Table 1. Pooled sensitivities and specificities of diagnostic studies on GCA with clinical diagnosis as reference standard

	Index test	Number of studies	Pooled sensitivity (95%CI)	Pooled specificity (95%CI)
All studies	US	23	0.76 (0.66,0.83)	0.91 (0.86,0.94)
	MRI	8	0.82 (0.76,0.86)	0.92 (0.84,0.97)
	PET-CT	5	0.80 (0.70,0.87)	0.91 (0.67,0.98)
Low risk of bias studies	US	8	0.88 (0.83,0.92)	0.96 (0.86,0.99)
	MRI	3	0.81 (0.71,0.89)	0.98 (0.89,1.00)
	PET-CT	4	0.76 (0.67,0.83)	0.95 (0.71,0.99)

GCA, giant cell arteritis; MRI, magnetic resonance imaging; PET-CT, positron emission tomography – computed tomography; US, ultrasound

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Talking about Remission

OP0189

REMISSION CRITERIA GUIDING IMMUNOSUPPRESSIVE THERAPY IN RA: WHICH IS BEST FITTED FOR THIS PURPOSE?

Keywords: Remission, Treat to target, Rheumatoid arthritis

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Background: Remission is the target for the management of rheumatoid arthritis (RA). However, the best definition of remission is still under debate, particularly regarding the inclusion of patient global assessment (PGA).[1] An increased cut-off for PGA (from ≤1 to ≤2cm) was recently proposed by ACR/EULAR for its Boolean-based criteria,[2] but others have suggested to replace PGA by the Physician's Global Assessment (PhGA)[3], or to simply drop PGA (ie, 3-Variable Boolean remission) when the objective is to guide immunosuppressive therapy.[2] Radiographic progression is a relevant reference standard to investigate as outcome of persistent/residual disease activity.

Objectives: To assess which definition of remission best predicts good radiographic outcome (GRO) in RA.

Methods: Meta-analyses using individual patient data (IPD) from 8 randomized controlled trials assessing the efficacy of bDMARDs on radiographic outcomes in RA. Six different definitions of remission were considered: i) The ACR/EULAR Boolean with 4 variables (Boolean 4v) with PGA≤1 (4vPGA); ii) SDAI≤3.3; iii) CDAI≤2.8; iv) Boolean 4v with PGA≤2 (4vPGA2); v) Boolean 4v replacing PGA by PhGA (4vPhGA), and vi) Boolean excluding PGA (3v). Good radiographic outcome (GRO) was defined as an increase of ≤0.5 modified Total Sharp score (mTSS) units. The relationship between achieving each remission definition at 6 and/or 12 months and GRO during the second year was analysed. The pooled probabilities of GRO for the different definitions of remission were estimated and compared, as well as their predictive accuracy (True Positive + True Negative). Meta-analyses were performed using the DerSimonian-Laird random-effects method.

Results: IPD from 4423 patients of 8 RCTs were analysed. 4vPGA remission was achieved by 24.3% of patients and 3V remission by 43.4%. The adoption of the recently proposed PGA≤2 cut-off results in an "in-between" rate of 32.4% (Table 1). GRO was observed in 77.6% of all patients, ranging from 65 to 91% in different trials. GRO among patients achieving remission ranged from 82.4% (3v) to 83.9% (SDAI), without any statistically significant difference between the 6 definitions considered. Boolean 3v remission showed a higher predictive accuracy (51.1%, 95%CI: 46.9-55.6%) than 4vPGA (38.8%, 95%CI: 34.1-43.5%). The 4vPhGA and the 4vPGA2 remission definitions performed in between, providing a correct prediction in 43.8 and 44.8% of the cases, respectively. The performance of SDAI- and CDAI-based definitions were, overall, very similar to that of 4vPGA. (Figure 1)

Table 1. Rates of remission and good radiographic outcomes in the included studies

		Remission at 6 and/or 12-months n (%)			Good Radiographic Outcome n (%)
Trial (year)	N	4vPGA	4vPGA2	3v	ΔmTSS≤0.5
DE019 (2004)	425	68 (16)	94 (22)	113 (27)	297 (70)
TEMPO (2004)	442	113 (26)	156 (35)	204 (46)	330 (75)
COMET (2008)	344	102 (30)	143 (42)	209 (61)	289 (84)
RAPID 1 (2008)	650	177 (27)	243 (37)	320 (49)	508 (78)
RAPID 2 (2009)	417	51 (12)	77 (19)	132 (32)	324 (78)
LITHE (2011)	761	141 (18)	209 (28)	307 (40)	610 (80)
DE013 (2013)	540	156 (29)	175 (32)	206 (38)	351 (65)
FUNCTION (2016)	844	308 (37)	381 (45)	459 (54)	766 (91)
Polled %		24	32*	43*	78
(95% CI)		(18 - 30)	(26 - 39)	(36 - 51)	(71 - 84)

ΔmTSS change in the modified total Sharp score during the second year of follow-up. *p<0.001 when compared with the 4vPGA definition.

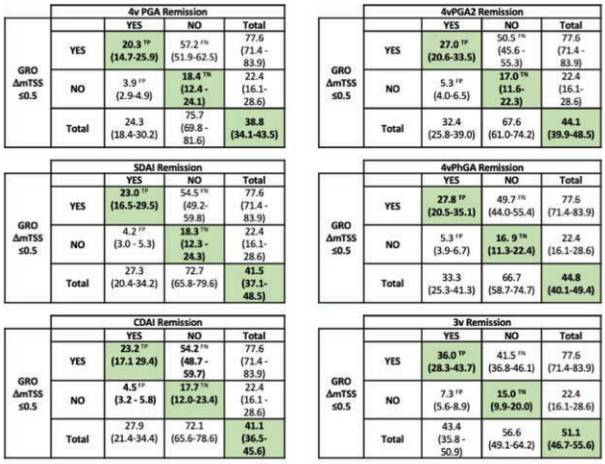

Figure 1: Accuracy of prediction of good radiographic outcome by remission criterion
All meta-analyses used the double arcsine transformation as the preferred method.; 4423 patients were included in GRO analysis; Legend: GRO: Good Radiographic Outcome; TP: True positive, TN: True negative, FP: False positive (risk of undertreatment); FN: False negative (risk of overtreatment). Accurately predicted= TP + TN. Between brackets is the pooled 95% CI.

Conclusion: The Boolean 3v remission provided the most accurate prediction of GRO, even better than 4vPGA2 and 4vPhGA remission. The use of the 3v definition in treatment recommendations would avoid the risk of overtreatment in a significant proportion of patients, with a minor increment in radiographic damage progression, validating 3v-remission as a preferable guide for immunosuppressive treatment. The patient's perspective, which must remain central, is best served by a dedicated autonomous target, rather than PGA: a dual-target approach.

REFERENCES:
[1] Studenic P, et al. Ann Rheum Dis. 2022. doi: 10.1136/ard-2022-223413
[2] Ferreira R, et al. Ann Rheum Dis. 2022. doi: 10.1136/annrheumdis-2021-221917
[3] Pazmino S, et al. J Rheumatol. 2021;48(2):174-8

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Artificial Intelligence in Medicine: Chances & Challenges

OP0190

A MACHINE LEARNING MODEL THAT PREDICTS RA PROGRESSION FROM UNDIFFERENTIATED ARTHRITIS -KURAMA AND ANSWER COHORT STUDY-

Keywords: Rheumatoid arthritis, Undifferentiated connective tissue disease, Real-world evidence

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Background: Early diagnosis and treatment of rheumatoid arthritis (RA) improve clinical outcomes. Undifferentiated arthritis (UA) is arthritis that does not fit a specific diagnosis. Half of the UA undergo spontaneous remission, while 30% of cases develop RA. Therefore, in UA, identifying patients at high risk for developing RA and providing close monitoring for those patients is required for early diagnosis and treatment [1]. However, predicting the evolution of UA to RA is still difficult.
Objectives: Machine learning, including deep learning, which is comparable to and in some cases surpasses the performance of human experts, is broadening its application in medicine. This study aims to build a machine-learning model that predicts the development of UA to RA.
Methods: For model training, a total of 322 UA patients in KURAMA cohort were analyzed (Table 1). For variables to train models, we chose 24 clinical features, which are easy to obtain in daily clinical practice. The target variable was the final diagnosis. We built models using Random forest (RF), XGBoost (XGB), Logistic regression (LR), and Deep neural network (DNN) and compared their performances. For model validation, we used data of 88 UA cases in ANSWER cohort (Table 1).
Results: We trained models using 24 clinical parameters at the first clinical visit, performed 10-fold cross-validation, and evaluated model performance by averaging accuracy and AUC. The performance of the models was 73.5%, 74.2%, 74.5%, and 85.1% in precision and 0.760, 0.734, 0.748, and 0.895 in AUC for RF, XGB, LR, and DNN, respectively. DNN showed the highest performance. We then applied the DNN model to external validation data from ANSWER cohort and found that the prediction accuracy was 80.0%.
Conclusion: Using parameters available in clinical practice, we developed a DNN model that effectively predicted RA development in internal and external UA datasets. Applying a machine learning approach might enable identifying patients at high risk of RA progression and improve the clinical management of UA patients.

REFERENCE:

[1] de la Calle-Fabregat C, Niemantsverdriet E, Cañete JD, Li T, van der Helm-van Mil AHM, Rodríguez-Ubreva J, Ballestar E. Prediction of the Progression of Undifferentiated Arthritis to Rheumatoid Arthritis Using DNA Methylation Profiling. Arthritis Rheumatol. 2021 Dec;73(12):2229-2239. doi: 10.1002/art.41885. Epub 2021 Nov 2. PMID: 34105306.

Table 1. Baseline patients' characteristics

	KURAMA		ANSWER	
Variables	RA (n=94)	Non-RA (n=228)	RA (n=14)	Non-RA (n=74)
age (median, yr)	60 [46.5-69]	53.5 [44-64]	44 [37.75-53.5]	63 [53.3-69.8]
sex (female%)	72.34%	78.07%	71.43%	64.86%
BMI (median, kg/m^2)	22.03 [20.09-24.29]	21.23 [19.22-23.90]	22.60 [20.85-28.37]	21.55 [19.68-23.44]
Family history of RA (positive %)	31.91%	27.19%	14.29%	17.57%
Smoking (current or past %)	35.11%	30.70%	57.14%	63.51%
CRP (median, mg/dL)	0.3 [0.1-1.1]	0.1 [0-0.1]	0.23 [0.078-0.63]	0.12 [0.04-1.09]
ESR_1h (median, mm)	19 [9-41]	12 [6-19.25]	11 [8-36.75]	13 [7.5-37.5]
RF (median, IU/mL)	8 [8-22.7]	8 [8-18.53]	6 [5-36.75]	7 [5-19]
ACPA (median, U/mL)	0.6 [0.6-0.7]	0.6 [0.6-0.6]	5.6 [0.675-263]	0.7 [0.5-3.05]
MMP-3 (median, ng/mL)	65.85 [43.15-137.58]	46.7 [31.9-62.13]	81.4 [49.03-98.78]	55.35 [39.16-128.15]
Dr_VAS (median, mm)	20 [9.25-33]	7 [2-17.25]	20 [10.5-32.25]	18 [10-33]
Pt_VAS (median, mm)	49.5 [22.25-67.75]	44 [15-55.25]	48.5 [31.5-64.5]	47 [21-68]
DAS28_CRP (median,)	3.22 [2.36-4.08]	2.38 [1.78-2.94]	3.27 [2.38-4.02]	3.09 [2.27-4.20]
HAQ (median)	0.5 [0.125-1]	0.25 [0-0.5]	0.313 [0-0.594]	0.375 [0.125-0.969]
ACR2010_points (median)	4 [3-5]	3 [2-4]	1 [0.25-2.75]	1 [0-2] [Q1-Q3]

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