Timing of PCR and Antibody Testing in Patients with COVID-19 associated dermatologic manifestations

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NOTE: This preprint reports new research that has not been certified by peer review and should not be used to guide clinical practice.
A recent study from France noted 40 patients with chilblain-like lesions in suspected COVID-19. None tested PCR positive for SARS-CoV-2, but 30% had detectable antibodies. The rapid increase in chilblain/pernio-like cases during the COVID-19 pandemic is likely SARS-CoV-2-associated. The relationship between skin symptom onset and COVID-19 PCR/antibody test timing, however, remains uncharacterized.

We established an international registry for cutaneous manifestations of COVID-19. Providers reported time between dermatologic symptom onset and positive/negative COVID-19 laboratory results, when available.

From 8 April-30 June, 2020, 906 laboratory-confirmed or suspected COVID-19 cases with dermatologic manifestations were reported, 534 of which were chilblains/pernio. Among PCR-tested patients, 57% (n=208) overall and 15% (n=23) of chilblains/pernio cases were PCR-positive. Antibody positivity was 37% (n=39) overall and 19% (n=15) for chilblains/pernio.

We evaluated 163 patients with timing information on PCR and/or antibody testing (Table 1). For patients with suspected COVID-19 and any cutaneous manifestation, PCR-positive testing occurred median 6 (IQR 1-14) days after dermatologic symptoms started while PCR-negative testing occurred median 14 (IQR 7-24) days later. For patients with pernio/chilblains, PCR-positivity was noted 8 (IQR 5-14) days after symptoms and negativity median 14 (IQR 7-28) days later. Antibody testing (IgM or IgG) was positive median 30 (IQR 19-39) days after symptom onset for all dermatologic manifestations and 27 (IQR 24-33) days after chilblains/pernio onset.

Like Hubiche et al, our data highlight the low frequency of SARS-CoV-2 PCR+ testing in COVID-19 patients with cutaneous manifestations. Positive predictive values for COVID-19 PCR are influenced by viral shedding kinetics, which are difficult to assess in non-respiratory presentations. Our data reveal that early PCR testing is more likely to be positive than later testing, even when date-of-onset is defined by cutaneous manifestations rather than systemic symptoms.

Most COVID-19 antibody data are from systemically-ill patients; the kinetics of antibody production in mild-to-moderate COVID-19 infections remain unclear. Here, positive antibodies resulted median 30 days from disease onset, beyond the frequently used 14-21 day testing window. In outpatients with true infection, many factors influence the likelihood of a positive antibody result: antibody production, test availability, assay sensitivity, and timing of care-seeking in relation to symptom-onset. These variables influence our interpretation of individual test results and our understanding of the association between pernio and COVID-19.
More population-level testing data is necessary to optimize diagnostic test timing. Positive identification of COVID-19 in minimally-symptomatic patients, including patients with skin findings, is critical to the public health effort.
**Table 1:** Distribution and timing of SARS-CoV-2 PCR and COVID-19 antibody test results in relation to dermatologic manifestations.

| Chilblains/Pernio | All dermatologic conditions |
|-------------------|-----------------------------|
|                   | Number of pernio patients | Number of pernio patients with timing data | Pernio onset to testing interval in days Median (IQR) | Number of patients | Number of patients with timing data | Dermatologic symptom onset to testing interval in days Median (IQR) |
|                   |                            |                                          |                                               |                   |                                   |                                                              |
| PCR Testing       |                            |                                          |                                               |                   |                                   |                                                              |
| PCR+              | 23                         | 5                                         | 8 (5-14)                                      | 208               | 67                                 | 6 (1-14)                                      |
| PCR-              | 134                        | 58                                        | 14 (7-28)                                     | 161               | 68                                 | 14 (7-24)                                     |
| SARS-CoV-2 Positive Antibody Testing |                   |                                          |                                               |                   |                                   |                                                              |
| IgM+ \ IgG+      | -                          | -                                         | -                                             | 1                 | 1                                  | 14                                           |
| IgM+ \ IgG-      | 7                          | 7                                         | 24 (23-28)                                    | 7                 | 7                                  | 24 (23-28)                                    |
| IgM- \ IgG+      | 1                          | 1                                         | 99                                            | 6                 | 6                                  | 32 (14-35)                                    |
| IgM unknown \ IgG+ | 2                        | 2                                         | 30 (25-35)                                    | 12                | 10                                 | 37 (25-40)                                    |
| Ig+ (isotype unknown) | 1                    | -                                         | -                                             | 5                 | 4                                  | 45 (20-84)                                    |
| SARS-CoV-2 Negative Antibody Testing |                   |                                          |                                               |                   |                                   |                                                              |
| IgM- \ IgG-      | 17                         | 5                                         | 37 (21-42)                                    | 18                | 5                                  | 37 (21-42)                                    |
| IgM unknown \ IgG- | 35                   | 16                                        | 38 (33-50)                                    | 37                | 18                                 | 36 (28-49)                                    |
| Ig- (isotype unknown) | 11                 | 6                                         | 34 (21-60)                                    | 11                | 6                                  | 34 (21-60)                                    |
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