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Quantitative cardiac MRI parameters for assessment of myocarditis in children and adolescents: a systematic review and meta-analysis

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AIM: To evaluate the role of quantitative cardiac magnetic resonance imaging (CMRI) parameters in myocarditis, including acute and chronic myocarditis (AM and CM), for children and adolescents.

MATERIALS AND METHODS: PRISMA principles were followed. PubMed, EMBASE, Web of Science, Cochrane Library, and grey literature were searched. The Newcastle-Ottawa Scale (NOS) and the Agency for Healthcare Research and Quality (AHRQ) checklist were utilised for quality assessment. Quantitative CMRI parameters were extracted and a meta-analysis was performed in comparison with healthy controls. The overall effect size was measured as the weighted mean difference (WMD).

RESULTS: Ten quantitative CMRI parameters of seven studies were analysed. Compared with the control group, the myocarditis group reported longer native T1 relaxation time (WMD=54.00, 95% confidence interval [CI]: 33.21,74.79, $p<0.001$), longer T2 relaxation time (WMD=2.13, 95% CI: 0.98, 3.28, $p<0.001$), increased extracellular volume (ECV; WMD=3.13, 95% CI: 1.34,4.91, $p=0.001$), elevated early gadolinium enhancement (EGE) ratio (WMD=1.47, 95% CI: 0.65,2.28, $p<0.001$), and increased T2-weighted ratio (WMD=0.43, 95% CI: 0.21,0.64, $p<0.001$). The AM group had longer native T1 relaxation times (WMD=72.02, 95% CI: 32.78,111.27, $p<0.001$), increased T2-weighted ratios (WMD=0.52, 95% CI: 0.21,0.84 $p=0.001$), and impaired left ventricular ejection fractions (LVEF; WMD=−5.84, 95% CI: -9.69, -1.99, $p=0.003$). Impaired LVEF (WMD=−2.24, 95% CI: -3.32, -1.17, $p<0.001$) was observed in the CM group.

CONCLUSION: Statistical differences can be observed in some CMRI parameters between patients with myocarditis and healthy controls; however, apart from native T1 mapping, there were no large differences in other parameters between two groups, which may reveal the limited benefit of CMRI in assessing myocarditis in children and adolescents.

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Introduction

Myocarditis occurs when inflammation develops in the myocardium.[1–7] Myocarditis presents with a host of non-specific symptoms and can be more complex[3,9] and atypical[8] in children and adolescents. Myocarditis can cause some severe outcomes, the potential threats to health should not be ignored.[10,11]

Appropriate diagnosis of myocarditis remains challenging, especially in children and adolescents. Endomyocardial biopsy (EMB) was considered as the reference standard[12,13]; however, the sensitivity was not satisfactory[14] and potential complications hamper its application.[9,15] Laboratory findings, electrocardiogram and echocardiogram have neither high sensitivity nor specificity.[3,8,9,11] cardiac magnetic resonance imaging (CMRI) has been proven to be a useful tool.[16] CMRI can not only evaluate myocarditis based on conventional sequences, but also provide new quantitative features using new techniques.[17,18] Some studies[19–22] have shown valuable diagnostic performance of these quantitative CMRI features for the assessment of myocarditis.

Several systematic reviews have evaluated the value of conventional CMRI[23–25] and quantitative CMRI features[22,24] for myocarditis in adults; however, the findings that focus on adults may not apply to children and adolescents.[3,9,26] Some original studies have investigated CMRI performance of myocarditis in children and adolescents, but as yet, no consensus has been reached. Therefore, an overall evaluation is required. The aim of this study was to evaluate CMRI quantitative measures in paediatric and adolescent patients with myocarditis (including AM and CM), compared to healthy controls.

Materials and methods

Study search

The study was performed in accordance with the guidelines of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.[27] The review protocol was registered with a Centre of Reviews and Dissemination (CRD) in the International Prospective Register of Systematic Reviews (PROSPERO). The search scope included MEDLINE, EMBASE, Cochrane Library, Web of Science, and grey literature using both free-text terms and Medical Subject Headings (MeSH) terms to select studies written in English, the search deadline was 26 July 2022. Detailed search strategies are presented in Electronic Supplementary Material S1. This study used existing literature with no new data from human, so there was no need for ethical review by the ethics committee.

Inclusion and exclusion criteria

Studies met the inclusion criteria if (a) they included children and adolescent patients[28] (<21 years) clinically diagnosed with AM or CM compared with healthy controls, (b) patients and controls all underwent CMRI assessments, and (c) results were able to be analysed statistically. Exclusion criteria were as follows: (a) the full text was not available after comprehensive and intensive search; (b) inappropriate study design, such as reviews, case reports, meta-analyses; (c) animal model studies and other non-clinical studies; (d) insufficient data for analysis; (e) studies using comparator groups other than healthy controls were also excluded.

Study selection and data extraction

After duplicates were removed, two investigators (W.B. and H.J.Z.) independently filtered retrieved studies by reading titles and abstracts. Selected articles were screened by reading the full text. Data collection and extraction were performed independently by two investigators (Y.Y. and Z.F.W.). Another investigator (X.Y.J.) double-checked the extracted data. Any disagreements were resolved by discussion until a consensus was reached.

Quality assessment

Two investigators (Y.Y. and Z.F.W.) independently assessed the quality of eligible studies and any discrepancies were resolved by the senior investigator (X.Y.J.). The Newcastle Ottawa Scale (NOS) was used to evaluate the quality of cohort and case–control studies.[29] The Agency for Healthcare Research and Quality (AHRQ) checklist was utilised for cross-sectional study assessment.[30]

Statistical analysis

Quantitative parameters were expressed as means and standard deviation (SD), weighted mean difference (WMD) were used for the description of outcomes. I^2 test and Q test were conducted to evaluate heterogeneity across included studies. Sensitivity analyses were assessed. STATA version 15.1 was the tool for analyses. A p-value of <0.05 was considered the threshold for statistical significance.

Results

Literature search and selection

The initial search produced 14,331 articles from databases and 191 articles of grey literature. After duplicates were removed, 10,135 studies were screened by reading titles and abstracts, and 10,068 studies were excluded according to predefined inclusion and exclusion criteria. Sixty-eight studies were left for screening of the full text. A total of 61 studies were excluded. Finally, seven studies were included. The PRISMA flow diagram[31] can be seen in Fig 1.

Baseline characteristics of included studies

The baseline characteristics of included studies[32–38] are shown in Table 1. The studies showed a broad geographical distribution, with two studies conducted in China, two in

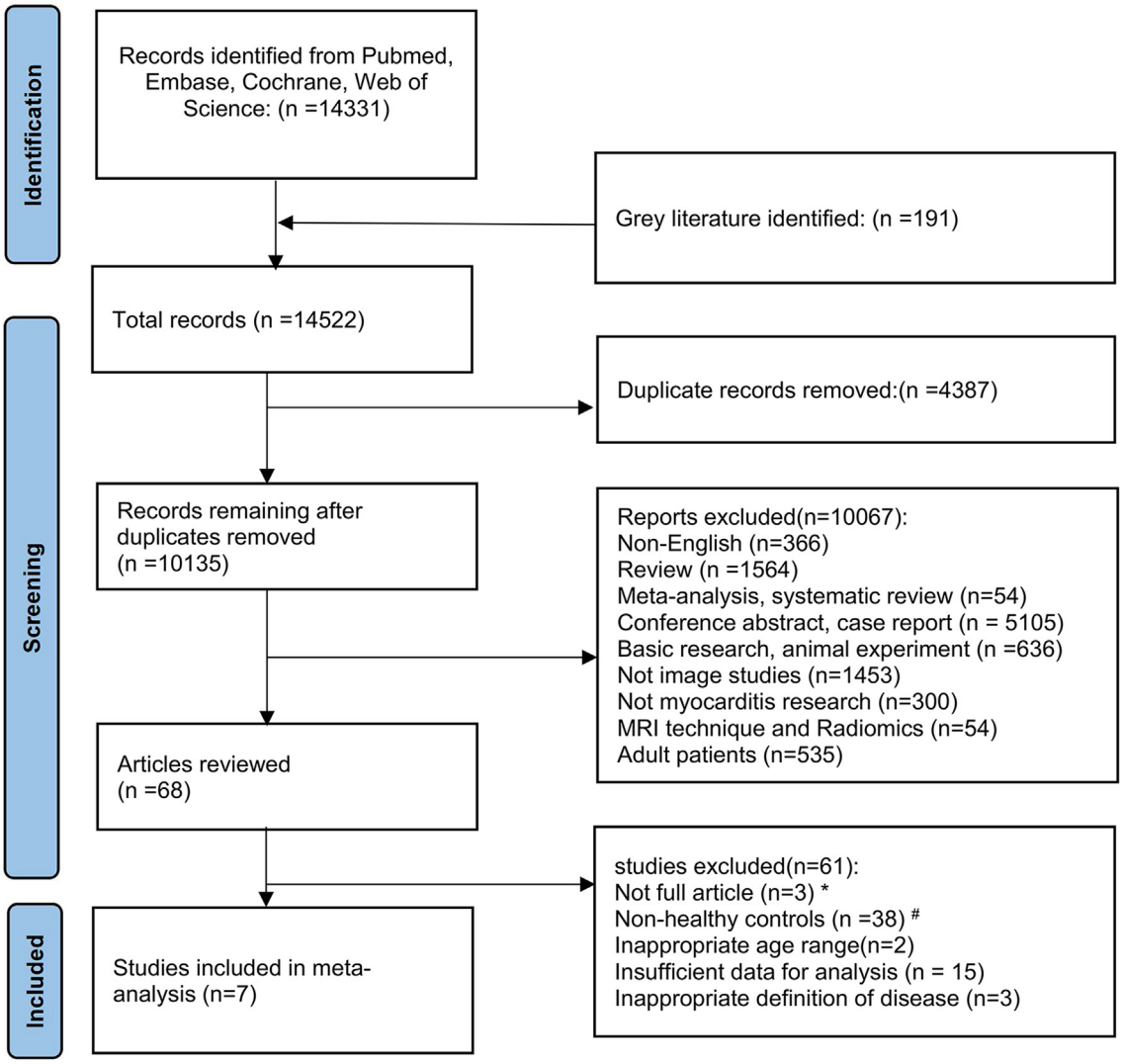

Figure 1 PRISMA flow diagram. *"Not full article" indicates full text was unavailable despite all efforts made, including requesting assistance through medical libraries and from the authors. #In the "Non-healthy controls" group, 25 studies had no control group. 13 studies had control groups with various types of diseases, such as arrhythmogenic right ventricular cardiomyopathy, hypertrophic cardiomyopathy, restrictive cardiomyopathy, etc.

Table 1
Baseline data of included studies.

Author &year	Country	Study design	Myocarditis group characters			Control group characters		Quantitative parameters extracted of each study	
			(*n*)	Age (year)	Sex (male, *n* , n%)	(*n*)	Age (years)	Sex (male, *n* , n%)	
Jia *et al.*, 2020	China	Cohort study	AM[25] CM[48]	AM(9.3 ± 3.4) CM(9.2 ± 3.2)	AM 14 (56%) CM 35 (72.8%)	17	7.5 ± 2.8	10 (58.8%)	④⑤⑥⑦
Cornicelli *et al.*, 2019	USA	Case–control study	AM[23]	16.3(14.7–17.7)	14(61%)	39	15.1 (11.3–17.2)	27(69.2%)	①②③④⑥⑧
Isaak *et al.*, 2021	Germany	Case–control study	AM[43]	17 ± 3	33 (77%)	16	17 ± 4	8 (50%)	①②③④⑥⑧
Wang *et al.*, 2020	China	Cohort study	AM[20] CM[11]	AM 9[2,14] CM 6[3,13]	AM 10 (50%) CM 9 (81.8%)	15	11[6,13]	9 (60%)	①②③⑥⑧⑨
Mavrogeni *et al.*, 2012	Greece	Cohort study	AM[20]	8–16	Unspecified	20	8–16	Unspecified	④⑤⑥⑦
Wisotzkey *et al.*, 2018	USA	Case–control study	AM[10]	15.5[14–17]	9 (90%)	10	15.5[12–18]	7 (70%)	⑥⑩
Seidel *et al.*, 2021	Germany	Cross-sectional study	AM[9]	10[4–16]	4 (44%)	7	15[10–19]	5(71%)	①②⑥⑧⑨

Quantitative parameters extracted of each study: ① native T1 relaxation time (ms), ② T2 relaxation time (ms), ③ extracellular volume fraction (ECV) (%), ④ T2-weighted ratio (%), ⑤ early gadolinium enhancement ratio (EGE ratio; %), ⑥ left ventricular ejection fraction (LVEF; %), ⑦ left ventricular end-diastolic volume (LVEDV; ml), ⑧ LVEDV index (LVEDVI; ml/m^2), ⑨ Left ventricular end-systolic volume index (LVESVI; ml/m^2), ⑩ radial strain (%).
AM, acute myocarditis; CM, chronic myocarditis.

the USA, and three in Europe. Among pooled studies, there were 124 healthy controls in total aged 4.7–21 years and 209 patients in total aged 2–20 years. Of 209 patients, 150 had AM (aged 2–20 years) and 59 had CM (aged 3–13 years).

Quality assessment results

The results of the quality assessment are shown in Electronic Supplementary Material S2 and S3. One study was identified to be of moderate quality and six studies were of high quality.

Results of meta-analysis

Ten CMRI quantitative parameters were extracted. The values for each parameter are shown in Electronic Supplementary Material S6. These parameters were independently analysed. Compared to controls, subgroup analyses of AM and CM groups were carried out separately. Meta-analyses were also performed between patients with AM and CM if there were sufficient related data. The summary of meta-analysis can be seen in Electronic Supplementary Material S5.

Native T1 relaxation time

Four studies[33–35,38] involving 89 patients (78 cases of AM and 11 cases of CM) and 77 controls investigated native T1 mapping. Longer native T1 relaxation time was observed in the myocarditis group. Using a random-effects model (I^2=90.30%), WMD for the overall effect size was 54 (95% CI: 33.21,74.79; $p<0.01$) between the myocarditis group and the control group. Statistical analysis between the AM group and the control group was conducted using a random-effects model (I^2=91.5%) and WMD was 72.02 (95% CI: 32.78, 111.27; $p<0.01$). Among the included studies, only one study[35] investigated the T1 relaxation time in patients with CM and controls, and no significant difference (p=0.50) was observed (Fig 2).

Extracellular volume fraction (ECV)

Three studies[33–35] reported ECV, involving 80 patients (69 cases of AM and 11 cases of CM) and 70 controls. Elevated ECV can be seen in patients. A random-effects model (I^2=93.8%) was used, and WMD was 3.13 (95% CI: 1.34, 4.91; $p<0.01$). A random-effects model was used (I^2=91.4%) to calculate WMD, which was 3.33 (95% CI: -0.12 , 6.78; p=0.06) between patients with AM and healthy controls. One included study[35] reported significantly increased ECV in the CM group compared with control group (p=0.004; Fig 3)

Early gadolinium enhancement ratio (EGE ratio)

Two studies[32,36] involving 93 patients (45 cases with AM and 48 cases with CM) and 37 controls, evaluated the EGE ratio. A random-effects model was used (I^2=95.2%) to calculate the WMD for the overall effect size, which was 1.47 (95% CI: 0.65, 2.28; $p<0.01$) between patients and controls, as a higher EGE ratio was observed in the myocarditis group. A random-effects model was used (I^2=97.4%) to calculate WMD, which was 2.75 (95% CI: -1.37, 6.88; p=0.19) between AM group and control group. Regarding EGE ratio in patients with CM, only one study by Jia *et al.*[32] reported a significantly elevated EGE ratio in patients with CM compared with healthy controls ($p<0.001$; Fig 4)

T2 relaxation time

Three studies[33–35] were used to conduct a meta-analysis for T2 relaxation time, involving 80 patients (69 cases with AM and 11 cases with CM) and 70 controls. A random-effects model was used (I^2=96.1%) to calculate the WMD for the overall effect size, which was 2.13 (95% CI: 0.98, 3.28; $p<0.01$), with significant prolonged T2 relaxation time in the patient group, while no significant difference was observed between the AM group and control group (WMD=4.35, 95% CI: -0.73, 9.43, p=0.09), according to the random-effects analysis (I^2=97.1%). Wang *et al.*[35] compared T2 relaxation time between CM and controls, but no significant difference emerged (p=0.65; Fig 5)

T2-weighted ratio

A total of 136 patients (88 cases with AM and 48 cases with CM) and 53 controls were included in three studies[32,34,36] that investigated the T2-weighted ratio. A random-effects model was used (I^2=90.3%) to calculate that WMD was 0.43 (95% CI: 0.21, 0.64). A higher T2-weighted ratio was reported in patients ($p<0.01$). T2-weighted ratio between AM group and the control group also showed a significant difference ($p<0.01$; WMD=0.52; 95% CI: 0.21, 0.84) according to the random-effects analysis (I^2=89.80%). Jia *et al.*[32] reported a significant difference (p=0.005) in this respect between the CM group and the control group (Fig 6).

Left ventricular ejection fraction (LVEF)

Seven studies[32–38] provided data for analysis of LVEF, involving a total of 209 patients (150 cases of AM and 59 cases of CM) and 124 controls. Heterogeneity differed between the AM (I^2=87.80%) and CM (I^2=0.01%) subgroups, so the WMD for the overall effect size was calculated separately. WMD for LVEF was −5.84 (95% CI: −9.68, −1.99; p=0.003) between the AM group and the control group. Two studies[32,35] offered data on the CM group, and WMD was −2.24 (95% CI: -3.32, -1.17; $p<0.001$) between the CM group and control group. Based on these two studies, WMD between the AM and CM subgroups was calculated to be −3.30 (95% CI: −12.91, 6.30) with p=0.50 according to the random-effects analysis model (I^2=97.1%; Figs 7–9).

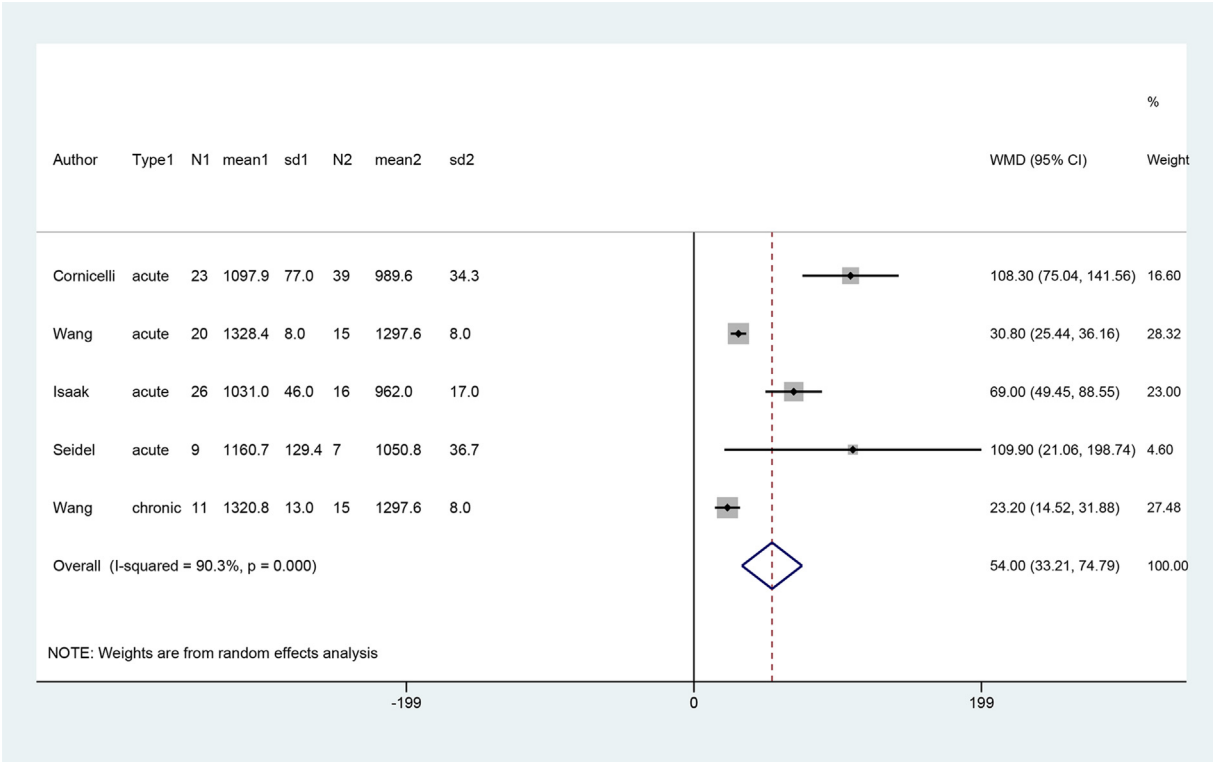

Figure 2 Pooled WMD for native T1 relaxation time from random-effects meta-analysis.

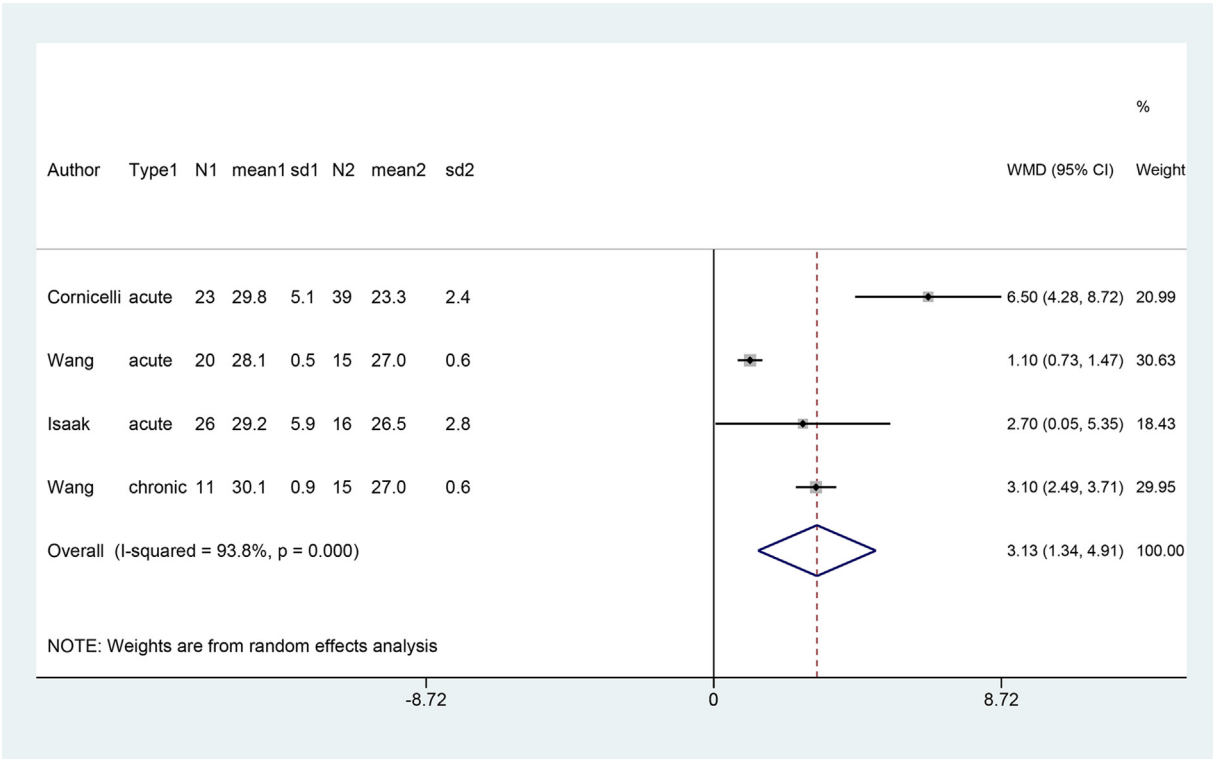

Figure 3 Pooled WMD for ECV from random-effects meta-analysis.

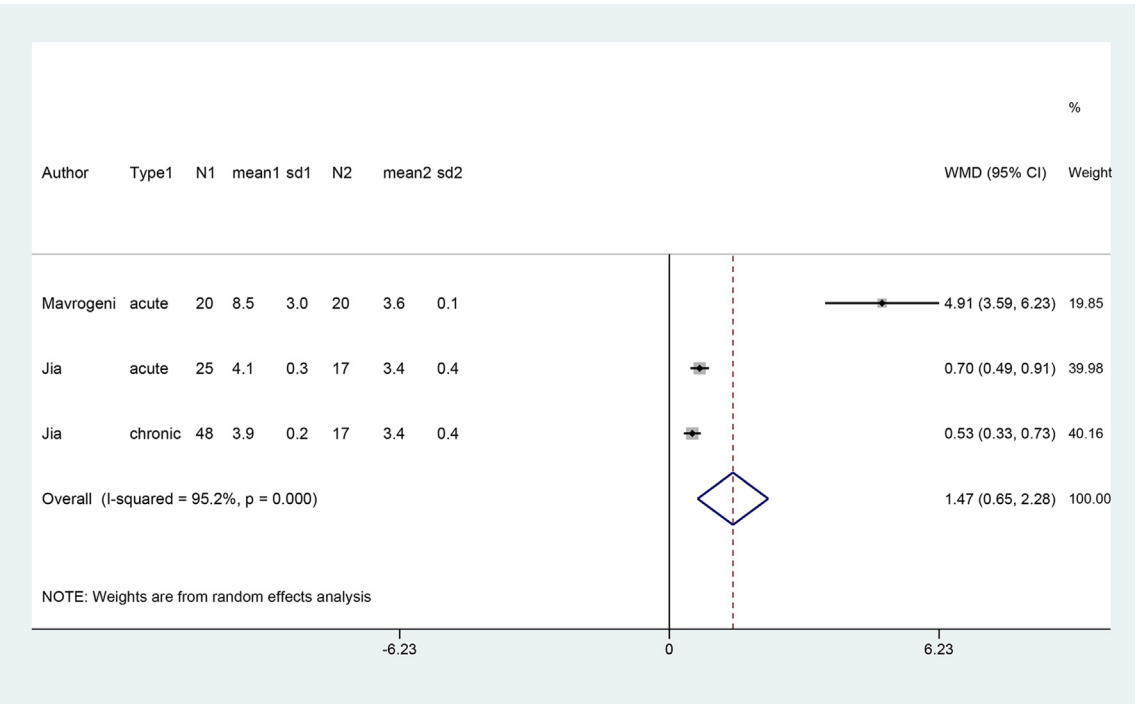

Figure 4 Pooled WMD for EGE ratio from random-effects meta-analysis.

Left ventricular end-diastolic volume (LVEDV) and LVEDV index (LVEDVI)

Two studies[32,36] reported LVEDV, involving 93 patients (45 cases of AM and 48 cases of CM) and 37 controls. WMD for the overall effect size was 4.14 (95% CI: −11.46, 19.74; p=0.60), according to the random-effects analysis (I^2=90%). No significant difference was found regarding LVEDV between the AM group and controls, (WMD=7.22; 95% CI: −12.92, 27.35; p=0.48) according to the random-effects

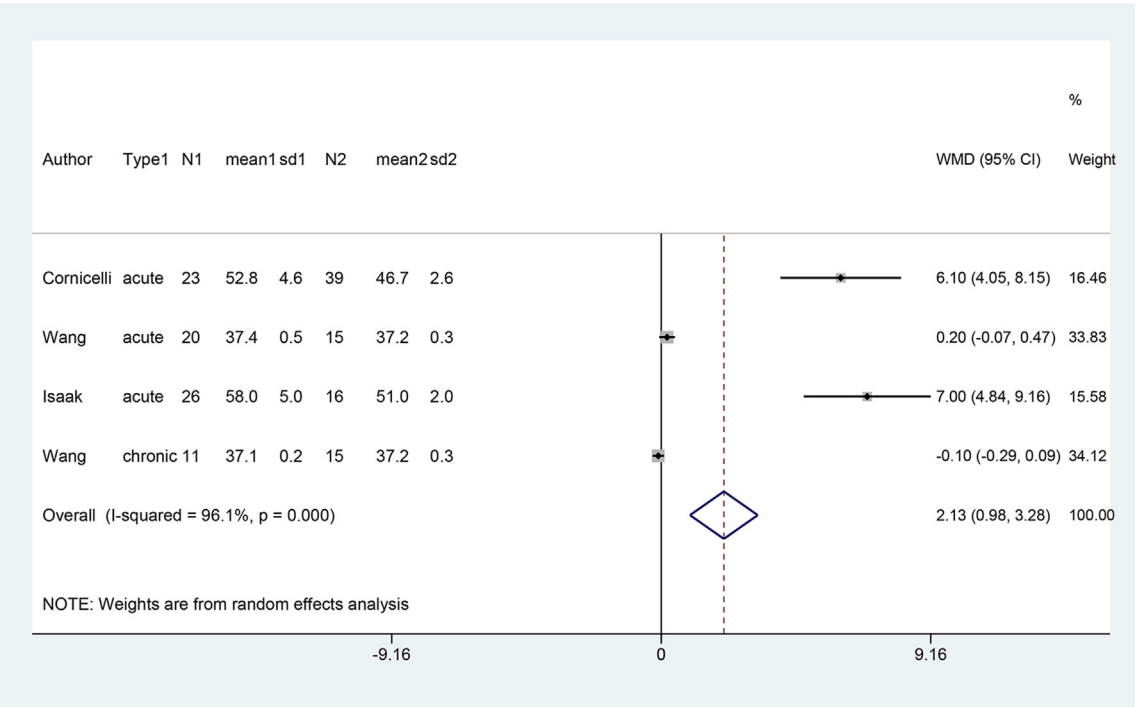

Figure 5 Pooled WMD for T2 relaxation time from random-effects meta-analysis.

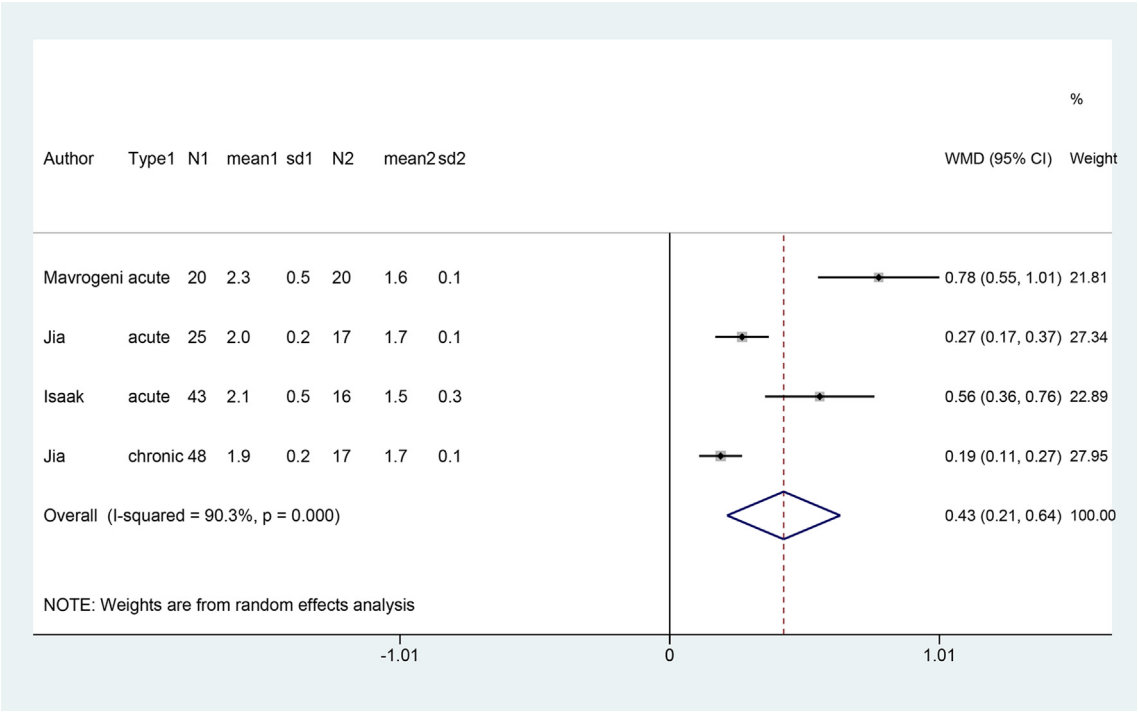

Figure 6 Pooled WMD for T2-weighted ratio from random-effects meta-analysis.

analysis (I^2=91.1%). The study by Jia *et al.*[32] reported no significant difference (p=0.74) in LVEDV between patients with CM and controls.

LVEDVI is defined as the LVESV indexed to the area of body surface. Four studies[33–35,38] reported LVEDVI involving 106 patients (95 cases of AM and 11 cases of CM) and 77 controls. WMD for overall effect size regarding LVEDVI was 0.46 (95% CI: −2.95, 3.86) with p=0.79 and significant heterogeneity was observed (I^2=51.7%). WMD was −1.581(95% CI: −3.99, 0.84; p=0.20) between the AM

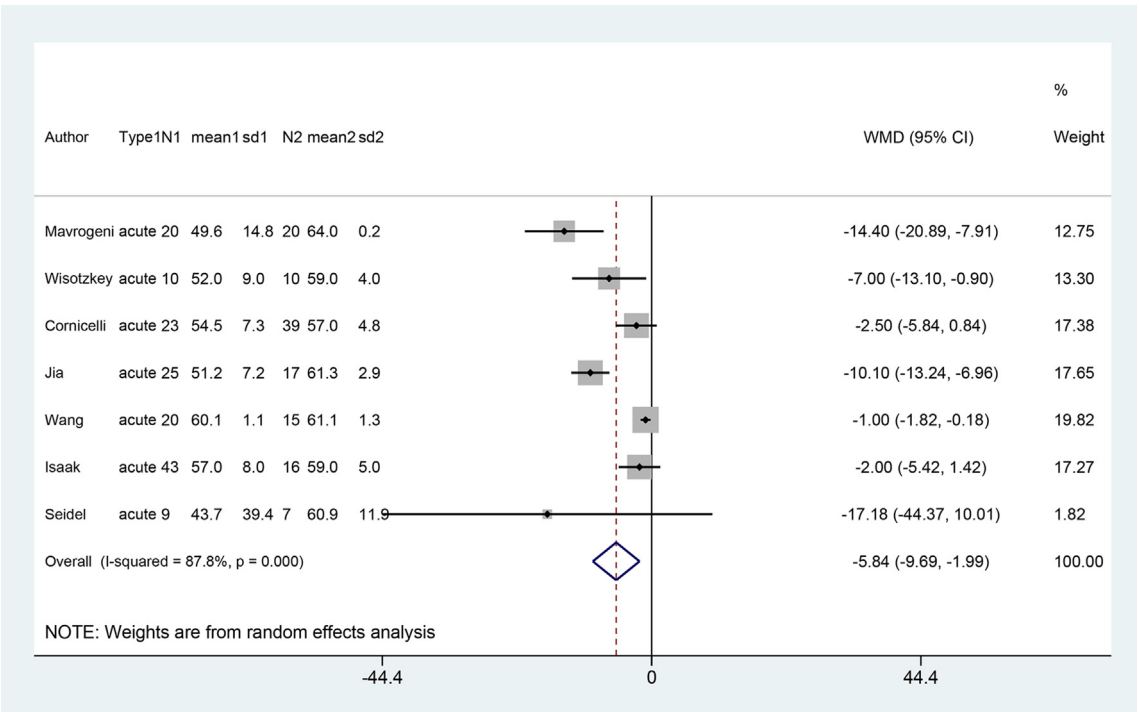

Figure 7 Pooled WMD for LVEF from random-effects meta-analysis between the AM and control group.

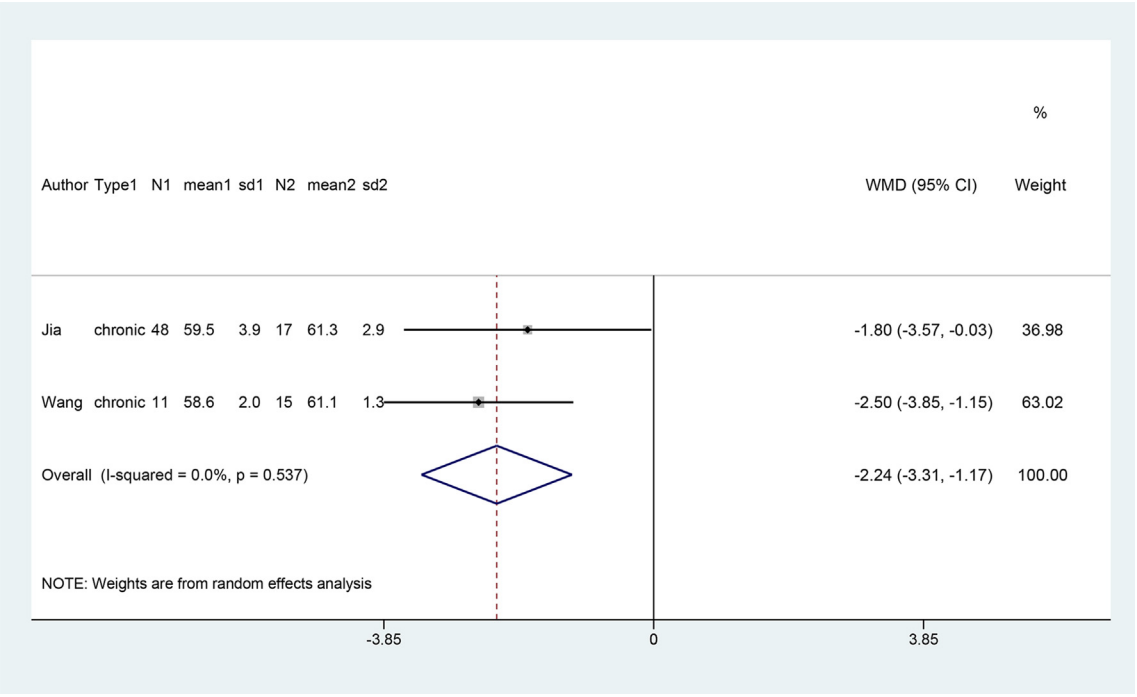

Figure 8 Pooled WMD for LVEF from random-effects meta-analysis between the CM and control group.

group and control group and no significant heterogeneity was found (I^2=44.6%). The study of wang *et al.*[35] demonstrated no significant difference in LVEDVI between patients with CM and controls (p=0.73; Fig 10; Electronic Supplementary Material Figs. S1 and S2)

Left ventricular end-systolic volume index (LVESVI)

Two studies[35,38] contributed to the statistical analysis of LVESVI, involving a total of 40 patients (29 cases of AM and 11 cases of CM) and 22 controls. WMD for overall effect size

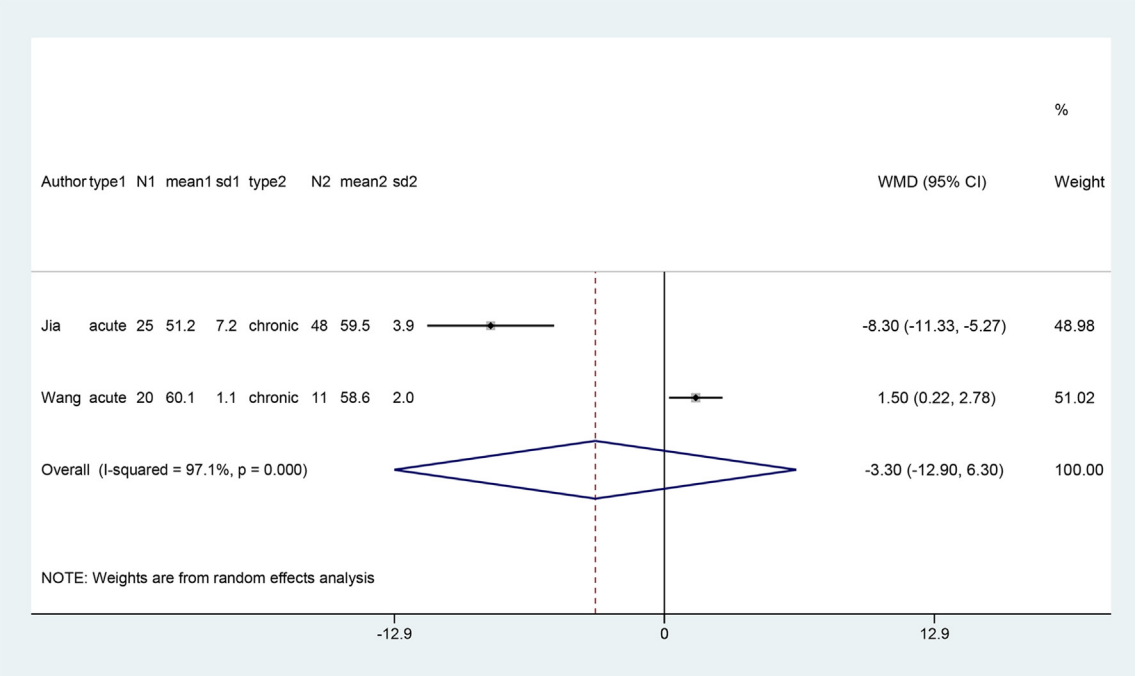

Figure 9 Pooled WMD for LVEF ratio from random effects meta-analysis between AM and CM patients.

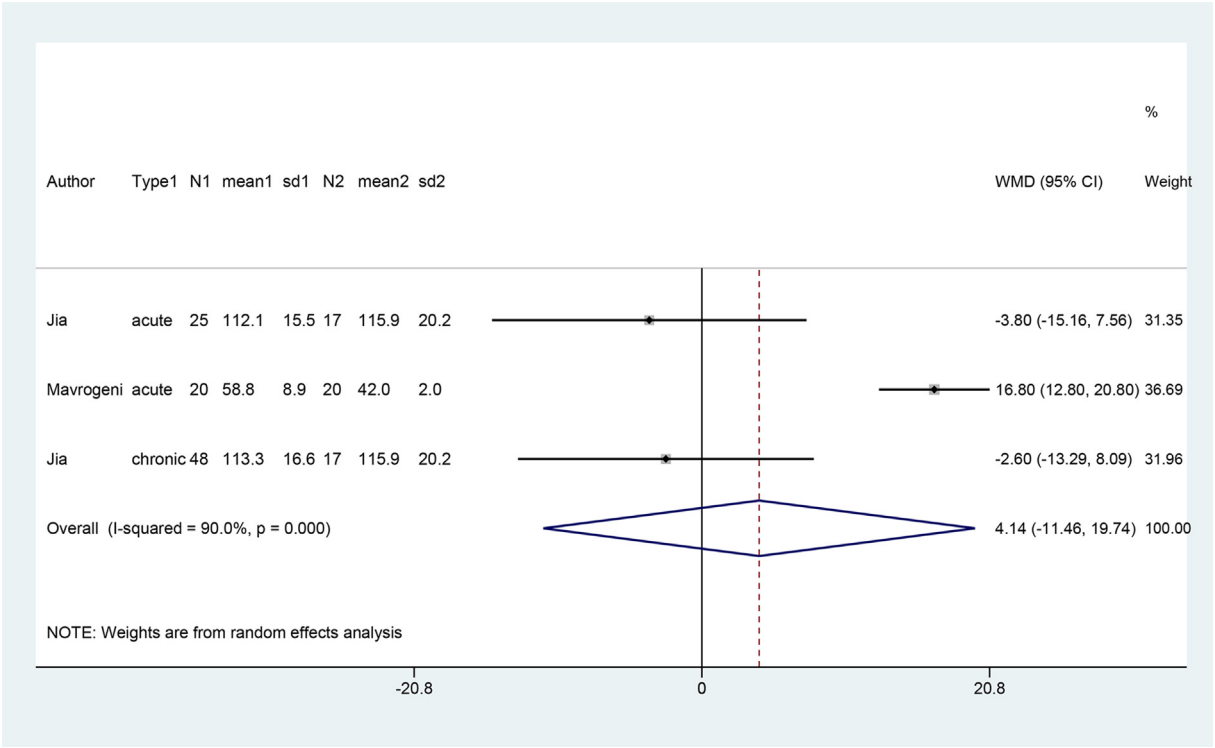

Figure 10 Pooled WMD for LVEDV from random-effects meta-analysis.

in was 0.99 (95% CI: −1.40, 3.39)[29] with p=0.42 between the myocarditis group and the control group and significant heterogeneity was observed (I^2=67.3%). No significant difference was observed between the AM group and the control group (WMD=-0.18; 95% CI: -1.64, 1.279; p=0.81) and no significant heterogeneity was seen (I^2=40.1%). No significant difference regarding LVESVI was seen between patients with CM and healthy controls (p=0.75), as reported by wang *et al.*[35] (Electronic Supplementary Material Figs. S3 and S4)

LV strain features

Two studies[37,38] offered data on LV radial strain, involving 19 patients with AM and 17 controls. No patients with CM were included. No significant difference was observed between patients with AM and healthy controls (WMD=−8.21; 95% CI: −20.76, 4.34; p=0.2) and significant heterogeneity was found (I^2=65.7%; Electronic Supplementary Material Figs. S5).

Features such as longitudinal strain and circumferential strain were reported in only one study, so a corresponding meta-analysis was not performed.

Assessment of sensitivity and publication bias

Sensitivity analysis showed no individual study significantly altered the results, as shown in Electronic Supplementary Material S4. There were only seven studies included and publication bias analysis was not performed.

Discussion

CMRI mapping parameters were included in the 2018 Lake Louise Criteria (LLC), which had good diagnostic performance in adult patients with myocarditis[22,39–45] as well as original studies on children and adolescents.[33–35,38]

Native T1 relaxation time was prolonged in myocarditis due to myocardial hyperaemia, oedema, and fibrosis.[39,46] In this study, native T1 relaxation time can discriminate paediatric patients with myocarditis from healthy controls. This parameter is also applicable to distinguish AM from healthy controls. This result is similar to the findings of previous meta-analyses targeted at adults.[22] The cut-off value of native T1 relaxation in adult patients was approximately 990 ms,[47] but no consensus has been reached in paediatric and adolescent patients. There were not enough data for CM group assessment. Only one study[35] demonstrated no significant difference regarding the native T1 relaxation time between CM group and healthy control, which may be explained by the inclusion of patients who were without positive results from conventional LLC. Although native T1 relaxation time was reported to discriminate acute and recovery stages of myocarditis in adults,[48] the use of this parameter to distinguish AM from CM was not evaluated in this study due to insufficient data for analysis.

The ECV value measures the quantitative change of the extracellular matrix. High ECV value in myocarditis is due to changes in the extracellular space of myocardium primarily caused by excessive collagen deposition.[34,49,50] In this meta-analysis, elevated ECV was reported in the myocarditis group, suggesting that ECV can distinguish patients

with myocarditis from healthy controls, which is consistent with previous studies on adults.[51–53] No significant difference was found regarding ECV between patients with AM and controls, possibly because extracellular space of myocardium may have slight changes in the early stage,[34] which is consistent with some studies.[21,24] Wang *et al.*[35] evaluated ECV in CM group and found that ECV may have benefit for chronic diffuse injury of myocarditis assessment, which may due to pathological basis of tissue fibrosis in CM. Therefore, ECV may be a good candidate to assess CM.

Prolonged T2 relaxation time is primarily underpinned by myocardial oedema in myocarditis.[54,55] In this meta-analysis, T2 relaxation time showed ability of discriminate myocarditis among children and adolescents; however, no significant difference emerged between patients with AM and healthy controls, differing from the results of many studies on adults.[19,40,55] Two[33,34] of the three included studies found significantly prolonged T2 relaxation time in patients with AM, but Wang *et al.*[35] revealed no significant difference, which affected the pooled results. As for the comparison of T2 relaxation time between patients with CM and healthy controls, Wang *et al.*[35] found no significant difference between these two groups. This may be attributed to insignificant myocardial oedema in patients with CM.

Conventional LLC (2009) included T2-weighted imaging (WI), EGE, and LGE, respectively representing myocardial oedema, hyperaemia, and fibrosis.[16] LGE was not investigated in the present study because it is not a continuous variable.[22]

T2-weighted ratio produced by comparing the signal intensity (SI) of myocardium to skeletal muscle at the same section[32] on T2WI. The present meta-analysis showed that the T2-weighted ratio helped to discriminate patients with myocarditis from healthy controls and distinguish AM from normal conditions, which may be attributed to significant myocardial oedema.[56] Jia *et al.*[32] found a significant difference in T2-weighted ratio between patients with CM and healthy controls, but an elevated T2-weighted ratio was observed in only 35.4% of patients with CM, indicating the limited diagnostic ability of it in CM.

EGE ratio is assessed by comparing myocardial SI to skeletal muscle the same section during the early period after injection of contrast agent. In this meta-analysis, the results indicating that the EGE ratio can be used statistically to distinguish myocarditis and controls. No significant difference was found to discriminate AM from normal conditions, which is not consistent with the results from Khanna *et al.*[22] This may be caused by a wide 95% CI range of WMD due to the significant heterogeneity between the two included studies. One included study[32] showed a statistically significant difference between CM and controls, but an elevated EGE ratio was observed in only 43.8% of patients.

Some CMRI parameters associated with ventricular size and function were investigated. Among them, a significant difference in LVEF was found between patients with AM and controls and between patients with CM and controls. Impaired LVEF was found in patients with AM or CM. To the authors' knowledge, LVEF is considered a vigorous prognostic marker for patients with myocarditis.[57,58] In one follow-up study[7] targeting children and adolescents with AM, persistent myocardial inflammation was found in patients during the short and medium follow-up, which may be related to myocardial systolic dysfunction presented by LVEF injury. In addition, two of the included studies compared the discrimination of LVEF between patients with AM from those with CM, and no significant difference emerged. This may be explained by persistent myocardial systolic dysfunction in the chronic phase.[7] No significant difference was observed regarding the diagnostic performance of other parameters including LVEDV, LVEDVI, and LVESVI, which may be affected by insufficient data and different levels of disease severity among patients.

CMRI feature tracking (CMRI-FT) can be used for quantitative analysis of strain for myocardial function. Some studies[57,59–61] identified CMRI-FT features, which can indicate early changes associated with mild impairment of myocardial function.[62,63] Two of included studies investigated the strain in children and adolescents with myocarditis; however, significant heterogeneity existed between these parameters. Thus, related data could not be summarised for meta-analysis. Although data on LV radial strain could be evaluated, no significant difference emerged between patients with AM and healthy controls due to the wide range of 95% CI for WMD. Strain analyses for patients with CM were not conducted in included studies.

The results above revealed statistical differences in the quantitative features of CMRI, including mapping parameters (native T1 relaxation time, ECV, and T2 relaxation time) and conventional quantitative parameters (EGE ratio and T2-weighted ratio) between paediatric and adolescent patients with myocarditis and healthy controls. Subgroup analyses of native T1 relaxation time, T2 weighted ratio, and LVEF can discriminate patients with AM from healthy controls. LVEF also can distinguish patients with CM from healthy controls. Although the results above showed statistical differences, all the results may not apply to clinical practice. For instance, T1 relaxation time with a WMD of 54 is clinically significant as it is significantly higher than T1 scan–scan reproducibility, so it is may be more valuable in the clinic. In comparison, other parameters, such as ECV, T2 relaxation time, EGE ratio, etc., with small WMD may be less likely to be useful clinically as scan–scan variability exists. In addition, despite the 5% WMD between in the LVEF, the mean LVEF in the myocarditis population was normal in most included studies. This limits the usefulness of LVEF in the discrimination between myocarditis and normal.

There are also some negative results. No significant differences emerged in light of some features such as LVEDV, LVEDVI, and LVESVI between patients with myocarditis and healthy controls. The meta-analysis of LVEF between patients with AM and those with CM, showed no significant difference. Left ventricular (LV) radial strain was the only parameter of myocardial deformation analysed, but no statistically significant difference was found between AM group and controls.

This study has some limitations (1): all the included studies were single centre and the comparator groups were healthy controls. According to the inclusion and exclusion

criteria, some studies were excluded because they chose patients with other cardiac diseases as the control group. It is essential to distinguish myocarditis and other heart diseases in clinic, thus these studies should be further meta-analysed in the near future (2). A summarised analysis of some parameters and investigation on the difference in the diagnostic value of a majority of parameters in AM and CM could not be conducted due to a small number of studies with insufficient data. Besides, publication bias assessment could not be carried out (3). The severity of myocarditis in study patients varied significantly and the stratification of AM and CM relies on symptom duration,[22] which may bias the analysis results (4). Significant heterogeneity was found regarding some CMRI parameters. This may be affected by patient conditions, MRI field strength,[50] scan sequences,[64] and imaging strategies and post-processing factors[34] and so on. No consensus has been reached on the cut-off value of these parameters in paediatric and adolescent patients with myocarditis.

In conclusion, statistical differences can be observed in a host of CMRI parameters including three mapping parameters, two classic parameters, and one functional parameter between patients with myocarditis and healthy controls; however, apart from native T1 myocardial mapping, there were no large differences in the assessed CMRI parameters, which may reveal the limited benefit of CMRI in assessing myocarditis in paediatric population. Multi-centre research with a large sample size is needed in the future.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crad.2023.05.019.

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