Silent hypoxia: pulse oximetry and its relation to COVID-19 in Singapore

From June 2021, each household in Singapore was eligible to obtain one free pulse oximeter from stores and pharmacies nationwide.[1] Prior to this, approximately 8,000 pulse oximeters had been issued to migrant workers in May 2020, when there were large outbreaks of the coronavirus disease 2019 (COVID-19) in dormitories.[1] The purported use of these pulse oximeters is to detect 'silent pneumonia' in the context of COVID-19.[2] Also termed 'happy hypoxia' or 'silent hypoxia', this condition has been reported to be a lethal but silent presentation of COVID-19.[3,4] It refers to a somewhat paradoxical state where a patient's oxygen levels are dangerously low (typically an oxygen saturation [SpO_2] of less than 90%) despite the absence of dyspnoea. This phenomenon has gained significant attention in popular media, having been reported in several global reputable news sources.[5,6] Understandably, with much that is unknown about this virus, atypical presentations with potentially devastating complications in otherwise seemingly asymptomatic individuals have caught the attention of the general public.[7]

SILENT HYPOXIA: INCIDENCE, PATHOPHYSIOLOGY AND IMPLICATIONS

Beyond the media attention and hype, silent hypoxia has also been shown to be of growing and sustained interest to the scientific community since April 2020, with at least 240 articles on 'silent pneumonia' in the context of COVID-19 indexed in PubMed as of June 2021. These articles range from case reports and vignettes, review and opinion articles to small observational studies. Despite the vast attention in the media, robust studies on its prevalence are limited. In one small, retrospective study of 213 hospitalised patients with hypoxia in Germany, a remarkable proportion (31.9% of the hypoxic patients) were asymptomatic, while the remaining demonstrated dyspnoea.[8] Among the general population of patients infected with COVID-19, the prevalence of this phenomenon remained unclear.

Potential pathophysiological mechanisms of silent hypoxia

Whether silent hypoxia is unique to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) remains a subject of debate and for further study. Many experts have proposed hypotheses as to how the virus could produce this paradoxical phenomenon in patients. SARS-CoV-2, like other coronaviruses, is predominantly a respiratory virus that can cause significant hypoxia due to pneumonia.[9] What is surprising is the fact that some patients would experience little to no dyspnoea despite having significant hypoxia.[10] One possible mechanism relates to the presence of angiotensin-converting enzyme 2 (ACE-2) receptors, found on both the carotid body and the olfactory bulb, which are targets for SARS-CoV-2.[11,12] Viral invasion of the olfactory bulb is believed to cause anosmia, which is a prominent symptom of COVID-19.[11] Although this remains to be determined, the carotid body is responsible for the detection of oxygen tension in the body. Viral invasion of the carotid body via ACE-2 receptors may thus contribute to the depressed sensation of dyspnoea.[12] Other authors have proposed that silent hypoxia may be related to the formation of pulmonary microthrombi related to COVID-19, which results in hypoxia in the absence of hypercapnia.[13] Because fluctuations in carbon dioxide levels result in more significant dyspnoea than fluctuations in oxygen levels, the symptoms related to hypoxia experienced in such patients may be more attenuated.[13] Nevertheless, it is clear that, while this phenomenon has been observed in a proportion of patients with COVID-19, more peer-reviewed scientific literature is needed to better describe and understand this clinical entity.[14]

Clinical implications of silent hypoxia

The implications of this phenomenon remain unclear as well. For example, certain symptoms like anosmia may confer better outcomes in patients with COVID-19.[15] In a small study of 213 hypoxic patients with COVID-19, patients who had silent hypoxia did not have poorer outcomes compared with those who were overtly dyspnoeic.[8] However, the danger lies in the situation where an asymptomatic patient with significant hypoxia does not present to a healthcare institution until much later in the disease course. Several case reports have reported the rapid progression of patients with initial silent hypoxia to critical illness requiring intensive care.[16,17] In one French study, asymptomatic hypoxia in elderly patients with COVID-19 was associated with a significantly higher risk of mortality; 33% of such patients were transferred to the intensive care unit (ICU) and 25.9% died.[18] However, it is important to note that this was an observational retrospective cohort, where of the 1,107 patients studied, only a small subset of patients ($n = 161$) had at least one blood gas analysis. Of these, it was observed that 27 out of 96 (28.1%) had hypoxia without dyspnoea at presentation.[18] The indication for blood gas analysis was not controlled for in this cohort, and being a small subset of the large study cohort, it may lend itself to inherent biases that may over-estimate the risk of mortality and adverse outcomes in this specific subgroup of patients.

POTENTIAL APPLICATIONS OF PULSE OXIMETRY

Applications in the prehospital setting

Widespread use of pulse oximetry by the general public is not new, with commercial devices becoming increasingly affordable and accessible. Such devices have existed in the market for several years, and even smartphones are now able to report oxygen saturations.[19] The accuracy of these equipment in measuring SpO_2 has been tested and verified.[20] One potential use of pulse oximetry is, therefore, home self-monitoring of oxygen levels in patients with suspected COVID-19.

The clinical efficacy of such an approach has not been tested in large, robust clinical trials, but it has been suggested that commercially available, home-based pulse oximeters may be used to detect patients with silent hypoxia, thus allowing these individuals to seek early and appropriate medical care before the condition progress to a potentially lethal complication of COVID-19.[21]

In one retrospective study on the use of prehospital pulse oximetry by paramedics, the authors reported significant discrepancy between the recorded SpO_2 and respiratory rate in patients with COVID-19 versus control patients three years prior to the pandemic.[22] The authors hypothesised that in a significant proportion of patients, profound hypoxia may be present despite a normal respiratory rate in patients with COVID-19. In such a setting, the use of prehospital pulse oximetry would help to guide early and appropriate oxygen supplementation.

Applications for inpatients with COVID-19

Within hospitals, continuous pulse oximetry is the standard of care in most ICUs.[23] In the context of COVID-19 illness, close monitoring in ICU will help in several ways, including avoiding hyperoxygenation and guiding fluid management in patients with acute respiratory distress syndrome from COVID-19.[24-26]

In the general ward setting, COVID-19 patients are often housed in specific isolation wards or zones that are segregated from the rest of the patient population. Healthcare workers would thus have to don personal protective equipment (PPE) in order to check the vital parameters of these patients.[27,28] Close monitoring of such patients is thus challenging, especially in the context where PPE may potentially be limited in supply.[29] In such a situation, continuous and automatic monitoring of patients with pulse oximetry may help to closely monitor these patients and identify those at risk of deterioration, even before they develop any symptoms.[26,30] It may also help to minimise the risk of exposure of healthcare workers to COVID-19.

In resource-poor countries, where access to oxygen supplementation is scarce, close monitoring of SpO_2 would be critical in guiding the judicious use of supplemental oxygen, where patients can be promptly weaned down to lower flow rates of oxygen when there is clinical improvement.[31] This would help ration the limited resource for other patients who may have a greater need for oxygen supplementation.[32]

Applications in the post-hospital setting

In Singapore, patients who have been diagnosed with COVID-19 in emergency departments, testing centres or primary healthcare centres are routinely admitted to hospitals for monitoring and observation.[33] Lower-risk patients are subsequently discharged to isolation facilities within the community.[34] Such facilities within the community have limited access to healthcare staff and monitoring. In such a setting, the use of self-monitoring with pulse oximetry may be useful to identify patients at risk for deterioration.

The ability to closely monitor such patients would permit easier and earlier discharge from hospitals, and thus reduce the burden on healthcare institutions. This has been tested in an outpatient setting in Chicago and found to be clinically effective.[35] Of the 209 patients with suspected COVID-19 who were discharged with home SpO_2 monitoring, 77 were subsequently diagnosed with COVID-19, and of these 77 patients, 22 (29%) were later readmitted. Home SpO_2 <92% was associated with the need for readmission, acute respiratory distress syndrome and septic shock. Applied to the Singapore context, pulse oximetry in community care facilities may help to appropriately identify patients who need to be transferred back to an acute hospital for further care and management. In conjunction with other symptoms, such as the presence of fever (which has been shown to be associated with adverse outcomes in COVID-19 patients in Singapore), pulse oximetry may add an additional data point to identify patients at risk of clinical deterioration.[36]

CONTROVERSIES AND APPLICATIONS IN A LOW-RISK CONTEXT

Although an appealing concept, the widespread use of pulse oximetry needs to be considered with some caution. In particular, the Singapore context is significantly different from that of other communities worldwide. With extensive efforts in active case-finding and isolation of positive cases, outbreaks within the local community have been relatively contained with a low mortality rate (62,981 cases and 36 deaths as of 17 July 2021).[37] The majority of these cases had also been in a relatively low-risk migrant worker population with few medical comorbidities.[33] COVID-19 vaccination uptake has also been robust, with 2,609,367 individuals (over one-third of the population) having completed two doses of vaccination as of 17 July 2021.[38] As such, the use of widespread pulse oximetry in our local context may result in many 'false-positive' cases being identified.

In Singapore, there is already an extensive use of rapid antigen tests (which can be self-administered and obtained from pharmacies), and nasopharyngeal swabs for polymerase chain reaction (PCR) tests for COVID-19 can be performed by most primary healthcare providers.[39] With the easy access

Box 1. Possible causes of low oxygen saturation (SpO_2) detection on pulse oximetry.[41]

Falsely low readings	True hypoxaemia
Abnormal haemoglobin variants	Hypoxia (e.g. carbon monoxide poisoning)
Methemoglobinaemia	Hypoventilation
Nail polish	Right-to-left shunting (e.g. ventricular septal defect)
Movement artefacts	Ventilation and perfusion mismatch (e.g. decompensated heart failure, asthma)
Vasoconstriction/peripheral hypoperfusion	Diffusion defects

to such tests and their excellent sensitivity and specificity for COVID-19, it is unclear if the use of pulse oximetry would increase the sensitivity of detecting cases of COVID-19. Conversely, low oxygen saturations with no symptoms may also be seen in patients due to inappropriate technique when operating the pulse oximeter, or in other pre-existing medical conditions such as in chronic smokers with chronic obstructive pulmonary disease.[40] Box 1 provides a non-exhaustive list of causes of low SpO_2 detection on pulse oximetry. In some settings, the readings may be falsely low, while in other settings, low SpO_2 from true hypoxia may result from a myriad of other medical conditions beyond pneumonia from COVID-19.[41] The presence of falsely low readings may, paradoxically, increase the burden on primary healthcare providers and emergency departments, as well as add to undue distress and anxiety.

Furthermore, in this age of misinformation, the general public may also develop the misconception that adequate oxygen saturation levels would exclude the diagnosis of COVID-19. This is not true, as patients with mild disease and minimal symptoms are at risk of transmission of COVID-19.[42] If such misconception becomes pervasive, it may lead to an uncontrolled spread of the disease in Singapore. Moreover, pulse oximetry is also limited in that it only identifies pulmonary complications of COVID-19. In many studies, COVID-19 has been increasingly recognised as a systemic disorder that affects multiple organ systems. Even in a low-risk context like Singapore, other systemic manifestations like thromboembolic complications, cardiac complications and liver dysfunction have been described, and these would not necessarily be identified by pulse oximetry.[43-45]

CONCLUSION

The use of pulse oximetry in Singapore may be beneficial for the purpose of closely monitoring confirmed cases of COVID-19 that are managed in community facilities in order to identify individuals at risk of clinical deterioration in a timely fashion. However, in a low-risk setting of the general public, the clinical efficacy of a widespread use of pulse oximetry remains to be studied in robust clinical trials and should be considered with caution.

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Conflicts of interest

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