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Value of cardiac magnetic resonance feature-tracking in Arrhythmogenic Cardiomyopathy (ACM): A systematic review and meta-analysis

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ABSTRACT

We aimed to assess the diagnostic performance of Cardiac Magnetic Resonance (CMR) strain parameters in ACM patients to evaluate their diagnostic role. We systematically searched MEDLINE, EMBASE, Scopus, and Web of Science. Of the 146 records, 16 were included. All Right Ventricle (RV) global strains were significantly reduced in ACM patients compared to controls (Standardized Mean Difference (SMD)[95 % Confidence Interval (CI)]: Longitudinal 1.31[0.79,1.83]; Circumferential 0.88[0.34,1.42]; Radial −1.14[−1.78,−0.51]). Similarly, all Left Ventricle (LV) global strains were significantly impaired in ACM compared to healthy controls (SDM [95 %CI]: Longitudinal 0.88[0.48,12.28], Circumferential 0.97[0.72,1.22], Radial −1.24[−1.49,−1.00]). Regarding regional RV strains, longitudinal and circumferential strains were significantly reduced in basal and mid-wall regions, while they were comparable to controls in the apical regions. The RV radial strain was reduced only within the basal region in the ACM group compared to controls. ACM patients exhibited significant impairment of regional LV strains in all regions–basal, mid-wall, and apical–compared to control subjects. Ultimately, despite the limitations of CMR-FT in terms of reproducibility, it is superior to qualitative assessment in detecting wall motion abnormalities. Thus, integrating CMR-FT with ACM diagnostic criteria seems to enhance its diagnostic yield.

1. Introduction

Arrhythmogenic Cardiomyopathy (ACM) is a condition characterized by progressive cardiomyocyte loss and subsequent fibrofatty tissue replacement [1,2]. ACM was historically deemed to predominantly involve the Right Ventricle (RV); nonetheless, Left Ventricular (LV) involvement is increasingly being recognized, and recent studies show that classic RV involvement is seen in more advanced stages [3]. ACM mainly manifests with cardiac electrical disturbances leading to potentially fatal ventricular arrhythmias [1]. Up to 20 % of sudden cardiac deaths in young individuals and athletes could be attributed to ACM [4].

The histopathological changes characteristically begin from the subepicardial myocardial layer with patchy distribution; thus, even myocardial biopsy has low diagnostic yield, especially in the early stages. ACM is diagnosed based on the Padua Criteria (International Criteria for ACM) [5–7]. The primary diagnostic criteria for ACM were the Task Force Criteria (TFC) originally introduced in 1994 and revised in 2010 [8,9]. Padua employs echocardiography, angiography, and CMR for assessment of dysfunction or structural alteration [7,10]. However, the wall motion abnormality is assessed qualitatively and is reported as akinesia, dyskinesia, or bulging [1,7,10].

CMR can accurately and reproducibly measure the Ejection Fraction (EF) and RV volume [11]. Moreover, CMR Feature Tracking (CMR-FT) is an emerging tool to assess global and regional strain and mechanical dispersion. Therefore, strain measures are more sensitive than global RV Ejection Fraction (RVEF) and can detect subclinical changes preceding

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the EF decline [1,11]. Diagnostic criteria for ACM are designed to be utterly specific, owing to several other diseases with significant overlapping presentations and findings. Using CMR-FT can increase the sensitivity of these criteria and improve the early detection of the disease [1].

With the advancement of imaging, ACM diagnostic guidelines incorporated imaging modalities to maintain the highest specificity and increase diagnostic sensitivity. There is growing evidence of the utility of Feature-Tracking (FT) strain analysis in ACM diagnosis. However, the available evidence is scattered. Thus, as a pioneering study, we aimed to comprehensively review and summarize the FT strain analysis findings in patients diagnosed with ACM compared to healthy controls.

2. Methods and materials

This study follows the recommendations outlined by the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement [12]. The study protocol was registered a priori in the International Prospective Register of Systematic Reviews (PROSPERO) under the register number CRD42023439364. Given that this study is a systematic review and meta-analysis of published research, no ethical approval was mandated.

2.1. Search strategy

We systematically searched the electronic databases, i.e., Scopus, MEDLINE, Embase, and Web of Science, on July 5th, 2023, using relevant keywords in three domains, i.e., "Cardiac Magnetic Resonance Imaging," "Strain Analysis," and "Arrhythmogenic Cardiomyopathy." The search was updated on January 28th, 2024. The key terms within each domain were connected by the Boolean operator "OR," and domains were connected using the Boolean operator "AND," tailored for each database. Additionally, the reference list and the first ten pages of related articles from Google Scholar were also screened for each included article to identify any possible records that might have been missed. We have detailed the search strategy in Supplementary Table 1. All retrieved records were imported into EndNote software (version 20, Captivate Analytics, California, USA), where duplicates were removed firstly by the automated duplicate finder and subsequently manually.

2.2. Study selection

Two independent reviewers (M.M. and A.A.) screened the imported records based on title and abstracts, followed by full texts to select eligible studies. In case of any disagreement, the opinion of a third researcher (A.S.) was sought to resolve the issue.

2.3. Inclusion criteria

Studies were included in this study if they met all of the following criteria:

(1) Were written in English.
(2) Were published in a peer-reviewed journal.
(3) Diagnosed ACM according to TFC.
(4) Performed Cardiac Magnetic Resonance Imaging (CMR) and FT strain analysis.
(5) Used an observational study design to evaluate strain analysis of ACM patients compared to healthy or athletic controls.

2.4. Exclusion criteria

Studies were excluded based on any of the following criteria:

(1) Studies on animal or in vitro.
(2) Studies including ischemic cardiomyopathy or dilated cardiomyopathies.
(3) Studies including patients with ischemic heart disease.

2.5. Data extraction

Two independent researchers extracted the data from the full-text articles using a data extraction form in Microsoft Excel (Version 2021, Microsoft Corp., Redmond, WA, USA). The extracted data included: the first author's name, country, publication year, study design, comparison group, diagnostic criteria, analysis software, sample size, patient characteristics, cardiovascular risk factors (i.e., diabetes, hypertension, dyslipidemia), and strain analysis findings, encompassing global and regional strains of right and left ventricle. Any disagreements were resolved through discussion.

2.6. Quality assessment

Two independent researchers conducted the quality assessment using the Newcastle-Ottawa Scale (NOS) appraisal tool for case-control studies [13] and the adjusted NOS appraisal tool for cross-sectional studies [14]. Any disagreement was resolved through discussion, or, if necessary, by consulting a third researcher. The NOS critical appraisal tool evaluates three broad dimensions: the selection of study groups (four questions), the comparability of groups (one question), and the ascertainment of the exposure (three questions). The NOS employs a star system wherein each question could earn a star (except for comparability, which can be awarded up to two stars). The total NOS score ranges from 0 to 9 and is categorized into three groups: 'poor' for scores of 0–3, 'fair' for scores of 4–6, and 'good' for scores of 7–9.

2.7. Statistical analysis

Primarily, we pooled the mean difference of strain analysis parameters between ACM and control groups using a standard meta-analysis method. Heterogeneity was assessed using the I-squared statistic and Q-test, to measure the magnitude and significance of heterogeneity, respectively. We employed a random-effects model for all variables, taking into account the variability among studies, particularly regarding the analysis software. The Standardized Mean Differences (SMDs) were pooled using the Cohen method. The meta-analyses were conducted using the 'meta' R package in R Studio software (version 2023.06.0 + 421). Forest plots were designed using the 'ggplot2′ R package in R Studio software. Publication bias was evaluated using Egger's regression asymmetry test, applicable for analyses including at least ten studies. A significance level of 0.05 was considered to assess potential publication bias. Based on data extracted from eligible studies, we calculated SMDs for all strain analysis parameters that were reported in at least three studies. A Leave-one-out sensitivity analysis was conducted for all variables reported in at least four studies. Changes in strain measures are presented as changes in their absolute values, with less negative values considered indicative of lower strain.

3. Results

3.1. Study selection

A total of 146 studies were retrieved, and after removing duplicates and screening titles, abstracts, and full texts for relevance, a total of 16 eligible studies were included, as illustrated in Fig. 1. The study conducted by Czimbalmos et al. compared athletic and non-athletic ACM patients and healthy athletes [4]; therefore, it was excluded from the meta-analysis due to its unique comparison groups.

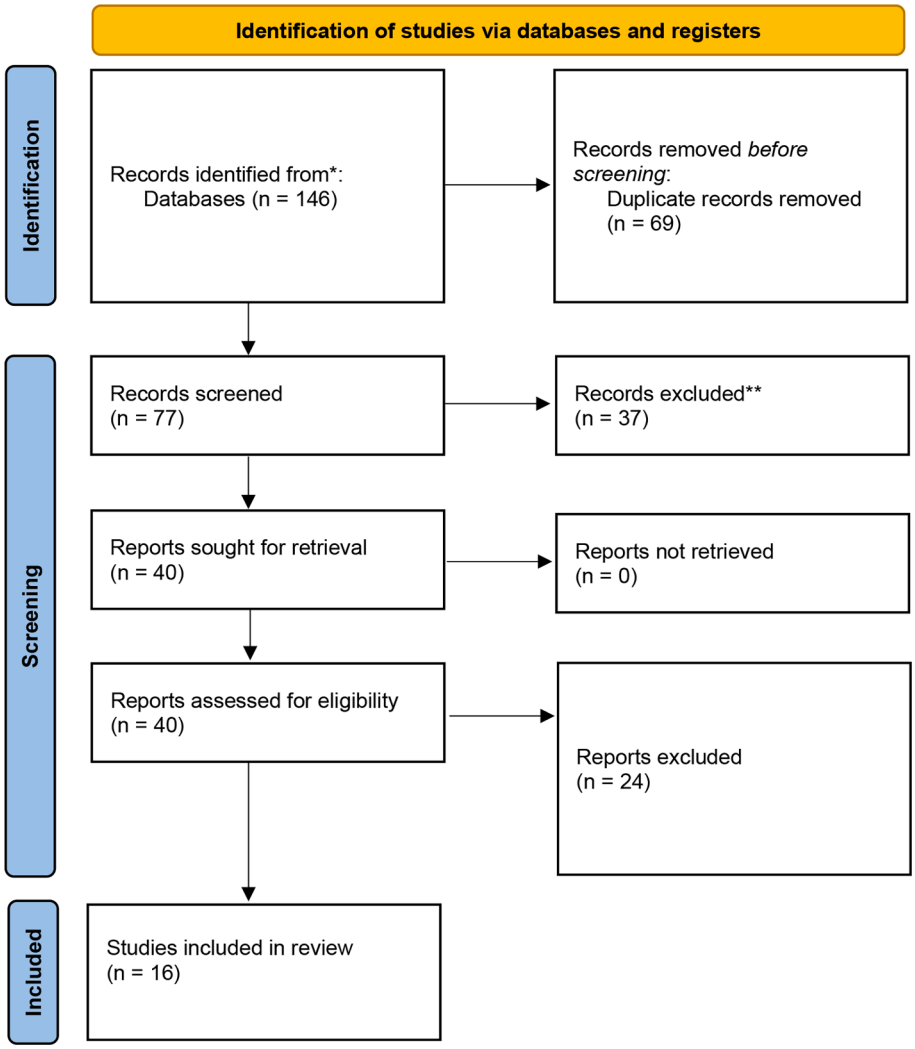

Fig. 1. PRISMA flowchart diagram of literature search and selection process. *Consider, if feasible to do so, reporting the number of records identified from each database or register searched (rather than the total number across all databases/registers). **If automation tools were used, indicate how many records were excluded by a human and how many were excluded by automation tools. *From:* Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71. For more information, visit: http://www.prisma-statement.org/.

3.2. Baseline characteristics

Three out of sixteen studies included in this study were conducted in China [15–17], two in Germany [5,6], two in Spain [18,19], two in Italy [1,20], two in the United States [21,22], and one each in Sweden [23], Canada [3], Hungary [4], France [24], and the Netherlands [25]. The sample size of eligible studies ranged from 30 [5,6] to 98 [15]. The mean age of ACM participants ranged from 32.3 [21,22] to 60.1 years [6]. The study by Chungsomprasong et al. included children and adolescents but did not report the mean age of their participants [3]. The study designs of the included studies were primarily case-control, except for the study by Chungsomprasong et al., which was a cross-sectional study [3].

All studies employed the 2010 TFC for diagnosing ACM except the study by Laredo et al., which employed the 2020 TFC [24], and the study by Vives-Gilabert et al. [18]. Although Vives-Gilabert et al. published their study in 2019, the criteria for diagnosing ACM were similar to those of the 2020 TFC [18].

One study stood out by utilizing and comparing four different software tools, TomTec, CVI42, MTT, and Medis, to analyze strain parameters [21]. Regarding the software used for strain analysis across the included studies, nine out of sixteen included studies utilized CVI-42 [26], five utilized TomTec [1,3,5,21,27], three implemented Medis [4,21,25], one employed MTT [21], and one of the most recent studies adopted Cardio Track for strain analysis [24].

3.3. Meta-analysis

The study characteristics of the included studies are summarized in Table 1. The pooled SMDs are presented in Table 2, offering a comprehensive overview of the strain analysis findings compared between ACM patients and control groups.

3.4. Strain analysis findings

3.4.1. Right ventricle strain

The meta-analyses of RV global and regional strains are summarized in Figs. 2, 3, and 4. Our meta-analysis demonstrated that global strains in all three dimensions, including RV GLS, GCS, and GRS are significantly decreased in ACM patients compared to their control counterparts (pooled SMD [95 %CI]: GLS 1.31 [0.79,1.83]; GCS 0.88 [0.34, 1.42]; GRS −1.14 [−1.78, −0.51], respectively, all p-values < 0.001). Regarding longitudinal regional strains of RV, basal and mid-wall strains of ACM patients were significantly lower than those in control groups (pooled SMD [95 %CI]: 0.95 [0.72,1.18]; 0.82 [0.48,1.16], respectively,

Table 1
Characteristics of included studies.

Study	Country	Design	Control	ACM	Diagnostic Criteria	Analysis Software	Sample Size		Age (mean ± SD)		Male (n)	
							ACM	Control	ACM	Control	ACM	Control
Aneq et al. 2018 [27]	Sweden	CC	Negative cardiac test	Definite ACM	2010 TFC	TomTec	27	24	48.4 ± 15.1	39.8 ± 16	16	19
Bourfiss et al. 2017 [21]	USA	CC	Mutation-free family members or not ACM with clinical evaluation	Definite ACM	2010 TFC	TomTec; CVI42; Medis	39	31	32.3 ± 13.5	37.2 ± 14.9	27	24
Chen et al. 2019 [15]	China	CC	Healthy matched for age and sex	Definite ACM	2010 TFC	CVI42	68	30	39.28 ± 13.88	40.2 ± 12.42	45	17
Chungsomprasong et al. 2017 [3]	Canada	CS	No ACM according to TFC	Definite ACM	2010 TFC	TomTec	24	56	NR	NR	NR	NR
Czimbalmos et al. 2019 [4]	Hungary	CC	Heathy Athletes	Definite ACM	2010 TFC	Medis	34	34	40.5 ± 7.7	31.8 ± 7.7	22	22
Heermann et al. 2014 [5]	Germany	CC	Healthy	Definite ACM	2010 TFC	TomTec	20	10	50.7 ± 16.9	24.3 ± 3	17	5
Heermann et al. 2019 [6]	Germany	CC	Healthy	Definite ACM	2010 TFC	CVI42	16	14	60.1 ± 15.5	48.8 ± 14.1	14	9
Laredo et al. 2023 [24]	France	CC	Healthy matched for age, sex, and BMI	Definite ACM with major structural criteria	2020 TFC	CardioTrack	26	39	46 ± 14	46 ± 12	22	22
Muscogiuri et al. 2021 [20]	Italy	CC	Healthy matched for age and sex	Definite ACM	2010 TFC*	CVI42	35	29	44 ± 15	41 ± 1	30	27
Prati et al. 2015 [1]	Italy	CC	Healthy matched for age and sex	At least borderline ACM	2010 TFC	TomTec	32	32	48.3 ± 18.8	43.9 ± 15.4	14	23
Shen et al. 2019 [17]	China	CC	Healthy matched for age and sex	Definite ACM	2010 TFC	CVI42	60	34	38.73 ± 17.65	42.32 ± 13.62	36	20
Taha et al. 2021 [25]	Netherlands	CC	Healthy non-athlete	Definite ACM	2010 TFC	Medis	34	46	43.4 ± 17.9	32.6 ± 16.8	18	21
Vigneault et al. 2016 [22]	USA	CC	Mutation-free family members or not ACM with clinical evaluation	Definite ACM	2010 TFC	CVI42	39	31	32.3 ± 13.5	37.2 ± 14.9	17	17
Vives-Gilabert et al. 2019 [18]	Spain	CC	Non-affected family members	Definite ACM with LV involvement	2010 TFC or histologically	CVI42	35	23	40.1 ± 17.9	49.6 ± 16.4	16	10
Vives Gilabert et al. 2020 [19]	Spain	CC	Non-affected family members	Definite ACM with LV involvement	2010 TFC	CVI42	35	23	39.4 ± 18.23	49.6 ± 16.4	17	10
Dong et al. 2023 [16]	China	CC	Healthy matched for age and sex	Definite ACM	2010 TFC	CVI42	37	37	39.0 ± 13.88	37.35 ± 14.65	27	30

Arrhythmogenic Right Ventricular Cardiomyopathy, BMI: Body Mass Index, CC: Case Control, CS: Cross-Sectional, LV: Left Ventricle, TFC: Task Force Criteria.
* This study cited the original 1994 TFC; however, their definition of positive CMR findings for ACM diagnosis was compatible with TFC 2010. Therefore, we presumed they had employed this criteria.

all p-values < 0.001); however, the apical strain was comparable between ACM and control groups (pooled SMD [95 %CI]: 0.43 [−0.05, 0.90], p-value: 0.077). Considering circumferential regional strains of RV, similar to that of longitudinal strains, ACM patients had significantly lower basal and mid-wall strain (pooled SMD [95 %CI]: 1.09 [0.78, 1.41]; 0.93 [0.55, 1.31], respectively, all p-values < 0.001), while apical strain did not reveal any significant difference between ACM and control groups (pooled SMD [95 %CI]: 0.18 [−0.17, 0.54], p-value: 0.312). The regional radial RV strains revealed that the ACM patients have significantly lower basal strain compared to control subjects (pooled SMD [95 %CI]: −0.97 [−1.45, −0.49], p-value < 0.001), while mid-wall and apical strains were comparable between groups (pooled SMD [95 %CI]: mid-wall −0.64 [−1.34, 0.06], p-value: 0.075; apical −0.09 [−0.45, 0.27], p-value: 0.634, respectively).

3.4.2. Left ventricular strain

Meta-analysis of LV global and regional strains are illustrated in Figs. 5 and 6. Similar to the RV, global strains of the LV in all three dimensions, including GLS, GCS, and GRS, were significantly lower in ACM patients compared to controls (pooled SMD [95 %CI]: GLS 0.88 [0.48, 1.28], p-value < 0.001; GCS 0.97 [0.72, 1.22], p-value < 0.001; GRS −1.24 [−1.49, −1.00], p-value < 0.001, respectively). The regional circumferential strains of the LV demonstrated that basal, mid-wall, and apical strains were significantly lower in ACM patients compared to control groups (pooled SMD [95 %CI]: basal 0.85 [0.55, 1.15], p-value < 0.001; mid-wall 0.60 [0.30, 0.90], p-value < 0.001; apical 0.49 [0.20, 0.79], p-value: 0.001, respectively).

3.4.3. Sensitivity analysis

The leave-one-out sensitivity analysis confirmed the robustness of

Table 2
Meta-analysis findings of age and strain analyses.

	Variable	SMD [CI95 %]	P value	k	I^2
1	Age	0.16 [−0.13,0.44]	0.277	13	0.71
2	RV GLS	1.31 [0.79, 1.83]	**<0.001**	9	0.86
3	RV GCS	0.88 [0.34, 1.42]	**0.001**	4	0.78
4	RV GRS	−1.14 [−1.78, −0.51]	**<0.001**	4	0.84
4	RV Longitudinal Basal Strain	0.95 [0.72, 1.18]	**<0.001**	5	0.00
5	RV Longitudinal Mid-wall Strain	0.82 [0.48, 1.16]	**<0.001**	4	0.43
6	RV Longitudinal apical Strain	0.43 [−0.05, 0.90]	0.077	4	0.71
7	RV Circumferential Basal Strain	1.09 [0.78, 1.41]	**<0.001**	4	0.00
8	RV Circumferential Mid-wall Strain	0.93 [0.55, 1.31]	**<0.001**	3	0.00
9	RV Circumferential Apical Strain	0.18 [−0.17, 0.54]	0.312	3	0.00
10	RV Radial Basal Strain	−0.97 [−1.45, −0.49]	**<0.001**	3	0.38
11	RV Radial Mid-wall Strain	−0.64 [−1.34, 0.06]	0.075	3	0.69
12	RV Radial Apical Strain	−0.09 [−0.45, 0.27]	0.634	3	0.00
13	LV GLS	0.88 [0.48, 1.28]	**<0.001**	6	0.70
14	LV GCS	0.97 [0.72, 1.22]	**<0.001**	6	0.37
15	LV GRS	−1.24 [−1.49, −1.00]	**<0.001**	4	0.00
16	LV Circumferential Basal Strain	0.85 [0.55, 1.15]	**<0.001**	3	0.00
17	LV Circumferential Mid-wall Strain	0.60 [0.30, 0.90]	**<0.001**	3	0.00
18	LV Circumferential Apical Strain	0.49 [0.20, 0.79]	**0.001**	3	0.00

CI: Confidence Interval, GCS: Global Circumferential Strain, GLS: Global Longitudinal Strain, GRS: Global Radial Strain, LV: Left Ventricle, RV: Right Ventricle, SMD: Standardized Mean Difference.

the effect size, demonstrating that the effect size was not driven by a single study for all aforementioned strain values except for the RV longitudinal apical strain. The meta-analysis did not detect a significant difference in RV longitudinal apical strain between patients with and without ACM, while leave-one-out sensitivity analysis of this variable revealed that when the study by Aneq et al. 2017 was excluded, the RV longitudinal apical strain was significantly lower in patients with ACM compare to the control group [27]. Therefore, the results of RV longitudinal apical should be interpreted with caution.

3.4.4. Subgroup analysis

The study by Bourfiss et al. highlighted that different strain analysis software reports different strain measurements [21]. Consequently, we performed subgroup analysis based on the analysis software used, even when heterogeneity was low. Details of subgroup analysis are illustrated in Figs. 2-6. Subgroup analysis of RV GLS revealed that ACM patients' RV GLS remained significantly lower compared to the control group when analyzed by TomTec and CVI42 software. Additionally, the two studies employing Medis software also reported a significantly lower RV GLS in ACM patients compared to healthy participants [21,25]. In terms of LV strain measurements, subgroup analysis of the GLS revealed that GLS measured by CVI42 was significantly lower in patients with ACM compared to healthy counterparts. Meanwhile, one study utilizing Cardio Track software did not detect a significant difference in LV GLS between the two groups [24].

3.5. Qualitative synthesis

Two studies demonstrated that RV longitudinal Standard Deviation of Time to Peak Strain (SD-TTP), indicative of mechanical dispersion and dyssynchrony, was significantly elevated in ACM patients compared to controls [1,27].

Czimbalmos et al.'s study compared healthy athletes and athletes with ACM. Findings indicated that while athletes with ACM exhibited normal RVEF and RV GLS, abnormalities were consistently observed in the regional longitudinal strains and strain rates of the RV mid-free wall among all eight athletes with ACM [4].

3.6. Diagnostic accuracy

The diagnostic value of FT in ACM diagnosis, as reported in the included studies, is detailed in Table 3. A novel regional myocardial strain parameter termed Longitudinal to Radial Strain Loop (LRSL), was introduced by Laredo et al., calculated from the longitudinal and radial motions of the basal sub-tricuspid segment in a four-chamber view [24]. LRSL demonstrated superior discriminatory accuracy to both RVEF and RV basal longitudinal strain in discriminating ACM patients, particularly those without any major structural criteria from healthy controls [24].

In one study comparing different software platforms, only Medis software was found to have adequate diagnostic accuracy to distinguish preclinical ACM from control subjects (AUC: 0.70). In contrast, other platforms, such as TomTec, MTT, and Circle, did not exhibit similar diagnostic capabilities [21].

3.7. Reproducibility

In terms of reproducibility, inter- and intra-observer variability of RV GLS was good to excellent in most studies [1,15,16,20,22,23], except for Heermann et al.'s study which reported moderate inter-observer correlation [6]. RV GCS exhibited good inter- and intra-observer variability [1,15,20,22], and RV GRS was deemed at least good in terms of reproducibility across three studies [15,16,20], whereas one study reported moderate inter- and intra-observer variability [1]. Despite its promising discriminatory power, LRSL was noted to have good inter-observer variability and moderate intra-observer variability [24]. Segmental strain measures attained the highest reproducibility when analyzed using CVI42 or Medis software; however, all measures, irrespective of the software used, resulted in moderate to good reproducibility [21]. Inter-observer correlations for regional radial peak strains (i.e., basal, apical, and RVOT endocardial) were moderate, while the medial radial peak strain exhibited weak inter-observer correlation [6]. With regard to dyssynchrony measures, circumferential SD TTP displayed the highest reproducibility among SD TTP measures. Circumferential and longitudinal SD TTP were moderately reproducible, while radial SD TTP suffered from poor inter-observer reproducibility [1].

3.8. Quality assessment

The results of the quality assessment of the included studies are detailed in Supplementary Table 2. All included studies received an NOS score of at least seven and were deemed of good quality, while the study by Aneq et al. 2017, which received an NOS score of six, was classified as fair in quality [27].

4. Discussion

The meta-analysis focused on ACM patients in comparison to control subjects unveiled significant differences in various strain parameters. The RV GLS, GCS, and GRS were consistently lower in ACM patients. For regional strains of the RV, the longitudinal and circumferential basal and mid-wall strains, were significantly lower in ACM patients, while apical strains exhibited no significant difference. Considering the radial regional strain, only basal strain was significantly lower in ACM patients compared to controls, while the mid-wall and apical regions had comparable radial strains between groups. Concerning LV strains, GLS, GCS, and GRS were significantly lower in ACM patients. Similarly, regional longitudinal strains of the LV were reduced in ACM patients at basal,

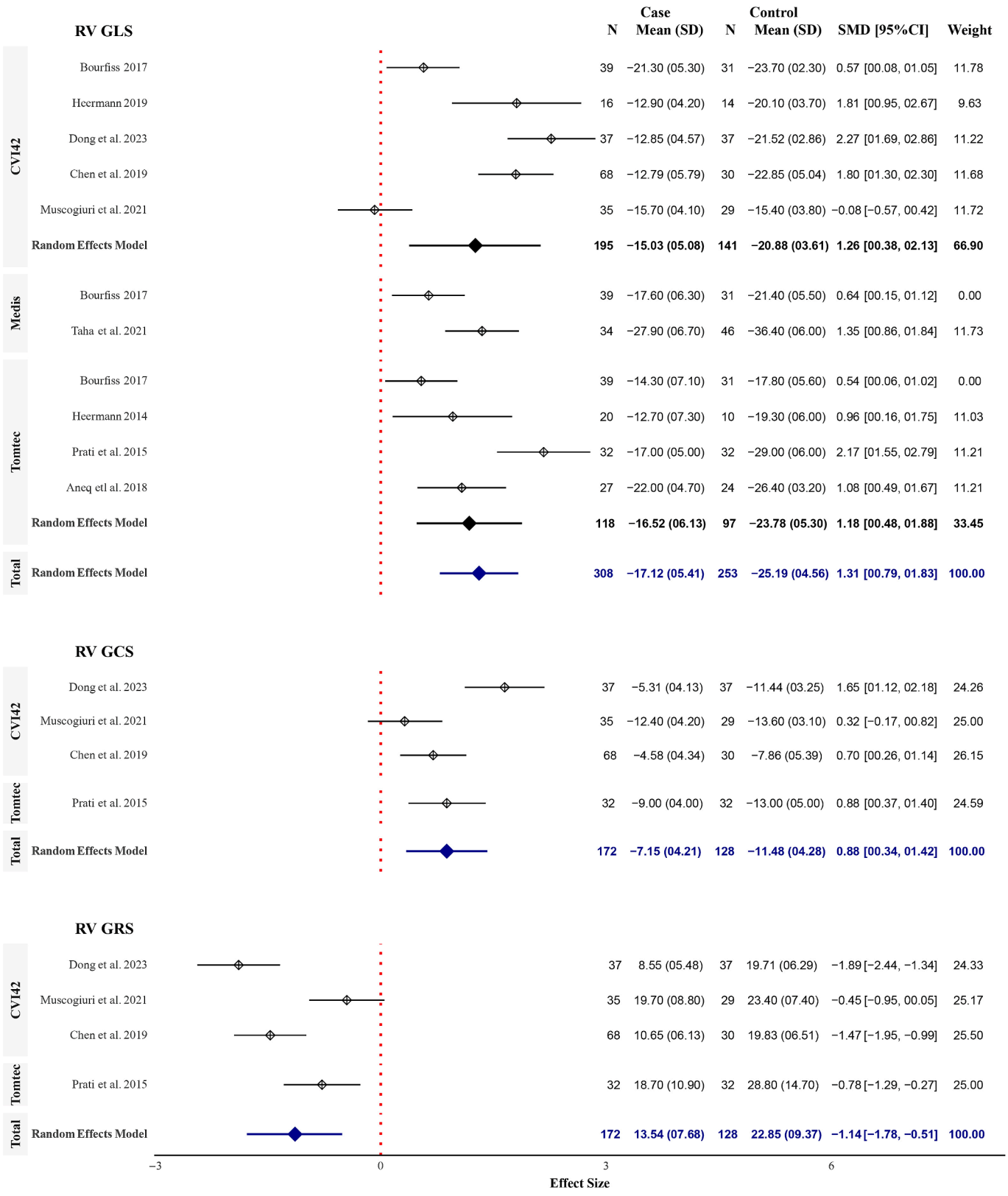

Fig. 2. Forest plots of pooled SMDs of RV GLC, GCS, and GRS Heterogeneity (I^2): RV GLS: 87 %, RV GCS: 78 %, RV GRS: 84 %.**GCS:** Global Circumferential Strain, **GLS:** Global Longitudinal Strain, **GRS:** Global Radial Strain.

mid-wall, and apical levels. When stratified by strain analysis software, the subgroup analysis maintained consistent findings of lower RV GLS in ACM patients across different software. The study acknowledges software-related variations in strain analysis.

The significance of CMR in ACM diagnosis is increasingly recognized [7]. Although CMR findings did not feature in the initial TFC criteria established in 1994, the 2010 TFC revision included them within the diagnostic criteria to address both global or regional dysfunction and

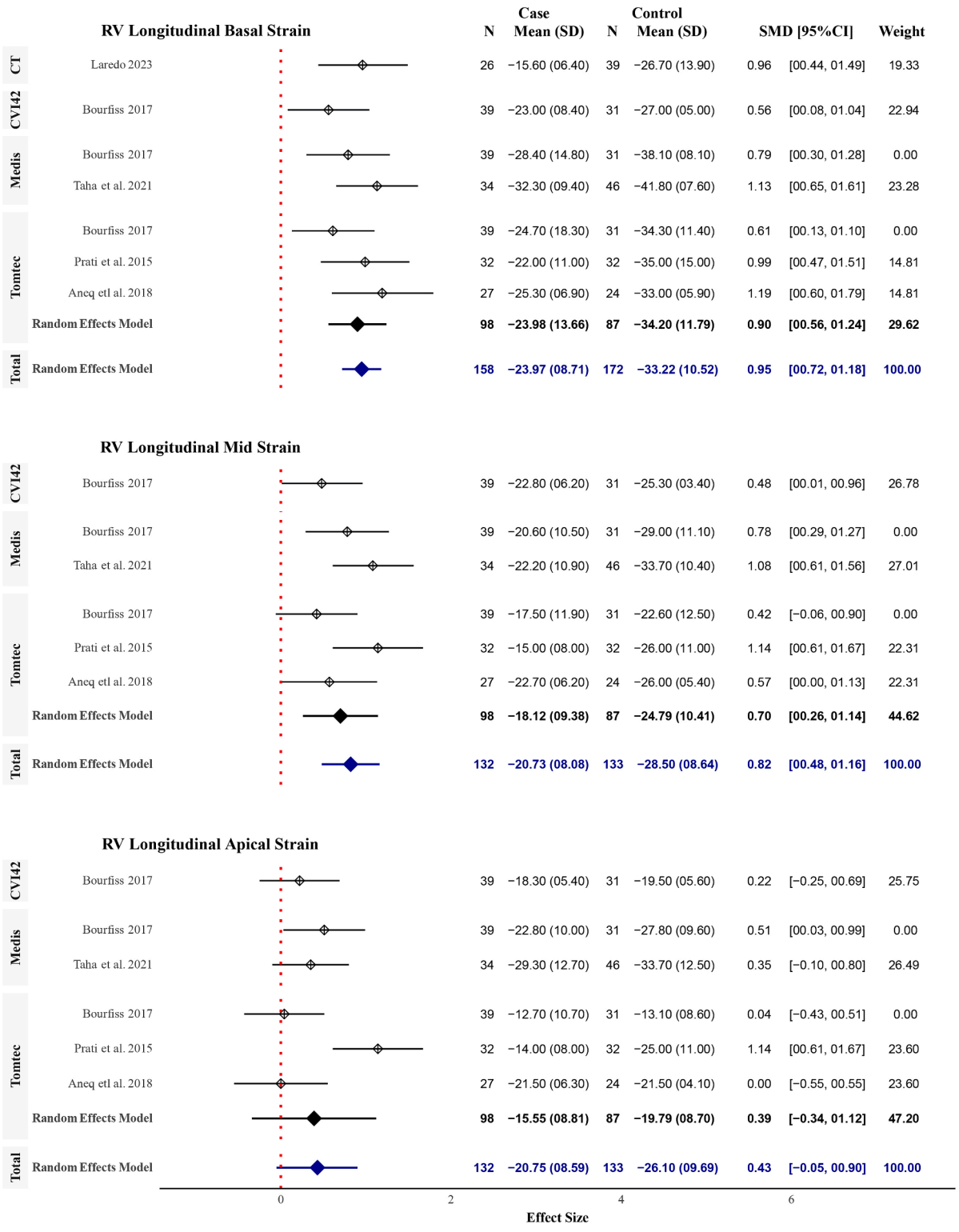

Fig. 3. Forest plots of pooled SMDs and subgroup analysis of RV longitudinal regional strains based on analytic software. Heterogeneity (I^2): RV Longitudinal Basal Strain: 0 %, RV Longitudinal Mid Strain: 43 %, RV Longitudinal Apical Strain: 71 %. **RV:** Right Ventricle.

structural changes [9]. Moreover, subsequent amendments in the Padua Criteria 2020 further underscored CMR's diagnostic importance by incorporating late gadolinium enhancement as a major diagnostic criterion in the tissue characterization section [7]. In a study comparing Padua Criteria 2020 with 2010 TFC, Padua Criteria reclassified 11 out of 15 patients classified as borderline by 2010 TFC to either right or biventricular ACM, given LGE findings. Furthermore, it reclassified 7 out of 9 patients classified as possible by 2010 TFC as left ACM [10].

As an example, a 60-year-old male with arrhythmia was referred to our outpatient clinic for ACM evaluation. CMR revealed RV enlargement (RVEDVI: 110 ml/m2) and reduced RVEF (40 %) with akinesia at the RV free wall. Ten minutes post-Gadolinium delayed enhancement sequence showed a transmural scar in the mid-wall region of the RV free wall (Fig. 7 **and** Supplementary video). The above finding is compatible with

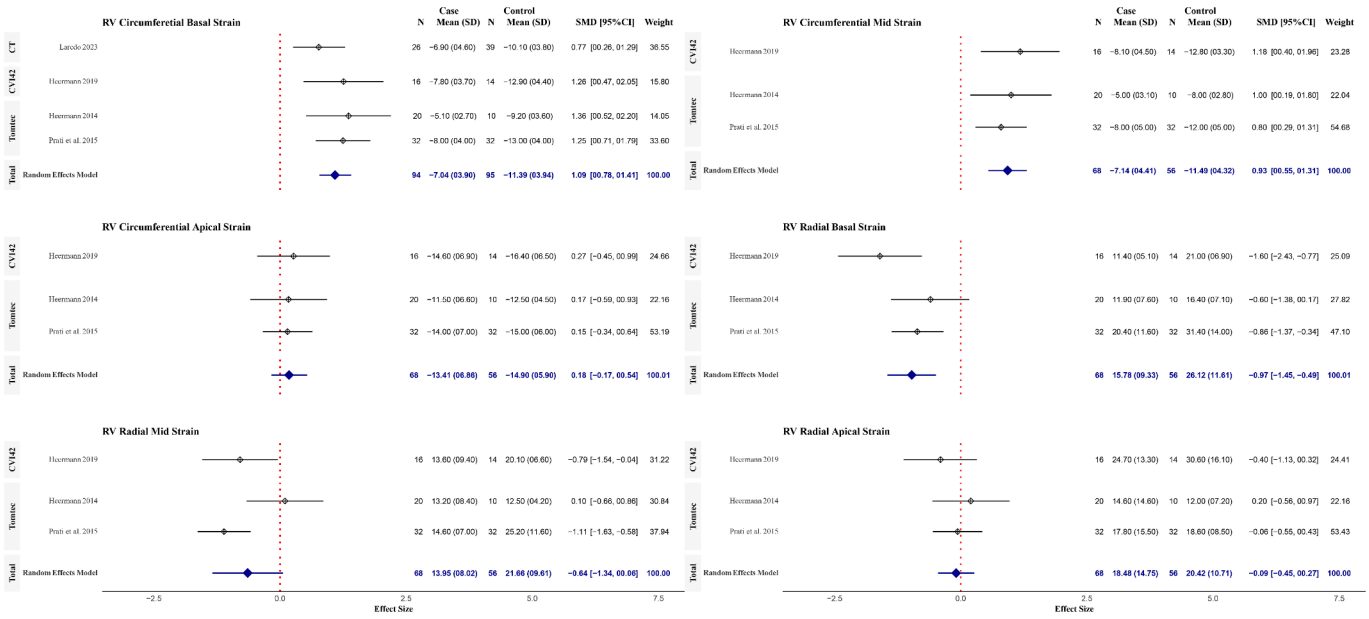

Fig. 4. Forest plots of pooled SMDs and subgroup analysis of RV circumferential and radial regional strains based on analytic software. Heterogeneity (I^2): RV Circumferential Basal Strain: 0 %, RV Circumferential Mid Strain: 0 %, RV Circumferential Apical Strain: 0 %, RV Radial Basal Strain: 38 %, RV Radial Mid Strain: 69 %, RV Radial Apical Strain: 0 %. **RV:** Right Ventricle.

one major criterion for ACM according to Padua Criteria 2020.

Both CMR-FT and Speckle Tracking Echocardiography (STE) are prevalently used for ventricular strain assessments. Prior echocardiographic studies indicate that patients with ACM exhibit reduced regional and global myocardial strain relative to healthy control [23,28]. Yet, significant discrepancies between the absolute strain values from the two methods highlight a poor correlation, indicating that CMR-FT and STE cannot be used interchangeably for patient monitoring over time [11,25]. Although each modality has its merits, CMR offers superior tissue characterization, clearer delineation of the endocardium, and the ability to acquire images in multiple planes. Nevertheless, its utility is constrained by factors such as limited availability, longer processing times, higher costs, and the requirement for contrast agents [1,17].

In the most recent diagnostic criteria for ACM, EF and ventricular dilation are utilized in the quantitative assessment of both ventricles, whereas the role of strain analysis is limited to SPE-derived GLS of the LV [7]. In comparison to echocardiography, CMR provides a more detailed evaluation of RV strains due to superior visualization of anterior and lateral RV walls [27,29]. Given that previous research supports the theory that ACM begins with regional myocardial involvement [30,31], the analysis of regional strains could be valuable for the early detection of ACM. Consequently, incorporating a reliable quantitative measure of ventricular strains into the diagnostic criteria should enhance the accuracy of ACM diagnostic [27].

Certain studies have explored FT findings in ACM across varied populations. Given that healthy athletes exhibit structural alterations similar to ACM, such as RV dilation, alternative diagnostic metrics like CMR-FT parameters (e.g., RV GLS, mid longitudinal strain, and minimum and average regional RV longitudinal strain) have demonstrated enhanced capability in distinguishing between athlete's heart and ACM. The study by Czimbalmos et al. revealed that while RVEF was shown to possess the strongest discriminatory power in contrast to strain measures, the study further indicates that RV GLS, mid-peak, and minimum peak strains in conjunction with minimum RV strain, also offer considerable discriminatory utility, thereby highlighting their potential complementary value to RVEF [4]. Integrating RVEF, RV end-diastolic index, and RV GLS surpassed the diagnostic accuracy of each [16].

The combination of LVEF and radial dyssynchrony achieved good diagnostic performance [18]. Moreover, when one study incorporated radial dyssynchrony into the 2010 TFC, the proposed criteria reclassified nearly one-third of grey zone patients (possible and borderline) to definite ACM [18]. Integrating mechanical function parameters from FT with timing variables achieved the highest discriminatory strength for ACM diagnosis [27]. Consequently, a combination of peak strains and mechanical dispersion appears to be superior to each parameter individually. The novel FT index of LRSL also exhibited strong performance in discriminating ACM from healthy individuals, as well as differentiating ACM without major structural criteria from healthy controls [24]. Therefore, the addition of a combination of strain and mechanical dispersion, or LRSL, might enhance the diagnostic accuracy of ACM criteria.

Research on Plakophilin-2 (*PKP2*) knockout mice revealed the onset of arrhythmia due to elevated intracellular calcium levels prior to any structural alterations, suggesting that arrhythmogenic triggers in these subjects may be primarily electrical rather than structural in nature [32].

Given the pathogenesis of ACM, alterations in cardiac contraction and time to peak contraction are anticipated. Therefore, integrating strain with time-to-peak strain parameters can enhance ACM detection compared to just qualitative assessments or using only strain measurements. This can compensate for the relatively low sensitivity of diagnostic criteria in clinical scenarios [1,18,19]. Also, in regard to prognostic evaluation, time-to-peak strain is a potential prognostic factor yet controversial results have been reported in the literature [27,33,34]. Considering that CMR T1 and T2 mapping is valuable in heart failure etiology assessment, their potential role in detecting fibrofatty change associated with ACM– alone and in conjunction with LGE–is yet to be elucidated [35,36].

Adverse cardiac events such as sustained ventricular tachycardia and cardiac death represent the most alarming complications for patients with ACM, causing significant morbidity and mortality [37,38]. In three studies, the incidence of adverse cardiac events ranged from 15 % to 32 % over follow-up periods ranging from one to five years [11,17,34]. CMR-FT strain analysis has proved capable of identifying subtle LV dysfunction, even in patients with a preserved EF. Moreover, LV GLS thresholds of −12.65 and − 18.3, as well as LV longitudinal dyssynchrony exceeding 89.15 ms, have been considered independent prognostic indicators for adverse cardiac events in individuals diagnosed

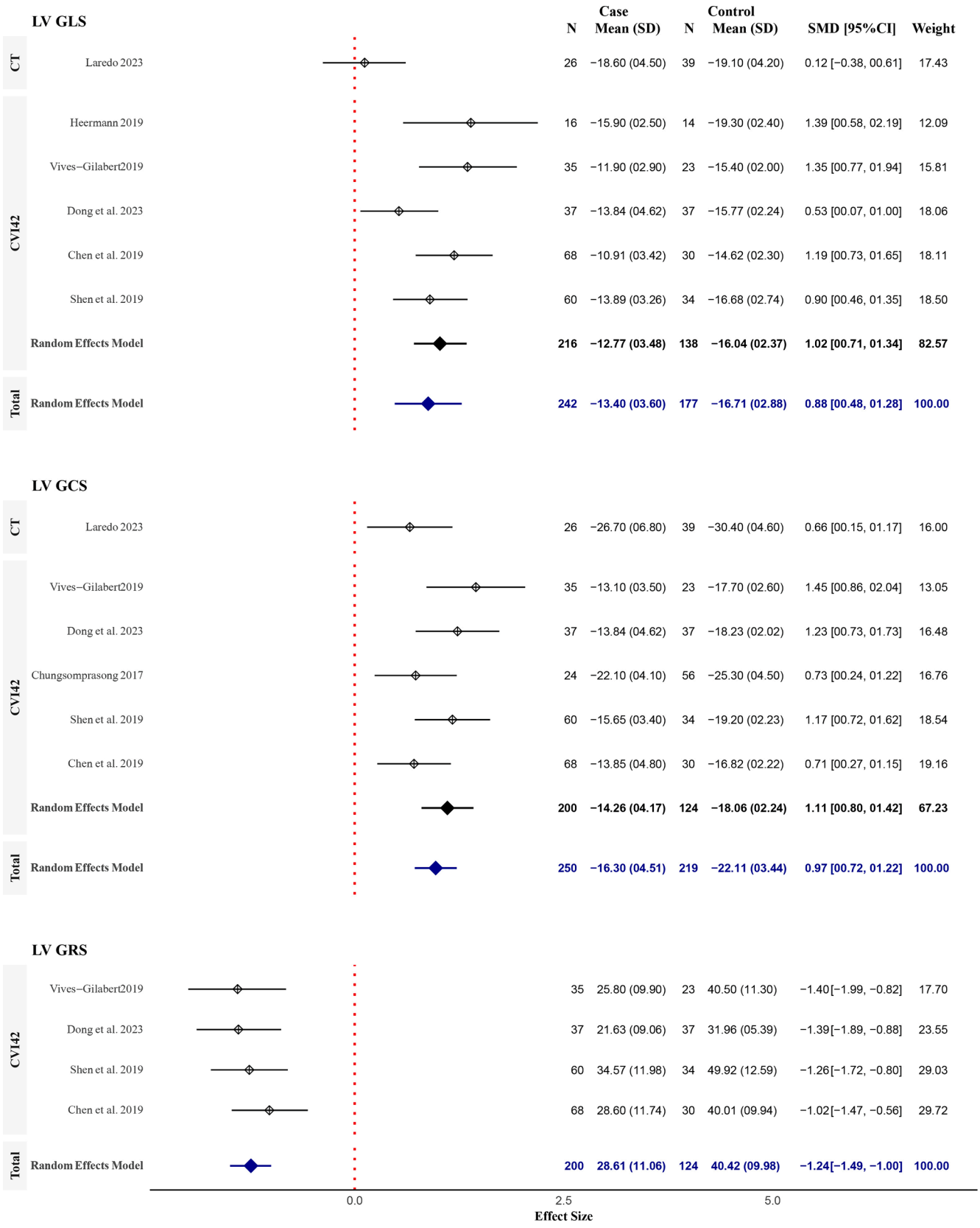

Fig. 5. Forest plots of pooled SMDs and subgroup analysis of LV GLS, GCS, and GRS based on analytic software Heterogeneity (I^2): LV GLS: 70 %, LV GCS: 37 %, LV GRS: 0 %.**GCS:** Global Circumferential Strain, **GLS:** Global Longitudinal Strain, **GRS:** Global Radial Strain, **LV:** Left Ventricle.

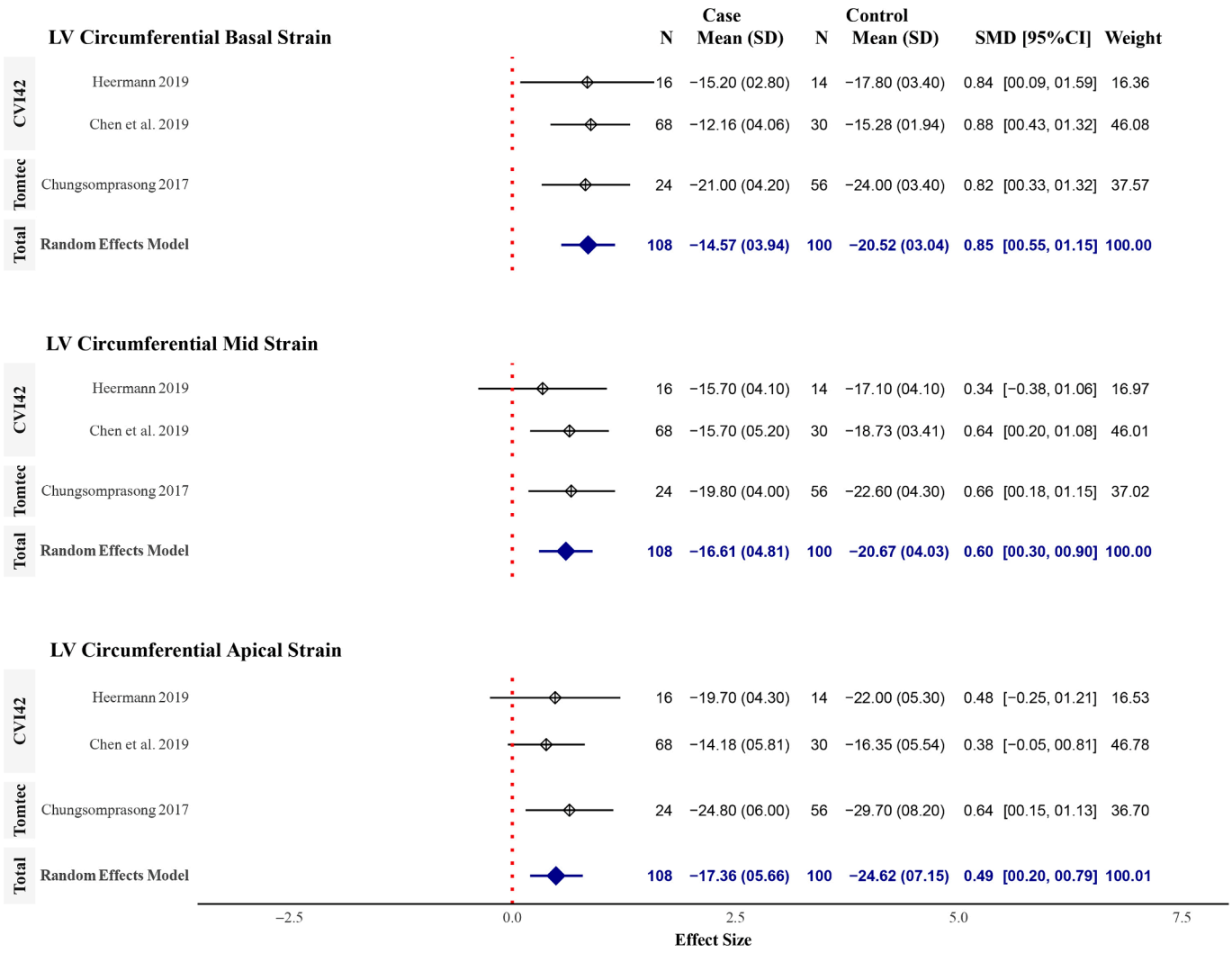

Fig. 6. Forest plots of pooled SMDs of LV circumferential regional strains Heterogeneity (I^2): LV circumferential basal strain: 0.0 %, LV circumferential mid-wall strain: 0.0 %, LV circumferential apical strain: 0.0 %.**LV:** Left Ventricle.

with ACM [15,17,34,39–41]. Therefore, CMR-FT augments early ACM detection, particularly in patients exhibiting minor alterations, and serves as a potential prognostic marker for cardiac adverse events. Although the reproducibility of strain measures is not consistently excellent, they offer adequate reproducibility when compared to the subjective evaluation of wall motion abnormality [6,17].

This highlights the complex cardiac contractile unit, and regional nature of ACM disease, which is so delicate that even precise measurements such as CMR-FT fall behind, underscoring the need for more quantitative criteria to evaluate these patients. Additionally, these results emphasize the critical need to enhance FT software to improve the reproducibility of these measures in the future.

5. Limitations

The primary limitations of this study include the significant heterogeneity of numerous variables and the insufficient number of studies, which hindered a pooled analysis of dyssynchrony parameters. Furthermore, there were no studies with large sample sizes, likely attributable to the rarity of ACM. Additionally, the variability in the cut-points used for assessing the sensitivity and specificity of outcome variables precluded conducting a meta-analysis.

6. Conclusion

Strain and dyssynchrony measures analyzed by CMR-FT may offer promising diagnostic value in ACM patients, particularly when used in conjunction. Additionally, these measures have the potential to enhance ACM diagnosis in special populations, such as athletes, ACM patients with preserved EF, and those in the grey zone. Despite the reproducibility challenges associated with CMR-FT, these methods are superior to the qualitative assessment of wall motion abnormalities.

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Table 3
Diagnostic accuracy of strain findings.

Ventricle	Variable	Discrimination between	Analysis Software	AUC [95 % CI]	Cut-point	Sensitivity	Specificity	Reference
RV	GLS	Definite ACM	Medis	0.67	NR	NR	NR	[21]
			CVI-42	0.94 [0.83, 1.00]	−17.10	0.94	0.89	[6]
				0.63	NR	NR	NR	[21]
				0.92	−19.95	0.97	0.90	[16]
			MTT	0.86	NR	NR	NR	[21]
			TomTec	0.78 [0.60, 0.96]	NR	NR	NR	[5]
				0.67	NR	NR	NR	[21]
			TomTec*	0.79 [0.65, 0.89]	NR	0.70	0.80	[27]
			TomTec†	0.84 [0.71, 0.93]	NR	NR	NR	[27]
		Preclinical	Medis	0.48	NR	NR	NR	[21]
			CVI-42	0.57	NR	NR	NR	[21]
			TomTec	0.50	NR	NR	NR	[21]
			MTT	0.56	NR	NR	NR	[21]
		Borderline ACM	CVI-42	NR	−19.95	0.81	0.90	[16]
		Definite ACM vs. RVOT-A and control	TomTec	0.90 [0.82, 0.95]	−0.23	0.91	0.75	[1]
		ACM vs. RVOT-VT	CVI-42	0.88 [0.77, 0.98]	−16.50	0.88	0.70	[6]
		ACM vs. BrS	CVI-42	0.79 [0.61, 0.98]	−16.00	0.75	0.67	[6]
		ACM vs. healthy athlete	Medis	0.73	−20.10	0.50	0.97	[4]
	GCS	Definite ACM	CVI-42	0.81	NR	NR	NR	[16]
			CardioTrack	0.60 [0.48, 0.72]	NR	0.48	0.77	[24]
		Definite ACM vs. RVOT-A and control	TomTec	0.71 [0.60, 0.79]	NR	NR	NR	[1]
		ACM w/o major structural criteria	CardioTrack	0.53 [0.37, 0.68]	NR	0.71	0.44	[24]
	GRS	Definite ACM	CVI-42	0.84	NR	NR	NR	[16]
			CardioTrack	0.61 [0.49, 0.73]	NR	0.52	0.69	[24]
		Definite ACM vs. RVOT-A and control	TomTec	0.66 [0.56, 0.75]	NR	NR	NR	[1]
		ACM w/o major structural criteria	CardioTrack	0.53 [0.38, 0.69]	NR	0.33	0.86	[24]
	Average Longitudinal Strain	ACM vs. healthy athlete	Medis	0.77	−29.40	0.73	0.76	[4]
	Global Longitudinal Strain Rrate	Definite ACM	TomTec	0.90 [0.78, 1.00]	−1.28	0.95	0.70	[5]
	Average Longitudinal Strain Rate	ACM vs. healthy athlete	Medis	0.67	−1.13	0.53	0.88	[4]
	Global Longitudinal SD TTP	Definite ACM vs. RVOT-A and control	TomTec	0.80 [0.70, 0.87]	113.10	0.59	0.95	[1]
	Global Circumferential SD TTP	Definite ACM vs. RVOT-A and control	TomTec	0.80 [0.71, 0.88]	177.10	0.66	0.83	[1]
	Global Radial SD TTP	Definite ACM vs. RVOT-A and control	TomTec	0.74 [0.64, 0.82]	NR	NR	NR	[1]
	Longitudinal Basal	Definite ACM	Medis	0.72	NR	NR	NR	[21]
			CVI-42	0.64	NR	NR	NR	[21]
				NR	−0.31	0.75	0.78	[22]
			MTT	0.80	NR	NR	NR	[21]
			TomTec	0.70	NR	NR	NR	[21]
			CardioTrack	0.72 [0.61, 0.83]	NR	0.67	0.72	[24]
		Preclinical	Medis	0.70	NR	NR	NR	[21]
			CVI-42	0.53	NR	NR	NR	[21]
			MTT	0.58	NR	NR	NR	[21]
			TomTec	0.53	NR	NR	NR	[21]
		ACM w/o major structural criteria	CardioTrack	0.61 [0.43, 0.72]	NR	0.95	0.28	[24]
		ACM vs. healthy athlete	Medis	0.63	−35.80	0.71	0.59	[4]
	Longitudinal Mid-wall	Definite ACM	Medis	0.71	NR	NR	NR	[21]
			CVI-42	0.61	NR	NR	NR	[21]
			MTT	0.74	NR	NR	NR	[21]
			TomTec	0.64	NR	NR	NR	[21]
		Preclinical	Medis	0.50	NR	NR	NR	[21]
			CVI-42	0.57	NR	NR	NR	[21]
			MTT	0.51	NR	NR	NR	[21]
			TomTec	0.56	NR	NR	NR	[21]

(*continued on next page*)

Table 3 (*continued*)

Ventricle	Variable	Discrimination between	Analysis Software	AUC [95 % CI]	Cut-point	Sensitivity	Specificity	Reference
		ACM vs. healthy athlete	Medis	0.77	−25.60	0.71	0.82	[4]
	Longitudinal Apica	Definite ACM	Medis	0.57	NR	NR	NR	[21]
			CVI-42	0.58	NR	NR	NR	[21]
			MTT	0.68	NR	NR	NR	[21]
			TomTec	0.47	NR	NR	NR	[21]
		Preclinical	Medis	0.43	NR	NR	NR	[21]
			CVI-42	0.49	NR	NR	NR	[21]
			MTT	0.56	NR	NR	NR	[21]
			TomTec	0.42	NR	NR	NR	[21]
		ACM vs. healthy athlete	Medis	0.69	−23.96	0.56	0.85	[4]
	Circumferential Basal	Definite ACM	CVI-42	0.87 [0.68, 1.00]	−12.40	0.94	0.78	[6]
			TomTec	0.82 [0.65, 1.00]	NR	NR	NR	[5]
	Circumferential Mid-wall	Definite ACM	CVI-42	0.83 [0.67, 0.99]	−13.30	0.88	0.67	[6]
			TomTec	0.79 [0.61, 0.96]	NR	NR	NR	[5]
	Circumferential Apical	Definite ACM	TomTec	0.52 [0.31, 0.73]	NR	NR	NR	[5]
	Radial Basal	Definite ACM	CVI-42	0.90 [0.77, 1.0]	16.70	0.81	0.78	[6]
			TomTec	0.68 [0.49, 0.87]	NR	NR	NR	[5]
		ACM vs. RVOT-VT	CVI-42	0.78 [0.63, 0.92]	15.10	0.75	0.70	[6]
	Radial Mid-wall	Definite ACM	CVI-42	0.80 [0.60, 1.0]	1.15	0.83	0.62	[6]
			TomTec	0.50 [0.29, 0.70]	NR	NR	NR	[5]
	Radial Apical	Definite ACM	TomTec	0.48 [0.26, 0.70]	NR	NR	NR	[5]
	Longitudinal Basal Strain Rate	Definite ACM	TomTec	NR	−2.41	0.95	0.70	[5]
		ACM vs. healthy athlete	Medis	0.67	−1.30	0.59	0.85	[4]
	Longitudinal Mid-wall Strain Rate	ACM vs. healthy athlete	Medis	0.69	−1.40	0.82	0.50	[4]
	Longitudinal Apical Strain Rate	ACM vs. healthy athlete	Medis	0.61	−0.90	0.38	0.91	[4]
	Circumferential Basal Strain Rate	Definite ACM	CVI-42	0.80 [0.55, 1.0]	−0.69	0.92	0.75	[6]
			TomTec	0.92 [0.81, 1.0]	−0.49	0.95	0.80	[5]
	Circumferential Mid-wall Strain Rate	Definite ACM	TomTec	0.78 [0.60, 0.95]	NR	NR	NR	[5]
	Circumferential Apical Strain Rate	Definite ACM	TomTec	0.52 [0.30, 0.74]	NR	NR	NR	[5]
	Radal Basal Strain Rate	Definite ACM	CVI-42	0.82 [0.62, 1.0]	1.03	0.83	0.75	[6]
			TomTec	0.82 [0.67, 0.98]	NR	NR	NR	[5]
	Radial Mid-wall Strain Rate	Definite ACM	TomTec	0.59 [0.37, 0.81]	NR	NR	NR	[5]
	RV Apical Strain Rate	Definite ACM	TomTec	0.56 [0.35, 0.77]	NR	NR	NR	[5]
	RVOT Endocardial Radial Strain	ACM vs. RVOT-VT	CVI-42	0.76 [0.59, 0.93]	55.40	0.79	0.58	[6]
	RVOT Endocardial Radial Strain Rate	ACM vs. RVOT-VT	CVI-42	0.79 [0.62, 0.97]	2.21	0.77	0.80	[6]
	Lateral TTP	Definite ACM	TomTec*	0.85 [0.72, 0.93]	NR	0.78	0.80	[27]
			TomTec†	0.85 [0.72, 0.93]	NR	NR	NR	[27]
	Lowest Longitudinal Strain	ACM vs. healthy athlete	Medis	0.79	−18.10	0.71	0.85	[4]
	Lowest Longitudinal Strain Rate	Definite ACM	TomTec	NR	−0.99	0.90	0.70	[5]
		ACM vs. healthy athlete	Medis	0.70	0.80	0.56	0.82	[4]
	LRSL	Definite ACM	CardioTrack	0.84 [0.75, 0.92]	NR	0.72	0.82	[24]
		ACM w/o major structural criteria	CardioTrack	0.75 [0.62, 0.88]	NR	0.62	0.79	[24]
LV	GLS	Definite ACM	CVI-42	0.82	−0.14	0.74	0.80	[15]
				0.79	NR	NR	NR	[17]
				0.93 [0.81, 1.00]	−18.30	0.93	0.89	[6]
		ACM with LV involvement	CVI-42	0.85	−9.50	0.26	1.00	[18]
		ACM vs. healthy athlete	Medis	0.60	−17.70	0.32	0.94	[4]

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Table 3 (*continued*)

Ventricle	Variable	Discrimination between	Analysis Software	AUC [95 % CI]	Cut-point	Sensitivity	Specificity	Reference
	GCS	Definite ACM	CVI-42	0.82	−17.68	0.81	0.77	[17]
		ACM with LV involvement	CVI-42	0.84	−14.00	0.51	1.00	[18]
		ACM vs. healthy athlete	Medis	0.64	−22.50	0.38	1.00	[4]
	GRS	Definite ACM	CVI-42	0.79	NR	NR	NR	[17]
		ACM with LV involvement	CVI-42	0.82	23.70	0.46	1.00	[18]
		ACM vs. healthy athlete	Medis	0.61	41.80	0.41	0.94	[4]
	Longitudinal Strain PCA	ACM with LV involvement (patients with moderate strain impairment)	CVI-42	0.78	−5.71	0.39	1.00	[19]
	Circumferential Strain PCA	ACM with LV involvement (patients with moderate strain impairment)	CVI-42	0.75	−6.91	0.35	1.00	[19]
	Radial Strain PCA	ACM with LV involvement (patients with moderate strain impairment)	CVI-42	0.71	14.93	0.39	1.00	[19]
	Longitudinal Mid-wall Strain	Definite ACM	CVI-42	0.82	−0.17	0.68	0.95	[15]
	Longitudinal Apical Strain	Definite ACM	CVI-42	0.84	−0.15	0.81	0.85	[15]
	Circumferential Dyssynchrony	ACM with LV involvement	CVI-42	0.74	55.60	0.31	1.00	[18]
	Radial Dyssynchrony	ACM with LV involvement	CVI-42	0.78	70.00	0.54	1.00	[18]
Index‡			TomTec*	0.94 [0.83, 0.99]	NR	0.93	0.80	[27]
Index§			TomTec†	0.94 [0.83, 0.99]	NR	NR	NR	[27]

ACM: Arrhythmogenic cardiomyopathy, AUC: Area Under the Curve, BrS: Brugada Syndrome, CI: Confidence Interval, GCS: Global Circumferential Strain, GLS: Global Longitudinal Strain, GRS: Global Radial Strain, LV: Left Ventricle, LRSL: Longitudinal Regional Strain of Left Ventricle, NR: Not Reported, PCA: Principal Component Analysis, RV: Right Ventricle, RVOT: Right Ventricular Outflow Tract, RVOT-A: Right ventricular outflow tract arrhythmias, RVOT-VT: Right ventricular outflow tract ventricular tachycardia, SD: Standard deviation, TTP: Time to Peak.
*: Based on the RV four-chamber view only
†: Based on RV four- and two-chamber view
‡: Index formula: (RV_TTP_lat_100*6.680 + RV_SD_TTP_average*0.097 + RVGLS*0.264)
§: Index formula: (RV_4ch*0.2763 + SD_4ch*0.0715 + Average_TTP_lat_RV_100*5.4575)

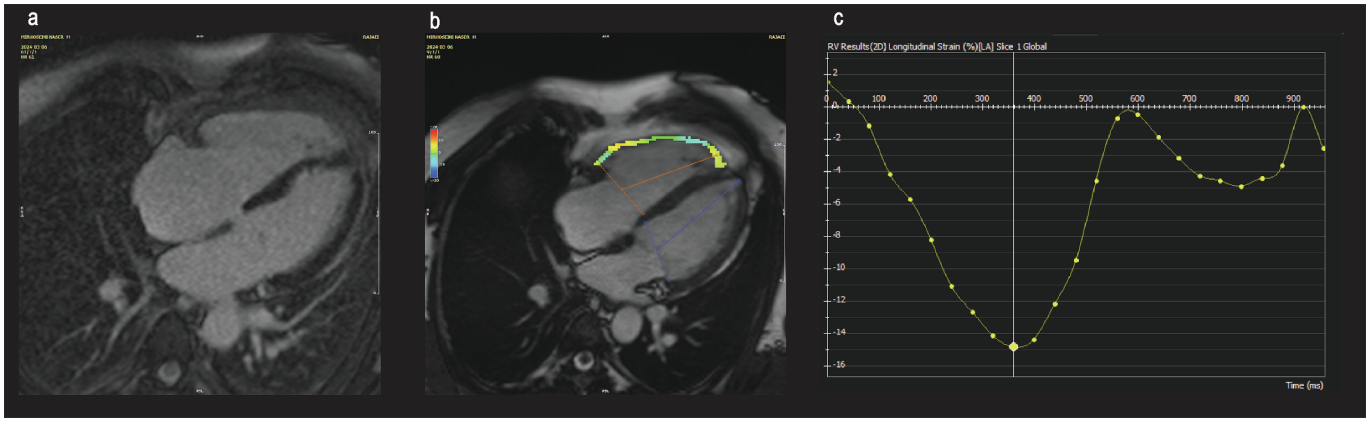

Fig. 7. (a) Delayed post-Gadolinium phase-sensitive inversion recovery sequence–four-chamber view–reveals RV free wall Gadolinium enhancement. (b) Global Longitudinal Strain (GLS) of RV free wall reveals a reduced GLS value of −14.0 % (lower limit of normal [95 %CI]: −16.4 % [−17.3 %, −15.5 %]) [42], and (c) color-coded image demonstrates reduced strain with RV free-wall turning green and yellow instead of blue. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

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Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijcha.2024.101455.

References

[1] G. Prati, G. Vitrella, G. Allocca, D. Muser, S.C. Buttignoni, G. Piccoli, et al., Right Ventricular Strain and Dyssynchrony Assessment in Arrhythmogenic Right Ventricular Cardiomyopathy: Cardiac Magnetic Resonance Feature-Tracking Study, Circ. Cardiovasc. Imaging 8 (2015) e003647, discussion e.
[2] A. Azimi, M. Pourirahim, G. Houshmand, S. Adimi, M. Maleki, S. Kalayinia, Arrhythmogenic left ventricular cardiomyopathy caused by a novel likely pathogenic DSP mutation, p.K1165Rfs*8, in a family with sudden cardiac death, BMC Med. Genomics 16 (2023) 266.

[3] P. Chungsomprasong, R. Hamilton, W. Luining, M. Fatah, S.J. Yoo, L. Grosse-Wortmann, Left Ventricular Function in Children and Adolescents With Arrhythmogenic Right Ventricular Cardiomyopathy, Am. J. Cardiol. 119 (2017) 778–784.

[4] C. Czimbalmos, I. Csecs, Z. Dohy, A. Toth, F.I. Suhai, A. Mussigbrodt, et al., Cardiac magnetic resonance based deformation imaging: role of feature tracking in athletes with suspected arrhythmogenic right ventricular cardiomyopathy, Int. J. Cardiovasc. Imaging 35 (2019) 529–538.

[5] P. Heermann, D.M. Hedderich, M. Paul, C. Schulke, J.R. Kroeger, B. Baessler, et al., Biventricular myocardial strain analysis in patients with arrhythmogenic right ventricular cardiomyopathy (ARVC) using cardiovascular magnetic resonance feature tracking, J. Cardiovasc. Magn. Reson. 16 (2014) 75.

[6] P. Heermann, H. Fritsch, M. Koopmann, P. Sporns, M. Paul, W. Heindel, et al., Biventricular myocardial strain analysis using cardiac magnetic resonance feature tracking (CMR-FT) in patients with distinct types of right ventricular diseases comparing arrhythmogenic right ventricular cardiomyopathy (ARVC), right ventricular outflow-tract tachycardia (RVOT-VT), and Brugada syndrome (BrS), Clin. Res. Cardiol. 108 (2019) 1147–1162.

[7] D. Corrado, M. Perazzolo Marra, A. Zorzi, G. Beffagna, A. Cipriani, M. Lazzari, et al., Diagnosis of arrhythmogenic cardiomyopathy: The Padua criteria, Int. J. Cardiol. 319 (2020) 106–114.

[8] W.J. McKenna, G. Thiene, A. Nava, F. Fontaliran, C. Blomstrom-Lundqvist, G. Fontaine, et al., Diagnosis of arrhythmogenic right ventricular dysplasia/ cardiomyopathy. Task Force of the Working Group Myocardial and Pericardial Disease of the European Society of Cardiology and of the Scientific Council on Cardiomyopathies of the International Society and Federation of Cardiology, Br. Heart J. 71 (1994) 215–218.

[9] F.I. Marcus, W.J. McKenna, D. Sherrill, C. Basso, B. Bauce, D.A. Bluemke, et al., Diagnosis of arrhythmogenic right ventricular cardiomyopathy/dysplasia: proposed modification of the task force criteria, Circulation 121 (2010) 1533–1541.

[10] D. Corrado, A. Zorzi, A. Cipriani, B. Bauce, R. Bariani, G. Beffagna, et al., Evolving Diagnostic Criteria for Arrhythmogenic Cardiomyopathy, J. Am. Heart Assoc. 10 (2021) e021987.

[11] M. Bourfiss, N.H.J. Prakken, C.A. James, R.N. Planken, S.M. Boekholdt, D. Ahmetagic, et al., Prognostic value of strain by feature-tracking cardiac magnetic resonance in arrhythmogenic right ventricular cardiomyopathy, Eur. Heart J. Cardiovasc. Imaging 24 (2022) 98–107.

[12] M.J. Page, J.E. McKenzie, P.M. Bossuyt, I. Boutron, T.C. Hoffmann, C.D. Mulrow, et al., The PRISMA 2020 statement: An updated guideline for reporting systematic reviews, Int. J. Surg. 88 (2021) 105906.

[13] G.A. Wells, B. Shea, D. O'Connell, J. Peterson, V. Welch, M. Losos et al., The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses, 2000.

[14] A. Alshabanat, Z. Zafari, O. Albanyan, M. Dairi, J.M. FitzGerald, Asthma and COPD Overlap Syndrome (ACOS): A Systematic Review and Meta Analysis, PLoS One 10 (2015) e0136065.

[15] X. Chen, L. Li, H. Cheng, Y. Song, K. Ji, L. Chen, et al., Early Left Ventricular Involvement Detected by Cardiovascular Magnetic Resonance Feature Tracking in Arrhythmogenic Right Ventricular Cardiomyopathy: The Effects of Left Ventricular Late Gadolinium Enhancement and Right Ventricular Dysfunction, J. Am. Heart Assoc. 8 (2019) e012989.

[16] Z. Dong, X. Ma, J. Wang, S. Yang, S. Yu, Y. Song, et al., Incremental Diagnostic Value of Right Ventricular Strain Analysis in Arrhythmogenic Right Ventricular Cardiomyopathy, J. Am. Heart Assoc. 13 (2024) e031403.

[17] M.T. Shen, Z.G. Yang, K.Y. Diao, L. Jiang, Y. Zhang, X. Liu, et al., Left Ventricular Involvement in Arrhythmogenic Right Ventricular Dysplasia/Cardiomyopathy Predicts Adverse Clinical Outcomes: A Cardiovascular Magnetic Resonance Feature Tracking Study, Sci. Rep. 9 (2019) 14235.

[18] Y. Vives-Gilabert, J. Sanz-Sanchez, P. Molina, A. Cebrian, B. Igual, P. Calvillo-Batlles, et al., Left ventricular myocardial dysfunction in arrhythmogenic cardiomyopathy with left ventricular involvement: A door to improving diagnosis, Int. J. Cardiol. 274 (2019) 237–244.

[19] Y. Vives-Gilabert, E. Zorio, J. Sanz-Sanchez, P. Calvillo-Batlles, J. Millet, F. Castells, Classification model based on strain measurements to identify patients with arrhythmogenic cardiomyopathy with left ventricular involvement, Comput. Methods Programs Biomed. 188 (2020) 105296.

[20] G. Muscogiuri, L. Fusini, F. Ricci, R. Sicuso, M. Guglielmo, A. Baggiano, et al., Additional diagnostic value of cardiac magnetic resonance feature tracking in patients with biopsy-proven arrhythmogenic cardiomyopathy, Int. J. Cardiol. 339 (2021) 203–210.

[21] M. Bourfiss, D.M. Vigneault, M. Aliyari Ghasebeh, B. Murray, C.A. James, C. Tichnell, et al., Feature tracking CMR reveals abnormal strain in preclinical arrhythmogenic right ventricular dysplasia/ cardiomyopathy: a multisoftware feasibility and clinical implementation study, J. Cardiovasc. Magn. Reson. 19 (2017) 66.

[22] D.M. Vigneault, A.S. te Riele, C.A. James, S.L. Zimmerman, M. Selwaness, B. Murray, et al., Right ventricular strain by MR quantitatively identifies regional dysfunction in patients with arrhythmogenic right ventricular cardiomyopathy, J. Magn. Reson. Imaging 43 (2016) 1132–1139.

[23] M.Å. Aneq, J. Engvall, L. Brudin, E. Nylander, Evaluation of right and left ventricular function using speckle tracking echocardiography in patients with arrhythmogenic right ventricular cardiomyopathy and their first degree relatives, Cardiovasc. Ultrasound 10 (2012) 1–9.

[24] M. Laredo, J. Lamy, K. Bouazizi-Verdier, M. Gueda, A. Giron, A. Gallo, et al., Feasibility of a New Regional Myocardial Strain Parameter for the Detection of Wall Motion Abnormalities in Arrhythmogenic Right Ventricular Cardiomyopathy, Radiol Cardiothorac Imaging. 5 (2023) e220160.

[25] K. Taha, M. Bourfiss, A. Te Riele, M.M. Cramer, J.F. van der Heijden, F. W. Asselbergs, et al., A head-to-head comparison of speckle tracking echocardiography and feature tracking cardiovascular magnetic resonance imaging in right ventricular deformation, Eur. Heart J. Cardiovasc. Imaging 22 (2021) 950–958.

[26] !!! INVALID CITATION !!! (6, 15-22).

[27] M. Astrom Aneq, E. Maret, L. Brudin, A. Svensson, J. Engvall, Right ventricular systolic function and mechanical dispersion identify patients with arrhythmogenic right ventricular cardiomyopathy, Clin. Physiol. Funct. Imaging 38 (2018) 779–787.

[28] A.J. Teske, M.G. Cox, A.S. Te Riele, B.W. De Boeck, P.A. Doevendans, R.N. Hauer, et al., Early detection of regional functional abnormalities in asymptomatic ARVD/C gene carriers, J. Am. Soc. Echocardiogr. 25 (2012) 997–1006.

[29] D. Corrado, C. Basso, G. Thiene, Arrhythmogenic right ventricular cardiomyopathy: diagnosis, prognosis, and treatment, Heart 83 (2000) 588–595.

[30] A.S. Te Riele, C.A. James, B. Philips, N. Rastegar, A. Bhonsale, J.A. Groeneweg, et al., Mutation-positive arrhythmogenic right ventricular dysplasia/cardiomyopathy: the triangle of dysplasia displaced, J. Cardiovasc. Electrophysiol. 24 (2013) 1311–1320.

[31] A. Te Riele, H. Tandri, D.M. Sanborn, D.A. Bluemke, Noninvasive Multimodality Imaging in ARVD/C, J. Am. Coll. Cardiol. Img. 8 (2015) 597–611.

[32] M. Cerrone, J. Montnach, X. Lin, Y.T. Zhao, M. Zhang, E. Agullo-Pascual, et al., Plakophilin-2 is required for transcription of genes that control calcium cycling and cardiac rhythm, Nat. Commun. 8 (2017) 106.

[33] D. Segura-Rodriguez, F.J. Bermudez-Jimenez, L. Gonzalez-Camacho, E. Moreno Escobar, R. Garcia-Orta, J.E. Alcala-Lopez, et al., Layer-Specific Global Longitudinal Strain Predicts Arrhythmic Risk in Arrhythmogenic Cardiomyopathy, Front Cardiovasc Med. 8 (2021) 748003.

[34] Y. Song, L. Li, X. Chen, K. Ji, M. Lu, R. Hauer, et al., Left Ventricular Longitudinal Dyssynchrony by CMR Feature Tracking Is Related to Adverse Prognosis in Advanced Arrhythmogenic Cardiomyopathy, Front Cardiovasc Med. 8 (2021) 712832.

[35] L.P. Bosman, A. Te Riele, Arrhythmogenic right ventricular cardiomyopathy: a focused update on diagnosis and risk stratification, Heart 108 (2022) 90–97.

[36] P.C. Almeida, V. Lopes, L.A. Ferreira, N. Moreira, C.M. Marto, L. Gonçalves, et al., Role of Cardiac Magnetic Resonance in the Diagnosis of Infiltrative, Hypertrophic, and Arrhythmogenic Cardiomyopathies, Front. Biosci. (Schol. Ed.) 14 (2022) 7.

[37] M. Odak, S. Douedi, A. Mararenko, A. Alshami, I. Elkherpitawy, H. Douedi, et al., Arrhythmogenic Right Ventricular Cardiomyopathy: The Role of Genetics in Diagnosis, Management, and Screening, Cardiol Res. 13 (2022) 177–184.

[38] S. Ermakov, M. Scheinman, Arrhythmogenic right ventricular cardiomyopathy–antiarrhythmic therapy, Arrhythmia Electrophysiol. Rev. 4 (2015) 86.

[39] E. Potter, T.H. Marwick, Assessment of Left Ventricular Function by Echocardiography: The Case for Routinely Adding Global Longitudinal Strain to Ejection Fraction, J. Am. Coll. Cardiol. Img. 11 (2018) 260–274.

[40] B.P. Halliday, R. Senior, D.J. Pennell, Assessing left ventricular systolic function: from ejection fraction to strain analysis, Eur. Heart J. 42 (2021) 789–797.

[41] J.L. Vos, T. Leiner, A.P.J. van Dijk, H.B. van der Zwaan, G.T. Sieswerda, R. J. Snijder, et al., Right atrial and ventricular strain detects subclinical changes in right ventricular function in precapillary pulmonary hypertension, Int. J. Cardiovasc. Imaging 38 (2022) 1699–1710.

[42] T.K.M. Wang, R.A. Grimm, L.L. Rodriguez, P. Collier, B.P. Griffin, Z.B. Popović, Defining the reference range for right ventricular systolic strain by echocardiography in healthy subjects: A meta-analysis, PLoS One 16 (2021) e0256547.