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Risk of aerosol transmission of SARS-CoV-2 in a clinical cardiology setting

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ABSTRACT

Cardiac exercise stress testing (CEST) is an important diagnostic tool in daily cardiology practice. However, during intense physical activity microdroplet aerosols, potentially containing SARS-CoV-2 particles, can persist in a room for a long time. This poses a potential infection risk for the medical staff involved in CEST, as well as for the patients entering the same room afterwards. We measured aerosol generation and persistence, to perform a risk assessment for SARS-CoV-2 transmission through aerosols during CEST. We find that during CEST, the aerosol levels remain low enough that SARS-CoV-2 transmission through aerosols is unlikely, with the room ventilation system producing 14 air changes per hour. A simple measurement of CO₂ concentration gives a good indication of the ventilation quality.

1. Introduction

Cardiology is an essential health care service that needs to be maintained during COVID-19 pandemic. The pandemic, caused by the Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is characterized by a high transmission rate and increased mortality from acute respiratory distress syndrome compared to other viruses. Especially for cardiovascular patients, SARS-CoV-2 infection is life-threatening [1–3] and they should be optimally protected against this viral infection. SARS-CoV-2 is transmitted through respiratory droplets from infected individuals produced by coughing, sneezing, and, even in asymptomatic patients, breathing [4–6]; already long ago the potential airborne transmission of SARS-type viruses was signaled and recently underlined also for SARS-CoV-2 [5–10]. Large respiratory droplets (60–100 μm in size) fall on the ground within 1–2 m after exhaling, which serves as the scientific basis for the social distancing; the CDC (in the US) recommended 2 m (6 feet) but the WHO recommended 1 m [7]. However, small aerosol microdroplets (<5 μm) remain airborne and inhalable for a longer time and can travel distances significantly larger than 2 m [8]. In daily cardiology practice, cardiac exercise stress testing (CEST) is an important diagnostic tool. During Cardiopulmonary stress testing, the increased intensity of breathing by the tested individual may cause an increase in production of small aerosol microdroplets. These potentially contain SARS-CoV-2 particles, and can persist in an enclosed space for a long time. Performing CEST in asymptomatic, but contagious

individuals poses a potential risk for medical staff in the same room, and for subsequent patients. Since no infection prevention guidelines are available for CEST testing with respect to SARS-CoV-2, we measured aerosol production and the persistence time of the aerosols during this diagnostic procedure and assessed the risk of SARS-CoV-2 transmission for different levels of ventilation. In addition, we explored whether a much simpler measurement of CO₂ concentration can also be used to assess the risk associated with aerosol production and persistence.

2. Methods

Patients referred to the clinic by a general practitioner for diagnosis were subjected to bicycle Cardiac exercise stress testing (CEST) for the diagnostic workup of exercise related chest pain, palpitations or dyspnea were included in the study; informed consent was obtained from all participants. The Medical Ethics Committee of the Amsterdam University Medical Centre approved the study protocol.

2.1. Experimental facility

CEST is performed in a 4.4·3 m³ exercise room. The aerosols produced by the exercising patients were measured at a distance of 2.5 m and a height of 1 m. The outpatient clinic has a dedicated HVAC system that produces 14,406 m³/h and extracts 13,720 m³/h. Taking into account the surface area and ceiling height of the clinic, this leads to 14 Air

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Changes per Hour (ACH).

2.2. Cardiac stress testing

Patients were subjected to a bicycle CEST. After taking an ECG the test starts with a workload of 60 Watts, which is increased by 20 Watts every 2 min, until a maximum safe heart rate was reached given by $((220 - \text{age}) * 0.85)$. Alternatively, the test was stopped when the patient experienced discomfort. Heart rate, workload, blood pressure and duration were all registered during the test. All experiments were carried out in accordance with relevant guidelines and regulations.

2.3. Aerosol measurement

Aerosol concentrations were measured with a Fluke 985 cleanroom particle counter which allows to measure concentrations without performing laser light scattering [8] which is difficult to implement in a clinical setting. The particle counter gives the amount of aerosol particles of a given size per liter of air, in different bins: 0.3 μm , 0.5 μm , 1.0 μm , 2.0 μm , 5.0 μm , and 10.0 μm . One usually assumes that the aerosols lose almost a factor of 10 in volume, which is roughly a factor of 2 in radius [8,14]. What we measure is already dried out; the aerosols are so small that they dry out almost instantly. We sum over all the channels (that are all in the airborne range) to obtain the total suspended particle concentration from the volume times the #copies/ml saliva, correcting for the drying; details can be found in Refs. [8–14]. The particles 2–5 μm constitute the major part of these, and are believed to be the most dangerous ones, since they deposit in the lungs. Larger particles deposit in the mouth and throat and even smaller particles are exhaled [17]. We specifically looked for variations in the amounts of aerosols produced by different patients, to see whether some might be “superspreaders”, shedding more aerosols than others [14]. In addition, we evaluated differences in aerosol persistence between different ventilation settings. 14 ACH is very good ventilation whereas 4 ACH is considered low ventilation.

2.4. CO₂ and ventilation measurement

In addition to the aerosol measurements, we also monitored the CO₂ concentration using a Testo 440 dP Air velocity & Indoor Air Quality measuring instrument using a Pitot tube differential measurement sensor. Measurements were performed with ACH of 14 and 4. The ventilation system of the clinic allows for different ventilation levels, on a scale of 1–5. In normal operation, the maximum ventilation level is used (ACH = 14); for reducing the ventilation level we simply decreased the ventilation level to 2 (ACH = 4). The change is relatively small since the medical staff did not want to operate under no ventilation conditions. However, there is good statistical data on the relation between ventilation rate (ACH) and aerosol persistence [10,14]. The air change rates in the different rooms of the clinic were measured also using the Testo device and the air change rates between the different rooms were found to be identical to within 5%.

2.5. Risk assessment (Aerosol concentration)

The role of respiratory aerosol microdroplets in the transmission of SARS-CoV-2 can be assessed by measuring the dynamics of exhaled respiratory droplets. We measured the evolution of the total number of aerosols in the exercise room of a given volume. Fig. 1 shows the exercise room with a patient on the exercise bike; the medical staff sits at the desk in the lower-left corner.

Under the assumption that during the stress test, aerosols would be produced by an infectious person, this allows for estimating the number of virus particles that the medical staff would be exposed to during the cardiac stress test. For this calculation, we assume a homogeneous distribution of the aerosols through the room and a normal breathing rate

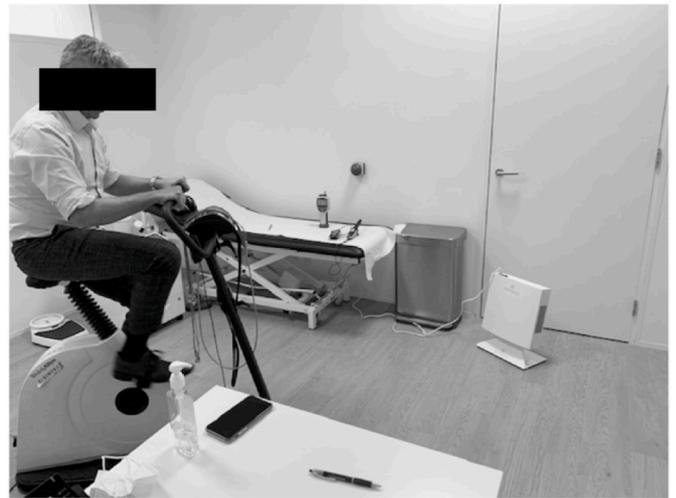


Fig. 1. The room where the measurements have been done.

of the staff of 8 l/min [9]. From averaging after background subtraction we obtain a maximum aerosol concentration, summed over all channels, of ~ 50 particles/l at the end of the exercise by a typical superspreader. Inhaling 8 L of air per minute then leads to 400 aerosol particles inhaled per minute, so a CEST taking 20 min, therefore, involves inhalation of 8000 aerosol particles produced by the person undergoing cardiac stress testing. The viral exposure can then be obtained by considering a viral load of 7×10^6 copies per milliliter of saliva [13], corresponding roughly to one copy per 1000 particles of 2 μm . The amount of viral particles that cause an infection N_{inf} also depends on factors such as the vulnerability/susceptibility of the host and viral characteristics. For SARS-CoV-2 N_{inf} is not yet well known [19]; however for other Coronaviruses, including SARS-CoV-1 $N_{inf} \sim 100 - 1000$ [19–21]. For safety, we assume the lower limit of this range ($N_{inf} \sim 100$) as safe (low risk of SARS-CoV-2 transmission). For the new Delta variant of the SARS-CoV-2 virus, the viral load in the saliva may be higher, and this potentially needs to be considered in the risk analysis.

3. Results

Twelve patients were included in the study. Patient characteristics are given in Ref. [16]. We found the time trace with a particle concentration of 5.0 μm per liter of air to be most accurate. At smaller concentration sizes increased background dust decreased the visibility of aerosols, whereas at higher concentrations only a few particles remain present, and measurements become noisy. We found that at test initiation, there were no detectable aerosol particles above baseline (background dust particles). Several minutes after starting the CEST, aerosol numbers increased. After the termination of the test, a rapid decay was observed. We first perform an aerosol persistence test to test the ventilation of the building. Fig. 2 shows a typical time trace of 5.0 μm particle concentrations (number of particles per liter of air) as a function of time (in seconds) with the standard ventilation setting (ACH = 14). At around 650 s we artificially generate aerosols. These then decay, mostly due to sedimentation and evacuation through the HVAC system, and the characteristic time of the exponential decay (here 110s, as indicated in the inset) is a good measure for the quality of ventilation. It should be underlined that these are NOT aerosols produced by the cardiac stress test. The other channels of the particle counter gave similar time traces, with the channels around 5.0 μm being the most accurate in terms of signal-to-noise.

We observed a large difference in aerosol production between patients. Fig. 3 shows a time trace of a session with 4 patients subsequently undergoing the CEST. Over 12 patients tested, the peak aerosol concentrations ranged from 400 particles/liter of air to zero

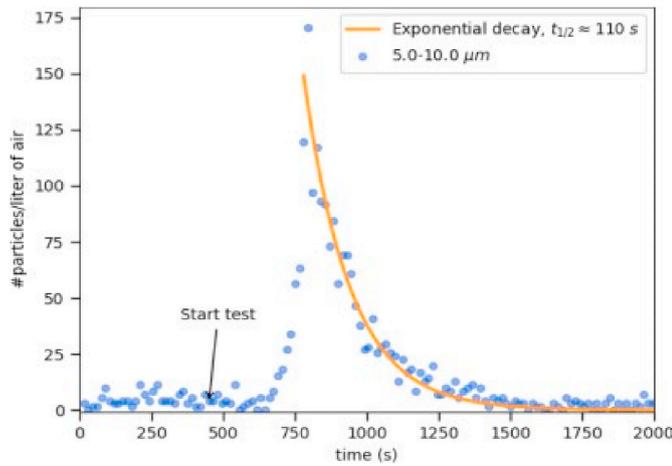


Fig. 2. A measured number of aerosol particles of sizes 5.0–10.0 μm as a function of time. The patient enters the exercise room at t = 0 s, starts the CEST at t = 450 s, and cycles for 10 min. The fit line after the peak shows an exponential decay, allowing to extract a characteristic time of aerosol persistence, which is < 2 min for standard ventilation (ACH = 14) during and after the CEST at the outpatient clinic of CCN.

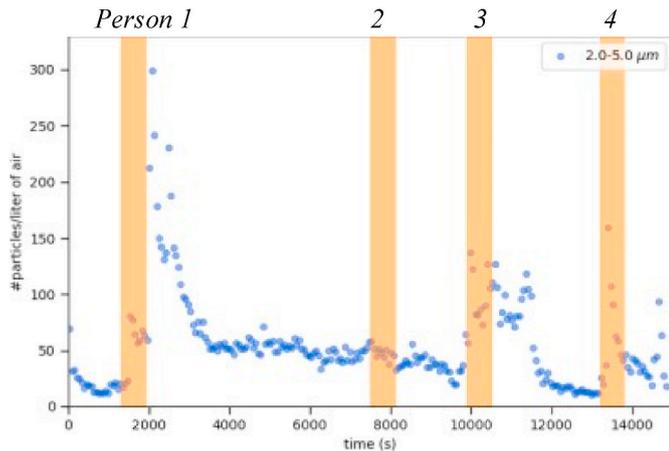


Fig. 3. The measured number of aerosol particles of sizes 2.0–5.0 μm as a function of time for four subsequent patients from continuous monitoring in the CEST room of the outpatient clinic at the standard ventilation setting (ACH = 14). The CEST periods for the four individuals are shown as the orange bars.

(indistinguishable from the background fine dust particle concentration). Six of these showed an aerosol concentration in excess of 100 particles/liter, six showed no significant increase over the background, similarly to patient #3 in Fig. 3. The data for the first individual shows a clear aerosol peak, but the second patient does not produce a number of aerosol particles that exceed the background dust particles. We found no correlation between maximum aerosol production and individual performance parameters (maximum workload, maximum heart rate, % of predicted workload, and the RPP) Table 1.

Table 1

R-squared analysis of the correlation between CEST characteristics and aerosol production.

Quantity	R squared
Double product	0,199
Power	0,058
% Target	0,0014

3.1. SARS-CoV-2 transmission risk

Considering the upper limit of $N_{inf} \sim 100$, and the viral load discussed above, we find that the cardiac stress test performed in a room with ACH of 14 leads to the inhalation of less than 10 viral particles, still an order of magnitude below the upper limit; the space is safe and there is a low risk of infection of the medical staff due to the aerosols produced during the stress test. Of course, the risk analysis is a subject of much current debate and necessarily such analyses rely on a number of assumptions [14,15]. Our direct study has the advantage of quantifying aerosol concentrations during CEST in normal operation of the clinic.

3.2. Aerosol persistence

The characteristic time of the (exponential decay of) aerosol concentration is about 2 min, even when the individual on the bicycle is still producing aerosols. This is very different from poorly ventilated spaces such as elevators where this same characteristic time can be as long as 15 min [9,10]. Fig. 4 in addition shows a very good correlation between the aerosol concentration and the amount of CO₂. For the well-ventilated room, both quantities decrease exponentially after the CEST has stopped, with a characteristic time of 2 min (Fig. 4). However, for the low ventilation setting, the aerosols persist and the CO₂ concentration remains high, even 5 min after the CEST has stopped. This underlines the importance of good ventilation: if the room is used all day for CEST and the ventilation is 4 ACH, the above estimate of the SARS-CoV-2 transmission risk becomes considerably larger.

4. Discussion

Since cardiology is considered an essential healthcare service,

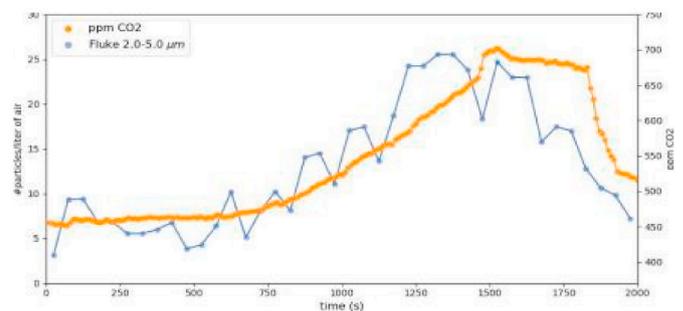
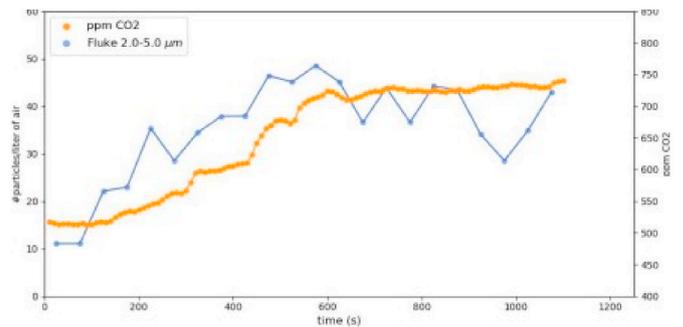


Fig. 4. Measured number of 2.0–5.0 μm aerosol particles of sizes 2.0–5.0 μm (blue symbols) compared to the CO₂ concentration (orange symbols) in the CEST room with the ventilation set to (a) ACH = 4 and (b) ACH = 14. There is a good correlation between the aerosol particle count in the room and the CO₂ concentration. The stress test starts at 0 s and stops at 600 s in the top figure, and 1500 s in the bottom figure.

diagnostic and therapeutic procedures should be maintained during the COVID-19 pandemic. Procedures that cannot be performed while adhering to at least 2 (WHO standard) meter distance to the patient, especially in poorly ventilated spaces, increase the risk of aerosol transmission of SARS-CoV-2. Although several health organizations have provided guidelines on interventions during the pandemic [11], so far due to the lack of quantifications of aerosol generation in clinical studies, no specific guideline can be designed for these laboratories to minimize transmission risk.

Cardiac exercise testing may harbor an increased risk of viral transmission due to increased and forced exhalation [12] and high-transmission risk procedures [13]. Although a significant number of aerosols is generated during this diagnostic procedure, we found that exercise testing can be safely performed. However, ventilation is crucial, as low ventilation rates increase the persistence of aerosols. Moreover, we found that large differences in aerosol production exist between patients; some individuals can be classified as superspreaders, as their aerosol production is much higher than others. Unfortunately, it remains difficult to predict the individual aerosol production in advance. Therefore, caution remains warranted for all diagnostic- and therapeutic procedures which require close interpersonal contact.

For the CCN clinic investigated, the ventilation system is dimensioned to have an ACH of 14, leading to the observed short persistence time of aerosols and hence the low aerosol concentration. Assessment of the ventilation capacity is crucial to determine viral transmission risk. One way of achieving this simply is to measure the CO₂ concentration, which correlates with aerosol concentration. Therefore, CO₂ measurement could potentially be used as a reliable and simple alternative for aerosol measurement and therefore the aerosol transmission risk in a working space. A typical level found in occupied spaces with good air exchange is below 1,000 ppm CO₂ concentration. The almost linear correlation between the number of aerosols and the CO₂ concentration suggests that for about 1000 ppm of CO₂, there will be on the order of ~100 aerosol particles per liter of air, which is still a safe level. The advice is then to keep the CO₂ below 1000 ppm levels to ensure a safe environment for patients and healthcare professionals. Ventilation can be increased to reduce CO₂ concentration and improve the safety of patients and medical staff. Of course, if many noninfected people are present in a room, CO₂ and aerosol levels will be elevated but not the virus concentration. CO₂ monitoring of indoor air as means of air quality assessment has of course already been known for decades and has been discussed for longer than the past few years as a means of assessing particulates in the air. What we do here goes one step farther in the sense that we couple a risk analysis to the aerosol persistence which in turn is correlated with the CO₂ levels.

It is also worthwhile noting that the infection risk in terms of the number of viral RNA copies is still the subject of a lot of discussions. Reference [18] for instance discusses that SARS-CoV-2 viral RNA levels e.g. in saliva are not the same thing as 'viral load'. Recently, Poydenot et al. [19] quantify the amount of virus by the number of infectious quanta. This is perhaps a better way to quantify but is harder to include in the risk analysis. As in Ref. [14], we here perform the risk analysis rather with the effective value of $N \sim 100$. It is worth noting that work of Bazant and Bush [20] suggests that these estimates of the viral load and infectivity are reasonable. They analyzed several superspreader events and came to the conclusion that the viral exhalation is around 72 viral quanta/m³ for a person who is speaking, corresponding to microscopic concentrations of $c_q = 2 \cdot 10^8$ and $7 \cdot 10^8$ quanta/mL in line with the idea that viral loads in sputum tend to peak in the range 10^8 to 10^{11} RNA copies per milliliter, in the range we used here.

5. Conclusion

This study shows a large inter-individual variation in the production of aerosols during cardiac stress testing. The persistence of aerosols is inversely related to the ventilation rate of the testing room. Risk

assessment assuming literature values for the viral load and infectivity of SARS-CoV-2 reveals that aerosol levels remain low inadequately ventilated space (ACH of 14) which makes SARS-CoV-2 transmission through aerosols is unlikely. This was shown for bicycle cardiac stress testing but may have implications for any other aerosol-generating diagnostic or therapeutic procedure. In addition, CO₂ concentration is strongly correlated with aerosol concentration and can potentially serve as a simple alternative to determine the aerosol transmission risk of any medical procedure.

CRedit authorship contribution statement

G. Aernout Somsen: Writing – review & editing, Investigation, Conceptualization. **Michiel M. Winter:** Investigation. **Igor I. Tulevski:** Investigation. **Stefan Kooij:** Investigation. **Daniel Bonn:** Writing – review & editing, Writing – original draft, Investigation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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