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

Cédric Annweiler, MD, PhD, Gaetan Gavazzi, MD, PhD, Gilles Berrut, MD, PhD, Guillaume Sacco, MD, PhD, Jean-Pierre Aquino, MD, Jennifer Gautier, MS, Nathalie Salles, MD, PhD, Olivier Guérin, MD, PhD, on behalf of the SFGG COVID-19 study group

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

Cédric Annweiler, MD, PhD a,b,c

Guillaume Sacco, MD, PhD a,b

Nathalie Salles, MD, PhD d

Jean-Pierre-Aquino, MD e

Jennifer Gautier, MS a

Gilles Berrut, MD, PhD f

Olivier Guérin, MD, PhD g,h

Gaetan Gavazzi, MD, PhD i

on behalf of the SFGG COVID-19 study group

a: Department of Geriatric Medicine and Memory Clinic, Research Center on Autonomy and Longevity, University Hospital, Angers, France; b:UPRES EA 4638, Université d'Angers, Angers, France; c: Robarts Research Institute, Department of Medical Biophysics, Schulich School of Medicine and Dentistry, the University of Western Ontario, London, ON, Canada; d: Department of Clinical Gerontology, University Hospital, Bordeaux, France; e: Délégation générale de la Société Française de Gériatrie et Gérontologie (SFGG); f: Pôle hospitalo-universitaire de gérontologie clinique, CHU de Nantes, France; g: Université Côte d'Azur, Centre Hospitalier Universitaire de Nice, Service de Médecine Gériatrique et Thérapeutique,

Nice; h: Université Côte d'Azur, CNRS UMR 7284/INSERM U108, Institute for Research on Cancer and Aging Nice (IRCAN), Faculté de médecine, Nice, France; i: Service Gériatrie Clinique, Centre Hospitalo-Universitaire Grenoble-Alpes, Saint-Martin-d'Hères, France

***Corresponding author:** Cédric Annweiler, MD, PhD, Department of Geriatric Medicine, Angers University Hospital, F-49933 Angers, France; E-mail: Cedric.Annweiler@chu-angers.fr; Phone: ++33 2 41 35 47 25; Fax: ++33 2 41 35 48 94

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 ≤3symptoms, 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 ≥70years 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

Technology and civil Liberties (ar20-0031v1), and was registered on clinicaltrials.gov under number NCT04343781.

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±7.0years; 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 80years 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 ≥80years 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
- Obtained funding: not applicable
- Statistical expertise: JG
- Administrative, technical, or material support: CA

Study supervision: CA

ACKNOWLEDGMENTS

The authors wish to thank all participants and services for their cooperation; Melinda Beaudenon, MS, and Romain Simon, MS, from the Research Center on Autonomy and Longevity, University Hospital of Angers, France; Caroline Pastorelli, from the French Society of Geriatrics and Gerontology (SFGG); and the COVID-19 study group of the SFGG. SFGG COVID-19 study group:

Didier Albert[1], Cédric Annweiler[2], Gaëlle Annweiler[3], Jean-Pierre-Aquino[4], Marine Asfar[2], Adeline Bannier[5], Jean Barré[2], Axel Bernard[6], Gilles Berrut[7], Mohand Chérif Bessai[8], Yves Beucher[9], Maëlle Beunardeau[10], Isabelle Biajoux[11], Clémence Boully[10],

Anne-Sophie Boureau[7], Antoine Brangier[2], Thomas Brunet[12], Hélène Campana Briault[13], Edouard Chaussade[10], Adrien Cohen[10], Julian Cornaglia[14], Axelle Courau[15], Nicolas Crochette[16], Sylvie Dardalhon[17], Guillaume Duval[2], Marine de La Chapelle[18], Séverine Deledicq[19], Mathilde Devaux[20], Gael Durel[21], Élise Fiaux[22], Thibaut Fraisse[23], Xavier Galimard[24], Jennifer Gautier[2], Gaetan Gavazzi[25], Béatrice Gonzalez[26], Olivier Guérin[27], Aline Gury[28], Valérie Haguenauer-Bariteau[29], Julie Hamrit[30], Céline Hervo[31], Béatrice Lacave[32], Maxime Le Floch[2], Gwenaël Le Moal[33], Pierre-Marie Liais[17], Matthieu Lilamand[34], Jocelyne Loison[2], Paul Loubet[35], Karin Maley[36], Hélène Mangeard[27], Géraldine Martin-Gaujard[37], Marc Mennecart[38], Hélène Meytadier[2], Jean-Marc Michel[39], Nathalie Michel-Laaengh[5], Elena Paillaud[40], Mathieu Priner[12], Emeline Proye[41], Guillaume Sacco[2], Nathalie Salle[42], Denis Soriano[43], Maturin Tabue Teguo[44], Julien Vernaudon[37], François Weill[45], Julien Zirnhelt[46].

1: Service de médecine gériatrique, CH Pau ; 2: Département de Gériatrie et Centre Mémoire Ressources Recherche, CHU Angers; 3: Service de médecine Polyvalente, Clinique de l'Anjou, Angers; 4: Délégation générale de la Société Française de Gériatrie et Gérontologie (SFGG); 5: Service de médecine gériatrique, CH Le Mans / CHU Angers; 6: service de médecine du vieillissement, Hospices Civils de Lyon hôpital Croix-Rousse; 7: Pôle de gérontologie clinique, CHU Nantes; 8: USLD, AP-HP Hôpital Paul Brousse; 9: EHPAD / USLD, CH Compiègne Noyon; 10: Service de gérontologie, AP-HP Hôpital Broca; 11: Service de SSR gériatrique, CH Valence; 12: Service de médecine gériatrique, CHU Poitiers; 13: Service de SSR gériatrique, AP-HP Hôpital Dupuytren Draveil; 14: Service de Maladies Infectieuses et Tropicales, CH Perpignan; 15 Service de gériatrie, CH Fourvière, Lyon; 16: Service de maladies infectieuses et tropicales, CH Le Mans; 17: Pôle gériatrique, GH Grand Est Clinique du Diaconat,

Colmar; 18: Service de maladies infectieuses et tropicales, CHU Angers; 19: Service de cours séjour gériatrique, CH Boulogne sur Mer; 20: Service de médecine interne, CHI Poissy Saint germain; 21: Medipole35 espace santé, Tinteniac; 22: Service de maladies infectieuses, CHU Rouen; 23: Service de cours séjour gériatrique, CH Ales Cévennes; 24: Service de médecine gériatrique aigue, CHI Poissy Saint germain; 25: Clinique universitaire de médecine gériatrique, CHU Grenoble; 26: CHI Créteil; 27: Service de Médecine Gériatrique et Thérapeutique, CHU Nice; 28: Service de médecine Interne et maladies vasculaires, CHU Angers; 29: Centre de soins Le Verger Des Balans, Annesse; 30: Service de court séjour gériatrique, CH Le Cateau-Cambrésis; 31: Service de SSR gériatrique, CH Valence; 32: Service de gériatrie / soins palliatifs, CH de Haguenau; 33: Service de maladies infectieuses, CHU Poitiers; 34: Service de Gériatrie, AP-HP Hôpital Bichat; 35: Service de maladies infectieuses et tropicales, CHU Nîmes; 36: Unité de gériatrie aiguë, Groupe hospitalier diaconesses Croix Simon Simon, Paris; 37: Institut du vieillissement, Hospices Civils de Lyon Hôpital Edouard Herriot; 38: Service de médecine gériatrique, CHU Tours Hôpital Bretonneau; 39: Pôle de gérontologie clinique, Hôpitaux Civils de Colmar; 40: Service de gériatrie, AP-HP Hôpital Européen Georges Pompidou; 41: Service de médecine aiguë de gériatrie, CH Valenciennes; 42: Pôle de Gérontologie Clinique, CHU Bordeaux; 43: EHPAD Clos de Cimiez, Nice; 44: Service de gériatrie, CHU de Guadeloupe; 45: Service de gériatrie aiguë – Pôle de gériatrie, CHU de Strasbourg; 46: Service de médecine gérontologique, Clinique St Barbe, Strasbourg. The authors have listed everyone who contributed significantly to the work in the Acknowledgments section. Permission has been obtained from all persons named in the Acknowledgments section. No participant objected to the use of anonymized clinical and biological data for research purposes. The study was conducted in accordance with the ethical standards set forth in the

Helsinki Declaration (1983). The study protocol was declared to the National Commission for Information Technology and civil Liberties (CNIL) under the number ar20-0031v1, and was registered on clinicaltrials.gov under number NCT04343781.

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.

REFERENCES

1. Sacco G, Brière O, Asfar M, Guérin O, Berrut G, Annweiler C. Symptoms of COVID-19 among older adults: systematic review of biomedical literature. Geriatr Psychol Neuropsychiatr Vieil*,* **2020;** [in press] doi:10.1684/pnv.2020.0863

2. Wang L, He W, Yu X, *et al*. Coronavirus Disease 2019 in elderly patients: characteristics and prognostic factors based on 4-week follow-up. J Infect, **2020**; 80: 639-645.

3. Chen T, Dai Z, Mo P, *et al*. Clinical characteristics and outcomes of older patients with coronavirus disease 2019 (COVID-19) in Wuhan, China (2019): a single-centered, retrospective study. J Gerontol A Biol Sci Med Sci, **2020;** [Epub ahead of print]. April 11, 2020. Available from: https://doi.org/10.1093/gerona/glaa089

4. Aguilova L, Sauzéon H, Balland É, Consel C, N'Kaoua B. [AGGIR scale: a contribution to specifying the needs of disabled elders]. Rev Neurol (Paris), **2014**; 170:216–221.

5. Borges do Nascimento IJ, Cacic N, Abdulazeem HM, *et al*. Novel Coronavirus Infection (COVID-19) in Humans: A Scoping Review and Meta-Analysis. J Clin Med, **2020**; 9: 941.

6. Yang J, Zheng Y, Gou X, *et al*. Prevalence of comorbidities in the novel Wuhan coronavirus (COVID-19) infection: a systematic review and meta-analysis. Int J Infect Dis, **2020**; 94: 91-95.

7. Sun P, Qie S, Liu Z, Ren J, Li K, Xi J. Clinical characteristics of hospitalized patients with SARS-CoV-2 infection: A single arm meta-analysis. J Med Virol [Epub ahead of print]. February 28, 2020. Available from: https://doi.org/10.1002/jmv.25735.

8. Jin X, Lian J-S, Hu J-H, *et al*. Epidemiological, clinical and virological characteristics of 74 cases of coronavirus-infected disease 2019 (COVID-19) with gastrointestinal symptoms. Gut, **2020**; 69(6): 1002-1009.

9. Gane SB, Kelly C, Hopkins C. Isolated sudden onset anosmia in COVID-19 infection. A novel syndrome? Rhinology, **2020**; 58(3): 299-301.

10. Zhang C, Wang X. Initiation of the age-related decline of odor identification in humans: A meta-analysis. Ageing Res Rev, **2017**; 40: 45-50.

11. Bender BS, Nagel JE, Adler WH, Andres R. Absolute Peripheral Blood Lymphocyte Count and Subsequent Mortality of Elderly Men. J Am Geriatr Soc, **1986**; 34: 649–654.

12. Yang Y, Yang M, Shen C, *et al*. Evaluating the accuracy of different respiratory specimens in the laboratory diagnosis and monitoring the viral shedding of 2019-nCoV infections. medRxiv 20021493 [Preprint]. February 17, **2020** [cited 2020 April 9]. Available from: https://doi.org/10.1101/2020.02.11.20021493

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)	P-value*	No major neurocognitive disorder (n=219)	With major neurocognitive disorder (n=134)	P-value*
Sociodemographic data							
Male gender	160 (45.3)	47 (52.8)	113 (42.8)	0.101	105 (48.0)	55 (41.0)	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				**0.0049**			
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	70 (21.5)	11 (13.8)	59 (24.0)		13 (6.5)	57 (44.9)	
3	47 (14.4)	8 (10.0)	39 (15.9)		24 (12.1)	23 (18.1)	
4	59 (18.1)	8 (10.0)	51 (20.7)		40 (20.1)	19 (15.0)	
5 and over	127 (39.0)	49 (61.3)	78 (31.7)		121 (60.8)	6 (4.7)	
Medical history							
Major neurocognitive disorders	134 (38.0)	21 (23.6)	113 (42.8)	**0.001**	0 (0.0)	134 (100.0)	-
Hypertension	234 (66.3)	50 (56.2)	184 (69.7)	**0.012**	144 (65.8)	90 (67.2)	0.786
Diabetes mellitus	80 (22.7)	23 (25.8)	57 (21.6)	0.407	52 (23.7)	28 (20.9)	0.535
Asthma or COPD	46 (13.0)	13 (14.6)	33 (12.5)	0.610	32 (14.6)	14 (10.5)	0.259
Cardiomyopathy	159 (45.0)	24 (27.0)	135 (51.1)	**<0.001**	92 (42.0)	67 (50.0)	0.143
Severe chronic renal failure	38 (10.8)	5 (5.6)	33 (12.5)	0.070	22 (10.1)	16 (11.9)	0.577
Solid or hematological cancer	67 (19.0)	15 (16.9)	52 (19.7)	0.554	45 (20.6)	22 (16.4)	0.337
General signs							
Sudden deterioration of general condition	186 (52.7)	34 (38.2)	152 (57.6)	**0.002**	113 (51.6)	73 (54.5)	0.599
Low blood pressure	51 (14.5)	8 (9.0)	43 (16.3)	0.090	31 (14.2)	20 (14.9)	0.842
Body temperature				**0.011**			**0.013**
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)	
Respiratory 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							

Falls	66 (18.7)	7 (7.9)	59 (22.4)	**0.002**	36 (16.4)	30 (22.4)	0.164
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							
Lymphopenia §	247 (74.6)	66 (78.6)	181 (73.3)	0.336	165 (79.3)	82 (66.7)	**0.011**
Lymphocytes / mm^3 (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°/°mm^3 (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°/°mm^3 (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.