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Cardiopulmonary exercise testing in the COVID-19 endemic phase

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The coronavirus disease 2019 (COVID-19) pandemic has presented significant challenges to healthcare systems across the world. The substantial need to provide acute COVID-19-related care resulted in non-COVID-19 care being immediately curtailed, with significant implications for the provision of normal or 'routine' healthcare. As the pressure from acute COVID-19 care begins to regress, it is timely to consider how certain services, including those undertaking physiological measurements, will re-open and how they will function within the constraints dictated by a COVID-19 endemic working environment.

Over the past decade, there has been evolving recognition of the importance and value of clinical cardiopulmonary exercise testing (CPET) within healthcare settings.[1] Primarily, CPET is used to evaluate the integrative response to incremental exercise, enabling clinicians to characterise cardiorespiratory fitness and reasons for physical impairment.[2] It is recognised that CPET plays an important role in clinical arenas including determining surgical operability and evaluating the risk of perioperative death and postoperative complications.[3] It also has a function in supporting preoperative planning algorithms,[4] and developing management strategies for pathological conditions (e.g. heart failure)[5] and in disease prognostication (e.g. pulmonary hypertension).[6] Whilst there is considerable uncertainty regarding the ability to safely undertake CPET at present, it remains an integral investigative tool in clinical practice, and urgent consideration needs to be given to determine how best to deliver CPET services in the COVID-19 endemic phase.

Role and delivery of CPET in the COVID-19 endemic phase

CPET remains highly relevant and indicated to help plan major surgical procedures for malignancy, even within a COVID-19 endemic phase. It is envisaged that an additional requirement for these procedures will emerge from requests to evaluate individuals recovering from severe COVID-19 infection.[7] In this context, measurements obtained from an assessment of cardiorespiratory responses to physiological stress could provide insight regarding the integrity of the pulmonary–vascular interface and characterisation of any impairment or abnormal cardiorespiratory function. CPET characterises oxygen consumption ($\dot{V}O_2$) for a given level of external work, and the relationship between carbon dioxide output and ventilation (e.g. as characterised by the $\dot{V}_E/\dot{V}CO_2$ slope) can detail pulmonary dead space. It also characterises exercise-associated desaturation and hypoxaemia (i.e. by allowing evaluation of the alveolar–arterial O_2 gradient and arterial to end-tidal CO_2 difference), and can be used to identify alterations in breathing patterns that may be relevant in the aetiology of exertional dyspnoea.[8] Data from severe acute respiratory syndrome (SARS)-related illness showed significant exercise limitation in the months after hospital discharge, and the pathophysiological mechanisms were described eloquently using CPET.[9] Functional disability and recovery have also been reported in the 5 yr after acute respiratory distress syndrome (ARDS).[10] In individuals requiring invasive ventilatory support for COVID-19, the profound musculoskeletal, neurological, and de-conditioning sequelae are compounded by de-conditioning from prolonged stays in critical care. Currently, there are no COVID-19-specific CPET data, but these are likely to be important to inform future decision making.[11] Indeed, CPET could be used to develop support strategies for those with long-term disability and to assess the efficacy of developed interventions.

Precautions and risk mitigation for CPET testing

Use of CPET in the COVID-19 endemic phase should be a priority, but must be undertaken safely and only when necessary. Indeed clinical resources will remain directed towards tackling the pandemic,[12] and shortages of personal protective equipment demand the correct use and deployment of any investigation (Fig 1).

Owing to the nature of CPET testing, the risk of infective transmission resulting from forced exhalation, even during sub-maximal exercise, is increased. There is controversy as to whether CPET is an aerosol-generating procedure,[13] and strong evidence, either way, is currently lacking. An additional consideration is that CPET does not incorporate bacterial and viral filters to collect exhaled particles. The potential to produce infected droplets from a positive COVID-19 patient will increase the risk of both airborne and surface transmission[14,15] and needs consideration regarding the potential for protracted viral shedding (i.e. the test lasts <10 min). Appropriate mitigation strategies are required to ensure that CPET can be conducted safely and without posing a risk of transmission and infection. Screening patients is a possible strategy but the reliability of the testing methods has been questioned[16]; therefore, additional approaches are needed which include the availability of appropriate personal protective equipment and other infection protection measures (see published guidelines from the Association for Respiratory Technology and Physiology,[13] Royal College of Physicians,[17] and the European Respiratory Society[18]).

Porous microbacterial/viral filters that partially restrict inspiration/expiration could be applied to reduce possible transmission. The use of fans or open windows in clinical or research laboratory settings are used regularly when environmental controls are not accessible; however, this is likely to spread any infected droplets and should be discouraged. Importantly the number of room air changes per hour (ACH) needs to be 6.0 for definite aerosol-generating procedure locations (e.g. noninvasive ventilation, continuous positive airway pressure treatments) but needs checking in exercise testing facilities.[15,19] Additional considerations are required to prevent surface transmission. Cleansing and sterilising of equipment is standard infection control practice; however, further precautions are required to reduce the risk of transmission to staff or subsequent patients. This includes reverting to single-use masks, sensors, turbines, and gas lines to prevent transmission from repeated use. Testing facilities should be left for a minimum of 20 min to allow airborne droplets to settle on surfaces and sterilised with appropriate cleaning solutions or by germicidal UV cleaning.

Impact of filters on measurement

We are not aware of cardiopulmonary exercise measurement systems that include a method of filtration of exhaled breath. Routine lung function testing filters with ~99.9% efficiency against viruses are available and guaranteed up to a flow rate that exceeds those achieved during CPET, to account for the measurement of peak flow rates in the average population. Anecdotal evidence suggests that these bacterial/viral filters have little impact on CPET measurements. These filters have an inherent resistance to flow which in most circumstances is in the region of 80 Pa at a flow rate of 90 L min^{-1}. This is unlikely to limit ventilation and impact exercise performance. However, at the ventilatory frequencies and tidal volumes associated with a maximal exercise test, the amount of water

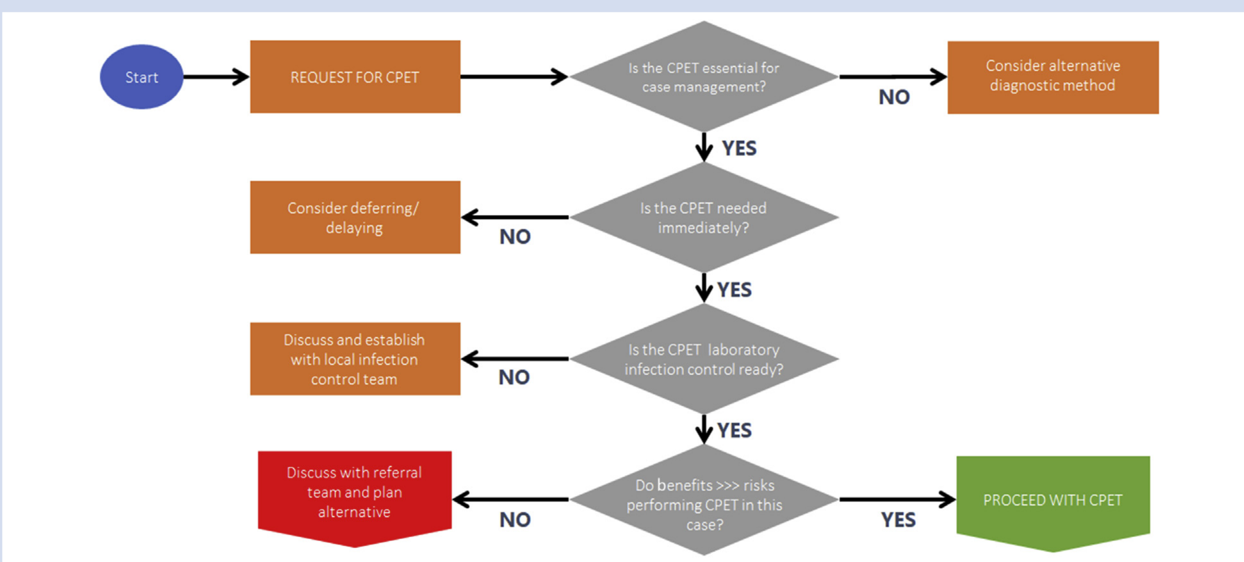

Fig 1. An approach to the logical use of clinical cardiopulmonary exercise testing (CPET) during the COVID-19 endemic phase.

vapour in exhaled breath will likely saturate the filter providing increased resistance to ventilation, impacting the time to volitional tolerance, especially in those where ventilatory capacity is limited. Therefore we would not recommend use of bacterial/viral filters manufactured specifically for lung function testing to be used to filter exhalation during CPET.

Novel ways of assessing cardiorespiratory function

A currently unquantified caseload of patients with a post-COVID-19 disability will require long-term support from healthcare services. Although validated approaches exist that can be conducted remotely (6 min walk test, accelerometers, and activity monitors) and in large volumes, these are subjective and provide somewhat cursory insight regarding cardiorespiratory function. Where possible interrogative procedures should be used. To alleviate the need for specialist laboratory space and testing in confined spaces (that pose an additional risk of infection transmission), it is plausible that portable CPET systems could be utilised to provide insight into day-to-day activities. Although a possible alternative, there is a need to develop standardisation approaches that are associated with the performance of a ramped exercise test.

Conclusions

CPET is an established investigative strategy for many clinical scenarios which includes preoperative evaluation of risk for postoperative complications. The list of indications is likely to be extended, and include post-COVID-19 complications in a currently unquantified caseload of patients. Implementation of CPET requires careful consideration alongside a risk/benefit analysis to ensure mitigation of sustained transmission. This may lead to shorter testing protocols and more use of 'threshold testing' to reduce the potential exposure to an undiagnosed virus. Urgent studies are also warranted to monitor the pathophysiological changes and identify the CPET parameters that might inform clinical management of COVID-19.

Authors' contributions

Devised the topic of the manuscript: MF, JH
Drafted sections of the manuscript: MF, JH, KS, BC
Finalised the manuscript: MF, JH, KS, BC

Declarations of interest

The authors declare that they have no conflicts of interest.

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