9 Hong J, Kong HJ, Yoon HJ. Web-based telepresence exercise program for community-dwelling elderly women with a high risk of falling: randomized controlled trial. *JMIR Mhealth Uhealth* 2018; **6**: e132.
10 Schwartz H, Har-Nir I, Wenhoda T, Halperin I. Staying physically active during the COVID-19 quarantine: exploring the feasibility of live, online, group training sessions among older adults. *Transl Behav Med* 2021; **11**: 314–322.

How to cite this article: Uemura K, Watanabe A, Kamitani T, Yamada M, Saho K, Okamoto H. Feasibility of active learning health education by video conferencing among older adults. Letters to the Editor - Research Studies. 2021;21:1064–1066. https://doi.org/10.1111/ggi.14281

Neutralizing antibodies directed against SARS-CoV-2 in a population residing in a nursing home and a long-term care unit

Dear Editor,

Ever since the beginning of the SARS-CoV-2 epidemic, much work has been carried out in order to better understand this infection in terms of its physiopathology, treatment and prevention, and towards scientific innovation, as seen with the design of the messenger RNA vaccines.[1] The importance of protective and persistent immunity is essential for avoiding new epidemic waves, brought on by the apparition of novel variants. In terms of morbidity and mortality, elderly and frail patients, especially those residing in nursing homes (NHs) or other long-term care units (LTCUs), have been identified as a population at particularly high risk in case of SARS-CoV-2 infection.[2] In order to establish the strategy of vaccination in this potentially immunosenescent population, the issue of post-infection and post-vaccination protective immunity must be taken into account. The persistence and effectiveness of post-infection/post-vaccination immunity have not been entirely clarified. It would seem that the development of herd immunity, capable of limiting epidemic outbreaks in the face of new variants, is dependent on the persistence of protective or neutralizing antibodies (NAb) in patients infected by SARS-CoV-2 or vaccinated against it. To date, multiple studies have proved the efficiency of these novel two-dose vaccines in terms of immune protection against potential reinfection, while suggesting that a single dose could suffice for those already infected and cured.[3–5] This latter strategy should confer long-term effective immunity in those having already contracted the disease. However, at this moment little data is available on the intensity and efficacy of the immune response in elderly frail patients infected by or vaccinated against SARS-CoV-2.

Following the first COVID-19 outbreak, in June 2020, a French university hospital organized a screening campaign at the heart of its (NHs) and (LTCUs). This campaign consisted of testing using Reverse Transcription - Polymerase Chain Reaction (RT-PCR) nasopharyngeal tests and ELISA (enzyme-linked-immuno-sorbent-assay) serological techniques that involved qualitative serological tests that detected antibodies against the SARS-CoV-2 nucleocapsid (Abbott Alinity SARS-Cov-2 IgG assay) and against the spike protein (Wantai SARS-CoV-2 Ab ELISA). Among the 221 patients screened, 147 (66.5%) showed seroconversion against SARS-CoV-2. A disparity between the two structure was found, with 88.7% seroconversion in the NH versus 45.6% seroconversion in the LTCU ($P < 0.001$) (Table 1).

Using the samples collected during the screening campaign, we went on to determine the anti-SARS-CoV-2 neutralizing antibody titer by means of neutralization tests using retroviral particles pseudotyped with the SARS-CoV-2 S glycoprotein (SARS-CoV-2pp PMID: 33193227), as previously described.[6,7] Pseudotyped retroviral particles containing the SARS-CoV-2 virus S glycoprotein (SARS-CoV-2pp) were produced, as described before, by transfection of a plasmid coding the S glycoprotein of SARS-CoV-2 and of a reporter plasmid coding for the luciferase enzyme. The pseudotyped particles were collected 48, 72 and 96 h after filtration through 0.45-μm pores. The plasma obtained for the serological tests was diluted by serial dilution ½ and then incubated with the SARS-CoV-2pp for an hour before being put in contact with 293T (ATCC® CRL-3216TM) cells, themselves transfected transitorily, 24 h before, with a plasmid coding for the human ACE2 receptor protein (pcDNA3.1-hACE2). The luciferase activity was measured 72 h after incubation. The NAb titer was defined as the plasma dilution inhibiting 50% of the luciferase activity. We thus compared the neutralizing antibody titers by the criteria of care unit, age and gender, by calculating the median antibody titers

Table 1 Characteristics and test results of the population

	All participants	LTCU residents	NH residents	*P*
Number (*n*)	261	139	122	
Age	84.8 ± 8.2	85.2 ± 8.4	84.4 ± 8.0	0.422
Sex M/F (%)	65/196 (24.9%/75.1%)	41/98 (29.5%/70.5%)	24/98 (19.7%/80.3%)	0.060
Age M/F	82.04 ± 7.3/85.7 ± 8.3	—	—	<0.001
Participants in the study *N* (%)	221 (84.7%)	114 (82.0%)	107(87.7%)	0.203
Positive serological test *N* (%)	147 (66.5%)	52 (45.6%)	95 (88.7%)	<0.001
Positive RT-PCR (*N*)	8	4	4	—

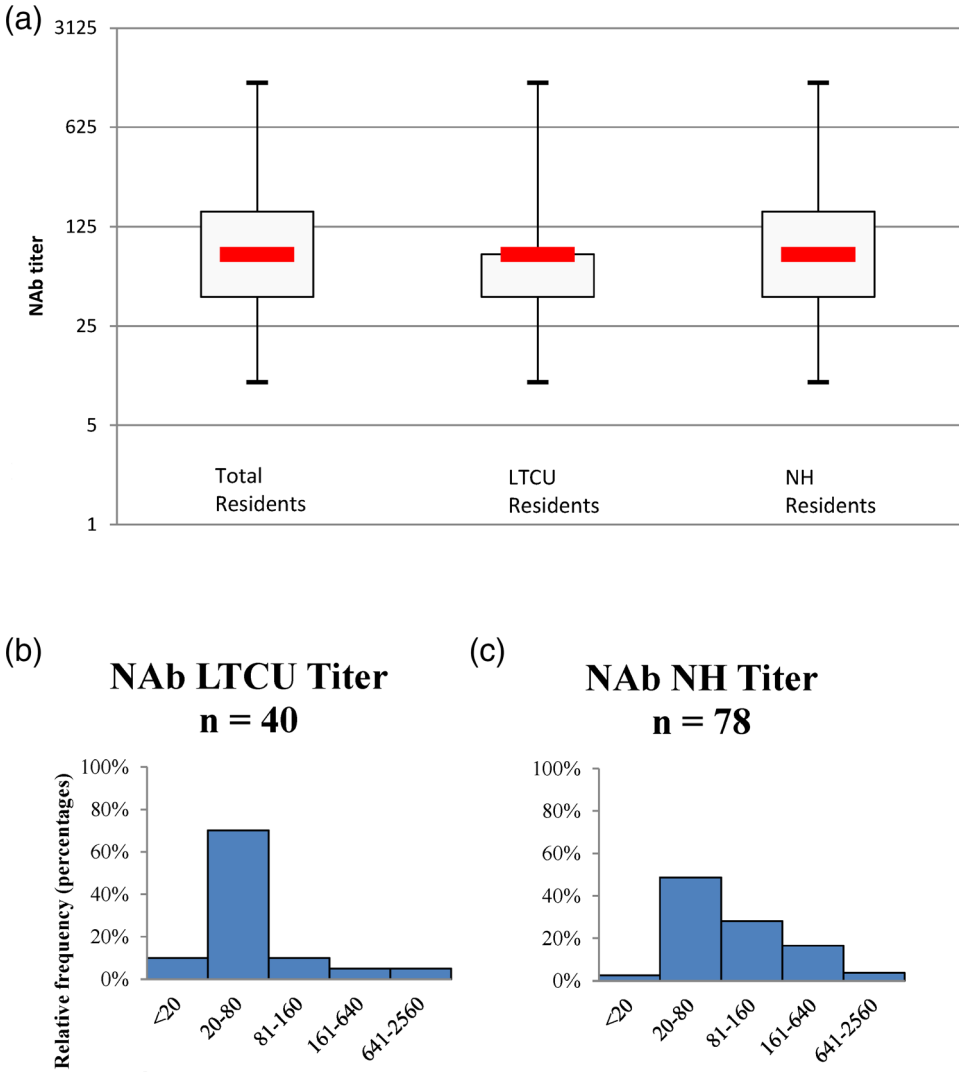

Figure 1 Median NAb titer determined during the June 2020 screening campaign with median IQR, and minimal and maximal values at the extremities (a). NAb titer distribution in the long-term care unit (LTCU) (b) and nursing home (NH) (c).

(interquartile range) and comparing them using Mann–Whitney or Kruskal–Wallis tests.

We were able to successfully determine the COVID-19 neutralizing antibody titer for 118 of the 147 (80%) residents having had a positive initial serology. The median antibody titer was calculated at 80 [40; 160]. The titer values ranged from 20 to 1280 (Fig. 1a). Among the LTCU residents and participants, 40 (79%) had a median titer of 80 [40; 80] and 32 (80%) had titers less than or equal to 80. Two of the patients had very high titers, at 1280 (Fig. 1b). In the NH, the median titer was 80 [40; 160] for the 78 (82%) patients analysed. The titer was less than or equal to 80 in 40 of them (52%). Sixteen (21%) had titers greater than 160, with a maximal value of 1280 found in three participants (Fig. 1a,c). The NAb titer was significantly higher in the NH ($P = 0.040$). No significant difference was found for the neutralizing antibody titer according to age (Median NAb =80 [40; 160] for residents under and over 90 years old; $P = 0.777$) and gender ($P = 0.320$). At this point we cannot conclude that the NH population had more effective immunity because of a lack of consensus regarding the minimal protecting NAb titer and because protection conferred by T-cell-mediated immunity was not taken into account.[8] It nevertheless seems that viral circulation was more important in the NH, thus conferring a more robust humoral immune response. Differences between transmission–precaution measures enforced in the two types of structure during the first viral outbreak are to be noted, with room-based isolation for the NH residents and isolation in a dedicated COVID-19 unit for the LTCU patients. Nevertheless, LTCU residents are by definition more fragile, have a higher burden of disease, and thus are potentially more immunosenescent. Accordingly, the issue of a lessened humoral immune response in these frailer and more immunodepressed patients can be raised knowing that in our study the median antibody titer was not impacted by age or gender. These antibody titers should therefore be analysed according to other clinical criteria (neurocognitive status, dependency, malnutrition, pathologies, immunosuppression, etc.) in order to determine criteria unfavourable to long-lasting immunity while taking into account the decrease over time of these specific antibodies.

By continuing to observe this cohort of NH and LTCU patients at the University Hospital Amiens Picardie, as part of the SERO-CoV-OLD trial (PI2020-843_0079) (ID ClinicalTrials.gov: NCT04563650), we have set about following the presence and kinetics of neutralizing COVID-19 antibodies over a longer period of time while also studying the residents immune profile. The included patients thus benefitted from follow-up qualitative and quantitative serological tests every 3 months for a year, with lymphocyte immunophenotyping and cytokine measurement done in

parallel in order to measure the impact of immunosenescence. It is to be noted that before the sampling scheduled at the 9-month time-mark, the residents were included in the Comirnaty (Pfizer BNT162b2) vaccination campaign. We therefore took the opportunity to evaluate the post-vaccination humoral and cellular immune response and to analyse the impact of prior seroconversion on vaccination response in the elderly. Studying this cohort of patients could help to guide vaccination strategy, most notably with regard to establishing the optimal number of doses that should be administered to elderly patients vulnerable to SARS-CoV-2 infection, by taking into account the many facets of the immune response.

Acknowledgements

The study was funded by a donation from the fund AGIPI (Association Générale Interprofessionnelle de Prévoyance et d'Investissement) for COVID-19 solidarity. AGIPI is an organization that was created in 1976. Since then, it has acted in relation to pensions, savings, providence and health. AGIPI offers solutions that match individual and professional protection needs and has almost 620 000 members.

Disclosure statement

The authors declare no conflict of interest.

Author contributions

All authors made substantial contributions to the conception or design of the work, or to the acquisition, analysis or interpretation of data for the work, critically reviewed it and approved the final version to be published.

Compliance with ethical standards

The study was conducted in accordance with the guidelines of the local hospital ethics committee.

Data availability statement

Data Availability Statement will be published alongside our manuscript, if it is accepted for publication.

Julien Moyet,[1] Francois Helle,[2] Gwladys Bourdenet,[3,4] Cédric Joseph,[5] Brigitte Gubler,[3,4,6] Etienne Brochot[2,7] and Frédéric Bloch[1,8]

[1]Department of Gerontology, Amiens University Hospital, Amiens, France
[2]AGIR Research Unit, UR UPJV 4294, Jules Verne University of Picardie, Amiens, France
[3]Department of Immunology, Amiens University Hospital, Amiens, France
[4]HEMATIM – EA4666, Jules Verne University of Picardie, Amiens, France
[5]Infectious Diseases Department, Amiens University Hospital, Amiens, France
[6]Department of Molecular Oncobiology, Amiens University Hospital, Amiens, France
[7]Department of Virology, Amiens University Hospital, Amiens, France
[8]Laboratory of Functional Neurosciences UR 4559, Jules Verne University of Picardie, Amiens, France

References

1 Krammer F. SARS-CoV-2 vaccines in development. *Nature* 2020; **586**: 516–527. https://doi.org/10.1038/s41586-020-2798-3.
2 Rydyznski Moderbacher C, Ramirez SI, Dan JM *et al*. Antigen-specific adaptive immunity to SARS-CoV-2 in acute COVID-19 and associations with age and disease severity. *Cell* 2020; **183**: 996–1012. https://doi.org/10.1016/j.cell.2020.09.038.
3 Baden LR, El Sahly HM, Essink B *et al*. Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. *N Engl J Med* 2021; **384**: 403–416. https://doi.org/10.1056/NEJMoa2035389.
4 Saadat S, Rikhtegaran Tehrani Z, Logue J *et al*. Binding and neutralization antibody titers after a single vaccine dose in health care workers previously infected with SARS-CoV-2. *JAMA* 2021; **325**: 1467–1469. https://doi.org/10.1001/jama.2021.3341.
5 Polack FP, Thomas SJ, Kitchin N *et al*. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. *N Engl J Med* 2020; **383**: 2603–2615. https://doi.org/10.1056/NEJMoa2034577.
6 Millet JK, Whittaker GR. Murine leukemia virus (MLV)-based coronavirus spike-pseudotyped particle production and infection. *Bio Protoc* 2016; **6**(23). https://doi.org/10.21769/BioProtoc.2035.
7 Brochot E, Demey B, Touzé A *et al*. Anti-spike, anti-nucleocapsid and neutralizing antibodies in SARS-CoV-2 inpatients and asymptomatic individuals. *Front Microbiol* 2020; **11**: 584251. https://doi.org/10.3389/fmicb.2020.584251.
8 Zuo J, Dowell AC, Pearce H *et al*. Robust SARS-CoV-2-specific T cell immunity is maintained at 6 months following primary infection. *Nat Immunol* 2021; **22**: 620–626. https://doi.org/10.1038/s41590-021-00902-8.

How to cite this article: Moyet J, Helle F, Bourdenet G, et al. Neutralizing antibodies directed against SARS-CoV-2 in a population residing in a nursing home and a long-term care unit. Geriatr. Gerontol. Int. 2021;21:1066–1068. https://doi.org/10.1111/ggi.14289