National French survey of COVID-19 symptoms in people aged 70 and over

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ABSTRACT

The objective of this national French survey was to determine the COVID-19 semiology in seniors (n=353; mean, 84.7±7.0y). 57.8% of patients exhibited ≤3 symptoms, including thermal dysregulation (83.6%), cough (58.9%), asthenia (52.7%), polypnea (39.9%), gastrointestinal signs (24.4%). Patients ≥80y exhibited falls (P=0.002) and asthenia (P=0.002). Patients with neurocognitive disorders exhibited delirium (P<0.001) and altered consciousness (P=0.001). Clinical peculiarities of COVID-19 were reported in seniors.

Keywords: COVID-19; SARS-Cov-2; semiology; symptomatology; older adults

Clinical Trials NCT04343781
INTRODUCTION

Since December 2019, the COVID-19 caused by SARS-CoV-2 is spreading worldwide from China, affecting millions of people. Although older adults do not appear more prone than younger ones to be infected, they are more at risk of developing severe and lethal forms of COVID-19 [1–3]. The core question is thus to properly discuss the diagnosis of COVID-19 in older patients. It is commonly admitted that the semiology of older adults differs from that encountered in younger ones. Changes in the clinical expression of the diseases and difficulties in interpreting the clinical signs in older patients could blur the diagnosis process. If these peculiarities were also retrieved with COVID-19, it could be the cause of delayed diagnosis among older patients, responsible for delayed care and isolation measures with subsequent higher risk of virus propagation. The objective of this national French survey was to describe and identify the symptoms most frequently encountered in people aged 70 and over diagnosed with COVID-19.

METHODS

This cross-sectional study was conducted by the French Society of Geriatrics and Gerontology (SFGG). An online standardized questionnaire was sent by email to all SFGG members and widely communicated through the professional networks in geriatrics and infectious diseases. Physicians were asked to report, between 22 March and 5 April 2020, their last 10 patients aged ≥70 years with confirmed SARS-CoV-2 infection (as defined as a positive RT-PCR test result). Those who had treated less than 10 diagnosed patients were asked to submit a questionnaire for each of them. The study was conducted in accordance with the ethical standards set forth in the Helsinki Declaration (1983), was declared to the National Commission for Information
The following characteristics were collected for each patient: demographic (age, gender, place of life, place of care, most recent disability score according to the Iso-Resource Group)[4], medical history (major neurocognitive disorders [MND], hypertension, diabetes mellitus, asthma or chronic obstructive pulmonary disease (COPD), cardiomyopathy, severe chronic renal failure defined as creatinine clearance under 30mL/min, solid or hematological cancer).

The following symptoms observed within the first 72 hours of SARS-CoV-2 infection (i.e., 72h from suspicion, possibly before diagnostic confirmation by RT-PCR test) were collected for each patient using yes/no questions: general signs (sudden deterioration of general condition, temperature, blood pressure), respiratory signs (cough, polypnea), ear nose and throat (ENT) signs (rhinorrhea, odynophagia, otalgia, conjunctivitis, dysgeusia or ageusia, anosmia), gastrointestinal signs (diarrhea, nausea or vomiting) and geriatric syndromes (falls, hypo or overactive delirium, altered consciousness). Changes in complete blood count (leukopenia, lymphopenia, thrombocytopenia) were also collected, with details when available.

Qualitative variables were described using numbers and percentages, and quantitative variables using means and standard deviations. Comparisons between participants aged ≥80years and <80years, and between those with and without MND, were performed using Chi² test for qualitative variables (or exact Fisher test where appropriate), and Student t test for quantitative variables (or Mann-Whitney U test where appropriate).

Univariate logistic regressions were conducted to determine the association of each COVID-19 sign with age≥80years and history of MND. Finally, the profiles of COVID-19 patients were determined according to their symptoms, age and history of MND.
using a multiple correspondence analysis (MCA). Two-sided P-values<0.05 were considered significant. Analyses were performed with SAS® (Sas Institute Inc.; v9.4) and R (R Core Team 2020; v3.6.3) using the FactoMineR and Factoshiny packages.

RESULTS
Older patients’ characteristics are presented in Table 1 (N=353; mean±SD, 84.7±7.0 years; 54.7% women). Most of patients (57.8%) exhibited ≤3 symptoms, and 15% had 0-1 symptom during the first 72h of the infection. The most frequent symptoms were thermal dysregulation (83.6%), cough (58.9%) and sudden deterioration of general condition (52.7%). Polypnea was found in 39.9% including n=47 with severe polypnea ≥30 cycles/minute, and gastrointestinal signs in 24.4% including n=77 with diarrhea. Biologically, 76.4% of the population had lymphopenia, with 725±267 lymphocytes per mm$^3$ on average.

Comparison of those under 80 and over 80 years of age showed that falls (22.4% versus 7.9%, P=0.002; odds ratio(OR)=3.37 [95% confidence interval(95CI):1.48-7.69]) and sudden deterioration of general condition (57.6% versus 38.2%, P=0.002; OR=2.20[95CI:1.34-3.59]) were more frequent above age 80, whereas fever was less frequent (51.5% versus 69.7%, P=0.011; OR=0.46[95CI:0.28-0.77]).

Comparison between patients with and without MND showed that those with MND exhibited more often hypoactive (27.6% versus 11.4%, P<0.001; OR=2.96[95CI:1.69-5.20]) and overactive delirium (14.9% versus 5.5%, P=0.003; OR=3.03[95CI:1.43-6.42]) and altered consciousness (17.2% versus 6.4%, P=0.001; OR=3.03[95CI:1.50-6.13]), and less often hyperthermia (47.0% versus 61.6 %, P=0.013; OR=0.55[95CI:0.36-0.85]), cough (46.3% versus 66.7%, P<0.001; OR=0.35[95CI:0.21-0.57]) and dysgeusia-ageusia (2.3% versus 10.1%, P=0.006; OR=0.21[95CI:0.06-0.70]).

Finally, the MCA results distinguished between two profiles of older patients. The first profile matched with patients under age 80 without MND, who exhibited more frequent hyperthermia and cough during the first 72h of the infection, but no fall, altered
consciousness or hypoactive delirium. In contrast, the second profile matched with patients aged 80 and over with MND; the latter exhibiting more frequently no specific symptoms, and most often an absence of hyperthermia, polypnea, cough and dysgeusia-ageusia.

DISCUSSION

This national French survey shows that older adults with COVID-19 exhibit a pauci-symptomatic clinical picture with less than 3 signs during the first 72h of the infection, generally combining general and respiratory signs (e.g. hyperthermia and cough) with peculiarities that should alert the clinician (e.g. sudden deterioration of general condition, diarrhea, lymphopenia, and/or geriatric syndromes including falls and delirium). Various clinical profiles were highlighted across older adults, especially among the oldest-old \( \geq \) 80 years and those with chronic diseases such as MND.

Our survey provides the first description of the COVID-19 signs in older, and even oldest-old, adults with comorbidities [1–3]. Compared to previous meta-analyses in younger adults [5–7], we found that older adults with COVID-19 often exhibit thermal dysregulation, which however results less often in hyperthermia (56% here versus 82% [5] to 91% [6] in younger adults) and more often in subfebrile temperatures or alternations of hyperthermia and hypothermia (not described thus far to our knowledge). The prevalence of cough was similar (59% here versus 61% [5] to 72% [7] in younger adults). In contrast, the sudden deterioration of general condition, mostly illustrated by marked asthenia, was particularly frequent in older adults (53% here versus 36% [5] to 51% [6] in younger adults). Also, older adults exhibited more often dyspnea (40% here versus 26% [5] to 30% [6] in younger adults) and gastrointestinal signs (24.4% here
with mostly diarrhea (21.8%) versus 10% in younger adults [5,8]). This should encourage clinicians to integrate the gastrointestinal signs into the diagnostic reasoning for SARS-CoV-2 infection in older adults. Older adults had less often anosmia (2% here versus 86% in younger adults [9]) and dysgeusia-ageusia (7% here versus 89% in younger adults [9]). The latter prevalence should however be cautiously interpreted due to olfactory and gustatory dysfunctions with advancing age [10]. Finally, we found a higher proportion of lymphopenia in older adults compared to the general population (75% here versus 55% [3]). The lymphopenia was more significant than that usually observed in the normal aging population (750/mm$^3$ versus 1432/mm$^3$ in the literature [11]), and may explain part of the excess mortality observed in older adults with COVID-19 [1].

Our study has a number of limitations. This is an observational cross-sectional study conducted on a panel of French older patients who may be not representative of the general older population. The 64 physicians who responded to the survey, however, came from all French regions. A reporting bias cannot be ruled out as the accuracy and completeness of the data were entirely reliant upon physicians’ declarations, although the questionnaire was designed to limit variability in readers’ interpretations by asking only factual data. Also, in the absence of mass screening policy in France, only patients for whom a biological test had been carried out because of suspected infection—for clinical reasons for example—could be included, which may have overestimated the prevalence of some signs. The lack of control group prevented to determine the average number of symptoms met in non-COVID-19 French older adults. Similarly, no data were available on the use of concomitant drugs, for example of antibiotics, which could partially explain increases in gastrointestinal signs. Finally, only patients diagnosed with RT-PCR test were included, although the sensitivity of this test presents a
relatively high risk of false negatives (sensitivity of 72%) [12], which may have excluded a number of patients with COVID-19.

In conclusion, this national French survey revealed that the clinical picture of older adults with COVID-19 includes both general and respiratory signs like in younger adults (e.g. hyperthermia and cough), but also more peculiar features such as marked asthenia, diarrhea, lymphopenia and geriatric syndromes. We also reported various clinical profiles across older adults, notably in those aged 80 years and over and those with a history of MND who appeared particularly pauci- or asymptomatic during the first 72h of the infection. These findings should be integrated into the clinical reasoning in geriatric medicine, and encourage the systematization of diagnostic tests for SARS-Cov-2 infection in older adults.
AUTHORS CONTRIBUTIONS

- CA has full access to all of the data in the study, takes responsibility for the data, the analyses and interpretation and has the right to publish any and all data, separate and apart from the attitudes of the sponsors. All authors have read and approved the manuscript.
- Study concept and design: CA, GS, NS, GB, OG and GG.
- Acquisition of data: CA, GS, NS, JPA, JG, GB, OG and GG
- Analysis and interpretation of data: CA, GS and JG
- Drafting of the manuscript: CA, GS and JG
- Critical revision of the manuscript for important intellectual content: NS, JPA, GB, OG and GG
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Study supervision: CA

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Patient level data are freely available from the corresponding author at Cedric.Annweiler@chu-angers.fr. There is no personal identification risk within this anonymized raw data, which is available after notification and authorization of the competent authorities.

COMPETING INTERESTS

All authors state that they have no conflicts of interest with this paper. The authors have no relevant personal financial interest in this manuscript.
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Table 1. Characteristics and comparisons of participants (N=353) separated according to their age and history of major neurocognitive disorders

|                                | Population of the study (N=353) | Comparison of patients under and over 80 years of age | Comparison of patients with and without major neurocognitive disorders |
|--------------------------------|---------------------------------|------------------------------------------------------|-----------------------------------------------------------------------|
|                                | Age < 80 y (n=89)               | Age ≥ 80 y (n=264)                                    | No major neurocognitive disorder (n=219)                                   | With major neurocognitive disorder (n=134)                                   |
|                                |                                 |                                                      | P-value*                                                              | P-value*                                                              |
| Male gender                    | 160 (45.3)                      | 47 (52.8)                                            | 113 (42.8)                                                           | 105 (48.0)                                                           | 55 (41.0)                                                           | 0.101                                                         | 0.206                                                         |
| Age (years), mean ± SD         | 84.7 ± 7.0                      | 75.4±2.9                                              | 87.8±4.8                                                             | -                                                                  | 83.7±7.2                                                             | 86.3±6.4                                                             | <0.001                                                        |
| Place of life                  |                                 |                                                      |                                                                      |                                                                     |                                                                      | <0.001                                                        |
| Community-dwelling             | 257 (72.8)                      | 75 (84.3)                                            | 182 (68.9)                                                           | 180 (82.2)                                                           | 77 (57.5)                                                           | <0.001                                                        |
| Institution-dwelling           | 96 (27.2)                       | 14 (15.7)                                            | 82 (31.1)                                                            | 39 (17.8)                                                           | 57 (42.5)                                                           |                                                                  |
| Place of care                  |                                 |                                                      |                                                                      |                                                                     |                                                                      | 0.1845                                                        | 0.173                                                         |
| Hospital                       | 324 (91.8)                      | 79 (88.8)                                            | 245 (92.8)                                                           | 204 (93.2)                                                           | 120 (89.6)                                                          |                                                                  |
| Nursing home                   | 23 (6.5)                        | 8 (9.0)                                              | 15 (5.7)                                                             | 11 (5.0)                                                            | 12 (9.0)                                                            |                                                                  |
| Services residence             | 3 (0.9)                         | 0 (0.0)                                              | 3 (1.1)                                                              | 1 (0.5)                                                             | 2 (1.5)                                                             |                                                                  |
| Personal residence             | 3 (0.9)                         | 2 (2.3)                                              | 1 (0.4)                                                              | 3 (1.4)                                                             | 0 (0.0)                                                             |                                                                  |
| GIR †                          |                                 |                                                      |                                                                      |                                                                     |                                                                      | <0.001                                                        | <0.001                                                        |
| 1                              | 23 (7.1)                        | 4 (5.0)                                              | 19 (7.7)                                                             | 1 (0.5)                                                             | 22 (17.3)                                                           |                                                                  |
|       | 2         | 3         | 4         | 5 and over | P-value |
|-------|-----------|-----------|-----------|------------|---------|
|       | 70 (21.5) | 11 (13.8) | 59 (24.0) | 13 (6.5)   | 57 (44.9)|
|       | 47 (14.4) | 8 (10.0)  | 39 (15.9) | 24 (12.1)  | 23 (18.1)|
|       | 59 (18.1) | 8 (10.0)  | 51 (20.7) | 40 (20.1)  | 19 (15.0)|
|       | 127 (39.0)| 49 (61.3) | 78 (31.7) | 121 (60.8) | 6 (4.7)  |

**Medical history**

| Condition                        | n (%)       | n (%)       | n (%)       | n (%)       | P-value |
|----------------------------------|-------------|-------------|-------------|-------------|---------|
| **Major neurocognitive disorders** | 134 (38.0)  | 21 (23.6)   | 113 (42.8)  | 0 (0.0)     | 134 (100.0) | -    |
| **Hypertension**                 | 234 (66.3)  | 50 (56.2)   | 184 (69.7)  | 144 (65.8)  | 90 (67.2)  | 0.786 |
| **Diabetes mellitus**            | 80 (22.7)   | 23 (25.8)   | 57 (21.6)   | 52 (23.7)   | 28 (20.9)  | 0.535 |
| **Asthma or COPD**               | 46 (13.0)   | 13 (14.6)   | 33 (12.5)   | 32 (14.6)   | 14 (10.5)  | 0.259 |
| **Cardiomyopathy**               | 159 (45.0)  | 24 (27.0)   | 135 (51.1)  | 92 (42.0)   | 67 (50.0)  | 0.143 |
| **Severe chronic renal failure** | 38 (10.8)   | 5 (5.6)     | 33 (12.5)   | 22 (10.1)   | 16 (11.9)  | 0.577 |
| **Solid or hematological cancer**| 67 (19.0)   | 15 (16.9)   | 52 (19.7)   | 45 (20.6)   | 22 (16.4)  | 0.337 |

**General signs**

| Condition                              | n (%)       | n (%)       | n (%)       | n (%)       | P-value |
|----------------------------------------|-------------|-------------|-------------|-------------|---------|
| **Sudden deterioration of general condition** | 186 (52.7)  | 34 (38.2)   | 152 (57.6)  | 113 (51.6)  | 73 (54.5)  | 0.599 |
| **Low blood pressure**                 | 51 (14.5)   | 8 (9.0)     | 43 (16.3)   | 31 (14.2)   | 20 (14.9)  | 0.842 |
| **Body temperature**                   |             |             |             |             |         |
| **No fever**                           | 58 (16.4)   | 14 (15.7)   | 44 (16.7)   | 36 (16.4)   | 22 (16.4)  |
| **Subfebrile temperature 37.5°-38°C**  | 75 (21.3)   | 10 (11.2)   | 65 (24.6)   | 35 (16.0)   | 40 (29.9)  |
| **Hyperthermia >38°C**                 | 198 (56.1)  | 62 (69.7)   | 136 (51.5)  | 135 (61.6)  | 63 (47.0)  |
| Alternation of hyperthermia and hypothermia | 22 (6.2) | 3 (3.4) | 19 (7.2) | 13 (5.9) | 9 (6.7) |
| Respiration signs | | | | | |
| Cough | 208 (58.9) | 0.153 | <0.001 |
| Sputum | 82 (23.2) | 14 (15.7) | 68 (25.8) | 49 (22.4) | 33 (24.6) |
| Dry | 126 (35.7) | 35 (39.3) | 91 (34.5) | 97 (44.3) | 29 (21.6) |
| Polypnea | 141 (39.9) | 0.165 | 0.014 |
| Between 23 and 29 / minute | 94 (26.6) | 17 (19.1) | 77 (29.2) | 58 (26.5) | 36 (26.9) |
| ≥ 30 / minute | 47 (13.3) | 12 (13.5) | 35 (13.3) | 38 (17.4) | 9 (6.7) |
| ENT signs | | | | | |
| Rhinorrhea | 32 (9.1) | 9 (10.1) | 23 (8.7) | 0.691 | 23 (10.5) | 9 (6.7) | 0.229 |
| Odynophagia | 9 (2.6) | 2 (2.3) | 7 (2.7) | 1.000 | 7 (3.2) | 2 (1.5) | 0.492 |
| Otalgia | 2 (0.6) | 1 (1.1) | 1 (0.4) | 0.441 | 2 (0.9) | 0 (0) | 0.528 |
| Conjunctivitis | 3 (0.9) | 1 (1.1) | 2 (0.8) | 1.000 | 1 (0.5) | 2 (1.5) | 0.560 |
| Dysgeusia - ageusia ‡ | 25 (7.1) | 8 (9.0) | 17 (6.5) | 0.428 | 22 (10.1) | 3 (2.3) | 0.006 |
| Anosmia ‡ | 7 (2.0) | 0 (0) | 7 (2.7) | 0.198 | 6 (2.8) | 1 (0.8) | 0.260 |
| Gastrointestinal signs | | | | | |
| Diarrhea | 77 (21.8) | 23 (25.8) | 54 (20.5) | 0.287 | 53 (24.2) | 24 (17.9) | 0.165 |
| Nausea - vomiting | 22 (6.2) | 3 (3.4) | 19 (7.2) | 0.197 | 16 (7.3) | 6 (4.5) | 0.286 |
| Geriatric syndromes | | | | | |
|                                | 66 (18.7) | 7 (7.9)  | 59 (22.4) | 0.002 | 36 (16.4) | 30 (22.4) | 0.164 |
|--------------------------------|-----------|----------|-----------|------|-----------|-----------|------|
| Falls                          |           |          |           |      |           |           |      |
| Hypoactive delirium            | 62 (17.6) | 14 (15.7)| 48 (18.2) | 0.599| 25 (11.4) | 37 (27.6) | <0.001|
| Overactive delirium            | 32 (9.1)  | 5 (5.6)  | 27 (10.2) | 0.190| 12 (5.5)  | 20 (14.9) | 0.003 |
| Altered consciousness          | 37 (10.5) | 6 (6.7)  | 31 (11.7) | 0.183| 14 (6.4)  | 23 (17.2) | 0.001 |

**Biology**

|                                | 247 (74.6)| 66 (78.6)| 181 (73.3)| 0.336| 165 (79.3)| 82 (66.7) | 0.011 |
|--------------------------------|-----------|----------|-----------|------|-----------|-----------|------|
| Lymphopenia §                  |           |          |           |      |           |           |      |
| Lymphocytes / mm³ (n=246), mean ± SD | 725 ± 267 | 730±285  | 723±261  | 0.856| 692±258  | 791±275  | 0.016 |
| Leukopenia ¶                   | 9 (2.7)   | 2 (2.4)  | 7 (2.8)   | 1.000| 5 (2.4)   | 4 (3.2)   | 0.733 |
| Leukocytes*/mm³ (n=17), mean ± SD | 2 394 ± 881 | 2613±1174 | 2327±818 | 0.571| 2261±1091 | 2545±603 | 0.630 |
| Thrombopenia |                    | 85 (25.4) | 24 (28.6) | 61 (24.3) | 0.436 | 58 (27.6) | 27 (21.6) | 0.244 |
| Thrombocytes°/°mm³ (n=84), mean ± SD | 115 523 ± 29 085 | 113 708±32 512 | 116 250±27 860 | 0.984 | 112 810±31 743 | 121 577±21 354 | 0.355 |

Data presented as n (%) where applicable; COPD: chronic obstructive pulmonary disease; ENT: ear nose and throat; GIR: iso resource group; N: total number of patient included in the study; n: number of patients according to the considered group; SD: standard deviation; y: years; *: comparisons based on Chi² test or exact Fisher test for qualitative variables, and Student t test or Mann-Whitney U test for quantitative variables, as appropriate; †: 27 missing data; ‡: 2 missing data; §: 22 missing data; ¶: 20 missing data; |: 18 missing data; P-values <0.05 indicated in bold.