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Efficacy of a Test-Retest Strategy in Residents and Health Care Personnel of a Nursing Home facing a COVID-19 Outbreak

Hubert Blain¹, Yves Rolland², Edouard Tuaillon³, Nadia Giacosa¹, Mylène Albrand¹, Audrey Jaussent⁴, Athanase Benetos⁵, Stéphanie Miot¹, and Jean Bousquet⁶

¹ Department of Geriatrics, Montpellier University Hospital, Montpellier University, France
² Gérontopôle de Toulouse, INSERM 1027; 31059 Toulouse, France
³ Department of Virology, Montpellier University Hospital, INSERM 1058, Montpellier University, France
⁴ Department of Medical Information, University Hospital of Montpellier, University of Montpellier, France
⁵ Department of Geriatrics, CHRU de Nancy and Inserm DCAC, Université de Lorraine, Nancy, France
⁶ Charité, Universitätsmedizin Berlin, Humboldt-Universität Berlin, and Berlin Institute of Health, Comprehensive Allergy Center, Department of Dermatology and Allergy, Berlin, Germany and MACVIA-France, Montpellier, France

Corresponding author: Prof Hubert BLAIN, Department of Geriatrics, Montpellier University Hospital, Montpellier University, France. Full postal address: Centre Antonin Balmes, Pôle de Gérontologie du Centre Hospitalier Universitaire de Montpellier, 39 avenue Charles Flahault, 34295 Montpellier Cedex 5, France. e-mail: h-blain@chu-montpellier.fr; tel: +33 467339957

Running title: Testing Efficacy in a Nursing Home facing COVID-19

Key words: COVID-19, nursing home, rRT-PCR, antibodies against SARS-CoV-2

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The present study did not require ethical approval. All materials and data are available.
Brief Summary:

A wide testing strategy is effective in detecting asymptomatic COVID-19 residents and HCP in a NH facing COVID-19 outbreak. Symptomatic residents and HCP as well as asymptomatic HCP with negative testing may also play a role in the virus spread within the NH.

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Abstract

Objective: To assess the American Testing Guidance for Nursing Homes (NHs) - updated May 19, 2020 - with a new COVID-19 case.

Design: Case investigation.

Setting and Subjects: All 79 residents and 34 Health Care Personnel (HCP) of a NH.

Methods: 7 days after identification of a COVID-19 resident, all residents and HCP underwent rRT-PCR testing for SARS-CoV-2 with nasopharyngeal swabs. This was repeated weekly in all previously negative subjects until the testing identified no new cases and in all positive subjects until the testing was negative. COVID-19 infection prevention and control (IPC) measures were implemented in all residents and HCP with positive testing or with COVID-19 symptoms. Standard IPC was also implemented in all HCP. Six weeks after initial testing, all residents underwent testing for ELISA-based IgG antibodies directed against the SARS-CoV-2. Symptoms were serially recorded in residents and HCP.

Results: 36 residents had a positive RT-PCR at baseline and two at day 7. Six HCP had a positive RT-PCR at baseline and two at day 7. No new COVID-19 cases were diagnosed later. Among the SARS-CoV-2-positive cases, six residents (16%) and three HCP (37%) were asymptomatic during the 14 days before testing. Twenty-five residents (92.3%) and all 8 HCP (100%) with a positive RT-PCR developed IgG antibodies against SARS-CoV-2. Among the residents and HCP always having tested negative, 2 (5%) and 5 (11.5%) developed IgG antibodies against SARS-CoV-2. These 2 residents had typical COVID-19 symptoms before and after testing and 2/5 HCP were asymptomatic before and after testing.

Conclusions and Implications: This study shows the validity of the updated American Testing Guidance for Nursing Homes (NHs). It suggests implementing COVID-19 IPC in both residents and HCP with positive testing or COVID-19 symptoms and warns that asymptomatic HCP with repeated negative RT-PCR testing can develop antibodies against SARS-CoV-2.

Key words: COVID-19, nursing home, rRT-PCR, antibodies against SARS-CoV-2

Introduction

After identification of a COVID-19 case in a Nursing Home (NH), residents are at high risk of serious illness and death from COVID-19, with a rapid and widespread transmission of
SARS-CoV-2 \(^1\),\(^2\) The standard COVID-19 diagnosis is based on SARS-CoV-2 nucleic acid testing by real-time reverse-transcriptase polymerase chain reaction (RT-PCR).\(^3\) Residents and health care personnel (HCP) with positive RT-PCR can be asymptomatic at the time of testing and may contribute to transmission.\(^2\) Control strategies focusing only on symptomatic residents are therefore insufficient. This explains why the recent American Testing Guidance for Nursing Homes recommends (i) testing of all residents and HCP in the NH if there is a confirmed case of COVID-19 and (ii) repeated weekly testing of all previously negative residents until no new cases of COVID-19 are detected for at least 14 days since the most recent positive result.\(^4\)

Seroconversion with SARS-CoV-2 antibodies generally occurs rapidly in adult subjects.\(^5\) The immune response to viruses may be influenced by aging, and seroconversion in frail older subjects is uncertain. It is unclear whether residents and HCP with repeated negative testing may develop antibodies against SARS-CoV-2.

A study was carried out on all residents and HCP of a NH facing a COVID-19 outbreak. The aim was to assess clinical and serological parameters for the efficacy of infection prevention and control (IPC) measures adapted to (i) symptoms and (ii) results of repeated testing.

**Methods**

**Setting:** Single NH

**Participants:** From March 3\(^{rd}\) to 6\(^{th}\), 2020, three NH residents were hospitalized for severe non-respiratory COVID-19 symptoms. All three developed respiratory symptoms (cough with fever and dyspnea) 7 to 10 days after admission, and RT-PCR following nasopharyngeal swab test confirmed COVID-19. Seven days after the first diagnosis, all residents or HCP were enrolled in the study.

No ethics committee was required as this is an observational study.

**Outcomes:** COVID-19 symptoms were examined for 14 days before the first test and then followed daily for 6 weeks.
Nasopharyngeal testing for SARS-CoV-2 using rRT-PCR was performed in all residents and HCP. It was repeated weekly in all previously negative subjects until no new cases were identified and in all positive subjects until testing was negative.

COVID-19 IPC measures were applied in all residents and HCP with positive testing or with new COVID-19 symptoms, including diarrhoea, delirium, or falls.

Six weeks after initial testing, all residents and HCP underwent blood testing for IgG antibodies directed against the SARS-CoV-2 nucleocapsid protein using an ELISA CE-IVD marked kit (ID screen® SARS-CoV-2-N IgG indirect ID. Vet, Montpellier, France).

**Results**

**Residents**

Among the 79 residents, 38 (48%) had a positive RT-PCR (Table 1). 36 were diagnosed at baseline and two at day 7. The residents who tested positive were distributed throughout the 4 floors of the NH (10, 9, 10, 9).

The mean age of residents was similar in positive and negative RT-PCR groups. Diabetes and renal disease were more common in RT-PCR positive residents.

Thirteen residents died two to seven days after testing due to respiratory symptoms. Twelve (7 men) had a positive RT-PCR. Six RT-PCR-positive residents (16%) were asymptomatic before testing.

Six weeks after initial testing, seven residents still had at least one typical COVID-19 symptom (particularly fever or cough) or a significant functional impairment. Among them, 5 (83%) were RT-PCR-positive.

The RT-PCR test became negative 14, 21, or 28 days after initial positive testing in 2 (14%), 7 (27%), and 12 (46%) residents. In the 5 (19%) who still had positive RT-PCR 28 days after initial testing, one recovered completely and 4 had long-lasting symptoms (fever and hypothermia; shortness of breath; dry cough; impaired health status).

**Health Care Personnel**
Among the 34 HCP, 6 had positive RT-PCR at baseline and 2 at day 7 (23.5%). No new COVID-19 diagnosis was made later. Two thirds of the positive RT-PCR HCP had COVID-19 symptoms, often mild.

**Seroconversion**

Six weeks after nasopharyngeal testing, 25 residents (92.3%) and all 8 HCP (100%) with positive RT-PCR developed SARS-CoV-2 IgG antibodies. Two (5%) RT-PCR negative residents and 5 (11.5%) RT-PCR negative HCP developed antibodies. All 2 residents and 3/5 HCPs had typical COVID-19 symptoms.

**Discussion**

The present study shows the clinical efficacy of a symptom- and repeated testing-based strategy in a NH facing a COVID-19 outbreak. This experience validates the American Testing Guidance for Nursing Homes updated in May 2020. All residents and HCP were tested and there was no selection bias. This study was conducted before any other COVID-19 cases had been detected in the county. The presence of antibodies in residents and HCP is therefore almost certainly linked with the COVID-19 outbreak in that NH.

In the present study, 16% of residents and one third of HCP with positive RT-PCR were asymptomatic in the 14 days before testing. This confirms that all residents and HCP should be tested if there is a confirmed case of COVID-19, whatever the symptoms. Two residents and two HCP who tested negative at baseline were tested positive for COVID-19 7 days after baseline. This suggests that a repeated weekly testing of all previously negative residents and HCP until no new COVID-19 cases are identified is also essential in preventing the SARS-CoV-2 spread.

Positive RT-PCR was associated with a severe prognosis (death in 32%), especially in men (death in 58%), confirming previous studies. Among the 22 negative RT-PCR residents presenting COVID-19 symptoms, one died and the others recovered completely, suggesting that severe COVID-19 outcomes could be generally, but not always, predicted by positive testing.
Testing remained positive for 3 weeks or more in two thirds of the RT-PCR positive residents. One remained positive for 8 weeks, indicating that NHs facing a COVID-19 outbreak should be prepared to maintain prolonged protective measures in residents tested positive for SARS-CoV-2. In accordance with our regional guidelines, this NH was considered to be COVID-19-free when none of the residents and HCP were diagnosed within the 14 days after the last positive result. COVID-19 free NHs apply regional recommended measures to prevent any further COVID entrance and spread. In our Occitanie region, these measures include:

1. Checking that RT-PCR testing in HCP and visitors with COVID-19 symptoms or in those having had contact with COVID-19 suspected or confirmed cases (daily screening) is negative before entering the premises.
2. Checking that RT-PCR testing in all new residents and in all residents having spent more than 24 h outside the NH (especially after hospitalization) is negative before entering.
3. Checking that residents, HCP, and visitors previously tested positive for COVID-19 meet all 3 follow-up NH entrance criteria: (i) resolution of fever (without use of fever-reducing medications) and of other COVID-19 symptoms within the past 48 hours; (ii) two consecutive negative RT-PCR results collected ≥24 hours apart, (iii) the first control test collected at least 7 days after the positive testing or 7 days after the first COVID-19 symptoms.
4. Obliging visitors allowed to enter the NH to sign a charter in which they agree to adhere to standard and transmission-based precautions to prevent COVID-19 spread in the NH (systematic face mask wearing, hand hygiene, and especially social distancing) as well as a registry with contact details to facilitate testing and contact tracing should a new case be diagnosed in the NH.
5. Admission to a private room and 14 days of isolation for every new resident and every resident having left the NH for at least 24h (especially after hospital stay).
6. Testing of every resident having left the NH for less than 24 hours (especially for medical consultation) 5 to 7 days after a possible contact with COVID-19.
7. Daily screening of all residents for COVID-19 symptoms (including atypical symptoms) and testing if there is any doubt.
8. If regular testing of HCP, visitors, and residents at high risk of encountering COVID-19 subjects outside the NH (health care workers who have a care activity outside the NH, visitors of several NHs, hemodialysed patients, etc...) can be justified in regions with moderate or substantial community transmission, this measure is not recommended in our region in which community transmission is now considered as low.
Residents and HCP with positive RT-PCR developed IgG antibodies against the SARS-CoV-2 in 96% and 100%, respectively, suggesting that most frail older adults living in a NH, as well as the HCP, can produce an antibody response against SARS-CoV-2.

Two residents (5%) with negative RT-PCR developed antibodies and all had fever or respiratory symptoms consistent with COVID-19 in the 14 days before. This suggests that residents with COVID-19 symptoms should benefit from the same IPC strategy as residents with positive RT-PCR, even if tested negative. Five HCP with negative testing developed antibodies against SARS-CoV-2 (11%) and some of them had no COVID-19 symptoms. This suggests that if specific COVID-19 IPC measures must be implemented in HCP with confirmed or suspected COVID-19, all HCP should wear a facemask, even if asymptomatic and with negative testing.

**Conclusions and Implications**

The present study supports the recent American testing guidance for NHs. It demonstrates that (i) testing all NH residents and HCP as soon as a new case of COVID-19 is diagnosed and (ii) repeating tests in all previously negative subjects once a week until the testing identifies no new COVID-19 cases is effective in detecting asymptomatic COVID-19 residents and HCP. It also shows that (iii) proposing COVID-19 IPC measures in residents and HCP tested positive or with COVID-19 symptoms and (iv) taking precautions in all other HCP should be effective in blocking the dissemination of the virus in NHs facing a COVID-19 outbreak.

**Conflicts of Interest:** The authors declare no conflicts of interest/Competing interests
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Table 1. Demographic Characteristics, Reported Symptoms at the Time of Initial Testing, and Occurrence of Antibodies against SARS-CoV-2 in Residents

| Characteristics                                      | Positive (N=38) | Negative (N=41) | P value* |
|------------------------------------------------------|-----------------|-----------------|----------|
| **Overall**                                          |                 |                 |          |
| Mean age (±SD) — yr                                   | 86 (15.5)       | 87 (9.8)        | 0.95     |
| Length of stay at Facility < 90 days before testing   | 4 (10)          | 5 (12)          | 1.00     |
| **Coexisting conditions—no %**                        |                 |                 |          |
| Any coexisting condition                              | 38 (100)        | 36 (88)         | 0.06     |
| Chronic lung disease                                  | 9 (23)          | 9 (21)          | 0.85     |
| Diabetes                                             | 9 (24)          | 3 (7)           | 0.04     |
| Cardiovascular disease                                | 32 (84)         | 32 (78)         | 0.49     |
| Cerebrovascular accident                              | 10 (26)         | 9 (22)          | 0.65     |
| Renal disease                                         | 26 (68)         | 7 (17)          | <0.0001  |
| Received hemodialysis                                 | 0               | 1 (2)           | 1.00     |
| **Cognitive impairment**                              |                 |                 |          |
| Moderate                                              | 18 (47)         | 20 (49)         | 0.90     |
| Severe                                                | 14 (37)         | 3 (7)           | 0.001    |
| Denutrition                                           | 12 (32)         | 14 (34)         | 0.80     |
| Obesity                                               | 10 (26)         | 9 (22)          | 0.65     |
| **Symptoms during the past 14 days—no. (%)**          |                 |                 |          |
| In symptomatic residents                              |                 |                 |          |
| At least one typical Covid 19 symptom                 | 32 (84)         | 22 (54)         | <0.01    |
| Temperature                                           | 28 (74)         | 19 (46)         | 0.01     |
| Cough                                                 | 27 (71)         | 14 (34)         | 0.001    |
| Shortness of breath                                   | 14 (37)         | 10 (24)         | 0.23     |
| Saturation rate less than 90%                         | 24 (63)         | 6 (15)          | <0.0001  |
| Respiratory rate more than 24                         | 21 (55)         | 5 (12)          | <0.0001  |
| Only atypical Covid 19 symptoms                       | 3 (8)           | 3 (7)           | 1.0000   |
| Asymptomatic residents                                | 3 (8)           | 3 (7)           | 1.0000   |
| Antibodies against SARS CoV-2                        | 25 (66)         | 2 (5)           | <0.0001  |

**P for chi-square test or Fisher’s exact test if chi-square was not a valid test for categorical variables, and Student test for continuous variables.
Nasopharyngeal swab testing repeated every week in all previously negative residents and HCP until testing identified no new cases and in all positive subjects until testing was negative.

Blood testing for antibodies against SARS-CoV-2

Assessment of COVID-19 symptoms

3 cases hospitalized for atypical COVID-19 symptoms

COVID-19 diagnosis in the first 3 residents

Implementation of IPC measures in the NH