A systematic review of radiological and lung functional sequelae of viral pneumonias in adults (SARS-CoV, MERS-CoV, SARS-Cov-2, H1N1, H1N2, H2N2, H3N2, H5N1 influenza)

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Citation

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Review question

Review question: What is the prevalence of radiological sequelae and pulmonary function abnormalities indicative of lung fibrosis in adults surviving viral pneumonia?

Participants:

Adults with microbiological confirmation of virus infection (through PCR, immunofluorescence, viral culture or serology testing) AND radiological features of viral pneumonia due to SARS-CoV, MERS-CoV, SARS-Cov-2, or influenza viruses H1N1, H1N2, H2N2, H3N2, H5N1

Interventions:

Hospitalization, oxygen therapy, invasive mechanical ventilation, non-invasive ventilation (NIV/CPAP), use of steroids and antivirals

Comparators:

Not applicable

Outcomes:

- Presence of radiologic sequelae at follow-up CT scans within a year of hospital discharge. Sequelae are defined as inflammatory (ground glass opacification, consolidation) or fibrotic (reticulation, lung architectural distortion, interlobular septal thickening, traction bronchiectasis and honeycombing).

- Presence of restrictive impairment at pulmonary function test, defined as reduced FVC with normal-to-high FEV1/FVC ratio; or total lung capacity (TLC) <80%, if available.

- Presence of reduced diffusing capacity for carbon monoxide (DLCO), defined as DLCO < 80% of LLN

Searches

Eligibility criteria:

All relevant original studies in human adult patients (aged >18) will be eligible for inclusion regardless of publication status, including conference abstracts and case reports and pre-prints.

Retrospective studies will also be eligible.

No language criteria will be applied.

Letters, commentaries, expert opinions, editorials, and other non-original studies will be excluded.

Information sources:

Electronic searches will be carried out in MEDLINE, EMBASE, Google Scholar the Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov using keywords and controlled vocabulary terms (i.e. medical subheading (MeSH) terms, EMTREE terms). Pre-print servers including medRxiv, bioRxiv and ChinaXiv will also be searched.

Search strategy:

Keywords will include patient-related terms (viral pneumonia, severe acute respiratory syndrome, Middle East respiratory syndrome, COVID19, influenza), treatment-related terms (hospitalization, oxygen therapy, mechanical ventilation, non-invasive ventilation, steroids, antivirals), and outcomes-related terms (CT, PFT, fibrosis).

In addition, hand searches will be conducted of the reference lists of eligible primary studies, and relevant review articles

Types of study to be included

Eligibility criteria:

All relevant original studies in human adult patients (aged >18) will be eligible for inclusion regardless of publication status, including conference abstracts and case reports and pre-prints.

Retrospective studies will also be eligible.

No language criteria will be applied.

Letters, commentaries, expert opinions, editorials, and other non-original studies will be excluded.

Condition or domain being studied

The Coronavirus Disease 2019 (COVID-19) is a viral infection caused by SARS-Cov-2, a member of the Coronaviridae family. It was declared a global pandemic by The World Health Organization (WHO) on March 11, 2020. Across the world, over 3 million individuals have been infected thus far. The illness is characterised by a broad spectrum of flu-like symptoms, from mild to severe. A subgroup of patients develops severe pneumonia, causing hypoxemic respiratory failure and acute respiratory distress syndrome (ARDS). The long-term sequelae of patients with severe Covid-19 are currently unknown, but there is evidence from previous viral pneumonias suggesting long term complications may include lung fibrosis. In a proportion of patients surviving SARS, there was evidence of restrictive impairments in pulmonary function tests and presence of ground-glass opacity, reticulation, and interlobular thickening on follow-up CT scans. Analogously, similar radiologic findings were described during the follow up of patients who had recovered from MERS and H1N1 influenza. We aim to perform a systematic review to assess the extent of radiologic sequelae and lung function impairment in survivors, drawing on published reports from past viral infections (SARS-CoV, MERS-CoV, H1N1, H1N2, H2N2, H3N2, H5N1 influenza)

Participants/population

Adults with microbiological confirmation of virus infection (through PCR, immunofluorescence, viral culture or serology testing) AND radiological features of viral pneumonia due to SARS-CoV, MERS-CoV, SARS-Cov-2, or influenza viruses H1N1, H1N2, H2N2, H3N2, H5N1

Intervention(s), exposure(s)

Hospitalization, oxygen therapy, invasive mechanical ventilation, non-invasive ventilation (NIV/CPAP), use of steroids and antivirals

Comparator(s)/control

Not applicable

Context

Main outcome(s)

- Presence of radiologic sequelae at follow-up CT scans within a year of hospital discharge. Sequelae are defined as inflammatory (ground glass opacification, consolidation) or fibrotic (reticulation, lung architectural distortion, interlobular septal thickening, traction bronchiectasis and honeycombing).

- Presence of restrictive impairment at pulmonary function test, defined as reduced FVC with normal-to-high FEV1/FVC ratio; or total lung capacity (TLC) <80%, if available.

- Presence of reduced diffusing capacity for carbon monoxide (DLCO), defined as DLCO < 80% of LLN

* Measures of effect

See above

Additional outcome(s)

- Quantitative increment of radiologic abnormal findings.

- FVC; FEV1; TLC; DLCO.

* Measures of effect

See above

Data extraction (selection and coding)

Data management:

Searches will be systematically assessed with exclusion decisions recorded. All data will be extracted and assessed using agreed upon proformas. Disagreement will be resolved by consensus. Quantitative synthesis will be performed in Microsoft Excel and assessed using Stata SE16.

Selection process:

The studies retrieved during the searches will be screened independently by two reviewers for relevance first using title and abstract. Those identified as being potentially eligible will be assessed using full-text against the inclusion/exclusion criteria, and selected or rejected, as appropriate. Rationale for exclusion will be recorded in a flow chart. Disagreements will be resolved by consensus or by third-person adjudication.

Data collection process:

Data from the chosen articles will be extracted using a pre-defined proforma independently by two reviewers and mutually confirmed. Data extraction from studies reporting the same cohort will be restricted in a hierarchical approach to the study with the most complete outcome data, followed by the largest sample size, and the longest follow-up.

Data items:

The data to be extracted will include:

Author details and year of publication;

Study design;

Sample size;

Viral agent;

Method(s) of diagnosis;

Participant demographics: age, gender, smoking status,

Requirement and duration of mechanical ventilation;

Use and dosage of oxygen;

Requirement and duration of non-invasive ventilation;

Duration of ICU stay;

Duration of hospital stay;

Survival outcome measures;

Follow up duration

Lung-function findings at baseline and follow-up;

CT findings at baseline and follow-up

Risk of bias (quality) assessment

Risk of bias in individual studies:

The risk of bias in studies will be assessed by two authors independently using study appropriate tools available from the CLARITY Group at McMaster University. Any disagreements will be resolved by consensus, or by the involvement of a third author, if necessary.

All studies will be included, irrespective of their risk of their bias rating.

Meta-Bias(es):

Where heterogeneity is high, defined by I^2 test, sensitivity analyses will be performed using inverse variance heterogeneity models. Analyses will be initially univariate, multivariate models will adjust for a priori confounders of age and gender. Where possible, study primary outcome effect sizes will be plotted with errors to obtain a risk of bias funnel plot, all studies will be reported regardless of bias.

Confidence in cumulative evidence:

The quality of the evidence will be evaluated using the GRADE guidance. Retrospective observational studies will be considered weak but may be upgraded. Risk of analytical and publication bias, and inconsistency in reporting, will be assessed. An overall judgement of ‘high’, ‘moderate’, ‘low’, or ‘very low’ will be provided for the quality of the cumulative evidence for review outcomes.

Strategy for data synthesis

Synthesis:

A narrative synthesis of the key findings from the included studies will be presented according to the review outcomes with quantitative synthesis of summary tables for study characteristics, participants and outcome details.

Outcomes from any individual case reports will also be combined for quantitative synthesis as a separate series by pooling of results in random effects models. Proportions of individuals meeting each outcome in the case series pool and independent clinical studies will be included in meta-analysis to provide summary estimates of proportions and errors. If sufficient data, random effects inverse variance method of meta-analysis will be performed with generalised linear models to evaluate the likelihood of primary outcomes according to defined subgroups.

Analysis of subgroups or subsets
Subgroup analysis will be performed where possible, according to viral agent, demographic data, and severity of disease as described using clinical intervention and hospital stay/mortality outcomes.

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Type and method of review
Meta-analysis, Systematic review

Anticipated or actual start date
01 May 2020

Anticipated completion date
01 November 2020

Funding sources/sponsors
Not applicable

Conflicts of interest
None known

Language
English

Country
England, United States of America

Published protocol
https://www.crd.york.ac.uk/PROSPEROFILES/183139_PROTOCOL_20200430.pdf

Stage of review
Review Ongoing

Subject index terms status
Subject indexing assigned by CRD

Subject index terms
Adult; COVID-19; Coronavirus Infections; Disease Progression; Humans; Influenza A Virus, H1N1 Subtype; Influenza A Virus, H1N2 Subtype; Influenza A Virus, H2N2 Subtype; Influenza A Virus, H3N2 Subtype;

Influenza A Virus, H5N1 Subtype; Influenza, Human; Middle East Respiratory Syndrome Coronavirus; Pneumonia, Viral; Radiography; Radiology; SARS Virus; severe acute respiratory syndrome coronavirus 2

Date of registration in PROSPERO
30 April 2020

Date of publication of this version
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Details of any existing review of the same topic by the same authors

Stage of review at time of this submission
The review has not started

Stage	Started	Completed
Preliminary searches	No	No
Piloting of the study selection process	No	No
Formal screening of search results against eligibility criteria	No	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions
30 April 2020

PROSPERO
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