CADTH COVID-19 PANDEMIC

Ventilation and Perfusion Imaging for the Diagnosis of Pulmonary Embolisms During the COVID-19 Pandemic: A Review of Safety and Guidelines

This report was published on October 2, 2020

To produce this report, CADTH used a modified approach to the selection, appraisal, and synthesis of the evidence to meet decision-making needs during the COVID-19 pandemic. Care has been taken to ensure the information is accurate and complete, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly

Abbreviations

COVID-19   coronavirus disease 2019

CTPA   computed tomography pulmonary angiography

Context and Policy Issues

Coronavirus disease 2019 (COVID-19), caused by the novel coronavirus known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in China in 2019, and then it spread worldwide.[1] On 11 March 2020, WHO declared COVID-19 as a pandemic.[2] The virus is thought to spread mainly from person to person through respiratory droplets produced when an infected person coughs, sneezes, or talks.[3]

COVID-19 is associated with considerable morbidity and mortality, resulting mainly from respiratory failure.[4] Incidences of venous thromboembolism complications, which mainly manifest as deep vein thrombosis and pulmonary embolism, have been reported in patients with COVID-19. Pulmonary embolism, if undiagnosed or untreated, may have serious consequences.[4] The diagnosis of pulmonary embolism is difficult and challenging in patients with COVID-19.[5,6] There appears to be no association between the traditional risk factors for pulmonary embolism (such as age, history of venous thromboembolism, smoking, diabetes, hypertension, and cardiovascular disease) and the occurrence of pulmonary embolism in patients with COVID-19.[5] One of the procedures used for diagnosis of pulmonary embolism is the lung ventilation-perfusion imaging scan. This nuclear medical procedure is comprised of a ventilation scan to investigate airflow in the lungs and a perfusion scan to investigate blood flow in the lungs.[7] For the perfusion scan, technetium 99m macroaggregated albumin is injected into the patient, and for the ventilation scan technetium-labelled aerosols, such as diethylenetriamine pentaacetate or sulphur colloid, are used.[8]

There is some concern regarding the use of ventilation-perfusion imaging scan tests for the diagnosis of pulmonary embolism during the COVID-19 pandemic, as the ventilation part of the procedure often induces coughing in the patient and there is potential for contamination and transmission of COVID-19 infection to health care providers. Considering these safety issues, it is unclear whether ventilation-perfusion or perfusion only (i.e., omitting the ventilation phase) imaging should be done during the pandemic for patients with suspected pulmonary embolism (with or without COVID-19).

The aim of this report is to summarize the evidence regarding the safety of ventilation-perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic. An additional aim is to summarize the evidence-based guidelines regarding the use of ventilation-perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic.

Research Questions

1. What is the clinical evidence regarding the safety of ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the coronavirus disease (COVID-19) pandemic?

2. What are the evidence-based guidelines regarding the use of ventilation and perfusion imaging for the diagnosis of pulmonary embolism in patients with COVID-19?

3. What are the evidence-based guidelines regarding the use of ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic?

Key Findings

No relevant evidence was identified regarding the safety of ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the coronavirus disease (COVID-19) pandemic.

No evidence-based guidelines were identified regarding the use of ventilation and perfusion imaging for the diagnosis of pulmonary embolism in patients with confirmed or presumptive COVID-19.

No evidence-based guidelines were identified regarding the use of ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic.

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources, including MEDLINE, PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were perfusion tests and COVID-19. No filters were applied to limit the retrieval by study type. An additional search was done for pulmonary embolisms and chest imaging, and filters were applied to limit retrieval of these to guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2019 and September 2, 2020.

Selection Criteria and Methods

One reviewer screened citations and selected studies. In the first level of screening, titles and abstracts were reviewed and potentially relevant articles were retrieved and assessed for inclusion. The final selection of full-text articles was based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

Population	Q1. Individuals with suspected pulmonary embolism during the COVID-19 pandemic Any individual providing care for patients with suspected pulmonary embolism during the COVID-19 pandemic
	Q2. Individuals with suspected pulmonary embolism with confirmed or presumptive COVID-19
	Q3. Individuals with suspected pulmonary embolism who have tested negative for COVID-19 or who have not been tested for COVID-19
Intervention	Q1. Nuclear medicine ventilation and perfusion imaging
	Q2,3. Nuclear medicine perfusion imaging only, or ventilation and perfusion imaging

Comparator	Q1. Nuclear medicine perfusion imaging, no comparator Q2,3. Not applicable
Outcomes	Q1. Safety (e.g., transmission of COVID-19 infection [from patient to clinician], accurate diagnosis of pulmonary embolism, mortality) Q2. Recommendations regarding best practices for the detection of pulmonary embolism in patients with COVID-19 (e.g., guidance regarding which imaging test(s) should be conducted, the safety precautions that should be implemented) Q3. Recommendations regarding best practices for the detection of pulmonary embolism during the COVID-19 pandemic (e.g., guidance regarding which imaging test(s) should be conducted, the safety precautions that should be implemented)
Study Designs	Health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, and evidence-based guidelines

COVID-19 = coronavirus disease 2019.

Exclusion Criteria

Articles were excluded if they did not meet the selection criteria outlined in Table 1, they were duplicate publications, or were published prior to 2019. Guidelines with unclear methodology were also excluded.

Summary of Evidence

Quantity of Research Available

A total of 283 citations were identified in the literature search. Following screening of titles and abstracts, 244 citations were excluded and 39 potentially relevant reports from the electronic search were retrieved for full-text review. Six potentially relevant publications were retrieved from the grey literature search for full-text review. Of these 45 potentially relevant articles, all 45 publications were excluded for various reasons. Appendix 1 presents the PRISMA[9] flowchart of the study selection.

Summary of Findings

No relevant health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, or evidence-based guidelines were identified regarding ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic; therefore, no summary can be provided.

Limitations

No health technology assessments, systematic reviews, randomized controlled trials, non-randomized studies, or evidence-based guidelines that met the inclusion criteria were identified; hence, no relevant evidence could be presented.

Conclusions and Implications for Decision- or Policy-Making

No relevant studies or evidence-based guidelines were identified regarding ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic. Some publications that did not meet the inclusion criteria, and hence were excluded from the current report, provided some useful insights regarding ventilation-perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic, and are discussed in this section. The methodology and/or evidence on which the conclusions or guidance were based were not reported in these publications; therefore, they were not eligible for inclusion in this report.

Overall, there appears to be uncertainty regarding the use of ventilation-perfusion scans for the diagnosis of pulmonary embolism during the COVID-19 pandemic. Some articles (a letter, narrative reviews, and guidelines with unclear methodology) suggested omitting,[10-13] or limiting,[14,15] the use of the ventilation portion of ventilation-perfusion testing for pulmonary embolism in the context of COVID-19. In contrast, other articles (a letter and guidelines with unclear methodology) indicated the importance of both ventilation and perfusion testing for the diagnosis of pulmonary embolism, even in the COVID-19 context.[16-18]

Specifically, considering the COVID-19 pandemic, Zuckier et al.[14] presented an algorithm for the diagnosis of pulmonary embolism so that use of ventilation studies could be minimized. In this algorithm, the prior probability of pulmonary embolus is determined using a scoring system such as Wells' criteria, Pulmonary Embolism Rule-out Criteria (PERC), or the Geneva scoring system. Patients with probable pulmonary embolism and who have no lung parenchymal opacities (assessed by chest X-ray or computed tomography) undergo perfusion-only scintigraphy and, if there are no segmental defects, then pulmonary embolism is excluded. For patients with lung parenchymal opacities, or with no lung parenchymal opacities but one or more segmental defects seen by perfusion-only scintigraphy, computed tomography pulmonary angiography (CTPA) is considered unless contraindicated (such as contrast agent allergy). If CTPA is contraindicated for these patients and if there are no leg symptoms, then ventilation-perfusion with appropriate aerosol protection is considered; if leg symptoms are present, then deep vein Doppler is considered.

According to the American College of Radiology,[10] the nuclear medicine department should consider not performing ventilation scans for the time being, due to the risk of exposure to COVID-19 to patients and nuclear medicine technologists. If the ventilation scan is thought to be clinically necessary, then further discussion is needed in the context of COVID 19 procedures and policies.

Ayan and Kirac[11] suggest that as lung ventilation procedures can cause aerosolization and the formation of microdroplets, they should not be performed in patients with probable pulmonary embolism during the pandemic.

According to the report by the Faculty of Intensive Care Medicine, the Intensive Care Society, the Association of Anaesthetists and the Royal College of Anaesthetists,[12] in the context of COVID-19, perfusion-only single-photon emission computed tomography (SPECT) with low-dose computed tomography (CT) (i.e., omitting the ventilation phase) is suggested to be a safe option, whereby the diagnostic quality of the scan could be preserved and unnecessary risk related to aerosolization and infection could be avoided. In

contrast, the report by the Canadian Association of Nuclear Medicine[16] suggested that omission of the ventilation phase and performing stand-alone perfusion with SPECT/CT is not advisable, as specificity of the study is reduced. Both perfusion and ventilation studies need to be conducted to rule out pulmonary embolism.

During the COVID-19 pandemic, for the diagnosis of pulmonary embolism, Kooraki et al.[15] suggest the use of CTPA as the preferred modality unless contraindicated, and suggest limiting the use of ventilation-perfusion imaging. In order to minimize contamination of the facility and personnel, they suggest eliminating the ventilation phase of the scan, limiting the use of ventilation-perfusion for cases when other options are not possible, using personal protective equipment, using negative airway pressure in the procedure room, and decontaminating the procedure room after each ventilation-perfusion scan.

Koutsikos and Angelidis[13] suggest that during the COVID-19 pandemic the investigation of pulmonary embolism by lung perfusion alone is advised in order to minimize the risk of contamination of personnel in the imaging suite. However, they caution that although elimination of the ventilation phase in the investigation of pulmonary embolism does not impact the sensitivity of the test, the rates of false positives are higher. They mention that in making recommendations for the practice of nuclear medicine during the pandemic and post-pandemic, the epidemic status, patient characteristics with respect to potential for infection, and available resources need to be considered.

Le Roux et al.[18] mention that diagnosis of pulmonary embolism using a perfusion scan alone is associated with an unacceptably high likelihood of false-positive results. A false-positive result will likely necessitate undue use of anticoagulation therapy, which also has associated risks for some patients. According to Le Roux et al.[18] the benefits of ventilation-perfusion scans outweigh the risks, and there is no justification for omitting the ventilation scan for non-COVID-19 patients, especially in regions with low disease prevalence. They suggest that if there is no shortage of personal protective equipment (such as FFP2 masks, eye protection, gloves and gowns) then even in COVID-19 patients it is advisable to use perfusion-ventilation for diagnosis of pulmonary embolism.

Lastly, according to the Société Française de Medicine Nucleaire (SFMC) working group,[17] if a chest CT is required for the diagnosis of pulmonary embolism, both ventilation and perfusion scans should be performed and the institution's COVID-19 precautions should be followed.

In summary, no relevant studies or evidence-based guidelines were identified regarding ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic. Concerns regarding the potential for virus transmission during the ventilation portion of the test have led to suggestions to omit this aspect of the test,[10-13] or limit use of the ventilation portion,[14,15] however this judgment is not unanimous.[16-18] At present, the safety of ventilation and perfusion imaging for the diagnosis of pulmonary embolism during the COVID-19 pandemic is unknown, and future work may help to reduce this uncertainty.

References

1. Alzghari SK, Acuña VS. Supportive Treatment with Tocilizumab for COVID-19: A Systematic Review. *J Clin Virol.* 2020;127:104380.

2. Dennie C, Hague C, Lim RS, et al. Canadian Society of Thoracic Radiology/Canadian Association of Radiologists Consensus Statement Regarding Chest Imaging in Suspected and Confirmed COVID-19. *Can Assoc Radiol J.* 2020:846537120924606.

3. Centers for Disease Control and Prevention. Coronavirus 2019 (COVID-19). How to protect yourself & others. 2020; https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html. Accessed 2020 Sep 23.

4. American Society of Hematology. COVID-19 and Pulmonary Embolism: Frequently Asked Questions. 2020; https://www.hematology.org/covid-19/covid-19-and-pulmonary-embolism. Accessed 2020 Sep 9.

5. Kermani-Alghoraishi M, Ghahramani R. A Review of Venous Thromboembolism Phenomena in COVID-19 Patients. *Curr Probl Cardiol.* 2020.

6. Cuker A. Coronavirus disease 2019 (COVID-19): Hypercoagulability. In: Post TW, ed. *UpToDate.* Waltham (MA): UpToDate; 2020: www.uptodate.com. Accessed 2020 Sep 10.

7. National Heart, Lung, and Blood Institute. Lung VQ scan. 2020; https://www.nhlbi.nih.gov/health-topics/lung-vq-scan. Accessed 2020 Sep 18.

8. Gulati A, Balasubramanya R. Lung Imaging. *StatPearls.* Treasure Island (FL): StatPears Publishing; 2020: https://www.ncbi.nlm.nih.gov/books/NBK558976/. Accessed 2020 Sep 9.

9. Liberati A, Altman DG, Tetzlaff J, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *J Clin Epidemiol.* 2009;62(10):e1-e34.

10. American College of Radiology. COVID-19: ACR Statement on Nuclear Medicine Ventilation Scans. 2020; https://www.acr.org/Advocacy-and-Economics/ACR-Position-Statements/COVID19-Nuclear-Medicine-Ventilation-Scans. Accessed 2020 Sep 10.

11. Ayan A, Kirac FS. Guide for Nuclear Medicine Applications During the COVID-19 Outbreak. *Mol Imaging Radionucl Ther.* 2020;29(2):49-58.

12. The Faculty of Intensive Care Medicine, The Intensive Care Society, The Association of Anaesthetists and The Royal College of Anaesthetists. Clinical guide for the prevention, detection and management of thromboembolic disease in patients with COVID-19. Information, guidance and resources supporting the understanding and management of Coronavirus (COVID-19). 2020; https://static1.squarespace.com/static/5e6613a1dc75b87df82b78e1/t/5eecb111fdd1e0249e31904a/1592570129615/VTE-Patients-with-COVID19.pdf. Accessed 2020 Sep 10.

13. Koutsikos J, Angelidis G. Challenges and priorities in skeletal, gastrointestinal, hepatobiliary, genitourinary and lung scintigraphy during the COVID-19 pandemic. *Hell J Nucl Med.* 2020;23 Suppl:21-25.

14. Zuckier LS, Moadel RM, Haramati LB, Freeman LM. Diagnostic Evaluation of Pulmonary Embolism During the COVID-19 Pandemic. *J Nucl Med.* 2020;61(5):630-631.

15. Kooraki S, Hosseiny M, Myers L, Gholamrezanezhad A. Re: Ventilation-Perfusion Scans During the Coronavirus Disease 2019 (COVID-19) Outbreak. *J Am Coll Radiol.* 2020;17(6):698-699.

16. Canadian Association of Nuclear Medicine. Recommendations for performing V/Q scans in the context of COVID19. 2020; https://canm-acmn.ca/resources/Documents/Email%20Blast%20Documents/Belnuc%20%20Recommendations%20for%20performing%20VQ%20scans%20in%20the%20context%20of%20COVID-19%20-%20Belnuc.pdf. Accessed 2020 Sep 10.

17. Société Française de Médecine Nucléaire et Imagerie Moléculaire, SFMC Working Group. Ventilatory and perfusion lung imaging. 2020; https://canm-acmn.ca/resources/Documents/Email%20Blast%20Documents/VQ%20scans%20and%20COVID-19.pdf. Accessed 2020 Sep 10.

18. Le Roux PY, Le Gal G, Salaun PY. Lung scintigraphy for pulmonary embolism diagnosis during the COVID-19 pandemic: does the benefit-risk ratio really justify omitting the ventilation study? *Eur J Nucl Med Mol Imaging.* 2020;22:22.

Appendix 1: Selection of Included Studies

```
┌─────────────────────────────────────────┐
│ 283 citations identified from electronic │
│     literature search and screened       │
└─────────────────────────────────────────┘
                    │
                    │────────────────┐
                    │                ▼
                    │     ┌──────────────────────────┐
                    │     │ 244 citations excluded    │
                    │     └──────────────────────────┘
                    ▼
┌─────────────────────────────────────────┐
│ 39 potentially relevant articles retrieved│
│  for scrutiny (full text, if available)  │
└─────────────────────────────────────────┘
                    │
┌──────────────────────────┐
│ 6 potentially relevant    │
│ reports retrieved from other│────▶
│ sources (grey literature) │
└──────────────────────────┘
                    ▼
┌─────────────────────────────────────────┐
│      45 potentially relevant reports     │
└─────────────────────────────────────────┘
                    │
                    │────────────────┐
                    ▼
```

45 reports excluded:
- irrelevant design (3)
- irrelevant population (3)
- irrelevant intervention (14)
- irrelevant outcomes (2)
- duplicate publications (2)
- guidelines with unclear methods (8)
- guideline with nothing specifically on perfusion / ventilation (1)
- published in language other than English (1)
- other (review article, letter, correspondence, commentary or editorial) (11)

```
┌─────────────────────────────────────────┐
│      No reports included in review       │
└─────────────────────────────────────────┘
```