UTILIZATION OF MULTIPLE DISEASE ACTIVITY MEASURES IN RHEUMATOID ARTHRTIS PATIENTS DETECTED A UNIQUE SUBTYPE OF RHEUMATOID ARTHRITIS

Craig Wiesenhutter
University of Washington School of Medicine, Seattle and Coeur d'Alene Arthritis Clinic, Coeur d'Alene

Conclusions

- The use of a diverse panel of disease activity measures (DAMs) in a rheumatology setting detected rare (4%) patients with a unique clinical profile.
- These patients demonstrated significant disease activity by traditional clinical assessments such as the disease activity score in 28 joints (DAS28) and the clinical disease activity index (CDAI) but not by two different objective measures of inflammation i.e. the ultrasound power Doppler joint count (UPDJC) and the multiple biomarker disease activity (MBDA) blood test.
- These patients would not be expected to respond to changes in their disease-modifying anti-rheumatic drug therapies.
- These patients would superficially appear to be good candidates for drug studies, but would not be expected to respond and should not be entered into clinical trials..

Introduction

- Routinely performing disease activity measures (DAMs) in a rheumatology clinic setting is required for proper decision making concerning treatments and for diagnostic purposes.
- The choice of the ideal combination of DAM instruments has yet to be determined.
- The most common and traditional instruments currently employed, such as the DAS28 and the CDAI, can lead to spurious results because of subjective patient impact on such items as joint counts.
- Including more diverse methods that determine disease activity by non-clinical, and more "technical" means would seem of possible benefit in this setting. The ultrasound power Doppler joint count (UPDJC), ultrasound grey scale joint count (USGSJC), and multiple biomarker disease activity (MBDA) blood test are three possible options.

Methods

- All patients with a diagnosis of rheumatoid arthritis in a long-standing rheumatology clinic underwent evaluation with DAMs including the DAS28, CDAI, and blood testing with a MBDA (Crescendo Bioscience).
- Also, methods for preforming a truncated UPDJC [1]. and an ultrasound grey scale joint count (USGSJC, see right panel) were adopted.

Demographics

Coeur d'Alene Arthritis Clinic & RA Patient Demographics	
Clinic Founded	1983
Male/Female Pt	22%/78%
SeroPos/SeroNeg	82%/18%
CCP Positive	41%
Pt Years in Clinic	9.5
New RA Pts per Month	1-2
N = 279	

Disease Activity Measures Severity Scales

Severity	Normal	Mild	Mod.	Severe
DAS28	<2.60	2.60-3.20	3.20-5.20	>5.20
MBDA	<25	26-30	31-44	>44
USPDJC	<5	5-6	7-10	>10
USGSJC	0-6	7-12	13-24	>24
CDAI	0-3	4-9	10-22	>22

Ultrasound Grey Scale JC
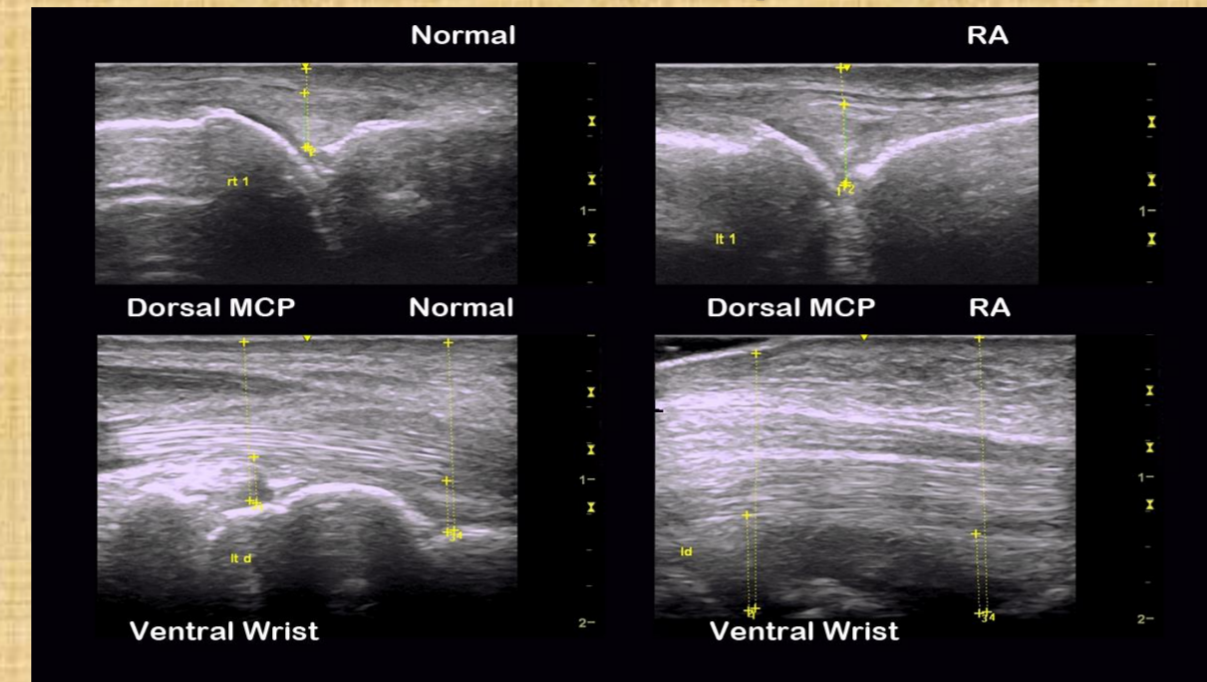
- 34 joint sites evaluated. Dorsal and ventral wrists, and dorsal and ventral 2nd-4th MCP and PIP joints bilaterally.
- Digital measurements at each location from joint surface to joint capsule and from joint surface to skin surface as shown above.
- If the distance measured is > the normal distance + 1.5 standard deviation then = 1 point with 68 points possible.
- In addition, each joint site was also graded using standard subjective scoring method with Grade II = ½ point and Grade III = 1 point and 30 subjective points possible..
- Joint count from digital measurements combined with subjective measurements = total possible UGSJC 0-98.

MBDA Blood Test

- Concentrations of 12 protein biomarkers (CRP, EGF, IL-6, Leptin, MMP-1, MMP-3, Resistin, SAA, TNF-RI, VCAM-1, VEGF-A, YKL-40) were measured in patient serum.
- Biomarker assays used electro-chemiluminescence detection on the Meso Scale Discovery Multi-ArrayTM platform.
- MBDA scores were generated using the same platform, reagents, and algorithm as the Vectra™ DA test, although the information systems and review procedures are different.
- Vectra DA is a validated measure of disease activity in patients with RA.
- The Vectra DA algorithm uses the concentrations of the 12 biomarkers to calculate an MBDA score between 1 and 100.

Results

- There were 279 patients tested with the diverse panel of DAMs in the clinic.
- There are significant correlations between the UPDJC and DAMs such as the DAS28, Vectra (MBDA), CRP, and CDAI (see table on the right).
- Therefore, in most patients, there were generally a positive correlation between the various DAMs.
- However, eleven patients (4%) stood out as outliers.
- The vast majority of these patients had low disease activity (LDA) or no disease activity (NDA) as demonstrated by the UPDJC and the MBDA, but showed moderate disease activity (MDA) to moderate-high disease activity by the DAS28-CRP.
- When the DAS28-CRP was broken down into its individual components, all of these patients showed high values for painful joint counts and patient global assessments.
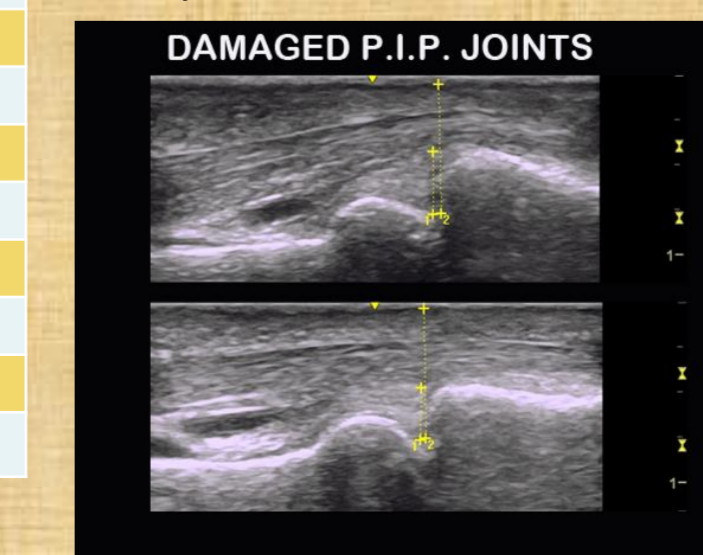
Ultrasound Power Doppler JC
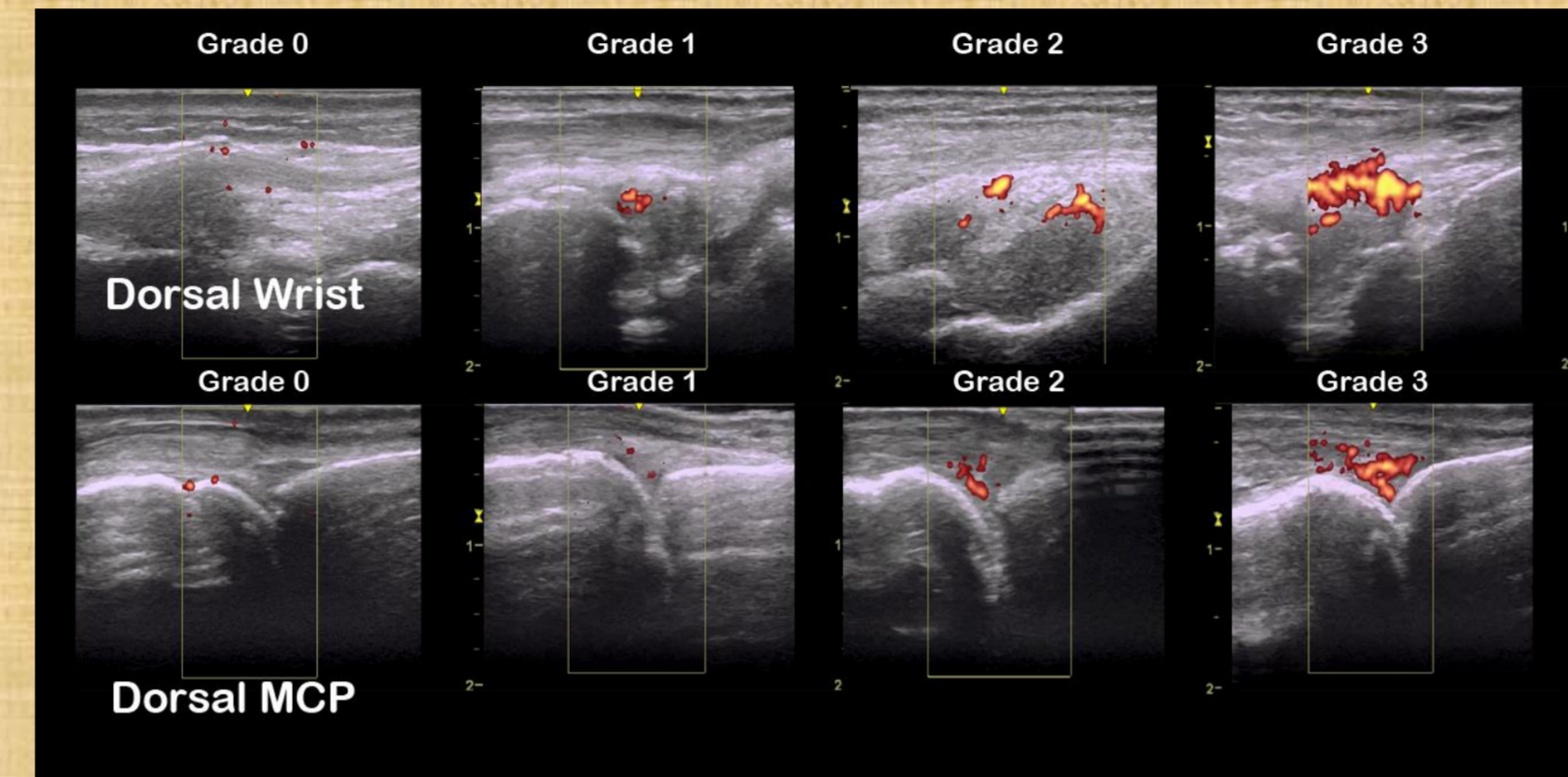
- The UPDJC analyzes six synovial sites [1] for a total of twelve sites with each site assessed by a subjective scale of Grade 0 (normal) to Grade 3 (severe) leading to a possible score of 0-36.
- The vast majority of increased vascularity in joints in RA occurs in the dorsal wrist, and dorsal MCPs > PIPs, allowing for the truncated version of this Doppler JC [1].

Correlations Between Disease Activity Measures

All Rheumatoid Arthritis Patients UPDJC CORRELATION VS	
Disease Activity Measure	Correlation
DAS28CRP	0.470
DAS28ESR	0.445
CRP	0.464
ESR	0.334
VECTRA	0.504
TJC	0.285
SJC	0.441
PT GLOBAL	0.263
DR GLOBAL	0.379
CDAI	0.437
USGSJC	0.142
N = 286	

- The majority of these patients related a history of having to maintain heavy physical labor during periods of high RA disease activity.
- The majority of these patients on USGS morphology demonstrated enlarged, and distended (dissected) joint capsules as shown below.

DAMAGED P.I.P. JOINTS

Clinical Disease Activity Profiles

Discussion

Currently, the treatment target for new and recent onset RA patients is LDA or NDA, especially with those patients with risk factors, such as being seropositive, erosive, or having high phase reactants.

INDIVIDUAL PATIENTS THAT ARE UNIQUE OUTLIERS

References

1. Shin-ya Kawashiri et. All. The power Doppler Ultrasonography Score from 24 Synovial Sites or 6 Synovial Sites, including the MCP joints, reflects the Clinical Disease Activity and Level of Serum Biomarkers in Patients with RA. Rheumatology (2011) 50 (5): 962-965.