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Bidirectional association between cardiovascular disease and hip fracture: a systematic review and meta-analysis

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Abstract

Background The aim of this study was to comprehensively analyze the bidirectional association between cardiovascular disease (CVD) and hip fracture (HF).

Methods We searched PubMed, EMBASE, Web of Sciences, Cochrane Library, ScienceDirect and China National Knowledge Infrastructure for relevant studies. The Newcastle-Ottawa scale was used to evaluate the risk of bias. We conducted random effects model for meta-analysis and subgroup analysis of different ethnic groups. Sensitivity analysis and publication bias of this study were also evaluated. This study followed the PRISMA and MOOSE guidelines for systematic reviews and meta-analyses.

Results This research included 18 cohort studies and case-control studies with a total sample of 1,854,441 individuals. The results showed ischemic heart disease might increase the risk of HF (OR = 1.41, 95%CI[1.05, 1.89], I^2 = 96%). Stroke might be a risk factor for HF (OR = 2.23, 95%[1.18, 4.19], I^2 = 97%), and HF might likewise be a risk factor for Stroke (OR = 2.22, 95% CI [1.81, 2.71], I^2 = 78%). Heart failure might increase the risk of HF (OR = 2.89, 95%CI [1.22, 6.85], I^2 = 91%), and HF might increase the risk of heart failure (OR = 2.74, 95%CI [1.27, 5.89], I^2 = 92%). Hypertension might increase the risk of HF (OR = 1.55, 95%CI[1.34, 1.8], I^2 = 87%), and HF might increase the risk of hypertension (OR = 3.75, 95%CI[3.3, 4.26], I^2 = 98%). Cerebrovascular disease (OR = 1.96, 95%CI[1.61, 2.4], I^2 = 79%) and diseases of arteries, arterioles, and capillaries (OR = 1.58, 95%CI[1.49, 1.68], I^2 = 0%) might increase the risk of HF. HF might increase the risk of myocardial infarction (OR = 2, 95%CI[1.17, 3.41], I^2 = 97%) and CVD-related death (OR = 1.78, 95%CI[1.05, 3.02], I^2 = 50%). Subgroup analyses showed that among Asians IHD might not raise the risk of HF (OR = 1.33, 95% CI [1.00, 1.78], I^2 = 95%). In caucasians, IHD might also not raise HF risk (OR = 1.52, 95%CI [0.64, 4.56], I^2 = 95%).

Conclusions This study supports possible bidirectional associations between CVD and HF, but more mechanistic studies of CVD and HF were warranted. However, high heterogeneity and potential confounding by unmeasured variables warrant cautious interpretation.

Keywords CVD, Hip fracture, Meta-analysis, Systematic review, Risk

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Introduction

Hip fracture (HF) is an emerging public health problem in an aging society with high morbidity and mortality [1, 2]. The 1-year mortality rate for patients with HF has been reported to be as high as 20–24%, and the risk of death may persist for more than 5 years [3, 4]. In our previous research showed that the incidence and prevalence of femur fractures in war-conflict zones and East Asia were on an upward trend from 1990 to 2019, with a significant increase in years of disability survival for femur fractures in populous countries, while predictive modeling suggested that in 2020–2030, although the global femur fracture incidence would decline, prevalence and disability living years would rise.

Cardiovascular disease (CVD) is likewise a significant threat to population health, with the burden of CVD reporting a 77.12% increase of CVD from 31.31 million in 1990 to 55.45 million in 2019, and a 53.81% increase in deaths from 12.07 million in 1990 to 18.56 million in 2019 [5, 6]. CVD and HF are common diseases in the elderly, and although they are two separate diseases, they share many common mechanisms [7, 8]. Bone and blood vessel formation are regulated by several common factors, and calcification of blood vessel walls resembles the process of bone formation in many ways. CVD and HF share common risk factors, such as poorer health, poor lifestyle, nutritional problems, hormonal secretion and metabolic disorders, vitamin D deficiency, and abnormal levels of inflammatory factors [9, 10].

Over the past two decades, the association between CVD and HF has gradually attracted the attention of scholars all over the world. While prior studies explored unidirectional associations, the bidirectional relationship remains understudied despite shared pathophysiology and overlapping risk factors. Investigating this reciprocity could inform integrated clinical management strategies. Previous researches reviewed CVD and HF, or conducted meta-analysis on the association between Stroke, Heart failure and HF independently. So far, there was no a quantitative and comprehensive analysis of the bidirectional association between CVD and HF. Therefore, we conducted the present meta-analysis and systematic review. While shared confounders like age, frailty, and polypharmacy may influence both CVD and HF, our analysis adjusts for these variables where possible, though residual confounding remains a limitation.

Methods

We conducted a systematic review and meta-analysis of the bidirectional association between CVD and HF based on a large sample of observational studies. This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [11, 12] and Meta-analysis of Observational Studies in Epidemiology (MOOSE) [13, 14] guidelines. We also registered this study with the International Platform of Registered Systematic Review and Meta-analysis Protocols (No. INPLASY2023110090).

Data sources and literature search

Two authors independently searched PubMed, EMBASE, Web of Sciences, Cochrane Library, ScienceDirect and China National Knowledge Infrastructure (CNKI) for relevant studies from 2000 to 2023. The search strategy was to combine the MeSH keywords "cardiovascular disease" OR "CVD", "Hip fracture" OR "Femur fracture" were combined, and other relevant MeSH keywords were also searched. If two authors disagreed with the inclusion, a third independent author was involved in the inclusion process. We also included relevant references from retrieved literature. There were no country or language restrictions on the included studies.

Inclusion criteria contained: [1] study was original; [2] the study design was a case-control, cohort, or nested case-control study; [3] the study was on the association between CVD and HF; [4] the study individual was human; and [5] the results reported relative risk (RR), odds ratio (OR), or hazard ratio (HR), or provided raw data that could be used to calculate OR.

Exclusion criteria contained: [1] studies were excluded if they were reviews, editorials, commentaries, case reports, or letters; [2] the results did not report the association between CVD and HF; and [3] animal and cellular experiments were not included in this study.

Data extraction and quality assessment

We extracted the following information from the included studies: study design, name of the first author, year of publication, country, gender, age, sample size and study period. Meanwhile, we extracted the risk estimates of CVD and HF, including adjusted hazard ratio (HR), adjusted risk ratio (RR), and adjusted odds ratio (OR) as well as 95% confidence intervals (95%CI). Newcastle-Ottawa scale (NOS) was used to assess the risk of bias of the included studies, including the following eight domains: representativeness of the exposed cohort, selection of the unexposed cohort, identification of the exposure, outcome of concern not present at the start of the study, comparability of cohorts, assessment of the outcome, duration of follow-up, and adequacy of cohort follow-up. There is limited cross-sectional study on this topic, and case-control and cohort study were better association evidence than cross-sectional study.

Statistical analysis

This study used the Higgins I^2 statistic to measure heterogeneity of included studies. When Heterogeneity was classified as low (I^2 < 25%), moderate (25–50%), or high

(I^2 > 50%) [12]. For random-effects meta-analyses, the restricted maximum likelihood (REML) estimator was used to calculate between-study variance. To account for uncertainty in heterogeneity estimation, the Knapp-Hartung adjustment was applied to all random-effects models, yielding conservative confidence intervals. Subgroup analyses by ethnicity were pre-specified to address potential population heterogeneity. However, subgroup analyses by age was not conducted since the age from included articles were between 70 and 80, which were similar. Gender subgroup analysis was not conducted because of the data limitation. Sensitivity analyses were performed using Leave-one-out plot to identify sources of heterogeneity. Publication bias was assessed using funnel plot, Begg's test, and Egger's test. All analyses in this study were performed using the R language (R Core Team, version 3.5.2, Vienna, Austria), and $P<0.05$ represented a statistically significance.

Results

Characteristics and quality of included articles

We initially searched a total of 2,674 literatures related with topic. According to the inclusion and exclusion criteria, after removing duplicates, unqualified data, we ended up with 18 literatures [15–32] (Fig. 1). Among the 18 literatures, 8 were case-control studies, 8 were cohort studies, and 2 were nested case-control studies. There were totaling 18,544,441 samples with 828,974 males and 10,254,667 females, with a mean age range from 55 to 86. The study publication was from 2007 to 2017, and study follow-up was from 1979 to 2015 (Table 1). We assessed the quality of the included literature using NOS scale, and all the literature scored between 7 and 8, which had good quality (STable 1).

Bidirectional association of CVD and HF

For ischemic heart disease (IHD), 5 papers reported IHD affecting HF, but no study reported the effect of HF on IHD. Four out of 5 studies considered IHD as a risk factor for HF. Despite the high heterogeneity of the meta-analysis, the results were meaningful in showing that IHD might increase the risk of HF (OR = 1.41, 95% CI [1.05, 1.89]) (Fig. 2).

Eight studies reported a bidirectional association between stroke and HF. Three studies suggested that stroke might increase the risk of HF, and similarly three papers suggested that HF might increase the risk of stroke. Meta-analysis showed that Stroke might be a risk factor for HF (OR = 2.23, 95% [1.18, 4.19]), and that HF was similarly may be a risk factor for Stroke (OR = 2.22, 95%CI [1.81, 2.71]) (Fig. 3).

Regarding the association between heart failure and HF, 2 studies reported that heart failure might raise the risk of HF (OR = 2.89, 95%CI [1.22, 6.85]). Meanwhile, 2 studies suggested that HF might raise the risk of heart failure (OR = 2.74, 95%CI [1.27, 5.89]) (Fig. 4).

Concerning hypertension and HF, 4 studies supported that hypertension might increase the risk of HF (OR = 1.55, 95%CI [1.34, 1.8]) and only 1 study reported that HF might increase the risk of hypertension (OR = 3.75, 95%CI [3.3, 4.26]) (Fig. 5).

In addition, due to data incompleteness, there were some unidirectional analyses of CVD with HF. The results showed that atherosclerosis might not raise the risk of HF (OR = 2.11, 95%CI[0.86, 5.17]) (Sfigure 1). Cerebrovascular disease (OR = 1.96, 95%CI[1.61, 2.4]) (Sfigure 2) and diseases of arteries, arterioles, and capillaries (AAC) (OR = 1.58, 95%CI[1.49, 1.68]) (Sfigure 3) might raise the risk of HF. HF might raise the risk of myocardial infarction (OR = 2, 95%CI[1.17, 3.41]) (Sfigure 4) and risk of CVD-related death (OR = 1.78, 95%CI [1.05, 3.02]) (Sfigure 5).

Subgroup analysis based on population

Subgroup analyses were performed according to the ethnicity, but due to missing data, we could only do subgroup analyses of IHD versus HF risk. The results showed that among Asians, IHD might not raise the risk of HF (OR = 1.33, 95% CI [1.00, 1.78]). In caucasians, IHD might also not raise HF risk (OR = 1.52, 95%CI [0.64, 4.56]) (Sfigure 6). This result suggested that ethnicity might be a confounding factor in the association between IHD and HF. Ethnicity may modulate IHD-HF associations due to genetic or lifestyle differences, though further studies are needed.

Risk of bias and sensitivity analysis

We analyzed the publication bias and sensitivity of the association between IHD and HF. The funnel plot showed the symmetry of the included studies and the absence of publication bias (Sfigure 7). Begg's test (Z = 0.98, $P = 0.33$) and Egger's test (t = 1.72, $P = 0.19$) verified lack of publication bias. Leave one out plot showed that the removal of Sennerby 2009 had the greatest effect on the overall OR (Sfigure 8).

Meta regression

Because of the high heterogeneity in this study, we also performed meta-regression to analyze the sources of heterogeneity in the association between IHD and HF (Table 2). The results showed that ethnicity, age, gender, and sample size were not causes of heterogeneity ($P>0.05$).

Discussion

To the best of our knowledge, this is the first meta-analysis that comprehensively analyzed the bidirectional association between CVD and HF. Our meta-analysis was

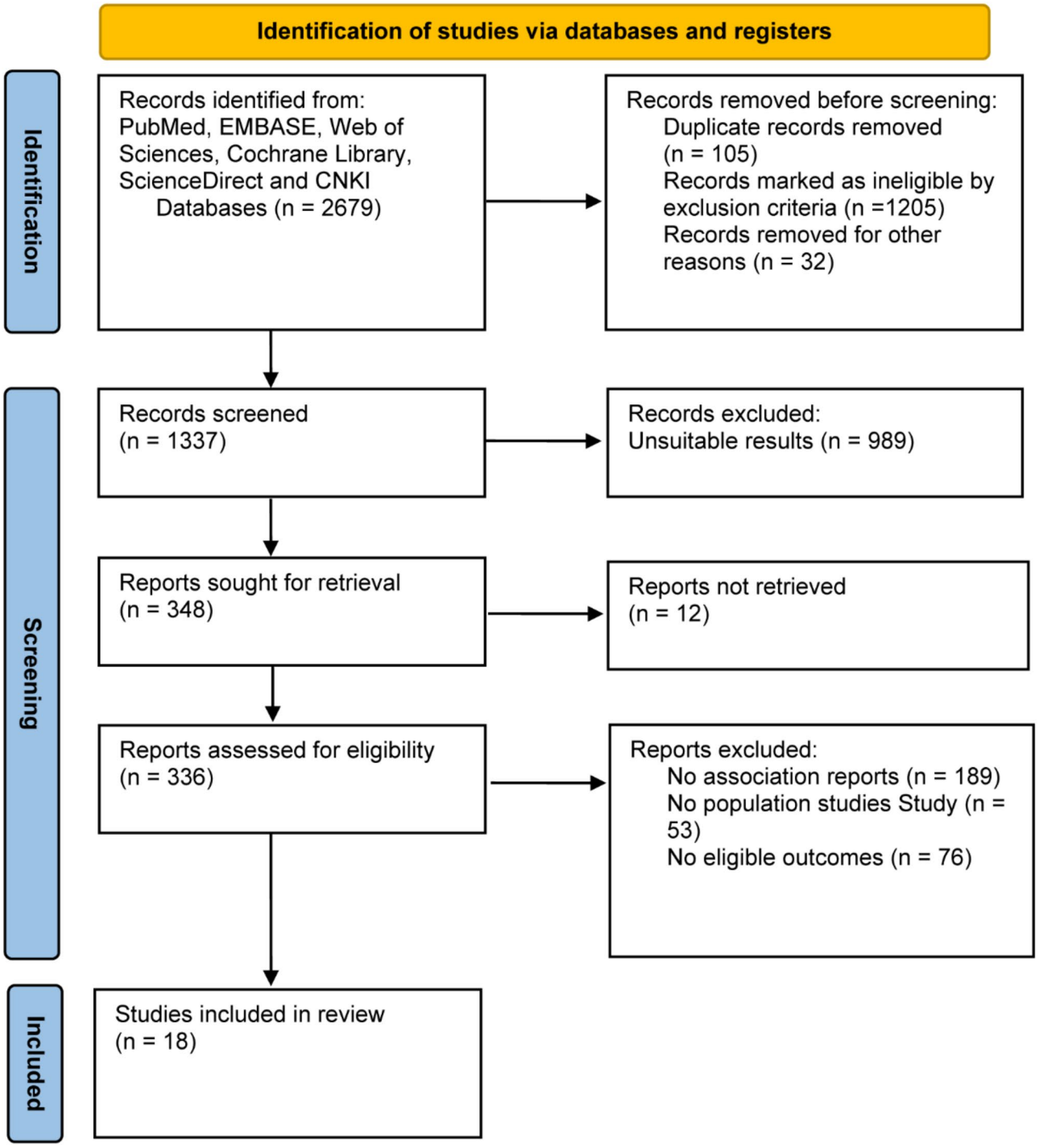

Fig. 1 PRISMA flow diagram of study selection process

robust because it included global multi-country studies, multiple types of CVDs, and large sample size.

The results showed some meaningful results in effect of CVD on HF. IHD, Stroke, heart failure, hypertension, cerebrovascular disease, and AAC might increase the risk of HF whereas atherosclerosis might not increase the risk of HF. The results that AAC may impair mobility, increasing fall risk, or reflect systemic vascular dysfunction affecting bone health, but it need more further study to support this finding. There were also some noteworthy results in terms of HF affecting the risk of CVD, and HF might raise the risk of Stroke, heart failure, hypertension, myocardial infarction, and CVD-related death. Previous literature reviews had consistent results with

Table 1 Characteristics of included articles

Study	Year	Language	Country	Groups	Male/Female	Age	*n*	Study design	Years of follow-up
Cameron	2010	English	Australia	Hip fractures	45/184	86.4 ± 6.3	229	nested case-control (CVD to HF)	1999 and 2003
				Controls	45/184	86.3 ± 6.0	229		
Carbone	2010	English	USA	CVDs	726/800	73.9 ± 5.7	1526	Cohort study (CVD to HF)	1989 and 1990
				Controls	1636/2451	72.3 ± 5.5	4087		
Chiang	2013	English	Taiwan	Hip fractures	3930/4828	70.0 ± 17.4	8758	Cohort study (HF to CVD)	2000 and 2009
				Controls	15,720/19,312	70.0 ± 17.4	35,032		
Friesendorff	2016	English	Sweden	Hip fractures	256/757	-	1013	Cohort study (CVD to HF)	1984 and 2005
				Controls	512/1514	-	2026		
Gerber	2011	English	Israel	CVDs	444/517	75.5 ± 12.7	961	Case-control study (HF to CVD)	1979 and 2002
				Controls	444/517	75.4 ± 12.6	961		
Gerber	2013	English	Israel	Hip fractures	460/1444	82.2 ± 9.5	1904	Case-control study (CVD to HF)	1985 and 2006
				Controls	460/1444	82.1 ± 9.4	1904		
Hyde	2013	English	Australia	Hip fractures	-	74.6	343	Cohort study (CVD to HF)	1996 and 1999
				Controls	-	72	11,751		
Kang	2010	English	Taiwan	Hip fractures	1183/918	76.7 ± 7.2	2101	Case-control study (HF to CVD)	2017 and 2019
				Controls	349/2754	77.4 ± 8.8	6303		
Liu	2017	English	Taiwan	CVDs	3224/3423	-	6647	nested case-control (CVD to HF)	2000 and 2004
				Controls	12,896/13,692	-	26,588		
Meng1	2015	Chinese	China	Hip fractures	121/194	76 ± 8	315	Case-control study (HF to CVD)	2010 and 2013
				Controls	132/183	75 ± 7	315		
Meng2	2015	Chinese	China	CVDs	7/10	77 ± 8	17	Case-control study (HF to CVD)	2006 and 2010
				Controls	496/240	77.6 ± 7.1	736		
Pedersen	2017	English	Denmark	Hip fractures	32,793/77,770	-	110,563	Cohort study (HF to CVD)	1995 and 2015
				Controls	163,951/388,823	-	552,774		
Pouwels	2009	English	UK	Hip fractures	1834/4929	75.7	6763	Case-control study (CVD to HF)	1991 and 2002
				Controls	7203/19,138	75.3	26,341		
Sennerby	2007	English	Sweden	Hip fractures	-	72.5 ± 6.8	1327	Case-control study (CVD to HF)	1993 and 1995
				Controls	-	70.7 ± 7.8	3170		
Sennerby	2009	English	Sweden	CVDs	6400/4762	-	11,162	Cohort study (CVD to HF)	1964 and 2005
				Controls	8408/10,681	-	19,089		
Tsai	2015	English	Taiwan	Hip fractures	11,662/13,496	71.0 ± 15.6	25,158	Cohort study (HF to CVD)	2000 and 2010
				Controls	2916/3424	72.2 ± 15.7	6340		
Wong	2017	English	Australia	CVDs	3024/2539	71.9 ± 13.4	5563	Cohort study (CVD to HF)	1999 and 2012
				Controls	57,613/50,424	55 ± 19.6	108,037		
Xu	2013	English	China	Hip fractures	4720/8351	68.8 ± 8.56	13,071	Case-control study (CVD to HF)	2006 and 2010
				Controls	476,719/374,618	68.1 ± 8.53	851,337		

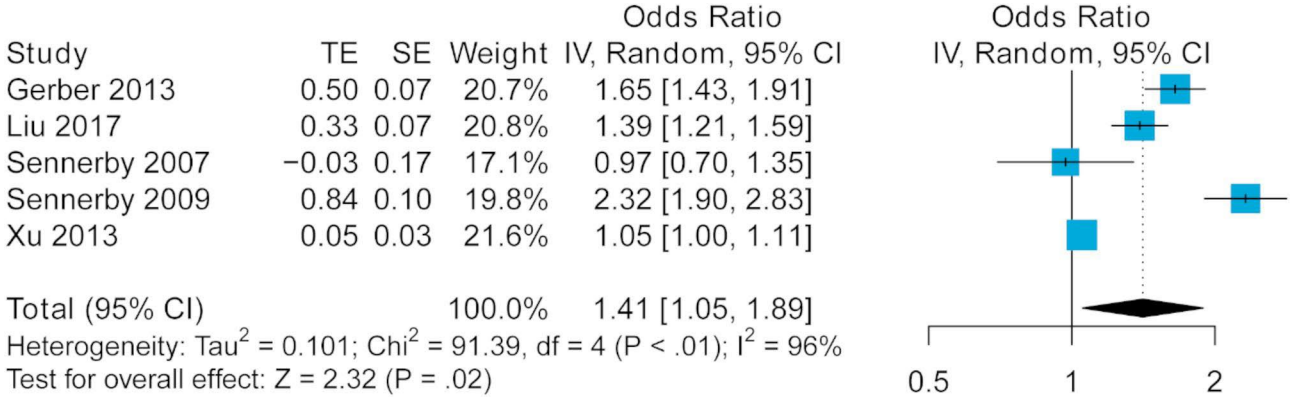

Fig. 2 Forest plots of HF risk between the IHD group and non-IHD group

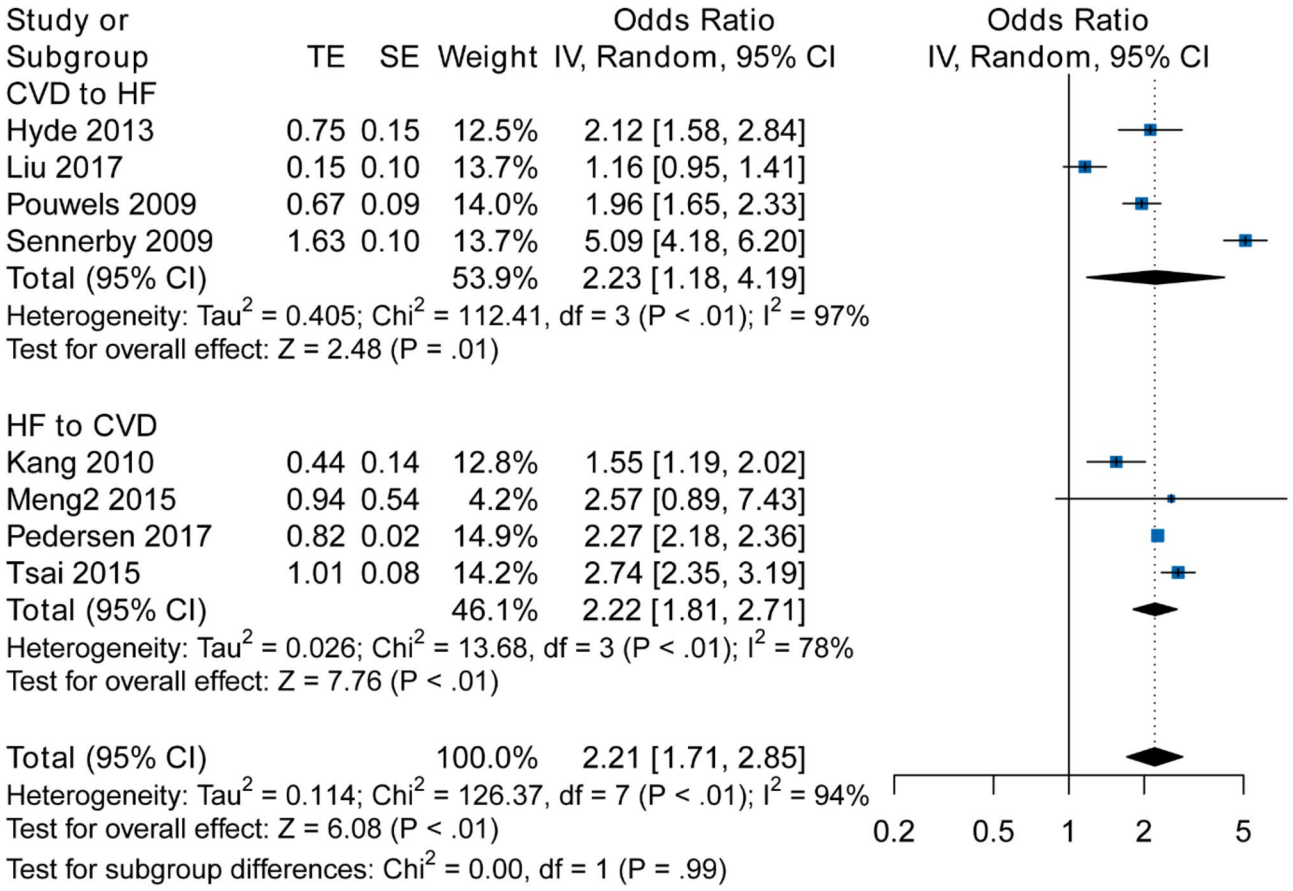

Fig. 3 Forest plots of bidirectional association between HF and stroke

ours [33–35], but it is widely believed that the association between cardiovascular disease and hip fractures is far from conclusive. We tried to systematically review the association mechanism from three perspectives: cardiovascular and bone metabolism, pathophysiology, and CVD and HF treatment.

In cardiovascular and bone metabolism. Troponin is one of the important cardiac markers, and elevated serum troponin can be used as an important basis for assessing possible heart failure and myocardial infarction in patients with HF. Previous studies have reported that the incidence of myocardial infarction and heart failure was significantly higher in patients with preoperative high-sensitivity troponin > 6.5 ng/L in HF within 90 d after surgery [36]. Elevated perioperative troponin was significantly associated with the development of postoperative cardiac complications, and a history of coronary artery disease, heart failure, hypertension, stroke, and myocardial infarction. Preoperative serum amino-terminal B-type natriuretic peptide precursor > 450 pg/mL was a risk factor for adverse cardiovascular events in HF patients within 6 months after surgery [37]. Preoperative serum albumin level is strongly associated with the development of postoperative cardiovascular complications. Patients with preoperative creatinine > 1 mg/mL had a higher likelihood of adverse cardiovascular events within 6 months after surgery [38].

Osteocalcin and the N-terminal prepeptide of type I procollagen are bone formation-specific markers, whereas bone resorption-specific markers include β-CrossLaps (β-CTx) [39]. β-CTx correlates with the severity of heart failure, and elevated serum levels of osteocalcin and β-CTx in patients with heart failure are indicative of a high rate of bone conversion. Nuclear factor-κB is an important transcription factor in many cell types, and its activation usually produces catabolic signals. Nuclear factor-κB ligand receptor activator (RANKL) and osteoprotegerin (OPG), derived from osteoblasts/stromal cells, are involved in osteoclast differentiation and activation of osteoblasts, whereas OPG is associated with osteoclast inhibition and bone necrosis [40]. OPG is elevated in patients with chronic HF, and there is an inverse association between OPG and BMD in HF patients.

In pathophysiologic perspective. Aging is the most prominent confounder in bone loss and CVD development [41]. The presence of dementia should be considered as a risk factor for bone loss, falls and HFs in elderly

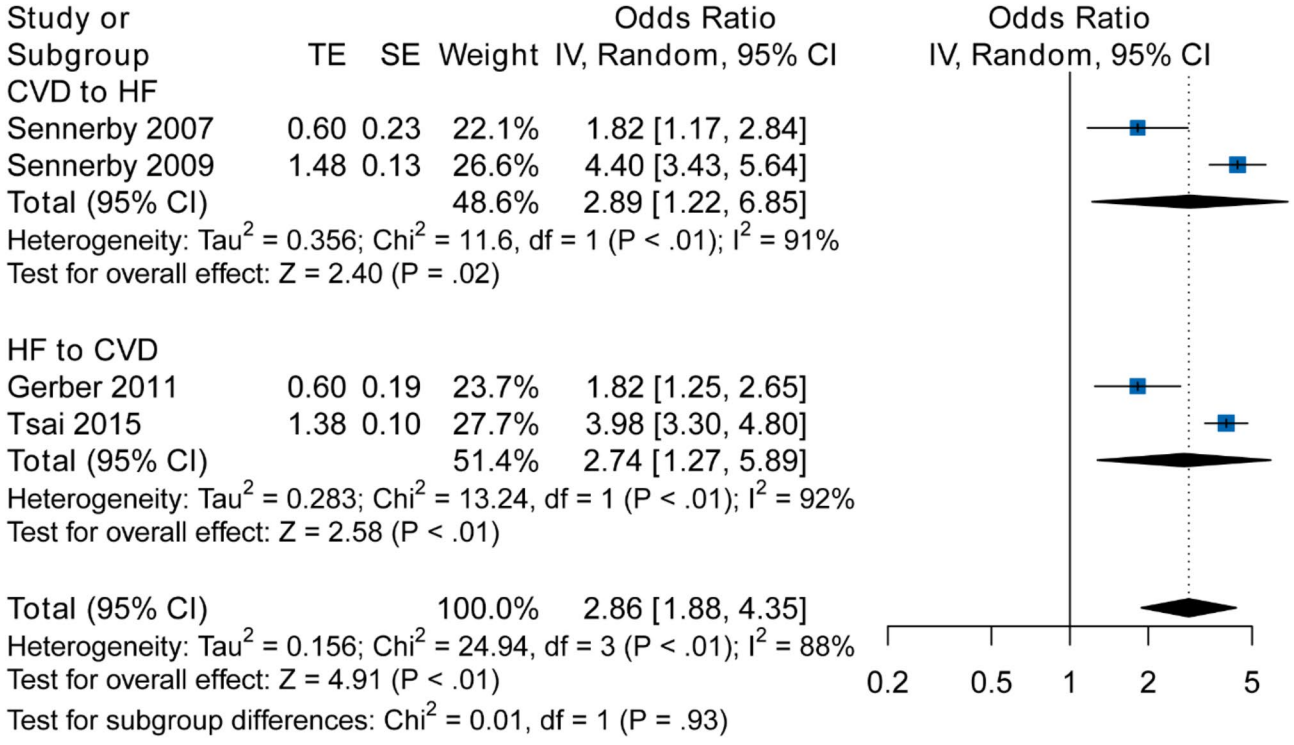

Fig. 4 Forest plots of bidirectional association between HF and heart failure

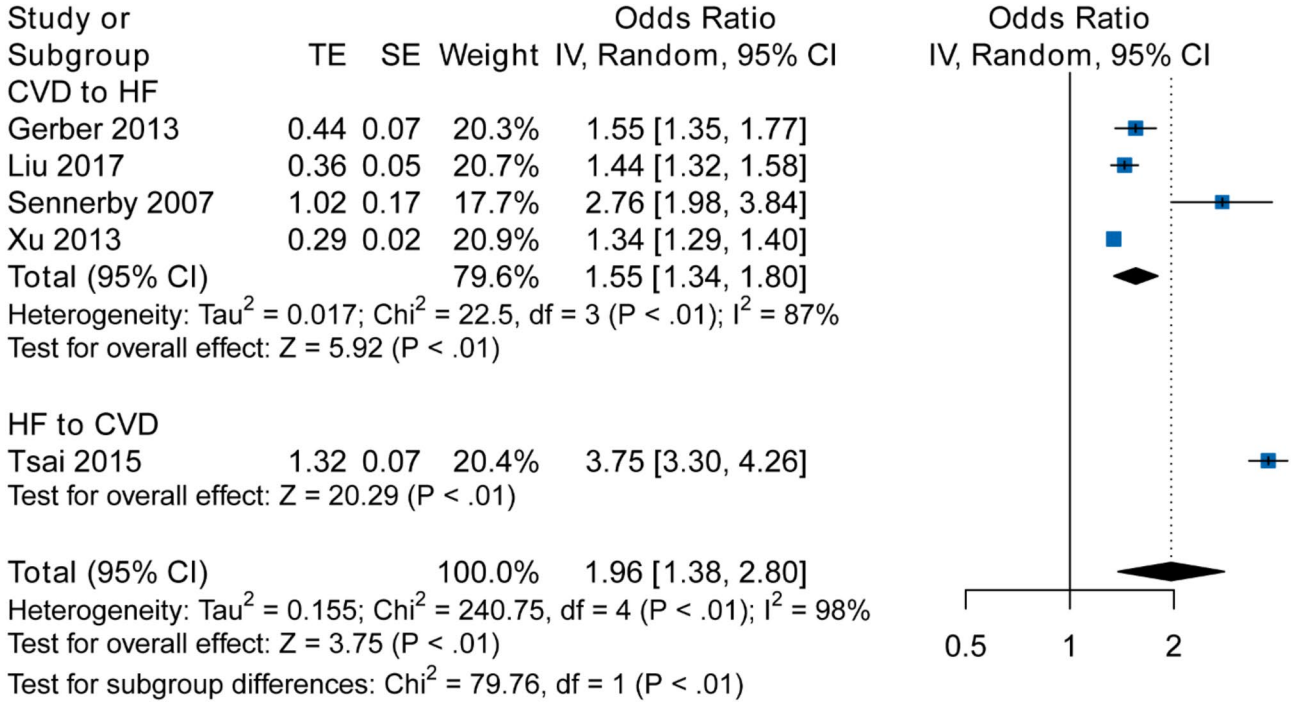

Fig. 5 Forest plots of bidirectional association between HF and hypertension

CVD patients. In addition to decreased physical activity in CVD patients and some common risk factors, accelerated bone loss in CVD subjects may also result from vitamin D deficiency and hyperparathyroidism, elevated aldosterone levels, and labeled diuretic use. Muscle strength imposes the greatest burden on the skeleton and the greatest bone strain. Skeletal unloading in CVD patients due to prolonged bed rest or poor exercise

Table 2 Meta-regression of HF risk between the IHD group and non-IHD group

	Coef	*P*	95%CI
Population	0.14	0.69	-0.56, 0.84
Age	0.02	0.61	-0.05, 0.09
Gender	-0.39	0.45	-1.42, 0.63
Size	0	0.31	-0.01, 0.01

capacity leads to bone loss through a reduction in the mechanical forces exerted on the skeleton. The presence of vitamin D deficiency is more pronounced in the CVD population than in the healthy population. Patients with CVD have a deficiency of vitamin D [42], even in sunny climates. The presence of vitamin D deficiency in the CVD population is more pronounced than in the healthy population. HF patients with secondary hyperparathyroidism are more severely affected than patients with normal serum parathyroid hormone (PTH) levels [43]. Elevated levels of PTH in patients with CVD may be a potential pathophysiologic pathway leading to bone loss or osteoporosis in patients. Lipocalin, an adipocytokine secreted by adipocytes, also plays a role in CVD and osteoporosis. Hypogonadism is a common condition in men with CVD, and hypogonadism is a risk factor for osteoporosis [44]. Oxidative stress contributes in part to the onset and progression of CVD, and the imbalance between oxidant and antioxidant status is associated with an increase in osteoblasts and a decrease in osteoclasts. Inflammatory cytokines may also alter bone metabolism [45]. Tumor necrosis factor and interleukin-6 are increased in patients with chronic CVD, and inflammation may play an important role in its development and progression [46].

In the treatment of CVD and HF. It has been found that delaying surgery for 24–72 h after diagnosis significantly increases the rate of mortality and major complications in patients with HFs [47]. The likelihood of heart failure as well as myocardial infarction was significantly higher in patients who delayed surgery for more than 2d [48]. Operations such as drilling of the femoral marrow cavity during HF surgery can lead to the entry of fat and bone marrow tissue into the circulation, which may lead to postoperative stroke [49]. Anesthesia may contribute to the occurrence of cardiovascular events in patients after surgery. Patients under local anesthesia are less likely to have a postoperative myocardial infarction compared to patients undergoing general anesthesia. The use of anesthetic agents such as remifentanil and etomidate may increase the likelihood of postoperative cardiovascular events in elderly HF patients [50]. About 75% of elderly HF patients are anemic, but the use of transfusion therapy in these patients is controversial, and the indications for blood transfusion in elderly HF patients remain unclear.

Exercise is the easiest way to maintain and increase muscle mass, and it is the most effective anabolic agent. Aerobic exercise training in CVD patients has been shown to be the best way to combat skeletal muscle wasting. Testosterone therapy has shown promising results in male patients with HF, and the direct anabolic properties of testosterone or the indirect effects of this therapy may also improve bone homeostasis in patients with HF [51]. Alendronate (one of the bisphosphonates) reduces the risk of CVD, and bisphosphonates are important agents in the treatment of osteoporosis [52, 53]. While our findings had heterogeneity, possibly due to differences in adjustment for frailty. Heterogeneity may stem from variability in study populations.

Conclusions

Overall, both CVD and HF are highly prevalent diseases of aging that have a huge impact on socioeconomic burden of disease and public health. Our study supports a bidirectional association between CVD and HF, though causal inference is limited by observational data., including the fact that IHD, Stroke, heart failure, hypertension, cerebrovascular disease, and AAC might increase the risk of HF. HF might raise the risk of Stroke, heart failure, hypertension, myocardial infarction, and CVD-related death. These results suggest that HF is never localized to a single discipline, but requires comprehensive multidisciplinary treatment. However, some of the associations between CVD and HF remain to be further confirmed, and the pathophysiologic mechanisms between these associations need to be further explored in the future. Clinicians should screen HF patients for CVD and vice versa. Multidisciplinary care addressing shared risk factors may reduce morbidity. Based on this study, the future co-treatment for both HF and CVD may be possible.

There were some limitations. First, we included only observational studies without randomized controlled trials. Future mechanistic research should focus on experimental models to isolate bidirectional pathways while controlling for age, sex, and comorbidities, thereby reducing heterogeneity. Second, the high heterogeneity of the results of this study needed to be interpreted with caution, which might be related to the operational details of the different studies, such as variability in data collection, analysis, and study processes. Third, despite our comprehensive search strategy, publication and selection bias might exist due to the inclusion of only published studies. Fourth, due to the limitation of the reported data, we were unable to perform subgroup analyses of gender and age. Finally, despite adjusting for age in meta-regression, residual confounding by frailty, polypharmacy, or unmeasured lifestyle factors ay persist.

Abbreviations

CVD	Cardiovascular disease
HF	Hip fracture
CNKI	China National Knowledge Infrastructure
IHD	Ischemic heart disease
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
MOOSE	Meta-analysis of Observational Studies in Epidemiology
INPLASY	International Platform of Registered Systematic Review and Meta-analysis Protocols
95%CI	95% confidence intervals
NOS	Newcastle-Ottawa scale
HR	Hazard ratio
RR	Risk ratio
OR	Odds ratio
AAC	Diseases of arteries, arterioles, and capillaries
β-CTx	β-CrossLaps
RANKL	Nuclear factor-κB ligand receptor activator
OPG	Osteoprotegerin
PTH	Parathyroid hormone

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04823-4.

Sfigure 1. Forest plots of HF risk between the atherosclerosis group and non- atherosclerosis group.1

Sfigure 2. Forest plots of HF risk between the cerebrovascular disease group and non-cerebrovascular disease group.

Sfigure 3. Forest plots of HF risk between the AAC disease group and non-AAC group. AAC, diseases of arteries, arterioles, and capillaries.

Sfigure 4. Forest plots of acute myocardial infarction risk between the HF group and non-HF group.

Sfigure 5. Forest plots of CVD related death risk between the HF group and non-HF group.

Sfigure 6. Subgroup forest plots of HF risk between the IHD group and non-IHD group based on race.

Sfigure 7. Funnel plot of HF risk between the IHD group and non-IHD group.

Sfigure 8. Leave one out plot of HF risk between the IHD group and non-IHD group.

Stable 1. Newcastle-Ottawa Scale of the included articles.

Supplementary Material 10

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Not applicable.

Author contributions
Jinyi Wu and Yan Zhang analyzed data and wrote the manuscript. Junwen Wang and Qingsong Zhang prepared the figures. Jun Jiang collected data. Qingwu Jiang and Yibiao Zhou provided the concept and validate the manuscript.

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Data availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
Since this research is a meta-analysis based on the published articles, there is no need for Ethics approval and consent.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Clinical trial number
Not applicable.

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