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超声联合手部滑膜炎与腱鞘炎判断 RA 患者的疾病活动度的可行性 *

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摘要 目的:探究超声联合手部滑膜炎与腱鞘炎判断 RA 患者的疾病活动度的可行性。**方法:**选择 2018 年 9 月至 2019 年 9 月我院收治的 103 例 RA 患者,采用 GS 和 PD 超声检查患者手部关节和腱鞘,比较超声指标与 DAS28-CRP 的相关性以及超声检查手部滑膜炎与联合检查手部滑膜炎和腱鞘炎对病情诊断情况的差异。**结果:**关节 GS 总分、关节 PD 总分、腱鞘 GS 总分、腱鞘 PD 总分、联合 GS 总分、联合 PD 总分与 DAS28-CRP 均显著相关($P<0.05$)。在基于 DAS28-CRP 的情况下,对比超声只检查手部滑膜炎与超声检查手部滑膜炎和腱鞘炎时发现:只存在腱鞘炎患者共有 9 名,即 9 名患者将被认为病情缓解,占有所有患者的 8.70%。**结论:**超声联合手部滑膜炎与腱鞘炎可以更准确地评估患者疾病活动度,减少误诊或遗漏的概率,值得在临床推广使用。

关键词:超声联合;滑膜炎;腱鞘炎;RA 患者;疾病活动度

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Feasibility of Ultrasound Combined with Handsynovitis and Tenosynovitis in Determination of Disease Activity of RA Patients*

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ABSTRACT Objective: To explore the feasibility of ultrasound combined with hand synovitis and tenosynovitis in the determination of the disease activity of RA patients. **Methods:** A total of 103 patients with RA, who were admitted to Second Affiliated Hospital of Nantong University from September 2018 to September 2019, were selected. The joint and tendon sheath of the patients were examined by GS and PD ultrasound. The correlation between ultrasound indexes and das28-crp was compared, and the difference between ultrasonic examination of hand synovitis and joint examination of hand synovitis and tenosynovitis were compared. **Results:** The total scores of GS, PD, GS, PD, GS and PD were significantly correlated with das28-crp ($P<0.05$). Based on das28-crp, the comparison of ultrasound examination of hand synovitis with ultrasound examination of hand synovitis and tenosynovitis showed that there were 9 patients with tenosynovitis only, that is, 9 patients would be considered as remission, accounting for 8.70% of all patients. **Conclusion:** Ultrasound combined with synovitis and tenosynovitis of hand can more accurately assess the disease activity of patients, reduce the probability of misdiagnosis or omission, which is worthy of clinical application.

Key words: Combined ultrasound; Synovitis; Tenosynovitis; RA patients; Disease activity

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前言

类风湿性关节炎(rheumatoid arthritis, RA)是继发于关节滑膜组织炎症的慢性炎症性疾病,这种关节炎症会导致结构损伤和残疾^[1-3]。美国风湿病学会(American College of Rheumatology, ACR)和欧洲抗风湿病联盟(european league against rheumatism, EULAR)最近强调了超声在风湿性关节炎诊断、监测疾病活动和治疗评价方面的作用^[4-7]。对早期 RA 的诊断并非

易事,部分不典型的早期患者常常被误诊、漏诊^[8,9]。目前常用超声检测 RA 患者的滑膜炎用于判断疾病活动度。Violeta Vlad 等人发现,RA 患者的腱鞘炎 US 评分可能与滑膜炎评分在描述疾病活动度和反应性上一样好^[10]。此外,在 RA 患者中,US 评估的腱鞘炎可能比 US 评估的滑膜炎更接近临床评估的缓解。目前国内外的研究中,鲜少将 RA 患者的滑膜炎和腱鞘炎联合评估。临床医生常用于判断疾病活动度的指标是 28 个关节疾病活动性评分(Disease Activity Score-28, DAS28)^[11]。本研

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究的目的是在检验超声检查结果与 DAS28 之间的相关性,并探究超声检查手部滑膜炎与检查手部的滑膜炎和腱鞘炎相比,是否低估了 RA 患者的疾病活动度。

1 资料与方法

1.1 一般资料

选择 2018 年 9 月至 2019 年 9 月南通大学第二附属医院风湿科门诊及住院的 RA 患者 103 例,其中男 24 例,女 79 例;年龄 25~78 岁,平均 58.3 ± 2.14 岁;病程 2~10 年,平均 4.38 ± 2.89 年。纳入标准:①符合 RA 分类诊断标准^[12];②均使用非生物疾病改良型抗风湿病药物治疗^[13]。排除标准:①急性或慢性活动性感染;②心力衰竭;③伴有其他弥漫性结缔组织病如系统性红斑狼疮、严重膝关节炎及干燥综合征等;④妊娠期、哺乳期及近期计划受孕的女性;⑤严重肝肾功能不全;⑥肿瘤或结核病史。

1.2 疾病的临床评估

我们搜集了病人的病程、28 个关节的疼痛数与肿胀数、视觉模拟评分的数值(范围 0-100)、C 反应蛋白(C-reaction protein,CRP)、红细胞沉降率(erythrocyte sedimentation rate,ESR)。由风湿科的一名主治医师和一名主任医师分别使用 DAS28 评估疾病活动度,得出结合 CRP 计算的 DAS28,即 DAS28-CRP,如果结果不一致,由两人协商后得到一致结果。本研究采用 DAS28-CRP 对病人进行分组,DAS28-CRP<2.3 为缓解组, $2.3 \leq \text{DAS28-CRP} < 2.7$ 为低疾病活动度组, $2.7 \leq \text{DAS28-CRP} \leq 4.1$ 为中疾病活动度组, $\text{DAS28-CRP} > 4.1$ 为高疾病活动度组,见表 1。

表 1 疾病的临床评估

Table 1 Clinical evaluation of diseases

Classification	RA patients(n=103)
DAS28-ESR*	3.01(2.65)
DAS28-CRP*	3.06(2.38)
TJC-28*	2(6)
SJC-28*	2(5)
VAS*	20(20)
CRP*	0.562(1.5)
ESR*	15(27)
Mitigation Group	33(32)
Low disease activity group	16(16)
Secondary Disease Activity Group	26(25)
High Disease Activity Group	28(27)

Note: * indicates the median (interquartile range), TJC-28: 28 joint tenderness. SJC-28: 28 joint swelling numbers. VAS: Visual analogue scoring method, ranging from 0 to 10.

1.3 超声检查方法

MSUS 检查由两名不知道临床指标的超声科医师进行,使用高分辨率机器(Affiniti70, PHILIPS, CHINA)和线性高频探头(5~18 MHz)。两名医师分别从事肌骨超声检查 1 年和 7 年,对于每个病人,每个关节进行超声评估,结果如果不一致,经协商

后决定。检查的关节包括:双手的掌指关节(metacarpophalangeal,MCP)、双手的近端指间关节(proximal interphalangeal, PIP)和双手腕关节,一共 22 个关节。检查的肌腱包括:双侧拇短伸-拇长展肌腱、桡侧腕伸肌腱、拇长伸肌腱、指总伸肌腱、小指伸肌腱、尺侧腕伸肌腱、双侧第 2~5 屈指肌腱、指浅-指深屈肌腱、拇长屈肌腱及桡侧腕屈肌腱。检查 PD 信号时,采用低通滤波,降低脉冲重复频率,将多普勒增益降低到刚好低于随机噪声的水平,以增加多普勒灵敏度。该设置被保存下来,用于本研究所有患者的检查。检查时取适量凝胶涂在皮肤上,检查者手腕轻悬,以免压迫血管。关节滑膜炎的 GS 和 PD 信号采用(0~3 分)半定量评分法(表 2)^[14],腱鞘炎的 GS 和 PD 信号采用(0~3 分)半定量评分法(表 3)^[15,16]。示例说明见图 1。每个患者的超声检查时间约 20 min。

表 2 关节滑膜炎的 GS 和 PD 信号半定量评分法

Table 2 GS and PD signal semi-quantitative scoring method for joint synovitis

Synovitis GS signal	Synovitis PD signal
0 points: no thickening of the synovium	0 points: None, for measuring blood flow signals
1 point: Mild, thickened synovium but not exceeding the line of bone vertex around the joint	1 point: Mild, measured point blood flow signal
2 points: Moderate, thickening of the synovium and beyond the line of the vertex of the bone around the joint	2 points: Moderate, measured sheet blood flow signal, but not more than half of the synovial area
3 points: Severe, the synovium thickens beyond the line of the bone apex around the joint and extends to at least one backbone	3 points: Severe, measured sheet blood flow signal, and more than half of the synovial area

表 3 腱鞘炎的 GS 和 PD 信号半定量评分法

Table 3 GS and PD signal semi-quantitative scoring method for tenosynovitis

Tenosynovitis GS signal	Tenosynovitis PD signal
0 points: normal	0 points: no PD
1 point: mild	1 point: mild
2 points: Moderate	2 points: Moderate
3 points: Severe	3 points: Severe

1.4 统计方法

所有数据均转移至微软的 Excel 表格中处理。使用 IBM SPSS 22.0 进行分析和统计处理。运用描述统计检验描述患者的群体特征。分类变量用数字和百分比来描述。非正态变量资料用中位数和四分位距描述。算出关节 GS 总分、关节 PD 总分、腱鞘 GS 总分、腱鞘 PD 总分、联合 GS 总分(关节 GS 总分与腱鞘 GS 总分之和)、联合 PD 总分(关节 PD 总分与腱鞘 PD 总分之和)。比较超声指标与 DAS28-CRP 的相关性用 Spearman 相关系数。

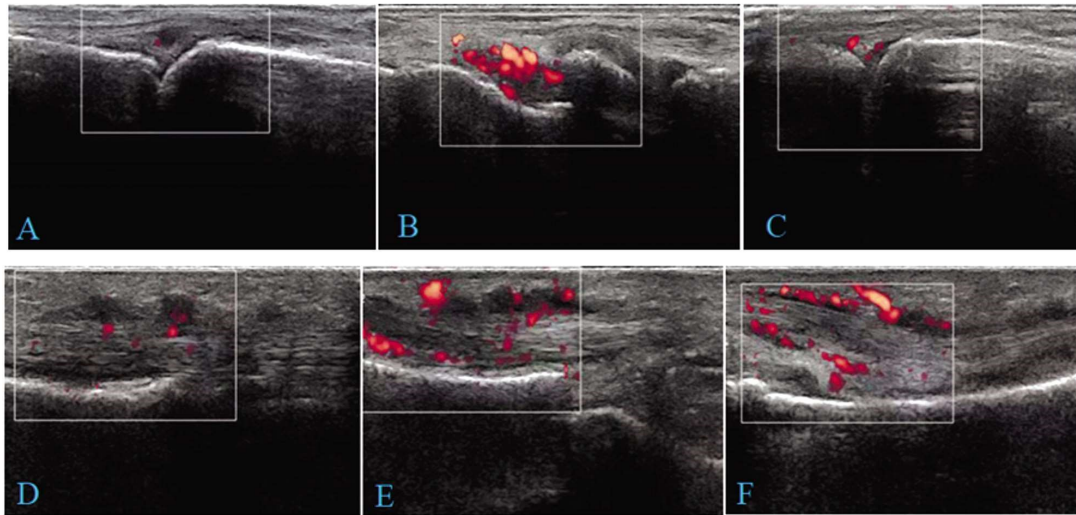


图 1 腱鞘炎患者的超声检测结果

注:(A:右手 PIP2,GS2 级,PD1 级;B:左手腕,GS2 级,PD3 级;C:左手 PIP3,GS1 级,PD2 级;D:腱鞘炎 GS2 级,PD1 级;E:腱鞘炎 GS2 级,PD2 级;F:腱鞘炎 GS1 级,PD3 级)。

Fig.1 Ultrasonic test results of tenosynovitis patients

Note: (A: right hand PIP2, GS2 grade, PD1 grade; B: left wrist, GS2 grade, PD3 grade; C: left hand PIP3, GS1 grade, PD2 grade; D: Tenosynovitis GS2 grade, PD1 grade; E: Tenosynovitis GS2 grade, PD2 grade; F: Tenosynovitis GS1 grade, PD3 grade).

2 结果

2.1 患者不同部位的 GS 评分和 PD 评分

本研究一共扫描了 2266 个关节和腱鞘。各个部位的 GS 评分和 PD 评分,见表 4。

表 4 不同部位的 GS 和 PD 的超声评分

Table 4 Ultrasound scores of GS and PD in different parts

Classification	Ultrasound score
Joint GS total	5.24± 5.81
Tendon sheath GS total	0.95± 2.19
Combined GS total	6.19± 6.69
Joint PD total	3.18± 4.51
Tendon sheath PD total	0.98± 2.39
Combined PD total	4.17± 5.66

表 5 不同部位的超声评分与 DAS28-CRP 的相关性

Table 5 Correlation between ultrasound scores of different parts and DAS28-CRP

Classification	P(r)
Joint GS total	0.000(0.497*)
Tendon sheath GS total	0.000(0.391*)
Combined GS total	0.000(0.575*)
Joint PD total	0.006(0.267*)
Tendon sheath PD total	0.029(0.215**)
Combined PD total	0.001(0.323*)

Note: The values in the table represent correlation coefficients. *Means that the correlation is significant on the 0.01 level (two-tailed). **Means that the correlation is significant at level 0.05 (two-tailed).

2.2 不同部位的 GS 和 PD 超声评分与 DAS28-CRP 的相关性比较

由表 5 可见,关节 GS 总分、关节 PD 总分、腱鞘 GS 总分、腱鞘 PD 总分、联合 GS 总分、联合 PD 总分与 DAS28-CRP 均显著相关($P<0.05$)。腱鞘 PD 总分与 DAS28-CRP 的相关性相对较弱, P 值在 0.05 层面上显著相关。其他各项指标与 DAS28-CRP 均在 0.01 层面上显著相关。

2.3 超声检查手部存在关节炎或腱鞘炎的情况对比

由于超声检查被认为比临床检查更敏感,本研究评估了患者超声检查出活动性炎症的比例。活动性炎症定义为至少一个关节或一根腱鞘的 $PD \geq 1$ 。如图 2 所见,缓解组的 33 位病人中,有 16 位能检查出活动性炎症,占 48%。低疾病活动组的 16 位病人中,有 12 位存在活动性炎症,占 75%。中疾病活动组的 26 位病人中,有 21 位存在超声下的活动性炎症,占 81%。高疾病活动组的 28 位病人中,有 22 位能检测出活动性炎症,占 79%。

在本研究中,根据 DAS28-CRP 患者处于缓解期,但患者不仅存在关节滑膜炎,仍有相当一部分患者存在腱鞘炎。由于本研究的主要目的之一是评估联合手部关节滑膜炎和腱鞘炎用于评估 RA 患者的疾病活动度的效用,我们比较了在基于 DAS28-CRP 的分组情况下,超声只检查手部关节与超声检查手部关节和腱鞘相比的敏感性,具体见表 6。结果显示,如果超声检查只做手部关节,有一部分患者将会被误以为疾病控制良好,缓解组中有 6.25%,低疾病活动组中有 16.67%,中疾病活动组中有 4.76%,高疾病活动组中有 22.73%。一共有 9 名患者,没有关节滑膜炎,只存在腱鞘炎,占有所有患者的 8.70%。如果只检测手部的关节滑膜炎,这些患者会被认为病情缓解。

3 讨论

类风湿性关节炎是一种以关节病变为主的慢性全身自身

免疫性疾病^[17]。在我国类风湿性关节炎任何年龄均可发病,发病人群主要以中老年人和女性为主^[18]。本疾病反复发作性,致残率较高,预后不良,发病机理不清楚,还没有很好的根治方

法^[19,20]。一旦治疗不理想可容易引发肺部疾病心血管疾病、恶性肿瘤及抑郁症等^[21]。

表 6 不同疾病活动度下超声只检查手部关节与超声检查手部关节和腱鞘相比的敏感性

Table 6 Sensitivity of ultrasound examination of hand joints compared with ultrasound examination of hand joints and tendon sheaths under different disease activities

DAS28-CRP	Joint synovitis (PD $\geq$ 1 in at least one joint)	Tenosynovitis (at least one tendon sheath PD $\geq$ 1)	Joint synovitis or tenosynovitis (PD $\geq$ 1 for at least one joint or one tendon sheath)	Ultrasound only examines the sensitivity of hand joints compared to ultrasound examination of hand joints and tendon sheaths
Mitigation Group	15	4	16	93.75 %
Low activity group	10	5	12	83.33 %
Middle Activity Group	20	4	21	95.24 %
High Activity Group	17	11	22	77.27 %
Total	62	24	71	-

在临床工作中正确评估患者的病情十分重要,DAS28-CRP是常用的 RA 病情活动度评分^[22]。但是发现 DAS28-CRP 评估有误诊的情况发生^[23]。换句话说,DAS28-CRP 并不是很可靠。目前,采用超声手段在诊断、监测疾病活动和治疗评价风湿性关节炎有着广泛的应用。灰阶超声(Gray scale ultrasound, GS)能识别形态学的改变,如积液、滑膜增生^[24]。能量多普勒超声(Power Doppler ultrasound, PD)能评价软组织内血流情况,间接反映炎症程度^[25,26]。类风湿性关节炎主要发生滑膜炎或腱鞘炎。常用超声检测 RA 患者的滑膜炎 US 评分用于判断疾病活动度,但是腱鞘炎 US 评估更为接近对疾病的评估。因此本研究探究了超声检查与 DAS28-CRP 评估患病情之间的相关性以及超声联合检查关节和腱鞘与单独检查关节对病情诊断情况的差异。研究表明,关节 GS 总分、关节 PD 总分、腱鞘 GS 总分、腱鞘 PD 总分、联合 GS 总分、联合 PD 总分与 DAS28-CRP 均显著相关。一共有 9 名患者,没有关节滑膜炎,只存在腱鞘炎,占有所有患者的 8.70 %。只存在腱鞘炎患者共有 9 名,即 9 名患者将被认为病情缓解,占有所有患者的 8.70 %。这些结果说明了 DAS28-CRP 虽然评价 RA 患者的病情,但是也存在一定的误诊或遗漏的情况。超声检查可较好的反应关节病变情况^[27]。与张斌^[28]等学者的研究类似,探讨高频超声检查在亚临床 RA 评估中的价值,纳入研究的 44 例 RA 患者中,达到 ACR/EULAR2011 缓解 26 例,达到 ACR 缓解标准 19 例,而达到超声缓解的仅 3 例;超声 GS 评分与病程,肿胀关节数之间存在相关性,超声 PD 评分则与患者疼痛评分,患者总体评分,ACR/EULAR2011、DAS28-ESR、DAS28-CRP 呈正相关。也有研究表明,仅凭 DAS28-CRP 判断 RA 患者的病情,临床医生可能会遗漏相当比例有活动性炎症的患者,而超声检查更直观看到患者缓解部位炎症或损伤^[29,30]。这与我们结论不谋而合。目前,滑膜炎未被充分认识,由此可以解释为什么由 DAS28 定义的疾病控制良好的病人仍然会出现骨侵蚀^[31]。我们为 RA 患者进行超声评估时,同时检查关节和腱鞘可以更准确地评估患者疾病活动度。我们的研究表明,对活动性滑膜炎的超声检测可以

有助于指导和改善对 RA 患者的治疗。本研究存在一定的不足,超声检查由两位经验不同的医师进行。虽然他们对每个病人的判断都是一致的,但结果还是不能被推广。我们的发现可能不直接适用于临床评估能明显发现的活性炎症的 RA 患者,因为他们通常不会选择做超声检查。

综上所述,我们的研究强调了 RA 患者检查腱鞘炎的重要性,以及忽视腱鞘炎的危害。我们还比较了 RA 患者只检查手部关节和同时检查手部关节和腱鞘相比的局限性。与临床检查和 DAS-28 评估相比,使用这种超声联合检查方案将有助于指导并改善 RA 患者的长期预测和临床跟踪服务,当然今后需要我们进一步研究,以评估其在常规实践中的潜在临床应用价值。

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