

FRAILITY AS A PREDICTOR OF MORTALITY AMONG ELDERLY PATIENTS WITH PNEUMONIA : A SYSTEMATIC REVIEW AND META-ANALYSIS

RA Tuty Kuswardhani¹, I Desak Putu Agung Krisdanti², Christina Permata Shalim³
¹Division of Geriatric Medicine, Department of Internal Medicine, Faculty of Medicine, Udayana University/Prof Dr. I.G.N.G. Ngoerah Hospital, Bali, Indonesia
²Department of Pulmonology and Respiratory, Faculty of Medicine, Udayana University/ Udayana University Hospital, Bali, Indonesia
³Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia

ABSTRACT

Introduction: Pneumonia is a significant cause of morbidity and mortality among elderly patients.

Assessing the prognostic factors associated with pneumonia outcomes is crucial for clinical decision-making. This systematic review and meta-analysis aimed to evaluate the impact of frailty on mortality in elderly patients with pneumonia.

Methods: We performed a systematic search on the electronic databases PubMed, Cochrane Library, and Science Direct up to June 12th, 2023. Studies reporting the association between frailty and mortality in elderly patients with pneumonia were included. Quality assessment of the included studies was appraised using a Newcastle-Ottawa Scale. Pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated using random-effects models.

Results: Seven studies involving a total of 376,170 elderly pneumonia patients were included in the meta-analysis. The pooled results demonstrated a significant association between frailty and mortality in this population (pooled OR = 2.76, 95% CI: 2.22-3.44; $p < 0.00001$). Frailty was also significantly associated with prolonged hospitalization (pooled OR = 2.74, 95% CI: 1.90-3.96; $p < 0.00001$).

Conclusion: Frailty is significantly associated with increased mortality and prolonged hospitalization in elderly patients with pneumonia.

Keywords: elderly, frailty, mortality, pneumonia

Correspondence :

Christina Permata Shalim

Siloam Hospitals Kebon Jeruk, Jakarta, Indonesia

Email : ina.j.chest@gmail.com

Ph : 0852 7647 0874

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FRAILITY AS A PREDICTOR OF MORTALITY AMONG ELDERLY PATIENTS WITH PNEUMONIA : A SYSTEMATIC REVIEW AND META-ANALYSIS

Introduction

Pneumonia, a common and serious respiratory infection, continues to be a significant cause of morbidity and mortality among elderly patients worldwide. According to data from the Centers for Disease Control and Prevention (CDC), pneumonia is associated with a substantial burden of hospitalizations and deaths among the elderly in the United States. In 2018, the death rate from influenza and pneumonia among persons aged ≥ 65 years was 93.2 deaths per 100,000 population. Death rates increased with age from 31.7 deaths per 100,000 population among adults aged 65–74 years, to 94.2 among adults aged 75–84 years, to 377.6 among those aged ≥ 85 years. Numerous studies from various countries also showed similar results with incidence of severe pneumonia and mortality rates of pneumonia increased with age.¹

With the global population aging rapidly, the burden of pneumonia-related complications in the elderly continues to rise emphasizes the importance of identifying factors that influence patient outcomes in this vulnerable population. Assessing these prognostic factors can aid healthcare providers in risk stratification, early intervention, and personalized treatment approaches that can improve patient outcomes.

Among the numerous prognostic factors that have been investigated, frailty has emerged as a crucial factor to consider within the geriatric population.² Frailty is a multidimensional syndrome that encompasses a decline in physiological reserve and an increased vulnerability to stressors. Having frailty is associated with higher risk of adverse health outcomes.³

In the context of pneumonia, the impact of frailty on patient outcomes has garnered increasing attention from researchers and clinicians alike. Frail elderly patients with pneumonia may face unique challenges due to compromised immune responses, impaired respiratory function, and reduced ability to mount effective physiological defenses against the infectious agent. These frailty-related factors may contribute to a heightened risk of

severe pneumonia, increased complications, and poorer clinical outcomes, including higher mortality rates and prolonged hospitalization.⁴

To evaluate the impact of frailty on mortality in elderly patients with pneumonia, we conducted this systematic review and meta-analysis. This thorough investigation aimed to consolidate the existing evidence from various studies, allowing for a quantitative synthesis and a more comprehensive understanding of the impact of frailty on pneumonia outcomes in this vulnerable population.

Methods

This meta-analysis conforms to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) standards.

Literature search

We performed a systematic literature search using PubMed, and Cochrane Library, and Science Direct to find eligible journals from their commencement to June 12th, 2023. We employed keywords ("frail" OR "frailty") AND "pneumonia" AND ("mortality" OR "prognosis" OR "survival"). Additionally, we examine the references of pertinent articles. Duplicate results were removed after the initial search.

Study selection

Two authors (CPS, IDPAK) independently performed study selection. A screening of study titles and abstracts was conducted to eliminate irrelevant literature. The inclusion and exclusion criteria for this review were applied to studies that passed the initial screening. The studies were included if they met all of the mentioned criteria: (1) observational studies reporting elderly patients with pneumonia, (2) reporting frailty assessment, (3) reporting patient's mortality, (4) articles in English or Indonesian. The studies were excluded if they meet one of the following criteria: (1) no full text available, (2) case reports, (3) conference papers, (4) review articles, (5) non research letters and (6)

commentaries, (7) did not provide the necessary data for conducting meta-analysis.

Data Extraction

Data of the included studies that were extracted are the first author's name, year of publication, country, type of study, number of patients, age, frailty status, and outcomes (death or alive). For the meta-analysis, we divided frailty status only into two groups: frail and non frail. Authors will combine two or more categories of frailty status if there are studies that categorized frailty status into more than two categories.

The primary outcome studied in the present systematic review and meta-analysis was patients' mortality. The secondary outcome was prolonged hospitalization. All authors utilized an electronic data collection form to acquire the necessary information from each article.

Risk of Bias

The Newcastle–Ottawa scale (NOS) was adopted to assess the risk of bias in each study included. Three authors (CPS, RTK, IDPAK) independently conducted this process. The risk of bias were divided into three categories: low risk (7-9), moderate risk (4-6), and high risk (0-3).

Statistical analysis

Review Manager 5.4 was used as the softwares for statistical analysis. Pooled odds ratios (OR) with 95% confidence intervals (CI) were calculated using random-effects models. Heterogeneity was assessed using the I^2 statistic, which reveals which percentage of the variation in observed impacts across studies is related to the variation in true effects, with values greater than 60% indicating significant heterogeneity. All P values were two-tailed, with <0.05 was regarded as statistically significant.

Results

Study selection and characteristics

The keywords search yielded a total of 177 publications. After eliminating the duplicates, we retrieved 174 publications. By screening the titles and abstracts, we excluded 156 studies, leaving us with 18 potential studies. Then, the full texts of the potential studies were obtained and assessed to see if they were eligible for inclusion in the meta-analysis. Publications that lacked essential data for this meta-analysis and failed to meet all inclusion criteria were excluded. Thereby, a total of 7 studies were included in the present study.⁵⁻¹¹ PRISMA study flow diagram is described in Figure 1.

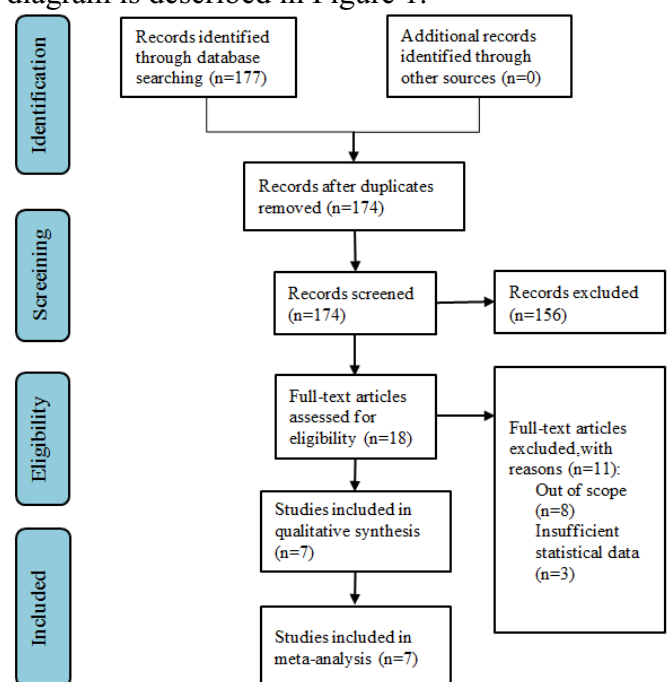


Figure 1. PRISMA Flow Diagram

Seven studies involving a total of 376,170 elderly pneumonia patients were included in the meta-analysis. Four included studies were retrospective cohorts and the other three studies were prospective cohorts. All studies were published in 2019–2023. Table 1 showed the characteristics of the included studies.

Table 1. Characteristics of the studies included in the meta-analysis

| No | Author | Country | Study design | Frailty assessment | Samples | Mean/median age (years) | Mortality rate | |
|----|------------|---------|----------------------|--------------------------|---------|-------------------------|----------------|------------|
| | | | | | | | Non frail | Frail |
| 1 | Huang 2022 | China | retrospective cohort | FI-Lab | 627 | 80 | 180/471 | 114/156 |
| 2 | Kundi 2019 | USA | retrospective cohort | HFRS | 270308 | 79.2 ± 8.9 | 23491/239342 | 5085/30966 |
| 3 | Kundi 2021 | Turkey | retrospective cohort | HFRS | 103449 | 77.4 ± 7.79 | 28466/99997 | 1553/3452 |
| 4 | Luo 2020 | China | prospective cohort | Fried Phenotype Criteria | 256 | 86 (81-90) | 0/85 | 14/171 |
| 5 | Park 2022 | Korea | prospective cohort | FI | 190 | 79 (74-85) | 12/90 | 41/100 |
| 6 | Park 2021 | Korea | prospective cohort | FI | 176 | 79 (75-84) | 4/81 | 15/95 |
| 7 | Zhao 2023 | China | retrospective cohort | FI-Lab | 1164 | 75 (69-82) | 141/656 | 267/508 |

Quality assessment

Using the NOS to evaluate the risk of bias, all seven studies were found to be at low risk. Table 2 showed the risk of bias assessment.

Table 2. NOS of the studies included in the meta-analysis

| Study | Selection | | | Demonstration that outcome of interest was not present at start of study | Comparability | | Outcome | | SCORE | Evidence quality |
|------------|--|------------------------------------|---------------------------|--|--------------------------|-----------------------|---|----------------------------------|-------|------------------|
| | Representativeness of the exposed cohort | Selection of the nonexposed cohort | Ascertainment of exposure | | Comparability of Cohorts | Assessment of outcome | Was follow-up long enough for outcomes to occur | Adequacy of follow up of cohorts | | |
| Huang 2022 | * | * | * | * | * | * | * | * | 7 | Low risk of bias |
| Kundi 2019 | * | * | * | * | * | * | * | * | 8 | Low risk of bias |
| Kundi 2021 | * | * | * | * | * | * | * | * | 8 | Low risk of bias |
| Luo 2020 | * | * | * | * | * | * | * | * | 7 | Low risk of bias |
| Park 2022 | * | * | * | * | * | * | * | * | 8 | Low risk of bias |
| Park 2021 | * | * | * | * | * | * | * | * | 8 | Low risk of bias |
| Zhao 2023 | * | * | * | * | * | * | * | * | 8 | Low risk of bias |

Frailty and mortality

The pooled results from these seven included studies demonstrated a significant association between frailty and mortality in elderly patients with pneumonia (pooled OR = 2.76, 95% CI: 2.22-3.44; p<0.00001) (Figure 2).

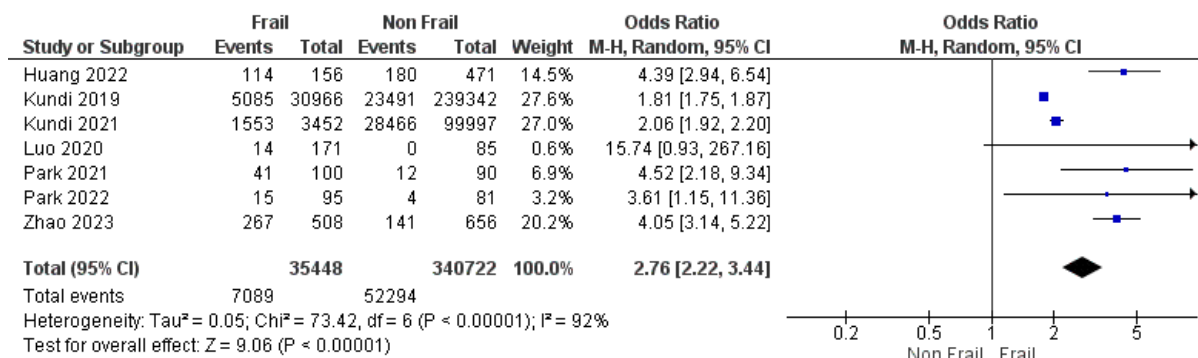


Figure 2. Forest plot of the effects of frailty on mortality among elderly patients with pneumonia

Frailty and prolonged hospitalization

From the included studies, we found only two studies reporting data about prolonged hospitalization. Based on these two studies, the analysis showed that frailty was significantly associated with prolonged hospitalization (pooled OR = 2.74, 95% CI: 1.90-3.96; p<0.00001) (Figure 3).

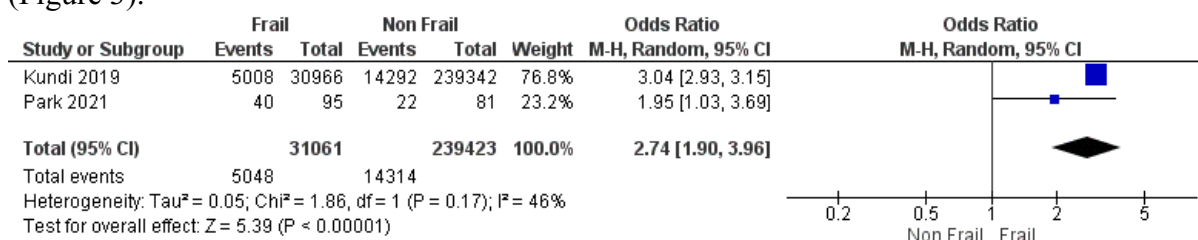


Figure 3. Forest plot of the effects of frailty on mortality among elderly patients with pneumonia

Discussion

In this meta-analysis, we noted that frailty is a significant predictor of mortality in patients with pneumonia, with frail patients having a higher mortality rate compared with the non frail ones. Studies that we included mostly came from Asia, with just one study conducted in the USA. Almost every study has different frailty assessment tools that they use, but all of them are standardized tools that have already been used in many previous studies.^{12,13}

The findings of this meta-analysis align with those of other previous studies that revealed that frailty is associated with a variety of adverse health outcomes, including falls, mortality, hospitalization, and reduced quality of life.¹⁴⁻¹⁶ In this study, we found that frailty was a predictor of mortality in elderly patients with pneumonia. Based on the pooled analysis, we also found that frailty is associated with prolonged hospitalization in this population, even though this result was only from two studies. There may be several reasons for these

results. First, frail elderly patients are particularly susceptible to the development of multiple chronic conditions that can interact synergistically with pneumonia, resulting in more severe and complex clinical courses. The presence of comorbidities in frailty adds to the challenges in managing these patients, as multiple medical conditions can influence treatment response and prognosis.¹⁷ Second, functional limitations that are a hallmark feature of frailty, also affecting mobility, activities of daily living, and overall physical independence. These limitations, combined with the debilitating effects of pneumonia, can lead to decreased physical function and deteriorating abilities, potentially prolonging hospitalization and recovery periods.^{18,19}

To the best of our knowledge, this is the first meta-analysis that evaluates frailty as a predictor of mortality in elderly patients with pneumonia. The impact of our study holds considerable importance in clinical practice. By recognizing frailty early in the course of pneumonia, healthcare providers can tailor

treatment plans, optimize resource allocation, and identify high-risk patients who may benefit from more aggressive interventions.

Addressing functional limitations through targeted rehabilitation and physical therapy interventions becomes essential in optimizing the recovery process and overall functional outcomes of frail elderly patients with pneumonia. Our study also highlights the need for continued research into interventions aimed at mitigating the impact of frailty on pneumonia outcomes.

Nevertheless, our research has its own limitations. First, during the study selection, a few studies reporting the association between frailty and mortality in elderly patients with pneumonia were excluded because they did not provide required data that we need to do the meta-analysis. We tried to contact each corresponding author of the study in question, but none gave a response. Second, the lack of standardized frailty assessment tools across studies may contribute to variability in results.

Conclusion

Our systematic review and meta-analysis showed that frailty is significantly associated with increased mortality and prolonged hospitalization in elderly patients with pneumonia. Thus, frailty assessment may serve as a valuable tool for risk stratification in this population.

Conflict of Interest

The authors declare that they have no conflict of interest.

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