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Juvenile Idiopathic Arthritis in adulthood: clinical pattern and long-term outcomes of 426 patients.

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Background

The adult impact of Juvenile Idiopathic Arthritis (JIA) is not fully understood:

- Inconsistencies of classification
- Barriers in the transition of care between paediatric environment and adult rheumatology
- Lack of integrated paediatric and adult registries

Objectives

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- To determine which adult JIA patients registered on the Rheumatic Diseases Portuguese Register (Reuma.pt) fulfill classification criteria for adult rheumatic diseases, evaluate their outcomes and determine clinical predictors of inactive disease, functional status and damage.

Methods

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- Cross-sectional analysis nested in a cohort study with the following inclusion criteria:
  - patients with JIA according to the 2001 revised International League of Associations for Rheumatology (ILAR) criteria
  - registered in Reuma.pt
  - older than 18 years old
  - disease duration greater than 5 years
  - available data in adulthood.

Methods

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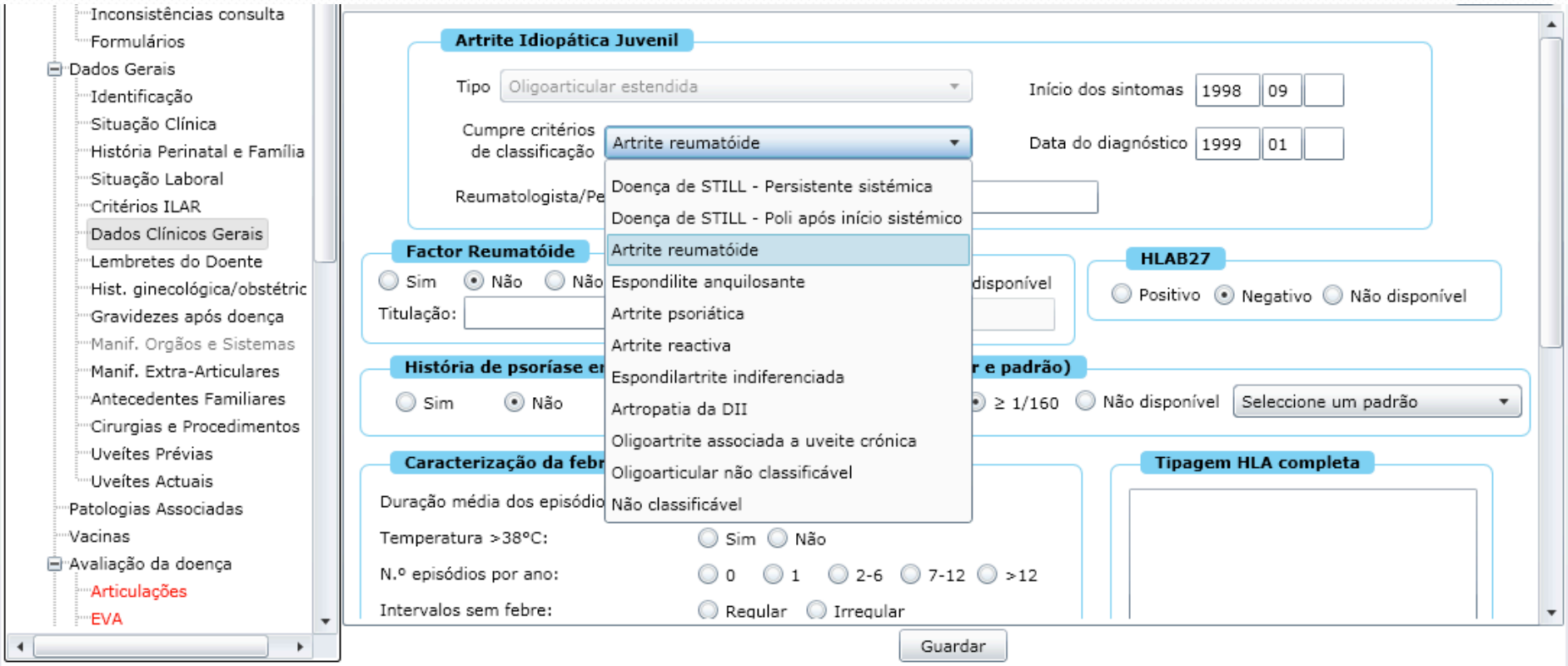
- Data from Reuma.pt regarding fulfilment of classification criteria of adult rheumatic diseases were analyzed.



Methods

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- Outcome assessments included:
  - Disease activity – inactive disease was defined based on index cut-offs according to current adult rheumatic disease:
    - DAS 28 < 2.6 for patients classified as RA
    - DAS 44<1.6 for PsA and peripheral SpA patients
    - ASDAS <1.3 for AS
    - Patients classified as ASD or with non-classifiable adult rheumatic disease, were considered to have inactive disease if they had: no active arthritis; no systemic sign/symptoms attributable to JIA; no active uveitis; normal ESR and/or CRP; a physician's global assessment of disease activity of 0

van Gestel AM, et al. *Arthritis Rheum* 1996; Fransen J, et al. *Rheumatology (Oxford) 2004*; Prevoo ML, et al. *Br J Rheumatol* 1996; Heimans L, et al. *Arthritis Res Ther* 2016; van der Heijde D, et al. *Ann Rheum Dis* 2009.

Methods

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- Outcome assessments included:
  - last year HAQ, articular (JADI-A) and extraarticular (JADI-E) damage index.
- Sociodemographic features, JIA related variables and concomitant therapies were analysed by univariate and multivariate regression analysis to identify predictors of inactive disease, functional status and damage.

Results: characteristics of the 426 study patients.

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Variables	No. (%) / Mean± Standard deviation
Female	288 (67.6%)
Age at disease onset (years) (n=423)	9.9± 4.8
Age at diagnosis (years) (n=399)	14.4 ± 9.9
Age at the time of last registered visit (years)	34.1 ± 12.8
Disease duration (years) (n=423)	22.5 ± 12.4
Years of education (n=234)	11.6 ± 3.7
Employed (n=234)	168 (71.8%)
Unemployed (n = 234)	24 (10.3%)
Retired due to JIA disability (n=234)	31 (13.2%)
Active /Inactive disease (n=300)	201 (67%)/ 99 (33%)
HAQ score (n=426)	0.5 ± 0.7
JADI - A score (n=140)	7.7 ± 14.5
JADI - E score (n=111)	0.8 ± 1.6
Previous / current therapy with corticosteroids (n=399)	80 (20%) / 103 (25.8%)
Previous /current therapy with synthetic DMARDs (n=399)	84 (21%) / 245 (61.4%)
Previous / current therapy with biologic DMARDs (n=399)	31 (7.8%) / 140 (35.1%)

Results: ILAR category at onset

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ILAR category at onset	N (%)
Persistent oligoarthritis	79 (18.5%)
Extended oligoarthritis	61 (14.3%)
RF-positive polyarthritis	71 (16.7%)
RF-negative polyarthritis	75 (17.6%)
Systemic	41 (9.6%)
Enthesitis related arthritis	80 (18.8%)
Psoriatic arthritis	13 (3.1%)
Undifferentiated arthritis	6 (1.4%)

Results: Classification according to adult rheumatic diseases

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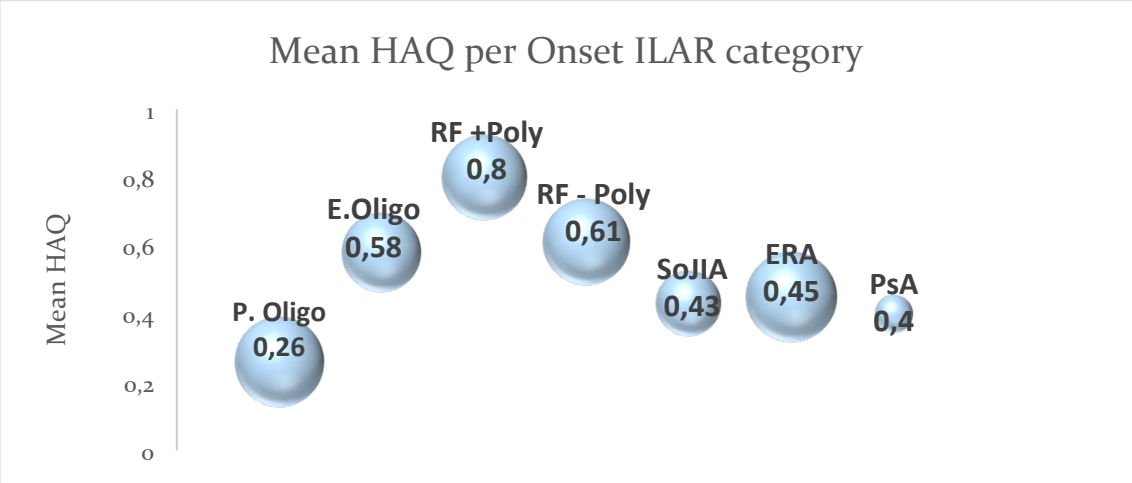
	Adult rheumatic disease classification at the last visit						
Onset ILAR category	RA	AS	USpA	EA	PsA	ASD	Non-classifiable
Systemic n=39	2 (5.1%)	0	0	0	0	36(92.3%)	1 (2.6%)
RF- Poly n=63	36 (57.1%)	2 (3.8%)	2 (3.8%)	0	8 (12.7%)	0	15 (23.8%)
RF+ Poly n=68	65 (95.6%)	1 (1.5%)	0	0	1 (1.5%)	0	1 (1.5%)
P. Oligo. n=66	4 (6.1%)	5 (7.6%)	9 (13.6%)	4 (6.1%)	5 (7.6%)	0	39 (59.1%)
E. Oligo. n=54	21 (38.9%)	2 (3.7%)	10 (18.5%)	1 (1.9%)	1 (1.9%)	0	19 (35.2%)
ERA n=76	0	41 (53.9%)	21 (27.6%)	4 (5.3%)	6 (7.9%)	0	4 (5.3%)
PsA n=13	0	0	0	0	12 (92.3%)	0	1 (7.7%)
Undif. n=6	3 (50%)	1 (16.7%)	0	1 (16.7%)	0	0	1 (16.7%)
Total	131 (34%)	52 (13.5%)	42 (10.9%)	10 (2.6%)	33 (8.6%)	36 (9.4%)	81 (21%)

Results: HAQ according to ILAR categories



Higher HAQ:

- Extended oligoarthritis (β=0.31, p=0.006)
- RF+ polyarthritis (β=0.54, p<0.001)
- RF-polyarthritis (β=0.35, p=0.001)

Results: JADI according to ILAR categories

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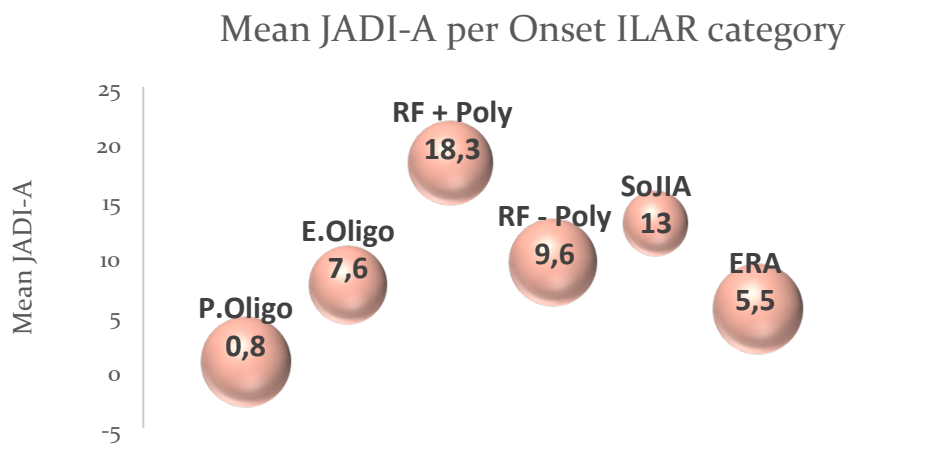

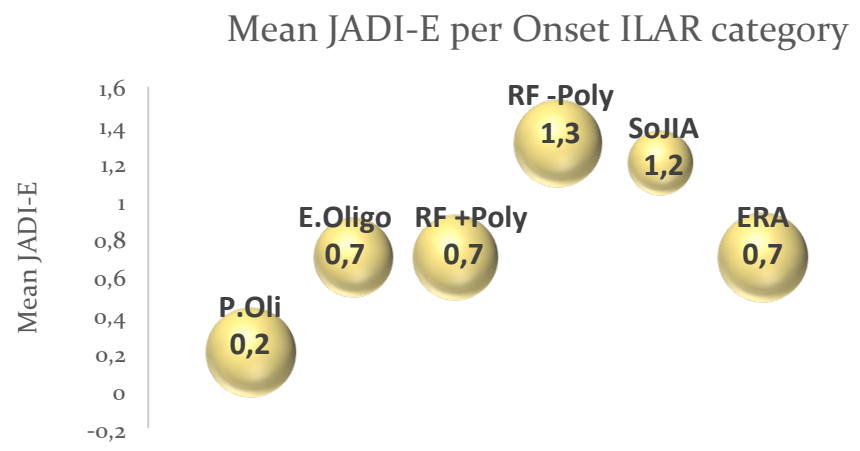

Higher JADI-A:

- RF+ polyarthritis (β=17.46, p<0.001)
- RF-polyarthritis (p=0.018)
- Systemic onset JIA (β=12.15, p=0.011)

JADI-E: similar across the different JIA categories

Results: Associations between baseline variables and disease activity

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Variables	Inactive disease	
	OR (95%CI)	p-value
Age of disease onset (years) *	1.0 (1.0;1.1)	0.186
ANA*	1.2 (0.5;2.5)	0.682
RF*	0.7 (0.2;2.0)	0.475
B27*	0.6 (0.2;2.2)	0.481
ACPA*	0.4 (0.1;1.8)	0.239
Disease duration*	**1.0 (0.9;1.0)**	**<0.001†**
HAQ score*	**0.1 (0.5;0.2)**	**<0.001†**
Exposure to corticosteroids*	0.6 (0.3;1.1)	0.077
Exposure to biologics*	0.8 (0.4;1.4)	0.375
Exposure to synthetic DMARD*	1.2 (0.6;2.4)	0.552
Delay in diagnosis*	**0.9 (0.9;0.9)**	**0.017†**
Unemployed[1]	1.8 (0.5;5.8)	0.352
Retired due to JIA disability	0.3 (0.1;1.3)	0.118
Years of education*	1.0 (0.9;1.1)	0.686

†p-value<0.05.*Adjusted for ILAR Category. . [1] – Compared to employed

Results: Associations between baseline variables, HAQ and JADI

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Variables	HAQ		JADI-A		JADI-E	
	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Age of disease onset*	-0.0(-0.0;0.0)	0.767	**-0.7 (-1.3;-0.2)**	**0.010†**	-0.1(-0.1;0.0)	0.095
ANA*	0.0 (-0.1;0.2)	0.732	6.0 (-1.2;13.3)	0.102	1.1 (0.1;2.1)	0.033†
RF*	0.1 (-0.2;0.4)	0.606	-1.5 (-11.9;8.8)	0.772	-0.2 (-1.8;1.3)	0.784
B27*	0.0 (-0.2;0.3)	0.748	-6.6 (-15.2;2.0)	0.132	-0.5 (-1.5;0.5)	0.286
ACPA*	0.2 (-0.3;0.7)	0.398	-3.5 (-31.9;24.9)	0.804	4.1×10^{-15} (-6.1;6.1)	≈1
Disease duration*	**0.02 (0.0;0.0)**	**<0.001†**	**0.3 (0.1;0.5)**	**0.001†**	**0.03 (0.0;0.1)**	**0.001†**
Exposure to corticosteroids*	**0.3 (0.2;0.5)**	**<0.001†**	4.5 (-1.1;10.2)	0.112	**1.2 (0.5;1.9)**	**0.001†**
Exposure to biologics*	**0.2 (0.0;0.3)**	**0.014†**	6.9 (1.3;12.5)	0.016†	0.6 (-0.1;1.3)	0.080
Exposure to synthetic DMARD*	-0.1 (-0.3;0.1)	0.394	-1.2 (-7.4;5.0)	0.699	-0.1 (-0.9;0.8)	0.864
Delay in diagnosis*	**0.01 (0.0;0.)**	**<0.001†**	-0.0 (-0.3;0.2)	0.787	-0.0 (-0.1;0.0)	0.157
Unemployed[1]	0.0 (-0.3;0.3)	0.904	1.1 (-7.8;10.0)	0.811	1.0 (-0.5;2.4)	0.178
Retired due to JIA disability	1.0 (0.7;1.3)	<0.001†	**29.1 (19.9;38.3)**	**<0.001†**	1.4 (0.2;2.6)	0.028†
Years of education*	-0.02 (-0.1; 0)	0.001†	-0.1 (-0.9;0.7)	0.795	-0.1 (-0.2;0.1)	0.367

†p-value<0.05.*Adjusted for ILAR Category.[1] –Compared to employed

Results: Predictors of functional status, damage and inactive disease

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Variables	Inactive disease		HAQ		JADI-A		JADI-E	
	OR (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value	β (95% CI)	p-value
Gender-Female	2.3 (0.2;31.3)	0.528	-0.03 (-0.2;0.2)	0.771	2.0 (-3.1;7.1)	0.436	-0.03 (-0,7;0.7)	0.937
Age at disease onset (years)	**1.4 (1.1;1.8)**	**0.008†**	**-0.02(-0.04;-0)**	**0.021†**	**-0.9 (-1.4;-0.3)**	**0.003†**	**-0.1 (-0.8;-0.0)**	**0.008†**
RF positive	12.9 (0.8;200.2)	0.068	-	-	-	-	-	-
ACPA +	**0.1 (0.0;0.7)**	**0.028†**	-	-	-	-	-	-
JIA ILAR category *	-	0.5123	-	0.4129	-	0.0349†	-	0.5406
E. Oligo	-	-	0.04 (-0.3;0.4)	0.798	4.5(-3.2;12.2)	0.246	0.5 (-0.6;1.5)	0.372
RF+ poly	8.6 (0.3;221.7)	0.194	0.34 (0.0;0.7)	0.036	**16.2 (6.8;25.6)**	**0.001†**	-0.2 (-1.6;1.2)	0.744
RF- poly	5.1 (0.2;116.9)	0.311	0.10 (-0.2;0.4)	0.501	6.2 (-0.8;13.2)	0.081	0.8 (-0.2;1.7)	0.124
SoJIA	4.2 (0.1;314.6)	0.513	0.05 (-0.4;0.5)	0.805	**10.2 (1.0;19.3)**	**0.029†**	0.3 (-1.0;1.7)	0.635
ERA	20.4 (0.5;853.8)	0.114	0.2 (-0.1;0.5)	0.116	6.4 (-0.8;13.6)	0.082	0.7 (-0.3;1.7)	0.148
PsA	-	-	0.1 (-0.5;0.6)	0.844	0.2 (19.2;19.5)	0.987	0.3 (-1.9;2.6)	0.773
Corticosteroid exposure	-	-	-	-	-	-	**1.1 (0.4;1.9)**	**0.002†**
Delay in diagnosis	0.01 (0.0;0.)	0.673	-0.0 (-0.3;0.2)	0.787	-0.0 (-0.1;0.0)	0.157	0.9 (0.9;0.9)	0.077
Retired due to JIA disability	1.0 (0.7;1.3)	0.437	29.1 (19.9;38.3)	0.932	1.4 (0.2;2.6)	0.132	0.3 (0.1;1.3)	0.218

*† Statistical significance * Persistent oligoarthritis used as comparator*

Study limitations

- Cross-sectional design may not accurately estimate the overall disease activity, as it misses fluctuations over time.

- Selection bias of the registry overrepresent more severe cases and some categories of JIA, as many patients in remission could have been lost for follow-up.

Conclusion

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- Most JIA patients followed in adult rheumatology clinics fulfilled classification criteria for adult rheumatic diseases, maintain active disease and functional impairment at long-term follow up.
- Younger age at disease onset was predictive of higher HAQ, JADI-A and JADI-E and decreased the chance of inactive disease in adulthood.
- ACPA positivity decreased the likelihood of disease inactivity and RF-positive polyarthritis and SoJIA were predictive of a worse JADI-A.

Conclusion

- JIA represents a group of very different diseases that evolve differently in adulthood.

- Understanding the way these juvenile diseases progress could help to establish a new classification capable of unifying the language between pediatric and adult care.

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