European Journal of Medical Research

REVIEW

Open Access

Effect of Astragalus injection treatment for viral myocarditis: a systematic review and meta-analysis

Dinala jialiken[1†], Lichao Qian[2†], Shiwu Wen[3], Shuai Ren[1], Yadong Fan[1], Yi xuan Dong[1] and Chong Zou[1*]

Abstract

Background Astragalus injection has been utilized in traditional Chinese medicine to treat a variety of diseases. The purpose of this systematic review was to evaluate the effectiveness of Astragalus injection in the treatment of viral myocarditis.

Methods English databases such as PubMed, Cochrane Library, and EMBASE, and Chinese databases of Sino Med, China National Knowledge Infrastructure (CNKI), the VIP Information Resource Integration Service Platform, and Wanfang Data Information Site, were searched from their inception until May 1, 2024. The outcome measures of this study included the effectiveness rate, creatine kinase (CK), aspartate aminotransferase (AST), creatine kinase Isoenzyme (CK-MB), lactate dehydrogenase (LDH), cardiac troponin I (cTnI), and electrocardiogram (ECG).

Results Twenty-six studies were included in this analysis, comprising a total of 2793 patients. Meta-analyses indicated that, compared to standard treatment alone, the Astragalus injection group demonstrated significant advantages, achieving an effectiveness rate of 92.79% (1094 cases). In contrast, the control group, which included 1108 cases, had an effectiveness rate of 77.71% (861 cases). Additionally, the Astragalus injection group exhibited the following benefits for patients affected by viral myocarditis: decreasing ΔAST [weighted mean difference (WMD) = − 14.23, 95% confidence interval (CI) (− 24.17, − 4.30), $P < 0.05$]; ΔCK [weighted mean difference (WMD) = − 34.84, 95% confidence interval (CI) (− 48.03, − 21.65), $P < 0.05$], lowering ΔCK-MB [WMD = − 7.64, 95% CI (− 9.30, − 5.99), $P < 0.001$], ΔcTnI [WMD = − 0.18, 95% CI (− 0.27, − 0.10), $P < 0.001$], ΔLDH [WMD = -41.93, 95% CI (− 55.97, − 27.90), $P < 0.05$], and ΔcTnI [WMD = − 0.18, 95% CI (− 0.28, − 0.08), $P < 0.05$].

Conclusion Astragalus injection may have a therapeutic effect in patients with viral myocarditis by reducing levels of AST, CK, CK-MB, LDH, and cTnI, improving ECG results, and increasing the overall effectiveness rate for those affected by this condition.

Trial registration: This study registered with PROSPERO before conducting the systematic review. The registration number is CRD42021239660.

Keywords Astragalus injection, Viral myocarditis, Meta-analysis, Systematic review, Traditional Chinese medicine

[†]Dinala jialiken and Lichao Qian are first author.

*Correspondence:
Chong Zou
yfy105@njucm.edu.cn
Full list of author information is available at the end of the article

Introduction

Viral myocarditis (VMC) is a potentially life-threatening condition, particularly in young adults [1]. The global incidence of VMC is estimated to be approximately 10 to 20 cases per 100,000 individuals. With advancements in diagnosis and survival rates, the prevalence of VMC is expected to increase by 46% by 2030 [2]. VMC is characterized by the degeneration and necrosis of cardiac myocytes and is an inflammatory myocardial lesion caused by viral invasion of the heart, with the Coxsackie B group being the most common viruses responsible for VMC [3, 4]. The infectious phase of VMC is marked by viral invasion and subsequent direct damage to the myocardium, which includes inflammation stemming from both innate and adaptive immune responses, as well as necrosis and apoptosis of cardiomyocytes [5]. Following viral infection, damage to cardiomyocytes occurs, leading to widespread inflammation that may also affect the pericardium, sinoatrial node, and conduction system to varying extents. Despite the emergence of immunosuppressive and antiviral therapies, supportive care, including mechanical circulatory support, remains the primary treatment approach for VMC. However, due to the absence of large-scale, randomized controlled trials assessing this treatment modality, current clinical guidelines do not endorse the use of immunoadsorption in VMC patients [6]. The underlying etiology and pathophysiological mechanisms of VMC are not yet fully understood, which complicates timely diagnosis and effective management for healthcare providers [7].

Coxsackie B viruses, recognized for their role in viral myocarditis, primarily impact the heart by directly infiltrating myocardial cells and eliciting localized inflammatory responses. In contrast, SARS-CoV-2, the etiological agent of coronavirus disease 2019 (COVID-19), primarily affects the respiratory system, but has also been associated with cardiac complications, including myocarditis, particularly in severe instances. Both viruses can provoke substantial immune responses; Coxsackie B may result in immune-mediated cardiac damage, whereas COVID-19 is frequently linked to a cytokine storm that intensifies cardiac injury. COVID-19, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in Wuhan, China, in December 2019 and rapidly spread worldwide. Severe manifestations of SARS-CoV-2 infection appear to elicit an inflammatory response in cardiac tissue, potentially leading to myocarditis [8].

Data from the National Health Commission of China indicate that 92% of confirmed COVID-19 patients received a combination of traditional Chinese medicine and Western medical treatments, which have demonstrated significant efficacy, particularly in patients with pre-existing health conditions. Early intervention with traditional Chinese medicine has been shown to effectively mitigate the progression of the disease to more severe forms. Accumulated clinical evidence suggests that early application of traditional Chinese medicine is vital for enhancing cure rates, shortening the duration of illness, delaying disease progression, and reducing mortality among COVID-19 patients [9].

Astragalus was first described in the renowned traditional Chinese medicine (TCM) text, "Shen Nong Ben Cao Jing". It is a quintessential Chinese herbal remedy for treating vital energy deficiency and holds a significant position in TCM. According to TCM theory, Astragalus can tonify Qi, lift yang, induce diuresis to alleviate edema, eliminate toxins, and promote tissue regeneration. The total flavonoids of Astragalus (TFA) are one of the primary active constituents found in Astragalus. The antiviral properties of Astragaloside IV against Coxsackievirus B3 are facilitated by the upregulation of interferon-gamma mRNA expression [10]. Additionally, Astragaloside IV influences the inflammatory response associated with CVB3-induced viral myocarditis by enhancing the expression of Tumor Necrosis Factor Alpha-Inducible Protein 20 [11].

Astragalus injection is derived from TFA and can be utilized to modulate the immune response, thereby achieving an antiviral effect. Previous studies indicate that Astragalus injection can enhance immune function in patients with VMC, reduce the activation and amplification of inflammatory pathways, mitigate myocardial cell damage, and improve the clinical efficacy of treatment [12]. In this paper, we aim to summarize all relevant studies to provide updated evidence on the effects of Astragalus injection treatment for viral myocarditis through a systematic review and meta-analysis.

Methods

We conducted this study in accordance with the PRISMA guidelines. All analyses were performed based on previously published reports; therefore, no ethical approval or patient consent was required (Prisma 2020 check list in Supplementary material).

Information sources and search strategy

Comprehensive literature searches were conducted in PubMed, Cochrane Library, EMBASE, SinoMed, China National Knowledge Infrastructure (CNKI), the VIP Information Resource Integration Service Platform, and Wanfang Data Information Site. The publication date range was set from the inception of each database to May 1, 2024. The reference lists of selected studies and

systematic reviews with a similar scope were examined for additional relevant studies. The search strategy was developed with the assistance of a medical librarian experienced in systematic review research. Medical Subject Headings (MeSH) and keywords pertinent to the study population, exposure, outcome, and study type were combined to formulate the search strategy. The complete search strategies for each database are shown in (Table 1, Figure 1 and Supplement 1).

Inclusion criteria

Inclusion criteria: (a) type of study (S): the included study was a randomized controlled trial; (b) type of participant (P): adult patients clinically diagnosed with viral myocarditis; (c) type of intervention (I): the experimental group was given Astragalus injection and conventional treatment; (d) type of comparator (C): the control group received conventional treatment; (e) type of prognostic measurement (O): these studies included one of the following outcomes: CK, CK-MB, LDH, cTnI, AST, and ECG results.

Exclusion criteria

Studies were excluded if they met any of the following criteria: (1) duplicate publications; (2) lack of relevant data from which clinical trial information could be extracted; (3) inclusion of single case reports, systematic reviews, essential scientific reports, and animal studies; (4) clinical trials that did not meet the above inclusion criteria.

The type of the outcome measurement

The outcome measures of this study included the effectiveness rate, creatine kinase (CK), aspartate aminotransferase (AST), creatine kinase isoenzyme (CK-MB), lactate dehydrogenase (LDH), cardiac troponin I (cTnI), and electrocardiogram (ECG).

Data extraction

Two reviewers independently extracted data from the included studies. A data extraction form was developed as a data collection tool and was modified based on group feedback. A calibration exercise was conducted by the reviewers to ensure consistent assessment methods. The principal investigator was involved whenever discrepancies arose between the reviewers. The following details were extracted from each study: (1) study characteristics: author, year of publication, study design, country of study, and study period; (2) study population; (3) diagnostic criteria; (4) outcome measures; (5) covariates: confounders were noted when the adjusted effect measures were reported.

Assessment of bias risk of included studies

The risk of bias in the studies included in our meta-analysis was independently assessed by two authors using the of Bias evaluation tool from the Cochrane Handbook for Systematic Reviews. The risk assessment covered seven items: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other sources of bias. We evaluated each of these aspects separately and categorized them as or based on the established assessment criteria.

The quality of evidence for outcome measures was assessed utilizing the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) methodology. Table 2.

Data analysis

The stata15.1 was used for the meta-analysis. We utilized WMD and CI as statistical analyses to determine changes in succession. WMDs and 95% CIs were extracted from the available publications when necessary. We calculated WMDs and CIs based on the original study data provided in the journals. To assess the level of heterogeneity among the included studies, we employed I^2 statistics and p-values. If $I^2 > 50\%$ or $P < 0.05$, we selected the random-effects model; otherwise, we chose the fixed-effects model Table 1.

Study characteristics

A total of 26 randomized controlled trials (RCTs) involving 2793 patients were included in the meta-analysis [12–37]. Among these studies, the experimental group comprised 1441 participants (652 males and 789 females), while the control group included 1352 participants (724 males and 628 females). The control group received standard treatment, whereas the experimental group received an Astragalus injection in addition to standard treatment. The duration of treatment varied from 10 days to 6 months. The outcome evaluation indicators included the effectiveness rate, improvements in electrocardiogram readings, and the myocardial enzyme profile (LDH, AST, CK-MB), as well as troponin cTnI levels, which are illustrated in Table 1.

Assessment of study quality

The analysis included 26 randomized controlled trials (RCTs), which were assessed using Review Manager for data processing and chart generation. The random number table method was employed for five items, while the implementation method for the remaining 21 items was not described. Assignment concealment was not

Table 1 Characteristics of 26 included studies

Author	Year	Intervention	Dose	Course of treatment	Gender (male/female)		Average age	Outcomes
					C	Astragalus injection		
Wang Zhaohui	2001	Astragalus injection + C	Astragalus injection 20 g + 5%GS 500ML, ivgtt, qd	3 m	30/20	27/39	32	CK, cTnI
Wu Qiaoyan	2009	Astragalus injection + C	Astragalus injection ~ 2 mL/kg, ivgtt, qd	11–31 d	17/13	18/12	7.5	ECG
Wang Fuyu	2001	Astragalus injection + C	Astragalus injection 20–30 ml + 5%GS 150–200ML, ivgtt, qd	3 w	23/27	22/28	24.72	LDH, AST, ECG
Xi Zhongxin	2012	Astragalus injection + C	Astragalus injection 40 ml + 5%GS 250ML, ivgtt, tid,	6 m	29/41	31/52	40.2	CK,CK-MB,LDH, AST,ECG
Sun XiangRong	2005	Astragalus injection + C	Astragalus injection 30 ml + 5%GS 150–200ML, ivgtt, qd	4 w	18/16	18/17	28	AST, CK-MB
Luo Chengxiang	2008	Astragalus injection + C	Astragalus injection 6–10 ml + 10%GS 250ML, ivgtt, qd	1–4 w	37/26	36/24	7.7	ECG
Peng Yongjun	2006	Astragalus injection + C	Astragalus injection 10–20 ml + 10%GS 50–100ML, ivgtt, qd	14 d	22/18	24/16	6	AST, CK-MB, LDH, CK, cTnI, ECG
Lu Zuozheng	2004	Astragalus injection + C	Astragalus injection 10 ml, ivgtt, qd	3–4 w	12/11	18/17	7	AST, CK-MB, LDH, CK
Liu Jin	2017	Astragalus injection + C	Astragalus injection 15 ml + 5%GS 100ML, ivgtt, qd	2 w	31/21	30/22	5.7	AST, CK-MB, LDH, CK
Wang Yuehua	2013	Astragalus injection + C	Astragalus injection 2.5 mg/kg·d + 5%GS 100–200ML, ivgtt, qd	15 d	16/15	26/21	7.4	CK-MB
Yuan Binli	2008	Astragalus injection + C	Astragalus injection 10–20 ml + 10%GS 150–200ML, ivgtt, qd	3 w	13/11	14/12	8	ECG
Lu Yanmei	2010	Astragalus injection + C	Astragalus injection 10–20 ml + 10%GS 100–250ML, ivgtt, qd	10–14 d	20/10	17/13	5	AST, CK-MB, LDH, CK
Zhang Lisheng	2010	Astragalus injection + C	Astragalus injection 1 mL/kg ~ 2 mL/kg, ivgtt, qd	42 d	22/18	23/17	9	CK-MB, cTnI
Xu Muzhen	2010	Astragalus injection + C	Astragalus injection 0.2 g/kg + 5%GS 10–20ML, ivgtt, qd	14 d	16/14	20/18	7.32	CK-MB, cTnI
Zhang Defeng	2001	Astragalus injection + C	Astragalus injection 1 ~ 2 m l / k g·d + 10%GS 100–250ML, ivgtt, qd	2 w	42/36	34/50	8.3	CK-MB, LDH
Hu Xiaofeng	2009	Astragalus injection + C	Astragalus injection 60 ml + 5%GS 250ML, ivgtt, bid	2 w	27/23	26/24	37	AST, CK-MB, LDH, CK, cTnI
Lu yingfen	2000	Astragalus injection + C	Astragalus injection 30 ml, ivgtt + 0.9%Nacl 500ML, ivgtt, qd	4 w	23/17	27/19	37.3	LDH, ECG
zhou zhilin	2003	Astragalus injection + C	Astragalus injection 30ml5%GS 250ML, ivgtt, qd	2 w	12/19	14/18	34	CK-MB, AST, ECG
Wei Ao	2020	Astragalus injection + C	Astragalus injection 20ml5%GS 250ML, ivgtt, qd	2 w	48/42	50/40	70	CK-MB, LDH, cTnI, ECG

Table 1 (continued)

Author	Year	Intervention	Dose	Course of treatment	Gender (male/female)		Average age	Outcomes
					C	Astragalus injection		
Zhang Yisheng	2013	Astragalus injection + C	Astragalus injection 30ml5%GS 250ML, ivgtt, qd	4 w	22/16	28/20	25	CK-MB, cTnI
Wu Bing	2016	Astragalus injection + C	Astragalus injection 20 ml + 5%GS 250ML, ivgtt, qd	2 w	24/23	21/26	26	CK-MB, cTnI, LDH
Xie Honhying	2021	Astragalus injection + C	Astragalus injection 20 ml + 5%GS 250ML, ivgtt, qd	2 w	42/38	43/37	45	CK-MB, cTnI
Yang Wenjun	2022	Astragalus injection + C	Astragalus injection 20 ml + 5%GS 250ML, ivgtt, qd	2 w	35/35	37/33	58.7	CK-MB, cTnI, LDH
Li Wangxuan	2018	Astragalus injection + C	Astragalus injection 20 ml, ivgtt, qd	2 w	36/26	38/24	30	CK-MB, cTnI, LDH, CK
Liu Ningning	2021	Astragalus injection + C	Astragalus injection 5 ~ 10 ml + 10%GS 100–150ML, ivgtt, qd	2 w	35/28	33/30	40	CK, CK-MB, LDH
Wang Honglei	2019	Astragalus injection + C	Astragalus injection 30 ml, ivgtt, qd	2 w	27/20	26/22	5	CK-MB, cTnI, LDH

T: treatment group; C: control group; Ivgtt: intravenous glucose tolerance test; CK: creatine kinase; CK-MB: creatine kinase isoenzyme; LDH: lactate dehydrogenase; cTnI: cardiac troponin I; AST: aspartate aminotransferase and electrocardiogram (ECG)

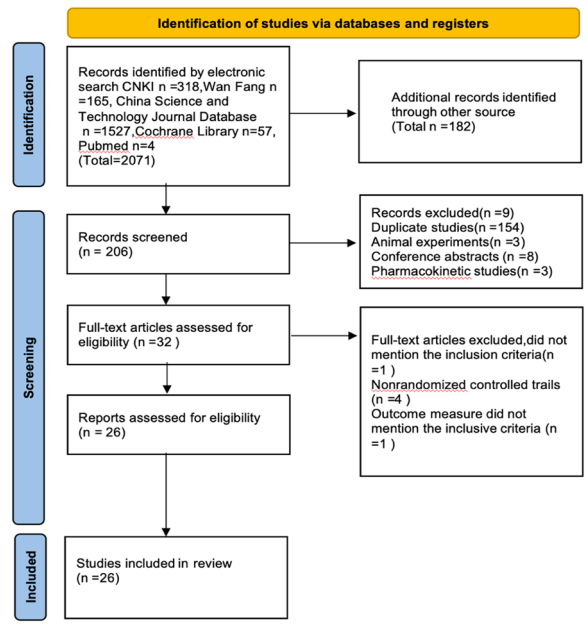

Fig. 1 PRISMA 2020 flow diagram

specified, and only two studies reported blinding of patients or participants. No information was provided regarding blinded outcome evaluations. All 26 follow-up datasets were complete, with no evidence of selection bias or other identified biases. Figures 2 and 3 present a summary of the risk of bias evaluation.

Result

Effectiveness

Astragalus injection group comprised 1179 cases across 22 studies, achieving an effectiveness rate of 92.79% (1094 cases). In contrast, the control group included 1108 cases with an effectiveness rate of 77.71% (861 cases). A meta-analysis was performed on the effective odds ratio (OR), indicating no significant heterogeneity ($I^2 = 0\%$, $P = 0.968$) and utilizing a fixed-effects model. The Astragalus injection group exhibited a significantly higher effective rate [OR = 3.82, 95% CI (2.93, 4.97)] compared to the control group, as illustrated in Fig. 3.

The efficacy rate of the electrocardiogram

Seven studies were included, comprising a total of 299 cases in the Astragalus injection group and 276 cases in the control group. A meta-analysis was conducted to determine the effective odds ratio (OR), revealing no significant heterogeneity ($I^2 = 0\%$, $P = 0.929$) when using a fixed-effects model. The electrocardiogram effective rate in the Astragalus injection group [OR = 2.51, 95% CI (1.66, 3.81)] was significantly higher than that in the control group (82.94% vs. 67.39%), with statistical significance achieved ($P < 0.05$) (Fig. 4).

Fig. 2 Assessment of study quality

ΔLDH, ΔAST, ΔCK and ΔcTnl

Significant heterogeneity was detected for the included studies ($P < 0.01$, $I^2 = 90.2\%$). As a result, random model was used in the analysis. The ΔLDH [WMD = − 41.93, 95%CI (− 55.97, − 27.90)] in the AI group showed a statistically significant difference compared to the control group, indicating a significant reduction ($P < 0.05$). This suggests that Astragalus injection effectively reduces LDH release, as depicted in A; the random model was employed due to significant heterogeneity ($P < 0.01$, $I^2 = 97.7\%$) among the eight included studies in ΔAST. The Astragalus injection group demonstrated a significantly lower ΔAST [WMD = − 14.23, 95%CI (− 24.17, − 4.30)] compared to the control group, with a statistically significant difference ($P < 0.05$). This indicates that Astragalus injection effectively reduces AST release, as depicted in B. The meta-analysis by ΔCK included 8 studies exhibiting significant heterogeneity ($P < 0.01$, $I^2 = 79.2\%$).

The Astragalus injection group demonstrated a significantly lower level of ΔCK [WMD = − 34.84, 95%CI (− 48.03, − 21.65)] compared to the control group, with statistical significance ($P < 0.05$), as depicted in D. The meta-analysis of 19 studies on ΔCK-MB, which exhibited significant heterogeneity ($P < 0.01$, $I^2 = 89.2\%$), necessitated the adoption of a random model. The Astragalus injection group demonstrated a significantly lower level of ΔCK-MB [WMD = − 7.64, 95%CI (− 9.30, − 5.99)] compared to the control group, with statistical significance ($P < 0.05$), as depicted in E. The changes of cTnl in the Astragalus injection group and the control group before and after intervention were statistically calculated, ΔcTnl included 10 studies with significant heterogeneity ($P < 0.01$, $I^2 = 97.1\%$), so the random model was adopted. Astragalus injection group ΔcTnl [WMD = − 0.18, 95%CI (− 0.27, − 0.10)] was significantly lower than that of control group, the difference was statistically significant ($P < 0.05$), Astragalus injection could reduce the level of serum cTnl (Fig. 5).

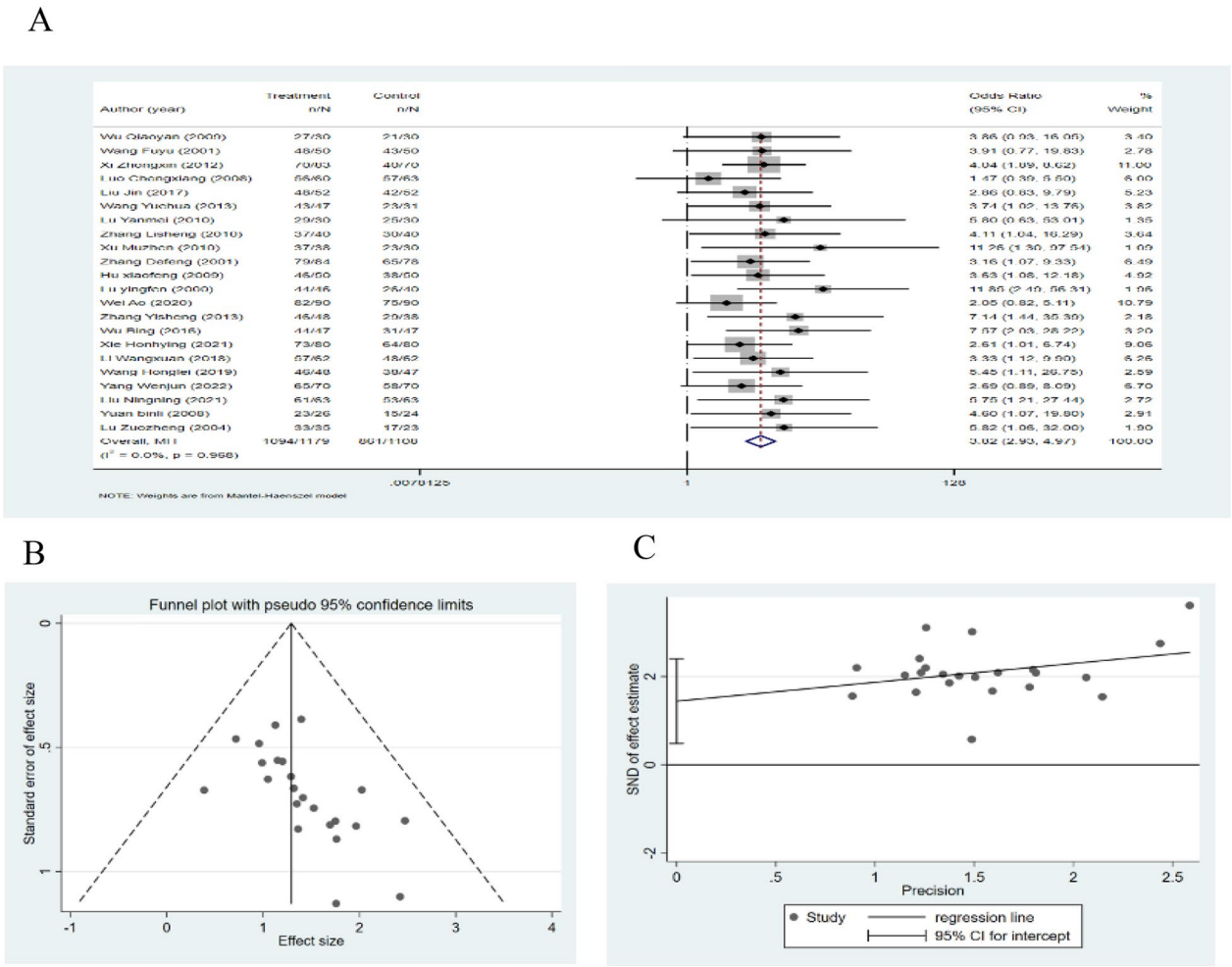

Fig. 3 **A** The forest plot of effectiveness; **B** the funnel plot for effectiveness; **C** the diagram of the Egger test

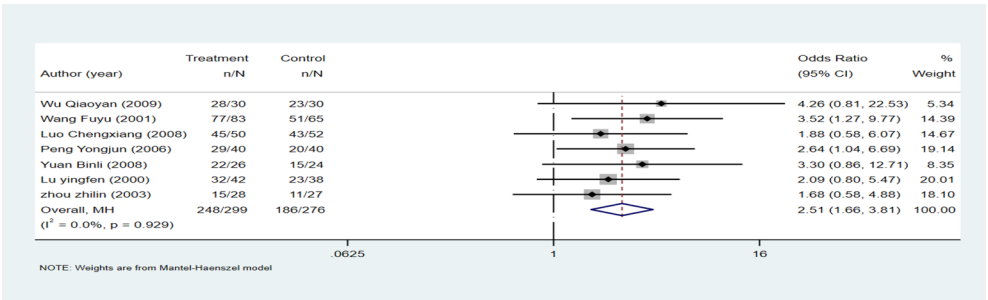

Fig. 4 The forest plot of ECG

Subgroup analysis

The effectiveness of different intervention courses

The effectiveness of various intervention courses was evaluated through subgroup analysis. Thirteen studies were included in the 2-week intervention course group, while ten studies were part of the group with interventions lasting more than 2 weeks. No significant heterogeneity (I^2 = 0%) was observed in either group, or a

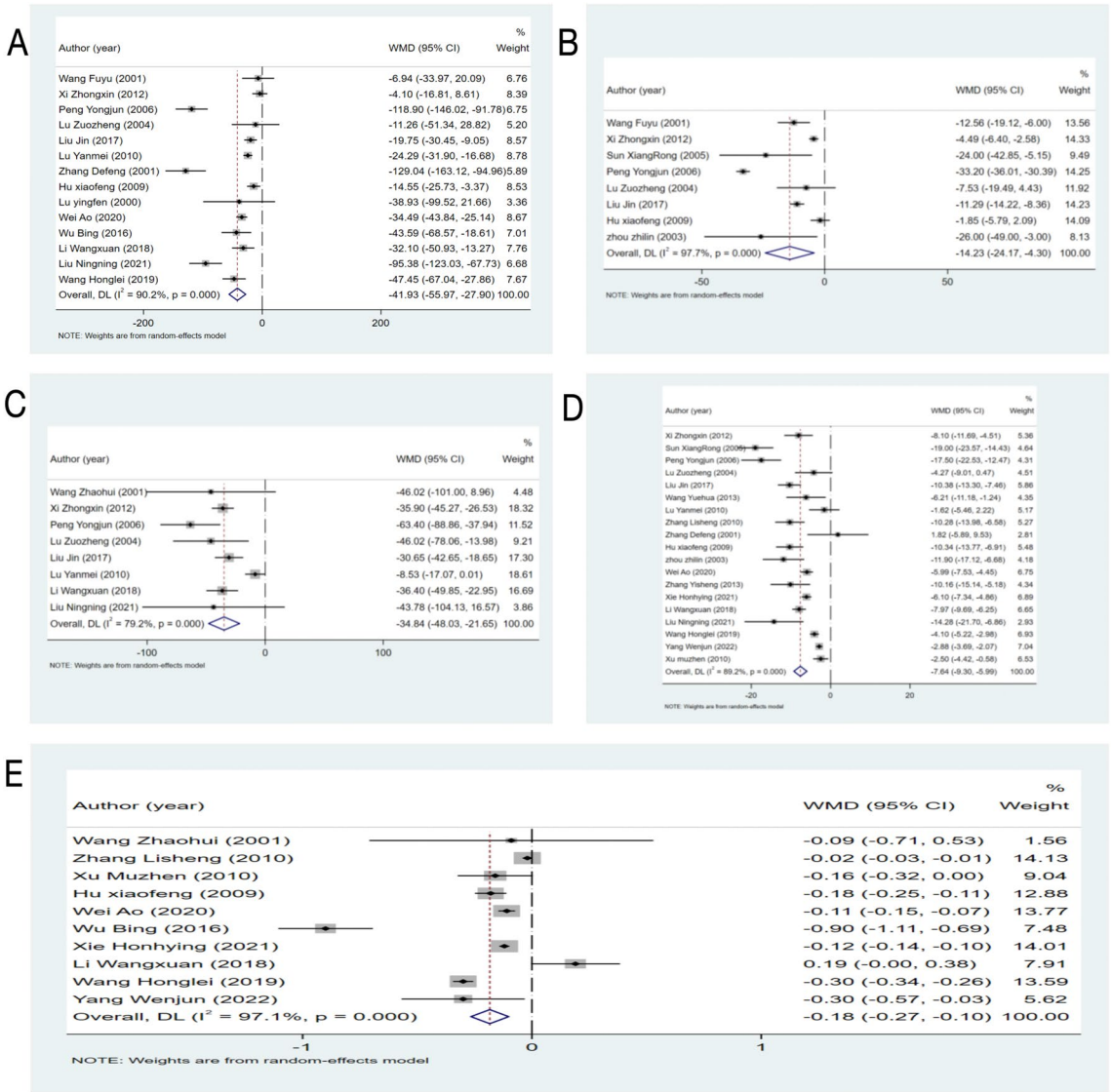

Fig. 5 The forest plot of ΔLDH, ΔAST, ΔCK, ΔCK-MB and ΔcTnI (**A**–**E**)

fixed-effects model was employed for the analysis. The Astragalus injection group demonstrated a higher effective rate at 2 weeks [OR = 3.52, 95% CI (2.52, 4.94)] compared to the control group. Furthermore, the Astragalus injection group exhibited a higher response rate at 2 weeks [OR = 4.34, 95% CI (2.84, 6.66)] than the control group, with a statistically significant difference between the two subgroups ($P < 0.05$) (Supplementary Fig. 1).

Effectiveness of electrocardiogram in different intervention courses

The subgroup analysis focused on the response rate of ECG during the intervention course, which included two studies conducted within two weeks and more than five studies conducted beyond 2 weeks. No significant heterogeneity ($I^2 = 0\%$) was observed in either group, and a fixed-effects model was employed. The ECG response rate within two weeks for the Astragalus injection group was higher compared to the control group, with an odds ratio (OR) of 2.17 and a 95% confidence interval (CI) of (1.08, 4.37) (64.71% vs. 46.27%). Furthermore, the Astragalus injection group demonstrated a higher ECG response rate beyond 2 weeks, with an OR of 2.71 and a 95% CI of (1.62, 4.56) (88.31% vs. 74.16%), indicating a statistically significant difference ($P < 0.05$) (Supplementary Fig. 2).

Alterations in myocardial enzyme profiles (ΔLDH, ΔAST, ΔCK, ΔCK-MB, and ΔcTnI) were analyzed for subgroup analysis based on different intervention durations (2 weeks and more than 2 weeks) (Supplementary Material, Figs. 3–6).

In the 2-week group, a total of 10 studies were included, with more than 4 studies incorporated within this timeframe. Heterogeneity analysis revealed no significant heterogeneity ($P=0.732$, $I^2=0\%$) in the 2-week group, while significant heterogeneity was observed in the > 2-week subgroup ($P<0.01$, $I^2=92\%$). Consequently, a random-effects model was adopted for the overall analysis. In the subgroup analysis of the 2-week duration [WMD = − 51.56, 95% CI (− 67.93, − 35.20)], it was found that the change in ΔLDH in the Astragalus injection group was significantly lower compared to the control group, with these differences being statistically significant ($P<0.05$). However, there was no statistically significant difference in ΔLDH at 2 weeks ($P>0.05$). Four studies included in the analysis of ΔAST over a period of 2 weeks demonstrated significant heterogeneity in both the 2-week group ($P=0.062$, $I^2=67.7\%$) and the > 2-week subgroup ($P<0.01$, $I^2=98.5\%$). Therefore, a random-effects model was employed for the overall analysis. In the 2-week subgroup [WMD = − 17.37, 95% CI (− 33.75, − 0.98)], as well as in the > 2-week subgroup [WMD = − 9.40, 95% CI (− 16.10, − 2.71)], there was a statistically significant decrease in ΔAST compared to the control group ($P<0.05$).

Four studies were included in the analysis of ΔCK over a 2-week period. No heterogeneity was observed in the 2-week subgroup ($P=0.794$, $I^2=0\%$), while significant heterogeneity was found in the same subgroup ($P<0.01$, $I^2=84.9\%$). Consequently, a random-effects model was adopted for the overall analysis. In the 2-week subgroup, WMD was -33.10 with a 95% CI of (− 51.51, − 14.69). Both subgroups exhibited significantly lower changes in ΔCK levels in the Astragalus injection group compared to the control group, and these differences were statistically significant ($P<0.05$). Fourteen studies were included in the analysis of ΔCK-MB over a 2-week period, with more than five studies in each subgroup. Both subgroups showed significant heterogeneity ($P<0.01$, $I^2=81.5\%$ for the > 2-week group and $P<0.01$, $I^2=88.8\%$ for the ≤ 2-week group). Therefore, a random-effects model was used for the overall analysis. In the > 2-week subgroup, the WMD was − 6.70 with a 95% CI of (− 8.40, − 5.00), and in the ≤ 2-week subgroup, the WMD was − 10.34 with a 95% CI of (− 14.77, − 5.92). Changes in ΔCK-MB were significantly lower in the Astragalus injection group compared to the control group ($P<0.05$).

Subgroup analyses were conducted for troponin ΔcTnl based on intervention durations of 2 weeks and greater than 2 weeks. Eight studies were included in the 2-week subgroup, while 2 studies were included in the subgroup for durations exceeding 2 weeks. There was no heterogeneity in the group with interventions lasting more than 2 weeks ($P=0.794$, $I^2=0\%$), whereas significant heterogeneity was observed in the 2-week group ($P<0.01$, $I^2=97.1\%$). Consequently, a random-effects model was applied to the overall analysis. In the 2-week subgroup, the weighted mean difference (WMD) was − 0.21 (95% CI − 0.31, − 0.12), and in the > 2 weeks subgroup, the WMD was − 0.02 (95% CI − 0.03, − 0.01). The change in ΔcTnl in the Astragalus injection group was significantly lower than that in the control group, with a statistically significant difference ($P<0.05$).

The analysis of bias

The indices (effective rate, ΔLDH, ΔCK-MB, ΔcTnI) that included ten or more items in the study underwent bias analysis. Stata 15 was used to generate funnel plots and conduct Egger tests for projects with more than ten included studies. The findings indicate no significant publication bias in the quantitative results for efficiency, ΔLDH, and ΔcTnI ($P>0.05$). However, there is evidence of publication bias in the quantitative results for ΔCK-MB ($P<0.05$). Please refer to Fig. 6, Tables 3, and Supplementary Fig. 7.

Discussion

Our updated systematic meta-analysis indicated that Astragalus injection could improve outcomes for patients affected by VMC. Specifically, Astragalus injection significantly reduced levels of inflammatory factors: CK, CK-MB, and LDH in the Astragalus injection group compared to conventional treatment alone Table 3.

Although the internationally recognized Dallas criteria exist for diagnosing myocarditis, they have limitations [38]. The presence of elevated myocardial markers is a critical criterion for diagnosing VMC. Furthermore, the commonly used myocardial enzyme indices in clinical practice include CK, CK-MB, LDH, and AST, with CK and CK-MB holding the greatest clinical significance [39]. In recent years, cTnI has also emerged as a highly sensitive and specific biomarker for diagnosing myocardial injury, making it increasingly valuable in the diagnosis of acute viral myocarditis [40]. CK plays a vital role in energy regulation as a myocardial enzyme and is found in the renal distal convoluted tubules, as well as in muscles and the brain. CK is a dimer composed of two subunits, M and B. CK-MB is a low molecular weight protein found in cardiac and skeletal muscle cells, and it is the first non-enzymatic protein used for the diagnosis of myocardial injury [41]. It is generally detectable in the bloodstream 1 to 2 h after myocardial damage [42].

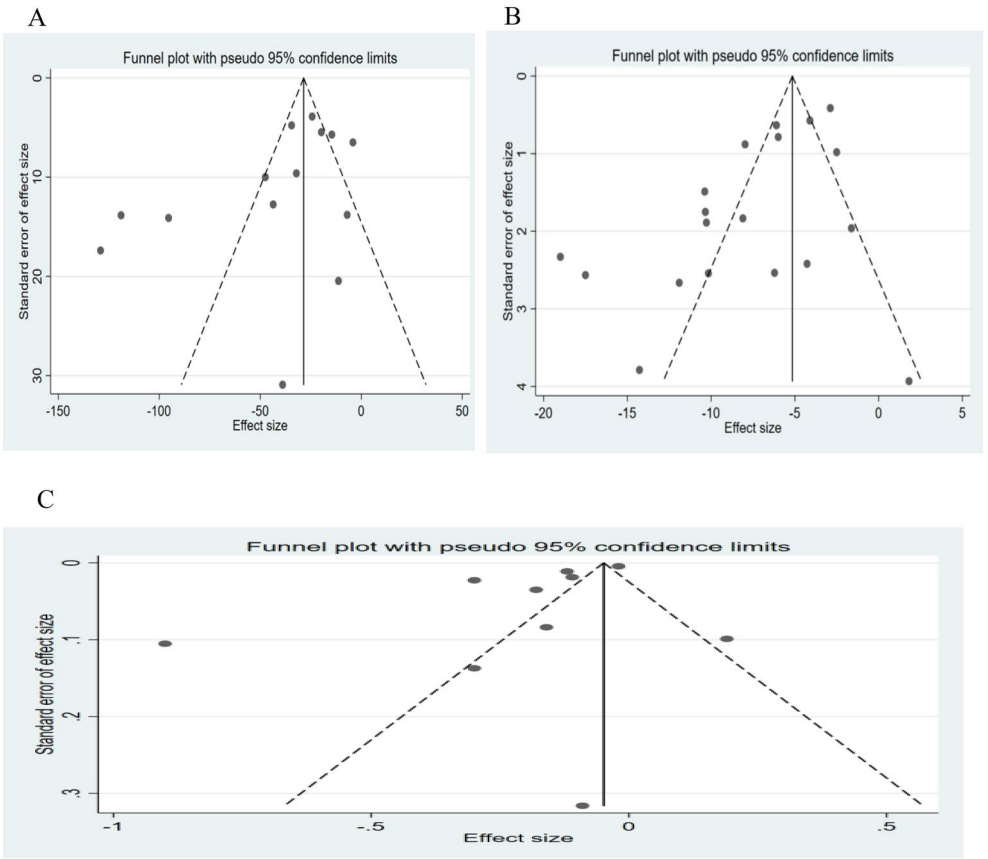

Fig. 6 The funnel plot of ΔLDH, ΔCK-MB and ΔcTnI (**A**–**C**)

Table 2 Grading of recommendations, assessment, development, and evaluation

Outcomes	N	Design	Certainty assessment					Patients		Effect WMD/OR(95%CI)	Quality
			Risk of bias	Inconsistency	Indirectness	Imprecision	Others	T	C		
CK	9	RCT	No serious	No serious	Serious	Serious	No serious	481	440	−34.83 (−48.03,−21.65)	Moderate
AST	9	RCT	No serious	No serious	Serious	No serious	No serious	407	380	−14.23 (−24.17,−4.30)	Moderate
CK-MB	20	RCT	No serious	No serious	Serious	No serious	No serious	1058	1022	−7.64 (−9.30,−5.99)	Moderate
LDH	14	RCT	No serious	No serious	Serious	No serious	No serious	850	812	−41.93 (−55.97,−27.90)	Moderate
cTnI	12	RCT	No serious	No serious	No serious	No serious	No serious	679	644	−0.18 (−0.27,−0.10)	High
ECG	9	RCT	No serious	No serious	No serious	No serious	No serious	457	438	2.51 (1.66, 3.81)	High

T: treatment group; C: control group; N: number

Lactate dehydrogenase (LDH) is a nonspecific myocardial enzyme found in the liver, skeletal muscle, erythrocytes, and other cells within the mitochondria. It serves as a marker in viral myocarditis (VMC), which can be effectively reduced by Astragalus injection interventions. Most of the cardiac troponin I (cTnI) binds to the myocardial contractile proteins in myocardial fibers, while a small portion remains free in the cytoplasm of cardiomyocytes. When the myocardium is damaged, cTnI can leak into the bloodstream through compromised myocardial cells, resulting in elevated levels of cTnI in the blood [43]. Additionally, cTnI plays a role in regulating myocardial contraction by influencing calcium metabolism, inhibiting kinin, and altering ATPase activity in muscle

Table 3 Egger test result

	Study	Coef	std	*P* > ltl	95% conf. interval	
Effectiveness	23	1.441	0.462	0.051	0.481	2.401
ΔLDH	14	−3.139	1.545	0.065	−6.506	0.226
ΔCK-MB	19	−3.108	0.949	0.004	−5.112	−1.105
ΔcTnI	10	−4.251	1.939	0.06	−8.723	0.221

fibers. Once myocardial damage subsides, cTnI levels will decrease. However, patients with VMC who exhibit a poor response to treatment may experience prolonged and more severe viral infections, leading to exacerbated chronic inflammation in cardiomyocytes and sustained elevated levels of cTnI [44]. Pharmaceutical studies have demonstrated that Astragalus injection can enhance the permeability of the blood–brain barrier and increase local blood flow.

Lactochrome is an extract derived from Astragalus membranaceus. It serves as an antioxidant and cardioprotective agent. The primary components of lactochrome, including astragaloside and isoflavonoids, are involved in various metabolic processes that effectively enhance myocardial contractility, reduce the replication of myotropic viruses, and protect heart function. Additionally, these compounds promote vascular dilation and help lower blood pressure. The combination of lactochrome with conventional therapies may yield synergistic effects through these mechanisms.

Astragalus membranaceus is a well-known traditional Chinese medicine celebrated for its immunomodulatory properties. The primary constituents of Astragalus include flavonoids, saponins, polysaccharides, amino acids, and trace elements. As a natural immune regulator, it is widely used in the treatment of various conditions, including nephritis, cancer-related immune responses, and other immune disorders. Furthermore, it demonstrates cardioprotective effects in cardiovascular diseases. In recent years, both clinical and fundamental studies have reported the beneficial therapeutic effects of Astragalus membranaceus against viral infections [45]. However, the clinical evidence remains fragmented, and the underlying mechanisms are still unclear, which limits the clinical application of Astragalus membranaceus.

The traditional Chinese medicine injection is an innovative formulation that integrates traditional Chinese medicine with modern science and technology, demonstrating high bioavailability and remarkable efficacy. It has been extensively used in the treatment of viral myocarditis [46]. A previous study examined the effects of Astragalus injection on inflammatory mediators in patients with viral myocarditis; however, this study only included Astragalus injection and highlighted its potential therapeutic role through immunomodulatory effects. Furthermore, subgroup analyses were not conducted to explore additional factors [47].

In our study, we found that the combination group exhibited significantly greater reductions in viral myocarditis-related indicators and enhanced clinical efficacy compared to the control group. Furthermore, no serious adverse events were observed in this meta-analysis. These findings suggest that the administration of Astragalus injection in conjunction with antihypertensive drugs has a cardioprotective effect on patients with viral myocarditis, making it a viable option for widespread use in clinical treatment. The significant heterogeneity observed in the included studies may pose a challenge in interpreting the results, despite the use of a random-effect model to account for this study. Thus the need for further research to strengthen the conclusions drawn in this article, including larger sample sizes and more diverse populations.

Currently, the concentration and compatibility of Astragalus injection require further optimization. Future research could focus on developing new formulation types, such as sustained-release formulations and nanodrugs, to enhance the drug's bioavailability and efficacy. Astragalus injection has demonstrated significant efficacy in treating viral myocarditis and also holds potential value in various cardiovascular diseases, including coronary heart disease and chronic heart failure. Future studies could broaden the application of Astragalus injection to other cardiovascular conditions and evaluate its overall therapeutic effects. Long-term efficacy and safety are critical indicators for assessing the clinical application of drugs. Therefore, future research should include long-term follow-up to evaluate the efficacy and safety of Astragalus injection in extended treatments, providing more comprehensive clinical data. By thoroughly exploring these research avenues, a more robust scientific foundation can be established for the clinical use of Astragalus injection in viral myocarditis and other cardiovascular diseases.

Limitations

There were several limitations in this study. First, there is controversy regarding the timing of CK-MB and CK index detection, making it difficult to reach a definitive conclusion about this indicator in our review. Second, the sample sizes of the included studies tended to be small. Third, in the original studies, the medications used in the conventional therapy group included only oxygen free radical scavengers, and it is unclear whether other drugs, such as immunosuppressants and interferons, were also utilized. Additionally, it is uncertain if, in the experimental group, other traditional Chinese medicines were used alongside Astragalus injection. Fourth, all included trials were conducted in China, which may introduce potential location bias. Finally, the quality of the included studies is relatively low; they were primarily short-term follow-up studies with small sample sizes, and they rarely employed allocation concealment or blinding methods. The types of interventions and the duration of the interventions in the included studies were also inconsistent. Therefore, caution should be exercised when interpreting the results. Despite these limitations, this investigation represents the first and most recent systematic assessment of Astragalus injection's efficacy in treating viral myocarditis, which could be beneficial for clinicians. The significant heterogeneity observed in the included studies may pose a challenge in interpreting the results, despite the use of a random-effects model to account for this variability. Therefore, there is a need for further research to strengthen the conclusions drawn in this article, including larger sample sizes, more diverse populations and more high-quality studies are needed to enhance the credibility of these findings.

Conclusion

Astragalus injection may have a therapeutic role in patients with viral myocarditis by reducing levels of AST, CK, CK-MB, LDH, and cTnI when compared to antiviral medications alone, thereby increasing the effectiveness rate for viral myocarditis. Well-designed and executed multicenter clinical trials are still needed to draw definitive conclusions regarding the effects of Astragalus injection treatment for viral myocarditis.

Abbreviations

CK	Creatine kinase
AST	Aspartate aminotransferase
CK-MB	Creatine kinase isoenzyme
LDH	Lactate dehydrogenase
cTnI	Cardiac troponin I
ECG	Electrocardiogram
VMC	Viral myocarditis

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s40001-024-02193-9.

Supplementary material 1.

Acknowledgements

Not applicable.

Author contributions

Conceptualization: Dinala jialiken, Shiwu Wen. Data curation: Yi xuan Dong, Shuai Ren. Formal analysis: Yadong Fan, Lichao Qian. Project administration: Yi xuan Dong. Supervision: Chong Zou and Lichao Qian. Writing—original draft: Dinala jialiken, Shiwu Wen. Writing—review and editing: Dinala jialiken, Chong Zou.

Funding

Design and Statistics of Clinical Trials in Traditional Chinese Medicine [A YXC2022-01–01 10]. Exploring the Mechanism of Qianyang Yuyin Granules in Improving Hypertensive Kidney Injury Based on the "Balance" Theory of the PPARγ/HGF and TGF-β1/Smads Signaling Pathways. [Y2022ZR09].] This study was supported by Clinical Design and Statistics of Chinese medicine (Grant No. A YXC2022-01-01 10), Innovative Development Foundation of Department in Jiangsu Hospital of Chinese Medicine (Grant No. Y2022ZR09), Natural Science Foundation of Nanjing University of Chinese Medicine (Grant No. XZR2021050), and Project of National Clinical Research Base of Traditional Chinese Medicine in Jiangsu Province, China (Grant No. JD2023SZ16).

Availability of data and materials

The data sets from this study are available from the first author upon request. No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

Author details

[1]Affiliated Hospital of Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China. [2]Nanjing Hospital of Chinese Medicine Affiliated to Nanjing University of Chinese Medicine, Nanjing, Jiangsu, China. [3]OMNI Research Group, Department of Obstetrics and Gynecology, University of Ottawa, Ottawa, Canada.

Received: 12 September 2024 Accepted: 2 December 2024
Published online: 03 January 2025

References

1. Schultz JC, Hilliard AA, Cooper LT, Rihal CS. Diagnosis and treatment of viral myocarditis. MayoClin Proc. 2009;84:1001–9. https://doi.org/10.1016/S0025-6196(11)60670-8.
2. Zheng Q, Zhuang Z, Wang ZH, Deng LH, Jin WJ, Huang ZJ, Zheng GQ, Wang Y. Clinical and preclinical systematic review of astragalus membranaceus for viral myocarditis. Oxid Med Cell Longev. 2020;2020:1560353. https://doi.org/10.1155/2020/1560353.
3. Mohamud Y, Li B, Bahreyni A, Luo H. Mitochondria dysfunction at the heart of viral myocarditis: mechanistic insights and therapeutic implications. Viruses. 2023;15:351. https://doi.org/10.3390/v15020351.

4. Kyaw T, Drummond G, Bobik A, Peter K. Myocarditis: causes, mechanisms, and evolving therapies. Expert Opin Ther Targets. 2023;27:225–38. https://doi.org/10.1080/14728222.2023.2193330.
5. Xu J, Zhou Z, Zheng Y, Yang S, Huang K, Li H. Roles of inflammasomes in viral myocarditis. Front Cell Infect Microbiol. 2023;13:1149911. https://doi.org/10.3389/fcimb.2023.1149911.
6. Menghini VV, Savcenko V, Olson LJ, Tazelaar HD, WilliamDec G, Kao A, Cooper LT. Combined immunosuppression for the treatment of idiopathic giant cell myocarditis. Mayo Clin Proc. 1999;74:1221–6. https://doi.org/10.4065/74.12.1221.
7. Olejniczak M, Schwartz M, Webber E, Shaffer A, Perry TE. Viral myocarditis—incidence, diagnosis and management. J Cardiothorac Vasc Anesth. 2020;34:1591–601. https://doi.org/10.1053/j.jvca.2019.12.052.
8. Clerkin KJ, Fried JA, Raikhelkar J, et al. COVID-19 and cardiovascular disease. Circulation. 2020;141(20):1648–55. https://doi.org/10.1161/120.046941. (**Epub 2020 Mar 21**).
9. Zhang Y, Li Y, Wang X, et al. Herbal plants coordinate COVID-19 in multiple dimensions-an insight analysis for clinically applied remedies. Int J Med Sci. 2020;17(18):3125–45. https://doi.org/10.7150/ijms.50260.
10. Zhang Y, Zhu H, Huang C, Cui X, Gao Y, Huang Y, Gong W, Zhao Y, Guo S. Astragaloside IV exerts antiviral effects against coxsackievirus B3 by upregulating interferon-gamma. J Cardiovasc Pharmacol. 2006;47(2):190–5.
11. Gui J, Chen R, Xu W, Xiong S. Remission of CVB3-induced myocarditis with Astragaloside IV treatment requires A20 (TNFAIP3) up-regulation. J Cell Mol Med. 2015;19(4):850–64.
12. Yang WJ, Luo QL, Zhang Q. Effects of Huangqi Injection on Th17 and Treg Cell Subsets in Peripheral Blood of Patients with Viral Myocarditis. West J Tradit Chin Med. 2022;35:91–4. https://doi.org/10.12174/j.issn.2096-9600.2022.09.17.
13. Wang ZH, Liao YH. Combined treatment of viral myocarditis with traditional Chinese medicine and Western medicine. J Clin Cardiol. 2001;17:353–5. https://doi.org/10.3969/j.issn.1001-1439.2001.08.006. (**In Chinese**).
14. Wu QY, Wu X. Observation of curative effect on treatment of viral myocarditis in children with combination of traditional chinese medicine and western medicine. Asia-Pac Tradit Med. 2009;5:33–4 (**In Chinese**).
15. Wang FY, Huo LY. Observation on the efficacy of integrated traditional Chinese and Western medicine in the treatment of 50 cases of viral myocarditis. Forum Tradit Chin Med. 2001;16:35–6. https://doi.org/10.3969/j.issn.1002-1078.2001.06.039. (**In Chinese**).
16. Xi ZX, Qiao SR. Analysis of the efficacy of Changcheng Astragalus Oral Liquid in the treatment of chronic viral myocarditis. Mod J Integr Tradit Chin West Med. 2012;21:629–30. https://doi.org/10.3969/j.issn.1008-8849.2012.06.033. (**In Chinese**).
17. Sun XR, Bie SX, Zhao YL. 35 cases of acute viral myocarditis treated with Meloxin combined with Astragalus injection. Chin J Emerg Med. 2005;14:78–9. https://doi.org/10.3760/j.issn:1671-0282.2005.01.022. (**In Chinese**).
18. Luo CY. Observation on the efficacy of Astragalus injection in the treatment of 60 cases of viral myocarditis in children. J Community Med. 2008;6:54–6. https://doi.org/10.3969/j.issn.1672-4208.2008.05.035. (**In Chinese**).
19. Peng YJ. Effect of radix astragali injection on children with viral myocarditis. J Pediatr Pharm. 2006;12:30–1. https://doi.org/10.3969/j.issn.1672-108X.2006.02.016. (**In Chinese**).
20. Lu ZZ, Wei Y. Observation on the efficacy of Astragalus injection in the treatment of viral myocarditis. J Tianjin Med Univ. 2004;10:576–7. https://doi.org/10.3969/j.issn.1006-8147.2004.04.032. (**In Chinese**).
21. Liu J, Yan H, Mu YP. The efficacy of Astragalus injection in the treatment of acute severe viral myocarditis in children and its effect on serum myocardial enzyme spectrum and related inflammatory factors. Mod J Integr Tradit Chin West Med. 2017;26:3623–5. https://doi.org/10.3969/j.issn.1008-8849.2017.32.032. (**In Chinese**).
22. Wang YH. Clinical observation on the treatment of viral myocarditis in children with Astragalus injection. Hubei J Tradit Chin Med. 2013;35:41–2 (**In Chinese**).
23. Li YB. Observation on the efficacy of Astragalus injection in the treatment of viral myocarditis in children, Shanxi. Med J. 2008;37:1078–9 (**In Chinese**).
24. Lu YM, Cao S. Observation on the efficacy of Astragalus injection in the treatment of viral myocarditis in children. Mod J Integr Tradit Chin West Med. 2010;19:181–2. https://doi.org/10.3969/j.issn.1008-8849.2010.02.027.[InChinese].
25. Zhang LS. Observation on the efficacy of Astragalus injection in the treatment of 40 cases of viral myocarditis in children. Chin J Integr Med CardioCerebrovascular Dis. 2010;8:749–50. https://doi.org/10.3969/j.issn.1672-1349.2010.06.062. (**In Chinese**).
26. Xu MZ, Huang XY, Zheng HX. Clinical Analysis of Astragalus Injection Treat the Pediatric Viral Myocarditis in 38 Cases. Sci Technol Eng. 2010;10:6986–8. https://doi.org/10.3969/j.issn.1671-1815.2010.28.031. (**In Chinese**).
27. Zhang DF. Astragalus injection for the treatment of viral myocarditis in children. Henan Med Inf. 2001;107:9–10 (**In Chinese**).
28. Hu XF. Huangqi the treatment of viral myocarditis caused by the clinical research of arrhythmia Master's Thesis. Hubei Univer Chinese Med. 2009;12:659707 (**In Chinese**).
29. Lu YF, Li HJ, Liu CB. Astragalus membranaceus injection clinical observation for the treatment of viral myocarditis. Clin Focus. 2000;15:549–50. https://doi.org/10.3969/j.issn.1004-583X.2000.12.016. (**In Chinese**).
30. Zhou ZL, Lin P, Lin D, Yu P, Jin MD. Clinical observation on 32 cases of viral myocarditis treated with Astragalus injection. Chin J Tradit Med Sci Technol. 2003;10:376–7. https://doi.org/10.3969/j.issn.1005-7072.2003.06.029. (**In Chinese**).
31. Wei Q, Li LX, Ding XH, Tan DM, Guo Q, Gu Y, Gou X. Zheng, Effect of Astragalus injection combined with trimetazidine on NLRP3 inflammasome and related downstream pathways in peripheral blood of elderly patients with viral myocarditis. Mod J Integr Tradit Chin West Med. 2020;29:815–8. https://doi.org/10.3969/j.issn.1008-8849.2020.08.005. (**In Chinese**).
32. Zhang YS. Observation on the efficacy of Astragalus injection combined with conventional Western medicine in the treatment of acute viral myocarditis. Mod J Integr Tradit Chin West Med. 2013;22:733–4. https://doi.org/10.3969/j.issn.1008-8849.2013.07.024. (**In Chinese**).
33. Wu B. Study on the effect of Astragalus injection on myocardial enzyme spectrum and cellular immunity in patients with viral myocarditis. Mod J Integr Tradit Chin West Med. 2016;25:2580–2. https://doi.org/10.3969/j.issn.1008-8849.2016.23.025. (**In Chinese**).
34. Xie HY, Luo XL, Lu H. Influence of huangqi injection on the expressions of NLRP3 inflammasome in peripheral blood of patients with viral myocarditis. West J Tradit Chin Med. 2021;34:94–7. https://doi.org/10.12174/j.issn.2096-9600.2021.07.24. (**In Chinese**).
35. Li WX. Clinical observation of Astragalus injection in the adjuvant treatment of viral myocarditis. J Pract Tradit Chin Med. 2018;34:1358–9. https://doi.org/10.3969/j.issn.1004-2814.2018.11.066. (**In Chinese**).
36. Liu NN. Observation on the pharmacological effects and efficacy of Astragalus injection in the treatment of viral myocarditis. Chin J Mod Drug Appl. 2021;15:168–70. https://doi.org/10.14164/j.cnki.cn11-5581/r.2021.13.062. (**In Chinese**).
37. Wang HL, Wang RJ, Meng NA. Clinical observation on the treatment of viral myocarditis in children with integrated traditional Chinese and Western medicine. J Pract Tradit Chin Med. 2019;35:68–9. https://doi.org/10.3969/j.issn.1004-2814.2019.01.056. (**In Chinese**).
38. Baughman KL. Diagnosis of myocarditis: death of dallas criteria. Circulation. 2006;113:593–5. https://doi.org/10.1161/CIRCULATIONAHA.105.589663.
39. Lee CH, Tsai WC, Hsu CH, Liu PY, Lin LJ, Chen JH. Predictive factors of a fulminant course in acute myocarditis. Int J Cardiol. 2006;109:142–5. https://doi.org/10.1016/j.ijcard.2005.04.014.
40. Kanda T, Koike H, Arai M, Wilson JE, Carthy CM, Yang D, McManus BM, Nagai R, Kobayashi I. Increased severity of viral myocarditis in mice lacking lymphocyte maturation. Int J Cardiol. 1999;68:13–22. https://doi.org/10.1016/S0167-5273(98)00250-2.
41. Lai YS, Zhao YJ, Liu JC, Wang LX, Li SE. Clinical value study of combined detection of CK-MB, hs-CRP and cTnI in children with viral myocarditis. Prog Mod Biomed. 2018;18:3937–40. https://doi.org/10.13241/j.cnki.pmb.2018.20.031. (**In Chinese**).
42. Nielsen TS, Hansen J, Nielsen LP, Baandrup UT, Banner J. The presence of enterovirus, adenovirus, and parvovirus B19 in myocardial tissue samples from autopsies: an evaluation of their frequencies in deceased individuals with myocarditis and in non-inflamed control hearts. Forensic Sci Med Pathol. 2014;10:344–50. https://doi.org/10.1007/s12024-014-9570-7.

43. Liu G, Chen X, Xu S, et al. The predictive value of anti-cardiac troponin I on the prognosis of viral myocarditis. Chinese J Nosoc Infect. 2017;7:1507–9 (**In Chinese**).
44. Luo Y, Ye J, Hui S, et al. The Value of dynamic electrocardiogram and myocardial injury markers in diagnosing acute viral myocarditis. Chinese J Coal Indust Med. 2018;21(3):293–7.
45. Chen XJ, Bian ZP, Lu S, Xu JD, Gu CR, Yang D, Zhang JN. Cardiac protective effect of astragalus on viral myocarditis mice: comparison with perindopril. Am J Chin Med. 2006;34:493–502. https://doi.org/10.1142/S0192415X06004028.
46. Li JP, Liu Y, Guo JM, Shang EX, Zhu ZH, Zhu KY, Tang YP, Zhao BC, Tang ZS, Duan JA. A comprehensive strategy to evaluate compatible stability of chinese medicine injection and infusion solutions based on chemical analysis and bioactivity assay. Front Pharmacol. 2017;8:833. https://doi.org/10.3389/fphar.2017.00833.
47. Guo J, Zhao N, Jin P, Yin Y. Effect of Astragalus injection on inflammatory mediators in patients with viral myocarditis: a systematic review and meta-analysis. Phytomedicine. 2022;107: 154436. https://doi.org/10.1016/j.phymed.2022.154436.

Publisher's Note