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**Impact of frailty on outcomes of elderly patients undergoing percutaneous coronary intervention: A systematic review and meta-analysis**

Impact of frailty on outcomes of elderly patients undergoing percutaneous coronary intervention

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**Abstract**

**BACKGROUND**

Frailty is a common condition in elderly patients who receive percutaneous coronary intervention (PCI). However, how frailty affects clinical outcomes in this group is unclear.

**AIM**

This study aims to assess the link between frailty and the outcomes, such as in-hospital complications, post-procedural complications, and mortality, in elderly patients post-PCI.

**METHODS**

PubMed/MEDLINE, Embase, Cochrane Library, and Web of Science databases were screened for publications up to August 2023. The primary outcomes assessed were In-hospital and all-cause mortality, major adverse cardiovascular events (MACE), and major bleeding. The new Castle-Ottawa scoring (NOS) scale was used for quality assessment.

## RESULTS

Twenty-one studies with 739,693 elderly patients undergoing PCI were included. Frailty was consistently associated with adverse outcomes. Frail patients had significantly higher risks of in-hospital mortality (Risk Ratio [RR]: 3.45, 95%CI: 1.90, 6.25), all-cause mortality (Hazard Ratio [HR]: 2.08, 95%CI: 1.78, 2.43), MACE (HR: 2.92, 95%CI: 1.85, 4.60), and major bleeding (HR: 4.60, 95%CI: 2.89, 7.32) compared to non-frail patients.

## CONCLUSION

Frailty is a pivotal determinant in the prediction of risk of mortality, development of MACE, and major bleeding in elderly individuals undergoing percutaneous coronary intervention.

**Key Words:** Frailty; Elderly; Percutaneous coronary intervention; Systematic review; Meta-analysis

Wang S, Liu W. Impact of frailty on outcomes of <sup>6</sup>elderly patients undergoing percutaneous coronary intervention: A systematic review and meta-analysis. *World J Clin Cases* 2023; In press

**Core Tip:** This comprehensive meta-analysis elucidates the significant impact of frailty on outcomes in elderly patients undergoing percutaneous coronary intervention (PCI). The study underscores the consistent association between frailty and heightened risks of in-hospital mortality, all-cause mortality, major adverse cardiovascular events (MACE), and major bleeding. The convergence of results across diverse study designs, patient populations, and methodological approaches underscores the robustness of these findings. Recognizing frailty as a potent predictor allows for tailored care plans,

emphasizing the need for standardized frailty assessment in the pre-PCI evaluation of elderly patients.

## **INTRODUCTION**

Gradual aging of the world population presents a significant challenge to healthcare systems globally <sup>[1]</sup>. Prolonged life expectancy correlates with an increased prevalence of cardiovascular diseases, which, in turn, requires complex interventions to effectively manage these conditions <sup>[2]</sup>. Percutaneous coronary intervention (PCI) is an essential modality in contemporary cardiovascular care, especially in elderly patients, who often present with complex comorbidities <sup>[3,4]</sup>.

Frailty is an important factor that impacts the outcomes of elderly patients undergoing PCI. It is characterized by diminished physiological reserves, reduced functional capacity, and elevated susceptibility to stressors <sup>[5-7]</sup>. Numerous studies show that frailty is a crucial determinant of healthcare outcomes in the elderly and has a profound influence on morbidity, mortality, and healthcare resource utilization <sup>[8,9]</sup>.

The precise impact of frailty post- PCI outcomes in the elderly remains a subject of ongoing scientific inquiry and discourse. Understanding the exact association between frailty and procedural outcomes, post-procedural complications, and long-term prognoses in this demographic is imperative for optimizing patient care and resource allocation <sup>[10,11]</sup>.

This study aims to assess the link between frailty and outcomes, such as in-hospital complications, post-procedural complications, and mortality, in elderly patients post-PCI.

## **MATERIALS AND METHODS**

The study was done per Preferred Reporting of Items for Systematic Review and Meta-analysis (PRISMA) guidelines <sup>[12]</sup>.

PubMed/MEDLINE, Embase, Cochrane Library (CENTRAL), and Web of Science databases were searched for publications up to 31<sup>st</sup> August 2023. The search strategy

was designed to identify studies exploring the link between frailty and outcomes in elderly PCI patients.

Prospero Registration Number: CRD42023446018.

Search Terms: We combined appropriate Medical Subject Headings (MeSH) terms and keywords, including "frailty," "elderly," "percutaneous coronary intervention," and associated synonyms. Only studies in English were considered (Table 1).

Additionally, a manual search was done, and the bibliography of the eligible studies was also thoroughly screened for any missed citations. No restrictions or filters were applied during the search.

Study Selection: Two authors screened titles and abstracts of identified articles independently for eligibility. Disputes were resolved by discussion. Full-texts of studies, selected at the first stage were then assessed for eligibility.

*Inclusion Criteria:*

Study Design: Randomized controlled trials (RCTs), cohort-, case-control-, and observational studies.

Population: Studies involving elderly coronary artery disease patients 65 years and older who underwent PCI.

Exposure Variable: Frailty status is assessed using validated tools or criteria, such as the Fried Frailty Phenotype, Clinical Frailty Scale, or other recognized measures.

Outcome Measures: Studies reporting on relevant clinical outcomes, including but not limited to procedural success rates, post-procedural complications (e.g., bleeding, vascular complications), in hospital and all-cause mortality, and MACE.

*Exclusion Criteria:*

Studies with insufficient data or outcomes that are not pertinent to the research question.

Studies with a sample size of fewer than 30 participants.

Studies with participants not undergoing PCI

Conference abstracts, case reports, series, blog spots.

Data Extraction

A standardized data extraction form included the following information: Study Characteristics: Author(s), publication year, study design, and setting; Participant Characteristics: Demographics, including age, sex, and comorbidities; Frailty Assessment: Details of the frailty assessment tool used and the criteria for categorizing participants as frail or non-frail; PCI Details: Information on the type of PCI, procedural details, and any relevant interventions; Outcome Measures: Data on primary and secondary outcomes, including post-procedural complications (e.g., bleeding, vascular complications), in hospital and all-cause mortality, and MACE.

Study Quality Assessment was done using the Newcastle-Ottawa Scale (NOS) for observational studies.

#### Data Analysis

The qualitative analysis included the summary of the findings of the eligible studies. Quantitative Synthesis or meta-analysis was performed if data were deemed suitable and sufficiently homogenous, using a random-effects model to calculate pooled effect estimates. Risk ratios (RR) and Hazard ratios (HR) were used for categorical outcomes like mortality, risk of developing MACE, and major bleeding, respectively. The adjusted HRs provided were plotted using a generic inverse variance model to calculate the cumulative estimate. Heterogeneity was measured by the  $I^2$  statistic. Subgroup analyses were done based on factors such as the study design, frailty assessment tools, and other relevant variables like age and type of patients undergoing PCI. Publication bias was evaluated using visualization of funnel plots and statistical tests, including Egger's and Begg's tests, if required.

## **RESULTS**

The literature search identified 439 records. Of them, 404 records remained after deduplication and underwent screening of title and abstract. Full-texts of 26 potentially eligible records were thoroughly assessed, and twenty-one studies [13–33] were deemed eligible for inclusion in the analysis (Figure 1). The details of the included studies are shown in Table 2. All studies were of moderate to high quality (NOS of 7-9) (Table 3).

Eleven studies [13–33], were retrospective cohorts [13,14,16–18,20,21,23,24,27,32], six were prospective cohorts [15,19,22,28,29,33] and four were cross-sectional studies [25,26,30,31]. Studies were conducted between 2015 and 2023, in various countries, and investigated the correlation between frailty and cardiovascular outcomes in different cardiac patient populations. The included studies employed a range of frailty assessment tools, including Gilbert's hospital frailty score, Clinical Frailty Scale (CFS), Fried criteria, Hospital Frailty Risk Score (HFRS), and other validated measures. The sample sizes varied significantly, ranging from as low as 42 participants to massive cohorts with over 7 million patients. Patient ages also exhibited considerable diversity, with mean ages ranging from approximately 62 to over 84 years.

In terms of gender distribution among participants, the included studies reported a range from 46.2% to 72.7% male patients. Frailty prevalence among these populations varied from 9.9% to 66.8%.

The relevant outcomes included a wide array of cardiovascular events, such as MACE, which encompassed outcomes such as myocardial infarction (MI), stroke, major bleeding, and all-cause mortality. Additionally, revascularization procedures, 30-day readmission rates, and in-hospital mortality were assessed. The follow-up periods ranged from 28 to 962 days.

#### Meta-analysis

The presented meta-analysis results demonstrate the significant impact of frailty on various outcomes in the aged population of patients undergoing PCI. The analysis categorized patients into "Frail" and "Non-Frail" groups, and the effect estimates (Risk Ratios (RR) for in-hospital mortality and Hazard Ratios (HR) for all-cause mortality, MACE, and major bleeding) were calculated.

#### *In-Hospital Mortality*

There was a substantial difference in in-hospital mortality between frail and non-frail patients. The overall RR was 3.45 (95%CI: 1.90 to 6.25), showing that frail patients have a significantly higher risk of in-hospital mortality after PCI.

As shown by the subgroup analyses, retrospective studies reported an RR of 2.92 (95%CI: 1.09 to 7.81), while prospective studies showed an even higher RR of 4.02 (95%CI: 1.62 to 9.97). These findings underscore the consistency and strength of the relationship between frailty and in-hospital mortality. (Figure 2)

#### *All-Cause Mortality*

The meta-analysis demonstrates a substantial impact of frailty on all-cause mortality. The HR was 2.08 (95%CI: 1.78 to 2.43), indicating over two-fold higher risk of all-cause mortality in frail than in non-frail patients after PCI. (Figure 3) The subgroup analysis demonstrated that frailty consistently predicted all-cause mortality across various subgroups, including different study designs, age groups, and indications for PCI. (Table 4) The funnel plot showed an evident skewness suggesting publication bias across the studies depicting the estimate of risk for all-cause mortality.

#### *MACE*

Frailty correlated with a significantly increased risk of MACE following PCI, with an HR of 2.92 (95%CI: 1.85 to 4.60). (Figure 4)

#### *Major Bleeding*

Frail patients undergoing PCI were at a considerably higher risk of experiencing major bleeding events. The HR was 4.60 (95%CI: 2.89 to 7.32), indicating that frailty is a strong predictor of major bleeding complications. (Figure 5)

### **DISCUSSION**

Our results reported that frailty significantly correlates with higher mortality rates in elderly patients undergoing PCI. Frail individuals had a threefold bigger risk of in-hospital mortality and a twofold higher risk of all-cause mortality. Frailty was also consistently linked to a nearly threefold increased risk of MACE and a 2-fold higher risk of major bleeding in elderly PCI patients.

The clinical implications of our findings are significant. Frailty has emerged as a significant factor affecting healthcare outcomes, particularly in cases of invasive procedures in the elderly population. Therefore, identifying frailty in elderly patients



who require PCI should prompt a comprehensive evaluation of potential risks and benefits [34,35]. Frailty assessments can aid clinicians in tailoring treatment plans, optimizing post-procedural care, and providing realistic expectations to patients and their families [36,37]. Interventions aimed at mitigating frailty and optimizing overall health may be crucial in improving PCI outcomes in this population. Moreover, frailty assessment can inform shared decision-making processes and guide discussions regarding the suitability of PCI *vs* alternative treatment strategies.

The subgroup analysis of all-cause mortality in our study demonstrated that frailty consistently predicts all-cause mortality across various subgroups, including different study designs, age groups, and indications for PCI. Our results confirm that frailty assessment is a valuable tool for risk stratification in elderly PCI patients, regardless of study design or age. Moreover, frailty appears to be particularly influential in predicting mortality in older patients and those with acute conditions like STEMI [38,39]. However, the substantial heterogeneity within some subgroups suggests the need for further investigation into potential sources of variation in the effect of frailty on mortality in these specific contexts.

Our results are in agreement with previous observations highlighting the adverse impact of frailty on various healthcare outcomes. A meta-analysis by He *et al* 2022 [40], with nine studies and a cohort of 2658 patients, showed that the occurrence of frailty was between 12.5 and 27.8% and correlated with higher in-hospital (OR 3.59, 95%CI 2.01 - 6.42; I2 = 35%), short-term (OR 6.61, 95%CI 2.89 -15.16; I2 = 0%), as well as long-term mortality (HR 3.24, 95%CI 2.04- 5.14; I2 = 70%) of PCI patients. A meta-analysis by Wang *et al* 2021 [41] demonstrated an independent positive association of frailty and all-cause mortality [adjusted RR=2.94, 95%CI: 1.90–4.56, I2 = 56%,  $P < 0.001$ ] and MACEs [adjusted RR =2.11, 95%CI: 1.32–3.66, I2 = 0%,  $P = 0.002$ ]. Similarly, a meta-analysis of six studies by Yu *et al* 2023 [42] reported higher rates of all- cause mortality (HR= 2.29, 95%CI: 1.65–3.16,  $P = 0.285$ ), rehospitalization (HR = 2.53, 95%CI: 1.38–4.63), and in- hospital major bleeding (HR = 1.93, 95%CI: 1.29–2.90,  $P = 0.825$ ) in PCI cohort. Our

findings corroborate and extend the understanding of frailty's role in predicting complications and mortality in this specific clinical scenario.

Heterogeneity among the included studies is an essential consideration. We observed variations in frailty assessment tools, study designs, and patient populations. Different frailty assessment methods may yield varying effect estimates, emphasizing the importance of standardized assessment tools in future research. Additionally, subgroup analyses by study design highlighted the robustness of the correlation of frailty with adverse PCI outcomes across different research methodologies.

While we detected certain variability in the quality of evidence across outcomes, it generally ranged from moderate to high. This suggests that further studies are needed to strengthen the certainty of the observed associations.

Our study has several limitations. First, the included studies exhibited substantial heterogeneity in frailty assessment methods, potentially influencing effect estimates. Second, our analysis relied on aggregate data rather than individual patient data, limiting our ability to control for confounders at the individual level. Third, we reported a potential publication bias across the studies, as shown in the forest plot for all-cause mortality. Therefore, our results need to be interpreted with caution.

The observed slight differences in ORs between retrospective and prospective studies could be attributed to several factors despite the consistent association between frailty and in-hospital mortality. Retrospective studies rely on historical data and may be subject to inherent biases related to data collection and documentation practices. On the other hand, prospective studies, by their nature, involve real-time data collection and standardized protocols, potentially providing a more accurate reflection of the studied outcomes. Also, Retrospective studies may include a broader range of patients over an extended period, leading to potential heterogeneity in patient characteristics, and Prospective studies, with their predefined inclusion criteria, might exhibit a more homogeneous patient population.

Future research should focus on standardizing frailty assessment methods and exploring the impact of various interventions to improve frailty in the PCI setting.

Longitudinal studies with larger sample sizes and more comprehensive patient data can enhance our understanding of the relationship between frailty and PCI outcomes. Additionally, more studies are needed to establish optimal timing and methods of frailty assessment during the pre-procedural evaluation.

## **CONCLUSION**

In conclusion, our study provides compelling evidence that frailty is a pivotal determinant of outcomes in elderly individuals undergoing percutaneous coronary intervention. This underscores the importance of frailty assessment as an integral component of patient management in this population of patients. While our study contributes valuable insights, further research is needed to refine risk stratification, optimize interventions, and improve outcomes for frail elderly patients undergoing PCI.

## **ARTICLE HIGHLIGHTS**

### ***Research background***

In exploring the intricate relationship between frailty and outcomes in elderly patients undergoing percutaneous coronary intervention (PCI), this study addresses existing gaps in understanding. The relevance of this issue is emphasized given the increasing prevalence of frailty in an aging population.

### ***Research motivation***

The motivation behind this research lies in recognizing the clinical significance of frailty in elderly PCI patients and its potential influence on short-term and long-term outcomes. The study aims to inform clinical practices and enhance patient care by comprehensively exploring the impact of frailty.

### ***Research objectives***

The research objectives encompass a thorough assessment of the association between frailty and key outcomes, including in-hospital mortality, all-cause mortality, major adverse cardiovascular events (MACE), and major bleeding. The investigation also seeks to identify potential outcome variations based on different study designs, patient characteristics, and indications for PCI. Furthermore, it explores the implications of frailty assessment on personalized care plans and its integration into routine clinical practice.

### ***Research methods***

Comprehensive search strategies are applied across PubMed/MEDLINE, Embase, Cochrane Library, and Web of Science databases. Statistical methods, including risk ratios (RR) and hazard ratios (HR), ensured a robust and standardized approach. Subgroup analyses were conducted to explore variations in outcomes across different study characteristics.

### ***Research results***

The results of the study establish a compelling association between frailty and adverse outcomes in elderly PCI patients. Specific risk increments, such as a threefold higher risk of in-hospital mortality and a twofold increase in all-cause mortality, underscore the comprehensive impact of frailty on cardiovascular health. The findings are consistent across retrospective and prospective study designs, affirming the robustness of the association.

### ***Research conclusions***

In conclusion, the study emphasizes the clinical significance of frailty assessment in the pre-PCI evaluation of elderly patients. It underscores the need for tailored care plans, acknowledging frailty as a potent predictor of adverse events. The research contributes to the existing knowledge by synthesizing key findings and provides a foundation for future research endeavors.

### ***Research perspectives***

Future research is encouraged to explore interventions targeting frailty and their potential to improve outcomes in elderly PCI patients, advocating for standardized frailty assessment tools and multidisciplinary approaches to enhance the holistic care of this vulnerable patient population.

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SIMILARITY INDEX

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