Body Mass Index Is Positively Correlated with Diverse Disease Activity Measures in Longstanding Rheumatoid Arthritis

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Abstract

- **Background/Purpose:** Obesity is a common problem with patients who have rheumatoid arthritis (RA). Adipose tissue has been shown to produce cytokines that are proinflammatory. The measurement of Body Mass Index (BMI) is a proxy for determining the amount of adipose tissue present in an individual. The impact of BMI on disease activity measures in RA have been contradictory, and, in fact, studies have shown that a high BMI is protective, as defined by x-ray changes for patients with early onset RA. The objective of this trial is to determine whether obesity and BMI are positively correlated with diverse disease activity measures (DAMs) in longstanding RA.

- **Methods:** Patients at a community based rheumatology clinic undergo DAM assessments on a routine basis as part of the implementation of a treat to target (T2T) strategy. These assessments include the disease activity score in 28 joints (DAS28CRP), the power Doppler joint count (UPD), and the multibiomarker disease activity test (MBDA), as well as several other commonly assessed DAMs. The UPD includes scoring at six dorsal wrist and six dorsal MCP sites. The average duration of RA in patients at this clinic is > 10 years. Also, as currently mandated by the authorities, BMI and other vital signs are obtained on a regular basis. Correlations were determined by Pearson's coefficients, and categorical data was compared by T tests. Patients were categorized as underweight (BMI < 18), normal weight (BMI > =18 and <25), overweight (BMI >=25 and <30), and obese (BMI >= 30).

- **Results:** Table 1 BMI and Comparisons with Diverse Disease Activity Measures

	N	BMI VS Prob	Normal Wt Avg +/- SD	Overweight Avg +/- SD	Obese Avg +/- SD	Prob NI vs Over	Prob NI vs Obese	Prob Over vs Obese
Leptin	241	r=.572 p<0.0001	11.8 +/- 19.7	19.2 +/- 18.4	30.4 +/- 23.9	p=0.001	p<0.0001	p<0.0001
DAS28CRP	260	r=.537 p<0.0001	3.63 +/- 1.62	3.86 +/- 1.24	4.47 +/- 1.32	NS	p<0.0001	p<0.0001
DAS28ESR	236	r=.285 p<0.005	4.11 +/- 1.38	4.10 +/- 1.45	4.47 +/- 1.32	NS	NS	p<0.0001
CRP	238	r=.340 p<0.0001	4.6 +/- 13.8	7.2 +/- 15.1	6.0 +/- 8.9	NS	NS	NS
ESR	236	r=.289 p<0.0001	18.3 +/- 13.7	19.0 +/- 20.4	21.9 +/- 19.4	NS	NS	p=0.02
MBDA	242	r=.300 p<0.0001	37.7 +/- 13.6	40.6 +/- 16.2	41.3 +/- 12.7	NS	p=0.05	p<0.0001
HAQ	233	r=.289 p<0.0001	1.9 +/- 1.6	1.8 +/- 1.4	2.7 +/- 1.8	NS	p=0.02	p=0.02
Pt Global	229	r=.228 p<0.001	3.5 +/- 2.4	3.5 +/- 2.2	5.0 +/- 2.3	NS	NS	p<0.0001
TJC	271	r=.222 p<0.001	7.1 +/- 6.8	7.6 +/- 9.7	11.4 +/- 7.5	NS	p=0.003	p<0.0001
CDAI	236	r=.206 p<0.001	18.6 +/- 12.2	19.0 +/- 20.4	21.9 +/- 19.4	p<0.001	NS	p=.003
RAPIDIII	244	r=.224 p<0.001	8.9 +/- 6.0	8.3 +/- 5.1	11.4 +/- 7.5	NS	NS	p=0.02

- There were only two patients in the underweight category, and that category was not included in this analysis.

- **Conclusion:** BMI positively correlates with, and shows significant increases in weight categories for several important measures of disease activity in patients with longstanding RA. Though the DAS28CRP, MBDA, and UPD generally correlate significantly in this clinic (r= 0.500), in this study, UPD was the only one of these measures that did not correlate with BMI (r = 0.090). One possible explanation is that power Doppler signals are very dependent on the distance of the probe from the site of the signals. The UPD method utilized includes assessments of the dorsal wrist at six out of twelve sites. Subcutaneous adipose tissue in overweight patients perhaps blunted the signals. Of interest, Leptin was significantly correlated with BMI and showed significant increases with weight categories. Leptin is produced by adipose tissue and is thought to be proinflammatory. Excess Leptin production might be contributory to the effects of BMI on RA disease activity. BMI is positively correlated with several important DAMs in patients with longstanding RA. Rheumatologists should significantly increase their efforts and resources to address and manage obesity in our RA patients.

Introduction

- Obesity is a common problem in patients who have rheumatoid arthritis (RA) and occurs more commonly than in the general population. In addition to contributing to mechanical stress in joints, adipose tissue has also been shown to produce cytokines that are proinflammatory. The measurement of Body Mass Index (BMI) is a proxy for determining the amount of adipose tissue present in an individual.

- The impact of BMI on disease activity measures in RA have been contradictory, and, in fact, studies have shown that a high BMI is protective, as defined by x-ray changes for patients with early onset RA.

- The objective for obtaining this data was to determine whether obesity and BMI are positively correlated with diverse disease activity measures (DAMs) and/or biomarkers in longstanding RA.

Methods

- Patients at a community based rheumatology clinic undergo DAM assessments on a routine basis as part of the implementation of a treat to target (T2T) strategy [1]. These assessments include the disease activity score in 28 joints (DAS28CRP), the ultrasound power Doppler joint count (UPDJC), the ultrasound grey scale joint count (UGSJC), and the multibiomarker disease activity test (MBDA), as well as several other commonly assessed DAMs. The UPDJC includes scoring at six dorsal wrist and six dorsal MCP sites [2]. RA disease duration in this clinic is > ten years.

- Also, as currently mandated by the authorities, BMI and other vital signs are obtained on a regular basis.

- Correlations were determined by Pearson's coefficients, and means data was analyzed by one way ANOVA using the SPSS v. 23 statistical software. Data from the two underweight patients was not analyzed. The remaining BMIs were divided into tertiles with tertile 1 = to a BMI of >18-26, tertile 2 = >26 -31, and tertile 3 = >31.

MBDA Blood Test

- Concentrations of 12 protein biomarkers (CRP, EGF, IL-6, Leptin, MMP-1, MMP-3, Resistin, SAA, TNF-R1, VCAM-1, VEGF-A, YKL-40) were measured in patient serum.
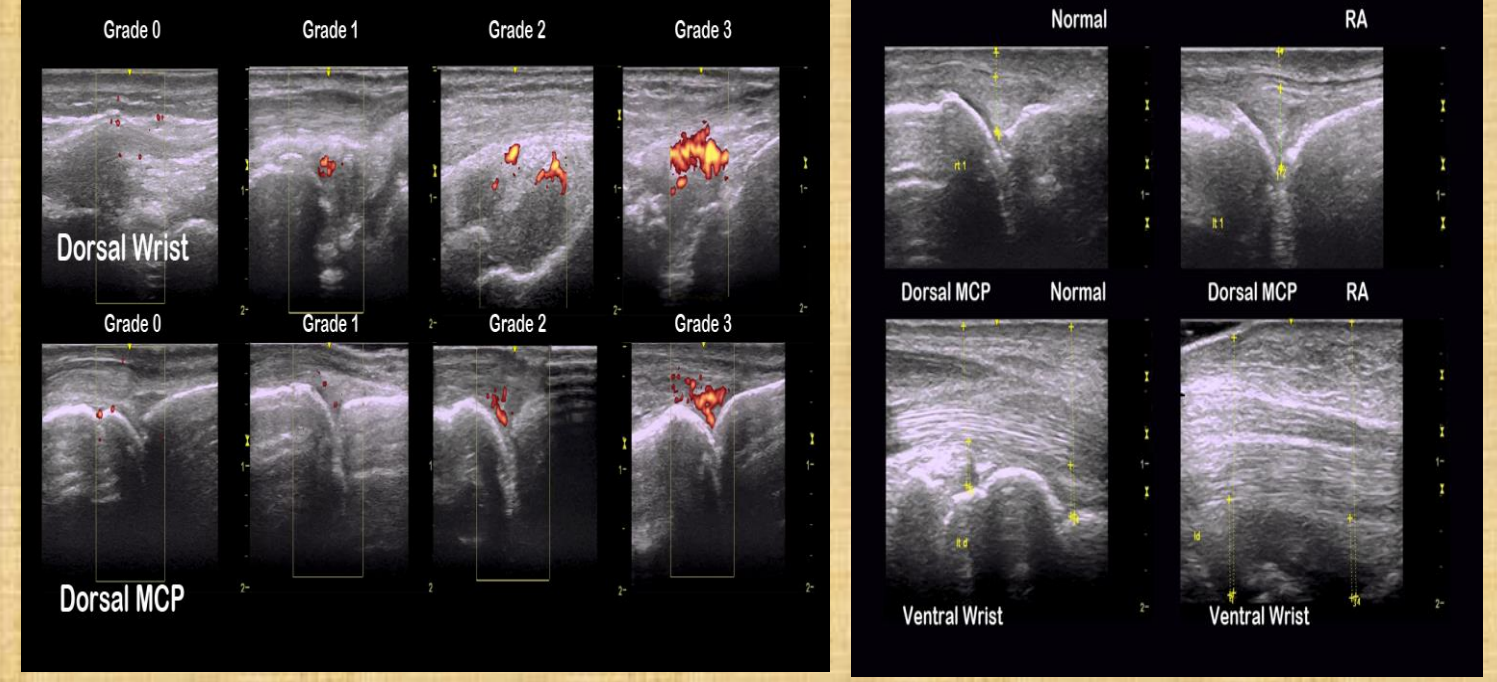
- MBDA scores were obtained from the Vectra DA test.

- Vectra DA is a validated measure of disease activity in patients with RA.

Patients with Long Standing RA

Figure 1.   Patients with long standing RA and deformities from the clinic are shown.

Ultrasound Joint Counts

Figure 2. UPDJC studies are shown on the left. The method for preforming a truncated UPDJC was adapted [2] for the clinic. UGSJC studies are shown on the right. 34 joint sites were evaluated. Dorsal and ventral wrists, and dorsal and ventral 2nd-4th MCP and PIP joints bilaterally with distances from joint to capsule and joint to surface measured at each joint..

Results

- Table 1 demonstrates that females consistently demonstrated higher correlations between BMI and all DAMs and biomarkers tested compared to males.

- There were no meaningful correlations between BMI and the nine MBDA biomarkers not shown in the table.

- There was a moderate to strong correlation with BMI and Leptin in patients with long standing RA.

- There were significant, but weak to moderate correlations between BMI and several other DAMs.

- Whereas there was a moderate strength correlation with BMI and UGSJC in females, no meaningful correlation was found with UPDJC.

Study	Female N Patients	BMI vs[2]	Prob[1]	Combined[3] BMI vs	Tertile 1[4] AVG	SD	Tertile 2[4] AVG	SD	Tertile 3[4] AVG	SD	ANOVA Prob[1]	Tertile 1 vs 2 Prob[1]	Tertile 1 vs 3 Prob[1]	Tertile 2 vs 3 Prob[1]
Leptin	259	r = .666	***	r = .624	15.8 ng/ml	(+/-)18.91	32.3 ng/ml	(+/-)22.19	61 ng/ml	(+/-)33.9	***	***	***	***
UGSSJC	112	r = .371	***	r = .228	12.0	(+/-)6.4	13.7	(+/-)14.3	17.21	(+/-)12.7	**	NS	**	NS
HAQ	122	r = .329	***	r = .292	1.93	(+/-)1.53	2.03	(+/-)1.37	3.07	(+/-)1.81	**	NS	**	*
Das28CRP	255	r = .321	***	r = .283	3.60	(+/-)1.07	4.16	(+/-)1.05	4.66	(+/-)1.32	***	*	***	*
MBDA	307	r = .307	***	r = .249	37.6	(+/-)15.5	41.3	(+/-)10.4	46.3	(+/-)9.5	***	NS	***	*
Das28ESR	254	r = .294	***	r = .283	4.13	(+/-)1.2	4.5	(+/-)1.13	5.11	(+/-)1.34	***	NS	***	**
Pt Global	257	r = .239	***	r = .224	3.6	(+/-)1.9	4.2	(+/-)2.5	4.9	(+/-)2.4	**	NS	**	NS
TJC	257	r = .239	***	r = .220	6.7	(+/-)6.6	8.7	(+/-)6.4	11.8	(+/-)7.8	***	NS	***	*
RAPIDIII	112	r = .221	*	r = .219	9.3	(+/-)5.8	9.2	(+/-)4.7	12.6	(+/-)6.3	*	NS	*	*
CDAI	256	r = .221	***	r = .133	18.2	(+/-)11.3	23.2	(+/-)11.8	26.5	(+/-)12.6	***	*	NS	***
CRP	254	r = .212	*	r = .111	3.2 mg/L	(+/-)4.6	5.1 mg/L	(+/-)7.6	8.6 mg/L	14.012.7	**	NS	**	*
RESISTEN	259	r = .191	**	r = .080	7.8 ng/ml	(+/-)2.8	7.8 ng/ml	(+/-)3.0	9.2 ng/ml	(+/-)3.4	**	NS	*	*
TNF-R1	259	r = .164	*	r = .052	1.7 ng/ml	(+/-)0.8	1.6 ng/ml	(+/-)0.4	2 ng/ml	(+/-)1.3	**	NS	*	**
ESR	358	r = .124	*	r = .124	19.1 mm/hr	(+/-)16.7	19.3 mm/hr	(+/-)19.7	22.6 mm/hr	(+/-)14.8	*	NS	NS	NS

[1]P = <0.05*, P = <0.005**,P = <0.0005***,   [2]Pearson's Coefficents,   [3]Males and Females Combined,   [4]Females Only

Table 1.   Correlations between BMI and several DAMs biomarkers and lab studies are show. Also, the female patients were analyzed by BMI tertiles, and the results are shown using one way ANOVA.

Discussion

- Obesity in the normal population has been correlated with elevated serum leptin levels [3] with leptin levels in normal weight subjects of 7.5 ng/ml +/- 9.3 and 31.3 ng/ml +/- 24 in obese individuals (BMI >27). Women with longstanding RA were found to have levels of Leptin that were twice as high.

- There were significant, but weak to moderate correlations between BMI and several other DAMs.

Conclusion

- BMI positively correlates with, and shows significant increases in weight categories for several important measures of disease activity in patients with longstanding RA, especially with female patients.
- Leptin was strongly correlated with BMI and showed significant increases with weight categories. Leptin is produced by adipose tissue and is thought to be proinflammatory. Excess Leptin production might be contributory to the effects of BMI on RA disease activity..
- Rheumatologists should significantly increase their efforts and resources to address and manage obesity in our RA patients.

References

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