INPLASY

Biomarkers in lower respiratory tract samples in diagnosis of ventilator associated pneumonia (VAP): a systematic review

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ADMINISTRATIVE INFORMATION

Support - Swedish society for medical research.

Review Stage at time of this submission - Completed but not published.

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 31 January 2024 and was last updated on 31 January 2024.

INTRODUCTION

Review question / Objective To identify studies reporting biomarkers for VAP in lower respiratory samples, and to assess the clinical utility of those.

Condition being studied Protein biomarker concentrations in samples from patients with VAP, compared to patients without VAP.

METHODS

Search strategy
Primary scout search

Date 5th of May 2022

Syntax used to search the Pubmed database:

Bronchoalveolar OR bronchopulmonary and lavage OR wash, lower airway sample, tracheobronchial toilet, tracheal aspirate, bronchoalveolar fluid, ventilator-associated pneumonia, vap, interleukins, neutrophils, heparin-binding proteins, biomarkers

Secondary search

Date 12th and 24th of May 2022
Database, search syntax and resulting number of hits.

Pubmed
#1"Bronchoalveolar Lavage"[Mesh]

#2
"bronchoalveolar lavage*" OR bronchoalveolar lavage* OR "broncho-alveolar lavage*" OR "broncho-alveolar lavage*" OR "bronchial lavage*" OR "bronchopulmonary lavage*" OR "broncho-pulmonary lavage*" OR BAL OR mini-BAL OR "tracheal aspirate*" OR "bronchial wash*" OR "lower airway sample*" OR tracheobronchial toilet

OR "bronchoalveolar fluid*" OR "bronchoalveolar fluid*" OR BALF

#3
#1 OR #2

#4
"Pneumonia, Ventilator-Associated"[Mesh]

#5
"ventilator-associated pneumonia" OR "ventilator associated pneumonia" OR "ventilatorassociated pneumonia" OR VAP

#6
#4 OR #5

#7
((((((((((((((((((((((((((((((((("Endothelin-1"[Mesh]) OR ("C-Reactive Protein"[Mesh] OR "CRP protein, human" [Supplementary Concept])) OR "Procalcitonin"[Mesh]) OR "Macrophage Migration-Inhibitory Factors"[Mesh]) OR "Monocyte Chemoattractant Proteins"[Mesh])) OR "Plasminogen Activators"[Mesh]) OR "Cytokines"[Mesh]) OR "Interleukins"[Mesh]) OR "Interferon-gamma"[Mesh]) OR "Vascular Endothelial Growth Factors"[Mesh]) OR "Granulocyte Colony-Stimulating Factor"[Mesh]) OR "SAA3P protein, human" [Supplementary Concept]) OR "Tumor Necrosis Factor-alpha"[Mesh]) OR "Complement System Proteins"[Mesh]) OR "Vitronectin"[Mesh]) OR "Mucins"[Mesh]) OR "S100 Proteins"[Mesh]) OR "Heat-Shock Proteins"[Mesh]) OR "Angiopoietins"[Mesh]) OR "Amylases"[Mesh]) OR "Serum Amyloid P-Component"[Mesh]) OR "Matrix Metalloproteinases"[Mesh]) OR "SCGB1A1 protein, human" [Supplementary Concept]) OR "Extracellular Traps"[Mesh]) OR "Peroxidase"[Mesh]) OR "Cell-Free Nucleic Acids"[Mesh]) OR "ESM1 protein, human" [Supplementary Concept]) OR "CCL5 protein, human" [Supplementary Concept]) OR "Endotoxins"[Mesh]) OR "lipopolysaccharide-binding protein" [Supplementary Concept]) OR "Lipopolysaccharides"[Mesh]) OR "Gelsolin"[Mesh]) OR "Vitamin D-Binding Protein"[Mesh]) OR "Pyruvate Kinase"[Mesh]) OR "Cell Count"[Mesh]) OR "cytology" [Subheading]) OR "CD14 protein, human" [Supplementary Concept]) OR "TREM1 protein, human" [Supplementary Concept]) OR "FGFBP1 protein, human" [Supplementary Concept]) OR "presepsin protein, human" [Supplementary Concept] OR biomarkers[Mesh]

#8
Endothelin-1 OR ET-1 OR C-reactive protein* OR CRP OR procalcitonin OR PCT OR macrophage migration inhibitory factor OR MIF OR monocyt chemoattractant protein* OR MCP-1 OR MIP-1 OR "Soluble urokinase plasminogen activator receptor*" OR suPAR OR plasminogen activator inhibitor-1 OR PAI-1 OR Plasminogen activator OR IL-1B beta OR cytokine OR interleukin*,IL-1b OR IL- 4 OR IL-6 OR IL-8 OR IL-10 OR IL-26 OR IL-17A OR IL-17 OR IL-1beta OR interferon-gamma OR IFNγ OR sTNFalphaRI OR "vascular endothelial growth factor*" OR VEGF-A OR myeloperoxidase OR MPO OR "granulocyte colony-stimulating factor*" OR G-CSF OR "serum amyloid A3" OR SAA3 OR "tumor necrosis factor-α" OR TNF-alpha OR TNFa OR TNF-a OR "complement system protein*" OR "complement protein*" OR c5 OR c5a OR c3 OR c3a OR factor h OR vitronectin OR mucin OR s100 OR heat shock protein OR HSP OR angiopoietin OR "soluble vascular cell adhesion molecule-1" OR sVCAM-1 OR VCAM OR ICAM OR "soluble endothelial selectin" sESEL OR cationic human neutrophil peptides OR α-amylase OR amylase* OR SAA OR "serum amyloid P-component*" OR protease* OR gelatinase* OR elastase* OR HNE OR Matrix metalloproteinase* OR MMP-8 OR MMP-9 OR TIMP OR TIMPs OR MUC1 OR MUC1-ED OR Clara cell protein 10 OR CC-10 OR Calprotectin OR NET OR NETs OR peroxidase* OR "cell-free DNA" OR "nitrated protein*" OR Endocan OR "High mobility group box-1 protein" OR HMGB1 OR CCL5 OR endotoxin OR LPS OR gelsolin OR "vitamin D-binding protein" OR "pyruvate kinase" OR s-IgA OR IgA OR Cell Count OR cytology OR CD14 OR intracellular organisms OR ICOs OR ICO OR neutrophil* OR "alveolar macrophage chemotactic factor-1" OR AMCF-1 OR "AMCF 1" OR AMCF1 OR "chemokine CXCL-8" OR "chemokine CXCL 8" OR "chemokine CXCL8" OR "chemokines CXCL-8" OR "chemokines CXCL 8" OR "chemokines CXCL8" OR "macrophage-derived chemotactic factor*" OR "macrophage derived chemotactic factor*" OR "granulocyte chemotactic peptide-interleukin-8" OR calcitonin-1 OR "macrophage inflammatory protein 1" OR MIP-1 OR SAA3 OR "ESMI protein*" OR lipopolysaccharide* OR sTREM-1 OR "sTREM 1" OR sTREM1 OR "triggering receptor expressed on myeloid cells 1" OR HBP OR "heparin-binding protein*" OR "heparin binding protein*"

#9
#7 OR #8

#10
#3 AND #6 AND #9

The same search terms were then used to search Cochrane, Embase, Scopus, CINAHL and Web of Science.

Participant or population Human subjects that were treated at an intensive care unit and that had clinical signs of VAP and positive microbial culture.

Intervention Measurement of potential biomarkers in lower respiratory tract samples.

Comparator Human subjects that were mechanically ventilated and samples from the lower respiratory tract were collected.

Study designs to be included Retrospective or prospective observational clinical studies reported in peer reviewed medical journals.

Eligibility criteria Report must be available in English language. Conference reports, case reports, guideline documents and reveiw articles were excluded. The following lower respiratory samples were considered: Bronchoalveolar lavage (BAL), mini-BAL, (endo-)tracheal aspirate, bronchial wash.

Information sources Pubmed, Cochrane, Embase, Scopus, CINAHL and Web of Science.

Main outcome(s) Concentration of biomarker and reported statistical comparison between patients with VAP and subjects without VAP. Reported p-values, sensitivity, specificity, AUC and cut-off values.

Additional outcome(s) Length of stay, duration of mechanical ventilation.

Data management Structured search performed in Endnote by medical science librarian at Lund university. Duplicates were identified and removed. Two reviewers independently assessed relevance based on screening of title and abstract according to compliance with a predefined protocol.

Quality assessment / Risk of bias analysis A structured two-step search strategy with a primary scout search to identify relevant search terms and an expanded secondary search was performed to minimize the risk of inclusion bias. Two independent reviewers assessed all identified articles to prevent individual errors. Only articles published in peer reviewed medical journals were considered. Study populations, definitions of VAP cohort and controls were recorded and will be presented in the final report to enable the reader to evaluate the reported results in relation to the studied cohort.

Strategy of data synthesis Extracted data will be presented in a table and a narrative summary will be provided. No statistical meta-analysis will be performed due to the expected limited number of articles and the large variations in demography and clinical characteristics of the studies cohorts.

Subgroup analysis No subgroup analysis are planned.

Sensitivity analysis Only reported sensitivities will be presented.

Language restriction English.

Country(ies) involved Sweden.

Keywords Ventilator-associated pneumonia; critical care; biomarkers; mechanical ventilation; bronchoalveolar lavage.

Dissemination plans The results will be published in an international peer-reviewed medical journal.

Contributions of each author

Author 1 - Emily Gromelsky - Author 1 designed the study and drafted the manuscript.
Email: emily.gromelsky@med.lu.se
Author 2 - Sanna Askman - Author 2 critically reviewed the manuscript and provided medical scientific expertise.
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Author 3 - Magnus Paulsson - Author 3 designed the study, supervised the analysis and critically reviewed the manuscript.
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