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OP0287

IMMUNOMODULATORY THERAPIES FOR SEVERE FORMS OF COVID-19: A SYSTEMATIC LITERATURE REVIEW TO INFORM EULAR POINTS TO CONSIDER

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Background: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV2) pandemic is a global health problem. Beside the specific pathogenic effect of SARS-CoV-2, a deleterious aberrant non-effective host immune response plays an important role especially in severe forms of COVID-19. There is intense investigation to explore the utility of immunomodulatory drugs commonly used in the Rheumatology arena as agents that may mitigate against COVID-19 to improve disease prognosis. Rheumatologists are used to the utilization of these immune targeted therapies.

Objectives: To summarize the available information on the use of immunomodulatory agents in severe COVID-19.

Methods: As part of a EULAR taskforce, a systematic literature search was conducted from January 2019 up to December 11, 2020. Two reviewers independently identified eligible studies according to the PICO framework P (population): patients with SARS-CoV-2 infection; I (intervention): any immunomodulator agent/strategy; C (comparator): any comparator; O (outcome) any clinical outcome including but not limited to mortality, admission to intensive care unit and clinical improvement. Data on efficacy and safety of immunomodulatory agents utilized therapeutically in SARS-CoV-2 infection at any stage were extracted. The risk of bias was assessed using validated tools.

Results: Of 60372 records, 401 articles were eligible for inclusion. Studies were at variable risk of bias. Randomised controlled trials (RCTs) were available for the following drugs: hydroxychloroquine (N=12), glucocorticoids (N=6), tocilizumab (N= 4), convalescent plasma (N=4), interferon beta (N=2), IVIg (N=2) and N=1 each for anakinra, baricitinib, colchicine, leflunomide, ruxolitinib, interferon kappa, and vilobelimab. For glucocorticoids, dexamethasone reduced mortality only in patients requiring respiratory support; while methylprednisolone reduced mortality in patients aged 60 years or over. Data from RCTs on tocilizumab are conflicting and definite conclusions cannot be drawn at this point in time, but recent studies suggest possible benefit in patients requiring respiratory support. Hydroxychloroquine was not beneficial at any disease stage, one RCT with anakinra was negative, one RCT with baricitinib+remdesivir was positive, and individual trials testing some other compounds provided interesting, albeit preliminary, results.

Conclusion: Although there is emerging evidence about immunomodulatory therapies for the management of COVID-19, conclusive data is scarce with some conflicting data. Since glucocorticoids seem to improve survival in some subsets of patients, RCTs comparing glucocorticoids alone versus glucocorticoids plus anti-cytokine/immunomodulatory treatment are warranted. This SLR informed the initiative to formulate EULAR points to consider on pathophysiology and use of immunomodulatory therapies in COVID-19.

Figure 1. Forest plots showing the risk ratio (RR) and 95% confidence interval for mortality in randomized controlled trials divided by intervention. The latest follow-up available is reported in the timing column.

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OP0288

MACHINE LEARNING ALGORITHMS TO PREDICT COVID-19 ACUTE RESPIRATORY DISTRESS SYNDROME IN PATIENTS WITH RHEUMATIC DISEASES: RESULTS FROM THE GLOBAL RHEUMATOLOGY ALLIANCE PROVIDER REGISTRY

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Background: Acute Respiratory Distress Syndrome (ARDS) is a life-threatening complication of COVID-19 and has been reported in approximately one-third of hospitalized patients with COVID-19¹. Risk factors associated with the development of ARDS include older age and diabetes². However, little is known about factors associated with ARDS in the setting of COVID-19, in patients with rheumatic disease or those receiving immunosuppressive medications. Prediction algorithms using traditional regression methods perform poorly with rare outcomes, often yielding high specificity but very low sensitivity. Machine learning algorithms optimized for rare events are an alternative approach with potentially improved sensitivity for rare events, such as ARDS in COVID-19 among patients with rheumatic disease.

Objectives: We aimed to develop a prediction model for ARDS in people with COVID-19 and pre-existing rheumatic disease using a series of machine learning algorithms and to identify risk factors associated with ARDS in this population.

Methods: We used data from the COVID-19 Global Rheumatology Alliance (GRA) Registry from March 24 to Nov 1, 2020. ARDS diagnosis was indicated by the reporting clinician. Five machine learning algorithms optimized for rare events predicted ARDS using 42 variables covering patient demographics, rheumatic disease diagnoses, medications used at the time of COVID-19 diagnosis, and comorbidities. Model performance was assessed using accuracy, area under curve, sensitivity, specificity, positive predictive value, and negative predictive value. Adjusted odds ratios corresponding to the 10 most influential predictors from the best performing model were derived using hierarchical multivariate mixed-effects logistic regression that accounted for within-country correlations.

Results: A total of 5,931 COVID-19 cases from 67 countries were included in the analysis. Mean (SD) age was 54.9 (16.0) years, 4,152 (70.0%) were female, and 2,399 (40.5%) were hospitalized. ARDS was reported in 388 (6.5% of total and 15.6% of hospitalized) cases. Statistically significant differences in the risk of ARDS were observed by demographics, diagnoses, medications, and comorbidities using unadjusted univariate comparisons (data not shown). Gradient boosting machine (GBM) had the highest sensitivity (0.81) and was considered the best performing model (Table 1). Hypertension, interstitial lung disease, kidney disease, diabetes, older age, glucocorticoids, and anti-CD20 monoclonal antibodies were associated with the development of ARDS while tumor necrosis factor inhibitors were associated with a protective effect (Figure 1).

Table 1. Performance of machine learning algorithms.

	GBM	SVM	GLMNET	NNET	RF
Accuracy	0.79	0.68	0.66	0.66	0.67
AUC	0.75	0.70	0.74	0.58	0.74
Sensitivity	0.81	0.68	0.65	0.68	0.67
Specificity	0.49	0.60	0.73	0.48	0.68
PPV	0.96	0.96	0.97	0.95	0.97
NPV	0.16	0.12	0.13	0.09	0.13

GBM: Gradient Boosting Machine, SVM: Support vector machines, GLMNET: Lasso and Elastic-Net Regularized Generalized Linear Models, NNET: Neural Networks, RF: Random Forest. AUC: Area Under Curve; PPV: Positive Predictive Value; NPV: Negative Predictive Value.

Conclusion: In this global cohort of patients with rheumatic disease, a machine learning model, GBM, predicted the onset of ARDS with 81% sensitivity using baseline information obtained at the time of COVID-19 diagnosis. These results identify patients who may be at higher risk of severe COVID-19 outcomes. Further studies are necessary to validate the proposed prediction model in external cohorts and to evaluate its clinical utility. Disclaimer: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance, and do not necessarily represent the views of the ACR, NIH, (UK) NHS, NIHR, or the department of Health.

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