BMC Cardiovascular Disorders

RESEARCH

Open Access

Relationship between comorbidity and health outcomes in patients with heart failure: a systematic review and meta-analysis

Kyoung Suk Lee[1], Da-In Park[2*], Jihyang Lee[1], Oonjee Oh[1], Nayoung Kim[1] and Gyumi Nam[3]

Abstract

Background The prevalence of heart failure (HF) is expected to rise due to increased survivorship and life expectancy of patients with acute heart conditions. Patients with HF and other multiple comorbid conditions are likely to have poor health outcomes. This study aimed to assimilate the current body of knowledge and to provide the pooled effect of HF patients' comorbid conditions on health outcomes.

Methods A systematic search was performed using MEDLINE, EMBASE and CINAHL databases. Observational studies evaluating the relationship between comorbid conditions and the health outcomes of HF were included. The pooled effect sizes of comorbidity on the identified health outcomes were calculated using a random effects model, and the heterogeneity was evaluated using I^2 statistics.

Results A total of 42 studies were included in this review, and a meta-analysis was performed using the results of 39 studies. In the pooled analysis, the presence of a comorbid condition showed a significant pooled effect size in relation to the prognostic health outcomes: all-cause mortality (HR 1.31; 95% CI 1.18, 1.45), all-cause readmission (HR 1.16; 95% CI 1.09, 1.23), HF-related readmission (HR 1.13; 95% CI 1.05, 1.23), and non-HF-related readmission (HR 1.17; 95% CI 1.07, 1.27). Also, comorbidity was significantly associated with health-related quality of life and self-care confidence. Furthermore, we identified a total of 32 comorbid conditions from included studies. From these, 16 individual conditions were included in the meta-analyses, and we identified 10 comorbid conditions to have negative effects on overall prognostic outcomes: DM (HR 1.16, 95% CI 1.11, 1.22), COPD (HR 1.31, 95% CI 1.23, 1.39), CKD (HR 1.18, 95% CI 1.14, 1.23, stroke (HR 1.25, 95% CI 1.17, 1.31), IHD (HR 1.17, 95% CI 1.11, 1.23), anemia (HR 1.42, 95% CI 1.14, 1.78), cancer (HR 1.17, 95% CI 1.04, 1.32), atrial fibrillation (HR 1.25, 95% CI 1.01, 1.54), dementia (HR 1.19, 95% CI 1.03, 1.36) and depression (HR 1.17, 95% CI 1.04, 1.31).

Conclusions Comorbid conditions have significantly negative pooled effects on HF patient health outcomes, especially in regard to the prognostic health outcomes. Clinicians should carefully identify and manage these conditions when implementing HF interventions to improve prognostic outcomes.

Keywords Heart failure, Comorbidity, Multimorbidity, Observational study, Systematic review, Meta-analysis

*Correspondence:
Da-In Park
dpark@hnu.kr
[1]College of Nursing, The Research Institute of Nursing Science, Seoul National University, Seoul, Republic of Korea
[2]Department of Nursing, College of Life Science and Nano Technology, Hannam University, Daejeon, Republic of Korea
[3]Seoul National University Hospital, Seoul, Republic of Korea

Background

Heart failure (HF) is a complex clinical syndrome associated with immense burden and reduced quality of life. It has become a major public health challenge worldwide with a substantially high prevalence among older adults [1]. As we face the forthcoming super-aged society, a continuous rise in HF prevalence is expected especially in more developed countries with improved survival rates for acute heart conditions [2]. Although advanced medicine has allowed better management of acute-stage heart conditions, the health outcomes of patients with HF remain poor, largely due to the chronicity of the illness and the presence of comorbidity [3].

Comorbidity in HF has recently gained considerable attention owing to its negative impact on health outcomes. Presence of both cardiovascular and non-cardiovascular comorbidities are frequently observed in HF patients [4, 5]. Recent review studies have indicated that HF research has shifted from focusing on acute care regimens to managing pre-existing comorbid conditions that have negative impacts on health outcomes [5, 6]. More than 40% of HF patients live with at least five comorbid conditions, which account for up to 80% of hospital care needs [5, 7]. This population presents high rates of unplanned readmissions and complications throughout their remaining lifetimes, and these costly medical needs derive largely from their comorbid conditions [8]. Thus, addressing and managing comorbidities should be recognized to achieve better quality of life and patient outcomes. Recent review studies have indicated that non-cardiovascular comorbidity significantly increases the risk of poor prognostic outcomes in patients with HF [6, 9]. However, given that these studies limited their search to non-cardiovascular conditions and mortality, there remains a paucity of data to fully understand the outcomes of HF patients with various comorbidities including both non-cardiovascular and cardiovascular comorbidities. For clinicians to stratify patients with a higher possibility of a worse prognosis and to provide more effective care, it is vital to understand the effects of common HF comorbid conditions on different health outcomes.

Methods

Aims

The purpose of this review was to provide a comprehensive understanding of the magnitude of the association between comorbid conditions and health outcomes in patients with HF. The specific aims were to synthesize and assimilate the current body of knowledge on comorbidity and health outcomes in HF, to provide pooled effect sizes of identified comorbid conditions in HF on health outcome measures, and to assess the quality of the current body of evidence.

Study design and search strategy

This study was conducted by systematically reviewing current literature and using meta-analysis. A focused systematic literature search was conducted to identify related studies published between January 2014 and September 2021 using MEDLINE, EMBASE, and CINAHL databases, with a guidance of a medical librarian. Search was restricted to studies published after 2013, considering that a previous meta-analysis study included articles published up to 2013 [6]. We also restricted the search language to English and study design to observational studies.

Relevant studies pertaining to the relationship between comorbid conditions and outcomes in patients with HF were identified using the following relevant search terms with abbreviations and truncation: "heart failure" and "comorbidity." Also, "multimorbidity" and its variations were combined with "comorbidity" and its variations using the "OR" operator. We did not set limitations for the outcome measures to synthesize the most literature possible. After reviewing the full texts of the articles, we further hand-searched the reference lists of each identified article.

The meta-analysis protocol was pre-registered with PROSPERO prior to the literature search process (CRD42020220021) in accordance with the recommendations of the Preferred Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement [10].

Study selection

Studies were included in the analyses if they met the following criteria: conducted with an adult population 18 years or above with HF diagnosis; reported original results (e.g., not a literature review, editorial, or case study); reported the relationships between health outcomes and comorbidities, which were defined as clinical diagnoses based on medical records, administration codes, or self-report (e.g., not a condition determined by questionnaires for screening, such as the presence of clinically significant depressive symptoms based on the Patient Health Questionnaire-9); and reported relevant statistical values. To calculate effect sizes for each health outcome, we excluded studies that reported composite outcomes, such as combined results of morbidity and hospital readmissions.

Data abstraction

Three reviewers (JL, OO, NK) independently screened all articles identified in the literature search process and retrieved full-text publications of all potentially eligible articles. The full-text articles were independently assessed by four reviewers (KSL, DP, JL, OO) for inclusion eligibility. Any discrepancies were resolved by discussion. A structured template was predefined and

designed prior to the literature search process to ensure consistency of data extraction. Data were extracted by four reviewers (DP, JL, OO, GN) using the pre-defined template. After data extraction, the accuracy of all data was independently verified by two reviewers (KSL, DP).

Quality appraisal

The Risk of Bias Assessment tool for Non-randomized Studies (RoBANS) (11) was used to assess the quality of each included study based on the risk of bias in six domains: the selection of participants, confounding variables, measurement of exposure, blinding of outcome assessment, incomplete outcome data, and selective outcome reporting. These six domains were judged to be "low," "high," or "unclear." Three reviewers (KSL, DP, JL) first rated the quality of three articles independently using the RoBANS, and any disagreement was resolved through discussion and/or consulting with a fourth reviewer (OO). The quality of the remaining articles was reviewed by the three reviewers as well.

Statistical analyses

Based on a predefined study protocol, we conducted a meta-analysis of the included studies. We used the RevMan software (version 5.4.1) and the CMA software (version 3.3.070) to perform all statistical analyses and to derive the forest plots. A meta-analysis was performed only when at least two studies provided data for each outcome of interest. We extracted adjusted hazard ratios (HR) or odds ratios (OR) with the corresponding 95% confidence intervals (CI) from the identified studies and used the inverse-variance method to calculate the overall effect size with 95% CI. HRs are considered a common measure of the association between comorbidities and HF prognostic outcomes with both ORs and RRs considered equivalent to HRs, given that the ORs and RRs provide similar estimates of risk when the outcome is rare [12]. If one study reported multiple adjusted HR or OR values for the same outcome measure, we calculated the pooled effect size that represented the outcome of the study.

The health outcome values were categorized into patient-reported and prognostic outcomes. The patient-reported outcomes included health-related quality of life (HRQoL) and self-care. The prognostic outcomes included mortality, hospital readmission and a longer hospital stay (>4 days). If possible, we further categorized the outcome results based on the follow-up period of each study. In accordance with recent multicenter cohort and meta-analysis studies, we used the 1-year mark as the dividing point between short-term and long- term periods [13–15]. We then synthesized the pooled effect sizes of the most common comorbid conditions on health outcomes.

Considering the observational design of the studies and methodological differences, the random effects model was used [16]. Statistical heterogeneity was assessed using I^2 statistics, where values of 25%, 50%, and 75% were considered as cut-off points for low, moderate, and high degrees of heterogeneity, respectively [17]. A p-value of <0.05 was considered statistically significant. All studies in each forest plot were organized in alphabetical order. We planned to perform a meta-regression using clinical characteristics (e.g., New York Heart Association functional classification, and ejection fraction). However, not all studies reported the exact values, so we could not conduct the meta-regression. Publication bias was assessed using Begg and Egger's test and funnel plot, and a p-value of >0.05 was considered statistical evidence for absence of publication bias (18). To determine the effect of publication bias on the robustness of the synthesized analysis, Duval and Tweedie's trim and fill method was used [18].

Results

After duplicate removal and title and abstract review, 98 articles were selected for full-text reviews. Additional 29 articles were retrieved during hand-search process. After independent full-text reviews and discussions, a total of 42 studies were eligible for the final inclusion. From the 42 identified studies, a meta-analysis was performed using 39 studies (Fig S1).

Narrative review of the included studies

The included 42 studies represented 2,814,442 HF patients recruited from inpatient [19–42], outpatient [43–53] or both settings [54–60] (Table S1).

The studies included mainly older adults with mean age ranging between 56 and 85 years. Included studies evaluated patients with both non-cardiovascular and cardiovascular comorbid conditions, yielding up to 32 individual conditions. The most commonly identified co-existing non-cardiovascular chronic conditions were diabetes mellitus (DM) [19–21, 24, 27, 29, 31–33, 35–37, 39, 42, 43, 46, 48, 50–52, 54, 56–59], chronic obstructive pulmonary disease (COPD) [27, 29, 31, 32, 36, 39–42, 44, 48, 51, 52, 56–60] and chronic kidney disease (CKD) [20, 22, 27, 29, 31, 36, 42, 46, 48–50, 52, 56–58], while the most frequently identified cardiovascular conditions were stroke [22, 23, 27, 29, 30, 32, 42, 51, 52, 54, 56–58], hypertension (HTN) [20, 29, 32, 36, 37, 50, 51, 54, 56, 58] and ischemic heart disease (IHD) [27, 31, 32, 36, 37, 39, 51, 54]. Some of the included studies defined comorbidity using the Charlson Comorbidity Index [23, 25, 26, 28, 32–34, 47, 51, 53, 55] or the total number of existing conditions [38, 45]. It should be noted that some of our included studies had exclusion criteria for patients who were diagnosed and receiving treatment for chronic

conditions such as CKD [26], thyroid conditions [21], respiratory conditions [44] or psychological conditions [23].

The patient-reported outcomes included HRQoL [40, 47, 57] and self-care [23, 43, 50, 53, 55]. The prognostic outcomes included in-hospital mortality [22, 24, 27, 30, 33, 34, 41, 58], all-cause mortality [19, 20, 25–28, 32, 37, 38, 44, 48, 49, 51, 52, 56, 58–60], all-cause readmission [28, 29, 31, 33, 35, 38, 39, 42, 45, 46, 56, 59], HF-related readmission [21, 29, 36, 38, 52, 54, 58], non-HF-related readmission [29, 54] and longer hospital stay [24, 33]. Further evaluation of the studies investigating all-cause mortality identified eight studies that reported the effect of comorbidities on short-term mortality [25, 27, 28, 32, 38, 52, 58, 60], and eleven reporting on long-term mortality [19, 20, 26, 32, 37, 44, 48, 49, 51, 56, 59].

Quality appraisal of included studies

Most included studies showed a low risk of bias in the selection of participants, confounding variables, measurement of exposure, blinding of outcome assessments, and incomplete outcome data domains. However, except for two studies that clearly reported the presence of the study protocol [28, 40], the majority of studies had unclear or a high risk of bias in selective reporting bias [20, 21, 23–27, 30, 33–36, 38, 39, 41, 43–45, 47, 49, 50, 52, 54–63] (Fig S2). Publication bias was, first, assessed by using the funnel plots of standard error with logit effect size. Examination of the funnel plots did not suggest publication bias as no asymmetry was observed. Additional Egger's regression tests were performed to confirm the absence of publication bias for included studies for calculation of the overall effect size of comorbid conditions on prognostic outcomes ($p=0.29$, two-tailed). Lastly, the trim and fill method revealed that no study was trimmed. As for studies that were included for other outcomes, the Egger's test was not used due to the small number. However, examination of the funnel plots indicated an absence of publication bias.

Quantitative analyses

Only a few studies were available for meta-analysis of patient-reported health outcomes. Although four studies investigated the relationship between comorbidity and HRQoL, only two were sufficient for the meta-analysis because of data limitations and differences in the questionnaires used to measure the level of HRQoL. The two studies used overall scores of the Kansas City Cardiomyopathy Questionnaire (KCCQ) [40, 57]. For self-care, studies that used Self-care of Heart Failure Index (SCHFI) were included in the meta-analysis [23, 43, 53]. We were able to perform the meta-analysis for three domains of the SCHFI: confidence, maintenance and management.

A total of 34 primary studies were pooled to calculate the overall effect size of comorbid conditions on prognostic outcomes: in-hospital mortality [22, 24, 27, 30, 33, 34, 41, 58], all-cause mortality [19, 20, 25–28, 37, 38, 44, 48, 49, 51, 52, 56, 58–60], all-cause readmission [28, 29, 31, 33, 35, 38, 39, 42, 45, 46, 56, 59], HF-related readmission [21, 29, 36, 38, 52, 54, 58], non-HF-related readmission [29, 54] and delayed length of hospital stay [24, 33]. Among the prognostic outcome measures, all-cause mortality was the only measure with sufficient data for the meta-analysis based on the follow-up periods. Eight studies were pooled to calculate the effect size of comorbid conditions on short-term all-cause mortality [25, 27, 28, 32, 38, 52, 58, 60], and 11 studies were pooled for long-term all-cause mortality [19, 20, 26, 32, 37, 44, 48, 49, 51, 56, 59].

Overall effects of comorbidity on HF outcome measures

From included studies, only five studies were available to pool the data on patient-reported health outcome measures [23, 40, 43, 53, 57]. Although the presence of comorbidity did not show significant pooled effect size on overall patient-reported outcomes, significance was noted for the HRQoL measured by KCCQ overall score (standardized mean difference (SMD) -5.86, 95% CI -8.51, -3.20, $p<0.001$) and the self-care confidence domain based on the SCHFI (SMD 1.91, 95% CI 0.31, 3.52, $p=0.02$) [23, 43, 53] (Fig. 1).

On the other hand, the pooled analysis showed that the presence of any comorbid condition was associated with a significantly higher risk of overall prognostic health outcome with HF 1.17 (95% CI 1.13, 1.21, $p<0.001$) (Fig. 2). The pooled analysis of 18 studies [19, 20, 25–28, 32, 37, 38, 44, 48, 49, 51, 52, 56, 58–60] indicated that HF patients with comorbidity had a statistically higher risk of all-cause mortality (HR 1.31, 95% CI 1.18, 1.45, $p<0.001$). In addition, the presence of comorbidity significantly increased the risk of all-cause readmission (HR 1.16, 95% CI 1.09, 1.23, $p<0.001$) [28, 29, 31, 33, 35, 38, 39, 42, 45, 46, 56, 59], HF-related readmission (HR 1.13, 95% CI 1.05, 1.23, $p=0.001$) [21, 29, 36, 38, 52, 54, 58] and non-HF-related readmission (HR 1.17, 95% CI 1.07, 1.27, $p<0.001$) [29, 54]. However, no significance was noted for in-hospital mortality and longer length of hospital stay (Fig. 2). When we further investigated the effects of coexisting conditions on all-cause mortality based on follow-up periods, we found a significant association for both short-term (HR 1.23, 95% CI 1.09, 1.38, $p<0.001$) [25, 27, 28, 32, 38, 52, 58, 60] and long-term risks (HR 1.35, 95% CI 1.21, 1.50, $p<0.001$) [19, 20, 26, 32, 37, 44, 48, 49, 51, 56, 59] (Fig S3).

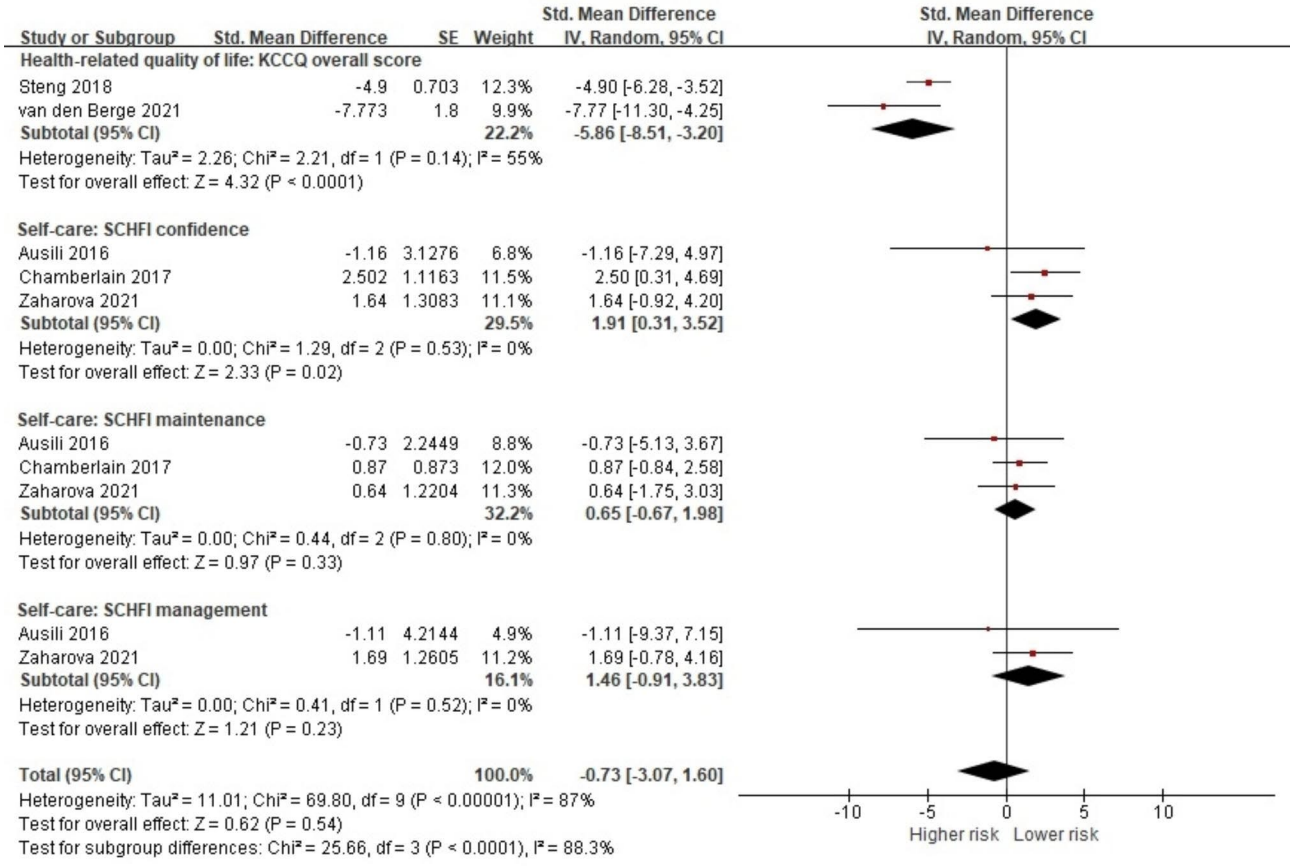

Fig. 1 Forest plot of the pooled analysis evaluating the effect of comorbidities on overall patient-reported outcomes in heart failure patients

Associated comorbid conditions

Although we identified various comorbid conditions, the following 16 individual conditions were identified for the meta-analysis: DM, COPD, CKD, stroke, HTN, IHD, anemia, cancer, atrial fibrillation, dementia, obesity, depression, arrhythmia, arthritis, asthma and valvular disease.

From 25 studies investigating DM, data from 22 studies were extracted to conduct a quantitative synthesis of the association between DM and the prognostic outcome measures [19–21, 24, 27, 29, 31–33, 35–37, 39, 42, 46, 48, 51, 52, 54, 56, 58, 59]. Diagnosis of DM was reported in 947,154 (34.8%) HF patients. Although the study results were highly heterogeneous (I^2=98.0%) and, thus, should be interpreted with caution, the pooled effect size indicated that the presence of DM was adversely associated with the overall prognostic outcomes (HR 1.16, 95% CI 1.11, 1.22, p<0.001) (Fig. 3). Our analysis indicated that, similar to the overall effect of any comorbid condition, HF patients with DM had an increased risk of all-cause mortality (HR 1.32, 95% CI 1.20, 1.44, p<0.001), all-cause readmission (HR 1.17, 95% CI 1.08, 1.26, p<0.001), HF-related readmission (HR 1.15, 95% CI 1.13, 1.17, p<0.001) and non-HF-related readmission (HR 1.10, 95% CI 1.03, 1.18, p=0.007). For all-cause mortality, further analysis was conducted using data from four studies with short-term follow-up [27, 32, 52, 58] and seven studies with long-term follow-up [19, 20, 32, 37, 48, 51, 56]. The presence of DM in HF significantly increased both short-term (HR 1.24, 95% CI 1.04, 1.46, p=0.01) and long-term all-cause mortality (HR 1.35, 95% CI 1.23, 1.49, p<0.001) (Fig S4).

From 18 studies that assessed COPD in HF, 16 reported the associations of COPD and in-hospital mortality [27, 41, 58], all-cause mortality [27, 32, 44, 48, 51, 52, 56, 58–60], all-cause readmission [29, 31, 39, 42, 56, 58] and HF-related readmission [36, 40]. Of the 783,940 HF patients, 108,488 (13.8%) were diagnosed with COPD, which increased the risk of poor overall prognostic health outcomes (HR 1.31, 95% CI 1.23, 1.39, p<0.001) (Fig. 4). Significant risks were noted for all-cause mortality, all-cause readmission and HF-related readmission (HR 1.36, 95% CI 1.21, 1.54; HR 1.33, 95% CI 1.23, 1.45; HR 1.16, 95% CI 1.10, 1.22, respectively). Additional analysis also showed that a COPD condition was statistically significantly associated with both short-term (HR 1.22, 95% CI 1.09, 1.37, p<0.001) [27, 32, 52, 58, 60] and long-term all-cause mortality risks (HR 1.43, 95% CI 1.20, 1.69, p<0.001) [32, 44, 48, 51, 56, 59] (Fig S5).

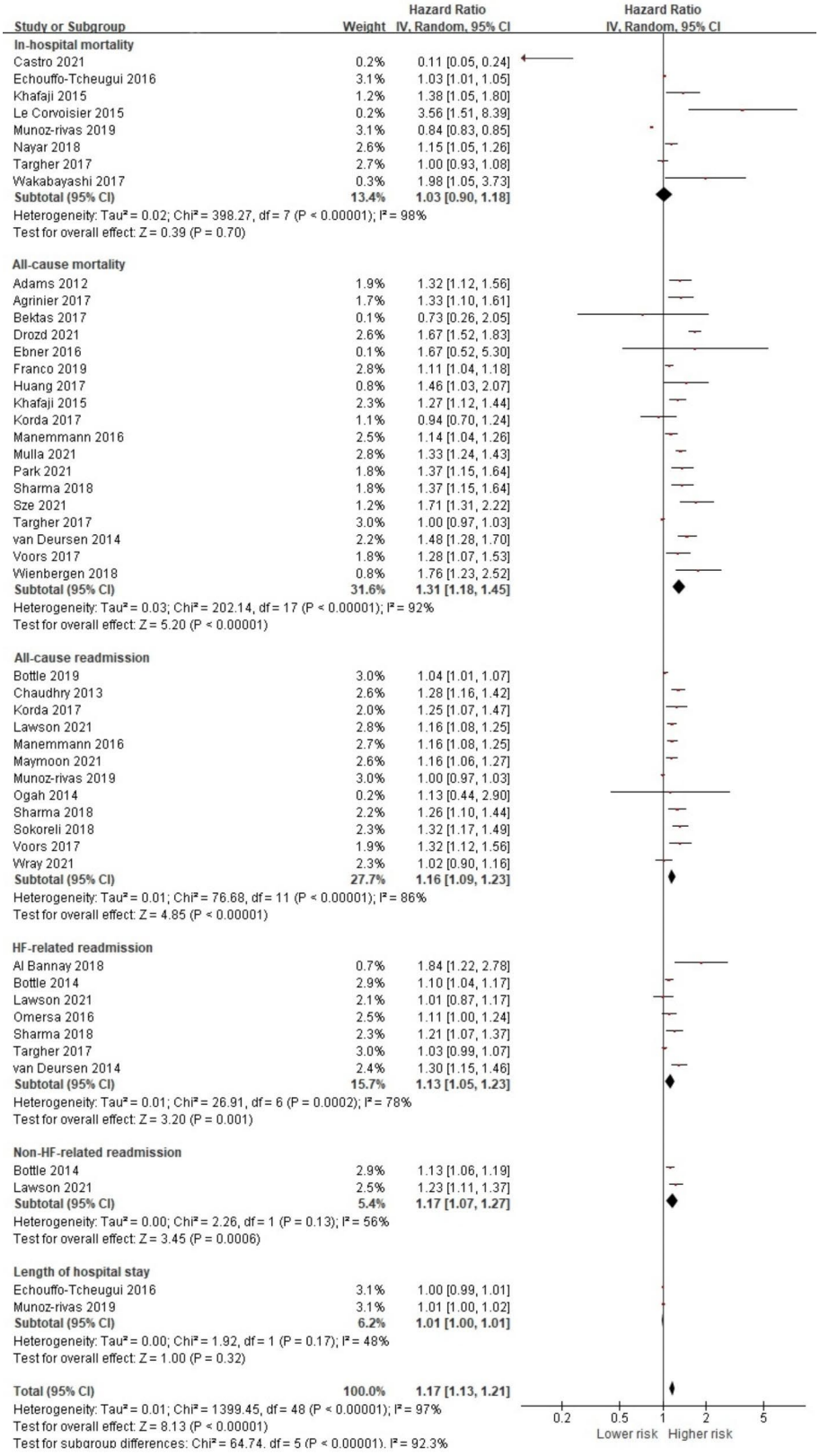

Fig. 2 Forest plot of the pooled analysis evaluating the effect of comorbidities on overall prognostic health outcomes in patients with heart failure

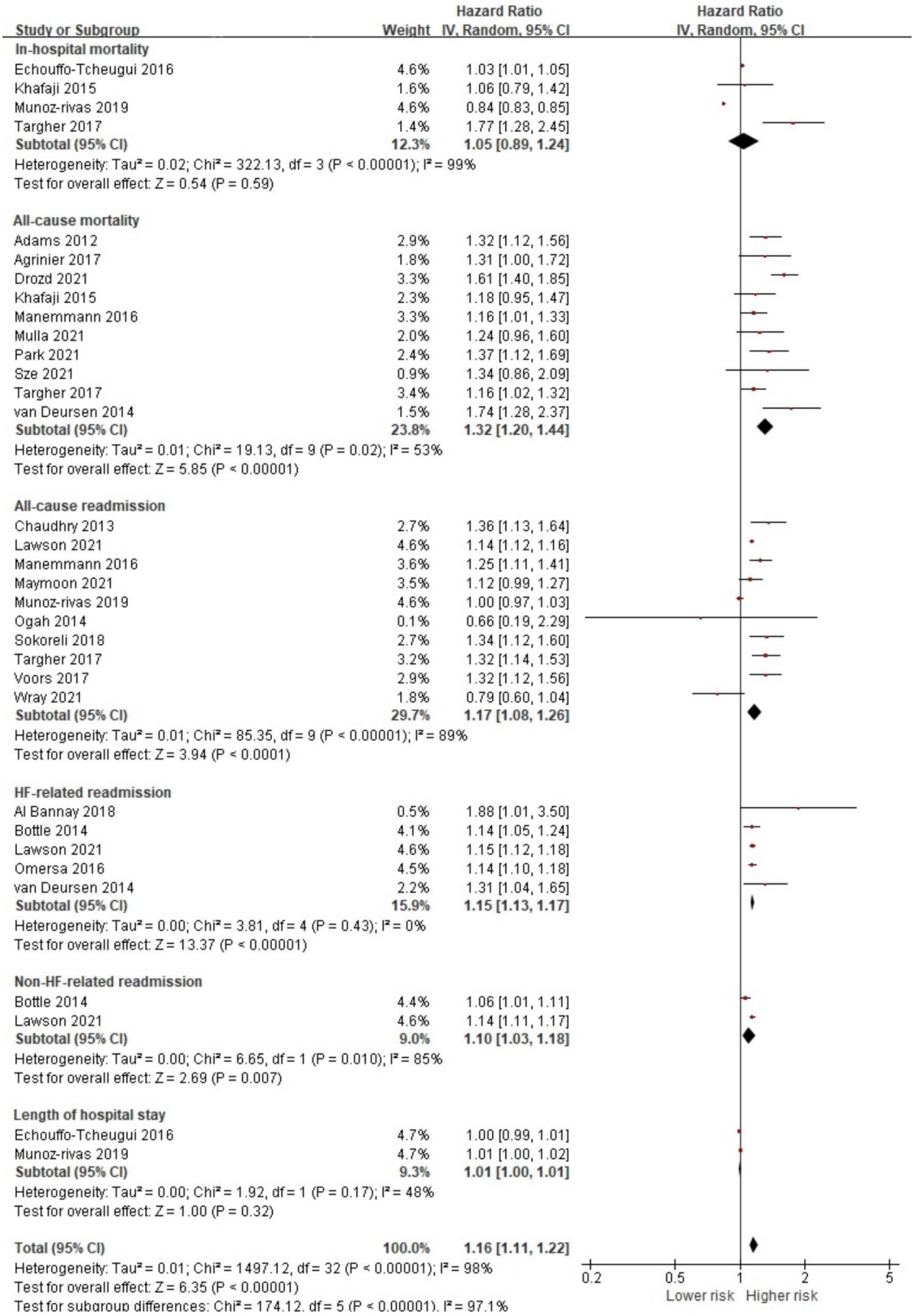

Fig. 3 Forest plot of the pooled analysis evaluating the effect of diabetes mellitus on health outcomes in patients with heart failure

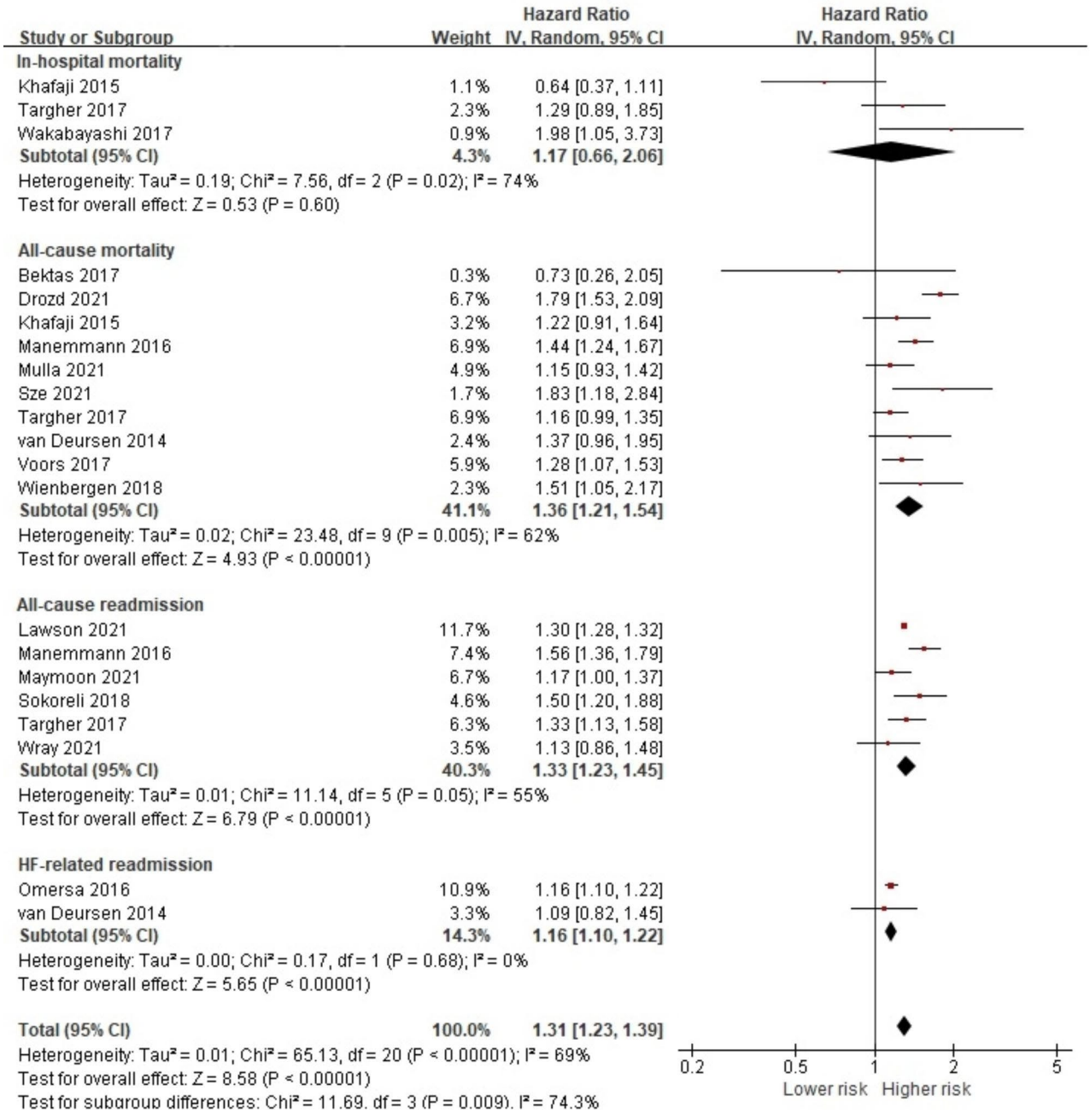

Fig. 4 Forest plot of the pooled analysis evaluating the effect of chronic obstructive pulmonary disease on health outcomes in heart failure patients

The presence of CKD was observed in 122,715 (15.8%) patients in 13 included studies [20, 22, 27, 29, 31, 36, 42, 46, 48, 49, 52, 56, 58]. Although two additional studies also included HF patients with an underlying CKD condition, they did not provide sufficient data for the meta-analysis [50, 57]. We also pooled the data in-hospital mortality [22, 27, 58], all-cause mortality [20, 27, 48, 49, 52, 56, 58], all-cause readmission [29, 31, 42, 46, 56, 58], and HF-related readmission [29, 36, 52]. A higher risk of a poor overall prognosis outcome was observed with CKD (HR 1.18, 95% CI 1.14, 1.23, $p<0.001$). HF patients with CKD showed a poorer prognosis in all-cause readmission (HR 1.22, 95% CI 1.05, 1.41, $p=0.009$) and HF-related readmission (HR 1.31, 95% CI 1.27, 1.36, $p<0.001$), but no significant relationship was noted for in-hospital mortality and all-cause mortality (Fig. 5 and S6).

A history of stroke, also reported as cerebrovascular accident, was indicated in 44,998 (5.6%) patients in 13 studies. Because only one of the 13 studies reported patient-reported outcome measures [57], only 12 studies

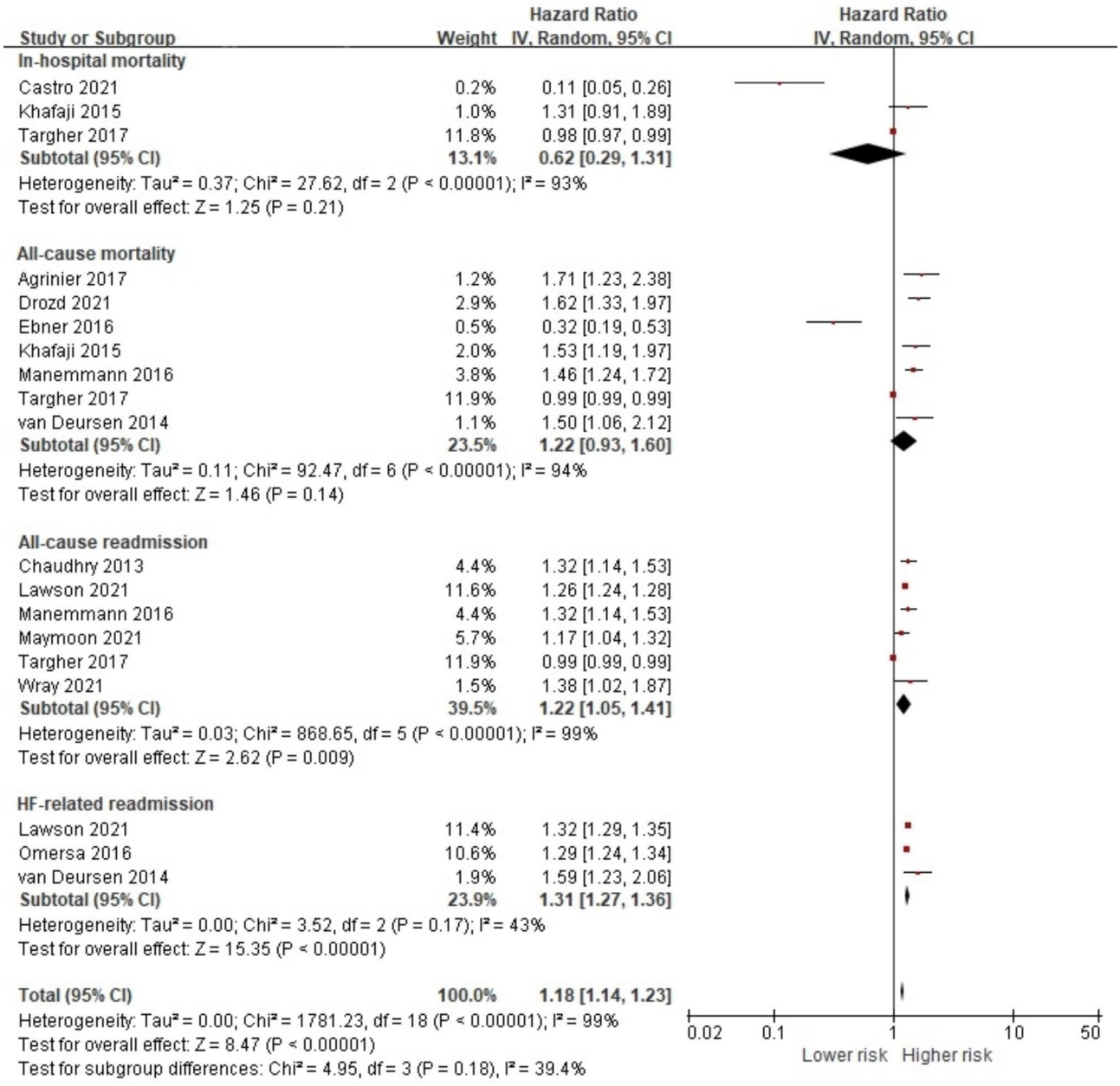

Fig. 5 Forest plot of the pooled analysis evaluating the effect of chronic kidney disease on health outcomes in heart failure patients

were pooled to calculate the effect size on the prognostic health outcomes: in-hospital mortality [22, 27, 30, 58], all-cause mortality [27, 32, 51, 52, 56, 58], all-cause readmission [29, 42, 46, 56, 58], HF-related readmission [52, 54] and non-HF-related readmission [29, 54]. A history of stroke had a significant pooled effect on a poor overall prognosis (HR 1.25, 95% CI 1.17, 1.33, $p<0.001$), specifically on all-cause mortality (HR 1.33, 95% CI 1.18, 1.50, $p<0.001$), all-cause readmission (HR 1.18, 95% CI 1.13, 1.24, $p<0.001$) and non-HF-related readmission risks (HR 1.25, 95% CI 1.19, 1.32, $p<0.001$) (Fig. 6). When we conducted a meta-analysis on all-cause mortality based on the follow-up periods, both short-term (HR 1.31, 95% CI 1.15, 1.51, $p<0.001$), and long-term all-cause mortality risks (HR 1.40, 95% CI 1.10, 1.79, $p<0.01$) significantly increased with a history of stroke (Fig S7).

The presence of HTN was observed in 386,154 (46.7%) patients in 11 studies, but data were extracted from 10 studies reporting the association of HTN with all-cause mortality [20, 32, 37, 51, 56, 58], all-cause readmission [29, 31, 56, 58], HF-related readmission [29, 36, 54] and non-HF-related readmission [29, 54]. The presence of HTN did not have a significant effect on the overall prognosis outcome in HF patients. In addition, it did not have

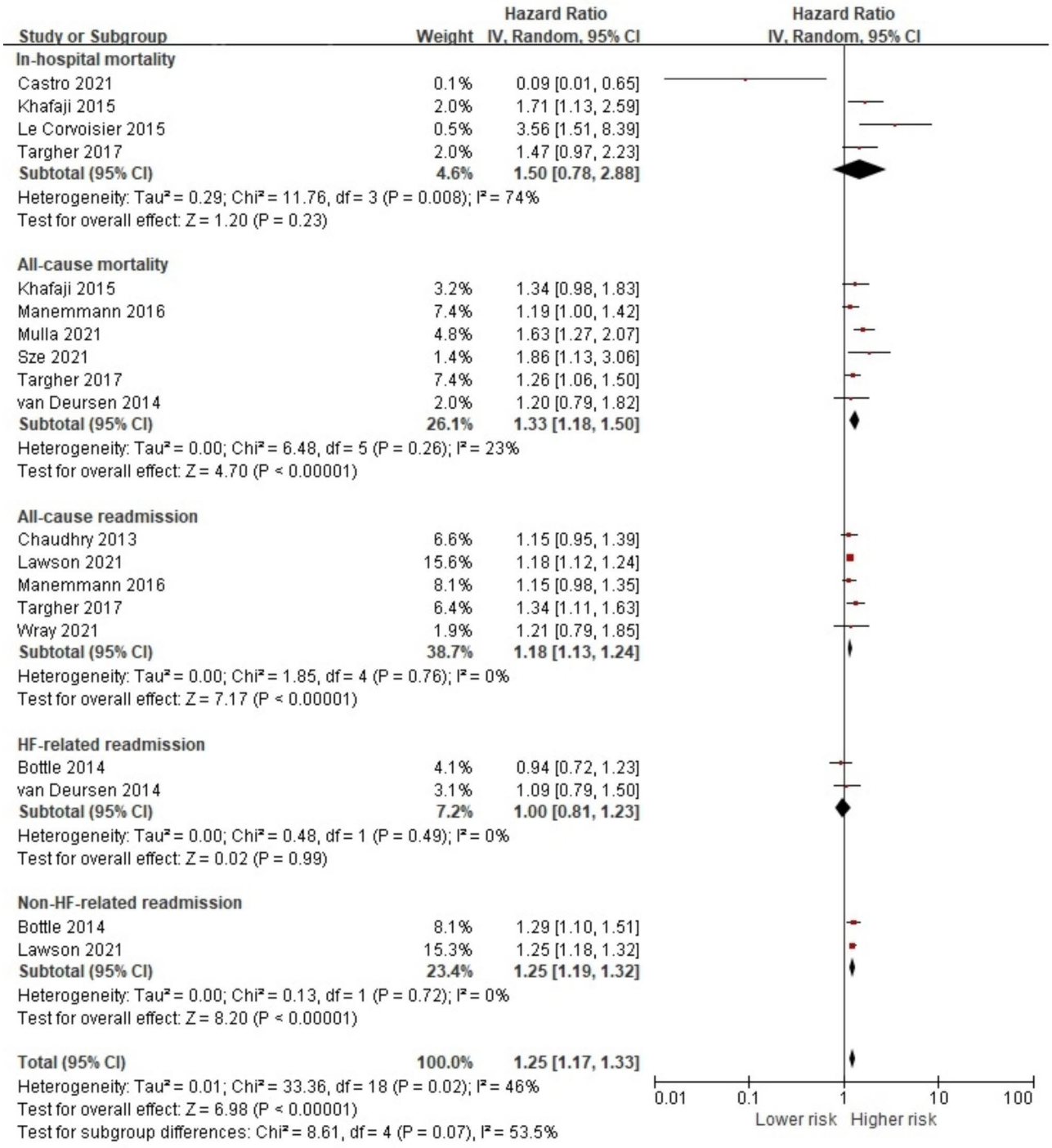

Fig. 6 Forest plot of the pooled analysis evaluating the effect of stroke on health outcomes in heart failure patients

a significant association with all-cause mortality, all-cause readmission, HF-related readmission, and short-term all-cause mortality risk (Fig. 7 and S8). However, HF patients with an HTN diagnosis showed a significantly higher long-term all-cause mortality (HR 1.16, 95% CI 1.01, 1.32, $p=0.03$) but lower risk of HF-related readmission (HR 0.90, 95% CI 0.83, 0.99, $p=0.02$).

We identified 42,773 (34.6%) HF patients with IHD in eight studies that observed the impact of IHD on all-cause mortality [27, 32, 37, 51], all-cause readmission [31, 39] and HF-related readmission [36, 54]. IHD in HF patients increased the risk of the overall prognostic outcome (HR 1.17, 95% CI 1.11, 1.23, $p<0.001$), especially in regard to all-cause readmission (HR 1.21, 95% CI 1.06,

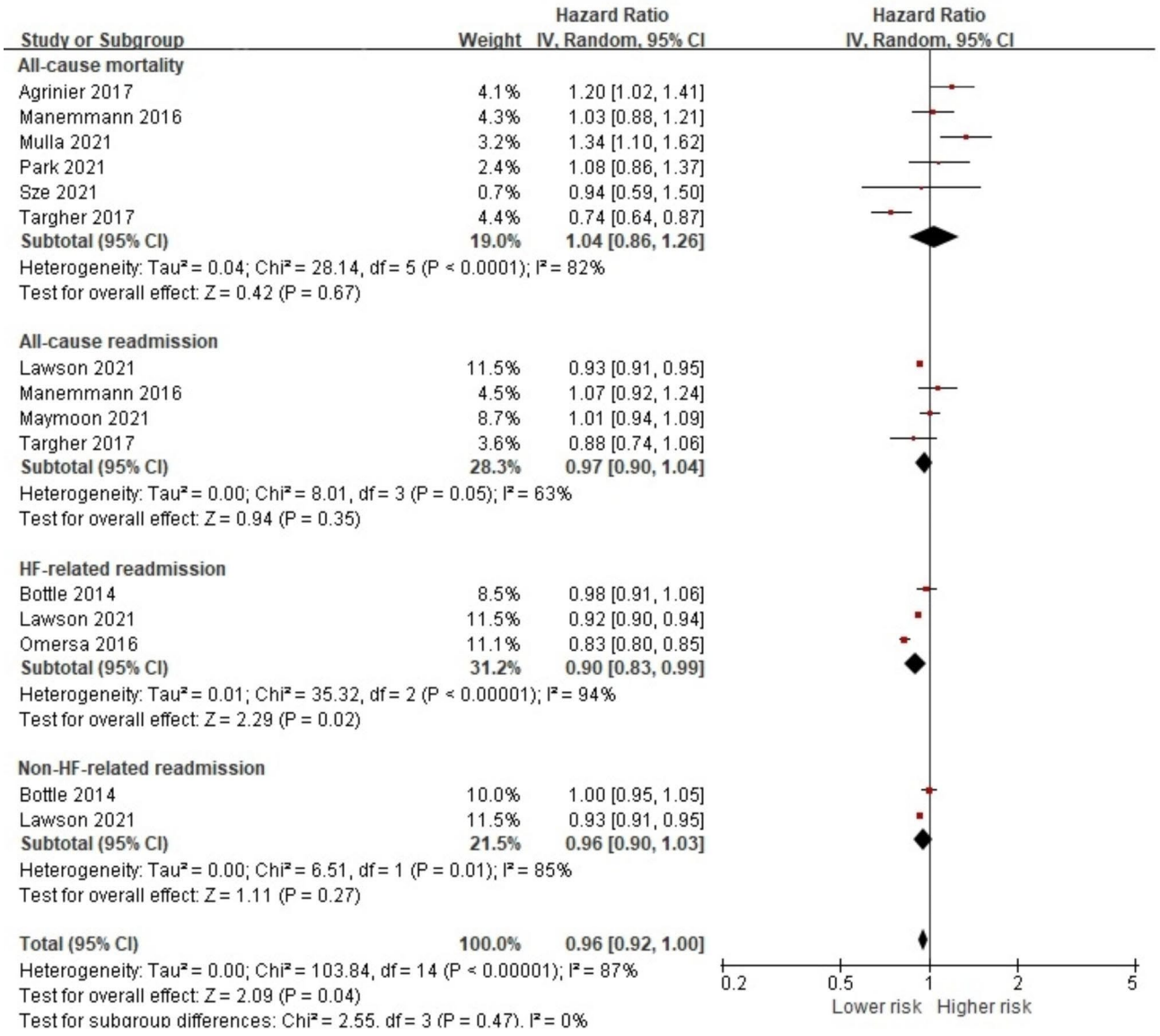

Fig. 7 Forest plot of the pooled analysis evaluating the effect of hypertension on health outcomes in heart failure patients

1.39, $p=0.006$) and HF-related readmission (HR 1.17, 95% CI 1.06, 1.29, $p=0.002$) (Fig. 8). However, it should be noted that only two studies were available for the meta-analysis for all-cause readmission and HF-related readmission. No statistical significance was noted for all-cause mortality and all-cause mortality based on the follow-up period (Fig S9).

A history of anemia (HR 1.42, 95% CI 1.14, 1.78, $p<0.01$) [28, 29, 31, 49, 51, 52, 60], cancer (HR 1.17, 95% CI 1.04, 1.32, $p=0.01$) [29, 36, 39, 42, 56, 60], atrial fibrillation (HR 1.25, 95% CI 1.01, 1.54, $p=0.04$) [31, 32, 35, 37], dementia (HR 1.19, 95% CI 1.03, 1.36, $p=0.02$) [28, 29, 42, 51, 54, 56] and depression (HR 1.17, 95% CI 1.04, 1.31, $p<0.01$) [29, 51, 56] were found to have a significant pooled effect on the overall prognostic outcomes in HF (Figures S10 to S15). However, no significant effect of obesity on prognostic outcomes was noted (HR 0.99, 95% CI 0.98, 1.00) [31, 49, 58]. Few studies reported HRs of arrhythmia [42, 56], arthritis [29, 56], asthma [29, 42, 56] and valvular disease [31, 42] for all-cause readmission. Of these conditions, HF patients who were diagnosed with arrhythmia and arthritis had an increased risk of all-cause readmission (HR 1.18, 95% CI 1.06, 1.31; HR 1.16, 95% CI 1.11, 1.20, respectively) (Fig S16).

Discussion

A total of 42 studies were included in this review, and the results of 39 studies were pooled to perform meta-analyses to calculate the overall effect size of presence of comorbidities on both patient-reported and prognostic

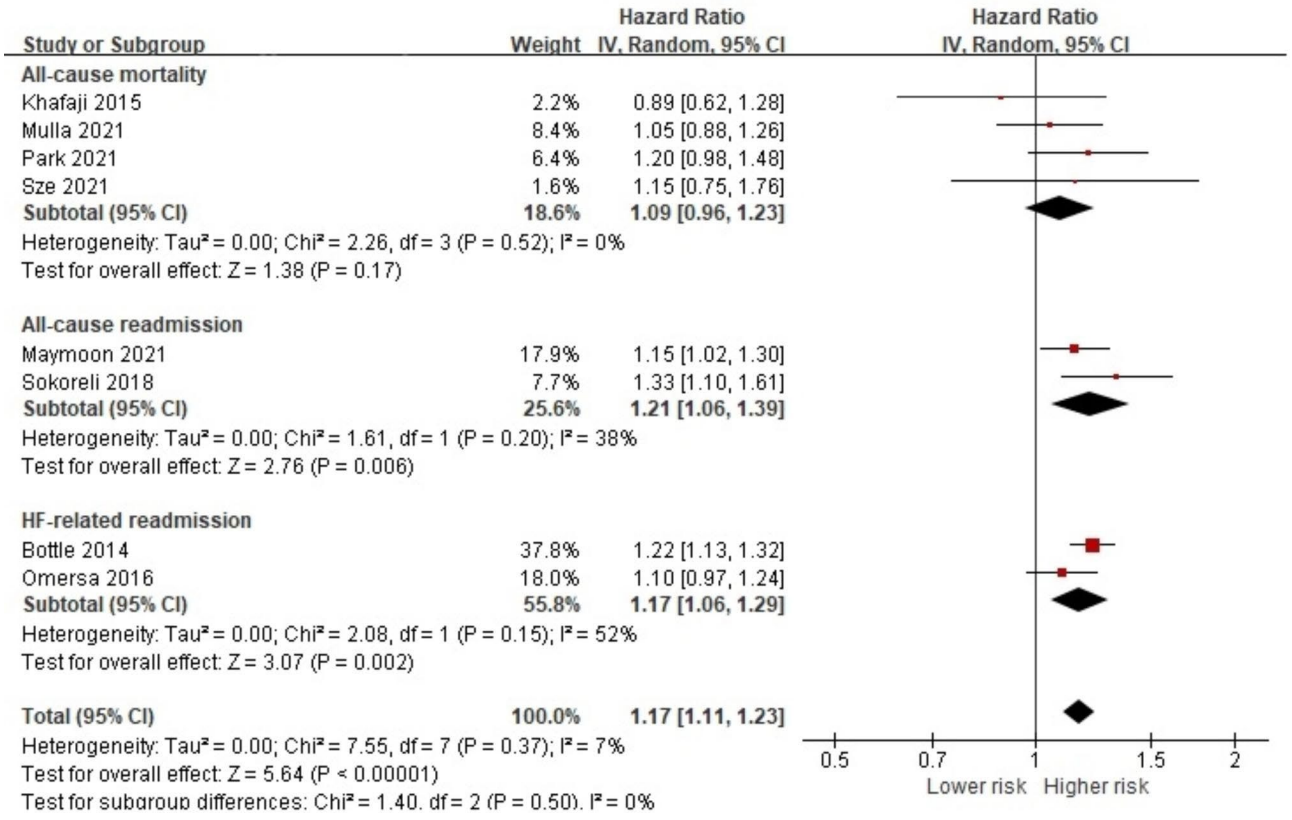

Fig. 8 Forest plot of the pooled analysis evaluating the effect of ischemic heart disease on health outcomes in heart failure patients

health outcomes and to calculate the effect size of individual comorbid condition on health outcomes as well. Due to the small number of studies that evaluated patient-reported outcomes, no significance was noted for the pooled effect size of comorbidities in HF on overall patient-reported outcomes. However, we found that the presence of comorbid conditions to have significant pooled effect on overall prognostic health outcomes. Further evaluation indicated that the presence of comorbidities had a significantly negative effect on all-cause mortality with both the short- and long-term follow-up periods. Although limited data was available to pool effect size of individual comorbid condition on patient-reported outcomes, we identified DM, COPD, CKD, stroke, IHD, anemia, cancer, atrial fibrillation, dementia, and depression to have significant pooled effect on poorer prognostic health outcomes. In addition, arrhythmia and arthritis were found to increase the risk of all-cause readmission.

Although the effect size on overall patient-reported outcomes was not significant, our quantitative analysis showed that the co-occurrence of HF and other chronic conditions is likely to result in poor HRQoL and self-care confidence levels. However, it should be noted that only a few of the included studies have measured patient-reported outcomes; therefore, our results may underrepresent patient-reported outcomes. Patient-reported outcomes include diverse factors that can be measured using various instruments. Because when it comes to patient-reported outcomes, such as HRQoL and self-care, similar outcomes can be measured with different instruments. A similar issue was raised in a previous scoping review, where the authors attempted to pool the effect of comorbidities on quality of life but were unable to do so due to wide variations in assessment methods between studies [64].

A previous meta-analytic study has also indicated that non-cardiovascular comorbidities in HF patients were associated with all-cause mortality (6). However, given that Rushton's review was only able to synthesize studies on mortality, our results further broaden the understanding of the effect of HF comorbidity on patient prognosis. In addition, to the best of our knowledge, no meta-analysis has been conducted to interpret the pooled effect of comorbidities on HF patient outcomes based on the follow-up periods. The results of this review indicate that multimorbidity increases both short- and long-term all-cause mortalities. This is consistent with previous findings that pre-existing or newly acquired comorbid conditions were more likely to be the main contributor to hospital readmission rates or death than HF exacerbation [3, 8, 65]. The results of our review may provide evidence

that those who have survived acute heart conditions and are discharged from hospital settings may struggle to manage HF together with coexisting conditions.

Very few guidelines articulate what chronic conditions to consider when providing care for HF patients. Although recent HF management guidelines by the American Heart Association/American College of Cardiology/Heart Failure Society of America (AHA/ACC/HFSA) have recognized the negative impact and the complexity of managing comorbidity, they do not clearly outline their effects on patient outcomes (66). Rushton's meta-analysis found DM, COPD, and renal dysfunction to be associated with all-cause mortality [6]. Similarly, DM and COPD were only conditions that are included in the Meta-analysis Global Group in Chronic Health Failure (MAGGIC), a relatively recently developed multivariable risk score to predict mortality in HF patients [67]. The developers of the MAGGIC risk scores have examined 30 cohort studies with a total of 39,372 HF patients for prognostic effects and reported that only DM and COPD were consistently included as comorbidity [67]. They also pointed out that of the 30 large cohort studies, the presence of DM was not assessed in one study and COPD was not assessed in 10 studies. In other words, even large-scale HF cohort studies may have overlooked some of the most important prognostic comorbidities.

On the other hand, we identified 32 individual conditions among HF patients from the included studies, and we were able to perform meta-analysis on 16 conditions. Our review found that DM, COPD, CKD, stroke, IHD, anemia, cancer, atrial fibrillation, dementia, depression, arrhythmia and arthritis to be statistically associated with higher mortality and hospital readmission rates in patients with HF. A previous narrative review also mentioned individual comorbid conditions that are associated with poor health outcomes in HF patients [5]. These conditions include all 16 conditions that were identified in the included studies. Although their narrative review also suggested conditions that were not included in our meta-analysis (e.g., thyroid and sleep disorders), they did not provide any quantitative results. It should be noted that although we identified 32 comorbid conditions, a meta-analysis could not be conducted for all conditions due to the lack of sufficient data. For example, only one of the included studies has study examined the effects of thyroid disorders and sleep apnea [52]. Our results suggest that a variety of comorbidities have yet to be investigated when examining the relationship between health outcomes and comorbidities. Also, the results of previous studies and those in our study indicate that among various comorbidities, DM, COPD, and renal dysfunction, especially CKD, may be the most important comorbidities to consider in relation to the prognosis of patients with HF.

Despite the importance of addressing multimorbid conditions in HF patients, this population has been either largely excluded or underrepresented from the most pivotal clinical trials and treatments [4, 5]. Contributing conditions have also been overlooked by researchers and clinicians when caring for the HF population even though this population puts considerable pressure on and presents significant challenges for cost-effective management. Even in some of our included studies, patients were excluded if they were diagnosed with chronic conditions or were receiving treatment for chronic conditions such as CKD [26], thyroid conditions [21], respiratory conditions [44] or psychological conditions [23]. Considering their negative effects on patient health outcomes, management of chronic conditions should be considered when providing care for HF patients.

Having multiple conditions can be a challenge for patients. Because medical systems are often fragmented, patients may have trouble comprehending and adhering to a variety of therapeutic regimens for each condition in a coherent manner. Intervention studies providing care coordination and/or supporting self-care have been effective to reduce the use of health services by patients with multi-morbidities [68, 69]. The need to address effective management of multimorbidity is critical, especially considering that the majority of the HF patients suffer from two or more coexisting chronic conditions.

Several limitations should be taken into consideration. Due to the lack of information in some of the included articles, we could not perform quantitative analyses on all studies due to lack of information. Therefore, some quantitative analyses were conducted based on only two studies, which may have led to heterogeneity between studies. In addition, our summary analyses included substantial heterogeneity, largely due to the observational study design of the included articles. Although the studies were mostly cohort studies with large sample sizes, studies with relatively small sample sizes were also included in the analyses. Although we confirmed a positive correlation between eight chronic conditions and poorer outcomes, it should be noted that this result may be underestimated. For example, COPD in HF is often underdiagnosed because its symptoms are similar to that of HF [9]. Lastly, eligible studies may have been excluded partly due to our inclusion criteria of selecting only publications written in English.

Conclusion

Comorbidities, including cardiovascular and non-cardiovascular related conditions, are very common among HF patients. Healthcare providers must address and provide comprehensive assessment and management of HF including comorbid conditions that negatively affect HF outcomes. Patients with HF must be screened for

comorbidities, especially DM, COPD, CKD, stroke, IHD, anemia, cancer, atrial fibrillation, dementia and depression, given that these conditions are likely to increase the risk of both mortality and hospital readmissions. Prompt and aggressive assessment, diagnosis, treatment, and coordinated care plans for these comorbidities should be reinforced to promote positive prognosis and patient-reported outcomes in the HF population.

List of Abbreviations

HF	Heart failure
PRISMA	The preferred items for systematic reviews and meta-analyses
RoBANS	The risk of bias assessment for non-randomized studies
HR	Hazard ratio
OR	Odds ratio
CI	Confidence interval
HRQoL	Health-related quality of life
DM	Diabetes mellitus
COPD	Chronic obstructive pulmonary disease
CKD	Chronic kidney disease
HTN	Hypertension
IHD	Ischemic heart disease
KCCQ	Kansas City Cardiomyopathy Questionnaire
SCHFI	Self-care of Heart Failure Index
SMD	Standardized mean difference
AHA/ACC/HFSA	American Heart Association/American College of Cardiology/Heart Failure Society of America
MAGGIC	Meta-analysis Global Group in Chronic Health Failure

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-023-03527-x.

Supplementary Material 1

Acknowledgements
All authors would like to thank the medical librarian for her help in establishing database-specific search strategies.

Author' contributions
KSL and DP designed the study; KSL, DP, JL, OO and NK conducted database searches and screened the data; DP, JL, OO and GN extracted the data, DP analyzed the data; and KSL and DP prepared and scientifically revised the manuscript. All authors reviewed and approved the final manuscript.

Funding
This work was supported by the National Research Foundation of Korea (NRF) grants funded by the Korea government (MSIT) (2021R1C1C100849812), the BK21 FOUR project (Center for Human-Caring Nurse Leaders for the Future) funded by the Ministry of Education (MOE, Korea) and the NRF, and the 2022 Hannam University Research Fund.

Data Availability
The data that support the findings of the study are available from individual included study, and the datasets analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Received: 2 May 2023 / Accepted: 21 September 2023
Published online: 10 October 2023

References

1. Tsao CW, Aday AW, Almarzooq ZI, Alonso A, Beaton AZ, Bittencourt MS, et al. Heart Disease and Stroke Statistics-2022 update: a Report from the American Heart Association. Circulation. 2022;145(8):e153–e639.
2. Okumura T, Sawamura A, Murohara T. Palliative and end-of-life care for heart failure patients in an aging society. Korean J Intern Med. 2018;33(6):1039–49.
3. Stewart S, Riegel B, Boyd C, Ahamed Y, Thompson DR, Burrell LM, et al. Establishing a pragmatic framework to optimise health outcomes in heart failure and multimorbidity (ARISE-HF): a multidisciplinary position statement. Int J Cardiol. 2016;212:1–10.
4. Dharmarajan K, Dunlay SM. Multimorbidity in older adults with heart failure. Clin Geriatr Med. 2016;32(2):277–89.
5. Stewart S, Riegel B, Thompson DR. Addressing the conundrum of multimorbidity in heart failure: do we need a more strategic approach to improve health outcomes? Eur J Cardiovasc Nurs. 2016;15(1):4–7.
6. Rushton CA, Satchithananda DK, Jones PW, Kadam UT. Non-cardiovascular comorbidity, severity and prognosis in non-selected heart failure populations: a systematic review and meta-analysis. Int J Cardiol. 2015;196:98–106.
7. Braunstein JB, Anderson GF, Gerstenblith G, Weller W, Niefeld M, Herbert R, et al. Noncardiac comorbidity increases preventable hospitalizations and mortality among Medicare beneficiaries with chronic heart failure. J Am Coll Cardiol. 2003;42(7):1226–33.
8. Kwok CS, Seferovic PM, Van Spall HG, Helliwell T, Clarson L, Lawson C, et al. Early unplanned readmissions after admission to Hospital with Heart failure. Am J Cardiol. 2019;124(5):736–45.
9. Correale M, Paolillo S, Mercurio V, Ruocco G, Tocchetti CG, Palazzuoli A. Non-cardiovascular comorbidities in heart failure patients and their impact on prognosis. Kardiol Pol. 2021;79(5):493–502.
10. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71.
11. Kim SY, Park JE, Lee YJ, Seo HJ, Sheen SS, Hahn S, et al. Testing a tool for assessing the risk of bias for nonrandomized studies showed moderate reliability and promising validity. J Clin Epidemiol. 2013;66(4):408–14.
12. Greenland S. Quantitative methods in the review of epidemiologic literature. Epidemiol Rev. 1987;9:1–30.
13. Verdu-Rotellar JM, Calero E, Abellana R, Verdu-Soriano J, Vinyoles E, Del Val-Garcia JL, et al. Short-term mortality in end-stage heart failure patients. Aten Primaria. 2020;52(7):477–87.
14. Dong G, Chen H, Zhang H, Gu Y. Long-term and short-term Prognostic Value of circulating Soluble suppression of Tumorigenicity-2 concentration in Chronic Heart failure: a systematic review and Meta-analysis. Cardiology. 2021;146(4):433–40.
15. Gu L, Li J. Short-term and long-term prognostic value of circulating soluble suppression of tumorigenicity-2 concentration in acute coronary syndrome: a meta-analysis. Biosci Rep. 2019;39(6).
16. Borenstein M, Hedges LV, Higgins JP, Rothstein HR. A basic introduction to fixed-effect and random-effects models for meta-analysis. Res Synth Methods. 2010;1(2):97–111.
17. Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. Stat Med. 2002;21(11):1539–58.
18. Polit DF, Beck CT. Nursing research: Generating and assessing evidence in nursing practice. 10th ed. ed. Philadelphia, PA: Lippincott Williams & Wilkins; 2016.
19. Adams J, Kuchibhatla M, Christopher EJ, Alexander JD, Clary GL, Cuffe MS, et al. Association of depression and survival in patients with chronic heart failure over 12 years. Psychosomatics. 2012;53(4):339–46.
20. Agrinier N, Thilly N, Briancon S, Juilliere Y, Mertes PM, Villemot JP, et al. Prognostic factors associated with 15-year mortality in patients with hospitalized systolic HF: results of the observational community-based EPICAL cohort study. Int J Cardiol. 2017;228:940–7.

21. Bannay RA, Husain A, Agarwal SK, AlHaiki W. Clinical characteristics of Acute Heart failure patients. Bahrain Med Bull. 2018;40(1):26–30.
22. Castro RRT, Lechnewski L, Homero A, Albuquerque DC, Rohde LE, Almeida D, et al. Acute hemodynamic index predicts In-Hospital mortality in Acute Decompensated Heart failure. Arq Bras Cardiol. 2021;116(1):77–86.
23. Chamberlain L. Perceived social support and self-care in patients hospitalized with heart failure. Eur J Cardiovasc Nurs. 2017;16(8):753–61.
24. Echouffo-Tcheugui JB, Xu H, DeVore AD, Schulte PJ, Butler J, Yancy CW, et al. Temporal trends and factors associated with diabetes mellitus among patients hospitalized with heart failure: findings from get with the Guidelines-Heart failure registry. Am Heart J. 2016;182:9–20.
25. Franco J, Formiga F, Corbella X, Conde-Martel A, Llacer P, Alvarez Rocha P, et al. De novo acute heart failure: clinical features and one-year mortality in the spanish nationwide Registry of Acute Heart failure. Med Clin (Barc). 2019;152(4):127–34.
26. Huang W, Chai SC, Lee SGS, MacDonald MR, Leong KTG. Prognostic factors after Index hospitalization for heart failure with preserved ejection fraction. Am J Cardiol. 2017;119(12):2017–20.
27. Khafaji HA, Sulaiman K, Singh R, AlHabib KF, Asaad N, Alsheikh-Ali A, et al. Clinical characteristics, precipitating factors, management and outcome of patients with prior stroke hospitalised with heart failure: an observational report from the Middle East. BMJ Open. 2015;5(4):e007148.
28. Korda RJ, Du W, Day C, Page K, Macdonald PS, Banks E. Variation in readmission and mortality following hospitalisation with a diagnosis of heart failure: prospective cohort study using linked data. BMC Health Serv Res. 2017;17(1):220.
29. Lawson C, Crothers H, Remsing S, Squire I, Zaccardi F, Davies M, et al. Trends in 30-day readmissions following hospitalisation for heart failure by sex, socioeconomic status and ethnicity. EClinicalMedicine. 2021;38:101008.
30. Le Corvoisier P, Bastuji-Garin S, Renaud B, Mahe I, Bergmann JF, Perchet H, et al. Functional status and co-morbidities are associated with in-hospital mortality among older patients with acute decompensated heart failure: a multicentre prospective cohort study. Age Ageing. 2015;44(2):225–31.
31. Maymon SL, Moravsky G, Marcus G, Shuvy M, Pereg D, Epstein D, et al. Disparities in the characteristics and outcomes of patients hospitalized with acute decompensated heart failure admitted to internal medicine and cardiology departments: a single-centre, retrospective cohort study. ESC Heart Fail. 2021;8(1):390–8.
32. Mulla W, Klempfner R, Natanzon S, Mazin I, Maizels L, Abu-Much A, et al. Female gender is associated with a worse prognosis amongst patients hospitalised for de-novo acute heart failure. Int J Clin Pract. 2021;75(4):e13902.
33. Munoz-Rivas N, Jimenez-Garcia R, Mendez-Bailon M, Hernandez-Barrera V, de Miguel-Diez J, Lorenzo-Villalba N, et al. Type 2 diabetes increases the risk of hospital admission for heart failure and reduces the risk of in hospital mortality in Spain (2001–2015). Eur J Intern Med. 2019;59:53–9.
34. Nayar P, Yu F, Chandak A, Kan GL, Lowes B, Apenteng BA. Risk factors for In-Hospital mortality in heart failure patients: does Rurality, Payer or Admission Source Matter? J Rural Health. 2018;34(1):103–8.
35. Ogah OS, Stewart S, Falase AO, Akinyemi JO, Adegbite GD, Alabi AA, et al. Predictors of rehospitalization in patients admitted with heart failure in Abeokuta, Nigeria: data from the Abeokuta heart failure registry. J Card Fail. 2014;20(11):833–40.
36. Omersa D, Farkas J, Erzen I, Lainscak M. National trends in heart failure hospitalization rates in Slovenia 2004–2012. Eur J Heart Fail. 2016;18(11):1321–8.
37. Park JH, Hwang IC, Park JJ, Park JB, Cho GY. Prognostic power of left atrial strain in patients with acute heart failure. Eur Heart J Cardiovasc Imaging. 2021;22(2):210–9.
38. Sharma A, Zhao X, Hammill BG, Hernandez AF, Fonarow GC, Felker GM, et al. Trends in Noncardiovascular Comorbidities among Patients hospitalized for heart failure: insights from the get with the Guidelines-Heart failure Registry. Circ Heart Fail. 2018;11(6):e004646.
39. Sokoreli I, Pauws SC, Steyerberg EW, de Vries GJ, Riistama JM, Tesanovic A, et al. Prognostic value of psychosocial factors for first and recurrent hospitalizations and mortality in heart failure patients: insights from the OPERA-HF study. Eur J Heart Fail. 2018;20(4):689–96.
40. van den Berge JC, van Vark LC, Postmus D, Utens E, Hillege HL, Boersma E, et al. Determinants of quality of life in acute heart failure patients with and without comorbidities: a prospective, observational study. Eur J Cardiovasc Nurs. 2022;21(3):205–12.
41. Wakabayashi K, Sato N, Kajimoto K, Minami Y, Mizuno M, Keida T, et al. Incidence and predictors of in-hospital non-cardiac death in patients with acute heart failure. Eur Heart J Acute Cardiovasc Care. 2017;6(5):441–9.
42. Wray CM, Vali M, Walter LC, Christensen L, Chapman W, Austin PC, et al. Examining the association of social risk with heart failure readmission in the Veterans Health Administration. BMC Health Serv Res. 2021;21(1):874.
43. Ausili D, Rebora P, Di Mauro S, Riegel B, Valsecchi MG, Paturzo M, et al. Clinical and socio-demographic determinants of self-care behaviours in patients with heart failure and diabetes mellitus: a multicentre cross-sectional study. Int J Nurs Stud. 2016;63:18–27.
44. Bektas S, Franssen FME, van Empel V, Uszko-Lencer N, Boyne J, Knackstedt C, et al. Impact of airflow limitation in chronic heart failure. Neth Heart J. 2017;25(5):335–42.
45. Bottle A, Kim D, Hayhoe B, Majeed A, Aylin P, Clegg A, et al. Frailty and co-morbidity predict first hospitalisation after heart failure diagnosis in primary care: population-based observational study in England. Age Ageing. 2019;48(3):347–54.
46. Chaudhry SI, McAvay G, Chen S, Whitson H, Newman AB, Krumholz HM, et al. Risk factors for hospital admission among older persons with newly diagnosed heart failure: findings from the Cardiovascular Health Study. J Am Coll Cardiol. 2013;61(6):635–42.
47. Comin-Colet J, Anguita M, Formiga F, Almenar L, Crespo-Leiro MG, Manzano L, et al. Health-related quality of life of patients with chronic systolic heart failure in Spain: results of the VIDA-IC study. Rev Esp Cardiol (Engl Ed). 2016;69(3):256–71.
48. Drozd M, Relton SD, Walker AMN, Slater TA, Gierula J, Paton MF, et al. Association of heart failure and its comorbidities with loss of life expectancy. Heart. 2021;107(17):1417–21.
49. Ebner N, Jankowska EA, Ponikowski P, Lainscak M, Elsner S, Sliziuk V, et al. The impact of iron deficiency and anaemia on exercise capacity and outcomes in patients with chronic heart failure. Results from the Studies investigating co-morbidities aggravating heart failure. Int J Cardiol. 2016;205:6–12.
50. Matsuoka S, Tsuchihashi-Makaya M, Kayane T, Yamada M, Wakabayashi R, Kato NP, et al. Health literacy is independently associated with self-care behavior in patients with heart failure. Patient Educ Couns. 2016;99(6):1026–32.
51. Sze S, Pellicori P, Zhang J, Weston J, Clark AL. The impact of malnutrition on short-term morbidity and mortality in ambulatory patients with heart failure. Am J Clin Nutr. 2021;113(3):695–705.
52. van Deursen VM, Urso R, Laroche C, Damman K, Dahlstrom U, Tavazzi L, et al. Co-morbidities in patients with heart failure: an analysis of the European Heart failure pilot survey. Eur J Heart Fail. 2014;16(1):103–11.
53. Zaharova S, Litwack K, Gopalakrishnan S, Ellis J, Saltzberg MT. Self-management in Heart failure: the importance of self-regulation but not complexity of Condition. West J Nurs Res. 2022;44(4):375–82.
54. Bottle A, Aylin P, Bell D. Effect of the readmission primary diagnosis and time interval in heart failure patients: analysis of English administrative data. Eur J Heart Fail. 2014;16(8):846–53.
55. Lee KS, Moser DK, Pelter MM, Nesbitt T, Dracup K. Self-care in rural residents with heart failure: what we are missing. Eur J Cardiovasc Nurs. 2017;16(4):326–33.
56. Manemann SM, Chamberlain AM, Boyd CM, Gerber Y, Dunlay SM, Weston SA, et al. Multimorbidity in Heart failure: Effect on Outcomes. J Am Geriatr Soc. 2016;64(7):1469–74.
57. Streng KW, Nauta JF, Hillege HL, Anker SD, Cleland JG, Dickstein K, et al. Non-cardiac comorbidities in heart failure with reduced, mid-range and preserved ejection fraction. Int J Cardiol. 2018;271:132–9.
58. Targher G, Dauriz M, Laroche C, Temporelli PL, Hassanein M, Seferovic PM, et al. In-hospital and 1-year mortality associated with diabetes in patients with acute heart failure: results from the ESC-HFA heart failure Long-Term Registry. Eur J Heart Fail. 2017;19(1):54–65.
59. Voors AA, Ouwerkerk W, Zannad F, van Veldhuisen DJ, Samani NJ, Ponikowski P, et al. Development and validation of multivariable models to predict mortality and hospitalization in patients with heart failure. Eur J Heart Fail. 2017;19(5):627–34.
60. Wienbergen H, Pfister O, Hochadel M, Fach A, Backhaus T, Bruder O, et al. Long-term effects of iron deficiency in patients with heart failure with or without anemia: the RAID-HF follow-up study. Clin Res Cardiol. 2019;108(1):93–100.
61. Ma C. Rehospitalisation rates and associated factors within 6 months after hospital discharge for patients with chronic heart failure: a longitudinal observational study. J Clin Nurs. 2019;28(13–14):2526–36.
62. Pantilat SZ, O'Riordan DL, Rathfon MA, Dracup KA, De Marco T. Etiology of Pain and its Association with Quality of Life among patients with heart failure. J Palliat Med. 2016;19(12):1254–9.

63. Tromp J, Tay WT, Ouwerkerk W, Teng TK, Yap J, MacDonald MR, et al. Correction: Multimorbidity in patients with heart failure from 11 asian regions: a prospective cohort study using the ASIAN-HF registry. PLoS Med. 2018;15(5):e1002583.
64. Comin-Colet J, Martin Lorenzo T, Gonzalez-Dominguez A, Oliva J, Jimenez Merino S. Impact of non-cardiovascular comorbidities on the quality of life of patients with chronic heart failure: a scoping review. Health Qual Life Outcomes. 2020;18(1):329.
65. Siga O, Wizner B, Piotrowicz K, Fedyk-Lukasik M, Grodzicki T. The prevalence and determinants of multimorbidity in hospitalized patients with heart failure. Folia Med Cracov. 2017;57(2):73–86.
66. Heidenreich PA, Bozkurt B, Aguilar D, Allen LA, Byun JJ, Colvin MM, et al. 2022 AHA/ACC/HFSA Guideline for the management of Heart failure: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2022;145(18):e895–e1032.
67. Pocock SJ, Ariti CA, McMurray JJ, Maggioni A, Kober L, Squire IB, et al. Predicting survival in heart failure: a risk score based on 39 372 patients from 30 studies. Eur Heart J. 2013;34(19):1404–13.
68. Boult C, Reider L, Leff B, Frick KD, Boyd CM, Wolff JL, et al. The effect of guided care teams on the use of health services: results from a cluster-randomized controlled trial. Arch Intern Med. 2011;171(5):460–6.
69. Gonzalez-Ortega M, Gene-Badia J, Kostov B, Garcia-Valdecasas V, Perez-Martin C. Randomized trial to reduce emergency visits or hospital admissions using telephone coaching to complex patients. Fam Pract. 2017;34(2):219–26.

Publisher's Note