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Severe COVID-19 outcomes in patients with psoriasis

Psoriasis is a chronic inflammatory disease associated with comorbidities known to increase risk of severe COVID-19, such as hypertension, cardiovascular disease, diabetes and obesity.^{1,2} Use of systemic therapies may increase a patient's risk of infections.³ Our study aims to evaluate the association of psoriasis systemic therapy and COVID outcomes.

This retrospective cohort study used RPDR, a clinical data registry, to identify patients with psoriasis (ICD-10 code L40) and positive COVID RT-PCR, between March and May/2020. By reviewing medical records on EPIC, active psoriasis prior to COVID was confirmed.

The exposure was psoriasis systemic therapy for at least three months prior to COVID. Our primary outcome was a composite of ICU admission, intubation and/or death.

Table 1 Demographic and clinical characteristics of patients†

	Biologic, n = 24	MTX, n = 10	Systemic therapy, n = 37	No systemic therapy, n = 67	P-value‡
Demographics					
Age (years)	51.9 ± 17.5	63.5 ± 10.6	55.1 ± 16.0	57.4 ± 18.4	0.51
Male	12 (50.0%)	7 (70.0%)	21 (56.8%)	38 (56.7%)	1.0
White	18 (75.0%)	7 (70.0%)	26 (70.3%)	43 (64.2%)	0.67
Comorbidities					
BMI (Kg/cm ²)	30.8 ± 6.8	30.3 ± 7.6	30.1 ± 7.0%	30.5 ± 6.3%	0.77
Current smoking	1 (4.2%)	1 (10.0%)	2 (5.4%)	3 (4.5%)	1.00
Alcohol abuse	1 (4.2%)	1 (10.0%)	2 (5.4%)	7 (10.4%)	0.49
Diabetes mellitus	5 (20.8%)	3 (30.0%)	9 (24.3%)	22 (32.8%)	0.50
Hypertension	15 (62.5%)	6 (60.0%)	22 (59.5%)	34 (50.7%)	0.42
Chronic respiratory disease	4 (16.7%)	4 (40.0%)	8 (21.6%)	16 (23.9%)	0.50
Cardiovascular disease	2 (8.3%)	2 (20.0%)	4 (10.8%)	11 (16.4%)	0.57
Renal disease	2 (8.3%)	0	2 (5.4%)	11 (16.4%)	0.13
Psoriatic Arthritis	16 (66.7%)	6 (60.0%)	24 (64.9%)	3 (4.5%)	<0.001
COVID-19 Outcomes					
Hospital admission			15 (40.5%)	26 (38.8%)	0.86
Supplemental oxygen			9 (24.3%)	24 (35.8%)	0.23
ICU admission			3 (8.3%)	10 (14.9%)	0.34
Orotracheal intubation			2 (5.6%)	6 (9.0%)	0.54
Death			2 (5.6%)	7 (10.8%)	0.39

†Continuous and categorical data are represented by mean ± SD and number of patients (%), respectively. Patients on both a biologic and methotrexate were not shown in the biologic and methotrexate columns, only in the combined systemic therapy column. MTX – methotrexate.

‡Comparison between patients on any systemic therapy and non-systemic therapy, using two-sided Student's *t*-test, Fisher's exact test or logistic regression for continuous and categorical data, respectively.

Table 2 Main composite outcome – univariable analysis

	Composite outcome, n (%)	Unadjusted OR (95% CI)	P-value†
Systemic therapy			
Yes (n = 37)	4 (10.8)	0.62 (0.18–2.10)	0.44
No (n = 67)	11 (16.4)		
Age			
≤ 60 (n = 61)	5 (8.2)	3.39 (1.07–10.79)	0.04
>60 (n = 43)	10 (23.3)		
Sex			
Male (n = 59)	7 (11.9)	1.61 (0.54–4.82)	0.40
Female (n = 45)	8 (17.8)		
Race			
White (n = 69)	9 (13.0)	0.73 (0.24–2.23)	0.58
Non-white (n = 35)	6 (17.1)		
Obesity			
Yes (n = 49)	9 (18.4)	1.84 (0.60–5.60)	0.29
No (n = 55)	6 (10.9)		
Current smoking			
Yes (n = 5)	0	–	1.00
No (n = 99)	15 (15.2)		
Alcohol abuse			
Yes (n = 9)	1 (11.1)	0.72 (0.08–6.24)	0.77
No (n = 95)	14 (14.7)		
Diabetes			
Yes (n = 31)	12 (38.7)	14.74 (3.77–57.58)	<0.001
No (n = 73)	3 (4.1)		
Hypertension			
Yes (n = 56)	13 (23.2)	6.95 (1.48–32.62)	0.01
No (n = 48)	2 (4.2)		
Respiratory disease			
Yes (n = 24)	4 (16.7)	1.26 (0.36–4.37)	0.72
No (n = 80)	11 (13.8)		
Cardiovascular disease			
Yes (n = 15)	6 (40.0)	5.93 (1.71–20.51)	0.005
No (n = 89)	9 (10.1)		
Renal disease			
Yes (n = 13)	5 (38.5)	5.06 (1.39–18.51)	0.01
No (n = 91)	10 (11.0)		
Arthritis			
Yes (n = 27)	3 (11.1)	0.68 (0.18–2.61)	0.57
No (n = 77)	12 (15.6)		

†Logistic regression.

Logistic regression assessed the association of therapy status with COVID-19 severe composite outcome (SCO). We adjusted for age and diabetes, based on prior knowledge. In addition, given the small number of outcomes, we used a propensity score (PS), calculated as a predicted probability of receiving or not systemic treatment as a function of all clinically relevant variables. The effect of systemic treatment was

adjusted using this PS as covariate in another model (SPSS 20.2, IBM, USA).

Our study included 104 patients. Among 37 patients on systemic therapy, 27 patients were using biologics (18, on anti-TNF α ; 4, on anti-IL17; 3, on anti-IL12/23; and 2, on anti-IL23). There were 13 patients on methotrexate (10 to 22.5 mg/week). Three patients were taking both. Most comorbidities and demographics were similar between groups. Analysing patients on methotrexate and biologics separately did not show differences (Table 1).

There were no significant differences in the SCO or other outcomes between patients taking or not systemic therapies. 8.3% of patients on biologics, 20% of patients on methotrexate and 16.4% of patients not on systemic therapy had the SCO. Older patients and the presence of diabetes mellitus, hypertension, cardiovascular and renal disease significantly increased the OR of developing the SCO (Table 2).

Adjusting for age and diabetes, systemic therapy remained not associated with our main outcome (OR 0.82, 0.21–3.24, $P = 0.77$). In another model, all covariates became balanced between exposure groups after adjusting for the PS and systemic treatment remained not associated with the SCO (OR 0.91, 0.17–4.81, $P = 0.92$).

Amidst this pandemic, dermatologists have to decide whether holding psoriasis therapies may protect patients or trigger a ‘cytokine storm’.⁴ In our study, we did not find increased rates of severe COVID in patients receiving systemic therapy.

Prior studies have not shown worsen COVID-19 outcomes among psoriasis patients on biologics.^{5–7} A large Italian study did not detect ICU admissions or deaths suspected for COVID-19.⁸ Few studies evaluated conventional systemic therapies. One study reported no deaths or hospitalizations in patients using cyclosporine.⁹ Methotrexate was associated with more hospitalizations in one study.¹⁰ In our study, methotrexate did not significantly increase severe outcomes.

In our cohort, by requiring confirmation of COVID by PCR testing, patients with more severe infection may have been included and 15 patients were admitted to an ICU, intubated and/or died. However, these proportions were similar in both exposure groups. As expected, increased age, diabetes, hypertension, cardiovascular and renal diseases increased the odds of SCO.

As a result of real-world data, patients with increased number of comorbidities may have decreased likelihood of receiving systemic therapy for psoriasis. As an attempt to circumvent that, we used PS analysis, comparing patients with similar chance of allocation in the exposure groups. Detection of COVID-confirmed severe outcomes in psoriasis population and detailed information on significant covariates allowed evaluation of crude and adjusted effect of systemic therapy. Our study suggests

that systemic psoriasis therapy does not worsen COVID-19. Larger detailed studies are needed.

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Patients in this manuscript have given written informed consent to publication of their case details.

Conflict of interest

Dr. Lima serves on the speakers' bureau for Abbvie. Mary Cueva has no relevant conflicts of interest. Dr. Lopes receives scholarship from CAPES - Brazilian Federal Agency for Support and Evolution of Graduate Education within the Ministry of Education of Brazil. Dr. Alora has been an investigator for Abbvie, Janssen, Celgene, Eli Lilly, Pfizer, Inc., Novartis.

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Delayed melanoma diagnosis in the COVID-19 era: increased breslow thickness in primary melanomas seen after the COVID-19 lockdown

Editor

For malignant melanoma (MM), the Breslow thickness and the presence of ulceration are important elements for determining the staging and prognosis.¹ Skin cancer screening and dermoscopic examination allowed an earlier recognition of cutaneous MM, causing especially an over-detection of thin lesions, without a proportional decline in later-stage disease.² Furthermore, the incidence of thicker MMs does not seem to be decreasing.^{3,4} Due to the COVID-19 pandemic, some planned medical activities have been postponed, for both national directives and out of concern of the patients who were afraid to go to hospitals.⁵ The aim of this study was to verify whether the Italian lockdown for the COVID-19 pandemic has had any detrimental effect on MM diagnosis. This cross-sectional study collected all consecutive primary MM from the Pathology Registry of IDI-IRCCS, a dermatological reference centre in Rome, Italy. Mean Breslow thickness (mm), ulceration (%) and other main histological features were collected. We divided the COVID-19 Italian pandemic into three phases: (i) prelockdown: from 1 January to 9 March; (ii) lockdown: from 10 March to 3 May; and (iii) postlockdown: from 4 May, when the lockdown measures started to be progressively eased, to 6 June – the last surgery date for which confirmed pathology results were available. Frequency distributions, means and proportions were obtained using the IBM SPSS Statistics for Windows, Version 26.0.0.1 (IBM Corp., Armonk, NY, USA). Differences between proportions were tested using the Fisher exact test. Differences between measures of central tendency were tested using the non-parametric Kruskal–Wallis one-way ANOVA on ranks. 95% confidence intervals (CIs) for the means and for the conditional maximum-likelihood estimates of the odds ratios (OR, in this case, Fisher's exact 95% CI) were computed using the OpenEpi online resource.⁶ During the 158 days of the study period, a total of 237 patients with primary MM were diagnosed: 128 (54.0%) were males, and average age was 57 years (standard deviation, 17). The mean number of MM diagnoses per day were as follows: 2.3 in the prelockdown phase, 0.6 during the lockdown and 1.3 after the lockdown (in 2018–2019, we had 2.3/day). The characteristics of the MMs are shown in Table 1. The OR for nodular MMs in the post- vs. prelockdown phases is 5.5 (exact 95% CI, 1.3–25.1), for SSM with nodule is 3.9 (exact 95% CI, 0.9–16.7), and for ulcerated MMs is 4.9 (exact 95% CI, 1.4–17.3). Proportion of ulceration was 5.9% (95% CI, 2.4–11.7%) prelockdown and 23.5% (95% CI 10.8–41.2%) postlockdown. Mean Breslow thickness was 0.88 (95%