ORIGINAL RESEARCH

76. Polypharmacy and Outcomes in Elderly Patients with Heart Failure: A Meta-Analysis

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Background: Polypharmacy, commonly defined as the use of five or more medications, is highly prevalent among elderly patients with heart failure. While guideline-directed therapy improves survival, excessive or inappropriate medication use may increase mortality, hospitalization, and treatment burden.

Aim: This study aimed to evaluate the association between polypharmacy and clinical outcomes in elderly patients with heart failure, including mortality, hospitalization, and quality of life.
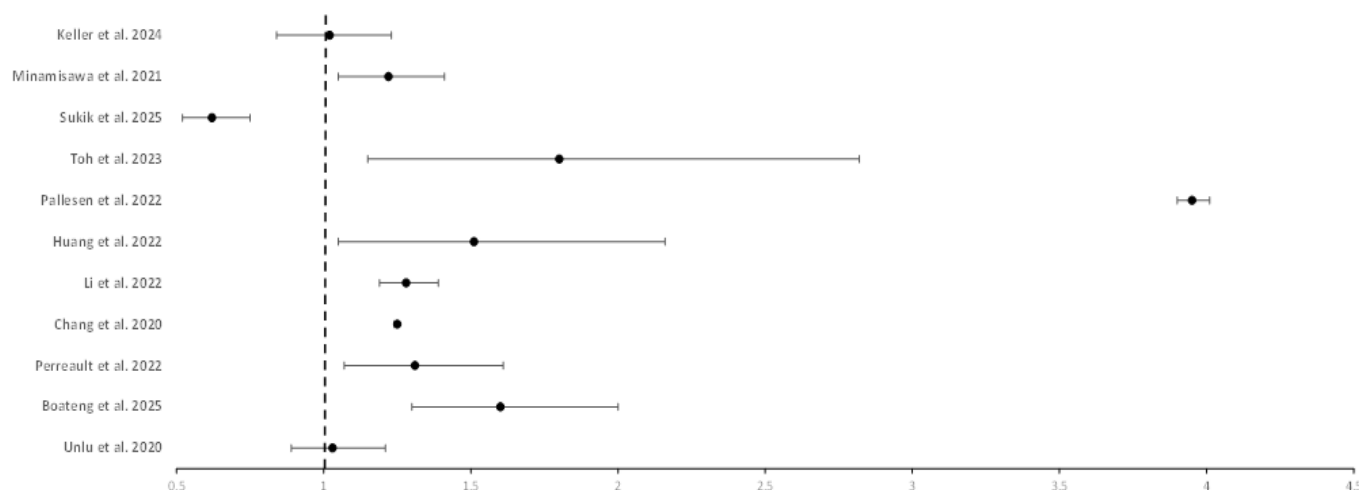
Methods: We conducted a systematic literature search in PubMed, Cochrane, and Scopus to identify observational studies assessing the impact of polypharmacy (defined as ≥5 medications) on elderly patients (≥65 years) with heart failure. Search strategies combined keywords (e.g., "heart failure", "polypharmacy") and subject headings (e.g., MeSH). The initial search yielded a total of 1,082 records. Studies were excluded if they were narrative reviews, case reports, or did not report quantitative outcomes of interest, such as mortality or hospitalization rates. After removing duplicates, titles and abstracts were screened based on predefined inclusion criteria. Following a full-text review of potentially eligible articles, 38 studies were included in the final systematic review, representing a pooled population of >250,000 participants. Of these, 11 studies provided sufficient quantitative data as Hazard Ratios with 95% Confidence Intervals and were included in the final meta-analysis for mortality and hospitalization. Findings from the remaining studies were synthesized narratively. Two reviewers independently screened, extracted data, and assessed study quality. A random-effects model was used to pool hazard ratios (HRs) and 95% confidence intervals (CIs). Statistical heterogeneity was assessed using the I^2 statistic. Subgroup analyses were performed by medication type (heart failure–specific vs. non-cardiovascular), setting (community vs. hospital), and frailty status.

Results: Polypharmacy was present in >70% of elderly patients with heart failure, with hyper-polypharmacy affecting 20–30%. Our pooled analysis, visualized in the accompanying forest plot (Figure 1), demonstrated increased all-cause mortality with polypharmacy (HR 1.38, 95% CI 1.25–1.60) and greater risk with hyper-polypharmacy (HR 2.29, 95% CI 1.80–2.70). Hospitalization risk was also elevated (HR 1.22, 95% CI 1.05–1.41; P=0.009), particularly when non-cardiovascular medications predominated. In contrast, studies examining guideline-directed medical therapy (GDMT) showed that appropriate polypharmacy could mitigate risk and improve survival, especially in HFpEF and HFmrEF populations. Quality of life outcomes were inconsistent, with most studies reporting no significant association; modest improvements were observed when inappropriate medications were discontinued. Frailty amplified risks of mortality and functional decline.

Conclusion: Polypharmacy in elderly heart failure patients is associated with higher mortality and hospitalization, particularly in the presence of frailty or inappropriate prescribing. However, polypharmacy driven by GDMT may confer survival benefits, underscoring the importance of medication appropriateness. Targeted deprescribing interventions and phenotype-specific management may reduce harm and improve outcomes in this vulnerable population.

Figure 1. Forest Plot of Study-Specific Effect Estimates with 95% Confidence Intervals.