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Title: Cardiac structure and function in resistance-trained and untrained adults: A systematic Review and Meta-Analysis.

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ABSTRACT

Background: Variations in the hemodynamic demands of specific training modalities may explain characteristic differences in cardiac structure and function amongst athletes. However, current consensus regarding these adaptations in highly resistance-trained athletes is yet to be established. **Objective:** To collate research investigating cardiac structure and function in resistance-trained athletes, exploring the defining characteristics of Athlete's Heart within these individuals. **Design:** Systematic selection and quality appraisal of articles was performed by two reviewers. A random effects meta-analysis model was applied to suitable studies. **Data sources:** Seven electronic databases were searched. **Eligibility criteria for selecting studies:** Studies which examined at least one measure of cardiac structure or function, included healthy, normotensive male or females (>18 years); and compared athletes engaged in a resistance training program (>12 months) to an untrained group engaged in no structured training program were included. Studies were limited to peer-reviewed articles and in English. **Results:** Resistance-trained athletes (n=949) demonstrated greater cardiac dimensions compared to their untrained counterparts. No clear impairments to systolic or diastolic cardiac function were observed in athletic population studied here. **Summary/Conclusion:** Resistance-trained athletes display some characteristics of the Athletes Heart phenomenon including greater wall thickening and chamber dilation compared to their untrained counterparts.

KEY WORDS: Hypertrophy; Exercise-induced; Exercise training; Echocardiography

INTRODUCTION

Substantial evidence of cardiac chamber enlargement and wall thickening in individuals exposed to chronic exercise training has been previously documented and reviewed [1, 2]. This phenomenon, known as the Athlete's Heart, may be described as morphological adaptations to any of the four chambers of the heart which leads to resultant distinctive changes in cardiac function following the physiological stress of chronic exercise [1]. It has been hypothesized that such adaptations may be training-specific, with endurance and resistance training both reflecting a differing hemodynamic demand [2, 3].

With cardiac output in endurance trained athletes being shown to increase from approximately 5 $L \cdot min^{-1}$ at rest, to nearly 40 $L \cdot min^{-1}$ during maximal exercise [4], dynamic aerobic exercise imposes a high hemodynamic volume overload on the left ventricle (LV). Over time these athletes have displayed structural alterations to the myocardium known as an eccentric pattern of hypertrophy whereby proportional increases in chamber dilation and wall thickness are observed [5]. Conversely, resistance training is characterized by static exercise, whereby, overload to the myocardium occurs following elevations in pressure and wall stress [3]. It is this exercising modality which when sustained, has been suggested to induce a concentric pattern of left ventricular hypertrophy where new sarcomeres are laid down in parallel to original ones increasing both LV wall thickness and overall LV mass (LVM) [5, 6].

Despite previous reviews indicating that resistance training increases ventricular septal wall thickness, posterior wall thickness and LVM [7], absence of a training-specific pattern of concentric hypertrophy in many resistance-trained athletes [3] has highlighted that the physiological stress experienced during lifting may not be sufficient to cause a distinct pressure overload, in part due to the involuntary implementation of a Valsalva maneuver [8, 9]. Moreover, the underlying use of anabolic steroids within this athletic population [10, 11], and the variation in resistance-training programs undertaken may lead to alterations to cardiac structure and function within these athletes which are not routinely acknowledged.

Non-invasive techniques including echocardiography and magnetic resonance imagining are modalities ideal for investigating LV geometry and the quantification of cardiac dimensions. However, whilst

77 further understanding of normative echocardiographic dimensions in resistance-trained athletes is
78 needed for clinicians to distinguish clearly between pathological and physiological hypertrophy, it is
79 important to remember the difficulties in standardizing and comparing cardiac parameters from
80 previous papers (e.g., due to sonographer experience, updated ultrasound technology and guidelines for
81 chamber quantification). Research examining the Athlete's Heart has primarily focused on younger,
82 elite-level males typically <50 years [2, 12], and rarely in older adults [13, 14]. With significant
83 variations in the degree of adaptations observed within this population in previous research it is
84 currently difficult to provide clear guidance to clinicians regarding normal reference values for cardiac
85 dimensions in adults exposed to chronic resistance training.

86 Therefore, the aim of this systematic review and meta-analysis is to examine (1) the morphology of the
87 resistance-trained heart; and (2) cardiac function in resistance-trained athletes. To the authors'
88 knowledge, this systematic review is the first to focus solely on directly comparing cardiac parameters
89 in resistance-trained individuals to untrained individuals across a wider age range and therefore is vital
90 for providing a more in-depth understanding of the typical characteristics of the Athlete's Heart which
91 are displayed in these athletes. Additionally, the information collected here can be used to inform
92 clinicians when examining cardiac structure and function, to establish the cardiac morphology of the
93 resistance-trained heart compared to that of untrained individuals.
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METHODS

This review was designed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [15]. Ethical approval was obtained from the University of Bedfordshire Institute of Sport and Physical Activity Research Committee (2020ISPAR004). The review was registered on PROSPERO (CRD42020197272).

Study search and selection

Seven electronic databases (PubMed, CINAHL, MEDLINE, ScienceDirect, EBSCO, Scopus, and Academic Search Elite) were systematically searched in November 2021, using Boolean operators for the terms (Appendix 1). Searches were limited to original peer-reviewed research articles published in English, with no date restriction applied. Search results were downloaded in Covidence online systematic review software (Veritas Health Innovation, Melbourne, Australia. Available at www.covidence.org) where duplicates were removed. Studies were identified for inclusion based on the population, intervention, comparator, and outcome (PICO) method outlined in Table 1. Studies without a clear statement regarding participants blood pressure, no clear evidence of a comparison to an untrained group and those that included individuals with any history, or immediate family history of cardiovascular disease were excluded, as well as any study investigating the effects of a resistance training intervention on previously untrained adults, rather than a direct comparison of a resistance-trained population versus an untrained population.

Table 1: Population, intervention, comparator, and outcome (PICO) model used for eligibility criteria and study selection

Patient, Population or Problem	Male or females, aged ≥18 years. Free from cardiovascular disease or immediate family history of cardiovascular disease. Normotensive.
Intervention or Exposure	Trained athletes engaged in a resistance training program of exercise for ≥12 months prior to data collection [3]
Comparison	Untrained individuals who engaged in no structured training program or competitive sport for the last 12 months.
Outcome	Studies must report on at least one cardiac parameter examining left ventricular structure or function measured by either echocardiography or magnetic resonance imaging.

Following the removal of duplicates, a two-phase search strategy was undertaken; study titles and abstracts were reviewed (AMS) before the remaining studies were retrieved and assessed against the inclusion/exclusion criteria (AMS and JR). Discrepancies were resolved through discussion between the first and second reviewer, any further disagreements were resolved by consulting a third reviewer (RLJ). The reference lists of relevant articles and review articles were hand-searched to identify any further studies and were added to full-text screening manually.

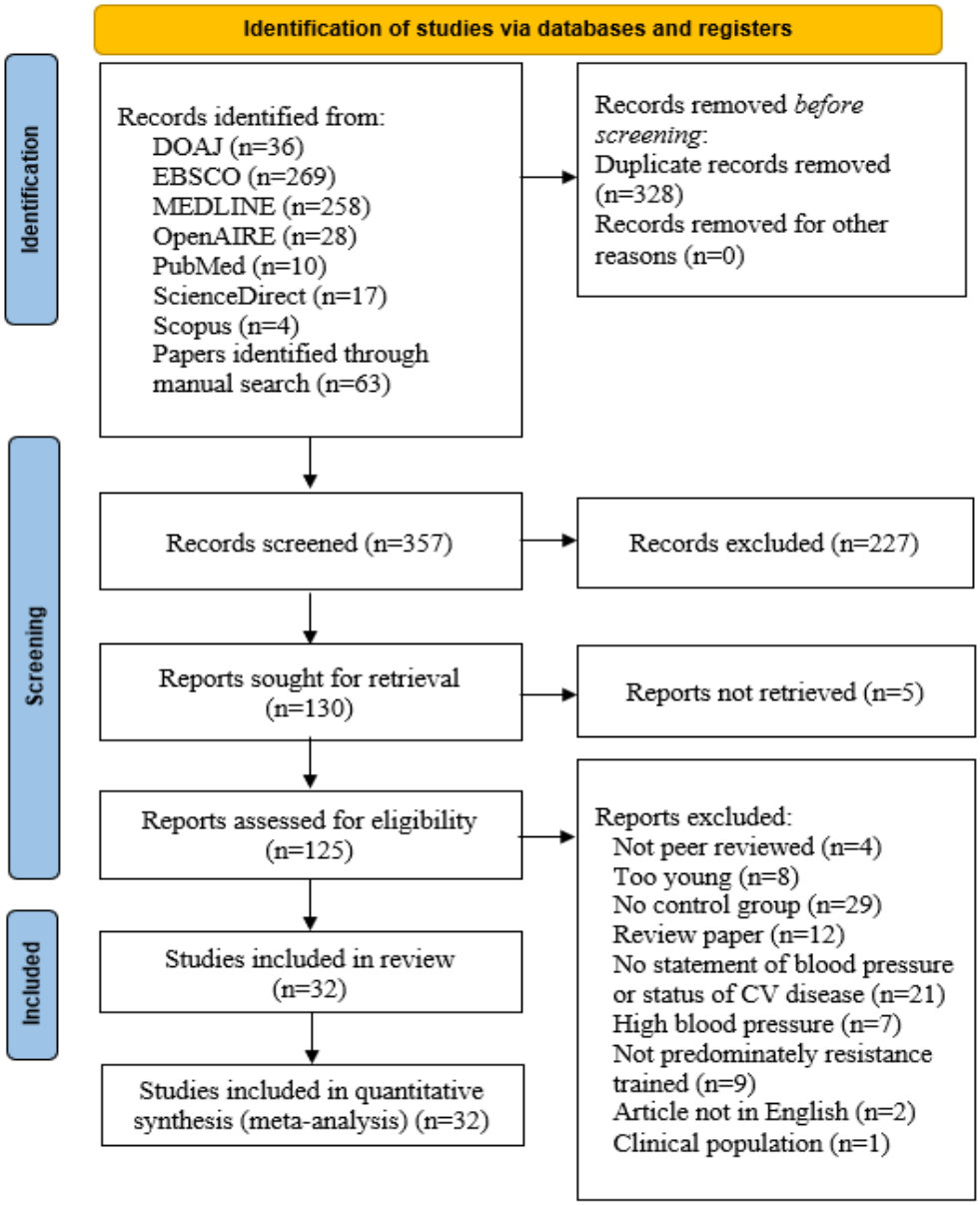

Figure 1: PRISMA Flow diagram of the study selection process for eligible studies in the systematic review and meta-analysis.

131 ***Quality appraisal and data extraction***

132 Two independent reviewers (AMS and JR) critically assessed methodological quality using the set
133 guidelines outlined by the appraisal tool for cross-sectional studies (AXIS) [16]. This tool consists of
134 20 components designed to aid researchers in evaluating study design, reporting quality and risk of bias
135 in cross-sectional studies across disciplines. Data extraction was independently conducted by the
136 primary author using a standardized and pre-piloted data extraction form (Excel Office 2016,
137 Microsoft). The data extracted from eligibility studies are outlined in Table 2. Other parameters
138 including right ventricle (RV) function were considered during initial data extraction but were reported
139 in less than three studies and therefore were not selected for analysis. For any studies included for
140 review with missing or incomplete data, the corresponding author was contacted and asked for the
141 necessary supplementary data.

Table 2: Data extracted from eligible studies

Characteristics	**Further details**
General information	Author names, publication year, country
Population	Overall sample size, number of participants in each relevant group, sex, age, height, body mass, body composition, resting heart rate, resting blood pressure
Exercise Exposure and Comparison Details	Predominate sport undertaken, hours trained per day/week, number of years this program had been followed, competitive status of athletic group, activity level (untrained comparison group)
Outcomes (Cardiac parameters)	Wall dimensions (interventricular septum (IVS), posterior wall (PWT), relative wall thickness (RWT)), chamber dimensions (LV internal diameter (LVID), aortic diameter (Ao), atrial diameter (AtrD), right ventricle area (RVarea), right ventricle diameter (RVdia)), LV end-systolic volume (ESV), LV end-diastolic volume (EDV) left ventricular mass (LVM), left ventricular mass indexed to body surface area (LVMi), stroke volume (SV), cardiac output (Q), fractional shortening (FS), ejection fraction (EF), trans-mitral blood flow velocities (LV peak early flow (E), LV peak atrial flow (A), E/A ratio, deceleration time (DT), isovolumic relaxation time (IVRT)), peak lateral tissue velocities (early diastole (e'), late diastole (a'), systolic phase (s'), e'/a' ratio), E/e' ratio, pulmonary pressure (PulP), global longitudinal strain (GLS)

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Data analysis

Data were reported as group mean ± 1 standard deviation (SD) in a spreadsheet (Excel Office 2016, Microsoft) for both the resistance-trained (RT) and untrained (UT) groups. To further explore the impact of a resistance training exercise modality on structural and functional cardiac parameters, a random effects meta-analysis model was applied using a pre-populated spreadsheet [17]. To quantify study-to-study heterogeneity both a Q statistic and an I^2 statistic were used. Studies with a Q statistic of >0.05 and an I^2 statistic of <75% were found to have no significant evidence of study-to-study heterogeneity. Levels of heterogeneity for each variable were categorized as low (<25%), moderate (≥25-50%) or high (≥50-75%) [18]. Additionally, further subgroup analyses exploring the impact of imaging modality (MRI) and anabolic steroid use was conducted using a random effect meta-analysis model. Cohens *d* levels (low: d=0.2-0.5, moderate: d=0.5-0.8, and high: d ≥0.8) were used to grade the effect size level [19]. Multiple two-sample independent t-tests were conducted for participant demographic data in a spreadsheet (Excel Office 2016, Microsoft). All statistical significance set at $p \leq 0.05$.

RESULTS

Study and sample characteristics

A total of 622 studies were identified and selected by the search process, with an additional 63 records identified through manual searching (Figure 1). Following duplication removal, 357 articles remained, with an additional 227 studies excluded during title and abstract screening. Following full-text screening, 32 studies remained for inclusion in the final synthesis (Figure 1). When examining the AXIS guidelines for assessing methodological quality the most frequent score was 17 out of 20 points. Over 70% of studies score ≥16 points with all studies scoring more than 13 out of 20 points. The most common issues highlighted were failures to justify the sample size used, describe methods detailed enough to be repeated, or form developed discussions on the limitations of the studies.

All 32 studies had two distinct populations – resistance-trained individuals and untrained individuals. Studies were conducted in 15 different countries: Australia (1), Brazil (2), Finland (1), France (2), Greece (1), Israel (4), Italy (7), Japan (1), Netherlands (2), New Zealand (1), Russia (1), Serbia (1), Turkey (1), the United Kingdom (4) and the United States (3). A total of 2,002 participants were included, with an average of 66 participants in each study (range: 17 to 334). Participants were predominately male (n=1,733) with females representing 16% of participants (n=269). Six studies reported mixed groups including males and females, whilst two studies used only female participants [20,21]. The 32 studies presented in this review provided data on 949 resistance-trained athletes and 1053 untrained individuals. Sixteen of these studies classified their athletic population as international or national-level, four as elite/sub-elite, four as competitive, and two as amateur athletes. The competitive status of athletes in the remaining six studies was not described. The average training program of the 949 athletes included consisted of 12 hours per week [95%CI: 10 - 15], four training sessions per week [95%CI: 3 - 5], for 5 years [95%CI: 4 – 6]. No studies reported the resistance trained athletes to be engaged in any aerobic exercise during their training programs.

General participant characteristics

The resistance-trained participants were similar in age (RT: 29 years [95%CI: 26 - 31]; CON: 29 years [95%CI: 27 - 32] and height (RT: 174 cm [95%CI: 172 - 177], CON: 175 cm [CI: 173 - 177]) to the

199 untrained individuals ($p > 0.05$). Body mass did not significantly differ between the RT (78.8 kg
200 [95%CI: 73.6 - 84.0]) and the untrained participants (74.2 kg [95%CI: 71.9 - 76.5]) ($p > 0.05$). The
201 average systolic (RT: 122 mmHg [95%CI: 121 - 125]; CON: 122 mmHg [95%CI: 120 - 124]) and
202 diastolic pressures (RT:75 mmHg [95%CI: 73 - 77]; CON: 76 mmHg [95%CI: 74 - 78] did not differ
203 greatly between the populations ($p > 0.05$). However, a significant difference was observed in resting
204 heart rate between the trained (65 bpm [95%CI: 63 - 67]) and untrained (69 bpm [95%CI: 68 - 71])
205 participants ($p = 0.005$).

206 ***Cardiac parameters***

207 The results demonstrating the impact of a resistance exercise training modality on various structural
208 and functional parameters of the heart are summarized in Table 3. The combined effect sizes of all
209 structural measurements with regards to cardiac mass and wall thickness demonstrated greater
210 dimensions in the resistance-trained participants compared to the untrained participants ($p <0.05$).
211 However, for each of these variables, high heterogeneity was evident (Table 3) and Egger's test
212 indicated there was publication bias ($p < 0.05$).

213 When examining chamber dimension, RT athletes displayed greater LV internal diameter (LVID)
214 during diastole than the untrained group (ES = -0.45, $p = 0.002$) with no obvious publication bias ($t = -$
215 1.46, $p = 0.16$). There were no significant differences between RT athletes and the untrained group of
216 untrained individuals with regards to LVID during systole with no obvious publication bias. The
217 combined effect sizes for both aortic and LV atrial diameter were non-significant with no publication
218 bias evident for either variable. When investigating the difference in end-systolic volume between RT
219 athletes and untrained individuals, data pooled from five data sets produced a non-significant combined
220 effect size (ES = -0.37, $p = 0.32$) however RT athletes did demonstrate greater end-diastolic volume
221 than their untrained counterparts when examining the combined effect size from a total of seven data
222 set (ES = -0.95, $p = 0.001$). There was no evidence of publication bias for any of the six variables above
223 ($p > 0.05$), but significant heterogeneity was also noted for each (Table 3).

The pooled data for general functional parameters showed no significant difference between RT athletes and untrained individuals with no obvious publication bias ($p > 0.05$) but significant heterogeneity noted when examining stroke volume, cardiac output, ejection fraction and fractional shortening (Table 3).

Transmitral blood flow velocity during early diastole was greater in RT athletes than CON individuals (ES = -0.45, $p = 0.016$), however there was significant heterogeneity between the studies and evidence of publication bias ($p < 0.05$). Furthermore, RT athletes demonstrated a greater E/A ratio than the untrained group (ES = -0.55, $p = 0.032$), with no evidence of publication bias from this pooled data ($t = -1.03$, $p = 0.31$). No significant difference in combined effect size were observed between RT athletes and untrained individuals with regards to transmitral blood flow velocity during late diastole, isovolumic relaxation time or deceleration time (Table 3).

Several studies (n = 4) presented data on tissue velocities of the LV lateral wall, with no significant differences between RT athletes and CON participants ($p > 0.05$), no publication bias was evident ($p > 0.05$). Peak lateral tissue velocity in late diastole was the only tissue velocity measure to display heterogeneity <75% (Table 3). There was no significant difference in global longitudinal strain between RT athletes and CON participants ($p > 0.05$).

A small number of studies (n=6) presented data on the RV of resistance-trained and untrained individuals (Table 3). No significant difference in RV area during systole, RV diameter in diastole or pulmonary pressure were seen between the two groups ($p>0.05$). However, the combined effect size for RV area during diastole that was reported in three studies found a significantly greater area in the RT athletes (ES = -0.43, p-0.008), with no obvious publication bias ($t= -0.77$, $p = 0.580$) or significant heterogeneity ($I^2 = 11\%$, $p = 0.324$). No studies in this review presented data for RV internal diameter in systole.

Table 3: Cardiac structural and functional parameters in resistance-trained and untrained adults.

Parameter	Resistance-trained (RT)	Untrained (UT)	Effect size	P value	Egger's test		Heterogeneity test		
					T value	P value	Q	I^2(%)	P value
LV mass (g)	197 (179 to 216) [n=20; 685]	158 (147 to 169) [n=20, 747]	-1.29	0.001	-2.73	0.013	347.9	94	<0.001
LV mass indexed (g/m^2)	107 (96 to 117) [n=17; 585]	83 (76 to 89) [n=17; 534]	-2.38	0.001	-4.39	0.001	362.3	95	<0.001
Interventricular septum in diastole (mm)	10.9 (10.3 to 11.6) [n=23; 610]	9.1 (8.7 to 9.4) [n=23; 673]	-1.76	0.001	-4.59	0.001	309.1	92	<0.001
Posterior wall thickness in diastole (mm)	10.7 (10.1 to 11.3) [n=22; 569]	8.8 (8.5 to 9.1) [n=22; 601]	-2.14	0.001	-5.53	0.001	269.7	91	<0.001
Relative wall thickness	0.42 (0.40 to 0.43) [n=11; 247]	0.36 (0.33 to 0.39) [n=11; 258]	-1.50	0.001	-2.62	0.028	98.5	89	<0.001
LV internal diameter in diastole (mm)	50.3 (48.6 to 51.9) [n=23; 642]	48.7 (47.5 to 49.8) [n=23; 689]	-0.47	0.001	-1.64	0.114	124.8	79	<0.001
LV internal diameter in systole (mm)	31.2 (29.7 to 32.6) [n=15; 435]	31.5 (30.3 to 32.7) [n=15; 446]	0.17	0.453	1.63	0.124	95.9	83	<0.001
End-diastolic volume (ml)	133.5 (111.3 to 155.8) [n=7; 186]	119.4 (94.4 to 144.5) [n=7;282]	-0.76	0.001	1.28	0.242	26.4	70	0.001
End-systolic volume (ml)	47.6 (35.0 to 60.2) [n=5; 100]	43.8 (28.6 to 58.9) [n=5;113]	-0.37	0.321	-1.17	0.306	26.71	81	<0.001
Aortic Diameter (mm)	30.2 (28.8 to 31.6) [n=7; 319]	26.9 (20.8 to 32.9) [n=7; 338]	-0.33	0.397	-0.33	0.753	47.5	87	<0.001
Atrial Diameter (mm)	32.6 (30.9 to 34.60) [n=9; 397]	32.2 (30.4 to 34.1) [n=7; 429]	-0.25	0.362	0.26	0.800	68.2	88	<0.001
Stroke volume (ml)	91 (77 to 104) [n=9; 264]	83 (71 to 95) [n=9; 200]	0.01	0984	-0.05	0.964	248.8	96	<0.001
Cardiac Output (L)	5.7 (4.5 to 6.9) [n=5; 171]	5.7 (4.9 to 6.4) [n=5; 107]	0.22	0.638	-1.23	0.274	46.2	89	<0.001
Ejection Fraction (%)	64 (62 to 67) [n=16; 591]	65 (63 to 67) [n=5; 766]	0.32	0.343	1.86	0.081	284.5	94	<0.001
Fractional shortening (%)	37 (35 to 39) [n=14; 311]	36 (35 to 37) [n=5; 260]	-0.18	0.334	0.37	0.714	58.07	74	<0.001
LV peak early trans-mitral flow velocity (cm/s)	78.6(73.3 to 83.9) [n=9; 298]	74.9 (69.4 to 80.3) [n=9;430]	-0.45	0.016	2.66	0.029	54.92	84	<0.001
LV peak late trans-mitral flow velocity (cm/s)	50.1 (45.2 to 54.9) [n=9; 298]	48.3 (44.0 to 52.6) [n=9; 430]	-0.11	0.606	1.09	0.308	88.8	90	<0.001
E/A ratio	1.8 (1.6 to 2.0) [n=16; 445]	1.7 (1.6 to 1.8) [n=16; 621]	-0.55	0.032	-1.03	0.317	162.7	90	<0.001
Deceleration Time (ms)	197 (174 to 219) [n=9; 311]	191 (172 to 210) [n=9; 393]					116.2	92	<0.001
Isovolumic relaxation time (ms)	78 (67 to 90) [n=6; 235]	74 (68 to 81) [n=6; 348]	0.16	0.701	0.63	0.554	107.4	94	<0.001
Peak lateral tissue velocity in early diastole (cm/s)	15.8 (14.2 to 17.6) [n=4; 101]	14.8 (12.0 to 17.7) [n=4; 93]	-0.17	0.633	0.70	0.522	23.31	79	<0.001

Peak lateral tissue velocity in late diastole (cm/s)	9.2 (8.1 to 10.3) [n=4; 101]	8.7 (7.5 to 9.9) [n=4; 93]	-0.01	0.942	-0.09	0.929	8.97	**44**	**0.110**
Peak lateral tissue velocity in systole (cm/s)	10.4 (9.7 to 11.2) [n=4; 101]	10.0 (9.0 to 11.0) [n=4; 93]	-0.08	0.755	0.39	0.719	16.33	69	0.006
LV lateral tissue e'/a' ratio	2.0 (1.4 to 2.7) [n=3; 81]	2.2 (1.9 to 2.5) [n=3; 83]	-0.05	0.885	0.98	0.430	10.2	71	0.017
E/e' ratio	6.2 (5.7 to 6.7) [n=4; 105]	6.6 (6.1 to 7.1) [n=4; 96]	-0.03	0.947	-0.56	0.616	27.5	86	<0.001
RV area in diastole (cm^2)	20.7 (16.0 to 25.4) [n=3; 84]	18.7 (14.6 to 22.70 [n=3; 82]	-0.43	0.008	-0.77	0.580	2.26	**11**	**0.324**
RV area in systole (cm^2)	10.8 (8.6 to 13.10) [n=3;84]	10.0 (8.0 to 11.9) [n=3; 82]	-0.23	0.341	-0.42	0.745	4.43	**55**	**0.109**
RV internal diameter in diastole (mm)	27.3 (22.9 to 31.70 [n=6; 253]	25.8 (22.0 to 29.5) [n=6; 342]	-0.82	0.099	-2.04	0.111	79.09	94	<0.001
Pulmonary Pressure (mmHg)	21.2 (19.2 to 23.1) [n=3; 79]	18.9 (18.3 to 19.4) [n=3; 81]	-1.06	0.206	-0.46	0.728	40.4	95	<0.001
Global longitudinal strain (%)	19 (16 to 22) [n=3; 101]	19 (18 to 20) [n=3; 102]	0.07	0.887	0.31	0.810	20.7	90	<0.001

Data presented mean (95% confidence interval) [Number of studies; Number of participants]. Bold = both a Q statistic at >0.05 and an I^2 statistic of <75% = non-significant heterogeneity.

There was significant evidence of study-to-study heterogeneity with I^2 statistic > 75% and p-values < 0.05 in many cardiac parameters (n = 25; Table 3). However, results of a random-effects meta-analysis model for the cardiac parameters with non-significant heterogeneity are presented in Table 4. Study-to-study heterogeneity was reported as moderate for peak tissue velocity of the LV lateral wall in late diastole, but no significant differences were observed between the two groups (ES = -0.01, p = 0.952). Additionally, RV area in systole showed high heterogeneity (I^2 = 55%, p = 0.109) with no significant difference between the RT athletes and untrained individuals (ES = -0.23, p = 0.341).

Evidence of high heterogeneity, in addition to previous research highlighting differences in imaging modality [2] and the impact of steroid use on cardiac parameters [12], gave a strong rationale to perform sub-group analysis on all variables. Following the removal of studies using MRI, an additional variable presented with non-significant heterogeneity. RT athletes demonstrated significantly larger LV end-diastolic volume than untrained individuals with a large effect size noted (ES = 0.95, p < 0.001). Study-to-study heterogeneity remained high for all other variables (data not reported). Studies including known steroid users were removed during sub-group analysis (n = 2) [22,23]. Following this, a meta-analysis random-effects model was applied to all cardiac parameters, but study-to-study heterogeneity remained high in all variables except the ratio of early-late tissue velocity of the lateral wall where no significant difference was found (ES = -0.31, p = 0.204).

				Heterogeneity test			
Parameter	**Subgroup analysis**	**Effect size**	**p-value**	**Q**	**I^2(%)**	**p-value**	**Categorization**
Peak lateral tissue velocity in late diastole (cm/s)		-0.01	0.952	8.97	44	0.110	Moderate
LV lateral tissue e/a ratio	Anabolic steroid users removed	-0.31	0.204	3.82	48	0.148	Moderate
End-diastolic volume (ml)	MRI removed	-0.95	**<0.001**	7.74	96	0.356	Low
RV area in diastole (cm^2)		-0.43	**0.008**	2.26	11	0.324	Low
RV area in systole (cm^2)		-0.23	0.341	4.43	55	0.109	High

Levels of heterogeneity for each variable was categorized as low (<25%), moderate (≥25-50%) or high (≥50%) [18]. Bold = Statistical significance set at p≤0.05.

DISCUSSION

The aim of this review was to examine the differences in cardiac structure and function between previously untrained adults and those engaged in a chronic resistance training program. Whilst the data presented here shows significantly greater wall thicknesses and left ventricular mass both in absolute and relative terms, in resistance-trained athletes compared to untrained individuals, this finding should be taken with great care given the significant heterogeneity observed and publication bias that is evident when examining these specific variables. It does appear that the current review agrees with previous work [2,7] highlighting how resistance-trained athletes present with some characteristics of the Athletes Heart phenomenon. However, interestingly, within this study athletes demonstrate greater LV mass than their untrained counterparts even when accounting for body size, which contradicts previous work suggesting that when correcting for body dimensions resistance-trained athletes present with standard heart sizes [24]. The current study is in agreement with previous work examining cardiac structure in RT athletes [25] but the lack of general consensus regarding body indexing measures in echocardiography highlights the importance of body composition analysis alongside cardiac parameters in future research. Improving understanding within this area will help to establish whether cardiac hypertrophy following training is a true physiological adaptation.

Of particular interest within this study, may be the finding that resistance-trained athletes showed not only greater wall thickness compared to the untrained individuals, but also greater LV chamber dimensions. The consequent suggestion that the greater LVM seen within the RT athletes is a result of both chamber dilation and myocardial thickening does not align with the well-known original research of Morganroth *et al.* [6] which first reported the pattern of concentric hypertrophy in this mode of athlete. The absence of concentric hypertrophy in the resistance-trained athletes may be explained by multiple factors including insufficient exposure to a pressure overload due to the small duration of time in each repetition [2]; variations in the type or intensity of resistance training undertaken by the athletes [26, 27]; or the influence of mixed-mode athletes who may have been described as ‘resistance-trained’ but did not correctly report their levels of aerobic exercise.

Minimal differences were observed in cardiac function between resistance-trained athletes and untrained individuals, with similar stroke volume, fractional shortening, and ejection fraction seen. This is in-line with previous work [2, 14] and suggests that changes to LV geometry following resistance training do not appear to be detrimental to normal cardiac function at rest. Furthermore, when examining tissue velocity of the LV wall during systole, no significant differences were observed between the resistance-trained athletes and untrained individuals, though it should be noted that measuring the velocity of myocardial motion using tissue Doppler imaging holds its own limitations, including being angle dependent and unable to differentiate passive motion from active motion [28]. Assessment of systolic function by 2D speckle tracking echocardiography, a technique previously shown to be a more reproducible method for the assessment of LV function [29] should be considered where possible – though this review found no difference in global longitudinal strain between resistance-trained individuals and untrained individuals, most likely due to the limited number of articles available. Of note, whilst resistance-trained athletes and non-athletes may not differ at rest, differences in systolic function (e.g. stroke volume) have been observed between these two groups during resistance exercise, therefore suggesting that favorable alterations in cardiac function in athletes occur acutely as an immediate response to the physiological stress of exercise [30].

The current review has presented findings on a greater number of cardiac parameters for diastolic function than previous systematic reviews and meta-analyses in this area [2, 7]. In these previous works, better diastolic function in parameters including trans-mitral flow during early diastole [2] and E/A ratio has been observed in endurance trained athletes compared to untrained individuals, with insufficient data available on diastolic function in resistance-trained athletes [7]. The results of this current review expand on this previous work, indicating that the greater diastolic function which has previously been documented in endurance trained athletes compared to untrained individuals is seen in athletes engaged in chronic resistance training also. Furthermore, as with systolic function, this systematic review most importantly highlights no significant impairments to diastolic function as a results of chronic resistance training; in agreement with previous studies [2, 31]. Consequently, with no negative impairments to diastolic function observed within the current review, individuals should have greater confidence in the

safety of undertaking this training modality for cardiac health. Further studies to investigate whether resistance training can be more frequently implemented within clinical populations to improve diastolic function are needed.

To be included in this review studies were required to provide data on the structural or functional parameters of the left ventricle. However, several studies (n = 6) also provided data on the right ventricle. Interestingly, the findings of this review showed a mirrored response to resistance exercise in both the left and right ventricle with regards to chamber dilation, supporting the suggestion of a balance morphological adaptation in response to long-term resistance training that has been described in aerobically trained athletes [2].

Although the current study found resistance-trained athletes demonstrated some structural and functional characteristics of the Athlete's Heart, however, these data should be taken with care. Significant evidence of study-to-study heterogeneity was found throughout this review, suggesting large variance between previous works. Whilst sub-group analysis was undertaken to account for differences in imaging modality (echocardiography, MRI), the significant heterogeneity observed may explained by differences in echocardiographic techniques between studies, including the use of M-mode imaging compared to 2-dimensional analysis for the measurement of LV wall thickness and internal diameters which was not always described in all papers [32]. Consequently, this review demonstrated the need for coherent guidelines for researchers using echocardiography to allow direct comparisons between athletic and non-athletic populations in future work - including clearer recommendations for when each mode of echocardiography should be used and appropriate definitions for endocardial borders, sample placement and offline analysis. Furthermore, the current meta-analysis removed studies including known steroid users [22, 23] during sub-group analysis due to the well-documented impact of these substances on cardiac function [11]. However, it should be noted that an additional limitation to this review is that many of the included studies relied on self-report of substance use rather than direct measures to confirm usage [26, 33-36]. Therefore, it is possible that the true extent of the impact of chronic resistance training on diastolic function may be masked in this review by the confounding effect

of unreported steroid users. Future studies should ensure objective forms of drug testing are conducted when directly comparing any athletic population to another.

In conclusion, this review informs current knowledge of the Athlete's Heart specifically within the previously underrepresented population of resistance-trained athletes. As previously discussed, this study demonstrates that while resistance-trained athletes may present with some physical attributes described in the widely acknowledged Morganroth Hypothesis, these individuals also display other characteristics of the Athlete's Heart phenomenon. Therefore, further work is needed to expand this currently scarce research area and reflect modern changes to resistance training and the exercise elements it incorporates. As previously stated, this work should include body composition analysis alongside echocardiography to determine the most appropriate indexing measure and data including exercise intensity, duration and type should be gathered to explore the contribution of other training modalities and any confounding effects. With the previous indication that most resistance training programmes may not provide sufficient haemodynamic load to cause cardiac remodelling this would also allow further subgroup analysis for training load to establish whether there is a dose effect or critical threshold for resistance training. Lastly, whilst cardiac dimensions were greater in resistance-trained athletes compared to untrained counterparts, these remain within normal parameters [37]. The results of meta-analyses included here are useful in identifying this central position of a dataset, but this is at the expense of outliers and therefore it should be noted that some resistance athletes may present with cardiac dimensions outside of normal parameters and should be clinically examined to exclude any underlying pathologies.

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