Surviving COVID-19 in Bergamo province: a post-acute outpatient re-evaluation

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Abstract

Bergamo province was badly hit by the coronavirus disease 2019 (COVID-19) epidemic. We organised a public-funded, multidisciplinary follow-up programme for COVID-19 patients discharged from the emergency department or from the inpatient wards of ‘Papa Giovanni XXIII’ Hospital, the largest public hospital in the area. As of 31 July, the first 767 patients had completed the first post-discharge multidisciplinary assessment. Patients entered our programme at a median time of 81 days after discharge. Among them, 51.4% still complained of symptoms, most commonly fatigue and exertional dyspnoea, and 30.5% were still experiencing post-traumatic psychological consequences. Impaired lung diffusion was found in 19%. Seventeen per cent had D-dimer values two times above the threshold for diagnosis of pulmonary embolism (two unexpected and clinically silent pulmonary thrombosis were discovered by investigating striking D-dimer elevation). Survivors of COVID-19 exhibit a complex array of symptoms, whose common underlying pathology, if any, has still to be elucidated; a multidisciplinary approach is fundamental, to address the different problems and to look for effective solutions.

Introduction

ASST ‘Papa Giovanni XXIII’ is the principal public hospital of the Bergamo province, serving a population of around 1 110 000. This province has been the hardest hit by the initial coronavirus disease 2019 (COVID-19) epidemic wave in Italy, starting from 22 February, with 2346 notified deaths and an estimated +568% increase in all-cause mortality (5058 excess deaths) over the period 20 February–31 March 2020, compared to the average of the same period in the years 2015–2019 [1]. Acute COVID-19 clinical manifestations have been described in detail [2–4], though little published data are available on the post-acute phase, medium-term complications and potential long-lasting harm. Anecdotal evidence is mounting about the so-called ‘long-COVID’: a hard-to-define syndrome, with some patients complaining of symptoms many months following recovery from the acute phase [5–9].

To mobilise health resources, to address the main clinical problems of survivors and to set public health priorities, in the wake of possible epidemic resurgences, a multidisciplinary evaluation of COVID-19 survivors appears of foremost importance [10–12].

At our institution, we organised a public-funded, dedicated outpatient service to follow-up survivors: by the end of September 2020, 1562 persons had completed their first post-discharge assessment; we present the preliminary data as observed in the first 767 patients (2 May through 31 July).

Methods

A list of all patients discharged from the emergency department (ED) or admitted to the wards of the hospital, with any condition possibly related to severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2) infection, was obtained from the hospital electronic health records database. We excluded asymptomatic pregnant women admitted for delivery and asymptomatic patients found positive to the molecular test admitted for planned procedures for other conditions.
All patients in the list, if reachable by phone or mail, have been offered to participate in the programme, with the exclusion of paediatric patients (<18 years). Patients still in-hospital were identified but put on a ‘waiting list’ to be recalled for the programme once discharged.

Enrolment into the programme was on a voluntary basis and required a double-negative nasopharyngeal swab for SARS-CoV-2 RNA (positive cases were re-tested regularly until a double-negative swab was obtained).

Cognitively impaired subjects were accompanied by a caregiver, who helped in providing information about the medical history and in recalling the pre-acute episode health status.

We offered a two-step assessment:

- **Step 1:** nurse assessment, blood tests (including full blood count, liver function tests, renal function tests, D-dimer, coagulation tests, thyroid function tests and thyroid antibodies, glucose, glycated haemoglobin, lactate dehydrogenase, brain natriuretic peptide, C-reactive protein), chest-X-ray, electrocardiogram, full pulmonary function testing with diffusion, psychological evaluation, assessment of rehabilitation needs.

- **Step 2** (three days later): infectious diseases consultation and subsequent referral to primary care or to other specialists (mainly respiratory medicine, cardiology, neurology, endocrinology, physical and rehabilitation medicine, haematology) as deemed appropriate.

Several assessment scales were adopted at step 1.

For psychological evaluation, self-report questionnaires were administered to evaluate post-traumatic stress disorder (PTSD), anxiety and depression symptoms and resilience. The following scales were used: Impact of Events Scale - Revised (IES-R) [13–19], Hospital Anxiety and Depression Scale (HADS) [18–21] and Resilience Scale for Adults (RSA) [22, 23].

Since July, a neuropsychological screening test, the Montreal Cognitive Assessment (MoCA) test [19, 24], was introduced to account for the increasing number of patients complaining of cognitive impairment (such as memory and attention deficit). The scale used was based on equivalent scores from 0 to 4, based on adjustment by age and education level of the MoCA scores [25]. In this modified scale, the ’pathologic’ score was 0. The results of the questionnaires were always discussed with the patients at the end of the clinical psychological interview.

For assessment of rehabilitation needs the Barthel Index and the Brief Fatigue Inventory scales were used [26–29]. Conditions pre-existing to the acute COVID-19 episode were scored using these two scales, by asking patients to recall their symptoms.

Ethics approval was granted from ASST ‘Papa Giovanni XXIII’ ethical committee. Data were collected using a Microsoft Access database. Written consent was obtained from all participants at enrolment. All patients had access to the follow-up programme regardless of their decision to participate in the study. The regional health system covered all the costs of the service, except for endocrinology, dermatology and rheumatology referrals [30].

**Results**

Up to 31 July, 2965 patients met the criteria (946 discharged from the ED and 2019 who were admitted). Six hundred forty-six of them had died (505 before discharge) and 405 declined participation. Of the remaining 1914, 767 had completed the two-step post-discharge assessment by 31 July. None of these patients declined to provide consent for data collection for this observational study.

COVID-19 was confirmed by a positive SARS-CoV-2-RNA PCR in all but 46 cases, among whom 37 had a positive serology (by LIAISON®, DiaSorin, Saluggia VC, until 10 July and by Elecsys®, Roche, afterwards). The clinical charts of the remaining nine patients were reviewed by a senior ID specialist and judged ‘probable COVID-19’.

Of the 767 enrolled patients, 252 were female (32.9%). The average age was 63 (s.d. 13.6, range 20–92).

The most relevant baseline patients’ characteristics and clinical details of the acute phase are summarised in Table 1.

Six hundred and sixty-eight persons were hospitalised with 66 (8.6%) of them requiring admission to the intensive care unit (ICU).

Eight per cent of the admitted patients had a total hospital stay of more than 60 days.

Survivors entered our programme at a median of 81 days (IQR = 66–106) after discharge from the ED or from the wards, and a median of 105 days (IQR = 84–127) after the appearance of the first symptoms related to COVID-19.

On the day of the first visit at our service, they had been at their home for a median of 68 days (IQR = 51–92) (332 patients, 43% of our cohort, was transferred to other facilities before returning home).

The main results are summarised in Table 2.

At the time of ID evaluation, 394 patients (51.4%) reported being still symptomatic, with fatigue and exertional dyspnoea as the most reported symptoms. Women were more symptomatic than men, with fatigue reported almost twice as frequently. Out of the symptomatic patients, 257 (33.5%) stated they were ‘not feeling fully recovered’, when specifically asked. The remaining 137 patients (17.9%) experienced only minor symptoms with little or no implications for their daily activities: as such, they considered themselves ‘recovered’.

One hundred and eighty-six patients (24.2%) were still on additional medical treatment, introduced during admission, with anticoagulants being the most frequent.

Self-reported dyspnoea using the Modified Medical Research Council Dyspnoea Scale (mMRC) was present in 228 patients (29.8%), of whom 52 patients had ‘moderate–severe’ dyspnoea.

Based on Barthel index scale results 121 patients (16%) were no longer fully independent, of these only six became moderately–severely dependent. The Brief Fatigue Inventory test found 334 patients (44.1%) complaining of new-onset fatigue (145 with moderate–severe fatigue).

While the Impact of Event Scale-Revised (IES-R) identified 222 patients (30.5% of 727) with COVID-19-related traumatic aspects, the RSA highlighted for 679 (95.5% of 711) they had enough resources to react. The MoCa screening, introduced in July, was pathologic in just 2 out of the 304 patients who were tested, despite 69 reporting related symptoms. Pulmonary function testing identified 27 patients (3.7%) with obstruction, 85 (11.8%) with restrictive pattern and 6 (0.9%) with mixed pattern. For 51 patients the test result was contraindicated or not diagnostic. Diffuse capacity of the lungs for carbon monoxide (DLCO) was reduced in 19% of patients.

C-reactive protein, D-dimer and lactate dehydrogenase were above the upper limit of normal (ULN) in 7%, 38% and 22% of cases, respectively. Two asymptomatic pulmonary sub-segmental thrombosis were discovered at follow-up, by investigating striking D-dimer elevation.
| Characteristic                                      | n   | %     | Sample size |
|----------------------------------------------------|-----|-------|-------------|
| **Age mean (s.d.) in years**                       | 63  | (13.6)| 767         |
| **Sex (M/F)**                                      | 515 | 252   | F = 32.9    |
| **Body mass index**                                |     |       | 742         |
| <18.5 – underweight                                | 0   | 0     |             |
| 18.5–24.9 – normal weight                         | 242 | 32.6  |             |
| 25–29.9 – overweight                               | 334 | 45    |             |
| >30 – obese                                        | 166 | 22.4  |             |
| **Smoking status**                                 |     |       | 767         |
| None                                               | 555 | 72.4  |             |
| Active                                             | 33  | 4.3   |             |
| Former                                             | 179 | 23.3  |             |
| **Comorbidities**                                  |     |       | 767         |
| Hypertension                                       | 169 | 21.7  |             |
| Coronary disease                                   | 73  | 9.5   |             |
| Diabetes                                           | 57  | 7.4   |             |
| Atrial fibrillation                                | 36  | 4.7   |             |
| COPD                                               | 36  | 4.7   |             |
| Heart failure                                      | 34  | 4.4   |             |
| Autoimmune disease                                 | 21  | 2.7   |             |
| Solid malignancy                                   | 15  | 2     |             |
| Haematologic malignancy                            | 11  | 1.4   |             |
| >1 comorbidity                                     | 158 | 20    |             |
| **Days from onset to 1st evaluation: median (IQR)**| 9   | (6–12)| 625         |
| **Admitted patients**                              | 678 | 88.4  | 767         |
| **ICU-treated patients**                           | 66  | 8.6   | 767         |
| **Transferred to other facilities:**               | 332 | 49    | 678         |
| Acute care (of whom in ICU)                        | 145 | 32    | 21.3 (0.05) |
| Post-acute care (nursing homes or rehabilitation) | 151 | 22.2  |             |
| Post-acute convalescence (e.g. hotels)             | 28  | 4.1   |             |
| **Duration of hospital stay in days: median (IQR):**|     |       | 678         |
| At our institution, not in ICU                     | 10  | (6–18)|             |
| At our institution, with ICU admission             | 30  | (19–41)|            |
| Overall* (without ICU admission)                   | 18  | (7–40)|             |
| Overall* (with ICU admission)                      | 58  | (40–77)|            |
| **Oxygen supplementation**                         |     |       | 749         |
| Room air                                           | 159 | 21.2  |             |
| Nasal prongs                                       | 213 | 28.4  |             |
| Venturi mask                                       | 77  | 10.3  |             |
| Reservoir mask                                     | 105 | 14    |             |
| CPAP or NIMV                                       | 133 | 17.8  |             |
| Mechanical ventilation                             | 62  | 8.3   |             |

COPD, chronic obstructive pulmonary disease.
*Overall stay, including hospital stay at other facilities.
Table 2. Follow-up multidisciplinary assessment

|                                | n     | %    | Sample size |
|--------------------------------|-------|------|-------------|
| Patients feeling recovered     | 510   | 66.5 | 767         |
| Days since patients have felt recovered, median (IQR) | 49 (30–72) | 510 |
| Persistent symptoms at follow-up visit |       |      |             |
| F                               | M     |       |             |
| None                            | 97    | 276   | 38.5        | 53.6 | 252 | 515 |
| Confusion                       | 7     | 16    | 2.8         | 3.1  | 252 | 515 |
| Asthenia                        | 93    | 93    | 36.9        | 18.1 | 252 | 515 |
| Dyspnoea                        | 66    | 101   | 26.2        | 19.6 | 252 | 515 |
| Fever                           | 1     | 3     | 0.4         | 0.6  | 252 | 515 |
| Myalgia                         | 9     | 20    | 3.6         | 3.9  | 252 | 515 |
| Cough                           | 8     | 15    | 3.2         | 2.9  | 252 | 515 |
| Headache                        | 1     | 3     | 0.4         | 0.6  | 252 | 515 |
| Chest pain                      | 9     | 15    | 3.6         | 2.9  | 252 | 515 |
| Palpitations                    | 18    | 12    | 7.1         | 2.3  | 252 | 515 |
| Syncope                         | 0     | 1     | 0.0         | 0.2  | 252 | 515 |
| Anosmia/Dysgeusia               | 11    | 12    | 4.4         | 2.3  | 252 | 515 |
| Upper gastro-intestinal symptoms| 1     | 0     | 0.4         | 0.0  | 252 | 515 |
| Lower gastro-intestinal symptoms| 4     | 3     | 1.6         | 0.6  | 252 | 515 |
| Others*                         | 13    | 46    | 5.2         | 8.9  | 252 | 515 |
| ⩾3 persistent symptoms         | 7     | 0     | 2.8         | 0.0  | 252 | 515 |
| Oxygen saturation on room air   |       |      |             |
| Mean (range)                    | 97.8 (91–100) | 767 |
| ⩾95%                            | 722   | 94.1 | 767         |
| 93-94%                          | 44    | 5.7  | 767         |
| <93%                            | 1     | 0.1  | 767         |
| Modified Medical Research Council dyspnoea Scale (mMRC) |       |      |             |
| Grade 0 – No dyspnoea           | 539   | 70.3 | 767         |
| Grade 1 – Mild dyspnoea         | 176   | 23.0 | 767         |
| Grade 2 – Moderate dyspnoea     | 42    | 5.5  | 767         |
| Grade 3 – Severe dyspnoea       | 10    | 1.3  | 767         |
| Grade 4 – Very severe dyspnoea  | 0     | 0.0  | 767         |
| Karnofsky performance status scale |     |      |             |
| >90%                            | 640   | 90.9 | 704         |
| 80-90%                          | 51    | 7.2  | 704         |
| <80%                            | 13    | 1.8  | 704         |
| Physical medicine evaluation    |       |      |             |
| Barthel index prior to COVID-19 |       |      |             |
| Total independent               | 690   | 91.0 | 758         |
| Semi-independent                | 34    | 4.5  | 758         |
| Slight dependency               | 14    | 1.8  | 758         |
| Moderate dependency             | 11    | 1.5  | 758         |
Table 2. (Continued.)

|                             | n   | %    | Sample size |
|-----------------------------|-----|------|-------------|
| Severe dependency           | 6   | 0.8  | 758         |
| Total dependency            | 2   | 0.3  | 758         |

Barthel Index at follow-up

|                             | n   | %    | Sample size |
|-----------------------------|-----|------|-------------|
| Total independent           | 569 | 75.1 | 758         |
| Semi-independent            | 138 | 18.2 | 758         |
| Slight dependency           | 20  | 2.6  | 758         |
| Moderate dependency         | 16  | 2.1  | 758         |
| Severe dependency           | 11  | 1.5  | 758         |
| Total dependency            | 3   | 0.4  | 758         |

Brief Fatigue Inventory prior to COVID-19

|                             | n   | %    | Sample size |
|-----------------------------|-----|------|-------------|
| No asthenia                 | 553 | 73.0 | 758         |
| Mild asthenia               | 134 | 17.7 | 758         |
| Moderate asthenia           | 53  | 7.0  | 758         |
| Severe asthenia             | 18  | 2.4  | 758         |

Brief Fatigue Inventory at follow-up

|                             | n   | %    | Sample size |
|-----------------------------|-----|------|-------------|
| No asthenia                 | 219 | 28.9 | 758         |
| Mild asthenia               | 98  | 12.9 | 758         |
| Moderate asthenia           | 247 | 32.6 | 758         |
| Severe asthenia             | 194 | 25.6 | 758         |

Psychological evaluation

|                             | n   | %    | Sample size |
|-----------------------------|-----|------|-------------|
| IES-R scale                 |     |      |             |
| Normal                      | 505 | 69.5 | 727         |
| Pathologic                  | 222 | 30.5 | 727         |
| HADS-Anxiety                |     |      |             |
| Normal                      | 645 | 88.7 | 727         |
| Pathologic                  | 82  | 11.3 | 727         |
| HADS-Depression             |     |      |             |
| Normal                      | 694 | 95.5 | 727         |
| Pathologic                  | 33  | 4.5  | 727         |
| RSA                         |     |      |             |
| Normal                      | 679 | 95.5 | 711         |
| Pathologic                  | 32  | 4.5  | 711         |
| MoCa                        |     |      |             |
| Normal                      | 302 | 99.3 | 304         |
| Pathologic                  | 2   | 0.7  | 304         |

Pulmonary Function Tests with CO diffusiona

|                             | n   | %    | Sample size |
|-----------------------------|-----|------|-------------|
| FEV1 (l), median (IQR)      | 2.97| (2.38–3.7)| 716         |
| FEV1% of expected, median (IQR) | 98  | (87–109)| 716         |
| FVC (l), median (IQR)       | 3.75| (3–4.55)| 717         |
| FVC% of expected, median (IQR) | 95  | (84–106)| 717         |
| DLCO (ml/min/mmHg), median (IQR) | 23.43| (18.16–29.16)| 680         |
| DLCO% of expected, median (IQR) | 96  | (81–112)| 680         |

(Continued)
Table 2. (Continued.)

|                         | n    | %     | Sample size |
|-------------------------|------|-------|-------------|
| FEV1/FVC, median (IQR)  | 0.81 (0.76–0.85) | 716   |
| FEV1/FVC LLN, median (IQR) | 0.65 (0.63–0.68) | 716   |
| Obstruction prevalence  | 3.7% |       |             |
| Restrictive pattern prevalence | 11.8% |       |             |
| Mixed pattern prevalence | 0.9% |       |             |
| DLCO reduction          | 19%  |       |             |

**Blood tests: principal findings**

| Test                        | n    | %     | Sample size |
|-----------------------------|------|-------|-------------|
| D-Dimer (ng/ml), mean (s.d.)| 700 (1021) | 743   |
| D-Dimer 500–999             | 163  | 22    | 743         |
| D-Dimer 1000–1999           | 88   | 12    | 743         |
| D-dimer ≥2000              | 39   | 5     | 743         |
| LDH (U/l), mean (s.d.)     | 222 (42) | 756   |
| LDH >256                   | 124  | 16    | 756         |
| Lymphocytes (cells/μl)     |      |       |             |
| Lymphocytes <3400          | 707  | 93    | 761         |
| Lymphocytes <1000          | 28   | 4     | 761         |
| C-reactive protein (mg/dl), mean (s.d.) | 0.36 (0.85) | 759   |
| C-reactive protein >1.0    | 52   | 7     | 759         |
| Creatinine (mg/dl)         |      |       |             |
| Creatinine >1.1 (females)  | 17   | 7     | 249         |
| Creatinine >1.3 (males)    | 37   | 7     | 509         |
| TSH (μU/ml)                |      |       |             |
| TSH >5 OR <0.3             | 24   | 4     | 657         |
| Anti-thyroid antibodies (UI/ml) | 61   | 9     | 656         |
| Anti-Thyroglobulin Ab >60  | 115  | 18    | 656         |
| Thyroid peroxidase Ab >60  | 115  | 18    | 656         |

**Complications**

| Complication                                         | F    | M    | F    | M    | F    | M    |
|------------------------------------------------------|------|------|------|------|------|------|
| None                                                 | 176  | 338  | 69.8 | 65.6 | 252  | 515  |
| Pulmonary (bacterial pneumonia, pleural effusion, pneumothorax) | 20   | 35   | 7.9  | 6.8  | 252  | 515  |
| Cardiac – arrhythmia                                  | 10   | 29   | 4.0  | 5.6  | 252  | 515  |
| Cardiac – ischaemia                                   | 2    | 12   | 0.8  | 2.3  | 252  | 515  |
| Cardiac – inflammatory                                | 2    | 10   | 0.8  | 1.9  | 252  | 515  |
| Renal (acute renal failure)                           | 5    | 11   | 2.0  | 2.1  | 252  | 515  |
| Thrombotic (pulmonary embolism, deep-vein thrombosis) | 10   | 37   | 4.0  | 7.2  | 252  | 515  |
| Haemorrhagic                                          | 3    | 6    | 1.2  | 1.2  | 252  | 515  |
| Psychiatric (delirium, depressive syndrome, psychosis) | 5    | 12   | 2.0  | 2.3  | 252  | 515  |
| Neurologic (CNS: stroke, encephalitis)                | 6    | 20   | 2.0  | 3.5  | 252  | 515  |
| Neurologic (PNS: Guillain Barré syndrome, polyneuropathy) | 6    | 20   | 2.4  | 3.9  | 252  | 515  |
| Infective (excluding pneumonia)                       | 7    | 18   | 2.8  | 3.5  | 252  | 515  |
| Rheumatologic/Dermatologic                            | 11   | 11   | 4.4  | 2.1  | 252  | 515  |

**Referrals**

| Referral                                                | n    | %     | Sample size |
|---------------------------------------------------------|------|-------|-------------|
| No referral (end of follow-up)                          | 388  | 50.6  | 767         |
| Pulmonary medicine consultation                         | 281  | 36.6  | 767         |

(Continued)
Anti-thyroglobulin and thyroid peroxidase antibodies were found elevated in 15% of the patients, with 5% of them (6 out of 115) showing concomitant derangement of the thyroid-stimulating hormone (TSH).

Two hundred and fifty-three patients (32.9%) had SARS-CoV-2 related complications during the acute phase, of whom the most frequent ones were:

- Neuropsychiatric (8.7%) (e.g. delirium, depressive syndrome, psychosis, stroke, encephalitis, Guillian–Barré syndrome, polyneuropathy).
- Cardiac (8.5%) (e.g. arrhythmia, ischaemia, myocarditis).
- Pulmonary additional complications (7.1%) (e.g. bacterial pneumonia, pleural effusion, pneumothorax).
- Thrombotic (6.1%) (e.g. pulmonary embolism, deep-vein thrombosis).

Complication almost exclusively occurred during the acute phase, but were assessed at follow-up to avoid missing the ones of late appearance.

Following ID evaluation, 379 patients (49.4%) were referred to specialty pathways. The majority (281 patients; 36.6%) were referred to respiratory medicine. Several patients were referred to more than one specialty.

Discussion

To our knowledge, our report represents one of the largest cohort to date, describing the medium-term consequences of SARS-CoV-2 infection.

It is a mono-centric study, referring to a homogeneous population, with a large majority (88.4%) of patients admitted to hospital of which 9.7% requiring intensive care: in other published cohorts so far, the selection criteria were based on just having a hospital stay of more than 60 days. We tracked down all the accessible information, for each case, along all these movements.

Of the admitted patients in our cohort, 43% were transferred to other facilities at least once during the hospital stay, experiencing what could be described as a ‘journey’ between different hospitals and hospital services (8% of patients had a total hospital stay of more than 60 days). We tracked down all the accessible information, for each case, along all these movements.

Another strength of this study is that patients were actively interviewed (in some cases, with the help of a caregiver): this provided equal access to the follow-up service, overcoming barriers posed by telephone and video consultations. Lastly, as long as COVID-19 appears to affect different organ systems, in some cases even without any relevant pulmonary disease, our large criteria of selection allowed us to depict a wide scenario of the consequences of COVID-19 in our population.

Patients surviving COVID-19 show a complex array of conditions, ranging from mild to potentially life-threatening (e.g. late-onset pulmonary embolism). Our intervention had the advantage of assessing health needs and, at the same time, offering interventions to address them, within the WHO-endorsed framework of ‘Recognition, research and rehabilitation’, as invoked for long-COVID sufferers [33].

Three hundred and ninety-four participants (51.4%) were still symptomatic at the ID evaluation, which is in line with other authors’ observations [31, 32, 34, 35]. In particular, 33.5% described themselves as ‘not yet recovered’: at a median time of 105 days since onset, these people probably fit into the ‘working definition’ (still to be strictly defined) of ‘long COVID sufferers’ [8].

The nature of the long-COVID symptoms has yet to be explained, however it appears reasonable to try and separate those symptoms related to post-viral chronic fatigue syndrome, from those due to post-critical-illness syndrome, or post-traumatic stress disorder, especially in a cohort with a high rate of hospitalisation and a long length of stay, as ours.

In this effort, a comprehensive and multidisciplinary assessment of patients after the acute episode of COVID-19 should be considered.

We adopted for each patient various scales of self-evaluation, comprehensive laboratory and instrumental tests: their correlation to the reported symptoms and their cross-concordance will be object of our next efforts.

Mid-term consequences of COVID-19 are not limited to lung disease and cover a wide range of organ systems: the underlying mechanism could be some kind of microcirculatory impairment [36, 37]. We propose that studies should be addressed in this direction.

Our study has a number of limitations. Firstly, the timeline of enrolment and assessments was not standardised: we have seen patients at variable intervals from the onset of COVID-19, making inter-group comparisons less stringent; this has to do with the immediate establishment of our intervention, right after the end of the first wave of the epidemic. Secondly, our inclusion criteria are pragmatic, but hardly representative of the actual case load in Bergamo province; during the initial epidemic, confounding factors altered the hospital case mix in both ways: severely ill patients did...
not gain access, due to ambulance system breakdown and less severely affected patients avoided consulting the ED due to overcrowding. Thirdly, the criterion of a double-negative test before enrolment delayed the evaluation of a part of our cohort: it’s not yet known if patients having a persistent positive swab share any relevant clinical characteristics, so that this delay could act as a source of variability. Fourthly, recall bias could have affected the scores given to the ‘pre-COVID’ assessment. Lastly, we censored our observations at the ID consultation, with a relevant percentage of the enrolled patients still to be seen by other specialists, who, in turn, may add further perspectives.

In conclusion, a large proportion of survivors of COVID-19 from our setting had significant ongoing health and psychosocial needs. Provision of a coordinated, multidisciplinary follow-up clinic offering a comprehensive medical and psychological assessment should be considered for such patients. Further research is required to better understand the burden of morbidity after acute COVID-19 infection, in order to plan and fund appropriate services.

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Data availability statements. The data that support the findings of this study are available on request from the corresponding author (s.venturelli[at]asst-pg23.it). The data are not publicly available due to their containing information that could compromise the privacy of research participants.

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