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Efficacy and safety of Chinese classical prescriptions for dilated cardiomyopathy: a systematic review and Bayesian network meta-analysis

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Abstract

Background Chinese classical prescriptions (CCPs) are commonly utilized in China as an adjuvant treatment for dilated cardiomyopathy (DCM). Nevertheless, there was insufficient systematic evidence data to show the advantages of CCPs plus current conventional therapy (CT) against DCM. This network meta-analysis (NMA) sought to evaluate and prioritize the six different CCP types' respective efficacies for DCM.

Methods A comprehensive search was conducted from the databases' inception to November 30, 2024, to extract RCTs that addressed the use of CCPs in conjunction with CT for DCM. The databases included PubMed, Embase, Web of Science Core Collection, Cochrane Library, ProQuest, China National Knowledge Infrastructure (CNKI), China Science Periodical Database (CSPD), Chinese Citation Database (CCD), Chinese Biomedical Literature Database (CBM), and ClinicalTrials.gov. The Cochrane Risk of Bias assessment tool was used to evaluate the quality of the included RCTs. Surface under the cumulative ranking curve (SUCRA) probability values was employed to rank the relative efficacy. Bayesian network meta-analysis was applied to evaluate the efficacy of various CCPs. This review was registered with PROSPERO (CRD42024586365).

Results Following the application of inclusion and exclusion criteria, 27 eligible RCTs involving 2019 patients were included. The evaluated outcomes included clinical effectiveness rate (CER), left ventricular ejection fraction (LVEF), left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), brain natriuretic peptide (BNP), cardiac output (CO), hypersensitive C-reactive protein (hs-CRP), and six-min walk test (6MWT). According to the NMA, Zhigancao decoction (ZGCD), Zhenwu decoction (ZWD), Shenfu decoction (SFD), Shengmai powder (SMP), Yangxin decoction (YXD), and Buyang Huanwu decoction (BYHW) in addition to CT considerably enhanced DCM treatment outcomes when compared to CT alone. SMP + CT (MD = 12.75, 95%CI 8.28–17.22) showed the highest probability of being the best treatment on account of the enhancement of LVEF. SFD + CT was most likely to be the optimal intervention for LVEDD decrease (MD = -4.68, 95%CI -8.73 to -0.62). YXD + CT (MD = -4.47, 95%CI -4.47 to -4.47) had the highest likelihood of being the optimal therapy for reducing LVESD. ZGCD + CT seemed to be the most promising intervention on the improvement in hs-CRP (MD = -2.82, 95%CI -3.60 to -2.04) and 6MWT (MD = 141.00, 95%CI 136.57 to 145.43). However, the optimal CCP for improving BNP and CO could not be identified based on the present studies. No significant adverse events emerged in the included studies.

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Conclusion This NMA indicated that adding CCPs to current CT treatment had a favorable effect on DCM. In light of the clinical efficacy and other outcomes, SMP + CT, SFD + CT, YXD + CT, and ZGCD + CT demonstrated a preferred improvement in patients with DCM when combined. Furthermore, additional larger RCTs with longer follow-up periods and standardized outcome reporting are required to give more solid evidence to support our findings due to the small sample size of the current studies and the presence of risk of bias.

Keywords Chinese classical prescription, Traditional Chinese medicine, Dilated cardiomyopathy, Network meta-analysis

Introduction

Cardiomyopathies are cardiac muscle illnesses that induce mechanical and/or electrical malfunction, leading to dilated, hypertrophic, or restrictive pathophysiology [1]. Dilated cardiomyopathy (DCM) is a clinical diagnosis characterized by left ventricular or biventricular dilatation and impaired contraction that cannot be explained by aberrant loading circumstances (such as hypertension and valvular heart disease) or coronary artery disease [2]. The American Heart Association categorizes DCM as genetic, mixed or acquired [3], whereas the European Society of Cardiology (ESC) groups cardiomyopathy into familial or nonfamilial forms [4]. According to a 2013 analysis, the prevalence of DCM was predicted to be more than one per 250 people based on recent clinical trials and associated data [5]. As DCM eventually causes reduced contractility, typical heart failure prevention or therapy procedures are the primary line of treatment for DCM patients [6]. Life-threatening arrhythmias may need to be avoided with the use of implantable cardioverter-defibrillators and cardiac resynchronization therapy [6]. The majority of heart failure caused by DCM occurs from pump failure owing to dilatation, with the remaining 30% triggered by sudden cardiac death from arrhythmias [7–9]. Therefore, it is critical to determine suitable adjuvant and alternative treatments for this serious medical requirement. Importantly, an improved approach to personalized clinical care driven by individual characteristics would benefit patients with DCM.

The expanding use of current complementary and alternative medicine in the treatment of DCM has gained a lot of attention in recent years. In China, Chinese classical prescriptions (CCPs) are widely used as an adjuvant treatment to DCM in addition to conventional therapy (CT). At present, the benefits of oral Chinese patent medicines [10] and Chinese medicine injections [11] on DCM have been well established. Moreover, several experiments have preliminarily confirmed the role of CCPs in reducing inflammation, inhibiting myocardial fibrosis and improving cardiac function in doxorubicin-induced DCM rats [12, 13]. Nonetheless, there was a lack of comprehensive and systematic evidence to support ranking the therapeutic effects of various types of CCPs combined with CT against DCM, and clinical trials evaluating CCPs combined with CT in the treatment of DCM were still insufficient. Compared to conventional meta-analyses, the network meta-analysis (NMA) can combine information from direct and indirect comparisons to determine the best therapeutic regimen, adding to evidence-based medical evidence for drug selection in clinical decision-making [14, 15].

Thus, six most commonly used CCPs for the treatment of DCM were gathered and analyzed (Table 1), namely Zhigancao decoction (ZGCD), Zhenwu decoction (ZWD), Shenfu decoction (SFD), Shengmai powder (SMP), Yangxin decoction (YXD), and Buyang Huanwu decoction (BYHW). A NMA of randomized controlled trials (RCTs) was conducted to systematically assess and rank the potential efficacy of CCPs for DCM across all accessible publications.

Materials and methods

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Extension Statement was followed when conducting this NMA [16]. As a supplementary file, a completed PRISMA checklist was provided (Additional file 1). The protocol for the current review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number of CRD42024586365.

Search strategy

Two researchers independently searched PubMed, Embase, Web of Science Core Collection, Cochrane Library, ProQuest, China National Knowledge Infrastructure (CNKI), China Science Periodical Database (CSPD), Chinese Citation Database (CCD), Chinese Biomedical Literature Database (CBM), and ClinicalTrials.gov from their inception to November 30, 2024 for ongoing and unpublished trials, as well as potential trials (Additional file 2). Our search method was adapted for each database, with search terms and MeSH headings relating to combinations of "Chinese classical prescription" and "dilated cardiomyopathy". In addition, relevant

Table 1 Details of six Chinese classical prescriptions

Chinese classical prescription	Chinese name	Latin name	Species	Family
Zhigancao decoction	Gancao	Glycyrrhizae Radix et Rhizoma	*Glycyrrhiza uralensis* Fisch	Fabaceae
	Renshen	Ginseng Radix et Rhizoma	*Panax ginseng* C.A.Mey	Araliaceae
	Shengjiang	Zingiberis Rhizoma Recens	*Zingiber officinale* Rosc	Zingiberaceae
	Guizhi	Cinnamomi Ramulus	*Cinnamomum cassia* Presl	Lauraceae
	Dihuang	Rehmanniae Radix	*Rehmannia glutinosa* Libosch	Scrophulariaceae
	Maidong	Ophiopogonis Radix	*Ophiopogon japonicus* (L.f) Ker-Gawl	Liliaceae
	Ejiao	Asini Corii Colla	*Equus asinus* L	Equidae
	Huomaren	Cannabis Fructus	*Cannabis sativa* L	Moraceae Gaudich
	Dazao	Jujubae Fructus	*Ziziphus jujuba* Mill	Rhamnaceae Juss
Zhenwu decoction	Fuzi	Aconiti Lateralis Radix Praeparata	*Aconitum carmichaeli* Debx	Ranunculaceae
	Fuling	Poria	*Poria cocos* (Schw.) Wolf	Polyporaceae
	Shaoyao	Paeoniae Radix Alba	*Paeonia lactiflora* Pall	Ranunculaceae
	Baizhu	Atractylodis Macrocephalae Rhizoma	*Atractylodes macrocephala* Koidz	Asteraceae
	Shengjiang	Zingiberis Rhizoma Recens	*Zingiber officinale* Rosc	Zingiberaceae
Shenfu decoction	Renshen	Ginseng Radix et Rhizoma	*Panax ginseng* C.A.Mey	Araliaceae
	Fuzi	Aconiti Lateralis Radix Praeparata	*Aconitum carmichaeli* Debx	Ranunculaceae
Shengmai powder	Renshen	Ginseng Radix et Rhizoma	*Panax ginseng* C.A.Mey	Araliaceae
	Maidong	Ophiopogonis Radix	*Ophiopogon japonicus* (L.f) Ker-Gawl	Liliaceae
	Wuweizi	Schisandrae Chinensis Fructus	Schisandra Chinensis (Turcz.) Baill	Magnoliaceae
Yangxin decoction	Huangqi	Astragali Radix	*Astragalus membranaceus* (Fisch.) Bge	Fabaceae
	Renshen	Ginseng Radix et Rhizoma	*Panax ginseng* C.A.Mey	Araliaceae
	Danggui	Angelicae Sinensis Radix	*Angelica sinensis* (Oliv.) Diels	Umbelliferae
	Fushen	Poria cum Radix Pini	*Poria cocos* (Schw.) Wolf	Polyporaceae
	Fuling	Poria	*Poria cocos* (Schw.) Wolf	Polyporaceae
	Suanzaoren	Ziziphi Spinosae Semen	*Ziziphus jujuba* Mill. var. spinosa (Bunge) Hu ex H. F. Chou	Rhamnaceae
	Baiziren	PLATYCLADI SEMEN	*Platycladus orientalis* (L.) Franco	Cupressaceae
	Yuanzhi	Polygalae Radix	*Polygala tenuifolia* Willd	Polygalaceae
	Wuweizi	Schisandrae Chinensis Fructus	Schisandra Chinensis (Turcz.) Baill	Magnoliaceae
	Banxia	Pinelliae Rhizoma	*Pinellia ternate (Thunb.)* Breit	Araceae
	Rougui	Cinnamomi Cortex	*Cinnamomum cassia* Presl	Lauraceae
	Chuanxiong	Chuanxiong Rhizoma	*Ligusticum chuanxiong* Hort	Umbelliferae
	Gancao	Glycyrrhizae Radix et Rhizoma	*Glycyrrhiza uralensis* Fisch	Fabaceae
Buyang Huanwu decoction	Huangqi	Astragali Radix	*Astragalus membranaceus* (Fisch.) Bge	Fabaceae
	Danggui	Angelicae Sinensis Radix	*Angelica sinensis* (Oliv.) Diels	Umbelliferae
	Chishao	Paeoniae Radix Rubra	*Paeonia lactiflora* Pall	Ranunculaceae
	Dilong	Pheretima	*Pheretima aspergillum* (E. Perrier)	Megascolecidae
	Chuanxiong	Chuanxiong Rhizoma	*Ligusticum chuanxiong* Hort	Umbelliferae
	Honghua	Carthami Flos	*Carthamus tinctorius* L	Asteraceae
	Taoren	Persicae Semen	*Prunus persica* (L.) Batsch	Rosaceae

systematic reviews and guideline references were also taken into consideration, and associated reference studies were manually gathered from the databases.

Study selection

The following criteria had to be satisfied for a study to be included: ① They had to be RCTs without restrictions on language, publication year, publication status, or blinding methods. ② Based on either the previous or current diagnostic criteria, patients recruited in the RCTs were diagnosed with DCM [1, 2]. Furthermore, their heart function was classified as grades II to IV by the New York Heart Association (NYHA) classification, with the patient's physical activity ranging from slight limitation to inability to engage in any physical activity [17]. Regarding gender, country, or ethnic origin, we placed

no restrictions. ③ While the control group received CT alone, patients in the experimental group received one of the six CCPs (ZGCD, ZWD, SFD, SMP, YXD, and BYHW) in addition to the current CT therapies for DCM. The use of CCPs was unrestricted in terms of dosage, frequency of administration, or course of treatment. ④ The primary outcome was clinical effectiveness rate (CER), and the secondary outcomes were left ventricular ejection fraction (LVEF), left ventricular end-diastolic dimension (LVEDD), left ventricular end-systolic dimension (LVESD), brain natriuretic peptide (BNP), cardiac output (CO), hypersensitive C-reactive protein (hs-CRP), and six-min walk test (6MWT). Moreover, adverse events were also collected and analyzed in this review. The therapeutic effect standard referred to the following definitions: ① Markedly effective: the improvement of NYHA was more than two grades, and there was an obvious improvement in the clinical symptom. ② Effective: the improvement of NYHA was more than one grade, and the clinical symptom improved partly. ③ Ineffective: it did not reach the above standards of efficiency, and even exacerbation. CER = markedly effective rate + effective rate.

Studies were disqualified if any of the subsequent conditions were satisfied: ① The intervention did not identify a therapeutic agent or combined several different therapies. ② Only iterations of a study with greater sample sizes and more thorough data would be kept if it was republished. ③ The full text was unavailable or the data was incomplete or imprecise.

Data extraction

The literature from various databases was organized using EndNote 20 software. Using the inclusion criteria as a guide, two researchers (ST and LY) independently examined the literature. Once duplicate studies were ruled out, the researchers went through the titles and abstracts to remove any unnecessary material. To select the studies that qualified, the entire text was finally read. Based on a specially designed form, the two researchers separately retrieved data from the qualifying RCTs. The first author, publication year, gender distribution, average age, sample sizes, cardiac function classification, randomization and blinding method, therapeutic regimen, outcomes, and details regarding RCT quality assessment were among the details that were recorded. Any disputes were settled through conversation or by consulting a third researcher (JL).

Quality assessment

Using the Cochrane Risk of Bias assessment tool, two reviewers (ST and LY) independently assessed the quality assessment. The following items were considered in the quality assessment of Cochrane tools: Detection bias: ① Selection bias: random sequence generation and allocation concealment, ② Performance bias: blinding of the participants and personnel, ③ Detection bias: blinding of the outcome assessment, ④ Attrition bias: incomplete outcome data, ⑤ Reporting bias: selective reporting, and ⑥ Other bias. Bias was classified as "low risk", "unclear risk", or "high risk" in each area. The third researcher (JL) was consulted or any differences that already existed were discussed.

Grading of the evidence

The evidence's degree of certainty was evaluated using the GRADE method [18]. RCT are initially rated as high by default and are subsequently downgraded according to the following pre-established criteria: risk of bias (the included studies were biased in randomization, allocation concealment and blinding), inconsistency (the overlapping degree of confidence intervals of different studies was poor, and the I^2 value of the combined results was > 50%), indirectness (presence of factors that limit the generalizability of the results), imprecision (the sample size of included studies was small and the confidence interval was wide), and other considerations. Finally, the evidence's level of certainty was classified as high, moderate, low, or extremely low.

Statistical analysis

Stata software (version 16) and Review Manager software (version 5.4) were used to conduct the NMA. The pooled data were converted to odds ratios (ORs) for dichotomous outcomes. For continuous outcomes, the mean and standard deviation of the change amount were computed using the pre- and post-treatment data, and the mean difference (MD) was utilized as the effect analysis metric. The effect sizes were reported as 95% confidence intervals (CIs). The differences between the groups were deemed statistically significant when neither the 95% CIs of the MD included one nor the 95% CIs of the ORs included zero. Stata software was used to create the network graph of the indirect comparative relationship between various interventions. If the closed loop of treatments was accessible, a loop-specific strategy was considered to investigate evidence inconsistency. The therapies were ranked using surface under the cumulative ranking curve (SUCRA) probability values, with 100% and 0% being the best and worst treatments, respectively. The higher the SUCRA value, the better the efficacy. To further investigate potential heterogeneity, sensitivity analysis and necessary subgroup analyses based on drug dosage, course of treatment, and sample size were carried out on included studies. Using Stata software, forest and funnel plots of the outcome indicators were created to show the comparative results and assess publication bias.

Results

Search results

The original search yielded a total of 1928 studies. One thousand thirty-four studies remained after duplicates were eliminated. Upon reviewing the abstracts and titles, 945 studies were deemed irrelevant due to their study design. After that, 89 papers were found to be eligible and subjected to examination. Of those, 63 were subsequently eliminated because of irrelevant study design ($n=41$), ineligible intervention ($n=9$), irrelevant outcome ($n=5$), and incomplete data ($n=8$). Additionally, 7 research were found via professional guidance and one-on-one conversations, and 1 study satisfied the requirements for inclusion.

Lastly, 27 eligible RCTs [19–45], including ZGCD (9 RCTs), ZWD (7 RCTs), SFD (3 RCTs), SMP (3 RCTs), YXD (3 RCTs), and BYHW (2 RCTs), were included in the NMA and investigated the use of 6 CPPs combined with CT against DCM. All of these RCTs were conducted in China between 2003 and 2023 (Fig. 1).

Study characteristics

Twenty-seven RCTs with 2019 patients accorded with the eligibility criteria, including 1018 patients in the experimental groups and 1001 patients in the control groups. Among the participants, men patients accounted for about 60% and the majority were middle-aged. Guideline-recommended optimal medical therapy was conducted in both groups, and the experimental group additionally received one of the CCPs. The duration of RCTs ranged from 10 days to 1 year, and it was 3 months in 26% of RCTs. The details of the study characteristics are presented in Table 2.

Figure 2 displays the compared relationships between the interventions for every outcome. There exists a positive correlation between the size of nodes and the number of patients, with each node representing a distinct intervention. The number of included studies for that intervention is reflected in the thickness of the line segment. The thicker the line segment, the more studies that are included for that intervention. Because no closed loops were constructed between the studies, this NMA did not rely on the premise of consistency between direct and indirect evidence.

Quality evaluation

Quality evaluation was carried out using the Cochrane risk-of-bias assessment tool (Fig. 3). Randomization was produced by eleven studies using a random number Table [19, 21, 25, 26, 31, 33, 34, 41–43, 45]. Three studies utilized randomization approaches that were high risk of bias, such as grouping by admission time and visiting sequence [27, 36, 38]. Concerning allocation concealment and blinding, none of the studies included

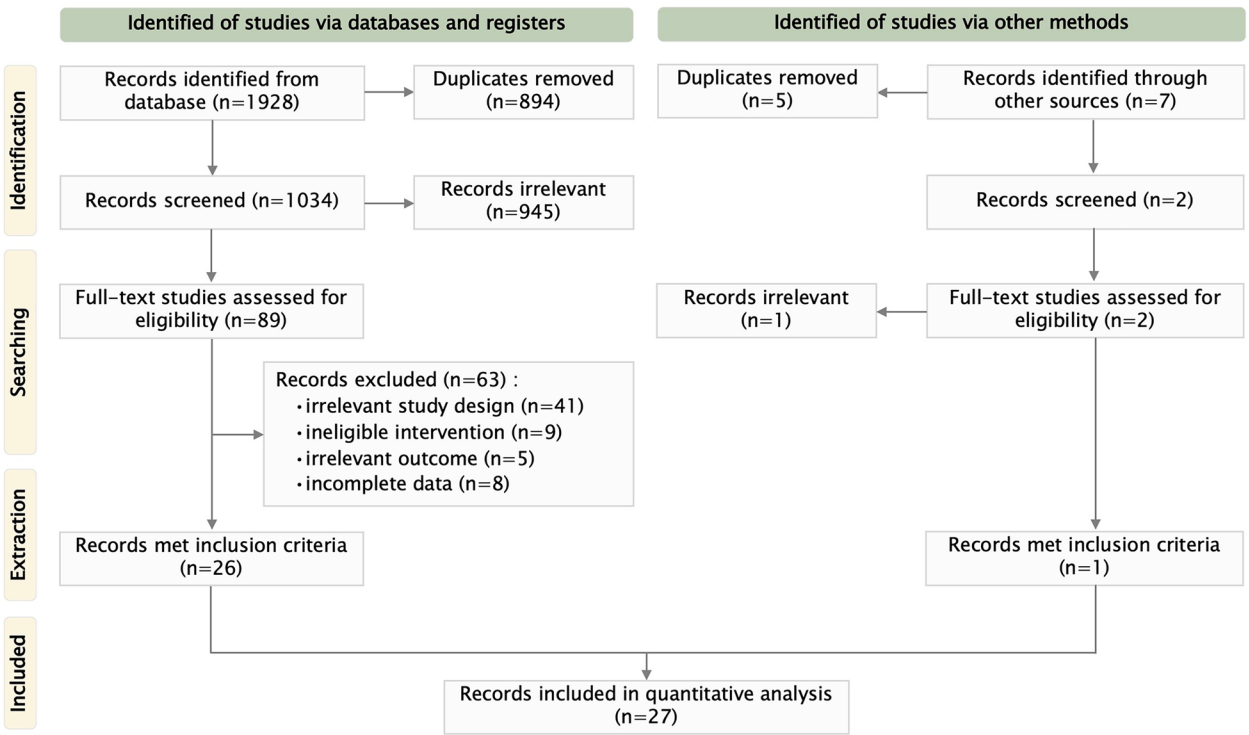

Fig. 1 Flow chart of the search for eligible studies

Table 2 Characteristics of the included studies

Study ID	N (E/C)	Male/Female		Age (years)		NYHA (I, II, III, IV)		Intervention		Duration	Outcomes
		E	C	E	C	E	C	E	C		
Wang et al. 2008 [19]	31/31	18/13	17/14	40.2 ± 3.1	40.6 ± 3.5	0, 10, 15, 6	0, 11, 13, 7	ZGCD + CT	CT	1y	①②③
Yang et al. 2008 [20]	35/30	21/14	19/11	30–61	28–63	0, 19, 14, 2	0, 17, 11, 2	ZGCD + CT	CT	1y	①②
Wang et al. 2009 [21]	35/35	20/15	22/13	38.7 ± 4.5	40.9 ± 3.8	0, 11, 18, 6	0, 13, 15, 7	ZGCD + CT	CT	3 m	①
Kong, 2010 [22]	25/24	34/15		18–73		0, 0, 19, 30		ZGCD + CT	CT	3w	①
Huang, 2012 [23]	32/30	20/12	19/11	41–78	40–73	0, 7, 19, 6	0, 6, 17, 7	ZGCD + CT	CT	3 m	①②③⑧
Li, 2013 [24]	50/50	28/22	29/21	30–56	30–55	0, 14, 26, 10	0, 15, 24, 11	ZGCD + CT	CT	-	①
Luo, 2016 [25]	40/40	19/21	24/16	38 ± 2.1	39.5 ± 2.6	0, 18, 10, 12	0, 14, 9, 17	ZGCD + CT	CT	6 m	①②⑤⑥
Cao, 2019 [26]	38/38	20/18	21/17	50.29 ± 5.59	50.27 ± 5.58	0, 15, 16, 7	0, 17, 15, 6	ZGCD + CT	CT	3 m	②③④⑦
Zhang et al. 2019 [27]	30/30	18/12	19/11	26–64	29–63	-		ZGCD + CT	CT	10d	①②
Ren et al. 2005 [28]	15/14	10/5	9/5	21–35	26–49	0, 1, 10, 4	0, 2, 8, 4	ZWD + CT	CT	15d	①
Wang et al. 2005 [29]	32/32	22/10	18/14	54–81	56–79	0, 8, 20, 4	0, 12, 18, 2	ZWD + CT	CT	1 m	②③④⑥⑦
Qian et al. 2008 [30]	29/29	32/26		52 ± 9.6		0, 12, 9, 8	0, 14, 8, 7	ZWD + CT	CT	8 m	①②③
Li et al. 2009 [31]	33/33	20/13	21/12	41.7 ± 4.8	42.1 ± 3.8	0, 9, 17, 7	0, 11, 15, 7	ZWD + CT	CT	3 m	①⑦
Jin et al. 2014 [32]	32/34	54/12		32–72		0, 18, 32, 16		ZWD + CT	CT	4w	①
Yu, 2017 [33]	20/20	8/12	11/9	44.9 ± 6.47	45.7 ± 7.56	-		ZWD + CT	CT	4w	①②③⑤
Hu, 2020 [34]	26/27	14/12	14/13	60.42 ± 8.71	59.56 ± 8.95	0, 12, 14, 0	0, 12, 15, 0	ZWD + CT	CT	6 m	①②③
Meng et al. 2017 [35]	40/38	30/10	26/12	28–65	25–70	-		SFD + CT	CT	4w	①②③⑤
Zhu, 2020 [36]	40/40	21/19	20/20	41.5 ± 9.7	43.3 ± 9.1	0, 0, 24, 16	0, 0, 27, 13	SFD + CT	CT	4w	①②
Han et al. 2020 [37]	20/20	29/11		48–72		0, 12, 19, 9		SFD + CT	CT	1y	①③⑤⑦
Shang, 2003 [38]	16/14	14/2	13/1	-		6, 6, 4, 0	5, 8, 1, 0	SMP + CT	CT	1 m	②⑥
Han et al. 2006 [39]	90/88	58/32	52/36	7–72	10–69	0, 0, 26, 64	0, 0, 22, 66	SMP + CT	CT	30d	①②⑥
Gong et al. 2015 [40]	33/30	19/14	17/13	38.30 ± 5.40	38.20 ± 5.20	2, 16, 10, 5	2, 14, 9, 5	SMP + CT	CT	12w	①②
Yang et al. 2018 [41]	54/53	35/19	36/17	45.29 ± 4.21	45.41 ± 4.13	0, 0, 37, 17	0, 0, 38, 15	YXD + CT	CT	3 m	①②⑧
Liu, 2019 [42]	84/84	52/32	48/36	52.63 ± 7.21	53.12 ± 7.47	0, 0, 56, 28	0, 0, 59, 25	YXD + CT	CT	3 m	①
Zhu, 2023 [43]	66/66	36/30	35/31	57.32 ± 8.47	57.49 ± 8.51	0, 29, 25, 12	0, 28, 27, 11	YXD + CT	CT	3 m	①②③④
Li, 2019 [44]	40/40	21/19	23/17	45.13 ± 8.16	44.37 ± 8.81	-		BYHW + CT	CT	6w	②③④
Chen, 2020 [45]	32/31	18/14	18/13	54.44 ± 9.26	58.00 ± 9.29	0, 11, 19, 10	0, 12, 17, 11	BYHW + CT	CT	12w	%1 ⑧

E experimental group, *C* control group, *ZGCD* Zhigancao decoction, *ZWD* Zhenwu decoction, *SFD* Shenfu decoction, *SMP* Shengmai powder, *YXD* Yangxin decoction, *BYHW* Buyang Huanwu decoction, *CT* conventional therapy. ① clinical effectiveness rate (CER); ② left ventricular ejection fraction (LVEF); ③ left ventricular end-diastolic dimension (LVEDD); ④ left ventricular end-systolic dimension (LVESD); ⑤ brain natriuretic peptide (BNP); ⑥ cardiac output (CO); ⑦ hypersensitive C-reactive protein(hs-CRP); ⑧ six-min walk test (6MWT)

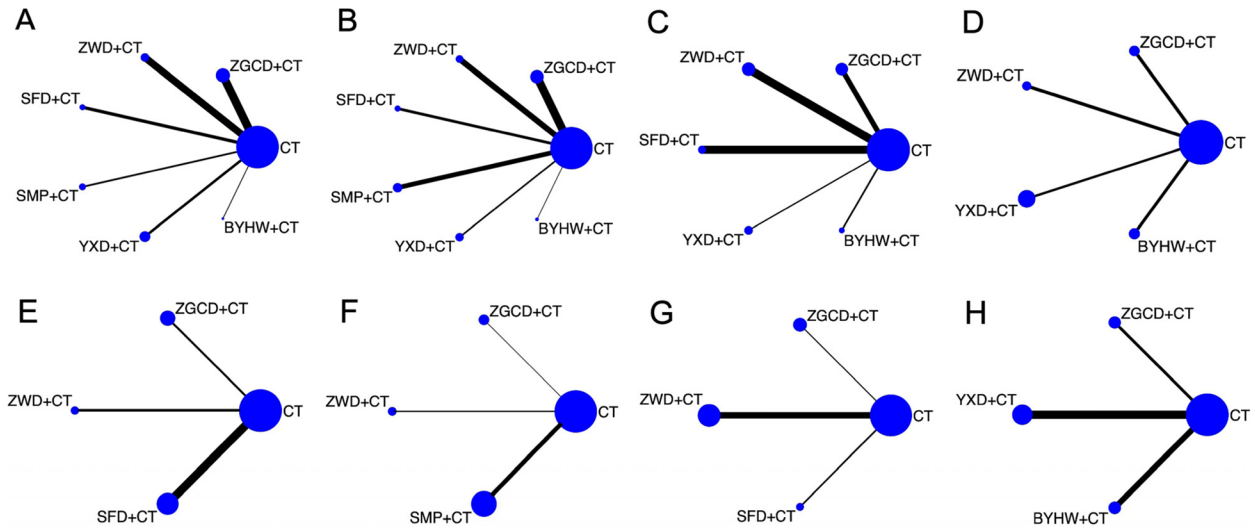

Fig. 2 Network graph of the outcomes. **A** clinical effectiveness rate (CER); **B** left ventricular ejection fraction (LVEF); **C** left ventricular end-diastolic dimension (LVEDD); **D** left ventricular end-systolic dimension (LVESD); **E** hypersensitive C-reactive protein (hs-CRP); **F** six-min walk test (6MWT); **G** brain natriuretic peptide (BNP); **H** cardiac output (CO); ZGCD, Zhigancao decoction; ZWD, Zhenwu decoction; SFD, Shenfu decoction; SMP, Shengmai powder; YXD, Yangxin decoction; BYHW, Buyang Huanwu decoction; CT, conventional therapy

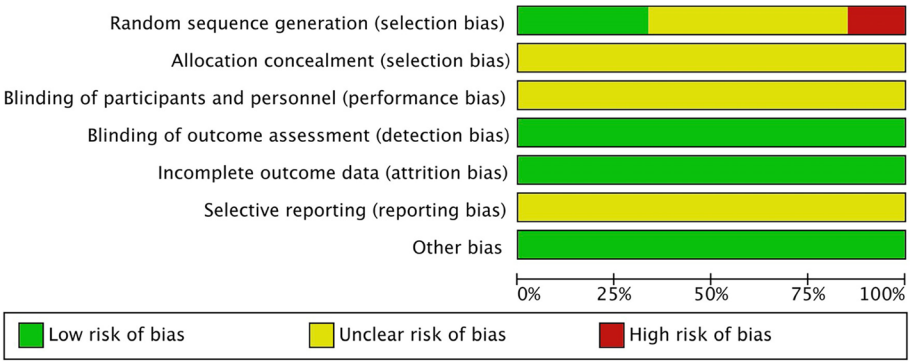

Fig. 3 Risk-of-bias graph

comprehensive information. Since the blinding toward the outcome assessors had no effect on the measurement of related results of the included studies, the detection bias was rated as "low risk". There was thought to be no chance of incomplete outcome data because all research outcome reports were comprehensive. Given the inability to obtain the entire implementation plan, the bias in reporting was assessed as "unclear risk". Because no other clear bias was found in any of the included studies, our review presumed that there were no further bias risks.

Outcomes

CER

Twenty-three RCTs involving 1769 participants reported the CER of six types of CCPs. Conventional Meta-analysis preliminarily showed that CER were significantly increased in the experimental group compared with the control group (OR = 3.93, 95%CI 3.01–5.13, $P < 0.001$), with low heterogeneity among studies ($I^2 = 0\%$, $P = 0.65$). Furthermore, NMA demonstrated that in BYHW + CT vs CT (OR = 10.59, 95%CI 3.26–34.43), SMP + CT vs CT (OR = 4.62, 95%CI 1.96–10.88), SFD + CT vs CT (OR = 4.16, 95%CI 1.77–9.74), ZGCD + CT vs CT (OR = 3.33, 95%CI 2.09–5.33), YXD + CT vs CT (OR = 3.25, 95%CI 1.77–5.96), and ZWD + CT vs CT (OR = 2.96, 95%CI 1.59–5.53), it was observed that the CCPs (BYHW, SMP, SFD, ZGCD, YXD, and ZWD) combined with CT had a better clinical effectiveness rate compared with CT alone (Fig. 4A and Table 3). The results of SUCRA suggested that BYHW + CT was the optimal combination, followed by SMP + CT, SFD + CT, and ZGCD + CT (Table 4 and Fig. 5A).

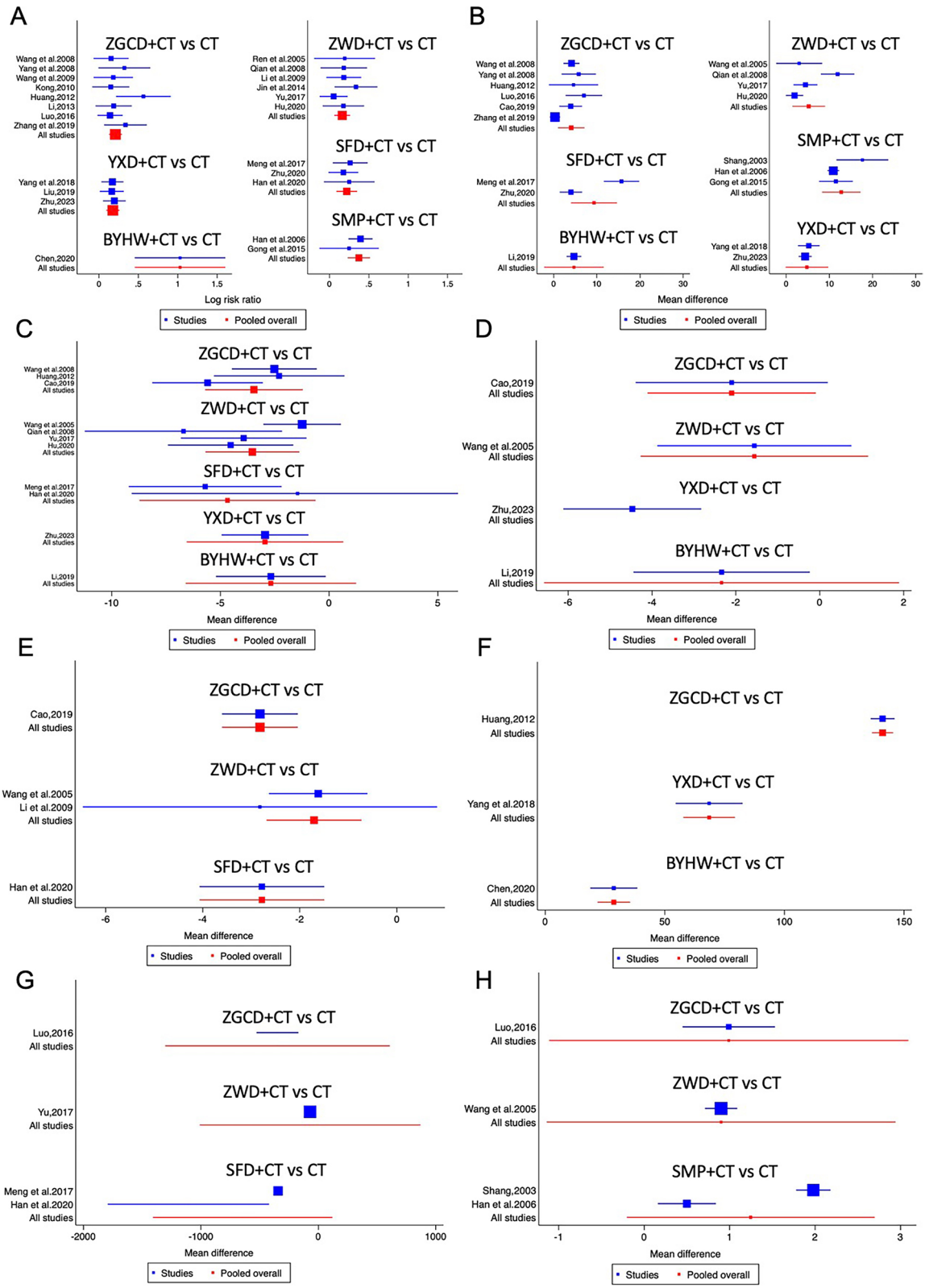

Fig. 4 Forest plot of the outcomes. **A** clinical effectiveness rate (CER); **B** left ventricular ejection fraction (LVEF); **C** left ventricular end-diastolic dimension (LVEDD); **D** left ventricular end-systolic dimension (LVESD); **E** hypersensitive C-reactive protein (hs-CRP); **F** six-min walk test (6MWT); **G** brain natriuretic peptide (BNP); **H** cardiac output (CO); ZGCD, Zhigancao decoction; ZWD, Zhenwu decoction; SFD, Shenfu decoction; SMP, Shengmai powder; YXD, Yangxin decoction; BYHW, Buyang Huanwu decoction; CT, conventional therapy

Table 3 Risk ratios/Mean difference (95%CIs) of the CER and LVEF

CER (Left lower part)				LVEF (Right upper part)		
BYHW + CT	−8.06 (−16.28, 0.16)	−4.64 (−13.35, 4.06)	−0.63 (−8.18, 6.92)	−0.10 (−8.59, 8.39)	−0.52 (−8.39, 7.35)	−4.69 (−11.59, 2.21)
2.29 (0.53,9.83)	**SMP + CT**	−3.41 (−10.33, 3.50)	−8.68 (−14.08, −3.28)	−7.95 (−14.62, −1.29)	−7.54 (−13.38, −1.69)	**−12.75 (−17.22, −8.28)**
2.55 (0.60,10.92)	1.11 (0.33,3.72)	**SFD + CT**	−5.27 (−11.39, 0.85)	−4.54 (−11.80, 2.72)	−4.12 (−10.63, 2.39)	**−9.33 (−14.64, −4.02)**
3.18 (0.89,11.30)	1.39 (0.52,3.68)	1.25 (0.47,3.30)	**ZGCD + CT**	−0.73 (−6.55, 5.09)	−1.15 (−6.01, 3.71)	**−4.06 (−7.12, −1.00)**
3.26 (0.87,12.29)	1.42 (0.50,4.07)	1.28 (0.45,3.64)	1.03 (0.48,2.21)	**YXD + CT**	−0.42 (−6.64, 5.81)	−4.79 (−9.74, 0.15)
3.58 (0.94,13.58)	1.56 (0.54,4.50)	1.40 (0.49,4.04)	1.13 (0.52,2.46)	1.10 (0.46,2.62)	**ZWD + CT**	**−5.21 (−8.99, −1.43)**
10.59 (3.26,34.43)	**4.62 (1.96,10.88)**	**4.16 (1.77,9.74)**	**3.33 (2.09,5.33)**	**3.25 (1.77,5.96)**	**2.96 (1.59,5.53)**	**CT**

The numbers in bold in the table indicate that there are statistically significant differences between this group and the CT group

CER clinical effectiveness rate, *LVEF* left ventricular ejection fraction, *ZGCD* Zhigancao decoction, *ZWD* Zhenwu decoction, *SFD* Shenfu decoction, *SMP* Shengmai powder, *YXD* Yangxin decoction, *BYHW* Buyang Huanwu decoction, *CT* conventional therapy

Table 4 Surface under the cumulative ranking curve results of the outcomes

Intervention	CER	LVEF	LVEDD	LVESD	Hs-CRP	6MWT	BNP	CO
ZGCD + CT	46.4%	36.6%	60.4%	53.0%	82.6%	84.5%	57.8%	58.6%
ZWD + CT	38.5%	48.0%	61.5%	40.2%	37.9%	-	36.0%	56.3%
SFD + CT	59.7%	79.3%	76.7%	-	79.5%	-	81.8%	-
SMP + CT	66.7%	96.5%	-	-	-	-	-	71.1%
YXD + CT	44.4%	44.4%	51.4%	95.2%	-	81.2%	-	-
BYHW + CT	94.4%	43.1%	46.9%	54.0%	-	59.6%	-	-
CT	0%	2.1%	3.2%	7.6%	0%	13.8%	24.3	14%

CER clinical effectiveness rate, *LVEF* left ventricular ejection fraction, *LVEDD* left ventricular end-diastolic dimension, *LVESD* left ventricular end-systolic dimension, *hs-CRP* hypersensitive C-reactive protein, *6MWT* six-min walk test, *BNP* brain natriuretic peptide, *CO* cardiac output, *ZGCD* Zhigancao decoction, *ZWD* Zhenwu decoction, *SFD* Shenfu decoction, *SMP* Shengmai powder, *YXD* Yangxin decoction, *BYHW* Buyang Huanwu decoction, *CT* conventional therapy

LVEF

Eighteen RCTs involving 1368 participants reported the LVEF of six types of CCPs. Conventional Meta-analysis preliminarily showed that LVEF were significantly improved in the experimental group compared with the control group (MD = 6.45, 95%CI 4.44–8.45, $P < 0.001$), with high heterogeneity among studies ($I^2 = 92\%$, $P < 0.001$). Sensitivity analysis was performed by excluding studies one by one, but the heterogeneity did not change remarkably. Subgroup analyses based on CCPs, dosage, course of treatment and sample size revealed that heterogeneity in each subgroup also remained high. NMA suggested that SMP + CT (MD = 12.75, 95%CI 8.28–17.22), SFD + CT (MD = 9.33, 95%CI 4.02–14.64), ZWD + CT (MD = 5.21, 95%CI 1.43–8.99), and ZGCD + CT (MD = 4.06, 95%CI 1.00–7.12) were more efficacious in improving LVEF compared with CT alone, while YXD + CT (MD = 4.79, 95%CI −0.15 to 9.743) and BYHW + CT (MD = 4.69, 95%CI −2.21 to 11.59) compared with CT alone had no statistical significance (Fig. 4B and Table 3). SMP + CT had the highest probability of being the best treatment on account of the enhancement of LVEF, and SFD + CT was the second most favorable intervention based on the SUCRA values (Table 4 and Fig. 5B).

LVEDD

Eleven RCTs of 745 participants involving five types of CCPs reported the LVEDD. Using conventional Meta-analysis, the fixed-effects model was performed due to the low heterogeneity of the results ($I^2 = 31\%$, $P = 0.15$). The overall mean difference favored the experimental group significantly (MD = −3.15, 95%CI −3.93 to −2.37, $P < 0.001$). Further NMA showed that SFD + CT (MD = −4.68, 95%CI −8.73 to −0.62), ZWD + CT (MD = −3.53, 95%CI −5.69 to −1.37), and ZGCD + CT (MD = −3.46, 95%CI −5.71 to −1.21) were more available in decreasing LVEDD compared with CT alone, while no significant difference was observed in YXD + CT vs CT (MD = −2.95, 95%CI −6.55 to 0.65) and BYHW + CT vs CT (MD = −2.68, 95%CI −6.60 to 1.24) (Fig. 4C and Table 5). According to the SUCRA values, SFD + CT

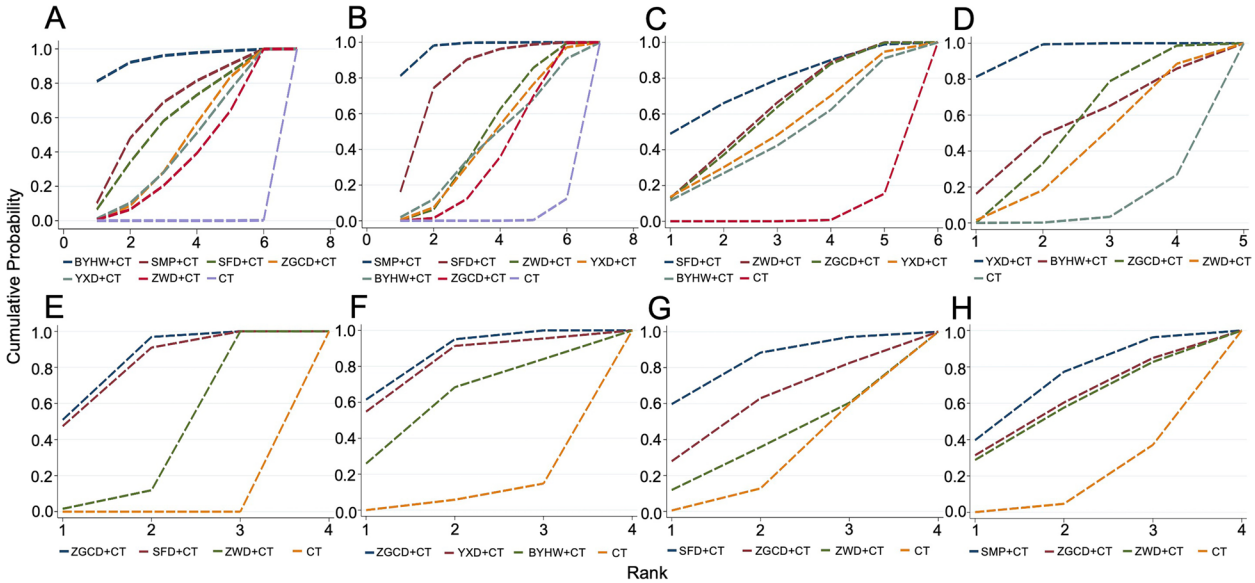

Fig. 5 Plot of the surface under the cumulative ranking curves for outcomes. **A** clinical effectiveness rate (CER); **B** left ventricular ejection fraction (LVEF); **C** left ventricular end-diastolic dimension (LVEDD); **D** left ventricular end-systolic dimension (LVESD); **E** hypersensitive C-reactive protein (hs-CRP); **F** six-min walk test (6MWT); **G** brain natriuretic peptide (BNP); **H** cardiac output (CO). ZGCD, Zhigancao decoction; ZWD, Zhenwu decoction; SFD, Shenfu decoction; SMP, Shengmai powder; YXD, Yangxin decoction; BYHW, Buyang Huanwu decoction; CT, conventional therapy

Table 5 Mean difference (95%CIs) of the LVEDD and LVESD

LVEDD (Left lower part)			**LVESD (Right upper part)**		
SFD + CT	-	-	-	-	-
−1.15 (−5.80, 3.51)	**ZWD + CT**	0.54 (−1.90, 2.98)	2.91 (0.20, 5.62)	0.78 (−4.25, 5.81)	1.56 (−1.15, 4.27)
−1.22 (−5.85, 3.42)	−0.07 (−3.18, 3.04)	**ZGCD + CT**	2.37 (0.36, 4.38)	0.24 (−4.44, 4.92)	**2.10 (0.09, 4.11)**
−1.73 (−7.15, 3.70)	−0.58 (−4.78, 3.62)	−0.51 (−4.76, 3.74)	**YXD + CT**	2.13 (−2.10, 6.36)	**4.47 (4.47, 4.47)**
−2.00 (−7.63, 3.64)	−0.85 (−5.33, 3.63)	−0.78 (−5.30, 3.74)	−0.27 (−5.59, 5.05)	**BYHW + CT**	2.34 (−1.89, 6.57)
−4.68 (−8.73, −0.62)	**−3.53 (−5.69, −1.37)**	**−3.46 (−5.71, −1.21)**	−2.95 (−6.55, 0.65)	−2.68 (−6.60, 1.24)	**CT**

The numbers in bold in the table indicate that there are statistically significant differences between this group and the CT group

LVEDD left ventricular end-diastolic dimension, *LVESD* left ventricular end-systolic dimension, *ZGCD* Zhigancao decoction, *ZWD* Zhenwu decoction, *SFD* Shenfu decoction, *YXD* Yangxin decoction, *BYHW* Buyang Huanwu decoction, *CT* conventional therapy

had the highest likelihood of being the best treatment for decreasing LVEDD, followed by ZWD + CT and ZGCD + CT (Table 4 and Fig. 5C).

LVESD

Four RCTs of 352 participants involving three types of CCPs (ZWD, YXD, and BYHW) reported the LVESD. Results from conventional Meta-analysis indicated that LVESD appeared substantially decreased in the experimental group compared with the control group (MD = −2.95, 95%CI −3.97 to −1.94, $P < 0.001$) through the fixed-effects model ($I^2 = 46\%$, $P = 0.14$). Moreover, NMA showed that YXD + CT (MD = −4.47, 95%CI −4.47 to −4.47) and ZGCD + CT (MD = −2.10, 95%CI −4.11 to −0.09) were more effective in decreasing LVESD compared with CT alone. However, BYHW + CT (MD = −2.34, 95%CI −6.57 to 1.89) and ZWD + CT (MD = −1.56, 95%CI −4.27 to 1.15) compared with CT alone had no statistical significance (Fig. 4D and Table 5). According to the SUCRA values, YXD + C had the highest likelihood of being the best treatment for decreasing LVEDD (Table 4 and Fig. 5D).

Hs-CRP

Four RCTs of 246 participants involving three types of CCPs (ZGCD, ZWD, and SFD) assessed the hs-CRP. Conventional Meta-analysis preliminarily showed that hs-CRP levels were markedly decrease in the experimental group compared with the control group (MD = −2.46, 95%CI −3.01 to −1.91, $P < 0.001$). Pooled analysis was

Table 6 Mean difference (95%CIs) of the Hs-CRP and 6MWT

Hs-CRP (Left lower part)			6MWT (Right upper part)		
ZGCD + CT	-	-	−72.47 (−81.90, −63.04)	−112.33 (−120.47, −104.19)	**−141.00 (−145.43, −136.57)**
−0.04 (−1.54, 1.46)	**SFD + CT**	-	-	**-**	-
−1.11 (−2.36, 0.14)	−1.07 (−2.69, 0.54)	**ZWD + CT**	-	-	-
-	-	-	**YXD + CT**	−39.86 (−52.66, −27.06)	**−68.53 (−79.35, −57.71)**
-	**-**	**-**	**-**	**BYHW + CT**	**−28.67 (−35.50, −21.84)**
−2.82 (−3.60, −2.04)	**−2.78 (−4.07, −1.49)**	**−1.71 (−2.68, −0.73)**	**-**	**-**	**CT**

The numbers in bold in the table indicate that there are statistically significant differences between this group and the CT group

Hs-CRP hypersensitive C-reactive protein, *6MWT* six-min walk test, *ZGCD* Zhigancao decoction, *ZWD* Zhenwu decoction, *SFD* Shenfu decoction, *YXD* Yangxin decoction, *BYHW* Buyang Huanwu decoction, *CT* conventional therapy

homogeneous ($I^2 = 20\%$, $P = 0.29$). Furthermore, NMA indicated that ZGCD + CT (MD = −2.82, 95%CI −3.60 to −2.04), SFD + CT (MD = −2.78, 95%CI −4.07 to −1.49), and ZWD + CT (MD = −1.71, 95%CI −2.68 to −0.73) were more efficacious in decreasing hs-CRP compared with CT alone (Fig. 4E and Table 6). Similarly, the SUCRA values suggested that ZGCD + CT had the highest likelihood of being the best intervention for the reduction in hs-CRP, followed by SFD + CT and ZWD + CT (Table 4 and Fig. 5E).

6MWT

Three RCTs involving 232 participants reported the 6MWT of three types of CCPs (ZGCD, YXD, and BYHW). The random-effects model indicated that 6MWT were significantly improved in the experimental group compared with the control group (MD = 79.50, 95%CI 1.41–157.59, $P < 0.001$), with high heterogeneity among studies ($I^2 = 92\%$, $P < 0.001$). NMA suggested that ZGCD + CT (MD = 141.00, 95%CI 136.57 to 145.43), YXD + CT (MD = 68.53, 95%CI 57.71 to 79.35), and BYHW + CT (MD = 28.67, 95%CI 21.84 to 35.50) effectively increased 6MWT compared with CT alone (Fig. 4F and Table 6). The SUCRA values affirmed that ZGCD + CT had the highest likelihood of being the best treatment for improving 6MWT, followed by YXD + CT and BYHW + CT (Table 4 and Fig. 5F).

BNP

Four RCTs involving 238 participants of three types of CCPs (ZGCD, ZWD, and SFD) reported the BNP. Conventional Meta-analysis preliminarily showed that BNP were significantly decreased in the experimental group compared with the control group (MD = −313.18, 95%CI −529.43 to −96.93, $P < 0.001$), with high heterogeneity among studies ($I^2 = 100\%$, $P < 0.001$). Sensitivity analysis was performed by excluding studies one by one, and heterogeneity decreased remarkably ($I^2 = 58\%$, $P = 0.09$) when the study of Yu, 2017 [33] was removed. However, NMA indicated that no significant difference was observed in SFD + CT vs CT (MD = −644.30, 95%CI −1408.65 to 120.05), ZGCD + CT vs CT (MD = −347.89, 95%CI −1304.43 to 608.65), and ZWD + CT vs CT (MD = −70.64, 95%CI −1010.49 to 869.21), respectively (Fig. 4G and Table 7). Additionally, SFD + CT had the largest SUCRA value, followed by ZGCD + CT and ZWD + CT (Table 4 and Fig. 5G).

CO

Four RCTs involving 352 participants of three types of CCPs (ZGCD, SMP, and ZWD) assessed CO. Results

Table 7 Mean difference (95%CIs) of the BNP and CO

BNP (Left lower part)		CO (Right upper part)		
SFD + CT	-	-	-	**-**
−296.41 (−1520.82, 928.01)	**ZGCD + CT**	−0.09 (−3.02, 2.84)	−0.26 (−2.81, 2.30)	−0.99 (−3.09, 1.11)
−573.66 (−1785.08, 637.77)	−277.25 (−1618.25, 1063.75)	**ZWD + CT**	−0.35 (−2.85, 2.16)	−0.90 (−2.94, 1.14)
-	-	-	**SMP + CT**	−1.25 (−2.70, 0.20)
−644.30 (−1408.65, 120.05)	−347.89 (−1304.43, 608.65)	−70.64 (−1010.49, 869.21)	**-**	**CT**

BNP brain natriuretic peptide, *CO* cardiac output, *ZGCD* Zhigancao decoction, *ZWD* Zhenwu decoction, *SFD* Shenfu decoction, *SMP* Shengmai powder, *CT* conventional therapy

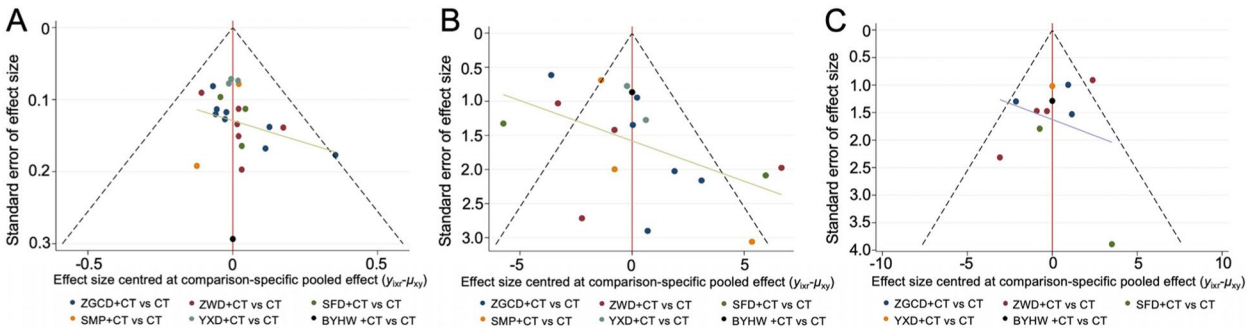

Fig. 6 Funnel plots of the CER, LVEF, and LVEDD. **A** clinical effectiveness rate (CER); **B** left ventricular ejection fraction (LVEF); **C** left ventricular end-diastolic dimension (LVEDD). ZGCD, Zhigancao decoction; ZWD, Zhenwu decoction; SFD, Shenfu decoction; SMP, Shengmai powder; YXD, Yangxin decoction; BYHW, Buyang Huanwu decoction; CT, conventional therapy

from conventional Meta-analysis indicated that CO appeared significantly improved in the experimental group compared with the control group (MD = 1.10, 95%CI 0.39–1.81, $P = 0.002$) through the fixed-effects model ($I^2 = 96\%$, $P < 0.001$). Sensitivity analysis was performed by excluding studies one by one, and heterogeneity decreased remarkably ($I^2 = 55\%$, $P = 0.11$) when the study of [38] was removed. Nevertheless, NMA showed that no significant difference was observed in SMP + CT vs CT (MD = 1.25, 95%CI −0.20 to 2.70), ZGCD + CT vs CT (MD = 0.99, 95%CI −1.11 to 3.09), and ZWD + CT vs CT (MD = 0.90, 95%CI −1.14 to 2.94), respectively (Fig. 4H and Table 7). Besides, SMP + CT had the largest SUCRA value, followed by ZGCD + CT and ZWD + CT (Table 4 and Fig. 5H.)

Adverse events

For adverse events, eight RCTs [19, 26, 27, 33, 34, 43–45] involving 566 participants provided detailed information on the conditions (Additional file 3). Adverse events such as constipation, nausea, vomiting, allergic rash, hypokalemia, and injection site abnormality were reported in three RCTs [26, 43, 44]. The fixed-effects model ($I^2 = 48\%$, $P = 0.15$) suggested that the overall mean difference of adverse events between the two groups was not statistically significant (OR = 0.59, 95%CI 0.33 to 1.05, $P = 0.07$).

Publication bias

Funnel plots were used to analyze the publication bias of the CER, LVEF, and LVEDD outcomes because there were more than 10 RCT trials reporting these data (Fig. 6). Different colored points indicate various comparisons between therapies. We found that the funnel plots of these results were almost visually symmetrical. Furthermore, the Egger's test indicated no significant potential publication bias of these studies in CER ($P = 0.104$), LVEF ($P = 0.984$), and LVEDD ($P = 0.736$).

GRADE assessment

The GRADE approach was used to provide a summary of the evidence grade evaluation of the included outcomes (Table 8). The findings confirmed that the evidence was categorized as extremely low to moderate. Inconsistency and imprecision were found to be the next

Table 8 GRADE assessment for the outcomes

Outcome	N (E/C)	Study Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Certainty of evidence
CER	892/877	RCT	Serious	Not serious	Not serious	Not serious	None	⊕⊕⊕◯ Moderate
LVEF	692/676	RCT	Serious	Serious	Not serious	Not serious	None	⊕⊕◯◯ Low
LVEDD	374/371	RCT	Serious	Not serious	Not serious	Not serious	None	⊕⊕⊕◯ Moderate
LVESD	176/1716	RCT	Serious	Not serious	Not serious	Serious	None	⊕⊕◯◯ Low
Hs-CRP	123/123	RCT	Serious	Not serious	Not serious	Serious	None	⊕⊕◯◯ Low
6MWT	118/114	RCT	Serious	Serious	Not serious	Serious	None	⊕◯◯◯ Very low
BNP	120/118	RCT	Serious	Serious	Not serious	Serious	None	⊕◯◯◯ Very low
CO	178/174	RCT	Serious	Serious	Not serious	Serious	None	⊕◯◯◯ Very low

CER clinical effectiveness rate, *LVEF* left ventricular ejection fraction, *LVEDD* left ventricular end-diastolic dimension, *LVESD* left ventricular end-systolic dimension, *hs-CRP* hypersensitive C-reactive protein, *6MWT* six-min walk test, *BNP* brain natriuretic peptide, *CO* cardiac output

most significant factors in evidence degradation, behind the risk of bias. Common biases in the included studies included blinding, randomization, and allocation concealment, indicating areas for improvement in the design of future trials on the use of CCPs to treat DCM.

Discussion

This NMA covered 27 RCTs with 2019 participants and found 6 CCPs for the treatment of DCM, including ZGCD, ZWD, SFD, SMP, YXD, and BYHW. Using NMA results and ranking analysis, we found that combining the aforementioned six CCPs with CT could not only optimize treatment efficacy but also improved LVEF, LVEDD, LVESD, hs-CRP, and 6MWT when compared to CT alone. SMP + CT had the highest chance of being the most effective treatment when it came to LVEF enhancement. SFD + CT had the highest chance of being the best intervention since it reduced LVEDD. YXD + CT had the greatest chance of being the optimal intervention in terms of lowering LVESD. For the enhancement of hs-CRP and 6MWT, ZGCD + CT may be the best option. However, the current studies did not allow for the identification of the ideal CCP for improving BNP and CO. Additionally, none of the examined studies revealed any serious adverse effects. The GRADE assessment identified only moderate certainty evidence for CER and LVEDD, with all other outcomes scoring low/very low. Comparatively speaking, we found that the six CCPs indicated above in addition to CT might help patients' CER and LVEDD more than CT alone. Given the limited degree of evidentiary certainty, it was unclear whether CCPs plus CT may enhance LVEF, LVESD, hs-CRP, and 6MWT. Still, it was quite evident that CCPs in addition to CT might raise CER among these patients, mostly based on NYHA, which led us to conclude that the combination of CCPs and CT could improve LVEF, LVESD, hs-CRP, and 6MWT to some amount. In summary, we should proceed with caution when evaluating these findings.

Overall, while taking into account the clinical effectiveness rate and other outcomes, SMP + CT, SFD + CT, YXD + CT, and ZGCD + CT presented a preferred improvement in patients with DCM. Clinical considerations about the optimal use of CCPs in the treatment of DCM should take the patient's condition into account, given the distinctiveness of the various CCPs. SMP is a famous traditional Chinese medicine formula, is mainly consisted of Renshen (Ginseng Radix et Rhizoma), Maidong (Ophiopogonis Radix), and Wuweizi (Schisandrae Chinensis Fructus). Pharmacological studies revealed that SMP could attenuate contractile dysfunction and structural damage [46], against inflammatory reaction to protect heart function [47]. Moreover, SMP may protect heart function through the restriction of doxorubicin-induced myocardial fibrosis and the regulation for cardiac immune microenvironment, indicating the potentially therapeutic effect of SMP on DOX-induced cardiomyopathy [48]. SFD, a clinical Chinese herbal prescription comprising Renshen (Ginseng Radix et Rhizoma) and Fuzi (Aconiti Lateralis Radix Praeparata), has been used for nearly 800 years. Modern chemical studies have shown that SFD mainly contains ginsenosides, aconite alkaloids, organic acids, nucleosides, amino acids and other components [49]. An experiment showed that SFD had positive effects on improving cardiac function in the rate model of congestive heart failure and attenuating ventricular remodeling and myocardial fibrosis [50]. A prospective, single-blind, randomized, controlled, and multicenter clinical trial demonstrated that SFD plus CT treatment can increase 6MWT and quality of life with heart failure patients [51]. YXD is based on the therapeutic approach of tonifying qi and activating blood in the theoretical sense of traditional Chinese medicine, and it mostly comprises of 13 different Chinese herbs. Previous study suggested that YXD can significantly improve the cardiac function, reduce CaN activity, decrease the expression levels of MMP-9, NFAT3 and GATA4, inhibit CaN/NFAT3 signaling pathway, increase myocardial remodeling and protect myocardial tissue in rats with congestive heart failure [52]. ZGCD, originated from *Treatise on Febrile Diseases* in the Eastern Han Dynasty (25–280 AD), is composed of 9 kinds of Chinese herbs. A Meta-analysis of 17 RCTs involving 1752 participants revealed that ZGCD combined with CT had better therapeutic effects and safety than CT alone, showing the characteristics and advantages of integrated Chinese and Western medicine in the treatment of cardiovascular diseases, which is worth recommending [53]. Furthermore, ZGCD might reverse the atrial electrical remodeling, and LC–MS/MS analysis confirmed that ZGCD contained several antiarrhythmic compounds including ginsenoside, isoliensinine, catalpol, glycyrrhizinate and hesperetin [54]. Consistent with our findings, the prior conventional meta-analysis also showed that Yiqi Yangyin prescription (Shengmai and Zhigancao decoction) may significantly improve the curative effect, increase LVEF, and reduce LVEDD in patients with DCM [55]. Importantly, our NMA showed a significant combined improvement in LVEF of 6.45% in the total combination therapy and 12.75% in the CMP group compared to CT alone, respectively. This result was more pronounced than the improvement in LVEF by CT alone in previous Meta [56], probably due to the synergistic effect of the combination therapy. However, only three RCTs were included in the CMP group in terms of

LVEF, thus the strength of the evidence needs to be further improved.

Enough consideration should be made to the safety of CCPs in the treatment of DCM-HF in addition to their efficacy. However, there is inadequate strong evidence of medication safety in the treatment of DCM since only 8 studies reported treatment-emergent adverse events, and 70% of RCTs did not especially mention the circumstances of using CCPs. CCPs, a classical formula consisting of various herbs containing complex components in specified ratios and doses, have been utilized effectively as alternative and complementary medicines in cardiovascular disorders in China, with the features of consistency and little side effects. Furthermore, practitioners were responsible for informing patients of any potential adverse responses in detail as soon as they received CCPs.

This NMA had indirectly analyzed the efficacy of various CCPs plus CT in the treatment of DCM and had thoroughly estimated the effectiveness of combinations of different CCPs with CT against DCM compared with WM alone. The results may serve as a guide for clinicians making decisions about treating DCM with CCPs and aid in the establishment of novel approaches to DCM management and treatment. Moreover, this review impartially assessed each piece of evidence, which will aid in directing the clinical application of CCPs in clinical decision-making.

Several limitations of this review need to be acknowledged. Firstly, the included RCTs had a low overall quality. Only eleven RCTs described the methods of generating random sequences, such as a random number table, and none of the studies included comprehensive information concerning allocation concealment and blinding, contributing to an exaggerated curative effect and decreased reliability of the evidence. Secondly, no direct comparisons were conducted between different CCPs, and all of the included RCTs were performed in China and the majority of them were single-center studies with short duration and small sample sizes, which reduced the generalizability of the results. Thirdly, almost all RCTs did not provided thorough details about CT treatment plans and only showed information including angiotensin II receptor antagonists, angiotensin-converting enzyme inhibitors, angiotensin receptor-neprilysin inhibitors, mineralocorticoid receptor antagonists, cardiac glycosides, nitrates, beta-blockers, and so on. This makes it impossible for us to conduct subgroup analysis for different CT treatment plans when doing a NMA to compare the efficacy of different CCPs. In addition, not all included RCTs provided a registration number and ethical approval. Therefore, emphasis should be placed on improving the methodological quality of clinical trials. It is recommended to conduct well-designed clinical studies in strict accordance with CONSORT statement to make relevant evidence-based evidence more convincing. Finally, the status of the patient, especially adverse events, should be recorded and reported in as much detail as possible.

Conclusion

Our NMA revealed that a combination of CCPs and CT was more effective in treating DCM than CT alone. When combined taking into account the clinical effectiveness rate and other outcomes, SMP + CT, SFD + CT, YXD + CT, and ZGCD + CT demonstrated a preferred improvement in patients with DCM. In addition, considering the unique properties of various CCPs, clinical recommendations ought to address the patient's actual condition. Even so, additional high-caliber studies focusing on the efficacy of CCPs for DCM are needed to offer stronger evidence to support our findings because of the paucity of data on CCPs for DCM and small sample size.

Abbreviations

CCP	Chinese classical prescription
DCM	Dilated cardiomyopathy
NMA	Network meta-analysis
RCT	Randomized controlled trial
ZGCD	Zhigancao decoction
ZWD	Zhenwu decoction
SFD	Shenfu decoction
SMP	Shengmai powder
YXD	Yangxin decoction
BYHW	Buyang Huanwu decoction
CT	Conventional therapy
CER	Clinical effectiveness rate
LVEF	Left ventricular ejection fraction
LVEDD	Left ventricular end-diastolic dimension
LVESD	Left ventricular end-systolic dimension
BNP	Brain natriuretic peptide
CO	Cardiac output
Hs-CRP	Hypersensitive C-reactive protein
6MWT	Six-min walk test
NYHA	New York Heart Association
SUCRA	Surface under the cumulative ranking curve
MD	Mean difference
OR	Odds ratio
CI	Confidence interval

Supplementary Information

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Supplementary Material 1. PRISMA checklist

Supplementary Material 2. Search strategy

Supplementary Material 3. Adverse events of the included studies

Authors' contributions

JL and ST contributed to the study concept and design. ST drafted the manuscript. ST and LY performed the meta-analysis and data interpretation. JL took responsibility for the integrity of the data and the accuracy of the data analysis. ST, LY, and JW were responsible for the literature search, data

collection, and quality assessment. XX and YL contributed to the data extraction. DY and WZ were involved in data checking. All authors critically revised the manuscript for important intellectual content and approved the final version of the manuscript.

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Data availability
The data used in this review were extracted from published studies, and the original data could be obtained by searching databases. Other data supporting the results of this review are available from the corresponding author upon reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
All authors have consent for publication.

Competing interests
The authors declare that they have no competing interests.

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