 2009, 5(11): 616-626. DOI:10.1038/nrrheum.2009.209.

[31] Kessel C, Hedrich C M, Foell D. Innately adaptive or truly autoimmune: is there something unique about systemic juvenile idiopathic arthritis?[J]. Arthritis Rheumatol, 2020, 72(2): 210-219. DOI:10.1002/art.41107.

[32] Rosina S, Rebollo-Giménez A I, Tarantola L, *et al*. Defining criteria for disease activity states in systemic juvenile idiopathic arthritis based on the systemic juvenile arthritis disease activity score[J]. Arthritis Rheumatol, 2024, 76(9): 1446-1454. DOI:10.1002/art.42865.

[33] Miotto E Silva V B, Mitraud S A V, Furtado R N V, *et al*. Patients with juvenile idiopathic arthritis in clinical remission with positive power Doppler signal in joint ultrasonography have an increased rate of clinical flare: a prospective study[J]. Pediatr Rheumatol Online J, 2017, 15(1): 80. DOI:10.1186/s12969-017-0208-7.

[34] de Lucia O, Ravagnani V, Pregnolato F, *et al*. Baseline ultrasound examination as possible predictor of relapse in patients affected by juvenile idiopathic arthritis (JIA)[J]. Ann Rheum Dis, 2018, 77(10): 1426-1431. DOI:10.1136/annrheumdis-2017-211696.

[35] Gmuca S, Xiao R, Brandon T G, *et al*. Multicenter inception cohort of enthesitis-related arthritis: variation in disease characteristics and treatment approaches[J]. Arthritis Res Ther, 2017, 19(1): 84. DOI: 10.1186/s13075-017-1297-x.

[36] Hahn Y S. Enthesitis-related arthritis[J]. J Rheum Dis, 2018, 25(4): 221. DOI:10.4078/jrd.2018.25.4.221.

(收稿:2026-06-02;修回:2026-08-04)

(编辑 严 涵)