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INPLASY

The global prevalence of interstitial lung disease in patients with rheumatoid arthritis: A systematic review and meta-analysis protocol

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Prasanna, H; Almutairi, K; Inderjeeth, C; Preen, D; Keen, H; Nossent, J.

Corresponding author:
Hari Prasanna

22981086@student.uwa.edu.au

Author Affiliation:
The University of Western Australia.

ADMINISTRATIVE INFORMATION

Support - Australian Rheumatology Association, and Arthritis & Osteoporosis WA.

Review Stage at time of this submission - Formal screening of search results.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 April 2024 and was last updated on 19 April 2024.

INTRODUCTION

Review question / Objective To estimate the global prevalence of interstitial lung disease in patients with rheumatoid arthritis and identify associated risk factors.

Rationale Patients with rheumatoid arthritis (RA) have a higher risk of developing interstitial lung disease (ILD). This results in poorer health outcomes and increased healthcare costs. Despite this impact, the prevalence of ILD in patients with RA is unclear with estimates ranging from 2 to 60%.

Condition being studied Rheumatoid arthritis (RA) is a chronic, autoimmune disease characterised by synovial inflammation and joint destruction. There is growing evidence that it can also have extra-articular manifestations in organs such as the heart, lungs, eyes, skin and kidneys. Interstitial lung disease (ILD) is a common manifestation of RA that is characterised by inflammation and fibrosis of the lungs. It severely impairs lung function and is associated with very high morbidity and mortality.

METHODS

Search strategy A literature search will be conducted in relevant databases, including MEDLINE (Ovid), EMBASE, Google Scholar, Scopus, Web of Science, Proquest Central and Cinahl. The search strategy was first developed in Medline using MeSH subject headings and free-text terms around the four search components 'Prevalence, 'Rheumatoid Arthritis', 'Interstitial Lung Disease' and 'X-ray Computed Tomography'. These terms were combined using 'AND' and 'OR' operators to conduct the search. This strategy will

be adapted to other databases' syntax and subject headings.

Participant or population Adults aged 18 and over with clinically diagnosed rheumatoid arthritis according to internationally recognised criteria.

Intervention Not Applicable.

Comparator Not Applicable.

Study designs to be included Our search strategy will include case-control studies, cross-sectional studies, and prospective or retrospective cohort studies.

Eligibility criteria Studies will be included if (1) participants had clinically diagnosed RA according to internationally recognised criteria, (2) ILD is defined based on the findings of the HRCT scan with or without surgical lung biopsy and is consistent with the American Thoracic Society/ European Respiratory society's guidelines on classifying Idiopathic Interstitial Pneumonias, (3) participants were aged 18 years or older, (4) a period or point prevalence is included as one of the outcomes of the study. Studies will be excluded if (1) participants were diagnosed with ILD before a diagnosis of RA, (2) participants were diagnosed with other causes of ILD such as Sarcoidosis, Systemic sclerosis, Myositis, Systemic Lupus Erythematosus, Sjögren's syndrome, Hypersensitivity Pneumonitis, Pneumoconiosis and Radiation Pneumonitis (3) participants were diagnosed with ILD without the use of a HRCT scan, (4) comprised non-primary literature like editorials, narratives, systematic reviews, case studies/series, (5) published in a language other than English.

Information sources Articles will be sourced from the following databases: MEDLINE (Ovid), EMBASE, Google Scholar, Scopus, Web of Science, Proquest Central and CINAHL.

Main outcome(s) The primary outcome is the point or period prevalence of RA-ILD. The prevalence of RA-ILD is assumed to be constant over the study period.

Additional outcome(s) Additional outcomes include the prevalence of specific radiological patterns of ILD. ILD patterns that are typically implicated in RA include usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), organising pneumonia (OP), lymphocytic interstitial pneumonia (LIP), diffuse alveolar damage (DAD) and desquamating interstitial pneumonia (DIP). Probable UIP will be considered as UIP in this study and other/ indeterminate types of ILD will be classified as 'other'.

Data management Literature search results will be uploaded to Endnote version 21 and RAYYAN AI software. Any duplicate or abstract-only publications will be discarded. Two authors will independently review the titles and abstracts identified through the search against the inclusion and exclusion criteria. Full reports will be obtained for titles that align with the inclusion criteria or in cases of uncertainty. The authors will then assess the full-text reports to determine whether they conform with the inclusion and exclusion criteria. If questions regarding eligibility arise, additional information will be sought from the study authors to address any uncertainties. The authors will resolve any disagreements by discussion and with the consultation of a third senior author.

Quality assessment / Risk of bias analysis The studies in this systematic review will be evaluated for risk of bias using a checklist by Hoy et al (2012), which classifies prevalence studies into low, moderate or high risk. Articles that meet the inclusion criteria will be scored using this criterion independently by an author (HP) and verified by the supervising author (KA).

Strategy of data synthesis Statistical analysis will be performed using the R programming language. The prevalence of RA-ILD will be calculated by dividing the number of RA-ILD cases by the total number of participants with RA. A meta-analysis will also be performed using a random effects model to account for the heterogeneity between studies. The Cochran's Q test and I2 test will be used to assess the magnitude of heterogeneity. The Begg and Egger tests will be used to find publication bias, with a p-value of less than 0.05 as the threshold for bias.

Subgroup analysis Subgroup analysis will be performed based on geographical locations, different time periods, patterns of ILD as well as risk factors like smoking and DMARD use if two or more studies can be found for each subgroup.

Sensitivity analysis Sensitivity analysis will be performed by leaving one study out at a time, including or excluding studies with moderate/high risk of bias and including or excluding studies with potential outliers.

Language restriction Included studies will be restricted to English.

Country(ies) involved Australia.

Other relevant information None

Keywords Rheumatoid Arthritis; Connective Tissue Diseases; Humans; Interstitial lung disease; Prevalence; Risk Factors.

Dissemination plans The findings of our final report will be disseminated to the scientific community through publication in a peer-reviewed journal and presentation at conferences.

Contributions of each author

Author 1 - Hari Prasanna - Conceptualisation and design of the study; Data acquisition; Data analysis; Writing the initial draft.
Email: 22981086@student.uwa.edu.au
Author 2 - Khalid Almutairi - Conceptualisation and design of the study; Data acquisition; Data analysis; Writing, reviewing and editing.
Email: khalid.almutairi@uwa.edu.au
Author 3 - Charles Inderjeeth - Conceptualisation and design of the study; Writing, reviewing and editing.
Email: charles.inderjeeth@health.wa.gov.au
Author 4 - David Preen - Conceptualisation and design of the study; Writing, reviewing and editing.
Email: david.preen@uwa.edu.au
Author 5 - Helen Keen - Conceptualisation and design of the study; Writing, reviewing and editing.
Email: helen.keen@uwa.edu.au
Author 6 - Johannes Nossent - Conceptualisation and design of the study; Writing, reviewing and editing.
Email: johannes.nossent@uwa.edu.au