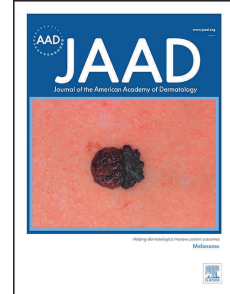


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The clinical spectrum of COVID-19-associated cutaneous manifestations: an Italian multicentre study of 200 adult patients

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61 **ABSTRACT**

62 **Background:** COVID-19 is associated with a wide range of skin manifestations.

63 **Objective:** To describe the clinical characteristics of COVID-19-associated skin manifestations, and
64 explore the relationships between the six main cutaneous phenotypes and systemic findings.

65 **Methods:** Twenty-one Italian Dermatology Units were asked to collect the demographic, clinical and
66 histopathological data of 200 patients with COVID-19-associated skin manifestations. The severity of
67 COVID-19 was classified as asymptomatic, mild, moderate, or severe.

68 **Results:** A chilblain-like acral pattern significantly associated with a younger age ($p < 0.0001$) and,
69 after adjusting for age, significantly associated with less severe COVID-19 ($p = 0.0009$). However, the
70 median duration of chilblain-like lesions was significantly longer than that of the other cutaneous
71 manifestations taken together ($p < 0.0001$). Patients with moderate/severe COVID-19 were more
72 represented than those with asymptomatic/mild COVID-19 among the patients with cutaneous
73 manifestations other than chilblain-like lesions, but only the confluent erythematous/maculo-
74 papular/morbilliform phenotype significantly associated with more severe COVID-19 ($p = 0.015$), and
75 this significance disappeared after adjusting for age.

76 **Limitations:** Laboratory confirmation of COVID-19 was not possible in all cases.

77 **Conclusions:** After adjusting for age, there was no clear-cut spectrum of COVID-19 severity in
78 patients with COVID-19-related skin manifestations although chilblain-like acral lesions were more
79 frequent in younger patients with asymptomatic/paucisymptomatic COVID-19.

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84 **CAPSULE SUMMARY**

85 • There are six main COVID-19-related cutaneous phenotypes, but only the chilblain-like acral
86 pattern significantly associated with younger age.

87 • After adjusting for patient age, there was no spectrum of COVID-19 severity in relation to
88 cutaneous phenotypes, although the longer-lasting chilblain-like acral pattern significantly
89 associated with milder disease.

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91 **INTRODUCTION**

92 Coronavirus disease 19 (COVID-19) is an infectious illness caused by severe acute respiratory
93 syndrome coronavirus 2 (SARS-CoV-2) that may affect multiple organs, including the skin (the
94 prevalence of cutaneous involvement was 7.8% in one bi-national Chinese-Italian cohort of 678
95 hospitalised adults with laboratory-confirmed disease).¹

96 A number of skin manifestations have been described in individual case reports and nationwide case
97 series. Galván Casas *et al.* published the first large clinical study of 375 patients with various COVID-
98 19-associated skin manifestations² and, on the basis of the available literature and direct clinical
99 experience, three of the authors of this paper (A.V. Marzano, G. Genovese and C. Moltrasio) have
100 identified six main phenotypes: i) urticarial rash; ii) confluent erythematous/maculo-
101 papular/morbilliform rash; iii) papulovesicular exanthem; iv) a chilblain-like acral pattern; v) a livedo
102 reticularis/racemosa-like pattern; and vi) a purpuric “vasculitic” pattern.³ However, there have been
103 reports of a miscellany of other cutaneous presentations that cannot be included in this
104 classification, including erythema multiforme-like⁴, pityriasis rosea-like⁵, and Grover’s disease-like
105 manifestations.⁶ Galván Casas *et al.* found maculopapular eruptions accounted for almost half of the
106 cutaneous manifestations in their study,² but the majority of published studies have focused on
107 chilblain-like acral lesions,⁷⁻¹⁰ which are generally associated with a benign clinical course and more
108 frequently reported in children.¹¹⁻¹³

109 The aim of this nationwide multicentre study was to provide clinical data concerning COVID-19-
110 associated skin manifestations in order to improve the clinical and demographic characterisation of
111 the cutaneous phenotypes that have previously been defined only on the basis of previously
112 published preliminary data.³ The main study objective was to explore the possible associations
113 between these phenotypes, extra-cutaneous symptoms, and the severity of COVID-19.

114

115 MATERIALS AND METHODS

116 Patients

117 With the support of the Italian Society of Dermatology and Sexually Transmitted Diseases
118 (SIDeMaST), 21 Italian Dermatology Units contributed to collecting the clinical data of patients with
119 COVID-19-associated skin manifestations who were examined between 1 and 18 March 2020. The
120 data included sex, age at the time of onset of COVID-19, the presence/absence of co-morbidities,
121 cutaneous patterns, the presence/absence of mucosal lesions, the duration of skin manifestations,
122 skin-related symptoms, systemic symptoms, the duration of systemic symptoms, the latency
123 between the cutaneous manifestations and systemic symptoms, death, and the severity of COVID-19.
124 Each participating centre was asked to provide data on the basis of the following patient inclusion
125 criteria: i) an age of ≥ 18 years; ii) probable or laboratory-confirmed COVID-19; and iii) the presence of
126 COVID-19-related skin manifestations confirmed by an expert dermatologist. A COVID-19 diagnosis
127 was considered to be laboratory-confirmed in the case of a nasopharyngeal swab positive for SARS-
128 CoV-2 RNA or positive serology for anti-SARS-CoV-2 IgG/IgM antibodies. COVID-19 was considered
129 probable in any patient meeting the clinical criteria (dry cough, fever, dyspnea, the sudden onset of
130 hyposmia or hypogeusia) who had been in close contact with someone with confirmed COVID-19 in
131 the 14 days before symptom onset. A history of new medications in the 15 days before the onset of
132 the skin manifestations was considered an exclusion criterion.

133 Clinical assessment

134 Systemic symptoms were taken from the charts of hospitalised patients or reported by outpatients,
135 and assessed by a physician (pulmonologist, or a specialist in internal/emergency medicine or
136 infectious diseases). The duration of the skin manifestations was directly evaluated by a
137 dermatologist in the case of hospitalised patients, or reported by outpatients. Each patient was
138 examined at least twice (during the period of skin manifestations and after their resolution).
139 The severity of COVID-19 was classified as asymptomatic, mild (in the presence of fever, cough
140 and/or gastrointestinal symptoms with no imaging sign of pneumonia), moderate (in the presence of

141 dyspnea and/or radiological findings of pneumonia) or severe (a need for invasive assisted
142 ventilation, the occurrence of thromboembolic events, or death),¹⁴ and was assessed by considering
143 the worst systemic symptoms over the entire course of the disease as shown in hospital records or
144 self-reported by outpatients.

145 **Statistical analysis**

146 Continuous variables are expressed as median values and interquartile ranges (IQR), and
147 dichotomous variables as absolute numbers and percentages. Quantitative variables (disease
148 severity, symptoms, cutaneous phenotypes) were compared between groups using the non-
149 parametric Wilcoxon-Mann-Whitney test.

150 Logistic regression analysis was used to assess the role of the six predefined skin phenotypes as risk
151 factors for extra-cutaneous symptoms (fever, cough, dyspnea, pneumonia, gastrointestinal
152 symptoms, hyposmia/hypogeusia) and the severity of COVID-19 (dichotomised as asymptomatic or
153 mild vs moderate or severe). Univariate logistic regression models of each cutaneous phenotype
154 were fitted by considering the severity of COVID-19 and the six extra-cutaneous symptoms as
155 dependent variables (seven separate models); the phenotype was considered an independent
156 variable. In addition, age-adjusted logistic regression analyses were made because of the possible
157 confounding effect of age on symptoms and the severity of COVID-19. Odds ratios (ORs) and their
158 95% confidence intervals (CI) were obtained from the estimates of the logistic model parameters.
159 Differences in the prevalence of symptoms between phenotypes were assessed using chi-square
160 tests. Given the small number of patients with a livedo reticularis-like/racemosa-like pattern, only
161 five phenotypes were considered (the purpuric and reticularis/racemosa-like patterns were merged).
162 Patients with more than one cutaneous phenotype were not included in the statistical analyses,
163 which were made using SAS statistical software (release 9.4, SAS Institute, Inc., Cary, North Carolina).
164 A two-sided P value of <0.05 was considered statistically significant

165 **Ethical approval and consent to participate**

166 The study was conducted in accordance with the Declaration of Helsinki, and the full protocol was
167 approved by the Institutional Review Board of the Ethics Committee of the Principal Investigator's
168 centre (Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Italy; Protocol No.
169 464_2020). All of the subjects enrolled in the study gave their written informed consent.

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170 RESULTS**171 Patients and cutaneous manifestations**

172 The demographic and clinical features of the 200 patients are summarised in Table 1. The patients
173 were predominantly males (n=108; 54%), and their median age at the time of the diagnosis of COVID-
174 19 was 57 years (IQR 40.25-72.25). Eighty-six of the 195 patients with available data (43%) had
175 experienced at least one co-morbidity.

176 Thirteen patients (6.5%) presented with more than one cutaneous phenotype. Of the 187 patients
177 with only one phenotype, 19 (10.2%) developed urticarial rash; 48 (25.7%) confluent
178 erythematous/maculo-papular/morbilliform rash; 29 (15.5%) papulovesicular exanthem; 46 (24.6%)
179 a chilblain-like acral pattern; 4 (2.1%) a livedo reticularis/racemosa-like pattern; and 13 (6.9%) a
180 purpuric “vasculitic” pattern (Supplemental Fig. 1). Cutaneous manifestations other than those
181 included in the classification mentioned above³ were observed in 28 patients (15.0%): pityriasis
182 rosea-like lesions in 10; erythema multiforme-like lesions in eight; erythema nodosum-like lesions in
183 four; panniculitis in four; and angioedema in two. No mucosal lesions were recorded. The most
184 frequent skin-related symptom was pruritus (n=81; 40.5%), followed by pain/burning (n=22; 11%).

185 Among the 168 patients for whom data were available, the median duration of the skin
186 manifestations was 12 days (IQR 8-20). However, the median duration of chilblain-like acral lesions
187 was significantly longer than that of the other cutaneous manifestations taken together (21.5 [15-31]
188 vs 10 [7-15] days; $p < 0.0001$). The median latency between the cutaneous manifestations and
189 systemic symptoms was 14 days (IQR 4-27) in the 155 patients for whom the data were available. The
190 median duration of the individual skin manifestations and the latency between these and systemic
191 symptoms are detailed in Table 1.

192 Interestingly, the median age of the patients with a chilblain-like acral pattern was significantly lower
193 than that of the patients with all of the other cutaneous phenotypes taken together (38.5 [23-55] vs
194 60 [50-75] years; $p < 0.0001$). The median age of the patients with purpuric and livedo reticularis-
195 like/racemosa-like patterns was significantly higher than that of the patients with the other

196 manifestations taken together (66 [58-84] vs 55 [39-71] years; $p=0.0022$), and the median age of the
197 patients with confluent erythematous/maculo-papular/morbilliform rash was also significantly higher
198 than that of the patients with the other manifestations taken together (61 [51.5-78] vs 55 [36-71]
199 years; $p=0.029$). There was no statistically significant association with age in the case of the
200 papulovesicular and urticarial phenotypes.

201 The median age of the patients with moderate/severe COVID-19 was significantly higher than that of
202 those with asymptomatic/mild COVID-19 (64 [54.5-78] vs 40 [27-57] years; $p<0.0001$). It was also
203 significantly higher in the patients with fever than in those without (59 [50-75] vs 38 [26-61] years;
204 $p<0.0001$), in those with cough than in those without (58.5 [50-74] vs 52 [30-71] years; $p=0.0077$), in
205 those with dyspnea than in those without (65 [55-78] vs 49 [30.5-63] years; $p<0.0001$), and in those
206 with pneumonia than in those without (65 [55-80] vs 41.5 [28-57] years; $p<0.0001$). There was no
207 statistically significant difference in median age in the case of gastrointestinal symptoms or
208 hypogeusia/hyposmia.

209 **Clinical features of COVID-19**

210 As shown in Table 2, COVID-19 was laboratory-confirmed in 124 patients, and regarded as probable
211 in the remaining 73. Thirty-one patients (15.5%) were asymptomatic; 51 (25.5%) had mild disease; 95
212 (47.5%) had moderate disease; and 23 (11.5%) had severe disease. Among the 124 patients for whom
213 the data were available, the median duration of systemic symptoms was 23 days (IQR: 12-31).

214 Skin signs pre-dated systemic symptoms in 11 patients; among the remaining 189, they followed
215 ($n=186$) or were concomitant with systemic symptoms ($n=3$). Fever was the most frequent systemic
216 symptom ($n=146$; 73%), followed by cough ($n=108$; 54%), pneumonia ($n=106$; 53%), dyspnea ($n=77$;
217 38.5%), gastrointestinal symptoms ($n=46$; 23%), and hypogeusia/hyposmia ($n=44$; 22%).
218 Thromboembolic complications occurred in 11 patients (5.5%), and death in seven (3.5%).

219 The median duration of systemic symptoms by each cutaneous phenotype is detailed in Table 2.

220

221 **Relationships between cutaneous phenotypes and the severity of COVID-19/extra-cutaneous**
222 **features**

223 It is worth noting that, after adjusting for age, chilblain-like acral lesions were associated with a
224 decreased risk of experiencing more severe COVID-19 (OR = 0.23, 95% CI 0.09-0.55; p=0.0009). On
225 the other hand, confluent erythematous/maculopapular/morbilliform rash was associated with more
226 severe COVID-19 before (OR = 2.49, 95% CI 1.19-5.18; p=0.015) but not after adjusting for age (OR =
227 1.9, 95% CI 0.83-4.37; p=0.1307).

228 Although patients with moderate/severe COVID-19 were more represented than those with
229 asymptomatic/mild COVID-19 among the patients with cutaneous phenotypes other than chilblain-
230 like lesions, there was no statistically significant association with the severity of COVID-19.

231 After adjusting for age, confluent erythematous/maculo-papular/morbilliform rash was identified as
232 a significant risk factor for cough (OR = 2.25, 95% CI 1.1-4.63; p=0.0269); the urticarial pattern as a
233 significant risk factor for gastrointestinal symptoms (OR = 6.10, 95% CI 2.25-16.59; p= 0.0004); and
234 the livedo-like/vasculitic pattern as a significant risk factor for dyspnea (OR =4.17, 95% CI 1.05-16.5;
235 p= 0.042).

236

237 **DISCUSSION**

238 With the exponential increase in the number of COVID-19 patients worldwide, the clinical features of
239 the disease are being better defined and a number of reports have documented the occurrence of
240 various cutaneous manifestations. In our nationwide cohort, the patients mainly presented with the
241 six cutaneous phenotypes previously identified by our group.³

242 The most frequent cutaneous phenotypes were confluent erythematous/maculo-
243 papular/morbilliform rash and a chilblain-like acral pattern, which affected respectively 25.7% and
244 24.6% of the 187 patients included in the statistical analysis, whereas the least frequent was a livedo
245 reticularis-like/racemosa-like pattern (2.1%). The median latency between the onset of the
246 cutaneous manifestations and systemic symptoms was 14 days (varying from four days in the case of
247 papulovesicular exanthem to 24.5 days in the case of a livedo reticularis-like/racemosa-like pattern).
248 The median duration of the cutaneous manifestations was 12 days (ranging from eight days in the
249 case of urticarial rash to 22 days in the case of a chilblain-like acral pattern).

250 Pityriasis rosea-like and erythema multiforme-like patterns were the most frequently reported skin
251 manifestations falling outside our classification, but it is still debated whether the former is directly
252 mediated by SARS-CoV-2 or caused by COVID-19-related immune system dysfunction leading to
253 human herpes virus(HHV)-6/HHV-7 reactivation,^{5,15,18} and whether the latter is triggered by SARS-
254 CoV-2 or other viruses.⁴

255 In line with previous observations, none of our patients experienced mucosal membrane lesions.¹⁶
256 Although the angiotensin-converting enzyme 2 (ACE2) receptor of the spike protein of SARS-CoV-2
257 has been described as being not only expressed on keratinocytes¹⁷ but also in the oral cavity,¹⁸
258 mucosal membrane lesions have very rarely been reported in patients with COVID-19¹⁶.

259 The main strength of this study is our exploration of the relationships between cutaneous
260 phenotypes and the severity of COVID-19. Two studies of large cohorts of patients with COVID-19-
261 related skin manifestations have found a gradient of increasingly severe systemic symptoms going
262 from chilblain-like lesions to a livedo/necrotic pattern.^{3,19} However, unlike these studies, our study

263 adjusted for patient age and failed to confirm this spectrum. Only the chilblain-like acral phenotype
264 significantly associated with less severe COVID-19 and, although patients with severe disease were
265 prevalent in each of the other five phenotypic categories, none of them significantly associated with
266 an increased risk of more severe COVID-19.

267 Moreover, in line with the findings of other studies,⁷ the chilblain-like acral phenotype was associated
268 with a younger age at the time of COVID-19 diagnosis, whereas the livedo-like/vasculitic and maculo-
269 papular phenotypes were associated with an older age at the time COVID-19 diagnosis. The
270 pathological mechanisms underlying these relationships remain unclear but, in line with the
271 acknowledged correlation between age and COVID-19 severity,²⁰ we found that patients with more
272 severe disease, fever or respiratory symptoms (cough, dyspnea and pneumonia) had a higher median
273 age, thus confirming the need for careful observation and an early intervention in order to prevent
274 the development of severe COVID-19 in the elderly.

275 The close association between the urticarial phenotype and gastrointestinal symptoms found in our
276 study is intriguing, and suggests that this phenotype is predictive of COVID-19-related
277 gastrointestinal involvement. The pathophysiological link between skin and digestive manifestations
278 needs further investigation, but it is likely that SARS-CoV-2 is a triggering factor for both.

279 The main limitation of this study is the absence of laboratory confirmation of COVID-19 in 73 patients
280 (36.5%), which was mainly due to the fact that asymptomatic and paucisymptomatic patients did not
281 undergo SARS-CoV-2 testing during the first wave of COVID-19 in Italy for economic reasons.

282 Selection bias due to the fact that the study only included patients whose COVID-19-related skin
283 lesions had been evaluated by an expert dermatologist may be considered another limitation, but we
284 believe that this is actually a strength insofar as it avoided the misdiagnoses that may have been
285 made by non-specialists.

286 In conclusion, this study further defines the demographic and clinical features of the six main clinical
287 phenotypes of COVID-19-associated skin manifestations by assessing the relationship between them
288 and the extra-cutaneous symptoms and severity of COVID-19. The only correlation between the

289 cutaneous phenotype and the severity of COVID-19 was observed in the case of chilblain-like acral
290 lesions, a phenotype that is generally associated with the benign/sub-clinical course of COVID-19.

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359 SUPPLEMENTARY MATERIAL

360 **Supplemental Figure 1.** Clinical features of COVID-19-associated skin manifestations. A) Urticarial rash on the lower limbs. B) Confluent erythematous rash
361 on the chest and abdomen. C) Papulovesicular exanthem. D) Chilblain-like acral lesions on the feet. E) Palpable purpura on the outside of the thigh. F) Livedo
362 reticularis-like lesions on the thighs. All photographs belong to the authors' own collections.

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363 **TABLE 1. Demographic data and clinical features of 200 patients with COVID-19-associated cutaneous manifestations**

Median age at the time of the onset of COVID-19, years (IQR)	57 (40.25-72.25)
Males, n (%)	108 (54)
Females, n (%)	92 (46)
Median latency between cutaneous manifestations and systemic symptoms, days (IQR)*	14 (4-27)
Median duration of cutaneous manifestations, days (IQR)**	12 (8-20)
Cutaneous phenotypes	
Urticarial rash, n (%) [§]	19 (10.2)
Confluent erythematous/maculo-papular/morbiliform rash, n (%) [§]	48 (25.7)
Papulovesicular exanthem, n (%) [§]	29 (15.5)
Chilblain-like acral pattern, n (%) [§]	46 (24.6)
Livedo reticularis-like/racemosa-like pattern, n (%) [§]	4 (2.1)
Purpuric “vasculitic” pattern, n (%) [§]	13 (6.9)
Other cutaneous phenotypes, n (%) [§]	28 (15)
More than one phenotype, n (%)	13 (6.5)
Median duration of cutaneous manifestations, days (IQR)	
Urticarial rash	8 (5-13) ^[1]
Confluent erythematous/maculo-papular/morbiliform rash	10 (7-14.5) ^[2]
Papulovesicular exanthem	10 (7-14) ^[3]
Chilblain-like acral pattern	22 (15-32) ^[4]
Livedo reticularis/racemosa-like pattern	14 (5-27) ^[5]
Purpuric “vasculitic” pattern	11 (6.5-15.5) ^[6]
Median latency between cutaneous manifestations and systemic symptoms, days	
Urticarial rash	12 (5-23) ^[1]
Confluent erythematous/maculo-papular/morbiliform rash	21.5 (12-28.75) ^[8]

(IQR)	Papulovesicular exanthem	4 (1.25-8) ^[9]
	Chilblain-like acral pattern	16 (9-39) ^[10]
	Livedo reticularis/racemosa-like pattern	24.5 (4-48.25) ^[11]
	Purpuric “vasculitic” pattern	16 (3.5-34) ^[12]
	Pruritus	81 (40.5)
Skin-related symptoms, n (%)	Pain/burning	22 (11)

364 Data available for the following numbers of patients: 155, 171, 19, 19, 49, 21, 41, 43, 5, 6, 17, 24, 24, 44, 28, 28, 23, 6, and 17.
 365 ^sPercentages of 187 patients (excluding the 13 with more than one cutaneous phenotype)

366 **TABLE 2. The severity of COVID-19 and the clinical features of its systemic symptoms**

Patients with at least one co-morbidity, n (%) [*]	86 (43)
Median duration of systemic symptoms, days (IQR)**	23 (12-31)
Systemic symptoms, n (%)	146 (73)
Fever	108 (54)
Cough	106 (53)
Pneumonia	77 (38.5)
Dyspnea	46 (23)
Gastrointestinal symptoms	44 (22)
Hypogeusia/hyposmia	11 (5.5)
Thromboembolic complications	7 (3.5)
Death	31 (15.5)
Disease severity, n (%)	51 (25.5)
Asymptomatic	95 (47.5)
Mild	23 (11.5)
Moderate	73 (36.5)
Severe	127 (63.5)
Diagnosis of COVID-19, n (%)	21 (11-39.5)
Suspected	28 (19-38)
Laboratory-confirmed	19 (12-28.5)
Median duration of systemic symptoms, days (IQR)	13 (7-21)
Urticarial rash ^[1]	26 (11.75-48.25)
Confluent erythematous/maculo-papular/morbiliform rash ^[2]	22 (8.75-33.5)
Papulovesicular exanthema ^[3]	
Chilblain-like acral pattern ^[4]	
Livedo reticularis/racemosa-like pattern ^[5]	
Purpuric "vasculitic" pattern ^[6]	

367 *Data available for 195 patients; **Data available for 124 patients. Data available for the following numbers of patients: ^[1] 17, ^[2] 39, ^[3] 13, ^[4] 21, ^[5] 6, and ^[6] 12

368 **TABLE 3. Age-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of COVID-19 severity and systemic symptoms by skin phenotype in**
 369 **patients with COVID-19-associated skin manifestations (n=187)***

	Moderate/severe COVID-19		Fever		Cough		Dyspnea		Pneumonia		Hyposmia/hyposgeusia		Gastrointestinal symptoms	
	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
Urticarial rash	1.24 (0.43-3.62)	0.6938	2.69 (0.72-10.10)	0.1418	1.036 (0.394-2.723)	0.9433	1.78 (0.63-5.02)	0.2781	1.351 (0.467-3.906)	0.579	2.23 (0.81-6.12)	0.1196	6.10 (2.25-16.59)	0.0004
Confluent erythematous/maculopapular/morbiliform rash	1.9 (0.83-4.37)	0.1307	0.83 (0.37-1.87)	0.6462	2.25 (1.1-4.63)	0.0269	2.05 (0.99-4.24)	0.0519	1.5 (0.7-3.3)	0.3121	0.67 (0.28-1.59)	0.3632	0.82 (0.37-1.85)	0.6391
Papulovesicular exanthem	1.44 (0.55-3.79)	0.4565	2.44 (0.77-7.71)	0.1283	0.96 (0.42-2.16)	0.9185	0.71 (0.29-1.74)	0.4507	1.34 (0.53-3.41)	0.5387	1.83 (0.76-4.41)	0.1814	0.65 (0.23-1.82)	0.4154
Chilblain-like acral pattern	0.23 (0.09-0.55)	0.0009	0.21 (0.1-0.46)	0.0001	0.28 (0.13-0.6)	0.001	0.2 (0.07-0.56)	0.0024	0.29 (0.12-0.70)	0.0063	0.19 (0.06-0.61)	0.0054	0.51 (0.2-1.30)	0.1579
Livedo reticularis/racemosa-like and purpuric "vasculitic" pattern	1.05 (0.25-4.39)	0.9462	1.18 (0.24-5.85)	0.8382	1.5 (0.43-5.18)	0.5223	4.17 (1.05-16.5)	0.0420	0.6 (0.17-2.16)	0.4302	1.19 (0.30-4.64)	0.8054	0.25 (0.03-1.97)	0.1864

370 *Patients with more than one cutaneous phenotype were excluded from the statistical analysis

371

372 **TABLE 4. Comparison of the median age of patients with COVID-19-associated skin manifestations (n=187)***

			Median (IQR)	P-value
Cutaneous phenotypes	Urticarial rash	Yes (n=19)	54 (36-58)	0.1663
		No (n=168)	57.5 (41-74)	
	Confluent erythematous/maculopapular/morbiliform rash	Yes (n=48)	61 (51.5-78)	0.029
		No (n=159)	55 (36-71)	
	Papulovesicular exanthem	Yes (n=29)	57 (44-75)	0.4863
		No (n=158)	57 (40-73)	
	Chilblain-like acral pattern	Yes (n=46)	38.5 (23-55)	<0.0001
		No (n=141)	60 (50-75)	
	Livedo reticularis/racemosa-like and purpuric "vasculitic" pattern	Yes (n=17)	66 (58-84)	0.0022
		No (n=170)	55 (39-71)	
Disease severity	Asymptomatic status and mild COVID-19 (n=75)		40 (27-57)	<0.0001
		Moderate and severe COVID-19 (n=112)	64 (54.5-78)	
Systemic symptoms	Fever	Yes (n=136)	59 (50-75)	<0.0001
		No (n=51)	38 (26-61)	
	Cough	Yes (n=102)	58.5 (50-74)	0.0077
		No (n=85)	52 (30-71)	
	Dyspnea	Yes (n=71)	65 (55-78)	<0.0001
		No (n=116)	49 (30.5-63)	
	Pneumonia	Yes (n=101)	65 (55-80)	<0.0001
		No (n=86)	41.5 (28-57)	
	Hyposmia/hypogeusia	Yes (n=41)	55 (44-65)	0.3337
		No (n=146)	57.5 (40-75)	
Gastrointestinal symptoms		Yes (n=43)	55 (44-71)	0.9462
		No (n=144)	57 (38.5-73.5)	

373 *Patients with more than one cutaneous phenotype were excluded from the statistical analysis

CAPSULE SUMMARY

- There are six main COVID-19-related cutaneous phenotypes, but only the chilblain-like acral pattern significantly associated with younger age.
- After adjusting for patient age, there was no spectrum of COVID-19 severity in relation to cutaneous phenotypes, although the longer-lasting chilblain-like acral pattern significantly associated with milder disease.

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