

Obesity is a Risk Factor for Worse Treatment Response in Rheumatoid Arthritis Patients - Results from Reuma.pt



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Introduction and Objectives

Obesity is a traditional cardiovascular risk factor that affects one third of rheumatoid arthritis (RA) patients. Moreover, an increase in body fat has a resulting increase in inflammatory cytokine production which would be expected to buffer treatment response. However, the importance of obesity in RA activity remains unclear. **This study aims to determine the influence of obesity on treatment response to biologic therapy evaluated by disease activity score (DAS28) at six months, in patients with RA, regardless of the targeted cytokine or cell, by analyzing a cohort of patients treated with anti-IL-6, anti-TNF or anti-CD20 drugs.**

Patients and Methods

We conducted a retrospective longitudinal cohort study using the National Rheumatic Diseases Register, Reuma.pt from the Portuguese Society of Rheumtology.

	Study Population	Control Group
Inclusion criteria	Meeting American College of Rheumatology 1987 revised criteria for RA	
	Available data on weight and height at baseline	
	≥ 6 months follow up after starting first biologic therapy (TNF i, IL6 i or anti-CD20)	≥ 6 months follow up after starting first non-biologic DMARD
Exclusion criteria	Patients previously or currently treated with other biological therapies	
	Under other DMARD than methotrexate	
	Prednisolone over 10mg/day or an equivalent dose of corticosteroid	

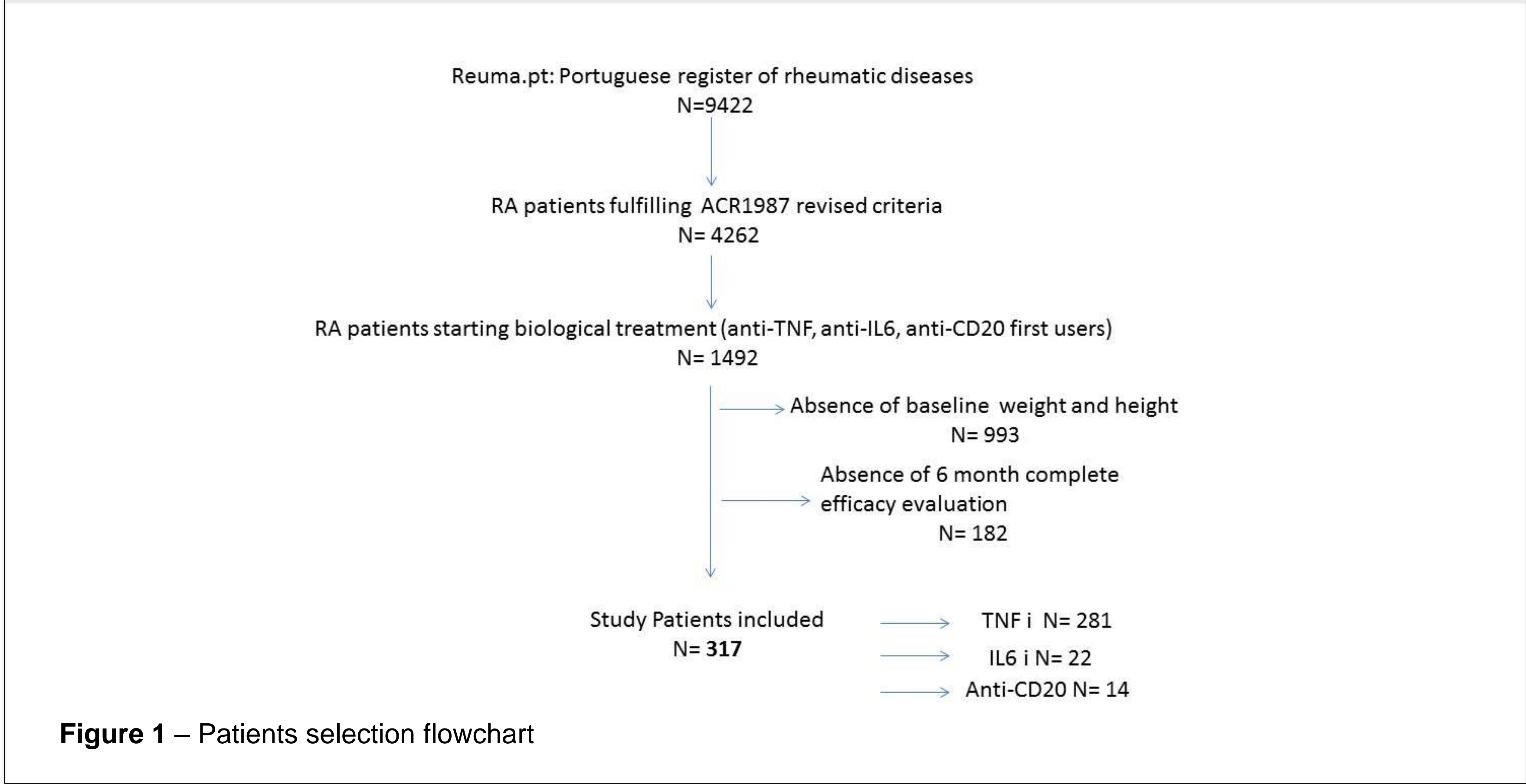


Table 1 - Baseline Characteristics of the total RA population starting biologic therapy and divided according to BMI category at the start of biologic treatment

	Study Population	BMI< 30 Kg/m ²	BMI≥ 30 Kg/m ²
N	317	244	73
Age (years)	53±0.7	52±0.8	55±0.9*
Female (%)	87	87	88
Disease duration (mean years)	10.5±0.5	10.4±0.5	10.8±1.0
Erosive disease (%)	71	70	71
RF positive (%)	72	72	73
Anti-CCP (%)	73	74	69
DAS28 (mean)	5.7±0.1	5.6±0.1	5.7±0.1
HAQ score (mean)	1.5±0.0	1.5±0.0	1.65±0.1*
Current smoking (%)	12	14	14
Education (average years)	7.2±0.3	7.6±0.3	6.0±0.5*
Concomitant MTX therapy (%)	82	83	77*
Concomitant low dose of steroid therapy (prednisolone< 5mg/day) (%)	79	82	71

Values represent means ± S.D. or n (%). BMI= body mass index; RF= Rheumatoid Factor; ACPA= anti-cyclic citrullinated peptide; DAS28= Disease activity index in 28 joints; HAQ= Health assessment questionnaire. For continuous variables, differences between obese and non-obese were assessed using t test and for categorical variables a qui-square. *Unadjusted p-value < 0.05

Results

317 RA biologic therapy first users from 16 Portuguese Rheumatology Centres met the inclusion and exclusion criteria. Most of the exclusions were due to missing data of weight and height (Figure 1). 23% were obese (Figure 1).

Table 2 - Multivariate model predicting the 6 month DAS28 after biologic therapy

	DAS28 at 6 months	
Dependent variables	β estimates (95%CI)	p-value
Obesity	0.413 (0.050-0.767)	0.022*
Age	0.060 (-0.005-0.024)	0.183
Gender	-0.289 (-0.752-0.174)	0.221
Disease duration	0.010 (-0.008-0.028)	0.280
RF positive	-0.274 (-0.613-0.064)	0.112
Baseline DAS28	0.514 (0.393-0.636)	<0.0001*
TNFi (yes/no)	1.22 (0.787-1.653)	<0.001*

Table 3 - Multivariate model predicting remission at 6 month after biologic therapy

	Remission	
Dependent variables	OR (95%CI)	p-value
Obesity	0.391 (0.132-1.161)	0.091
Age	0.959 0.924-0.995)	0.026*
Gender	1.332 (0.429-4.132)	0.620
Disease duration	0.979 (0.929-1.032)	0.442
RF positive	1.340 (0.581-3.090)	0.493
Baseline DAS28	0.384 (0.264-0.597)	<0.0001*
TNFi (yes/no)	0.037 (0.012-0.111)	<0.0001*

Thirty-five RA patients DMARD naïve were included in the control group. There were also 23% of obese people (N=8). As expected, this group is composed by patients with lower disease duration (p<0.001), less erosive disease (p<0.001) and with less disease burden (HAQ) (p=0.003) than the study population (table 4).

Table 4 - Baseline Characteristics DMARD naive RA population and according to BMI category - the control group

	Control Population	BMI< 30 Kg/m ²	BMI≥ 30 Kg/m ²
N	35	27	8
Age (years)	56±2.5	57±3.0	55±4.1
Female (%)	74	74	75*
Disease duration (mean years)	2.4±0.6	2.6±0.7	2.0±1.0*
Erosive disease (%)	25.7	55	25*
RF positive (%)	48.6	33.3	25
Anti-CCP (%)	28.6	33	25
DAS28 (mean)	4.8±0.2	4.9±0.3	4.5±0.4
HAQ score (mean)	1.1±0.1	1.0±0.1	1.4±0.26
Current smoking (%)	12.4	22	-
Education (average years)	8.2±2.8	8.0±4.0	9.0±1.0
Concomitant low dose of steroid therapy (prednisolone< 5mg/day) (%)	89	89	88

Values shown are means ± S.D. or n (%). BMI= body mass index; RF= Rheumatoid Factor; CCP= anti-cyclic citrullinated peptide; DAS28= Disease activity index in 28 joints; HAQ= Health assessment questionnaire. For continuous variables, differences between obese and non-obese were assessed using t test and for categorical variables a qui-square. *Unadjusted p-value < 0.05

Table 5 - Multivariate model predicting the 6 month DAS28 in DMARD naïve group

	DAS28 at 6 months	
Dependent variables	β estimates (95%CI)	p-value
Obesity	0.993 (0.149-0.838)	0.023*
Age	0.007 (-0.019-0.034)	0.582
Gender	0.224 (-0.632-1.081)	0.596
Baseline DAS28	-1.739 (-0.467-0.119)	0.235
RF positive	-0.450 (-0.807-0.717)	0.905

Table 6 - Multivariate model predicting the 6 month DAS28 in DMARD naïve group

	Remission at 6 months	
Dependent variables	OR (95%CI)	p-value
Obesity	0.240 (0.031-1.859)	0.172
Age	0.998 (0.939-1.060)	0.936
Gender	0.556 (0.059-5.213)	0.608
Baseline DAS28	2.675 (1.183-0.047)	0.018*
RF positive	2.411 (0.365-15.915)	0.361

Conclusions

In our study, we have found that in longstanding RA patients (starting their first biologic therapy) obesity was significantly associated to DAS 28 at 6 months but not with disease remission. Moreover, in a control group of patients of early RA patients (DMARD first users) we also found a statistically significant association between obesity and worst treatment response but not with remission.

It seems that obesity negatively influences the first six month of treatment response independently of treatment options and disease characteristics.