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A meta-analysis of wenxin granule and metoprolol for the treatment of coronary heart disease and arrhythmia

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Abstract

Background: This meta-analysis aimed to systematically and comprehensively assess the effectiveness and safety of wenxin granule (WXG) and metoprolol in the treatment of elderly patients with coronary heart disease (CHD) and arrhythmia.

Methods: We searched the electronic databases of the Cochrane Library, PUBMED, EMBASE, CNKI, Wangfang, and CBM from initiation to May 1, 2022, and selected a set of clinical indicators for WXG and metoprolol for CHD and arrhythmia. The methodological quality of the included studies was analyzed using the Cochrane risk-of-bias tool. Data were pooled using a fixed-effects or random-effects model, and a meta-analysis was conducted.

Results: Eight randomized controlled trials involving 722 patients with CHD and arrhythmia were included. Our findings showed that WXG and metoprolol showed better effects than metoprolol alone on electrocardiogram change (odds ratio [OR] = 7.21, 95% confidence interval [CI] [1.48, 35.07]), clinical symptom improvement (OR = 5.83, 95% CI [1.52, 22.35]), overall clinical effect (OR = 5.51, 95% CI [2.65, 11.44], $P < .001$), atrial premature beat (mean difference [MD] = −109.85, 95% CI [−171.25, −48.46], $P < .001$), ventricular premature beat (MD = −195.43, 95% CI [−334.09, −56.77], $P < .001$), borderline premature beat (MD = −42.92, 95% CI [−77.18, −8.67], $P = .01$), short-burst ventricular tachycardia (MD = −35.98, 95% CI [−39.66, −32.30], $P < .001$), ST segment reduction (MD = −0.47, 95% CI [−0.54, −0.40], $P < .001$), ST segment decrease duration (MD = −0.76, 95% CI [−0.95, −0.57], $P < .001$). However, no significant differences were observed in adverse reactions (OR = 0.54, 95% CI [0.27, 1.09], $P = .09$).

Conclusion: Compared to metoprolol alone, WXG and metoprolol can more effectively manage patients with CHD and arrhythmia. However, additional large-scale, multicenter, rigorous, and high-quality randomized controlled trials are warranted to verify the present findings.

Abbreviations: APB = atrial premature beat, ARs = adverse reactions, BPB = borderline premature beat, CHD = coronary heart disease, CI = confidence interval, CYI = clinical symptom improvement, ECG-C = electrocardiogram change, MD = mean difference, OCE = overall clinical effect, OR = odds ratio, RCTs = randomized controlled trials, STSD = ST segment decrease duration, STSR = ST segment reduction, STVT = short-burst ventricular tachycardia, VPB = ventricular premature beat, WXG = wenxin granule.

Keywords: arrhythmia, coronary heart disease, meta-analysis, metoprolol, wenxin granule

1. Introduction

Coronary heart disease (CHD) is characterized by occlusion or vascular stenosis leading to myocardial ischemia, hypoxia, and necrosis.[1–4] It is one of the most common risk factors for cardiovascular diseases and a major public health problem worldwide.[5–7] It has been reported that CHD primarily leads to cardiovascular-related mortality, with approximately 7.3 million annual deaths, and China has contributed about 130,000 deaths.[8,9] Together with arrhythmia, it is responsible for the largest number of cardiac-associated mortality and morbidity worldwide.[10–12] Thus, it is important to manage patients with CHD and arrhythmia.

Metoprolol, a class II antiarrhythmic agent, is currently utilized clinically for the management of arrhythmias and CHD.[13–15] According to previous experimental and clinical studies, it can significantly decrease the occurrence of CHD and arrhythmia.[13–16] Studies have reported that it can slow heart rate, inhibit cardiac contractility by blocking β-adrenoceptors, and enhance cardiac autonomic function.[17] However, its efficacy remains unsatisfactory and is accompanied by a variety of adverse events, such as nausea, dizziness, headache, and bradycardia.[18]

Fortunately, the traditional Chinese herbal medicine, wenxin granule (WXG), has also been reported to manage such conditions with promising outcomes.[19–21] WXG comprises of 5

The authors have no conflicts of interest to disclose.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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herbal medicines including *Ginseng*, *Polygonatum*, *pseudo-ginseng*, *lamber*, and *Nardostachys Chinensis*. It has been widely used for the management of CHD and arrhythmia in China.[19–21] Studies have reported that it benefits CHD and arrhythmia by tonifying Qi, nourishing Yin, and promoting blood circulation, in accordance with the theory of traditional Chinese medicine.[22,23] Other pharmacological studies have reported that WXG has electrophysiological effects on blocking I_{Na} and I_K, which helps to relieve CHD and arrhythmia.[24–27]

A variety of clinical trials have explored the effectiveness and safety of WXG and metoprolol in the treatment of patients with CHD and arrhythmia.[28–35] However, there is still limited evidence to systematically and comprehensively investigate the effectiveness and safety of WXG and metoprolol in the treatment of elderly patients with CHD and arrhythmia. Therefore, this study systematically and comprehensively summarized the latest clinical trials to evaluate the effectiveness and safety of WXG and metoprolol in the treatment of patients with CHD and arrhythmia. Our findings provide evidence for the clinical practice of treating CHD and arrhythmia.

2. Methods

We reported this meta-analysis based on the PRISMA statement.

2.1. Ethic approval statement

This study did not require ethical approval because it analyzed secondary data from potential publications.

2.2. Eligibility criteria

We included the following trials: randomized controlled trial (RCT); patients aged >60 years; diagnosed with CHD and arrhythmia; experimental group treated with WXG and metoprolol and the control group treated with metoprolol alone; and no gender, race, or nationality limitations.

We excluded the following studies: duplicate records; irrelevant studies, including animal studies, experimental studies, reviews, conference summaries, case reports, case series, non-controlled clinical studies, and retrospective studies; and not RCT, combined therapies, wrong comparisons, quasi-RCTs, and studies with incomplete data.

2.3. Search strategy for eligible records

Six electronic databases were searched from initiation to May 1, 2022: Cochrane Library, PUBMED, EMBASE, CNKI, Wangfang, and CBM. There were no limitations to the language of the search results. Keywords used to search were: "Wenxin granule," OR "Wenxin keli," OR "Betaloc," OR "metoprolol," OR "coronary heart disease," OR "arrhythmia," OR "cardiac arrhythmia," OR "clinical trial," OR "RCT," OR "randomized controlled trial." The search strategy of PUBMED is given in Table 1. This study included RCT that investigated the effectiveness and safety of WXG as adjunctive therapy to metoprolol in elderly patients with CHD and arrhythmia.

2.4. Outcome measurement

The outcomes were electrocardiogram change (ECG-C), clinical symptom improvement (CYI), overall clinical effect (OCE), atrial premature beat (APB), ventricular premature beat (VPB), borderline premature beat (BPB), short-burst ventricular tachycardia (STVT), ST segment reduction (STSR), ST segment decrease duration (STSD), and adverse reactions (ARs).

2.5. Study selection, data extraction, and risk of bias assessment

Record screening, data extraction, and risk of bias assessment were independently performed by 2 authors and cross-checked. Any disagreement was resolved through consultation or discussion with the third author. All records were selected based on eligibility criteria. Data from the included trials were extracted using a previously designed data collection form, including general data summary (e.g., title, first author, year of publication), basic patient and study information (e.g., age, gender, sample size, details of intervention and comparison), and outcomes. The methodological quality of all the included trials was evaluated using the Cochrane risk-of-bias tool in 7 domains. Each study was assessed through 7 domains, and each was rated as having a low, unclear, or high risk of bias.

2.6. Statistical analysis

This study analyzed data and conducted a meta-analysis using RevMan 5.3 software (Copenhagen: The Nordic Cochrane Center, The Cochrane Collaboration). Continuous data were calculated using the mean difference (MD) and 95% confidence interval (CI), and dichotomous data were calculated using odds ratios (OR) and 95% CI. Statistical heterogeneity across the included studies was checked using I^2 index. A fixed-effects model was used to synthesize the data if I^2 was <50%, and a random-effects model was used to pool the data if I^2 was ≥50%.

3. Results

3.1. Study characteristics

In total, 938 records were identified in this study (Fig. 1). A total of 930 citations were excluded because of duplication, irrelevant studies, non-RCT, combined therapy, wrong comparison, quasi-RCT, and trials with incomplete data (Fig. 1). Finally, 8 eligible studies involving 722 patients focusing on WXG and metoprolol for CHD and arrhythmia were included, and the data were analyzed (Fig. 1). The sample sizes varied from 60 to 148 and all were prospective studies. The general characteristics of the 8 eligible studies are summarized in Table 2.

Table 1

Search strategy of PUBMED.

Number	Search terms
1	Coronary heart disease
2	Cardiac arrhythmia
3	Arrhythmia
4	Or 1–3
5	Chinese medicine
6	Herbal medicine
7	Chinese herbal medicine
8	Wenxin granule
9	Wenxin keli
10	Betaloc
11	Metoprolol
12	Or 5–11
13	Clinical trial
14	Controlled clinical trial
15	Randomized controlled trial
16	Case-control study
17	Observational study
18	Or 13–17
19	4 AND 12 AND 18

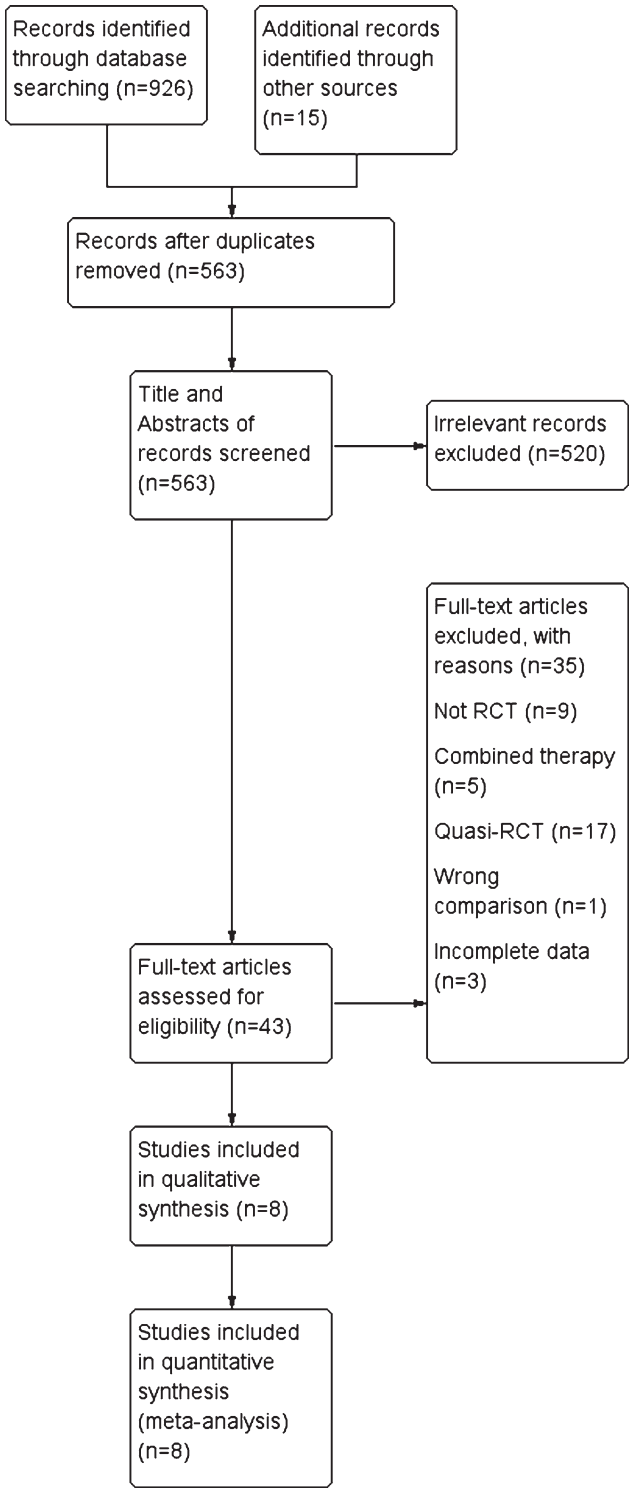

Figure 1. Flow diagram of study selection.

3.2. Study quality assessment

The Cochrane risk-of-bias tool was used to assess the quality of the 8 included trials (Fig. 2). All 8 studies reported details of random sequence generation.[28–35] However, none of the included trials provided insufficient information on allocation concealment and blinding to participants, investigators, and outcome assessors[28–35] (Fig. 2). Regarding incomplete outcome data, all studies reported sufficient data, except for 3 studies with insufficient outcome indicators. All trials reported selective reporting and other biases with sufficient information[28–35] (Fig. 2).

Table 2

General characteristics of included studies.

Study	No. of patients (T/C)	Age (yr, T/C)	Intervention	Control	Outcomes	Follow-up
Gu 2019	40/40	T: 69.7 ± 3.4; C: 69.5 ± 3.5	Metoprolol + WXG	Metoprolol	ECG-C	1 mo
Guo 2018	50/50	T: 68.3 ± 4.6; C: 69.1 ± 4.7	Metoprolol + WXG	Metoprolol	OCE, STVT, STSR, STSD, ARs	1 mo
Luo 2018	40/40	T: 70.5 ± 1.1; C: 71.5 ± 1.3	Metoprolol + WXG	Metoprolol	OCE	1 mo
Tan 2021	30/30	T: 72.6 ± 2.4; C: 72.1 ± 2.3	Metoprolol + WXG	Metoprolol	OCE, APB, VPB, ARs	2 mo
Wang 2017	42/42	T: 71.0 ± 2.6; C: 71.0 ± 2.4	Metoprolol + WXG	Metoprolol	CYI, APB, VPB, BPB	1 mo
Wang 2019	46/46	T: 71.1 ± 2.4; C: 70.5 ± 2.6	Metoprolol + WXG	Metoprolol	OCE, ARs	5 wk
Zhang 2019	39/39	T: 63.3 ± 3.1; C: 63.2 ± 3.1	Metoprolol + WXG	Metoprolol	APB, VPB, BPB, STVT, STSR, STSD	1 mo
Zhu 2019	74/74	T: 74.3 ± 9.1; C: 74.3 ± 9.1	Metoprolol + WXG	Metoprolol	APB, VPB, ARs	3 mo

APB = atrial premature beat, ARs = adverse reactions, BPB = borderline premature beat, C = control group, CYI = clinical symptom improvement, ECG-C = electrocardiogram change, OCE = overall clinical effect, STSD = ST segment decrease duration, STSR = ST segment reduction, STVT = short-burst ventricular tachycardia, T = treatment group, VPB = ventricular premature beat, WXG = wenxin granule.

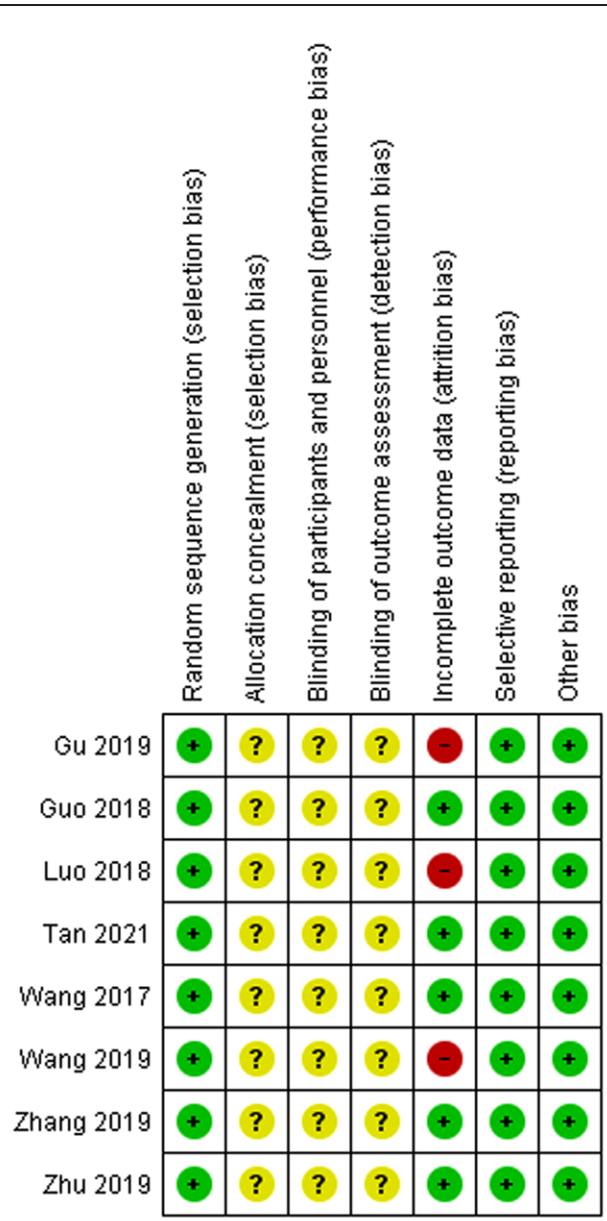

Figure 2. Risk of bias summary.

3.3. ECG-C and CYI

One study involving 80 patients evaluated the ECG-C (OR = 7.21, 95% CI [1.48, 35.07], Table 3)[28] and another study investigated CYI (OR = 5.83, 95% CI [1.52, 22.35], Table 3).[32]

3.4. Meta-analysis of OCE

Four trials involving 332 patients assessed the OCE. Its results showed that WXG and metoprolol showed better effects than metoprolol alone on OCE (OR = 5.51, 95% CI [2.65, 11.44], I^2 = 0%, P < .001, Table 3, Fig. 3).[29–31,33]

3.5. Meta-analysis of APB and VPB

Four studies with 370 patients explored APB and VPB (Table 3). Statistically significant differences were found in APB (MD = −109.85, 95% CI [−171.25, −48.46], I^2 = 97%, P < .001; Table 3, Fig. 4), and VPB (MD = −195.43, 95% CI [−334.09, −56.77], I^2 = 99%, P < .001; Table 3, Fig. 5).

Table 3

Qualitative synthesis of included trials.

Outcome or subgroup	Studies	Participants	Statistical method	Effect estimate
1.1 Electrocardiogram change	1	80	Odds ratio (M-H, fixed, 95% CI)	7.21 [1.48, 35.07]
1.2 Clinical symptom improvement	1	84	Odds ratio (M-H, fixed, 95% CI)	5.83 [1.52, 22.35]
1.3 Overall clinical effect	4	332	Odds ratio (M-H, fixed, 95% CI)	5.51 [2.65, 11.44]
1.4 Atrial premature beat	4	370	Mean difference (IV, random, 95% CI)	−109.85 [−171.25, −48.46]
1.5 Ventricular premature beat	4	370	Mean difference (IV, random, 95% CI)	−195.43 [−334.09, −56.77]
1.6 Borderline premature beat	2	162	Mean difference (IV, random, 95% CI)	−42.92 [−77.18, −8.67]
1.7 Short-burst ventricular tachycardia	2	178	Mean difference (IV, fixed, 95% CI)	−35.98 [−39.66, −32.30]
1.8 ST segment reduction	2	178	Mean difference (IV, fixed, 95% CI)	−0.47 [−0.54, −0.40]
1.9 ST segment decrease duration	2	178	Mean difference (IV, fixed, 95% CI)	−0.76 [−0.95, −0.57]
1.10 Adverse reactions	4	400	Odds ratio (M-H, fixed, 95% CI)	0.54 [0.27, 1.09]

CI = confidence interval, IV = inverse variance, M-H = Mantel-Haenszel.

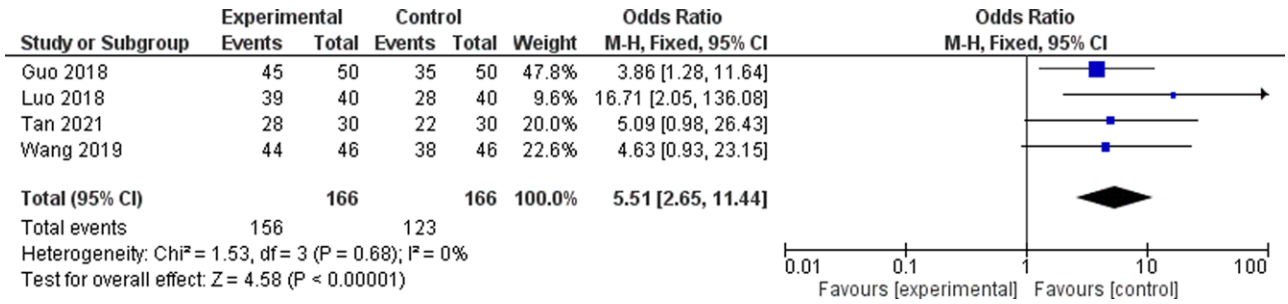

Figure 3. Meta-analysis of overall clinical effect.

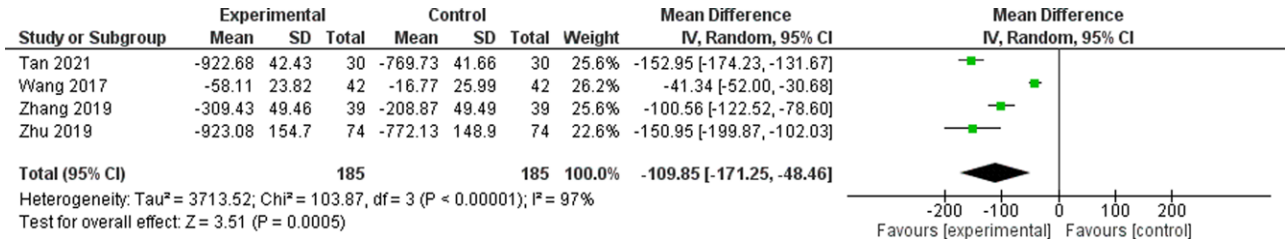

Figure 4. Meta-analysis of atrial premature beat.

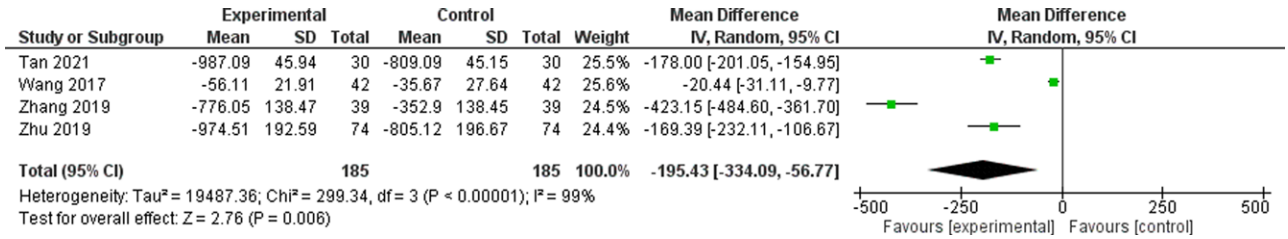

Figure 5. Meta-analysis of ventricular premature beat.

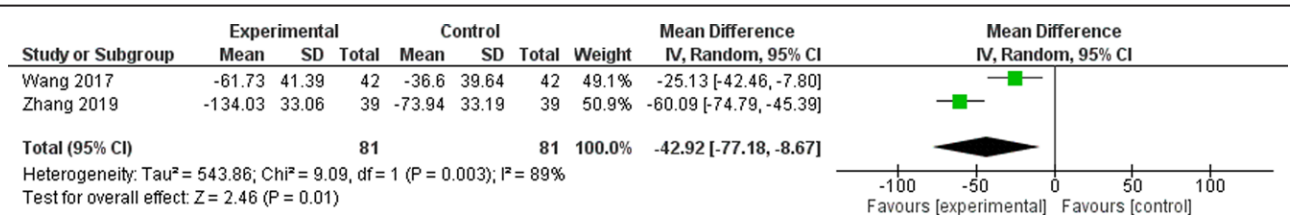

Figure 6. Meta-analysis of borderline premature beat.

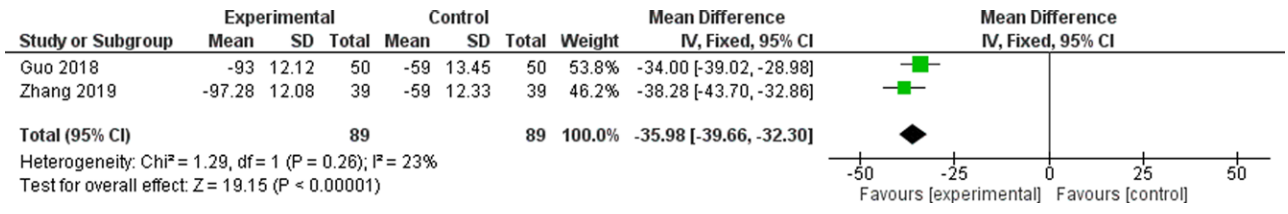

Figure 7. Meta-analysis of short-burst ventricular tachycardia.

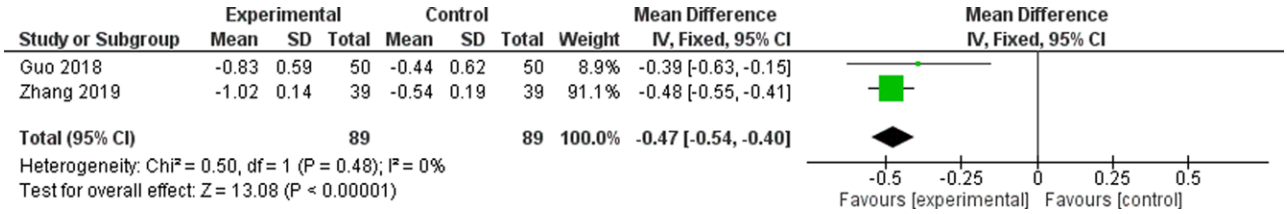

Figure 8. Meta-analysis of ST segment reduction.

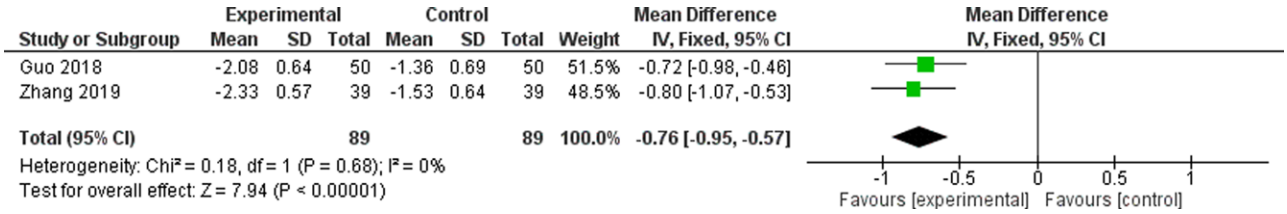

Figure 9. Meta-analysis of ST segment decrease duration.

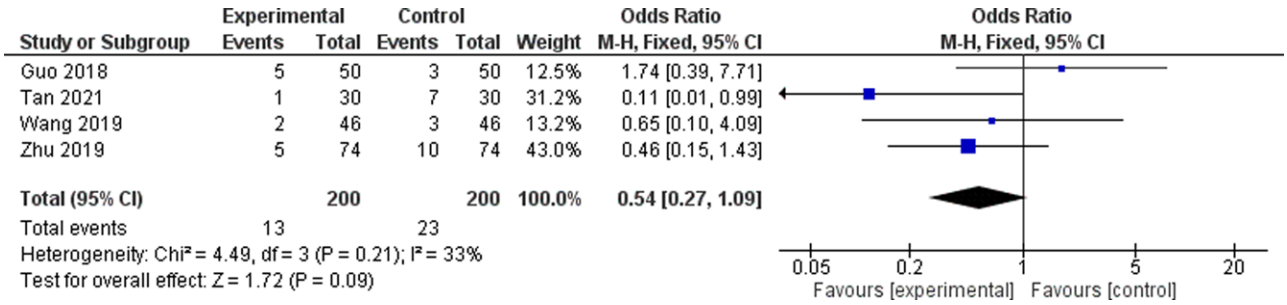

Figure 10. Meta-analysis of adverse reactions.

3.6. Meta-analysis of BPB

Two studies involving 162 patients evaluated BPB, and the results showed a statistically significant difference on BPB (MD = −42.92, 95% CI [−77.18, −8.67], I^2 = 89%, P = .01; Table 3, Fig. 6).

3.7. Meta-analysis of STVT, STSR, and STSD

Two trials with 178 participants examined STVT, STSR, and STSD[29,34] (Table 3). There were significant differences between 2 groups on STVT (MD = −35.98, 95% CI [−39.66, −32.30], I^2 = 23%, P < .001; Fig. 7), STSR (MD = −0.47, 95% CI [−0.54, −0.40], I^2 = 0%, P < .001; Fig. 8), and STSD (MD = −0.76, 95% CI [−0.95, −0.57], I^2 = 0%, P < .001; Fig. 9).

3.8. Meta-analysis of ARs

A total of 4 studies with 400 patients explored ARs[29,31,34,35] (Table 3). No significant difference was observed in ARs (OR = 0.54, 95% CI [0.27, 1.09], I^2 = 33%, P = .09; Fig. 10).

4. Discussion

CHD is still one of the most significant risk factors that can result in major public health problems or even cardiovascular-related deaths worldwide.[5–9] In addition to arrhythmia, previous studies have reported that such conditions account for more cardiac-associated mortality and morbidity.[10–12] Metoprolol has been reported to relieve both CHD and arrhythmia symptoms.[13–15] Furthermore, a variety of clinical trials have explored the effects and safety of WXG and metoprolol in the treatment of elderly patients with CHD and arrhythmia. However, there is limited evidence supporting this hypothesis.

This meta-analysis included a total of 8 trials involving 722 patients. This study comprehensively and systematically investigated the effects and safety of WXG and metoprolol in the treatment of elderly patients with CHD and arrhythmia. The results showed that patients who received WXG and metoprolol had better outcomes than those who received metoprolol alone. Effectiveness of WXG and metoprolol on ECG-C, CYI, OCE, APB, VPB, BPB, STVT, STSR, and STSD indicates that the effects of WXG and metoprolol are superior to those of metoprolol alone for the management of CHD and arrhythmia.

In addition, 4 trials involving 400 participants reported adverse events. There were no significant differences in the ARs when the data were pooled. This indicates that both modalities have similar safety profiles.

The present study has certain limitations as follows: there were certain risk of bias in the included trials, and all included studies did not fully describe the procedures of allocation and blind implementation; the sample size of some of the included studies was small, and their effectiveness tests were restricted; all studies were conducted in China and were published in Chinese journals, which may have caused bias. Therefore, further studies with larger sample sizes and multicenter designs are needed to validate the current findings.

5. Conclusion

The findings of this study showed that WXG and metoprolol was more effective than metoprolol for the treatment of elderly patients with CHD and arrhythmia.

Author contributions

Conceptualization: Ling-Li Meng and Wei Huang.
Data curation: Ling-Li Meng and Wei Huang.
Formal analysis:Ling-Li Meng.
Investigation: Wei Huang.
Methodology: Ling-Li Meng.
Supervision: Wei Huang.
Validation: Wei Huang.
Writing–original draft: Ling-Li Meng and Wei Huang.
Writing–review & editing: Ling-Li Meng and Wei Huang

References

[1] Mozaffarian D, Benjamin EJ, Go AS, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. Circulation. 2015;131:e29–322.
[2] Dibben G, Faulkner J, Oldridge N, et al. Exercise-based cardiac rehabilitation for coronary heart disease. Cochrane Database Syst Rev. 2021;11:CD001800.
[3] Zhang S, Chen ZL, Tang YP, et al. Efficacy and safety of xue-fu-zhu-yu decoction for patients with coronary heart disease: a systematic review and meta-analysis. Evid Based Complement Alternat Med. 2021;2021:9931826.
[4] Nowbar AN, Howard JP, Finegold JA, et al. Global geographic analysis of mortality from ischaemic heart disease by country, age and income: statistics from World Health Organisation and United Nations. Int J Cardiol. 2014;174:293–8.
[5] Tsao CW, Aday AW, Almarzooq ZI, et al. Heart disease and stroke statistics—2022 update: a report from the American Heart Association. Circulation. 2022;145:e153–639.
[6] Jousilahti P, Laatikainen T, Peltonen M, et al. Primary prevention and risk factor reduction in coronary heart disease mortality among working aged men and women in Eastern Finland over 40 years: population based observational study. BMJ. 2016;352:i721.
[7] Vedin O, Hagström E, Stewart R, et al. Secondary prevention and risk factor target achievement in a global, high-risk population with established coronary heart disease: baseline results from the stability study. Eur J Prev Cardiol. 2013;20:678–85.
[8] Gaziano TA, Bitton A, Anand S, et al. Growing epidemic of coronary heart disease in low- and middle-income countries. Curr Probl Cardiol. 2010;35:72–115.
[9] Bechthold A, Boeing H, Schwedhelm C, et al. Food groups and risk of coronary heart disease, stroke and heart failure: a systematic review and dose-response meta-analysis of prospective studies. Crit Rev Food Sci Nutr. 2019;59:1071–90.
[10] John RM, Tedrow UB, Koplan BA, et al. Ventricular arrhythmias and sudden cardiac death. Lancet. 2012;380:1520–9.
[11] Tung P, Albert C. M. Causes and prevention of sudden cardiac death in the elderly. Nat Rev Cardiol. 2013;10:135–42.
[12] Liu Y. Analysis of clinical related factors of arrhythmia in elderly patients with acute and chronic myocardial ischemia. Jilin Univ. 2017 (Dissertation).
[13] Zhou P, Huang J, Ding W. Effect of ling-gui-zhu-gan decoction major components on the plasma protein binding of metoprolol using UPLC analysis coupled with ultrafiltration. RSC Adv. 2018;8:35981–8.
[14] Jiang W, Chen C, Huo J, et al. Comparison between renal denervation and metoprolol on the susceptibility of ventricular arrhythmias in rats with myocardial infarction. Sci Rep. 2018;8:10206.
[15] Zhang Q, Lu XN, Sun NL. Effects of verapamil and metoprolol on heart rate variability in patients with coronary heart disease. J Peking Univ (Health Sci). 2007;39:610–3.
[16] Tölg R, Witt M, Schwarz B, et al. Comparison of carvedilol and metoprolol in patients with acute myocardial infarction undergoing primary coronary intervention—the PASSAT Study. Clin Res Cardiol. 2006;95:31–41.
[17] Wehrens SM, Hampton SM, Skene DJ. Heart rate variability and endothelial function after sleep deprivation and recovery sleep among male shift and non-shift workers. Scand J Work Env Hea. 2012;38:171–81.
[18] Li YQ. Effect of moricizine combined with metoprolol on heart rate variability and adverse reactions in patients with ventricular arrhythmia. J North Pharm. 2020;17:167–8.
[19] Wei ZW, Li H. Effect and safety of wenxin granule in treating arrhythmia of senile coronary heart disease. J Clin Rational Drug Use. 2021;5:52–5.
[20] Geng GZ. Clinical observation and analysis of wenxin granule in treating chronic pulmonary heart disease complicated with coronary heart disease arrhythmia. J Math Med. 2021;2:284–5.
[21] Han XB. Study on mechanism and effect of wenxin granule in treating arrhythmia of coronary heart disease. J Pharm Forum. 2018;5:167–8.
[22] Niu ZH, Zhao YJ, Niu JX, et al. Research progress in the treatment of arrhythmia with the method of replenishing qi and nourishing yin. Guangming Tradit Chin Med. 2022;37:223–5.
[23] Wei RL, Wang ZF, Ma XC, et al. Clinical comprehensive evaluation of wenxin granule in treating arrhythmia (deficiency of both Qi and Yin). Chin J Tradit Chin Med. 2021;46:6068–77.
[24] Xue X, Guo D, Sun H, et al. Wenxin Keli suppresses ventricular triggered arrhythmias via selective inhibition of late sodium current. Pacing Clin Electrophysiol. 2013;36:732–40.
[25] Tian G, Sun Y, Liu S, et al. Therapeutic effects of wenxin keli in cardiovascular diseases: an experimental and mechanism overview. Front Pharmacol. 2018;9:1005.
[26] Hu D, Barajas-Martinez H, Burashnikov A, et al. Mechanisms underlying atrial-selective block of sodium channels by wenxin keli: experimental and theoretical analysis. Int J Cardiol. 2016;207:326–34.
[27] Wang P, He T, Zheng R, et al. Applying cooperative module pair analysis to uncover compatibility mechanism of fangjis: an example of wenxin keli decoction. J Ethnopharmacol. 2021;278:114214.
[28] Gu LY. Clinical effect of Wenxin granule combined with metoprolol on arrhythmia in elderly patients with coronary heart disease. People Health. 2019;17:71–2.
[29] Guo L. Efficacy and safety of Wenxin granule combined with metoprolol in elderly patients with coronary heart disease arrhythmia. Primary Care Forum. 2018;22:3523–5.
[30] Luo LK, Wu Y. Effect of wenxin granule combined with metoprolol on arrhythmia in elderly patients with coronary heart disease. Health Nutr Chin. 2018;28:236–7.
[31] Tan GC, Wu MJ, Wu WP. Clinical effect of wenxin granule combined with metoprolol on arrhythmia in elderly patients with coronary heart disease and its influence on hemorheology index. Clin Med Res Pract. 2021;6:117–9.
[32] Wang GJ, Chen YH, Mao LJ. Effect and safety of wenxin granule combined with metoprolol on arrhythmia in elderly patients with coronary heart disease. Chin J Biochem Med. 2017;37:325–7.
[33] Wang DM. Effect of Wenxin granule combined with metoprolol on arrhythmia in elderly patients with coronary heart disease. Chin Health Nutr. 2019;29:225–6.
[34] Zhang SK. Effect of Wenxin granule combined with metoprolol on arrhythmia in elderly patients with coronary heart disease. Ration Drug Use Chin. 2019;192:141–2.
[35] Zhu K. Analysis of the clinical effect of metoprolol combined with Wenxin granule on arrhythmia in elderly patients with coronary heart disease. Wisdom Health. 2019;5:165–6.