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Research Article

Clinical Efficacy of Qili Qiangxin Capsule Combined with Western Medicine in the Treatment of Chronic Heart Failure: A Systematic Review and Meta-Analysis

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Qili Qiangxin capsule (QQC) is a formulation of traditional Chinese medicine commonly used for the treatment of heart failure in China. This meta-analysis aimed to assess the clinical efficacy of QQC combined with western medicine in the treatment of chronic heart failure (CHF). We conducted a systematic review and meta-analysis abided by the PRISMA guidelines. Literature search was conducted in the China National Knowledge Infrastructure, Wanfang Database, Chinese Scientific Journals Database, PubMed, and Web of Science from inception to August 2020. A total of 52 eligible studies were obtained, and 42 of these studies were included in the meta-analysis. The results showed that, compared with western medicine alone, the combination of Qili Qingxin capsule and Western medicine treatment has better efficacy (metoprolol: RR: 1.24, 95%CI 1.14–1.34; carvedilol: RR: 1.24, 95%CI 1.14–1.34; trimetazidine: RR: 1.20, 95%CI: 1.12–1.27; sacubitril valsartan sodium: RR: 1.23, 95%CI: 1.11–1.36; sodium nitroprusside: RR: 1.33, 95%CI: 1.23–1.45; and bisoprolol: RR: 1.31, 95%CI: 1.15–1.49) and increased the level of LVEF, LVEDD, and 6MWT of patients with CHF and reduced the adverse effects and the level of HR, LVESD, BNP, and Hs-cTnT as well. However, there is high heterogeneity in the meta-analysis of LVEDV, BNP, NT-proBNP, Hs-cTnT, 6MWT, and adverse effects, and the methodological quality of the included studies was poor. Therefore, further studies with good methodological quality and large sample size are required to validate our findings. In our study, evidence suggests that Qili Qiangxin capsule combined with Western medicine may improve therapeutic effect and the quality of life of patients with CHF.

1. Introduction

Chronic heart failure (CHF) has been recognized as one of the major global health issue which is associated with high risk of morbidity, mortality, and cost [1]. According to the survey, there are 23 million patients with CHF worldwide, approximately 5.7 million in the US and over 4.2 million in China [1]. The pathogenesis of CHF mainly includes primary myocardial damage resulted from long-term glucose and lipid metabolism disorder and ischemic myocardial damage [2]. Especially, the elderly showed higher morbidity of CHF [3]. In the future, the number of patients with CHF would increase significantly with the aging of the population [4].

Conventional Western medicine for CHF treatment includes beta-blockers, cardiotonic steroids, diuretics, and angiotensin-converting enzyme inhibitors (ACEI). Although these treatments have certain therapeutic effects, such as a reduction of heart rate and left ventricular filling pressure and an improvement in exercise capacity [4], an improvement in the curative effect is still necessary because of the adverse effects and short-term effects. For example, the metoprolol, a beta-blocker, may cause depression and anxiety during the CHF treatment [5]. With the development of science and technology, more and more anti-CHF ingredients have also been discovered [6–8]. Complementary and alternative medicine therapies have

become increasingly popular and are used regularly by patients with chronic disorders [9]. Currently, the combination of traditional Chinese medicine (TCM) and western medicine has been widely used for the CHF treatment [10–12]. According to the perspective of TCM, the etiology of CHF is the yang deficiency of heart which is the result of the inadequacy of Qi and blood, blood stasis, and phlegm-dampness. With the in-depth research of TCM, the main CHF treatment is replenishing Qi and nourishing Yin [13].

Qili Qiangxin capsule (QQC) is a traditional Chinese herbal remedy that was mentioned as a treatment with certain therapeutic effects, such as reducing heart rate and revering ventricular remodeling, for the CHF by China Food and Drug Administration [14]. QQC is a standardized Chinese herbal extract prepared from 11 Chinese herbs, including dry root of Astragalus membranaceus (Fisch.) Bge. var. mongholicus (Bge.), Hsiao or Astragalus membranaceus (Fisch.) Bge., dry root of Panax ginseng C. A. Meyer, Aconitum carmichaeli Debx., dry root of Salvia miltiorrhiza Bunge, dry seeds of Lepidium apetalum Willd. or Descurainia Sophia (L.) Webb ex prantl., dry tubers of Alisma orientalis (Sam.) Juzep., dry rhizome of Polygonatum odoratum (Mill.) Druce, dry twigs of Cinnamomum cassia Presl, dry flower of Carthamus tinctorius L., dry root bark of Periploca sepium Bge., and dried ripe peel of Citrus reticulata Blanco. Previous studies have reported that QQC played a role in the treatment of CHF through multiple mechanisms, such as reducing cardiac fibrosis remolding, improving cardiac function, reducing NT-proBNP, and regulating the inflammatory responses [13-16]. In addition, the efficacy and safety also have been proved in a study of the effects of QQC on 512 patients with CHF [17].

Currently, QQC combined with Western medicine has been widely used for the treatment of CHF. A lot of studies have reported that QQC combined with Western medicine can improve clinical outcomes compared to Western medicine treatment [18-20]. Sun et al. performed a metaanalysis in 2016 and concluded that QQC plus conventional treatment showed better efficiency than conventional treatment alone in the treatment of heart failure [21]. However, a subgroup analysis based on conventional treatments was not conducted in the meta-analysis. With the deepening of research on QQC in CHF in recent years, it is necessary to conduct an in-depth analysis of the clinical effects of QQC plus Western medicine on CHF patients. Given the small sample sizes and inconsistent results of previous research studies, this study aimed at conducting a systematic review and meta-analysis of the efficacy and safety of QQC combined with Western medicine in the treatment of CHF and providing reference for clinical diagnosis and treatment.

2. Method

This study was compiled based on the Preferred Reporting Items for Systematic reviews and Meta-Analyses statement (PRISMA) (Supplementary Materials S1) [22].

- 2.1. Search Strategy. We searched the following five data-bases from their start date to August 2020: China National Knowledge Infrastructure (CNKI), Wanfang Database, Chinese Scientific Journals Database (VIP), PubMed, and Web of Science. We used the following keywords and medical subject heading terms: ("Qili Qiangxin" OR "qili-qiangxin" OR "qiangxinli") and ("Chronic heart failure" OR "Chronic cardiac failure" OR "Chronic heart decompensation"). We also hand-searched the reference lists of all full text papers for additional relevant reports. We did not impose any language restrictions.
- 2.2. Eligibility and Exclusion Criteria. Trials were considered eligible if they were (a) randomized controlled trials (RCTs); (b) enrolled participants with CHF; (c) compared the curative effects of the combination of QQC and Western drugs with Western drugs alone. The following studies were excluded, including repeated publication, literature with incomplete or incorrect data, and the control group without a description of the Western drugs used in this study.
- 2.3. Study Selection. At first, the duplicates of all records obtained from the electronic databases were removed. Then, two researchers read the titles and abstracts independently to identify the eligible studies. Full texts of the studies were read to determine whether they met the eligibility criteria. The disagreements were resolved by discussing with a third researcher.
- 2.4. Outcomes. Our primary outcome measures were the clinical efficiency. Secondary outcomes measures were heart rate (HR), left ventricular ejection fractions (LVEF), left ventricular end-diastolic dimension (LVEDD), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic diameter (LVESD), brain natriuretic peptide (BNP), N-terminal Pro B-type natriuretic peptide (NT-proBNP), high-sensitivity cardiac troponin T (Hs-cTnT), 6-min walk test (6MWT). We also collected adverse events data. RCTs reporting one or more of these outcomes were included.
- 2.5. Data Extraction and Quality Assessment. The following details were extracted by two researchers independently from included studies: first author; year; sample size; age; gender; course of treatment; the intervention of experimental group; the intervention of control group; and outcome data. The methodological quality of the included studies was used Cochrane 5.1.0 assessment tool. It includes following seven aspects: (1) random sequence generation; (2) allocation concealment; (3) blinding of participants and personnel; (4) blinding of outcome assessment; (5) incomplete outcome data; (6) selective reporting; and (7) other bias. Each domain of the included studies was evaluated as having a low, high, or unclear risk of bias. It was also independently completed by two researchers. The disagreements were resolved by discussing with a third researcher.

2.6. Data Analysis. The meta-analysis was performed by using RevMan 5.3 software. The relative risk (RR) and 95% confidence intervals (95% CI) were used for dichotomous variables, and the mean difference (MD) and 95% CI were used for continuous variables. This study used I^2 and Q tests to evaluate heterogeneity of study. When the I^2 >50% or P < 0.01 in the Q test, the random model would be used for meta-analysis. Otherwise, we used fixed model for meta-analysis.

3. Results

- 3.1. Description of Studies. As shown in Figure 1, a total of 1623 studies were obtained from five databases. After removing the 552 duplicates, 281 mechanism studies, 268 animal experiments, 298 reviews, protocols, and case reports, we included 224 studies. By screening the full text articles, we removed 67 studies of no control group, 48 studies of incomplete or incorrect data, 57 studies of the control group without a description of the Western drugs used in study. Finally, we included 52 studies for the quality assessment, and 42 of these studies were included for meta-analysis.
- 3.2. Characteristics of Study. The characteristics of the 52 included studies are shown in Table 1. All included studies were conducted in China and published in Chinese. Among the included studies, 11 studies [18–20, 37, 40, 45, 46, 57–60] were related to clinical efficacy of QQC combined with metoprolol. 3 studies [36, 42, 53] were related to clinical efficacy of QQC combined with bisoprolol. 3 studies [51, 69, 70] were related to clinical efficacy of QQC combined with levocarnitine oral solution. 5 studies [31, 43, 44, 55, 56] were related to clinical efficacy of QQC combined with carvedilol. 10 studies [24, 26, 27, 32–35, 47–49] were related to clinical efficacy of QQC combined with trimetazidine. 1 study [23] was related to clinical efficacy of QQC combined with digoxin. 2 studies [54, 64] were related to clinical efficacy of QQC combined with coenzyme Q10. 1 study [65] was related to clinical efficacy of QQC combined with enalapril maleate and folic acid tablets. 4 studies [61, 66-68] were related to clinical efficacy of QQC combined with sacubitril valsartan sodium tablets. 1 study [30] was related to clinical efficacy of QQC combined with benazepril hydrochloride. 9 studies [25, 28, 29, 38, 39, 41, 52, 63, 71] were related to clinical efficacy of QQC combined with sodium nitroprusside, and 2 studies [50, 62] were elated to clinical efficacy of QQC combined with ivabradine.
- 3.3. Risk of Bias. As shown in Figure 2, for the random sequence generation, 6 studies were high risk of bias, and the rest were low risk of bias. One study specified the methods of allocation, and the rest were unclear. One study blinded participants, personnel, and outcome assessment, whereas the rest had no description about the methods of the blinding. There were complete data in all studies, and all studies had low risk of bias in selective reporting and other source of bias.

- 3.4. Clinical Efficacy. In Figures 3 and 4, the meta-analysis results showed that the clinical efficacy of QQC plus Western drugs treatment was significantly better than Western drugs treatment alone. The following data showed the meta-analysis of QQC combined with different Western drugs treatment: (1) metoprolol (n = 9 trials, RR: 1.21, 95%CI: 1.14 to 1.29, Figure 3(a)); (2) carvedilol (n = 5 trials, RR: 1.24, 95% CI 1.14 to 1.34, Figure 3(b)); (3) trimetazidine (n = 8 trials, RR: 1.20, 95%CI: 1.12 to 1.27, Figure 3(c)); (4) sacubitril valsartan sodium (n = 4 trials, RR: 1.23, 95%CI: 1.11 to 1.36, Figure 4(a)); (5) sodium nitroprusside (n = 8 trials, RR: 1.33, 95%CI: 1.23 to 1.45, Figure 4(b)); and (6) bisoprolol (n = 3 trials, RR: 1.31, 95%CI: 1.15 to 1.49, Figure 4(c)).
- 3.5. Heart Rate (HR). The meta-analysis with a random model showed that the HR of QQC plus metoprolol treatment was significantly lower than metoprolol treatment alone (n = 8 trials, MD: -8.71, 95%CI: -10.93 to -6.50, P < 0.00001, heterogeneity $\chi^2 = 66.92$, P < 0.00001, $I^2 = 90$, Figure 5).
- 3.6. Left Ventricular Ejection Fractions (LVEF). The meta-analysis results showed that the LVEF of QQC plus Western drugs treatment was significantly higher than Western drugs treatment alone (Figures 6 and 7). The following data showed the meta-analysis of QQC combined with different Western drugs treatment: (1) metoprolol (n = 7 trials, MD: 3.86, 95%CI: 2.92 to 4.80, Figure 6(a)); (2) carvedilol (n = 5 trials, MD: 11.02, 95%CI: 6.68 to 15.36, Figure 6(b)); (3) trimetazidine (n = 8 trials, MD: 8.08, 95%CI: 4.99 to 11.17, Figure 6(c)); (4) sacubitril valsartan sodium (n = 4 trials, MD: 6.78, 95%CI: 4.53 to 9.04, Figure 7(a)); (5) sodium nitroprusside (n = 6 trials, MD: 4.37, 95%CI: 3.33 to 5.40, Figure 7(b)).
- 3.7. Left Ventricular End-Diastolic Dimension (LVEDD). The meta-analysis results showed that the LVEDD of QQC plus Western drugs treatment was significantly higher than Western drugs treatment alone (Figure 8). The following data showed the meta-analysis of QQC combined with different Western drugs treatment: (1) metoprolol (n=3 trials, MD: -2.98, 95%CI: -4.21 to -1.75, Figure 8(a)); (2) carvedilol (n=3 trials, MD: -7.51, 95%CI: -9.85 to -5.81, Figure 8(b)); (3) trimetazidine (n=5 trials, MD: -4.61, 95% CI: -7.26 to -1.07, Figure 8(c)); (4) sodium nitroprusside (n=5 trials, MD: -5.72, 95%CI: -6.95 to -4.50, Figure 8(d)).
- 3.8. Left Ventricular End-Diastolic Volume (LVEDV). The meta-analysis with a random model showed that the LVEDV of QQC plus trimetazidine treatment was significantly lower than trimetazidine treatment alone (n = 3 trials, MD: -25.19, 95%CI: -37.69 to -12.68, P < 0.0001, heterogeneity $\chi^2 = 14.99$, P = 0.0006, $I^2 = 87\%$, Figure 9).
- 3.9. Left Ventricular End-Systolic Diameter (LVESD). The meta-analysis with a random model showed that the LVESD of QQC plus sodium nitroprusside treatment was

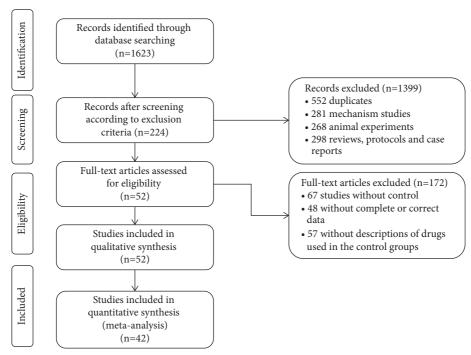


FIGURE 1: Flow chart of study searching and selection.

significantly lower than sodium nitroprusside treatment alone (n = 4 trials, MD: -5.64, 95%CI: -6.75 to -4.53, P < 0.0001, heterogeneity $\chi^2 = 0.87$, P = 0.83, $I^2 = 0\%$, Figure 10).

3.10. Brain Natriuretic Peptide (BNP). The meta-analysis results showed that the BNP of QQC plus Western drugs treatment was significantly lower than Western drugs treatment alone (Figure 11). The following data showed the meta-analysis of QQC combined with different Western drugs treatment: (1) metoprolol (n = 8 trials, MD: -388.94, 95%CI: -488.23 to -289.64, Figure 11(a)) and (2) bisoprolol (n = 3 trials, MD: -242.41, 95%CI: -428.59 to -56.24, Figure 11(b)).

3.11. N-Terminal Pro-B-Type Natriuretic Peptide (NT-ProBNP). The meta-analysis results showed that there was no significant difference between the NT-proBNP of QQC plus Western drugs treatment and Western drugs treatment alone (Figure 12). The following data showed the meta-analysis of QQC combined with different Western drugs treatment: (1) trimetazidine (n = 3 trials, MD: -0.47, 95%CI: -1.01 to 0.07, Figure 12(a)) and (2) sacubitril valsartan sodium (n = 3 trials, MD: -0.61, 95%CI: -1.38 to 0.15, P = 0.12, heterogeneity $\chi^2 = 171.01$, Figure 12(b)).

3.12. High-Sensitivity Cardiac Troponin T (Hs-cTnT). The meta-analysis with a random model showed that the Hs-cTnT of QQC plus metoprolol treatment was significantly lower than metoprolol treatment alone (n=3 trials, MD: -5.93, 95%CI: -9.92 to -1.95, P=0.004, heterogeneity $\chi^2=69.45$, P<0.0001, $I^2=97\%$, Figure 13).

3.13. 6-Min Walk Test (6MWT). The meta-analysis with a random model showed that the 6MWT of QQC plus trimetazidine treatment was higher than trimetazidine treatment alone (n = 3 trials, MD: 37.61, 95%CI: 10.93 to 64.29, P = 0.006, heterogeneity $\chi^2 = 15.94$, P = 0.0003, $I^2 = 87\%$, Figure 14).

3.14. Adverse Effects. The adverse effects occurred in the included studies included headache, hypotension, hyponatremia, nausea, cough, arrhythmia, and fatigue. The meta-analysis with a random model showed that the adverse events of QQC plus metoprolol treatment was lower than metoprolol treatment alone (n=8 trials, RR: 0.48, 95%CI: 0.28 to 0.81, P=0.006, heterogeneity $\chi^2=16.47$, P=0.02, $I^2=58\%$, Figure 15(a)). There was no significant differences between the group treated with QQC plus trimetazidine and the group treated with trimetazidine alone (n=3 trials, RR: 0.83, 95%CI: 0.26 to 2.67, P=0.76, heterogeneity $\chi^2=0.77$, P=0.68, $I^2=0\%$, Figure 15(b)).

4. Discussion

The characteristics of CHF are high risk of hospitalization, readmissions, mortality, morbidity, and cost. Patients with CHF suffer from a low quality of life with dyspnea, fatigue, physical exertion, mood disorders, and so on [72]. In recent years, the angiotensin-converting enzyme inhibitors, betablockers, aldosterone antagonists, digoxin, and diuretics as standard Western medicine have been widely used for the treatment of CHF to delay the development of myocardial remodeling [10]. However, owing to the adverse reaction, poor compliance, lower heart rate, and so on, the desired application of these drugs is restricted [2]. The combination

TABLE 1: Characteristics of included studies.

QQC+ digostiv/digostin QQC QQC+ digostiv/digostin QQC+ digostiv/digostin QQC QQC+ improved QQC	ID (Author year)	Intervention (T/C)	Sample size	Age (T/C)	Gender (men/women)-T	Gender (men/women)-C	Outcome indicator	Course of treatment	Reference
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QQC++stantium intropersisted sodium 4440 Sk ±4472±14 38/6 33.7 QQC++stantium intropersisted sodium intropersisted codium intropersisted c	Liu HL 2008	QQC + digoxin/digoxin	20/36	76±11			Clinical efficacy, LVEF, CO, CI, SV, 6MWT, adverse reaction	4 w	[23]
QQC+ trimmetabline proposation and proposation of the proposation	Ding XZ 2011	QQC + sodium nitroprusside/sodium	44/40		38/6	33/7	Clinical efficacy, LVEF, LVEDD, BNP, FS		[2]
90QC+ sodium nitropusside sodium 1972 39.26 65.2±5.5(64.5±2.5 15/15 17/13 17/1	Chen WQ 2012	OOC+ trimetazidine/trimetazidine	09/09	$58 \pm 14/57 \pm 14$	36/24	35/25	Clinical efficacy, LVEF, LVEDD, 6MWT, FS, E/A, adverse reaction	6 m	[24]
QQC+ Timmexialmentation 974 97.55.616.2.5.3 20.10 1711 QQC+ Timmexialment Timexeraline 90.30 65.5.45.616.2.5.3 15/15 17/13 QQC+ timmexialment Timexeraline 90.30 65.5.45.616.2.5.3 15/15 17/13 QQC+ sodium nitroprusside-sodium 56/56 63.5.4.36 17/18 17/13 QQC+ stammer nitroprusside continum nitropru	CIOC MA SHOULD	QQC + sodium nitroprusside/sodium	10/06	2 + 02/2 + 02	01/00	11/01	Claim of the state		. 2
QQC+ Finnexadine (Trinetaidine) 1920 65.5±5/645±25 15115 17113 QQC+ Finnexadine frimetaidine (Trinetaidine frimetaidine frimetaidine frimetaidine frimetaidine frimetaidine frimetaidine (Trinetaidine QQC+ sodium interprasside/sodium) 50/56 53.2±5.2/58.8±4.1 23/27 1713 QQC+ sodium interprasside/sodium 30/30 58.2±5.2/58.8±4.1 23/27 27/23 QQC+ solium interprasside formate and interprass	Huang AM 2012	nitroprusside	39/21	59±6/60±5	20/10	19/11	Clinical efficacy, LVEF, LVEDD, LVESD		[67]
QQC+ stellam interpressides defined 90.90 0.03±0.50±3±1.2.0 17/13 17/13 QQC+ stellam interpressides defined 56.56 63.5±3.6 17/13 17/13 17/13 QQC+ stellam interpressides defined 56.56 63.5±3.6 17/13 18/17 17/13 18/17 QQC+ stellam grid QQC+ stellam grid 20.30 88±15.52/58.8±4.1 20.02 19/13 QQC+ trimeardial refuneration 42.42 64.12.8 686.87.7±8.1 20.02 19/13 QQC+ trimeardial refuneration for trimeardial displaced from transition 42.42 64.12.86.12.6 20.02 19/13 QQC+ trimeardial refuneration displaced from transition 42.42 64.12.86.2.4.8 20.02 19/13 QQC+ trimeardial refuneration displaced from transition 43.44 61.2.5.12.48.5.4.4.5 15/14 16/24 QQC+ trimeardial refuneration displaced from transition 43.44 61.2.5.12.48.5.4.4.5 15/15 18/15 QQC+ trimeardial refuneration 43.44 64.2.4.5.6.6.2.4.6.5 15/15 18/15 18/15 QQC+ trimeardial refuneration 43.44 64.2.5.6.6.6.	Zhou FZ 2013	QQC + Trimetazidine/Trimetazidine	19/20		1	Č.	Clinical efficacy, LVEF, CO, SV, LVESV, LVEDV	12 w	[26]
QQC+ sedium introprusside sodium 59/50 59.2 ± 52/59.8 ± 41 24/27 27/23 QQC+ sedium introprusside sodium 56/56 63.5 ± 3.6 17/18 18/17 27/23 ModC+ sedium introprusside sodium 56/56 63.5 ± 3.6 17/18 18/17 18/17 ModC+ borderide/chenzepril 30/30 88.1 ± 15/79 ± 18 18/17 19/11 QQC+ chrine/adian/chrinectardine 47/42 64.12 ± 8.68(6.57 ± 8.54 20/22 19/23 QQC+ transcrandine/trimectardine 47/42 64.2 ± 8.68(6.57 ± 8.1 20/22 19/13 QQC+ transcrandine/trimectardine 47/42 64.2 ± 8.68(6.57 ± 8.1 20/22 19/13 QQC+ trimectardine/trimectardine 40/49 61.6 ± 7.4(6.7 ± 8.1 14/25 19/12 QQC+ trimectardine/trimectardine 40/49 61.6 ± 7.4(6.7 ± 8.1 14/25 19/12 QQC+ trimectardine/trinectardine 47/47 58.2 ± 4.7/58.9 ± 4.6 27/20 19/12 QQC+ trimectardine/trimectardine 47/47 58.2 ± 4.7/58.9 ± 4.6 27/20 26/21 QQC+ trimectardine/trimectardine 47/47	Huang XY 2013	QQC + trimetazidine/trimetazidine	30/30	$65.5 \pm 5.5/64.5 \pm 2.5$	15/15	17/13	Clinical efficacy, LVEF, LVEDD, BNP	3 m	[27]
QQC+ sodium nitroprusside/sodium 56/56 635±3.6 17/18 18/17 PydCock branzprill 35/35 66/56 17/18 18/17 18/17 PydCock branzprill 36/36 38±15/37±18 18/12 19/11 19/11 QQC+ branzprill reduction deviron transcription of deviron transcription of the transcription of transcription of the transcription of tra	Zhen XJ 2013	QQC + sodium nitroprusside/sodium nitroprusside	50/50	$59.2 \pm 5.2/59.8 \pm 4.1$	23/27	27/23	Clinical efficiency	8 w	[28]
hydrochloride/benazepil 35/35 66667 17/18 18/17 hydrochloride/benazepil 35/35 66667 17/18 18/17 hydrochloride/benazepil 35/35 6665.7 ± 8.54 20/22 19/13 QQC+ chrinecabilar/chrinecabiline 42/42 64.12 ± 86/86.5 7 ± 8.5 20/22 19/13 QQC+ timerazidiar/chrinecabiline 41/41 64.12 ± 86/86.5 7 ± 8.5 20/22 19/13 QQC+ timerazidiar/chrinecabiline 40/49 64.6 ± 7.4(6.2.7 ± 8.1 14/25 16/24 QQC+ sodium introprusside/sodium 34/34 64.9 ± 5.6(6.5.2 ± 6.8 15/15 18/15 QQC+ sodium introprusside/sodium 47/47 38.5 ± 4.5(6.5.3 ± 7.9 15/15 18/15 QQC+ sodium introprusside/sodium 47/47 38.5 ± 7.64(6.3.8 ± 7.9 15/15 18/15 QQC+ sodium introprusside/sodium 47/47 38.5 ± 7.64(6.3.8 ± 7.9 16/15 16/12 QQC+ sodium introprusside/sodium 47/47 38.5 ± 7.64(6.3.8 ± 7.9 16/15 16/15 QQC+ sodium introprusside/sodium 47/47 38.5 ± 7.64(6.3.8 ± 7.9 16/15 16/15 QQC+ sodium introprusside/sodium 47/47 38.5 ± 7.64(6.3.8 ± 7.9 16/15 16/15 QQC+ sodium introprusside/sodium 47/47 38.2 ± 7.64(6.3.8 ± 7.9 16/15 16/15 QQC+ christoproloh/metoprolol 39/39 38.4 ± 5.94(5.3.7 ± 3.2 17/19 18/18 QQC+ christoproloh/metoprolol 39/39 38.4 ± 5.94(5.3.2 ± 2.2 17/19 18/18 QQC+ christoproloh/metoprolol 39/39 38.4 ± 5.94(5.3.2 ± 2.2 2.0/24 2.0/21 QQC+ christoproloh/metoprolol 39/39 38.4 ± 5.94(5.3.2 ± 2.2 2.0/24 2.0/21 QQC+ trinecabiline/trinecabiline 40/40 39/39 38.4 ± 5.94(5.3.2 ± 2.2 2.0/24 2.0/21 QQC+ trinecabiline/trinecabiline 40/40 30/39 3.0/39 3.0/19 3.0/19 QQC+ trinecabiline/trinecabiline 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40 40/40	Du XC 2013	QQC + sodium nitroprusside/sodium	26/56	635+36			Clinical efficacy TVEE TVEDD: TVESD: MTWHE		[67]
hydrochloride chematerial 35/35 66/67 17/18 18/17 COC+ chraceful chematerial 30/30 58 ± 15/57 ± 18 18/12 OQC+ chraceful chematerial 42/42 64.12 ± 8.68/63.7 ± 8.54 20/22 19/23 OQC+ trimetazidine trimetazidine chematerial 41/41 61.2 ± 8.68/63.7 ± 8.54 20/22 19/23 OQC+ trimetazidine trimetazidine chematerial 41/42 61.6 ± 7.46.2 ± 8.1 14/26 16/24 OQC+ trimetazidine trimetazidine 41/41 30/30 48.12 ± 5.12/48.5 ± 4.25 15/15 18.Dec OQC+ metoprolol attrate metoprolol 30/30 48.12 ± 5.12/48.5 ± 4.25 15/15 18.Dec OQC+ metoprolol attrate 47/47 58.5 ± 4.7/58.9 ± 46 27/20 26/21 OQC+ metoprolol metoprolol 47/47 58.5 ± 4.7/58.9 ± 46 27/20 26/21 OQC+ metoprolol/metoprolol 47/47 58.5 ± 4.7/58.9 ± 46 27/20 26/21 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/53.7 ± 5.2/20 27/20 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/20 27/20 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/20 27/20 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/20 27/20 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/20 27/20 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/20 27/20 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/53.7 ± 5.2/20 OQC+ metoprolol/metoprolol 47/47 52.19 ± 5.1/58.3 ± 5.2/20 27/20 OQC+ metoprolol/metoprolol 47/47 57/47 27/47 27/20 27/20 OQC+ metoprolol/metoprolol 47/47 57/47 27/20 27/20 OQC+ metoprolol/metoprolol 47/47 47/4		nitroprusside							[
hydrochlordec 2013 2014 2015	7014	QQCs + Denazeprii	35/35	19(33	01/21	71/01	Clinical efficacy, LVEF, LVEDD, SBP, DBP, HR, E/A,	9	[30]
QQC+ -timetacidine charaction 30,30 SR ± 18,57 ± 18 18/12 19/11 QQC+ timetacidine charaction 4,42 64,12 ± 86,865.7 ± 8.54 20/22 19/23 QQC+ timetacalidine charactione charaction	Guo L 2014	nydrochloridec hydrochloridec	66/66	00/07	1//10	10/17/	adverse reaction	10 111	[06]
QQC+ timetaxidine/timetaxidine 42,42 64,12±6.868.83.57±8.54 20/22 19/23 QQC+ timetaxidine/timetaxidine 42,42 64,12±6.868.83.57±8.54 20/22 19/23 QQC+ timetaxidine/timetaxidine 49,49 61.6±7.462.7±8.1 14.26 15/15 23/12 QQC+ timetaxidine/timetaxidine 40,40 61.6±7.462.7±8.1 14.26 15/12 23/12 QQC+ timetaxidine/timetaxidine 40,40 61.6±7.462.7±8.1 14.26 15/12 15/12 QQC+ sockium introprusside/sodium 47/47 58.5±4.7/58.9±4.6 27/20 26/21 QQC+ sockium introprusside/sodium 47/47 58.5±4.7/58.9±4.6 27/20 26/21 QQC+ sockium introprusside/sodium 47/47 52.19±5.17/53.3±5.43 25/22 26/21 QQC+ sockium introprusside/sodium 47/47 52.19±5.17/53.3±4.23 26/22 26/21 QQC+ sockyolol/metoprolol 49/49 67.8±5.665.2±5.8 20/10 18/13 QQC+ timetoprolol/metoprolol 30/39 70.2±9.11/17.14±9.35 20/10 18/13 QQC+ timetoprolol/metoprolol 30/20 </td <td>Feng CY 2015</td> <td>QQC + Carvedilol/Carvedilol</td> <td>30/30</td> <td>$58 \pm 15/57 \pm 18$</td> <td>18/12</td> <td>19/11</td> <td>Clinical efficacy, LVEF, LVEDD, adverse reaction</td> <td>6 m</td> <td>[31]</td>	Feng CY 2015	QQC + Carvedilol/Carvedilol	30/30	$58 \pm 15/57 \pm 18$	18/12	19/11	Clinical efficacy, LVEF, LVEDD, adverse reaction	6 m	[31]
QQC+ timetaxidine trimetaxidine 42,42 64±9/64±8 20/12 19/13 QQC+ timetaxidine chindrataxidine 49,49 61.6±7.466.7±8.1 42/2 17/22 QQC+ timetaxidine chindrataxidine 49,49 61.6±7.466.7±8.1 14/25 15/24 27/22 QQC+ bisoprolo/lisoprolod tartate/metoprolod 30,30 48,12±5.12/48.56±4.25 15/15 18-Dec QQC+ sodium intoprasside/sodium 47/47 38.5±4.7/38.9±4.6 27/20 26/21 QQC+ sodium intoprasside/sodium 47/47 38.5±4.7/38.9±4.6 27/20 26/21 QQC+ sodium intoprasside/sodium 47/47 22.19±5.17/33.1±5.43 25/22 26/21 QQC+ sodium intoprasside/sodium 47/47 38.5±4.64/38.9±4.8 25/22 26/21 QQC+ sodium intoprasside/sodium 47/47 38.5±4.7/38.9±4.8 25/22 26/21 QQC+ sodium intoprasside/sodium 47/47 38.5±4.56/65.2±5.3 25/22 26/21 QQC+ socytum intoprasside/sodium 47/47 35.945.35.9±5.3 20/19 18/18 QQC+ metoprolol/metoprolol 38/39 38.45±4.56/65.2±5.3	Wei HC 2015	QQC + trimetazidine/trimetazidine	42/42	$64.12 \pm 8.68/63.57 \pm 8.54$	20/22	19/23	Clinical efficacy, NT-proBNP, NO, APN	e m	[32]
QQC + trimetazidine dihydrochloride/trimetazidine dihydrochloride/trimetazidine/trimetazidine/trimetazidine/trimetazidine/trimetazidine/trimetazidine/trimetazidine	Yin YS 2015	QQC + trimetazidine/trimetazidine	42/42	$64 \pm 9/64 \pm 8$	20/22	19/23	Clinical efficacy, LVEF, LVEDD, LVESD, 6MWT, HR	6 m	[33]
QQC+ trimetaxidine dihytochloride (trimetaxidine dihytochloride) 49/40 61.6 ± 7.4/6.2 ± 8.1 14/26 25/24 27/12 QQC+ bisoprolo/bisoprolol 30/30 48.12 ± 5.12/48.56 ± 4.5 15/15 18-Dec QQC+ sodium nitroprusside sodium sodium sodium sodium sodium sod	Li WH 2015	QQC + trimetazidine/trimetazidine	41/41		25/16	23/18	Clinical efficacy, LVEF, LVEDD, NT-proBNP, adverse reaction	8 w	[34]
QQC+ histoprolobil supprolobil	Zhang HY 2015	QQC + trimetazidine dihydrochloride/trimetazidine	49/49		25/24	27/22	Clinical efficacy, LVEF, 6MWT, NT-proBNP	5 m	[32]
QQC+ metoprolol tartate/metoprolol autroprusside/sodium 47/47 38.5 ± 4.7/58.9 ± 4.6 15/15 18-Dec QQC+ sodium nitroprusside/sodium 34/34 64.9 ± 5.6/65.2 ± 6.8 15/19 17/17 QQC+ sodium nitroprusside/sodium 34/34 64.9 ± 5.6/65.2 ± 6.8 15/19 17/17 QQC+ sodium nitroprusside/sodium 47/47 52.19 ± 5.17/53.3 ± 5.43 25/22 26/21 QQC+ metoprolol/metoprolol 49/49 67.87 ± 7.64/66.3 ± 7.94 26/23 27/12 QQC+ carvedilo/carvediol 49/49 67.87 ± 7.64/66.3 ± 7.94 26/23 25/19 QQC+ carvedilo/carvediol 49/49 67.87 ± 7.64/66.3 ± 7.94 26/21 23/19 QQC+ carvediol/carvediol 49/49 67.87 ± 7.64/66.3 ± 7.94 26/23 25/19 QQC+ carvediol/carvediol 49/49 67.87 ± 7.64/66.3 ± 7.94 26/23 25/19 QQC+ metoprolol/metoprolol 48/42 22.94/53.95 ± 6.18 21/19 24/19 QQC+ metoprolol/metoprolol 39/39 65.94 ± 3.56/6.3 ± 7.5 26/24 25/22 QQC+ metoprolol/metoprolol 29/29 63.89 ± 1.12.6 (63.	2100 WW 20047	unyarocnionae	40/40	1 8 + 7 63/4 7 + 9 1	30/1/1	10/31	Clinical office are BND CBD DBD advanced and the	3	[36]
QQC+ sodium intoprusside/sodium 47/47 38.5 ± 4.7/58.9 ± 4.6 25/12 18-Dec QQC+ sodium intoprusside/sodium 34/34 64.9 ± 5.6/65.2 ± 6.8 15/19 17/17 QQC+ sodium intoprusside/sodium 47/47 32.5 ± 4.7/58.9 ± 4.6 27/20 26/21 QQC+ metoprolol/metoprolol 62/63 45/42 52.19 ± 5.17/53.3 ± 5.4 22/22 26/21 QQC+ metoprolol/metoprusside/sodium 47/47 52.19 ± 5.17/53.3 ± 5.4 22/22 26/21 QQC+ metoprolol/bisoprolol 43/42 52.3 ± 4.52/53.3 ± 5.4 22/21 26/21 QQC+ metoprolol/metoprolol 39/39 88.45 ± 5.94/53.97 ± 6.8 21/18 24/15 QQC+ metoprolol/metoprolol 39/39 6.54 ± 3.62/63.2 ± 5.2 26/21 26/21 QQC+ metoprolol/metoprolol 39/39 6.64 ± 3.62/63.2 ± 5.2 26/11 18/15 QQC+ metoprolol/metoprolol 39/39 6.64 ± 5.36/63.2 ± 5.3 20/10 18/13 QQC+ metoprolol/metoprolol 39/39 6.11 ± 1.1.26/63.2 ± 1.5 20/10 18/13 QQC+ trimetazidine (trimetazidine (trimetazidine (trimetazidine (trimetazidine (Zilalig A W 2010	OOC + metonrolol tartrate/metonrolol	40/40	01.0 T /.4/02./ T 0.1	14/20	10/ 24	Clinical efficacy RNP SRP DBP clinical efficacy HR Hs-cTn-T	3 1111	[96]
QQC + sodium nitroprusside column introprusside column nitroprusside column c	Gai YB 2016	tartrate	30/30	$48.12 \pm 5.12/48.56 \pm 4.25$	15/15	18-Dec	adverse reaction	3 m	[37]
QQC+ sodium introprusside/sodium 34/34 64.9±5.6/65.2±6.8 15/19 17/17 qQC+ sodium introprusside codium coprolol/metoprolol code conservation code code conservation code code conservation code code code code code code code code	Wang ZX 2016	QQC + sodium nitroprusside/sodium	47/47	$58.5 \pm 4.7/58.9 \pm 4.6$	27/20	26/21	Clinical efficiency	2 w	[38]
QCC+ metoprolof metoprolof 62/63 64.9±5.6/65.2±6.8 15/19 17/17 QQC+ metoprolof/metoprolof 62/63 62/19±5.17/53.31±5.43 25/22 26/21 QQC+ sodium nitroprusside/sodium 47/47 52.19±5.17/53.31±5.43 25/22 26/21 QQC+ bisoprolof/metoprolof 49/49 67.87±7.64/66.38±7.94 26/22 27/12 QQC+ carvedilof carvedilof arceliol (arceliol arceliol arce		OOC + sodium nitroprusside/sodium							
QQC+ metoprolol/metoprolol 62/63 26/21 QQC + bisoprolol/metoprolol 47/47 52.19±5.17/53.31±5.43 25/22 26/21 QQC + bisoprolol/bisoprolol 49/49 67.87±7.64/66.38±7.94 26/23 27/22 QQC + bisoprolol/bisoprolol 39/39 58.45±5.94/53.71±3.24 22/21 23/19 QQC + carvedilol/carvedilol 36/36 65.41±3.62/65.32±3.52 17/18 24/15 QQC + metoprolol/metoprolol 30/30 70.21±9.11/7.1.04±9.35 20/10 18/18 QQC + metoprolol/metoprolol 30/30 70.21±9.11/7.1.04±9.35 20/10 18/18 QQC + metoprolol/metoprolol 30/30 70.21±9.11/7.1.04±9.35 20/10 18/18 QQC + metoprolol/metoprolol 30/30 63.9±1.2/66.3.2±1.2.4 26/24 25/21 QQC + trimetazidine/trimetazidine 46/46 61.85±4.33/61.7±1.14 24/23 26/24 QQC + trimetazidine/trimetazidine 46/46 61.85±4.33/61.7±1.14 24/23 26/24 QQC + trimetazidine/trimetazidine 40/46 61.85±4.33/61.7±1.2 23/17 22/18 QQC +	Sun FR 2016	ACC + southin introp usside	34/34	$64.9 \pm 5.6/65.2 \pm 6.8$	15/19	17/17	Clinical efficacy, LVEF, plasma ADH value	2 w	[39]
QQC+ sodium nitroprusside/sodium 47/47 52.19±5.17/53.31±5.43 25/22 26/21 QQC+ bioproblosioprolol of Control bisoprolol/bisoprolol of Control bisoprolol/bisoprolol of Control bisoprolol/bisoprolol and Control bisoprolol/metoprolol and Control bisoprolol and Control bisoprolol and Control bisoprolol/metoprolol and Control bisoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metoprolol/metop	Hu S 2017	QQC+metoprolol/metoprolol	62/63				Clinical efficacy, LVEF, BNP, HR	12 m	[40]
QQC+ bisoprolol/bisoprolol 49/49 67.87±7.64/66.38±7.94 26/23 27/22 QQC+ carvedilol/carvedilol 39/39 58.45±5.94/53.97±6.18 21/18 24/15 QQC+ carvedilol/carvedilol 39/39 58.45±5.94/53.97±6.18 21/18 24/15 QQC+ metoprolol/metoprolol 36/36 65.41±3.62/65.32±1.25 17/19 18/18 QQC+ metoprolol/metoprolol 30/30 70.21±9.11/71.04±9.35 20/10 18/18 QQC+ metoprolol/metoprolol 29/29 63.3±7.9/64.5±7.5 26/14 25/25 QQC+ metoprolol/metoprolol 50/50 63.3±7.9/64.5±7.5 26/24 25/25 QQC+ trimetazidine/trimetazidine 40/4 61.85±4.33/61.47±5.14 24/23 26/21 QQC+ trimetazidine/trimetazidine 40/4 61.85±4.33/61.27±1.13 24/23 26/21 QQC+ trimetazidine/trimetazidine 40/4 70.39±8.43/71.23±9.95 23/17 23/17 QQC+ ivabradine/rabradine 51/51 55.09±7.41/54.63±7.3 20/19 21/18 QQC+ sogrammine/levocarmine 40/40 70.39±8.43/71.23±9.95 23/17 23/18 </td <td>Han CX 2017</td> <td>QQC + sodium nitroprusside/sodium</td> <td>47/47</td> <td>$52.19 \pm 5.17/53.31 \pm 5.43$</td> <td>25/22</td> <td>26/21</td> <td>Clinical efficacy, LVEF, LVEDD, LVESD, SF-36</td> <td>6 m</td> <td>[41]</td>	Han CX 2017	QQC + sodium nitroprusside/sodium	47/47	$52.19 \pm 5.17/53.31 \pm 5.43$	25/22	26/21	Clinical efficacy, LVEF, LVEDD, LVESD, SF-36	6 m	[41]
QQC+ carvedilol/carvedilol 49/49 07.81 ± 1.6406.38 ± 1.794 20/12 2/12 QQC+ carvedilol/carvedilol 39/39 58.44 ± 5.2/3.71 ± 3.24 22/21 23/19 QQC+ carvedilol/carvedilol 39/39 58.44 ± 5.2/3.71 ± 3.24 21/21 23/19 QQC+ carvedilol/carvedilol 36/36 65.41 ± 3.62/65.32 ± 3.52 17/19 18/18 QQC+ metoprolol/metoprolol 30/30 70.21 ± 9.11/71.04 ± 9.35 20/10 18/12 QQC+ trimetazidine/trimetazidine 50/50 63.3 ± 7.9/64.5 ± 7.5 26/24 25/21 QQC+ trimetazidine/trimetazidine/trimetazidine/trimetazidine/trimetazidine/trimetazidine/trimetazidine/trimetazidine 46/46 61.85 ± 4.33/61.27 ± 9.2 26/20 25/21 QQC+ trimetazidine/trimetazidine 47/47 60.14 ± 11.28/61.27 ± 11.4 24/23 26/20 QQC+ trimetazidine/trimetazidine 47/47 60.14 ± 11.28/61.27 ± 11.4 24/23 26/21 QQC+ trimetazidine/trimetazidine/trimetazidine 40/40 70.39 ± 8.43/71.23 ± 9.95 23/19 30/21 QQC+ kodulum nitroprusside/sodium 40/40 70.39 ± 8.43/71.23 ± 9.95 23/15 22/18	0100 281 1	nitroprusside	07,07	110000000000000000000000000000000000000	20,70	6	מזאת זיי מתחוון תחוון אין ויייור		. 3
QQC+ carveditol/carveditol 3/37	Zhon VE 2018	QQC + pisoproiol/pisoproiol	49/49	6/.8/ ± /.04/66.38 ± /.94 52 34 ± 4 52/53 71 ± 3 24	26/23	27/177	Cimical efficacy, LVEF, LVEDD, SV, BINF	m y	[42]
QQC+ metoprolol/metoprolol 36/36 65.41±3.62/65.32±5.22 17/19 18/18 QQC+ metoprolol tartrate/metoprolol 30/30 70.21±9.11/710.4±9.35 20/10 18/12 QQC+ metoprolol/metoprolol 29/29 63.69±12.76/63.2±12.36 14/15 16/13 QQC+ trimetazidine/trimetazidine 50/50 63.9±12.76/63.2±11.36 26/20 25/25 QQC+ trimetazidine/trimetazidine 46/46 61.85±4.33/61.47±5.14 26/20 25/21 QQC+ trimetazidine/trimetazidine 47/47 60.14±11.28/61.27±11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 47/47 60.14±11.28/61.27±11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 47/47 60.14±11.28/61.27±11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 40/40 70.39±8.43/71.23±9.95 23/17 23/17 QQC+ levocarnitine/elvocarnitine 40/40 70.39±8.43/71.23±9.95 23/17 22/18 QQC+ socarvitine/lol/bisoprolol 39/39 61.7±2.1/62.5±2.3 20/19 21/18 QQC+ carvedilol/carvedilol 39/39 67.2±0.6/67.4±0.	Ren WW 2018	OOC + carvedilol	39/39	58 45 + 5 94/53 97 + 618	21/18	24/15	Clinical efficacy, LVEF, LVEDD, LVESD, ADL	0 m 9	[44]
QQC+ metoprolol tartrate/metoprolol 30/30 70.21±9.11/71.04±9.35 20/10 18/12 tartrate QQC+ metoprolol/metoprolol 29/29 63.69±12.76/63.25±12.36 14/15 16/13 QQC+ trimetazidine/trimetazidine 50/50 63.9±12.76/63.25±12.36 14/15 16/13 QQC+ trimetazidine/trimetazidine 46/46 61.85±4.33/61.47±5.14 26/20 25/25 QQC+ trimetazidine/trimetazidine 47/47 60.14±11.28/61.27±11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 47/47 60.14±11.28/61.27±11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 40/40 70.39±8.43/71.23±9.95 23/17 26/21 QQC+ levocarnitine/levocarnitine 40/40 70.39±8.43/71.23±9.95 23/17 23/17 QQC+ levocarnitine/levocarnitine 40/40 70.39±8.43/71.23±9.95 23/17 23/18 QQC+ levocarnitine/levocarnitine 40/40 70.39±8.43/71.23±9.95 23/17 23/18 QQC+ levocarnitine/levocarnitine 40/40 70.39±8.43/71.23±9.95 23/15 11/18 QQC+ socarnitine/levocarnitine <t< td=""><td>Li J 2018</td><td>QQC+ metoprolol/metoprolol</td><td>36/36</td><td>65.41 ± 3.62/65.32 ± 3.52</td><td>17/19</td><td>18/18</td><td>Clinical efficacy, BNP, Hs-cTnT</td><td>3 m</td><td>[45]</td></t<>	Li J 2018	QQC+ metoprolol/metoprolol	36/36	65.41 ± 3.62/65.32 ± 3.52	17/19	18/18	Clinical efficacy, BNP, Hs-cTnT	3 m	[45]
QQC+ metoprolol/metoprolol 29/20 0.0.2 ± 9.11/1.0.4 ± 7.5.3 20/10 18/11 QQC+ trimetazidine/trimetazidine 46/46 63.54 ± 12.76/63.25 ± 12.36 14/15 16/13 QQC+ trimetazidine/trimetazidine 46/46 63.58 ± 4.33/61.47 ± 5.14 26/24 25/25 QQC+ trimetazidine/trimetazidine 47/47 60.14 ± 11.28/61.27 ± 11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 47/47 60.14 ± 11.28/61.27 ± 11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 47/47 60.14 ± 11.28/61.27 ± 11.41 24/23 26/21 QQC+ trimetazidine/trimetazidine 40/40 70.39 ± 8.43/71.23 ± 995 23/17 23/17 QQC+ levocarmitine/evocarmitine 40/40 70.39 ± 8.43/71.23 ± 995 23/17 23/17 QQC+ sodium nitroprussides 40/40 70.39 ± 8.43/71.23 ± 995 23/17 23/18 QQC+ sodium nitroprusside 39/39 61.7 ± 2.1/62.5 ± 2.3 20/19 21/18 QQC+ soprolol/bisoprolol 38/33 56.01 ± 13.55/55.11± 12.12 23/15 18/15 QQC+ carvediol/carvediol 41/41	010C dV W	QQC+metoprolol tartrate/metoprolol	00/00	700.1011	01,00	61/01	ביין איזם מומם ממחיזו איז מומם ממחיזו איז מומם ממחיזו איז מיזם מיזם ביין ביין ביין כיין		
QQC+ metoprolol/metoprolol 29/29 63.69 ± 12.76(63.25 ± 12.36 14/15 16/13 QQC+ trimetazidine/trimetazidine 50.65 63.3 ± 7.9(64.3 ± 7.5 26/24 25/25 QQC+ trimetazidine/trimetazidine 46/46 60.14 ± 11.28(61.27 ± 11.4 24/23 26/21 QQC+ trimetazidine/trimetazidine 47/47 60.14 ± 11.28(61.27 ± 11.4 24/23 26/21 QQC+ trimetazidine/trimetazidine 47/47 60.14 ± 11.28(61.27 ± 11.4 24/23 26/21 QQC+ trimetazidine/trimetazidine 40/40 70.39 ± 8.43/71.23 ± 9.95 23/19 30/21 QQC+ trimetazidine/trimetazidine 40/40 70.39 ± 8.43/71.23 ± 9.95 23/17 23/17 QQC+ trimetazidine/trimetazidine/carvadiol 39/39 61.7 ± 2.1/62.5 ± 2.3 20/19 21/18 QQC+ carvediol/biarvediol 38/33 56.01 ± 13.55/55.11 ± 12.12 23/15 18/15 QQC+ metoprolol/metoprolol 41/41 59.4 ± 11.5/88 ± 12.4 20/21 22/19 QQC+ metoprolol/metoprolol 42/42 70.56±9.68/706.2± 9.06 25/17 22/19 QQC+ metoprolol/metoprolol 42/42	wallg AF 2010	tartrate	06/06	/0.21 ± 9.11//1.04 ± 9.33	20/10	10/12	Chincal enicacy, LVEDD, DINF, E/A, auverse reaction	0 111	[40]
QQC+ trimetazidine frimetazidine 50/50 63.3 ± 7.9(45.5 ± 7.5 26/24 25/22 QQC+ trimetazidine/trimetazidine frimetazidine frimetazidine/trimetazidine frimetazidine frimeta	Wang QM 2018	QQC + metoprolol/metoprolol	29/29	$63.69 \pm 12.76/63.25 \pm 12.36$	14/15	16/13	Clinical efficacy, LVEF, HR	8 w	[18]
QQC+ trimetazidine/trimetazidine QQC+ trimetazidine/trim	Liu LP 2018	QQC + trimetazidine/trimetazidine	50/50	63.3 ± 7.9/64.5 ± 7.5	26/24	25/25	Clinical efficacy, LVEF, LVESV, LVEDV	e m	[47]
QQC + Unintegration for the following and the following the following discontinuous and the following discontinuous discontinuous declaration for the following discontinuous declaration for the following discontinuous declaration for following discontinuous declaration for following discontinuous declaration for following discontinuous declaration for following discontinuous declaration following discontinuous discontinuou	Wang XF 2018	QQC + trimetazidine/trimetazidine	46/46	$61.85 \pm 4.33/61.47 \pm 5.14$	26/20	25/21	Clinical efficient MIMINI consists of a sequence	o m	[48]
QQC+structural introprusside sodium 40/40 70.39 ± 8.43/71.23 ± 9.95 23/17 23/18 22/17 21/18 22/19	Wang VI, 2018	OOC + transetazionie/transetazionie	51/51	55 09 + 7 41/54 63 + 7 92	32/19	30/21	Chincal enicacy, MLW11r, copepuit, Gal-3, auverse reaction Clinical efficacy HR adverse reaction	3 K	[49]
QQC+ sodium nitroprusside nitroprusside dQC+ bisoprolol/bisoprolol 40/40 64/66 19/21 22/18 QQC+ bisoprolol/bisoprolol 38/33 56.01 ± 13.55/55.12 ± 12.12 20/19 21/18 QQC+ carvedilol/carvedilol 38/39 67.2 ± 0.6/67.4 ± 0.3 22/17 18/15 QQC+ carvedilol/carvedilol 53/53 66.49 ± 5.37/67.31 ± 5.24 33/20 31/22 QQC+ metoprolol/metoprolol 41/41 59.4 ± 11.5/58.8 ± 1.2.4 20/21 22/19 QQC+ metoprolol/metoprolol 42/42 70.56 ± 9.68/70.6.2 ± 9.06 25/17 28/14 QQC+ metoprolol/metoprolol 42/40 70.56 ± 9.68/70.6.2 ± 9.06 25/17 28/14 QQC+ metoprolol/metoprolol 40/40 62.11 ± 9.2/6(1.4 ± 9.3 26/14 25/15 QQC+ metoprolol tartrate/metoprolol 39/39 62.01 ± 5.62/61.6.8 ± 5.79 17/22 18/21 QQC+ metoprolol tartrate/metoprolol 53/53 69/21 ± 1.10/69.51 ± 1.28 30/23 29/24	Wang CF 2018	QQC + levocarnitine/levocarnitine	40/40	70.39 ± 8.43/71.23 ± 9.95	23/17	23/17	Clinical efficacy, 6MWT, IL-6, IL-10, TNF-a	1 m	[51]
nitroprusside 40,40 61.7±2.1/62.5±2.3 20/19 22.10 QQC+bisoprolol/bisoprolol 38/33 56.01±13.55/53.12±12.12 23/15 18/15 QQC+coenzymeQ10+/coenzymeQ10 38/33 56.01±13.55/53.12±12.12 23/15 18/15 QQC+carvediol/carvedilol 53/53 66.49±5.37/67.31±5.24 33/20 31/22 QQC+metoprolol/metoprolol 41/41 59.4±11.5/58.8±12.4 20/21 22/19 QQC+metoprolol/metoprolol 40/40 62.1±9.2/6(1.4±9.3 25/17 28/14 QQC+metoprolol/metoprolol 39/39 62.1±5.62/61.68±5.79 17/22 18/21 QQC+metoprolol/metoprolol 53/53 69/1±1.10/69.51±1.28 30/23 29/24	1 v V 2018	QQC + sodium nitroprusside/sodium	40/40	64/66	16/51	22/18	Olinical officery LVED RNP	, m	[52]
QQC+ bisoprolol/bisoprolol 39/39 61.7±2.1/62.5±2.3 20/19 21/18 QQC+ coenzymeQ10+/coenzymeQ10 38/33 56.01±13.55/53.12±12.12 23/15 18/15 QQC+ carvediol/carvediol 39/39 67.2±0.6/67.4±0.3 22/17 21/18 QQC+ carvediol/carvediol 53/53 66.49±5.37/67.31±5.24 33/20 31/22 QQC+ metoprolol/metoprolol 41/41 59.4±11.5/58.8±12.4 20/21 22/19 QQC+ metoprolol/metoprolol 42/14 70.56±9.8/7.06.2±9.06 25/17 28/14 QQC+ metoprolol/metoprolol 40/40 6.21±9.2/61.4±9.3 26/14 25/15 QQC+ metoprolol tartrate/metoprolol 39/39 6.01±5.62/61.68±5.79 17/22 18/21 QQC+ metoprolol tartrate/metoprolol 53/53 69/71±1.10/69.51±1.28 30/23 29/24		nitroprusside				i i	The fact of fa	1	1
QQC+ coenzymeQ10+/coenzymeQ10 38/33 56.01±13.55/55.12±12.12 23/15 18/15 QQC+ carvediol/carvediol 59/39 67.2±0.6/67.4±0.3 22/17 21/18 QQC+ carvediol/carvediol 53/53 66.49±5.37/67.31±5.24 33/20 31/22 QQC+ metoprolol/metoprolol 41/41 59.4±11.578.8±12.4 20/21 22/19 QQC+ metoprolol/metoprolol 42/2 70.56±9.68/70.6±9.06 25/17 28/14 QQC+ metoprolol/metoprolol 40/40 6.2.1±9.2/6(1.4±9.3 26/14 25/15 QQC+ metoprolol tartrate/metoprolol 39/39 6.01±5.62/61.68±5.79 17/22 18/21 QQC+ metoprolol tartrate/metoprolol 53/53 69/71±1.10/69.51±1.28 30/23 29/24	Zhang M 2019	QQC + bisoprolol/bisoprolol	39/39	$61.7 \pm 2.1/62.5 \pm 2.3$	20/19	21/18	Clinical efficacy	3 m	[53]
QQC+carvediol/carvediol 39/39 67.2±0.6/67.4±0.3 22/17 21/18 QQC+carvediol/carvediol 53/53 66.49±5.37/67.31±5.24 33/20 31/22 QQC+metoprolol/metoprolol 41/41 59.4±11.578.8±12.4 20/21 22/19 QQC+metoprolol/metoprolol 42/42 70.56±9.68/7.062±9.06 25/17 28/14 QQC+metoprolol/metoprolol 40/40 6.21±9.2/61.4±9.3 26/14 25/15 QQC+metoprolol tartrate/metoprolol 39/39 6.01±5.62/61.68±5.79 17/22 18/21 QQC+metoprolol tartrate/metoprolol 53/53 69/71±1.10/69.51±1.28 30/23 29/24	Wu B 2019	QQC + coenzymeQ10+/coenzymeQ10	38/33	$56.01 \pm 13.55/55.12 \pm 12.12$	23/15	18/15	Clinical emcacy, LVEF, LVEDD, 6MW 1, NI-probNF, adverse reaction	2 m	[54]
QQC+ carvedilol/carvedilol 53/53 66.49 ± 5.37/67.31 ± 5.2 4 33/20 31/22 QQC+ metoprolol/metoprolol 41/41 59.4 ± 11.5/58.8 ± 12.4 20/21 22/19 QQC+ metoprolol/metoprolol 42/42 70.56.98/70.62 ± 90.6 25/17 28/14 QQC+ metoprolol/metoprolol 40/40 62.1 ± 92.6(1.4 ± 9.3) 26/14 25/15 QQC+ metoprolol tartrate/metoprolol 39/39 62.01 ± 5.62/61.68 ± 5.79 17/22 18/21 QQC+ metoprolol tartrate/metoprolol 53/53 69/21 ± 1.10/69.51 ± 1.28 30/23 29/24	Yang QY 2019	QQC + carvedilol/carvedilol	39/39	$67.2 \pm 0.6/67.4 \pm 0.3$	22/17	21/18	Clinical efficacy, LVEF, LVEDD, LVESD, SF-36, ADL	9 m	[55]
QQC+ metoprolol/metoprolol 41/41 59.4 ± 11.5/58.8 ± 12.4 20/21 22/19 QQC+ metoprolol/metoprolol 42/42 70.56 ± 9.68/70.62 ± 9.06 25/17 28/14 QQC+ metoprolol/metoprolol 40/40 62.1 ± 9.2/61.4 ± 9.3 26/14 25/15 QQC+ metoprolol/metoprolol 39/39 62.0 1 ± 5.62/61.68 ± 5.79 17/22 18/21 QQC+ metoprolol tartrate/metoprolol 53/53 69.71 ± 1.10/69.51 ± 1.28 30/23 28/24	Meng JC 2019	QQC + carvedilol/carvedilol	53/53	$66.49 \pm 5.37/67.31 \pm 5.24$	33/20	31/22	Clinical efficacy, LVEF, CI, NT-proBNP, APN	3 m	[26]
QQC+ metoprolol/metoprolol 42/42 70.56 ± 9.68/70.62 ± 9.06 25/17 28/14 QQC+ metoprolol/metoprolol 40/40 62.1 ± 9.2/61.4 ± 9.3 26/14 25/15 QQC+ metoprolol/metoprolol 39/39 62.0 1 ± 5.62/61.68 ± 5.79 17/22 18/21 QQC+ metoprolol tartrate/metoprolol 53/53 69/71 ± 1.10/69.51 ± 1.28 30/23 28/24	Tan X 2019	QQC + metoprolol/metoprolol	41/41	$59.4 \pm 11.5/58.8 \pm 12.4$	20/21	22/19	Clinical efficacy, LVEF, BNP, HR, Hs-cTnT, adverse reaction	8 w	[19]
QQC+ metoprolol/metoprolol $40/40$ $62.1\pm9.2/61.4\pm9.3$ $26/14$ $25/15$ QQC+ metoprolol/metoprolol $39/39$ $62.01\pm5.62/61.68\pm5.79$ $17/22$ $18/21$ QQC+ metoprolol tartrate/metoprolol $53/53$ $69/71\pm1.10/69.51\pm1.28$ $30/23$ $29/24$	Lv DS 2019	QQC + metoprolol/metoprolol	42/42	$70.56 \pm 9.68 / 70.62 \pm 9.06$	25/17	28/14	Clinical efficacy, LVEF, BNP, HR, adverse reaction	e m	[57]
QQC + metoprotol tartrate/metoprotol 53/53 69.71 + 1.10/69.51 + 1.28 30/23 29/24	Liu L 2019	QQC + metoprolol/metoprolol	40/40	$62.1 \pm 9.2/61.4 \pm 9.3$	26/14	25/15	Clinical efficacy, LVEDD, BNP, HR, E/A	e m	[28]
を表で、1.11copt.com and architectures 53/53 69.71 ± 1.10/69.51 ± 1.28 30/23 29/24	Liu r 2019	QQC + metoprolol/metoprolol	66/66	62.01 ± 5.62/61.68 ± 5./9	1/177	18/21	Climical emcacy, LVEF, LVEDD, Cl, adverse reaction	90.0	[66]
tartrate	He W 2019	tartrate	53/53	$69.71 \pm 1.10/69.51 \pm 1.28$	30/23	29/24	Clinical efficacy, LVEF, HR, adverse reaction	w 9	[09]

TABLE 1: Continued.

ID (Author year)	Intervention (T/C)	Sample size (T/C)	Age (T/C)	Gender (men/women)-T	Gender Gender (men/women)-T (men/women)-C	Outcome indicator	Course of treatment	Reference
Wang L 2019	QQC + sacubitril valsartan sodium tablets/sacubitril valsartan sodium tablets	57/57				Clinical efficacy, LVEF, 6MWT, NT-proBNP	1 m	[61]
Zhou Y 2019	QQC+ivabradine/ivabradine	30/30	$55.12 \pm 7.99/54.98 \pm 8.07$	17/13	18/12	Clinical efficacy, ST2, LVEF, BNP, 6MWT, HR, Gal-3, adverse reaction	3 m	[62]
Zhang XN 2019	QQC + sodium nitroprusside/sodium nitroprusside	46/46	$58.36 \pm 5.24/56.75 \pm 5.36$	20/26	22/24	Clinical efficacy, LVEF, LVEDD, LVESD, SF-36	2 m	[63]
Li SJ 2020	QQC + coenzymeQ10/coenzymeQ10	92/92	$67.0 \pm 4.7/66.1 \pm 4.9$	48/44	51/41	Clinical efficacy, LVEF, LVEDD, SV, copeptin, Gal-3	1 m	[64]
Guo C 2020	QQC + enalapril maleate and folic acid tablets/enalapril maleate and folic acid tablets	99/99	$65.2 \pm 13.6/64.3 \pm 11.7$	32/24	31/25	Clinical efficacy, LVEF, LVEDD, LVESD, SV, BNP, 6MWT, hs-CRP, adverse reaction	*	[69]
Lu C 2020	QQC + metoprolol tartrate/metoprolol tartrate	53/53	$62.19 \pm 9.82/62.54 \pm 9.11$	30/23	32/21	Clinical efficacy, LVEF, 7, BNP, 6MWT, Gal-3, HO-1, hcy, adverse reaction	12 w	[20]
Su CB 2020	QQC + sacubitril valsartan sodium tablets/sacubitril valsartan sodium tablets	37/37	$59.06 \pm 8.52/58.39 \pm 8.06$	22/15	21/16	Clinical efficacy, ST2, LVEF, CO, SV, NT-proBNP	1 m	[99]
Xu JF 2020	QQC + carvedilol + sacubitril valsartan sodium tablets/carvedilol + sacubitril valsartan sodium tablets	50/50	53.79 ± 4.46/54.13 ± 7.42	22/28	27/23	Clinical efficacy, LVEF, LVEDD, LVESD, 6MWT, NT-proBNP, MLWHF	12 w	[67]
Li CY 2020	QQC + sacubitril valsartan sodium tablets/sacubitril valsartan sodium tablets	35/35	$38.5 \pm 4.1/35.2 \pm 3.9$	13/22	18/17	Clinical efficacy, LVEF, LVEDD, LVESD, BNP, Hs-cfnT, adverse reaction		[89]
Wang L 2020	QQC + levocarnitine/levocarnitine	32/32	$64.21 \pm 4.30/65.31 \pm 5.46$	18/14	17/15	Clinical efficacy, LVEF, BNP	1 w	[69]
Liu CY 2020	QQC+;evocarnitine/levocarnitine	39/39	$70.23 \pm 4.65/69.78 \pm 4.52$	22/17	21/18	Clinical efficacy, LVEF, LVEDD	1 m	[20]

short-axis shortening rate; SF-36: the MOS item short from health survey; ADH: antidiuretic hormone; MLWHF: Minnesota Living with Heart Failure; SBP: systolic blood pressure; DBP: diastolic blood pressure; LVESV: left ventricular end-systolic volume; ADL: activities of daily living; APN: adiponectin; hs-CRP: hypersensitive C-reactive protein; HR: heart rate; Hs-cTnT: high-sensitivity cardiac troponin T; Gal-3: galectin-3; HO-1: heme oxygenase-1; Hcy: homocysteine; LVEDV: left ventricular end-diastolic volume; IL-6: interleukin-6; IL-10: interleukin-10; TNF- α: tumor necrosis factor-α QQC: Qili Qiangxin capsule; ST2: growth stimulation expressed gene 2; LVEF: left ventricular ejection fractions; LVEDD: left ventricular end-diastolic dimension; LVESD: left ventricular end-systolic diameter; CO: carbon monoxide; CI: cardial indexes; SV: stroke volume; BNP: brain natriuretic peptide; 6MWT: 6-min walk test; NT-proBNP: N-terminal pro-B-type natriuretic peptide; NO: nitric oxide; FS: left ventricular

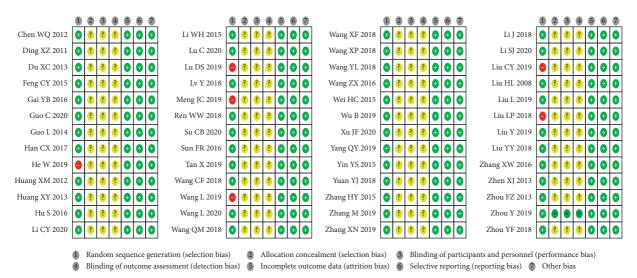


FIGURE 2: Risk of bias summary.

Study or Subgroup	QQC+Me Events	toprolol Total	Metop Events	rolol Total	Weight (%)	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Gai YB 2016	28	30	20	30	7.4	1.40 [1.07, 1.83]	
Li J 2018	33	36	27	36	10.1	1.22 [0.99, 1.51]	-
Liu L 2019	39	40	33	40	12.3	1.18 [1.02, 1.37]	-
Liu Y 2019	37	39	31	39	11.5	1.19 [1.00, 1.42]	-
Lu C 2020	51	53	45	53	16.8	1.13 [1.00, 1.28]	—
Lu DS 2019	40	42	28	42	10.4	1.43 [1.14, 1.79]	
Tan X 2019	40	41	34	41	12.7	1.18 [1.02, 1.36]	-
Wang QM 2018	27	29	22	29	8.2	1.23 [0.98, 1.54]	
Wang XP 2018	30	30	28	30	10.6	1.07 [0.96, 1.20]	+-
Total (95% CI)		340		340	100.0	1.21 [1.14, 1.29]	•
Total events	325		268				
Heterogeneity: Chi ² =	= 9.20, df = 8 (P	= 0.33);	$I^2 = 13\%$				0.5 0.7 1 1.5 2
Test for overall effect:	Z = 6.34 (P < 0)	0.00001)					Metoprolo QQC+Metoprolol

					(a)	
Study or Subgroup	QQC+Car Events	vedilol Total	Carve Events	dilol Total	Weight (%)	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Feng CY 2015	28	30	21	30	13.4	1.33 [1.04, 1.72]	
Meng JC 2019	50	53	42	53	26.9	1.19 [1.02, 1.39]	
Ren WW 2018	37	39	28	39	17.9	1.32 [1.07, 1.63]	
Yang QY 2019	38	39	34	39	21.7	1.12 [0.98, 1.27]	 -
Zhou YF 2018	41	43	31	42	20.1	1.29 [1.07, 1.57]	
Total (95% CI)		204		203	100.0	1.24 [1.14, 1.34]	•
Total events	194		156				
Heterogeneity: Chi ² =	3.49, df = 4 (P	= 0.48);	$I^2 = 0\%$			_	0.5 0.7 1 1.5 2
Test for overall effect: 2	Z = 5.13 (P < 0)	.00001)					Carvedilol QQC+Carvedilol

Risk Ratio

Study or Subgroup	QQC+Trim Events	netazidine Total	Trimeta Events		Weight (%)	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Chen WQ 2012	58	60	50	60	19.2	1.16 [1.03, 1.31]	
Huang XY 2013	29	30	24	30	9.2	1.21 [1.00, 1.46]	
Li WH 2015	39	41	34	41	13.1	1.15 [0.98, 1.34]	-
Liu LP 2018	50	50	43	50	16.7	1.16 [1.03, 1.31]	
Wei HC 2015	40	42	32	42	12.3	1.25 [1.04, 1.50]	
Yin YS 2015	40	42	32	42	12.3	1.25 [1.04, 1.50]	
Zhang HY 2015	36	49	32	49	12.3	1.13 [0.86, 1.47]	
Zhou FZ 2013	18	19	13	20	4.9	1.46 [1.04, 2.04]	
Total (95% CI)		333		334	100.0	1.20 [1.12, 1.27]	•
Total events	310		260				
Heterogeneity: Chi ² =	= 2.73, df = 7 (F	P = 0.91);	$I^2 = 0\%$			_	0.5 0.7 1 1.5 0
Test for overall effect:							0.5 0.7 1 1.5 2 Trimetazidine QQC+Trimetazidine
					(c)	

FIGURE 3: Forest plot of QQC plus Western medicine treatment versus Western medicine only for clinical efficiency (part 1). QQC: Qili Qiangxin capsule.

Weight

Risk Ratio

SVS

QQC+SVS

Study or Subgroup

Study or Subgroup	Events	Total	Events	Total	(%)	M-H, Fixed, 95% CI	M-H, Fixed, 95% CI
Li CY 2020	29	35	25	35	19.1	1.16 [0.90, 1.50]	
Su CB 2020	35	37	27	37	20.6	1.30 [1.05, 1.60]	
Wang L 2019	51	57	41	57	31.3	1.24 [1.03, 1.50]	
Xu JF 2020	46	50	38	50	29.0	1.21 [1.02, 1.44]	-
Total (95% CI)		179		179	100.0	1.23 [1.11, 1.36]	•
Total events	161		131				
Heterogeneity: Chi ² =	0.48, df = 3	(P = 0.9)	$(92); I^2 = 0$	1%		_	0.5 0.7 1 1.5 2
Test for overall effect: 2	Z = 3.99 (P	< 0.000	1)				0.5 0.7 1 1.5 2 SVS QQC+SVS
						(a)	
Study or Subgroup	QQ0 Events	C+SN Total	S Events	N Total	Weight (%)	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Ding XZ 2011	38	44	26	40	11.7	1.33 [1.03, 1.72]	
Du XC 2013	49	56	32	56	13.7	1.53 [1.20, 1.96]	
Han CX 2017	40	47	30	47	12.9	1.33 [1.04, 1.71]	
Huang XM 2012	26	30	18	30	7.7	1.44 [1.04, 2.00]	_
Sun FR 2016	32	34	25	34	10.7	1.28 [1.03, 1.59]	
Wang ZX 2016	43	47	35	47	15.0	1.23 [1.02, 1.48]	
Zhang XN 2019	39	46	30	46	12.9	1.30 [1.02, 1.66]	
Zhen XJ 2013	46	50	36	50	15.4	1.28 [1.06, 1.55]	
Total (95% CI)		354		350	100.0	1.33 [1.23, 1.45]	•
Total events	313		232				
Heterogeneity: $Chi^2 =$	2.53, df = 7	(P = 0.9)	$(92); I^2 = 0$	%			0.5 0.7 1 1.5 2
Test for overall effect: 2	Z = 6.78 (P	< 0.0000	01)				SN QQC+SN

QQC+Bi Events	isoprolo Total			Weight (%)	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
46	49	38	49	43.2	1.21 [1.02, 1.43]	-
34	39	25	39	28.4	1.36 [1.04, 1.77]	
35	40	25	40	28.4	1.40 [1.07, 1.83]	-
	128		128	100.0	1.31 [1.15, 1.49]	•
115		88				
.15, df = 2	(P = 0.5)	(6); $I^2 = 0$	%		_	05 07 1 15 0
= 4.04 (P	< 0.0001)				0.5 0.7 1 1.5 2 Bisoprolol QQC+Bisoprolol
	Events 46 34 35 115 1.15, df = 2	Events Total 46	Events Total Events 46 49 38 34 39 25 35 40 25 128 115 88	Events Total Events Total 46 49 38 49 34 39 25 39 35 40 25 40 128 128 115 88 1.15, df = 2 (P = 0.56); I² = 0%	Events Total Events Total (%) 46 49 38 49 43.2 34 39 25 39 28.4 35 40 25 40 28.4 128 128 100.0 115 88 1.15, df = 2 (P = 0.56); I² = 0%	Events Total Events Total (%) M-H, Fixed, 95% CI 46 49 38 49 43.2 1.21 [1.02, 1.43] 34 39 25 39 28.4 1.36 [1.04, 1.77] 35 40 25 40 28.4 1.40 [1.07, 1.83] 128 128 100.0 1.31 [1.15, 1.49] 115 88 1.15, df = 2 (P = 0.56); I² = 0%

Figure 4: Forest plot of QQC plus Western medicine treatment versus Western medicine only for clinical efficiency (part 2). QQC: Qili Qiangxin capsule, SVS: aacubitril valsartan sodium, and SN: sodium nitroprusside.

Study or Subgroup	QQC	+Meto	prolol	Me	etopro	lol	Weight	Mean Difference	Mean D	ifference	
Study of Subgroup	Mean	SD	Total	Mean	SD	Total	(%)	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Gai YB 2016	72	10	30	94	13	30	7.4	-22.00 [-27.87, -16.13]			
He W 2019	62.12	1.05	53	70.26	1.08	53	15.4	-8.14 [-8.55, -7.73]			
Hu S 2016	63.7	5.4	62	69.2	6.4	63	13.6	-5.50 [-7.57, -3.43]	-		
Liu L 2019	63.6	6.4	40	69.8	5.7	40	12.7	-6.20 [-8.86, -3.54]	+		
Lu DS 2019	60.02	5.25	42	69.99	6.89	42	12.7	-9.97 [-12.59, -7.35]	-		
Tan X 2019	63.5	5.7	41	68.3	5.8	41	13.0	-4.80 [-7.29, -2.31]	+		
Wang QM 2018	60.18	2.26	29	73.57	5.19	29	13.7	-13.39 [-15.45, -11.33]	-		
Wang XP 2018	64.28	6.63	30	69.25	6.47	30	11.5	-4.97 [-8.28, -1.66]	-		
Total (95% CI)			327			328	100.0	-8.71 [-10.93, -6.50]	♦		
Heterogeneity: Tau ²	= 8.23; C	$2hi^2 = 6$	6.92, d	f = 7 (P	< 0.00	0001); 1	$I^2 = 90\%$				
Test for overall effect	z = 7.7	2 (P < 0	0.00001)				-50		0 25	50
									Metoprolol	QQC+Metoprolo	DI

FIGURE 5: Forest plot of QQC plus Western medicine treatment versus Western medicine only for HR. QQC: Qili Qiangxin capsule, HR: heart rate.

Study or Subgroup	QQC Mean	+Meto SD	1	Mean	etopro SD		Weight (%)	Mean Difference IV, Random, 95% C	
He W 2019	45.02	0.16	53	41.62	0.21	53	30.3	3.40 [3.33, 3.47]	
Hu S 2016	43.8	6.5	62	40.5	6.3	63	11.1	3.30 [1.06, 5.54]	
Liu Y 2019	53.79	6.01	39	47.23	5.41	39	9.4	6.56 [4.02, 9.10]	
Lu C 2020	44.98	4.93	53	41.87	4.56	53	14.3	3.11 [1.30, 4.92]	
Lu DS 2019	45.68	6.52	42	39.02	6.08	42	8.7	6.66 [3.96, 9.36]	
Tan X 2019	58.5	7.3	41	53.6	6.7	41	7.3	4.90 [1.87, 7.93]	
Wang QM 2018	46.18	0.58	29	43.72	3.57	29	19.0	2.46 [1.14, 3.78]	+
Total (95% CI)			319			320	100.0	3.86 [2.92, 4.80]	•
Heterogeneity: Tau ²	= 0.76; C	$hi^2 = 1$	4.57, di	f = 6 (P	= 0.0	2); I ² =	59%		-20 -10 0 10 20
Test for overall effect	z = 8.00	6 (P < 0	0.00001)					Metoprolol QQC+Metoprolol

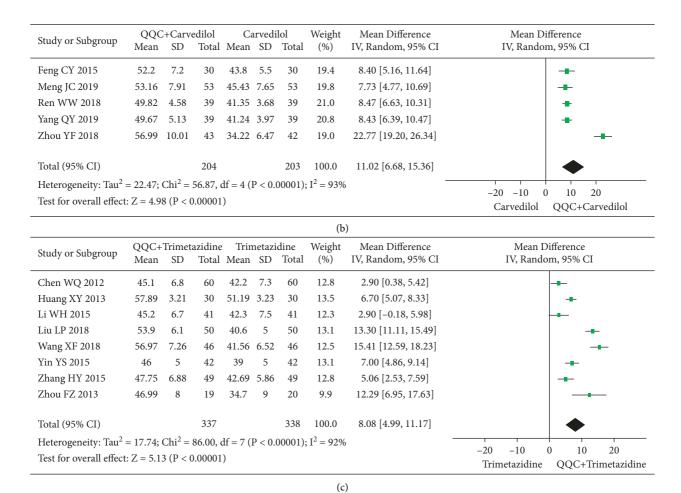


FIGURE 6: Forest plot of QQC plus Western medicine treatment versus Western medicine only for LVEF (part 1). QQC: Qili Qiangxin capsule, LVEF: left ventricular ejection fractions.

Ct., I., C., I	Q	QC+S	VS		SVS		Weight	Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	(%)	IV, Random, 95% CI	IV, Random, 95% CI
Li CY 2020	52.17	9.34	35	41.01	8.55	35	15.4	11.16 [6.96, 15.36]	
Su CB 2020	53.08	3.82	37	49.26	4.03	37	27.3	3.82 [2.03, 5.61]	-
Wang L 2019	58.04	5.96	57	48.89	6.82	57	24.3	9.15 [6.80, 11.50]	-
Xu JF 2020	49.68	0.37	50	44.23	0.36	50	33.0	5.45 [5.31, 5.59]	•
Total (95% CI)			179			179	100.0	6.78 [4.53, 9.04]	•
Heterogeneity: Tau ² Test for overall effect					= 0.00	002); I ²	= 85%	-	-20 -10 0 10 20 SVS QQC+SVS

(a)

FIGURE 7: Continued.

Ct., dr. on C., bono	Q	QC+S	N		SN		Weight	Mean Difference	2	M	ean Differe	nce	
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	(%)	IV, Fixed, 95% C	I	IV	, Fixed, 95%	S CI	
Du XC 2013	44.1	6.4	56	39.6	5.4	56	22.3	4.50 [2.31, 6.69]				_	
Han CX 2017	43.27	6.37	47	39.85	5.96	47	17.2	3.42 [0.93, 5.91]			-	_	
Huang XM 2012	43.2	6.3	30	39.8	5.9	30	11.2	3.40 [0.31, 6.49]					
Lv Y 2018	42	7	40	37	6	40	13.1	5.00 [2.14, 7.86]			_	-	
Sun FR 2016	54.4	2.9	34	49.8	6.5	34	18.7	4.60 [2.21, 6.99]			_	-	
Zhang XN 2019	45.14	6.28	46	40.1	5.81	46	17.5	5.04 [2.57, 7.51]			-	•	
Total (95% CI)			253			253	100.0	4.37 [3.33, 5.40]				•	
Heterogeneity: Chi ²	= 1.45, d	f = 5 (F	P = 0.92); $I^2 = 0$)%				20	-10	0	10	20
Test for overall effect	Z = 8.23	8 (P < 0	0.00001)					-20	-10	•	C+SN	20

Figure 7: Forest plot of QQC plus Western medicine treatment versus Western medicine only for LVEF (part 2). QQC: Qili Qiangxin capsule, SVS: sacubitril valsartan sodium, SN: sodium nitroprusside, LVEF: left ventricular ejection fractions.

Study or Subgroup	QQC- Mean	+Meto SD	prolol Total	Mean	etopro SD	olol Total	Weight (%)	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
Liu L 2019	40	4.3	40	43.4	5.1	40	35.5%	-3.40 [-5.47, -1.33]	
Liu Y 2019	39.14	4.15	39	42.12	4.92	39	37.2%	-2.98 [-5.00, -0.96]	-
Wang XP 2018	40.01	4.27	30	42.45	5.02	30	27.3%	-2.44 [-4.80, -0.08]	
Total (95% CI)			109			109	100.0%	-2.98 [-4.21, -1.75]	•
Heterogeneity: Chi ²	= 0.36, di	f = 2 (I	P = 0.84); $I^2 = 0$	1%				
Test for overall effect	: Z = 4.74	4 (P < 0	0.00001)				-20	-10 0 10 20 Metoprolol QQC+Metoprolol
							(a)	
Study or Subgroup	QQC Mean	+Carv SD		Ca Mean	rvedi SD	lol Total	Weight (%)	Mean Difference IV, Random, 95% CI	Mean Difference IV, Random, 95% CI
Feng CY 2015	46	3	30	51.4	2	30	34.9%	-5.40 [-6.69, -4.11]	+
Ren WW 2018	49.15	3.41	39	57.35	4.18	39	32.4%	-8.20 [-9.89, -6.51]	-
Yang QY 2019	48.17	3.16	39	57.26	4.16	39	32.7%	-9.09 [-10.73, -7.45]	+
Total (95% CI)			108			108	100.0%	-7.51 [-9.85, -5.18]	•
Heterogeneity: Tau ² Test for overall effect					= 0.0	009); I ²	= 86%	-2(O -10 0 10 20 Carvedilol QQC+Carvedilol
							(b)	
Study or Subgroup	QQC+' Mean	Trimet SD		Trin Mean	netazi SD	dine Total	Weight (%)	Mean Difference IV, Fixed, 95% CI	Mean Difference IV, Fixed, 95% CI
Chen WQ 2012	57.6	6.2	60	58.7	6.5	60	16.5%	-1.10 [-3.37, 1.17]	
Huang XY 2013	55.65	3.45	30	60.65	2.21	30	39.6%	-5.00 [-6.47, -3.53]	-
Li WH 2015	63.7	7.3	41	64.1	6.9	41	9.0%	-0.40 [-3.47, 2.67]	
Wang XF 2018	57.74	5.31	46	61.62	5.86	46	16.3%	-3.88 [-6.17, -1.59]	
Yin YS 2015	45	5	42	55	5	42	18.6%	-10.00 [-12.14, -7.86]	-
Total (95% CI)			219			219	100.0%	-4.69 [-5.61, -3.77]	♦
Heterogeneity: Chi ² Test for overall effect					$[^2 = 90]$)%		-2	20 –10 0 10 20 Trimetazidine QQC+Trimetazidine

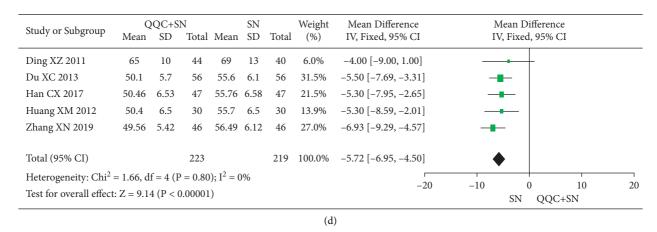


FIGURE 8: Forest plot of QQC plus Western medicine treatment versus Western medicine only for LVEDD. QQC: Qili Qiangxin capsule, SN: sodium nitroprusside, LVEDD: left ventricular end-diastolic dimension.

Study or Subgroup	QQC+					Weight			Mean Difference				
	Mean	SD	Total	Mean	SD	Total	(%)	IV, Random, 95% CI		IV, Rando	om, 95% CI		
Liu LP 2018	88.9	10.2	50	123.6	15.1	50	39.0	-34.70 [-39.75, -29.65]		-			
Wang XF 2018	112.48	11.35	46	131.59	19.4	46	37.4	-19.11 [-25.61, -12.61]		-			
Zhou FZ 2013	129.1	25	19	148.2	29	20	23.6	-19.10 [-36.07, -2.13]					
Total (95% CI)			115			116	100.0	-25.19 [-37.69, -12.68]					
Heterogeneity: Tau ²	= 97.77;	Chi ² =	14.99,	df = 2 (1	P = 0.0	0006);]	$I^2 = 87\%$		-50	-25	0	25	50
Test for overall effect	t: $Z = 3.9$	5 (P < 0	0.0001)						-30	Trimetazidine	-	QC+Trimetaz	

FIGURE 9: Forest plot of QQC plus Western medicine treatment versus Western medicine only for LVEDV. QQC: Qili Qiangxin capsule, LVEDV: left ventricular end-diastolic volume.

Study or Subgroup	Q	QQC+SN					Weight	Mean Difference	Mean Difference		
	Mean	SD	Total	Mean	SD	Total	(%)	IV, Fixed, 95% CI	IV, Fixed, 95% CI		
Du XC 2013	38.2	5.1	56	43.6	4.8	56	36.7	-5.40 [-7.23, -3.57]	-		
Han CX 2017	39.76	5.41	47	44.98	6.54	47	21.0	-5.22 [-7.65, -2.79]	-		
Huang XM 2012	39.7	5.4	30	44.9	6.5	30	13.5	-5.20 [-8.22, -2.18]			
Zhang XN 2019	38.66	4.35	46	45.12	5.69	46	28.8	-6.46 [-8.53, -4.39]	-		
Total (95% CI)			179			179	100.0	-5.64 [-6.75, -4.53]	•		
Heterogeneity: Chi ²		•)%		-20	-10	0 10	20	
Test for overall effect	: Z = 9.95	5 (P < 0	0.00001)				SN	QQC+SN		

FIGURE 10: Forest plot of QQC plus Western medicine treatment versus Western medicine only for LVESD. QQC: Qili Qiangxin capsule, SN: sodium nitroprusside, LVESD: left ventricular end-systolic diameter.

of TCM with western medicine has been developed as a novel therapeutic approach for the treatment of CHF. It has the unique advantage of reducing the adverse reactions compared with Western medicine alone [21]. In this study, we revealed that compared with Western medicine alone, the combination of QQC with Western medicine for CHF showed better clinical efficiency. However, more evidence was required to validate the advantage of QQC plus Western medicine on reducing the occurrence of adverse effects.

QQC is a traditional Chinese medical formulation, which has been demonstrated to improve cardiac function and urine volume of CHF patients. Previous studies have found that the possible mechanisms of QQC in the treatment of CHF might be connected with reversing the increases of both AQP2 and pS256-AQP2 expression and involving the inhibition of V2R and AT1R [13, 73]. The research of the effects of QQC on cardiac function in rats with myocardial infarction suggested that it improved

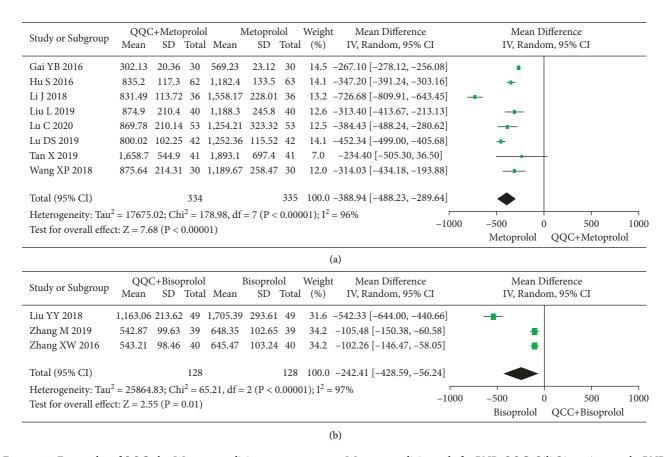


FIGURE 11: Forest plot of QQC plus Western medicine treatment versus Western medicine only for BNP. QQC: Qili Qiangxin capsule, BNP: brain natriuretic peptide.

Study or Subgroup	QQC+	Trimet	azidine	Trin	netazi	dine	Weight	Mean Difference	Mean Difference
study of subgroup	Mean	SD	Total	Mean	SD	Total	(%)	IV, Random, 95% CI	IV, Random, 95% CI
Li WH 2015	0.52	0.17	41	0.66	0.18	41	33.8	-0.14 [-0.22, -0.06]	•
Wei HC 2015	1.33	0.24	42	2.36	0.41	42	33.2	-1.03 [-1.17, -0.89]	•
Zhang HY 2015	1.76	0.38	49	2.01	0.42	49	33.0	-0.25 [-0.41, -0.09]	•
Total (95% CI)			132			132	100.0	-0.47 [-1.01, 0.07]	
Heterogeneity: Tau ²	= 0.23; C	$2hi^2 = 1$	16.22,	df = 2 (P < 0.0	00001);	$I^2 = 98\%$	Ó	$\begin{array}{c ccccccccccccccccccccccccccccccccccc$
Test for overall effect	: Z = 1.70	0 (P =	0.09)						Trimetazidine QCC+Trimetazidin
							(a	.)	
C: 1 C.1	Q	QC+S	VS		SVS		Weight	Mean Difference	Mean Difference
Study or Subgroup	Mean	Total	Mean	SD	Total	(%)	IV, Random, 95% CI	IV, Random, 95% CI	
Su CB 2020	1.52	2.94	37	2.29	3.42	37	16.7	-0.77 [-2.22, 0.68]	
Wang L 2019	1.3	0.28	57	2.31	0.32	57	41.5	-1.01 [-1.12, -0.90]	•
Xu JF 2020	0.34	0.16	50	0.49	0.18	50	41.8	-0.15 [-0.22, -0.08]	•
Total (95% CI)			144			144	100.0	-0.61 [-1.38, 0.15]	
Heterogeneity: Tau ²	= 0.36; C	$2hi^2 = 1$	71.01,	df = 2 (P < 0.0	00001);	$I^2 = 99\%$	_	-2 -1 0 1 2
	: Z = 1.50	SVS QQC+SVS							

FIGURE 12: Forest plot of QQC plus Western medicine treatment versus Western medicine only for NT-proBNP. QQC: Qili Qiangxin capsule, SVS: sacubitril valsartan sodium, NT-proBNP: N-terminal pro-B-type natriuretic peptide.

Study or Subgroup	QQC	+Meto	prolol	Metoprolol V			Weight	Mean Difference	Mean Difference		
	Mean	SD	Total	Mean	SD	Total	(%)	IV, Random, 95% CI	IV, Rando	m, 95% CI	
Gai YB 2016	9	1	30	12	1.2	30	34.3	-3.00 [-3.56, -2.44]			
Li J 2018	8.72	4.28	36	18.75	2.27	36	32.7	-10.03 [-11.61, -8.45]	-		
Tan X 2019	9.29	3.2	41	14.2	3.5	41	33.0	-4.91 [-6.36, -3.46]	-		
Total (95% CI)			107			107	100.0	-5.93 [-9.92, -1.95]			
Heterogeneity: Tau ² Test for overall effect				df = 2 (P < 0.	00001);	$I^2 = 979$	6 –20	-10 (0 10 QQC+Metopro	20 olol

FIGURE 13: Forest plot of QQC plus Western medicine treatment versus Western medicine only for Hs-cTnT. QQC: Qili Qiangxin capsule, Hs-cTnT: high-sensitivity cardiac troponin T.

Study or Subgroup	QQC+ Mean	Trimet SD		Trir Mean	netazi SD		Weight (%)	Mean Difference IV, Random, 95% Cl	[om, 95% CI	
Chen WQ 2012	391.8	32.3	60	377.3	31.6	60	36.0	14.50 [3.07, 25.93]			-	
Yin YS 2015	279	54	42	227	48	42	30.6	52.00 [30.15, 73.85]				_
Zhang HY 2015	529.71	46.59	49	480.37	38.71	49	33.4	49.34 [32.38, 66.30]			-	
Total (95% CI)			151			151	100.0	37.61 [10.93, 64.29]				
Heterogeneity: Tau ² Test for overall effec				df = 2	(P = 0	.0003);	$I^2 = 87\%$)	-100	–50 Trimetazidine	0 50 QQC+Trimet	100 azidine

FIGURE 14: Forest plot of QQC plus Western medicine treatment versus Western medicine only for 6MWT. QQC: Qili Qiangxin capsule, 6MWT: 6-min walk test.

Study or Subgroup	QQC+Metoprolol Events Total		Metoprolol V Events Total		Weight (%)	Risk Ratio M-H, Random, 95% C	Risk Ratio CI M-H, Random, 95% CI
Gai YB 2016	1	30	4	30	4.9	0.25 [0.03, 2.11]	
He W 2019	1	53	7	53	5.1	0.14 [0.02, 1.12]	
Hu S 2016	9	62	24	63	17.8	0.38 [0.19, 0.75]	
Liu Y 2019	1	39	7	39	5.2	0.14 [0.02, 1.11]	
Lu C 2020	9	53	14	53	16.7	0.64 [0.30, 1.36]	
Lu DS 2019	6	42	20	42	15.8	0.30 [0.13, 0.67]	
Tan X 2019	6	41	9	41	14.0	0.67 [0.26, 1.70]	
Wang XP 2018	16	30	14	30	20.5	1.14 [0.69, 1.90]	+
Total (95% CI)		350		351	100.0	0.48 [0.28, 0.81]	•
Total events	49		99				
Heterogeneity: Tau ² =	= 0.28; Chi ² =	= 16.47, df	= 7 (P = 0)	.02); I ²	= 58%		
Test for overall effect:	Z = 2.75 (P)	= 0.006)			0	0.01 0.1 1 10 100 Metoprolol QQC+Metoprolol	

(a)

Figure 15: Continued.

Study or Subgroup	QQC+Trin	Trimetazidine		Weight	Risk Ratio		Risk Ratio		
orday or odogroup	Events	Total	Events	Total (%)	(%)	M-H, Fixed, 95% CI	M-H, Fix	ed, 95% CI	
Chen WQ 2012	2	60	1	60	16.7	2.00 [0.19, 21.47]		-	
Li WH 2015	1	41	2	41	33.3	0.50 [0.05, 5.30]		 	
Yuan YJ 2018	2	47	3	47	50.0	0.67 [0.12, 3.81]			
Total (95% CI)		148		148	100.0	0.83 [0.26, 2.67]	■		
Total events	5		6						
Heterogeneity: Chi ²	= 0.77, df = 2	(P = 0.68)	$I^2 = 0\%$						
Test for overall effect	z = 0.31 (P)	= 0.76)			0.01	0.1 Trimetazidine	1 10 QCC+Trimetaz	100 cidine	
					(l	p)			

FIGURE 15: Forest plot of QQC plus Western medicine treatment versus Western medicine only for adverse effects. QQC: Qili Qiangxin capsule.

cardiac function by keeping the balance between proinflammatory and anti-inflammatory of cardiomyocytes [74]. The LVEF, LVEDD, LVEDV, LVESD, BNP, NT-proBNP, Hs-cTnT, and 6MWT are important indicators to reflect the cardiac function of CHF patients [17, 72, 75]. The results of this research showed that compared with Western medicine alone, the combination of QQC with Western medicine exerted positive effects on improving efficacy of CHF, with increased level of LVEF, LVEDD, and 6MWT and reduced level of HR, LVESD, BNP, and Hs-cTnT of patients with CHF. This research also suggested that QQC could improve the quality of life in patients with CHF, which was in agreement with the research in 2016 [21].

In our research, there is high heterogeneity in the meta-analysis of LVEDV, BNP, NT-proBNP, Hs-cTnT, 6MWT, and adverse effects. The level of cardiac function index is influenced by the age and gander. Moreover, etiology (type 2 diabetes mellitus, obesity, valvular heart disease, and others) and underlying disease (depression, kidney disease, sleep disordered, and others) also significantly affected the cardiovascular system [76]. These factors have not been strictly described and controlled in the included studies, which may lead to the high heterogeneity in the meta-analysis of LVEDV, BNP, NT-proBNP, Hs-cTnT, 6MWT, and adverse effects

This research comprehensively identified the relevant literature, developed evaluation plans, and strictly implemented those plans. These methodological advantages can improve the accuracy and clinical applicability of the results of this study. However, there are several limitations in this research: (1) few studies included for meta-analysis of each indicator may lead to publication bias; (2) the description of allocation concealment is inadequate; (3) the blinding of participants personnel and outcome assessment of included studies are unclear; (4) the overall risk of bias in the included studies was generally high; (5) all subjects included in this study belong to China, it cannot account for ethnic and regional differences. Therefore, more high quality studies were required to find more convincing proof. We recommend researchers report in full their trial methodology such as random sequence generation, allocation concealment, and internationally recognized diagnosis of CHF in future publications.

5. Conclusion

This meta-analysis demonstrated that, compared with Western medicine alone, the combination of QQC and Western medicine exerted more positive effects on improving efficacy and increasing the level of LVEF, LVEDD, and 6MWT, as well as reducs the adverse effects and the level of HR, LVESD, BNP, Hs-cTnT of patients with CHF. The results further proved the efficacy and safety of QQC for CHF patients. However, there are several limitations in our included studies, and more high quality studies are required to provide more convincing proof.

Data Availability

All datasets used and analyzed during this study can be available from the corresponding author upon reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Acknowledgments

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Supplementary Materials

The PRISMA 2020 checklist for the meta-analysis. (Supplementary Materials)

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