[10]*Laboratoire de Virologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France*
[11]*INSERM, UMR_S1109, LabEx TRANSPLANTEX, Research Center for Immunology and Hematology, Faculty of Medicine, University Hospital Federation (FHU) OMICARE, Federation of Translational Medicine of Strasbourg (FMTS), University of Strasbourg, Strasbourg, France*

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Quantitative description of SARS-CoV-2 RT-PCR, a cohort of 76 COVID-19 older hospitalized adults

INTRODUCTION

During the first wave of the COVID-19 pandemic, many recommendations emerged regarding patient testing for COVID-19 to plan transfers between medical units and entry into retirement/care homes in the almost complete absence of evidence on the duration of SARS-CoV-2 viral carriage and especially SARS-CoV-2 RT-PCR quantitative description over time in older adult patients.

Here, we report a quantitative description of the natural evolution over time of SARS-CoV-2 RT-PCR results of a cohort of 76 COVID-19 older hospitalized adults followed until death or RT-PCR negative conversion.

METHODS

The observational cohort study was approved by the institutional ethics board of the University Hospital of Strasbourg,[1] consent was collected for all patients.

From March 10 to June 9, 2020, we included all patients aged 70 and older with a COVID-19 confirmed

by SARS-CoV-2 RT-PCR, hospitalized in the COVID geriatric units. Patients with lack of data regarding the date of first symptom onset (dso) were excluded.

SARS-CoV-2 nasopharyngeal RT-PCR was performed 1 month after the dso and repeated until the advent of final negative sample.

In a real time or quantitative-RT-PCR, the cycle threshold (Ct) value is the number of PCR cycles required to amplify the target nucleic acid to reach the threshold level of detection. The greater the initial quantity of genetic material/virus, the lower the number of RT-PCR cycles required for its detection. The SARS-CoV-2 RT-PCR test is detailed in the Supplementary text S1.

Temporal patterns of viral shedding were modeled with generalized additive models,[2] using a total of 235 nasopharyngeal swabs from 76 patients.

The survival analysis, representing the expected time duration until the final RT-PCR negative conversion, is shown in a Kaplan–Meier curve. In this representation model, a test is considered positive until the final SARS-CoV-2 RT-PCR negative conversion for that patient.

RESULTS

Seventy-six patients with COVID-19 were included. Twenty-two patients died before reaching virological evaluation at 1 month after dso. Of the 54 surviving patients, 52 had a RT-PCR reassessment at 1 month after dso and were followed-up until SARS-CoV-2 nasopharyngeal RT-PCR negative conversion. The average age was 86.0 (6.37) years.

Temporal patterns of viral shedding are shown in the Figure S1.

The survival analysis, representing the expected time duration until the final RT-PCR negative conversion, is shown in Figure 1. The maximum time point of RT-PCR negative conversion was 66 days. At day 40 after dso, 51 out of 52 patients (98.1%) had received a reassessment test after 1 month, and 19 patients (36.5%) had not yet developed a negative RT-PCR test. At day 50 after dso all the 52 patients had already received a reassessment test after 1 month, 8 patients (15.4%) had still not developed a negative RT-PCR test result. When applying a Ct cut-off above 35 for conversion to a negative test, 9 patients (17.3%) at 40 dso and 2 patients (3.9%) at 50 dso had not yet developed a negative RT-PCR test result.

The risk of a persistently positive test at 1 month was associated with a higher Charlson comorbidity index odds ratio (OR) 1.27 (95% CI, 1.01–1.68), $p = 0.027$, when applying a Ct cut-off above 37 Ct: OR 1.66 (95% CI, 1.21–2.65), $p = 0.001$.

Among patients with persistent positive results between 30 and 60 days after dso, the median Ct value was 39 (37–40). Seven patients presented Ct value ≤35 after 1 month.

DISCUSSION

We provided evidence for longer detection of SARS-CoV-2 in serial RT-PCRs on affected patients than previously reported.[3-5] Prolonged detection of positive RT-PCR is expected among older adults. The Ct is then generally high suggesting very little viral genetic material, but this trend was not exclusive.

Older age and severity of the disease have often been identified as risk factors for prolonged viral shedding; however, hypertension, diabetes, and coronary artery disease were inconstantly identified.[6] Among older adults, the Charlson comorbidity index could be a more potent marker of prolonged viral excretion than comorbidities taken one by one.

Limitations

All RT-PCR tests that produced a reaction were interpreted as positive regardless of the Ct value, which may be debatable, but no clear guidelines were available. When specified in studies, Ct value cut-offs were between 34 and 45.[4,7-9]

In an attempt to present data that may be comparable with other studies however we presented survival curves with different Ct cut-offs.

For 12 patients we were limited to one final negative.

To the best of our knowledge, despite the plethora of literature on COVID-19 there are no studies on the quantitative description of viral shedding in older adult patients for the prolonged duration of 2 months.

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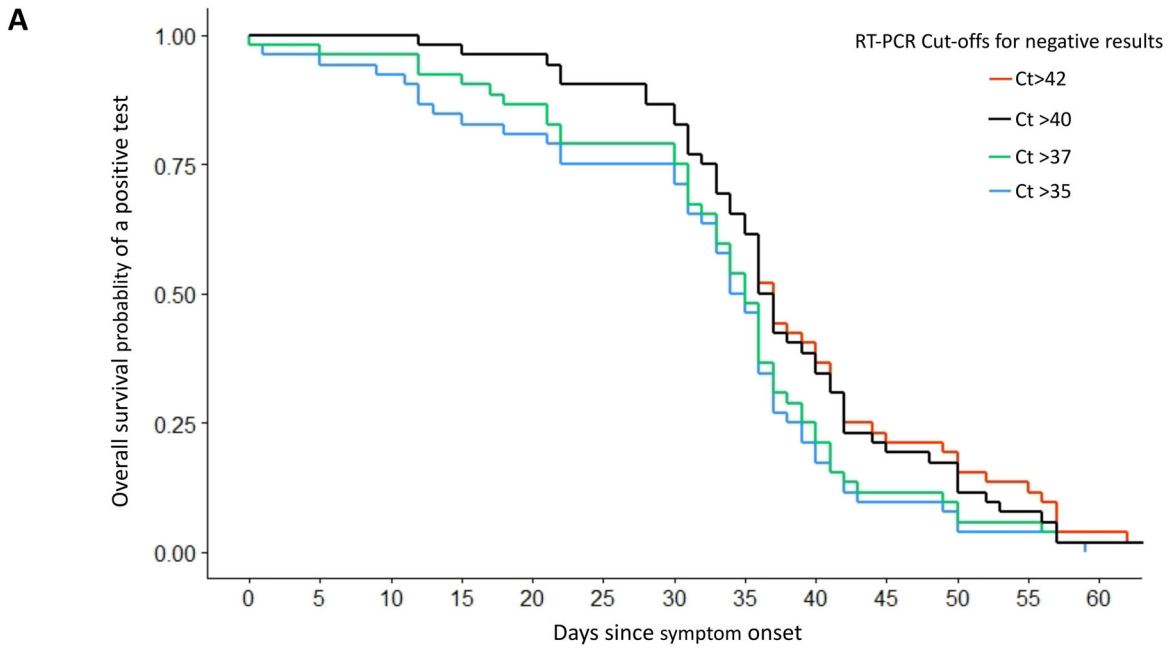
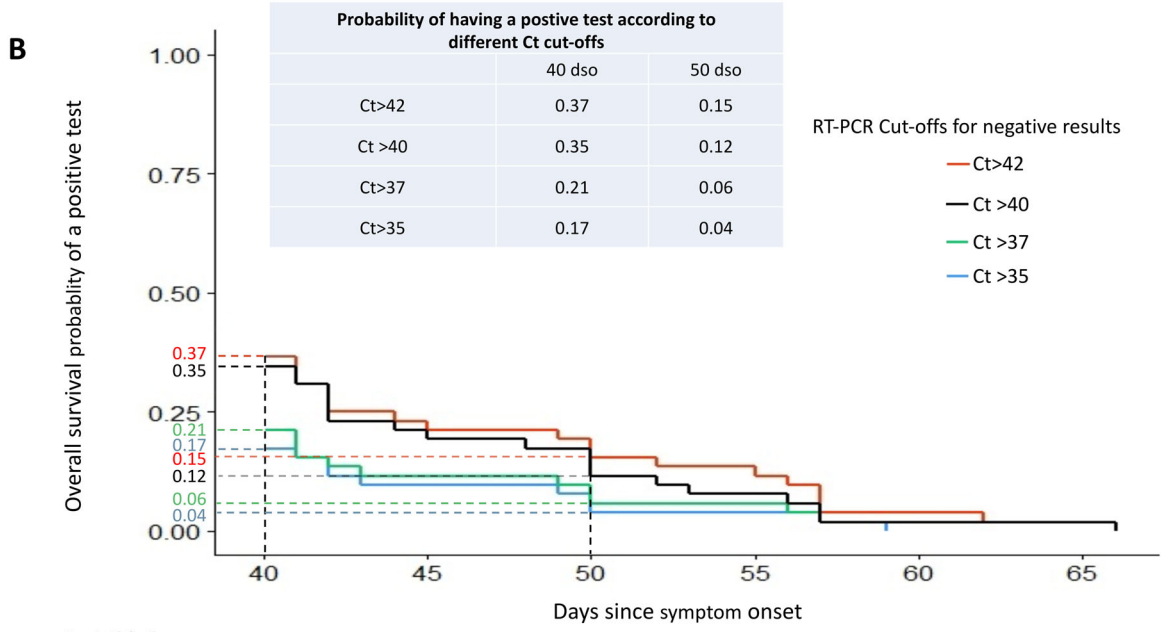


No. at risk for the group Absence of RT-PCR reaction	52	52	50	45	21	10	2
Number of tests every 10 days	58	13	19	53	44	19	7
Different patients tested every 10 days	52	12	15	45	35	13	6
Ct, Mean (SD) and Median (IQR) for positive results every 10 days	25.9 (7.0) 25 (21-30.75)	34.2 (5.2) 33.5 (33-37.75)	36.7 (2.6) 37.5 (35-38.75)	37.1 (3.8) 39 (35-40)	38.3 (3.0) 39 (37.75-40)	37.25 (3.3) 36 (35-38.25)	-



No. at risk for the group Absence of RT-PCR reaction	21	12	10	7	2	1
Number of tests every 10 days	44		19			7
Different patients tested every 10 days	35		13			6
Ct, Mean (SD) and Median (IQR) for positive results every 10 days	38.3 (3.0) 39 (37.75-40)		37.25 (3.3) 36 (35-38.25)			-

FIGURE 1 Legend on next page.

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Maxence Meyer MD[1]
Anita Meyer MD[2]
Lidia Calabrese MD[1]
Florentin Constancias PhD[3]
Louise F. Porter MD, PhD[4]
Marion Muller MD[1]
Manon Leitner MD[1]
Amandine Leitner MD[1]
Antonin Michaud MD[1]
Alexandre Boussuge MD[1]
Georges Kaltenbach MD, PhD[1]
Elise Schmitt MD, PhD[1]
Patrick Karcher MD[1]
Erik Sauleau MD, PhD[5]
Saïd Chayer PhD, HDR[6]
Frédéric Blanc MD, PhD[1]
Samira Fafi-Kremer PharmD, PhD[7,8]
Aurélie Velay PharmD, PhD[7,8]
Thomas Vogel MD, PhD[1]

[1]*Department of Geriatric, University Hospitals of Strasbourg, Strasbourg, France*
[2]*Department of Nephrology, Klinikum Offenburg, Offenburg, Germany*
[3]*Department of Health Sciences and Technology, ETH Zürich, Zurich, Switzerland*
[4]*Department of Medical Genetics, University Hospital of Strasbourg, Strasbourg, France*
[5]*Department of Public Health, Methods in clinical research, University Hospitals of Strasbourg, Strasbourg, France*
[6]*Department of Clinical Research and Innovations, University Hospitals of Strasbourg, Strasbourg, France*
[7]*Laboratoire de Virologie, Hôpitaux Universitaires de Strasbourg, Strasbourg, France*
[8]*INSERM, UMR_S1109, LabEx TRANSPLANTEX, Research Center for Immunology and Hematology, Faculty of Medicine, University Hospital Federation (FHU) OMICARE, Federation of Translational Medicine of Strasbourg (FMTS), University of Strasbourg, Strasbourg, France*

See related letter by Meyer et al.

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FIGURE 1 The survival analysis, analyzing expected duration of time until RT-PCR negative conversion. (A and B) In this representation a RT-PCR test is considered positive on a particular D-day for a patient if the last test performed on the D-day is positive or if the last test performed on the D-day is negative but the patient presented a subsequent positive test after the D-day. For example, if the patient had RT-PCR positive on day 3, 15, 30, 37 then negative on 42 and 47 the test is considered negative from day 42. If the patients had RT-PCR positive on day 3, 15, 30, 37, then negative on day 42, then positive on day 47, then negative on day 52 and 57. The test is considered negative from day 52. We included in this analysis the results of a total of 213 RT-PCR tests among the 52 patients who survived. Number of tests performed, different patients tested and the RT-PCR cycle threshold (Ct) value with its mean and standard deviation (SD) and median and interquartile range (IQR) are presented for every 10 days. The survival curves are presented with different cut-offs defining a negative RT-PCR test depending on whether the Ct is greater than 35, 37, 40, 42. Because the study is designed to reassess the RT-PCR 1 month after dso, the survival analysis plot makes sense from the 40th day after dso (panel B)

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

Appendix S1. Supplementary Text S1. Details of the SARS-CoV-2 RT-PCR test on nasopharyngeal swab.

Figure S1. Graphical representation of temporal patterns of viral shedding The attached graphs represent the smoothing curves of the delay: X = Days since symptom onset, Y = RT-PCR Cycle threshold (Ct) value. Comparison of RT-PCR initial Ct value and death at 1 month and comparison of a persistently RT-PCR positive test at 1 month and the Charlson Comorbidity Index were performed using the Mann–Whitney Wilcoxon Test. Odds-ratio (OR), is the multiplication of the risk that PCR is positive at 1 month when the Charlson Index increases by 1.

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Medical students' motivations to help older adults during the COVID-19 pandemic

INTRODUCTION

Across the globe, the Coronavirus disease 2019 (COVID-19) pandemic continues to disproportionately impact the older population. Adults aged 65 years and older are at a greater risk of contracting the virus due to close living quarters in long-term care facilities, a less robust immune system, and a systemic unawareness of their unique health needs.[1,2] Ironically, the continued social distancing mandate may present as a risk factor for poorer mental and physical health outcomes among older adults.[3,4]

The pandemic has also impacted the medical student experience. Clinical rotations were halted abruptly, leaving students with limited patient interaction during a time when exposure to patients is critical for their personal and professional development.[5] Social distancing guidelines have placed both the older population and medical students in an unusual and troubling position. The pandemic has elucidated an unaddressed problem with respect to socially isolated older adults, simultaneously leaving medical students willing and able to assist without knowing how to help.[6]

Our initiative at Rutgers Robert Wood Johnson Medical School (RWJMS), "Caring Companions" (CC), connected medical students with older patients in the Rutgers RWJMS General Internal Medicine practice. The CC pilot was created at the onset of the pandemic and recruited medical students to volunteer and make weekly telephone calls to patients. Telephone initiatives such as CC represent cost-effective and easily implementable solutions to ameliorate the consequences of isolation in the older population, simultaneously providing medical students quality experiences through engagement with persons aged 65 years and older. Other medical schools have also recognized this opportunity and created similar telephone initiatives to connect medical students to older adults.[7-9] Although prior research on medical student telephone initiatives with older adults during the pandemic has examined benefits to both students and older adults, little is known about why students choose to volunteer with older adults. We examine student motivations to provide medical schools with insight on how to engage student volunteers with the older population during and after the COVID-19 pandemic.

METHODS

An email was sent to Rutgers RWJMS students seeking volunteers for the CC initiative at the onset of the pandemic in April, 2020. Interested students completed a questionnaire indicating their year in school, professional interest, and motivation to participate in CC. Seventy-one students signed up to volunteer (39% 1st year, 11% 2nd year, 29% 3rd year, and 21% 4th year). Students' open-ended responses were deidentified and classified using the six functional motivations for volunteering detailed in the Volunteer Functions Inventory[10]: Values, Understanding, Enhancement, Protective, Career, and Social.