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REVIEW

Mortality and Readmission Rates After Heart Failure: A Systematic Review and Meta-Analysis

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Objective: The current work aimed to examine the rates of and risk factors for mortality and readmission after heart failure (HF).

Setting: A systematic search was carried out in PubMed, the Cochrane Library, and EMBASE to identify eligible reports. The random-effects model was utilized to evaluate the pooled results.

Participants: A total of 27 studies with 515,238 participants were finally meta-analysed. The HF patients had an average age of 76.3 years, with 51% of the sample being male, in the pooled analysis.

Primary and Secondary Outcome Measures: The outcome measures were 30-day and 1-year readmission rates, mortality, and risk factors for readmission and mortality.

Results: The effect sizes for readmission and mortality were estimated as the mean and 95% confidence interval (CI). The estimated 30-day and 1-year all-cause readmission rates were 0.19 (95% CI 0.14–0.23) and 0.53 (95% CI 0.46–0.59), respectively, while the all-cause mortality rates were 0.14 (95% CI 0.10–0.18) and 0.29 (95% CI 0.25–0.33), respectively. Comorbidities were highly prevalent in individuals with HF.

Conclusion: Heart failure hospitalization is followed by high readmission and mortality rates.

Keywords: heart failure, meta-analysis, prevalence, readmission, mortality, hospitalization

Background

Heart failure (HF) represents a global public health threat. The effect of HF on the elderly population is disproportionate. Even assuming that the incidence for a specific age, sex, or ethnicity is stable, heart failure prevalence shows a steady elevation over the next 20 years,[1] mainly in association with population ageing.[2] Epidemiological changes in usual risk factors for heart failure may influence the above prediction. Even if the incidence for a specific age, sex, or race remains stable, the prevalence rates of hypertension and coronary heart disease would rise due to demographic changes.[3] Meanwhile, the incidence rates of obesity[4] and diabetes[5] for specific ages, sexes, and races are also expected to increase, and the increased prevalence rates of these risk factors may further elevate the prevalence of HF. As a result, heart failure remains a substantial and growing public health burden. According to available data in Europe and the United States,[2–6] the prevalence of heart failure ranges from 1% to 14%. When all adults are included, heart failure is considered a chronic debilitating disease regardless of age.[2,5]

In other developed countries, the one-year mortality rate after hospitalization for HF is 25%-30%,[7] which is higher than those of many common cancers.[8] The

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prevalence of heart failure increases with age.[9,10] In addition, heart failure is the main cause of hospitalization in individuals over 64 years of age.[11] The treatment of heart failure is important for improving the prognosis of patients and reducing health system expenditures.[12] In addition, the in-hospital mortality rate of HF patients is relatively low; however, high rates of death and readmission are found after discharge.[13]

Readmission constitutes a common negative result for health care facilities and patients and a huge financial burden imposed on medical insurance beneficiaries and private payers.[11] Decreased 30-day readmission and 30-day hospital mortality rates are weak but significantly correlated.[14] From 2001–2003 to 2009–2011, the 30-day readmission rate following myocardial infarction declined from 20.5% to 15.8%, although the trend decreased slightly upon adjustment for patient features and treatments.[15] Predicting the risk factors for and causes of 30-day rehospitalization would help optimize the allocation of meagre medical resources and design profitable and viable interventions.[16,17]

However, multiple previous trials have been conducted in single centres with few patients, with inconsistent readmission and mortality rates in heart failure patients. For instance, 30-day readmission rates for heart failure in previous reports ranged between 4.3% and 30.4%.[18–28] Based on the above, further assessing the prevalence and potential causes of and risk factors for readmission is of prime importance. Therefore, this meta-analysis aimed to examine the prevalence of readmission after HF, as well as the potential risk factors for and causes of HF. In addition, we discussed potential intervention approaches for mitigating the risk of readmission after HF.

Methods

Search Strategy

Two independent medical librarians systematically searched three electronic databases, including PubMed,

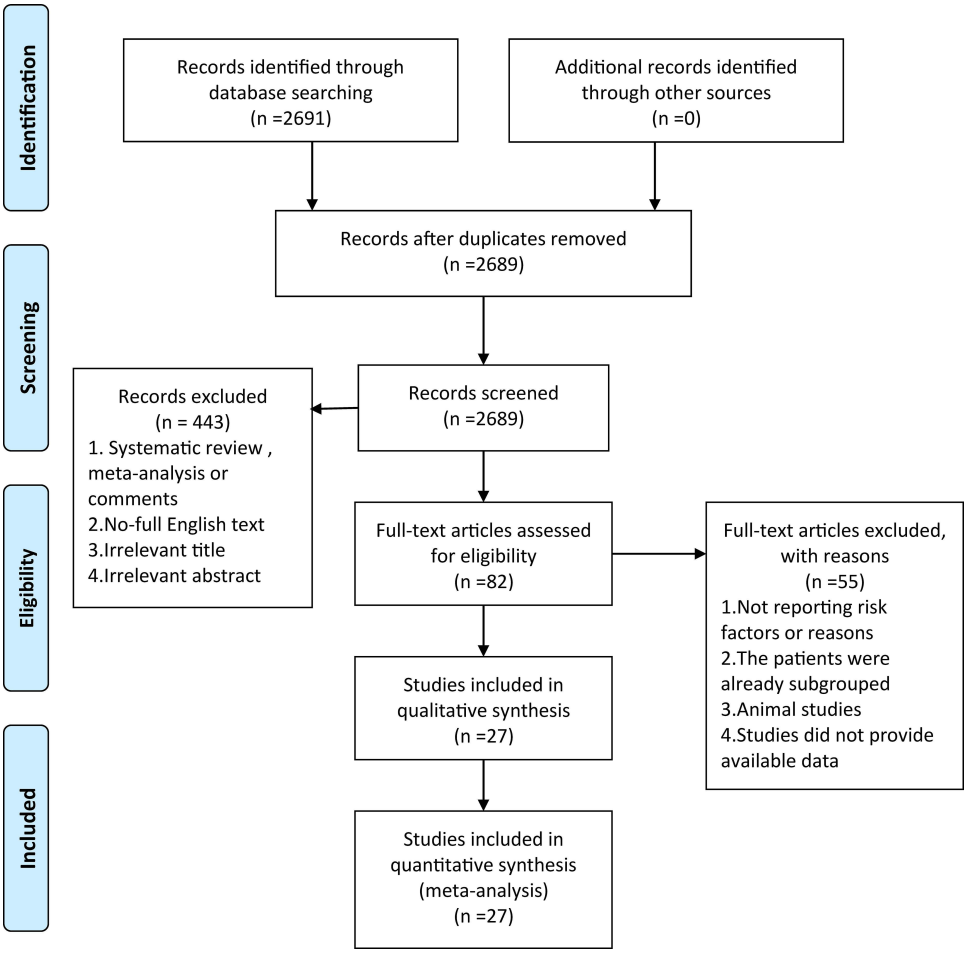

Figure 1 Flow diagram of the study.

Table 1 Characteristics of Included Studies

Author (Year)	Country	Study Period	Method of HF Diagnosis	Data Source	Study Type	Study Population
Aizawa H 2015[18]	Japan	2012.4.1–2013.3.31	ICD-10	DPC database	Retrospective cohort study	≥15
Arenja N 2011[32]	Switzerland	2001.5–2002.4, 2006.4–2007.3	Two independent cardiologists	University Hospital of Basel	Prospective study	–
Babayan ZV 2003[33]	USA	1996.1.1–1997.12.31	Modified Framingham criteria	Johns Hopkins Hospital	Retrospective cohort	–
Bradford C 2016[19]	USA	2008.10–2014.11	ICD-9-CM	Sharp Memorial Hospital	Retrospective observational study	–
Chaudhry SI 2010[34]	USA	1998.4–1999.3, 2000.7–2001.6	ICD-9-CM	Medicare	–	–
Choi DJ 2011[35]	Korea	2004.6–2009.4	Framingham criteria	KorHF Registry database	–	–
Coles AH 2015[36]	USA	1995, 2000, 2002, 2004, 2006	Framingham criteria, ICD-9	Massachusetts medical centers	–	–
Corrao G 2015[20]	Italy	2011	ICD-9	HCU Databases	Retrospective cohort study	≥50
Costa D 2018[37]	Argentina	2016.6.1–2017.5.31	Framingham criteria	University Hospital in Buenos Aires	Prospective, observational study	–
Dai S 2016[21]	USA	–	–	Florida Hospital	Prospective study	20~89
Eapen ZJ 2013[38]	USA	2005.1–2009.12	ICD-9	CMS	–	≥65
Fernandez-Gasso L 2017[22]	Spain	2003–2013	ICD-9	Minimum Basic Set discharge registry	Retrospective observational study	–
Formiga F 2018[39]	Spain	2012.1–2014.12	Framingham criteria	Bellvitge University Hospital	–	>70
Golas SB 2018[23]	USA	2014.10~2015.9	ICD-9-CM	PHS	Retrospective study	≥18
Harikrishnan S 2017[40]	India	2013–2014	European Society of HF	THFR	–	–
Leong KT 2007[41]	Singapore	2003.11.10–2004.4.10	Modified Framingham criteria	Changi General Hospital	Observational prospective study	–
Mavrea AM 2015[42]	Romania	2013.1.1–2013.12.31	LVEF	Timisoara City Hospital	Prospectively	–

(*Continued*)

Table 1 (Continued).

Author (Year)	Country	Study Period	Method of HF Diagnosis	Data Source	Study Type	Study Population
McLaren DP 2016[24]	USA	2007.1.1–2007.12.31	ICD-9	Rochester Medical Center	Retrospective	≥18
Mwita JC 2017[43]	South Africa	2014.2–2015.2	–	PMH	Observational study	≥18
Reynolds K 2015[44]	USA	2008–2011	ICD-9-CM	KPNW, Kaiser Permanente Georgia	Retrospective cohort	–
Rudiger A 2005[45]	European	2001.12–2003.2	Physicians	University Hospital of Zurich, Helsinki University Central Hospital	Prospective study	–
Siirila-Waris K 2006[46]	England	2004.2.2–2004.5.30	ESC AHF guideline criteria	Hospitals in Finland	Prospective multicenter study	–
Stampehl M 2019[47]	USA	2010.1.1–2014.12.31	ICD-9-CM	Medicare	Retrospective study	–
Sterling MR 2018[25]	USA	2011–2015	–	Vanderbilt University Medical Center	Prospective observational study	≥18
Tuppin P 2013[26]	France	2009	ICD-10	SNIIRAM	–	–
Whittaker BD 2014[27]	USA	2009.7.1–2010.6.30	ICD-9	Core Measures databases	Retrospective cohort study	≥18
Wiley JF 2017[28]	Australia	–	Cardiologist	Multicenter RCT	RCT	≥18

Abbreviations: ICD-10, Codes of the 10th Revision of the International Statistical Classification of Diseases; DPC, Diagnosis Procedure Combination; ICD-9-CM, International Classification of Diseases-9th Revision-Clinical Modification codes; KorHF, Korean Heart Failure; ICD-9, International Classification of Diseases 9th Revision codes; HCU, Healthcare Utilization; CMS, Centers for Medicare and Medicaid Services; PHS, Partners Healthcare System; HF, Heart Failure; THFR, Trivandrum Heart Failure Registry; LVEF, Left Ventricular Ejection Fraction; PMH, Princess Marina Hospital; KPNW, Kaiser Permanente Northwest; ESC, European Society of Cardiology; AHF, Acute heart failure; SNIIRAM, National Health Insurance Information System; RCT, randomized controlled trial.

Web of Science, and the Cochrane Library. All articles published in English were obtained before May 26, 2019. The Keywords/terms were "Heart Failure", "Patient Readmission" and "Mortality".

Selection Criteria

Two investigators performed screening of all titles and abstracts in an independent fashion, retrieving and evaluating the retrieved studies based on full texts. In the final analysis, studies selected for inclusion must have provided data for 30-day and/or 1-year readmission or mortality in hospitalized individuals with HF. Studies were excluded for the following reasons: 1) Did not report risk factors or causes; 2) had already subgrouped patients; 3) were cell culture or animal studies; 4) provided no available data; 5) had a small sample size (<100); and 6) was a systematic review, meta-analysis, case report or comments. In the case of patient cohort overlap, studies with the longest follow-up were included.

Data Extraction and Methodological Quality Assessment

To facilitate the data extraction process, two researchers generated a standardized form and independently extracted the data. From all eligible articles, the extracted information included the first author, year, country, study period, method of HF diagnosis and data source, study design, study population, sample size, demographic features, 30-day and 1-year readmission rates, mortality, and risk factors for readmission and mortality.

Study quality was evaluated based on the Critical Appraisal of the Health Research Literature[29] taking into account the sample size, sample design, sampling frame, study and setting, measures, unbiased assessors, response rate and refusers, and prevalence rates. Each item was given a score. A study with a total score below 6 was considered to be of low quality; otherwise, it was considered to be of high quality (≥6).

Statistical Analysis

The estimated effect sizes for readmission and mortality are expressed as the mean and 95% confidence interval (CI). The random-effects model was used to pool 30-day and 1-year mortality or readmission rates across studies, as well as the mean age, sex, and comorbidities.[30] Heterogeneity was assessed by I^2 statistics. Subgroup analysis was carried out based on the region, study population, and study quality to determine the sources of heterogeneity. The median and interquartile range for age were converted to the mean and standard deviation (SD) as previously proposed.[31] Inverse funnel plots were generated to visually assess publication bias. STATA/SE 15.1 was utilized for data analysis.

Patient and Public Involvement Statement

No patients were involved.

Results

Study Characteristics

In total, 2691 articles were reviewed for titles/abstracts, and 2609 articles were excluded. The remaining 27 reports were further assessed. The flow diagram of the study selection process is shown in Figure 1. We identified 27 studies included in this meta-analysis that reported 30-day and 1-year readmission data and mortality after HF,[18–28,32–47] including 1 trial conducted in

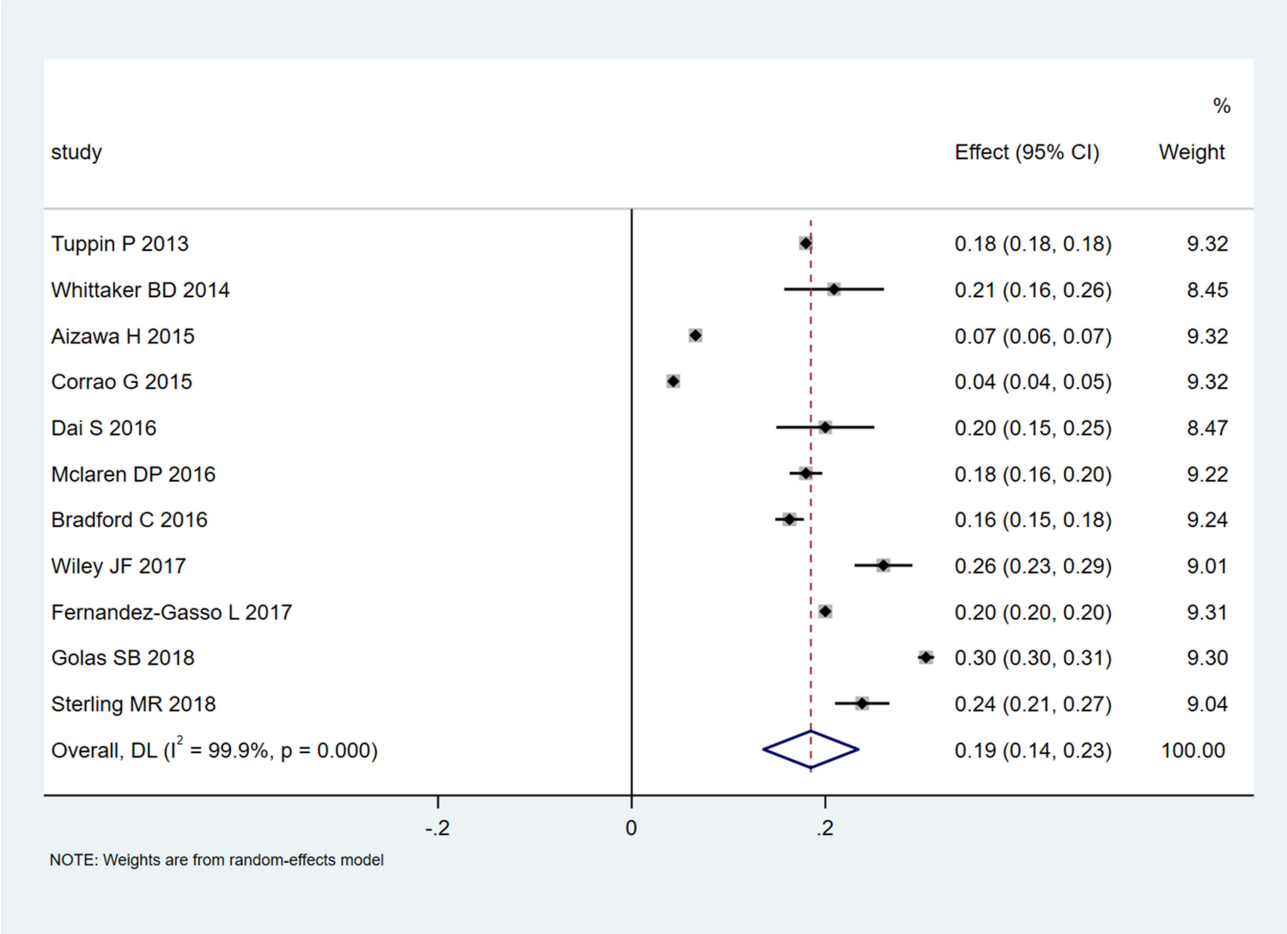

Figure 2 Meta-analysis of 30-day readmission rates.

Japan,[18] 12 in the US,[19,21,23–25,27,33,34,36,38,44,47] 1 in Italy,[20] 2 in Spain,[22,39] 1 in India,[40] 1 in Singapore,[41] 1 in Romania,[42] 1 in France,[26] 1 in Australia,[28] 1 in Switzerland,[32] 1 in Korea,[35] 1 in Argentina,[37] 1 in South Africa,[43] 1 in Europe[45] and 1 in England.[46] The total number of participants was 515,238. Two articles reported both mortality and readmission rates, eleven reported mortality only, and fourteen assessed readmissions only. Ten and four studies were single centre and multicentre trials, respectively, and 13 assessed data from a large national database (Table 1). Twenty-one and 8 studies were of low and high quality, respectively (Tables S1 and S2).

30-Day and 1-Year Readmission Rates

A pooled 30-day readmission rate of 0.19 (95% CI 0.14–0.23; Figure 2) was recorded in 11 studies that included 194,161 patients. Heterogeneity was extremely high (I^2=99.9%, P<0.001), and the funnel plot displayed asymmetry. Then, the studies were grouped by region, sample size, and quality for the subgroup analysis (Table S2). The rate was reduced for the non-American region (0.15, 95% CI 0.08–0.21) compared with the American region (0.22, 95% CI, 0.15–0.28) at 30 days (Table S3). The 30-day readmission rates in studies with sample sizes<10,000 (0.21, 95% CI 0.18–0.24) and high quality (score ≥6; 0.22, 95% CI 0.16–0.27) were higher than those for trials with sample sizes>10,000 (0.16, 95% CI 0.09–0.23) and low quality (score<6; 0.17, 95% CI 0.11–0.23). For 1-year readmissions, the results were similar. The rate was lower for the non-American region (0.50, 95% CI 0.31–0.68) than for the American region (0.59, 95% CI 0.56–0.62, Table S4). However, the 1-year admission rate was lower in studies with sample sizes <10,000 (0.49, 95% CI 0.30–0.69) compared with those with sample sizes >10,000 (0.59, 95% CI 0.56–0.61). Only one study had a quality assessment score above 6.

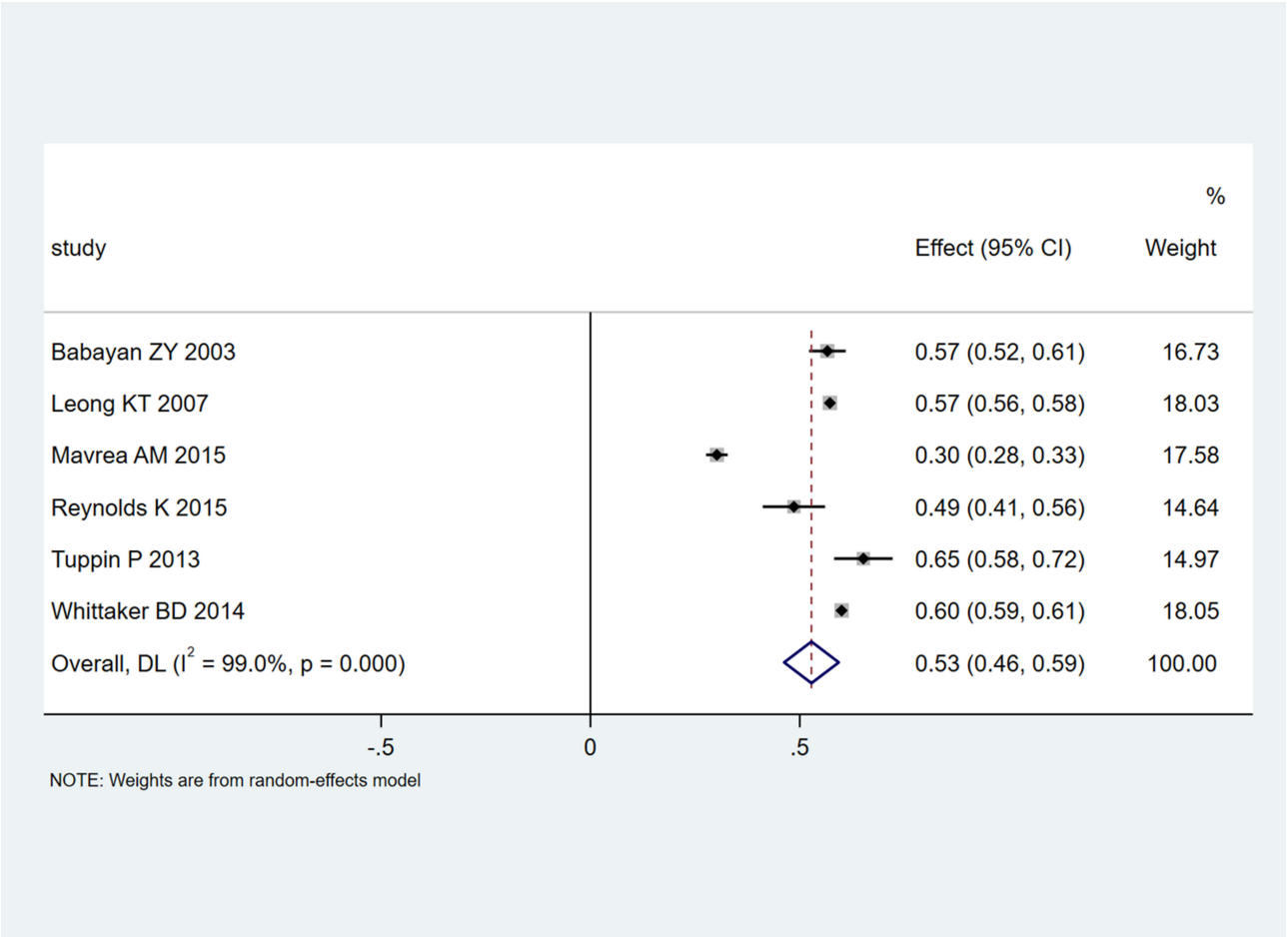

Figure 3 Meta-analysis of 1-year readmission rates.

Table 2 Risk Factors for Readmission

Author (Year)	Age	Male	DM	HTN	IHD	CKD	AF	COPD	EF	HF Type	Beta-Blockers	ACEI/ ARB	AA	Diuretics	Digoxin	LOS	30-Day Readmission/ Total Patients	1-Year Readmission/ Total Patients
Aizawa H 2015[18]		36,313 (53.2)									26,825 (39.3)	38,292 (56.1)	23,890 (35)	53,309 (78.1)	7850 (11.5)	19 (Median)	4479/68,257 (6.56)	
Babayan ZY 2003[33]		236 (47.87)	199 (40.37)	344 (69.78)			96 (19.47)	166 (33.67)										279/493 (56.6)
Bradford C 2016[19]	72	1331 (55)	721 (29.8)		56 (2.3)	1087 (44.9)		1031 (42.6)									394/2420 (16.28)	
Corrao G 2015[20]	79.3 (9.5)	6103 (46.3)			CAD 2081 (15.8)	886 (6.7)	2441 (18.5)	RD 2459 (18.7)			5537 (42)	8739 (66.4)	1163 (8.8)	6334 (48.1)		12.0 (10.3)	566/13,171 (4.3)	7534/13,171 (57.2)
Dai S 2016[21]		173 (72.1)	129 (53.75)	194 (80.83)	165 (68.75)			54 (22.5)	≤40%	Decompensated HF	233 (97.08)	135 (56.25)	121 (50.4)	208 (86.6)			48/240 (20)	
Fernandez-Gasso L 2017[22]	76.9	10,601 (43)	814 (3.3)	3156 (12.8)													4938/24,654 (20)	
Golas SB 2018[23]	75.7	6073 (52.8)	2470 (21.46)	4293 (37.3)		3004 (26.1)					4949 (43)	4259 (37)		6909 (60)			3502/11,510 (30.4)	
Harikrishnan S 2017[40]	61.2 (13.7)	831 (69)	662 (54.94)	696 (57.76)	866 (71.87)	216 (17.93)	177 (14.69)	186 (15.44)										333/1205 (30.2)
Leong KT 2007[41]	68.7	89 (51.4)	87 (50.3)	117 (67.6)		81 (46.8)	29 (16.5)				72 (41.6)	130 (75.1)	63 (36.4)	155 (89.6)	33 (19.1)			84/173 (48.55)
Mavrea AM 2015[42]	64.6	98 (55)	57 (32.02)	136 (76.4)	CAD 108 (60.67)	CKD 87 (48.88)	70 (39.33)	44 (24.72)		HFpEF	152 (85.39)		129 (72.4)	129 (72.4)				116/178 (65.17)
McLaren DP 2016[24]	68.2 (15.6)	1175 (59)		714 (36)	718 (36)		784 (39)									7.9 ± 15.2	366/1999 (18)	
Reynolds K 2015[44]	73.9	10,541 (52.9)	9326 (46.8)	17,077 (85.7)	CAD 9047 (45.4)	CKD 12415 (62.3)					10,003 (50.2)	9206 (46.2)		9386 (47.1)	2013 (10.1)			11,956/19,927 (60)
Sterling MR 2018[25]	60	477 (54)	377 (44)		CAD 375 (43)			COPD 242 (27.4)	40 (15, 60)								210/883 (23.8)	

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Table 2 (Continued).

Author (Year)	Age	Male	DM	HTN	IHD	CKD	AF	COPD	EF	HF Type	Beta-Blockers	ACEI/ ARB	AA	Diuretics	Digoxin	LOS	30-Day Readmission/ Total Patients	1-Year Readmission/ Total Patients
Tuppin P 2013[26]	78	33,580 (48)	13,852 (19.8)	6996 (1)	CAD 10704 (15.3)						27,703 (39.6)	39,176 (56)		41,835 (59.8)		9	12,592/69,958 (18)	
Whittaker BD 2014[27]	59 (17)	148 (61.9)	88 (36.8)	117 (49)	CHD 90 (37.7)	119 (49.8)		COPD 43 (18.0)				119 (49.8)				9.7 ± 14.9	50/239 (20.9)	
Wiley JF 2017[28]	73 (13)	540 (65)	510 (61)	590 (71)	CAD 494 (60)			RD 409 (49)		CHF							216/830 (26)	

Abbreviations: DM, Diabetes Mellitus; HTN, Hypertension; IHD, Ischemic Heart Disease; CKD, Chronic Kidney Disease; AF, Atrial Fibrillation; COPD, Chronic Obstructive Pulmonary Disease; EF, Ejection Fraction; HF, Heart Failure; ACEI/ARB, Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers; AA, Aldosterone Antagonist; LOS, Length Of Stay; CAD, Coronary Artery Disease; RD, Respiratory Disease; HFpEF, Heart Failure with preserved Ejection Fraction; CHD, Coronary Heart Disease; CHF, Chronic Heart Failure.

Six studies with 35,147 patients reported 1-year readmission rates. A pooled 1-year readmission rate of 0.53 (95% CI 0.46–0.59; Figure 3) was obtained, with significant heterogeneity among the trials (I^2=99%, P<0.001).

Risk Factors for Readmission

Fourteen risk factors were revealed by ≥2 trials by multivariate analysis. Common comorbidities, including kidney disease, diabetes, chronic obstructive pulmonary disease (COPD), and cardiac arrhythmia, were tightly associated with elevated 30-day readmission rates. Table 2 depicts all the risk factors for readmission.

30-Day and 1-Year Mortality Rates

A pooled 30-day mortality rate of 0.14 (95% CI 0.10–0.18; Figure 4) in 7 studies that included 317,128 participants was found. Heterogeneity was extremely high (I^2=99.9%, P<0.001), and the funnel plot showed asymmetry. The results of the subgroup analyses were not significantly different for 30-day mortality rates (Table S5). It is worth noting that heterogeneity for studies with a sample size<10,000 was low (I^2=23%). The 1-year mortality rate for the non-American region (0.28, 95% CI 0.25–0.32) was reduced in comparison with the American rate (0.31, 95% CI 0.31–0.31; I^2=0%) (Table S6).

A pooled 1-year mortality rate of 0.29 (95% CI 0.25–0.33; Figure 5) was obtained in 10 studies that included 231,019 participants. Heterogeneity was extremely high (I^2=98.8%, P<0.001), and the funnel plot showed asymmetry.

Risk Factors for Mortality

Fifteen risk factors were revealed by the multivariable analysis in 2 or more trials (Table 3). The risk factors for 30-day mortality included ischaemic heart disease (IHD) in 4 studies. The use of beta-blockers was positively correlated with elevated readmission rates in 3 trials. Meanwhile, a history of lung disease was negatively correlated with readmission in 3 trials.

Heterogeneity Analysis

The results of this study may be more than expected based on chance alone, with a P ≤0.10 in the heterogeneity test. Given the potential statistical heterogeneity, we formed a hypothesis before conducting the above

analysis, which may help explain the differences in the results: differences in intervention methods, such as telephone follow-up, home visits, and heart failure clinic visits, may explain the variability leading to the differences in the results.

Discussion

This was the first comprehensive systematic review and meta-analysis of 30-day and 1-year readmission and mortality rates following HF. Readmission and mortality mostly resulted from cardiac and noncardiac factors. Nonspecific chest pain was the top noncardiac cause of readmission, while cardiac factors encompassed angina and acute ischaemic heart disease, chest pain, etc. In addition, kidney disease, female sex, diabetes mellitus, chronic obstructive pulmonary disease (COPD), and HF were the major predictive factors of early readmission,[48] which may provide a possible correct direction for reducing the readmission rate of HF patients. Among the 13,171 newly hospitalized HF patients, respiratory disease accounted for 18.7%, arrhythmia accounted for 18.5%, coronary/aortic disease accounted for 15.8%, and renal dysfunction accounted for 6.7%.[20] The 3 most common reasons for readmission were HF (36.0%), renal disorders (8.4%), and other cardiac diseases (6.9%).[19] In addition, comparing the baseline patients and clinical characteristics of the readmission and nonrehospitalization HF patient groups, COPD and renal disease accounted for the majority of readmissions.[19]

The results indicated that the 30-day readmission rate recorded in 11 studies was 0.19 (95% CI 0.14–0.23; Figure 2). Our findings corroborate the data from other nations. For instance, 30-day HF readmission rates after HF hospitalization in the USA and France are both 18%.[24,26] Meanwhile, the 1-year HF readmission and 30-day mortality rates in South Africa are 14.7%.[43] Most of

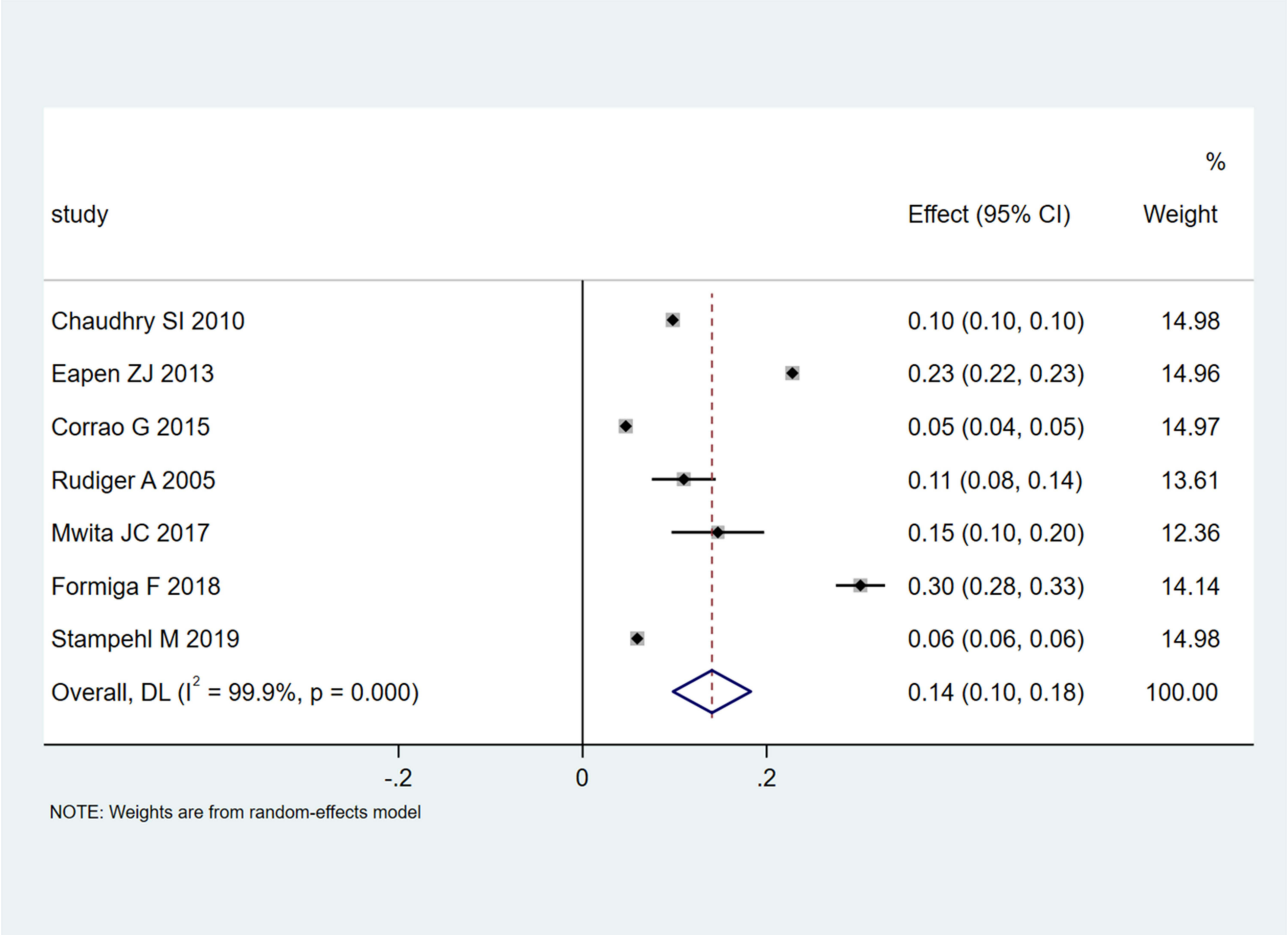

Figure 4 Meta-analysis of 30-day mortality rates.

the articles reported similar data for 1-year all-cause mortality, ie, 29%.[32,34,36,38–40,43,45–47] The careful management of HF outpatients who are elderly, high disease severity, multiple comorbidities, or taking beta-blockers, loop diuretics, thiazide, or nitrates when discharged from the hospital may be critical to reducing the 30-day readmission.[18]

In some studies assessed in this meta-analysis, the authors identified multiple predictive factors of readmission, including age[18,20,21] and clinical comorbidities.[20,33,40–42] Some reports revealed multiple parameters that increased 30-day readmission rates, including elevated New York Heart Association functional class (NYHA) and Charlson Comorbidity Index (CCI) and treatment with beta-blockers, loop diuretics, thiazide, or nitrates.[18] In addition, retired and/or disabled patients had one or more emergency room visits in the last 3 months, hospitalization durations above 5 days, and BUN levels >45 mg/dL at discharge.[19] However, only one study reported that age, sex, race, marital status, payer type, and multiple patient features did not predict readmission in their model from Bradford et al.[19]

This study had limitations. First, due to limited data, the original causes or comorbidities of CHF patients are not yet clear. Second, multiple risk factors for and/or causes of readmission had no clear definitions, and various reports classified and grouped the causes and risk factors differently with variable definitions of the parameters, which were hardly combined for the meta-analysis. Finally, the studies were highly heterogeneous. Most reports had incomplete datasets, and subgroup analyses could not be performed for all variables.

Conclusions

We found that multiple diseases are very common in hospitalized chronic HF patients. In addition, the increase in recurrent diseases itself was shown to be parallel to an elevated all-cause 30-day readmission

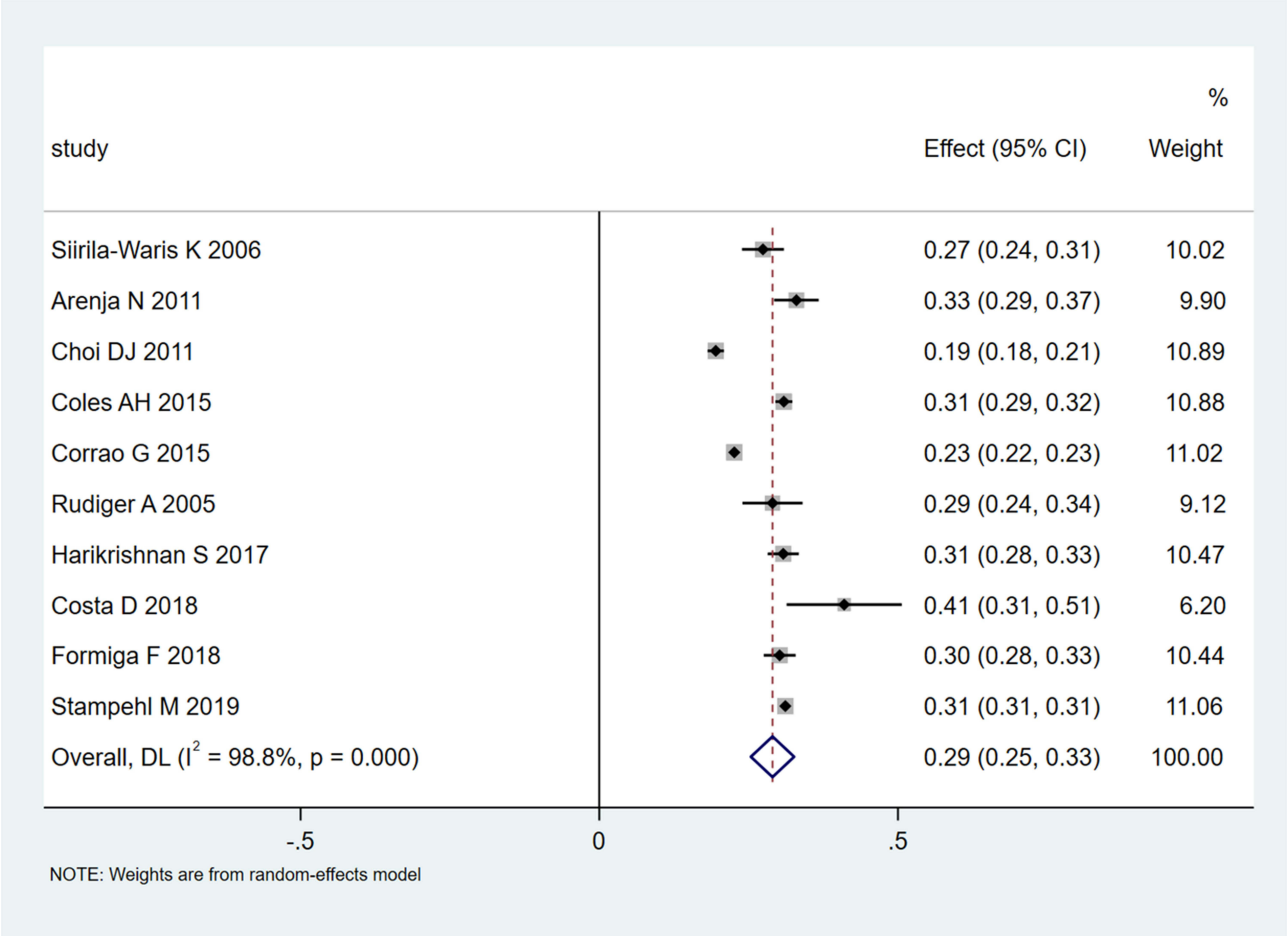

Figure 5 Meta-analysis of 1-year mortality rates.

Table 3 Risk Factors for Mortality

Author (Year)	Age	Male	DM	HTN	IHD	CKD	AF	CLRD	EF	HF Type	Beta-Blockers	ACEI/ ARB	AA	Diuretics	Digoxin	LOS	COPD	30-Day Mortality/ Total Patients	1-Year Mortality/ Total Patients
Arenja N 2011[32]	82 (median)	330 (54)	180 (30)	430 (71)	–	243 (39)	–	–	–	AHF	357 (61)	440 (76)	–	475 (82)	Digitalis 51 (9)	–	154 (25)	–	201/610 (33)
Chaudhry SI 2010[34]	79.6 (7.8)	25,867 (41.5)	24,745 (39.7)	39,704 (63.7)	CAD35653 (57.2)	–	–	–	–	–	–	–	–	–	–	–	21,379 (34.3)	6124/62,330 (9.8)	–
Choi DJ 2011[35]	67.6 (14.3)	1600 (50)	975 (30.5)	1486 (46.5)	1544 (52.3)	295 (9.2)	–	104 (3.5)	38.5 ±15.70	–	1109 (58.6)	648 (53.7)	913 (53.1)	1982 (68.1)	Inotropic agents 711 (21.7)	–	1289 (32.2)	–	625/3200 (0.195)
Coles AH 2015[36]	75	1771 (44)	1493 (37.1)	2874 (71.4)	CHD 2028 (50.4)	1027 (25.5)	1453 (36.1)	–	–	ADHF	2290 (56.9)	2228 (55.4)	255 (6.34)	3201 (79.5)	1423 (35.4)	–	403 (10)	–	1245/4025 (30.9)
Corrao G 2015[20]	79.3 (9.5)	6103 (46.3)	–	–	CAD 2081 (15.8)	886 (6.7)	Arrhythmia 2441 (18.5)	RD 2459 (18.7)	–	–	5537 (42)	8739 (66.4)	1163 (8.8)	6334 (48.1)	–	12.0 (10.3)	–	619/13,171 (4.7)	2977/13,171 (22.6)
Costa 2018[37]	77 (13.4)	56 (56)	36%	78%	–	–	33%	–	–	AHF	60%	63%	24%	–	3%	–	–	–	41/100 (41)
Eapen ZJ 2013[38]	80 (74, 86)	15, 221 (45.6)	13, 002 (39.7)	24, 673 (75.3)	20, 308 (60.9)	–	11, 817 (36.1)	–	43 (30, 55)	–	–	–	–	–	–	–	–	7020/33,349 (22.8)	–
Formiga F 2018[39]	81.6	484 (42.8)	460 (40.6)	978 (86.4)	CAD 267 (23.6)	298 (26.3)	444 (39.2)	–	–	AHF	539 (47.6)	586 (51.8)	164 (14.5)	–	–	–	267 (23.6)	117/1132 (10.3)	342/1132 (30.2)
Harikrishnan S 2017[40]	61.2 (13.7)	831 (69)	662	696	866	216	177	–	–	–	–	–	–	–	–	–	186	–	371/1205 (0.308)
Mwita JC 2017[43]	54.2 (17.1)	104 (53.9)	30 (15.5)	106 (54.9)	11 (5.7)	–	19 (9.8)	–	41.8 (20)	AHF	124 (72.1)	126 (73.2)	-	148 (86)	38 (22.1)	9medium	-	28/190 (14.7)	–
Rudiger A 2005[45]	73 (12)	176 (56.4)	100 (32.1)		78 (25)	–	91 (29.2)	–	–	AHF	–	–	–	–	–	–	–	34/312 (11)	90/312 (29)
Siirila- Waris K 2006[46]	75.1 (10.4)	312 (50.4)	32.3	54.7	CAD 55.2	9.4	29.4	–	–	–	–	–	–	–	–	–	12.6	–	170/620 (27.4)

(*Continued*)

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Table 3 (Continued).

Author (Year)	Age	Male	DM	HTN	IHD	CKD	AF	CLRD	EF	HF Type	Beta-Blockers	ACEI/ARB	AA	Diuretics	Digoxin	LOS	COPD	30-Day Mortality/Total Patients	1-Year Mortality/Total Patients
Stampehl M 2019[47]	80.5 (11.2)	79, 076 (39.3)	107, 540 (52.0)	199, 439 (96.5)	753 (0.4)	102, 546 (49.6)	113, 163 (54.8)	–	–	–	–	–	–	–	–	–	92,688 (44.9)	12,278/ 206,644 (5.94)	64,363/ 206,644 (31.15)

Abbreviations: DM, Diabetes Mellitus; HTN, Hypertension; IHD, Ischemic Heart Disease; CKD, Chronic Kidney Disease; AF, Atrial Fibrillation; CLRD, Chronic Lower Respiratory Disease; EF, Ejection Fraction; HF, Heart failure; ACEI/ARB, Angiotensin-Converting Enzyme Inhibitors/Angiotensin Receptor Blockers; AA, Aldosterone Antagonist; LOS, Length of Stay; COPD, Chronic Obstructive Pulmonary Disease; AHF, Acute Heart Failure; CHD, Coronary Heart Disease; ADHF, Acute Decompensated Heart Failure; CAD, Coronary Artery Disease; RD, Respiratory Disease.

rate. This is a major problem for individuals and the health care system as a whole. Based on the present evidence of common comorbid disease clusters in chronic HF, the development and testing of new interventions tailored to patients in each cluster may be a key direction for future clinical trials.

Data Sharing Statement

No additional data available.

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Disclosure

The authors declare that they have no conflict of interest.

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