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REVIEW

Effects of exercise on cardiac structure and function in patients with type 2 diabetes: a narrative review of prospective imaging studies

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Abstract

Around 30% of patients with type 2 diabetes(T2D) develop heart failure and this leads to poor prognosis. Treatment with exercise intervention can improve left cardiac function at rest in T2D, but its effects on subclinical HF markers, maximal cardiac function during exercise, and right cardiac function are unknown. This review aimed to synthesize the effects of exercise on cardiac structure and function in patients with T2D from prospective cardiac imaging trials. The secondary aim was to address the methodological shortcomings of previous studies and map future avenues. Our synthesis showed that exercise interventions can improve left ventricular structure and systolic and diastolic function at rest and during exercise, and right ventricular systolic function at rest in patients with T2D. Study shortcomings were inadequate reporting of randomization, concealment, between-group point estimates, intervention adherence, attendance and adverse events. Future studies should investigate sex- and phenotype-specific effects of exercise on the left and especially right heart during rest and peak exercise, determine the optimal exercise intensity, duration and volume for inducing cardiac changes, and determine if cardiac changes translate to a long-term prognosis.

Keywords Exercise · Training · Type 2 diabetes · Heart failure · Cardiac dysfunction · Diabetic cardiomyopathy

Abbreviations

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Cardiac structure	diastolic interventricular septal diameter (IVSd), systolic and diastolic left ventricle posterior wall diameter (LVPWs, LVPWd), left ventricle diastolic diameter (LVDd), left ventricle systolic diameter (LVSd), eccentricity ratio, left ventricle end-diastolic volume (LVEDV), left ventricle end-diastolic volume per body surface area or fat-free mass (LVEDV/(BSA or FFM), left ventricle end-systolic volume (LVESV), left ventricle end-systolic volume per body surface area or fat-free mass (LVESV/(BSA or FFM), left ventricle mass (LVM), left ventricle mass per body surface area or volume (LVMi), left ventricle outflow tract diameter (LVOT), left atrial volume (LAV), right ventricle mass (RVmass), right ventricle mass per body surface area of fat-free mass (RVmass/BSA), right ventricle end-systolic volume (RVEDV), right ventricle end-systolic volume (RVESV), right ventricle end-systolic volume per body surface area (RVESV/BSA), and calibrated integrated backscatter.
Systolic function	tricuspid annulus systolic velocity via pulsed wave (pwTDI) or colored(cTDI) tissue doppler imaging (s'), isovolumetric contraction time (IVCT), ejection time (ET), left ventricle ejection fraction (LVEF), left ventricle stroke volume (LVSV), left ventricle stroke volume per body surface area or fat-free mass (LVSV/(BSA or FFM)), left ventricle cardiac output (LVCO), left ventricle cardiac output per body surface area or fat-free mass (LVCO/(BSA or FFM)), stroke work (SW), left ventricle displacement (LVdis), right ventricle stroke volume (RVSV), right ventricle stroke volume per body surface area (RVSV/BSA), right ventricle cardiac output (RVCO), right ventricle ejection fraction (RVEF), tricuspid annular plane systolic excursion (TAPSE), global strain, strain rate, peak endocardial circumferential strain, peak whole wall circumferential strain, peak twist, peak LV basal rotation, LV basal twist rate, time to peak basal untwist rate, peak LV apical rotation, LV apical twist rate, LV apical untwist rate, time to LV apical untwist rate, peak LV twist rate, peak LV untwist rate, time to peak untwist rate, and cardiac index (CI).

Diastolic function early inflow velocity at mitral annulus (E), early tissue velocity at mitral annulus via pulsed wave tissue Doppler imaging (e'pwTDI), early tissue velocity at mitral annulus via colored tissue Doppler imaging(e' colorTDI), early inflow velocity at mitral annulus by early tissue velocity at mitral annulus(E/e'), late inflow velocity at mitral annulus (A), late tissue velocity at mitral annulus (a'), late LV filling rate, early by late inflow velocity at mitral annulus (E/A), peak E-deceleration, E-deceleration, isovolumetric relaxation time (IVRT), left ventricle peak early diastolic strain rate (LVPEDSR), myocardial perfusion reserve, aortic distensibility, pulmonary venous flow during atrial systole (Pva), and pulmonary venous flow in systole by pulmonary venous flow in diastole (Pvs/Pvd).

Introduction

In the early 1970 s, postmortem examinations of patients with type 2 diabetes (T2D) for the first time revealed the development of heart failure (HF) without accompanying hypertension, myocardial ischemia, or congenital or valvular heart disease [1]. This signaled a causal relationship between T2D and HF, giving rise to the new condition called diabetic cardiomyopathy [1]. Diabetic cardiomyopathy is characterized by negative structural, functional and metabolic cardiac remodelling that increases the risk of HF [2, 3]. About 30% of patients with T2D have HF [4–6], and 28% of patients with T2D receive HF diagnosis in the first five years of follow-up [7]. The coexistence of T2D and HF exacerbates the risk of adverse events and death [7–9], emphasizing preventive needs.

Exercise training is a widely-recognized intervention for improving glycemic profile, cardiovascular risk factors and cardiorespiratory fitness in patients with T2D [10–12]. Cardiac imaging studies showed that exercise intervention, next to pharmacological agents [13, 14], weight loss procedures [15], and dietary interventions [16], protects the heart of a patient with T2D [17, 18]. A meta-analysis of the effects of exercise on the heart in patients with type 2 diabetes showed that exercise intervention improves imaging markers of subclinical HF by increasing early diastolic tissue velocity and global longitudinal strain [18]. However, this meta-analysis did not include data on left atrial function, and right atrial and ventricular function, which are also negatively affected by T2D [19]. Additionally, the meta-analysis did not include cardiac imaging markers during exercise, although they improve the detection of subclinical HF [20, 21].

Building upon this meta-analysis, through the inclusion of new prospective evidence [22–25], and the advancement of the subclinical HF paradigm from cardiac imaging at rest to exercise [20, 21], this review aimed to address the full scope of prospective imaging evidence on the effects of exercise interventions on cardiac structure and function at rest and exercise in patients with T2D. The secondary aim was to address the methodological shortcomings of previous studies and outline the future directions.

Methods in brief

We searched two databases (PUBMED and SCOPUS) from inception to 2021 and PUBMED alone in 2024, to find randomized controlled trials (RCT), randomized trials (RT), controlled trials (CT), and single-group (SG) studies in adults with T2D, with exercise interventions of at least four weeks containing cardiac imaging outcomes. Mesh terms were "type 2 diabetes", "exercise" and "training", and the query box contained: (((type 2 diabetes) OR (t2d) OR (t2dm) OR (non-insulin-dependent diabetes)) AND ((exercise) OR (training)). The filters were "clinical trials" and "English language" (Fig. 1). We used Rayyan software [26], Zotero reference manager (George Mason University, VG), and spreadsheet Excel 2019 to eliminate duplicates and extract data. We noted between-group differences or group-time interactions (#), within-group changes (↑ or ↓), and time effects (†). Study quality was assessed with the TESTEX scale (Supplement 5) [27]. Tabular data are preintervention values. Supplement 1 contains methods according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) Statement.

Results and discussion

Study retrieval, populations, and interventions

From the initial 26,882 records, eighteen studies remained, of which two presumably fragmented [28–31] (Supplement 2 - Flowchart). Twelve studies were RCTs, one CT, two RTs and three SG (Table 1). In total, 570 men and women with T2D were enrolled (353 in exercise groups, and 217 in control groups, Table 1). Studies included patients with T2D with and without insulin use, and predominantly no diabetic

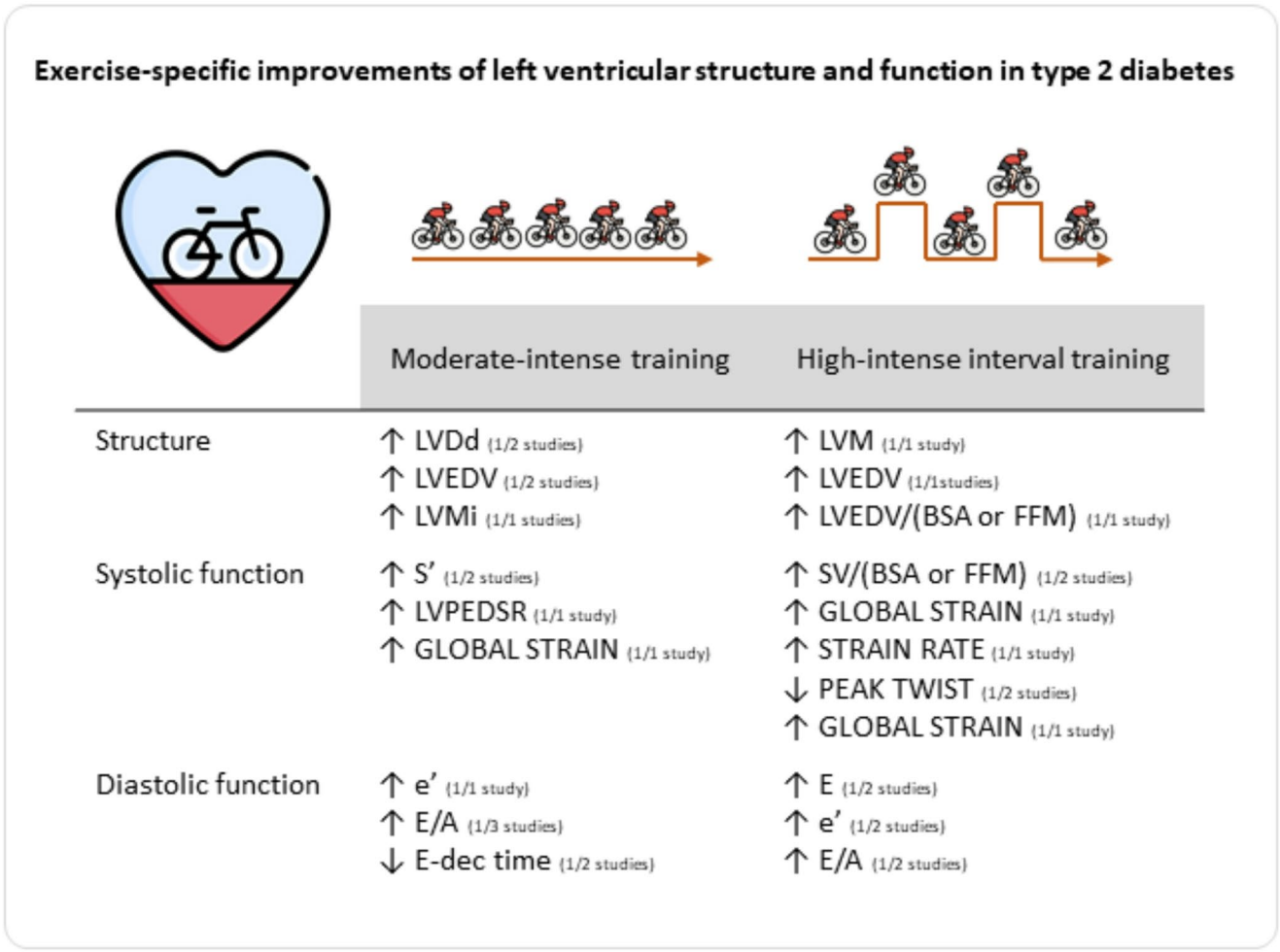

Fig. 1 Central illustration– Exercise-specific effects of exercise on cardiac function in patients with type 2 diabetes

complications nor known cardiovascular disease (Supplement 3). Patients were overweight or obese (BMI:28–35 kg/m²), middle-aged (age:46-66y), with a poor-to-well-controlled glycemic state (Hba1c: 5.8–8.2%), blood pressure (122-146mmHg) and lipid profile (total cholesterol: 151-205 mg/dl, triglycerides: 97-195 mg/dl, LDL: 89-135 mg/dl) (Supplement 3).

Two studies investigated the effects of moderate-intensity exercise training (MIT) or moderate-intensity continuous exercise training (MICT), seven combined moderate-intensity and dynamic resistance exercise training (MIT + RT), five high-intensity interval exercise training (HIIT), one MICT vs. sprint-interval exercise training (SIT), one MICT vs. HIIT, one soccer training and one aquatic training (Table 2). Interventions lasted 2.5–12 months, training frequency was 3-4x/week, endurance exercise intensity between 55 and 100% of the maximal heart rate or maximal oxygen consumption or wattage, and resistance training intensity 55–80% of one maximal repetition or maximal voluntary contraction (Table 2). Eight studies reported supervised exercise training, three semi-supervised exercise training, and five unclear supervision. Training attendance was reported in 6/18 studies and ranged from 60 to 100% (Table 2).

Effects of exercise on the left cardiac structure

Table 3 and the central illustration (Fig. 1) qualitatively summarize the effects of exercise on cardiac structure and function in patients with T2D stratified per exercise intervention type. Exercise interventions had mixed between-group effects on the left ventricle diastolic diameter (LVDd) [28, 31–33], left ventricle end-diastolic volume (LVEDV) [22, 32, 34], LVEDV per body surface area or fat-free mass

Table 1 Baseline characteristics, body composition, metabolic profile and blood pressure of participants in included studies

Study	Design	Group	n	Sample size calculation* (yes/no/unclear)	Age (years)	Sex (M/F)	BMI (kg/m^2)	Hba1C*(%)*	SBP (mmHg)	DBP (mmHg)	Cholesterol(mg/dl)
McGavock 2004(39)	RCT	CON	11	no	58±7	0/11	34±5	6.6±0.9	133±15	76±9	
		MICT+RT	7		59±5	0/7	34±7	7.4±1.1	139±17	74±11	
Van Ryckeghem 2022(23)	RT	MICT	9	no	66±11	8/1	30±7	6.8±0.5			160±40
		HIIT	10		61±5	9/1	30±5	6.6±0.7			164±19
Brassard 2007(33)	RCT	MICT	11	no	58±5		28±3	5.8±1.3	132±13	76±10	205±43
		CON	12		57±6		31±3	6.4±1.2	142±17	75±11	205±31
Loimaala 2007(40)	RCT	MICT+RT	24	unclear	52±8	24/0		8.2(2.1)	144(17)	88(9)	179(7)
		CON	24		52±8	24/0		8.0(1.3)	146(15)	89(6)	188(7)
Hordern 2014 & Hare 2011(28,31)	RCT	MICT+RT+Diet	88	yes	56±12	46/34	32±5	7.5±1.6	137±17	83±10	189±35
		CON	88		55±9	50/38	32±6	7.6±1.3	129±15	80±9	186±39
Schrauwen-Hinderling 2011(35)	SGT	MICT+RT	11	unclear	60[1]	11/0	30[1]	7.1[0.2]			190[8]
Schmidt 2013(32)	CT	SOCCER	12	no	51±7	12/0	30±3	7.4±1.2	138±15	89±7	170±35
		CON	9		49±9	9/0	30±7	7.5±1.2	126±14	84±8	151±35
Gulsin 2020(22)	RCT	MIT	22	yes			33(32-35)	7.4(1.1)	136 (17)	87(8)	
		CON	30				35(33-41)	7.3(0.9)	138 (13)	85(7)	
Wilson 2019(24)	RCT	HIIT	11	no	52±5	7/4	34±2	7.7±3.1			
		CON	5		51±5	3/2	32±3	7.8±3.3			
Suryanegara 2019(25)	RCT	HIIT	13	yes	61±9	3/10	31±5	7.1±3.1	142±17	89±13	162±43
		CON	13		60±9	3/10	32±5	7.0±2.7	141±14	86±10	167±39
Cassidy 2016(34)	RCT	HIIT	12	unclear	61±9	10/2	31±5	7.0±1	123±4	81±2	155±39
		CON	11		59±9	8/3	32±6	7.0±0.5	126±3	84±2	174±35
Heiskanen 2017(38)	RT	SIT	11	no	49(47,51)	7/4	31(29,33)	5.7(5.4,6.0)	135(129,142)	86(81,90)	
		MICT	10		49(46,51)	6/4	31(29,33)	5.8(5.5,6.0)	146(141,152)	89(85,93)	
Sacre 2014(37)	RCT	MIT+RT+HOME	24	no	59±10	13/11	32±6	7.7±1.6	131(3)	76(1)	179±40
		CON	25		60±9	10/15	32±5	7.7±1.7	122(3)	70(1)	184±37
Hollekim-Strand 2014 & 2016(29,30)	RCT	Home MIT	17	no	55±5	11/6	30±4	6.7±0.7	135±12	81±7	
		HIIT	20		59±5	12/8	30±3	7.0±1.2	142±18	81±7	
Cugusi 2015(36)	SGT	AQUATIC	18	no	52±9	18/0	31±5	8.1±0.8	131±17	83±10	
Jonker 2013(16)	SGT	MIT+RT+Trekking	12	no	46±2	7/5	29±1	6.7±0.3	142±7	87±4	

Data are mean±SD, mean[SEM] or median(IQ) of baseline data. RCT-randomized controlled trial, SGT-single group trial, CON-control, MI(C)T-moderate intense (continuous) training, RT-resistance training, HOME-home training, AQUA-aquatic training, BMI-body mass index, Hba1c-hemoglobin A1C, SBP-systolic blood pressure, DBP-diastolic blood pressure, Cholesterol-total cholesterol, sample size calculation– "yes" if based on the cardiac outcome with the reference provided

(LVEDV/(BSA or FFM) [22, 24], left ventricle mass and left ventricle mass index (LVM or LVMi) [22, 24, 28, 31–34](Supplement 4: Table 1, and 2), but no between-group effects on diastolic interventricular septal diameter (IVSd) [33], systolic and diastolic left ventricle posterior wall diameter (LVPWs, LVPWd) [33, 34], eccentricity ratio [34], left ventricle end-systolic volume (LVESV) [34], LVESV by body surface area or fat-free mass (LVESV/(BSA or FFM)) [24], and left atrial volume (LAV) [33] (Supplement 4: Table 1, and 2). One single group study showed a reduction in LVESV [35], two no effects on LVESV [16, 36], and three no effects on LVEDV [16, 35, 36].

Effects of exercise on the left systolic function

Exercise interventions showed between-group increases in relative left ventricle stroke volume (LVSV/(BSA or FFM)) [24], and mixed effects on increases in the mitral annulus systolic velocity (s') [24, 28–32, 37], global strain [22, 30, 32, 34, 37, 38], and global strain rate [22, 29–31, 37], and decreases in peak twists [29, 30, 34]. Exercise intervention also showed between-group effects via decreases in the LVEF and stroke work (SW) at iso-intensity during low- and moderate-intense exercise (Supplement 4: Tables 4, 5, 6, 7, 8 and 9) [24]. Single-group studies had mixed effects on s' [36], LVCO and LVCO/BSA [16, 35](Supplement 4: Table 4, and 5).

Exercise interventions did not show between-group effects in the left ventricle ejection fraction (LVEF) [22, 24, 28, 31–34, 37], cardiac output (CO) [25, 34], CO/(BSA or FFM) [24], LVSV [25, 34], global systolic contraction amplitude (LV displacement) [32], peak endocardial and whole wall circumferential strains [34], peak left ventricular basal and apical rotations [30], twist and untwist rates [30], peak twist rates [30], and times to peak basal, apical, total untwist rates [30] and SW at rest [24] (Supplement 4: Tables 4, 5, 6, 7 and 8). Single-group studies did not affect LVEF [16, 36], LVSV [16], and strain rate [36] (Supplement 4: Tables 4 and 6).

Effects of exercise on the left diastolic function

Exercise interventions showed between-group effects via increases in the early left ventricular filling rate [34], and left ventricular peak early diastolic strain rate (LVPEDSR) [39] (Supplement 4: Tables 10 & 12). Exercise had mixed between-group effects on the increases in early inflow velocity at mitral annulus (E) [24, 29, 33, 39, 40], early tissue velocity at mitral annulus (e') [24, 28–32, 37], E/A [22, 24, 29, 30, 32, 33, 37, 39], and decreases in E-deceleration time [32, 33, 37, 39] (Supplement 4: Table 10, and 11). However, exercise did not show between-group effects in E/e' [22, 24, 29, 32, 37, 40], late inflow velocity at the mitral annulus (A) [24, 33, 39, 40], late left ventricular filling rate [34], isovolumetric relaxation time (IVRT) [33], pulmonary venous flow during atrial systole (Pva) [39], pulmonary venous flow in systole by diastole (Pvs/Pvd) [39], myocardial perfusion reserve [22] and aortic distensibility [22] (Supplement 4: Table 11, and 12). Single-group studies had mixed effects on decreases in E/e' [32, 37], and no effects on E/A [16] and E-deceleration peak [16] (Supplement 4: Table 10, and 11).

Effects of exercise on the right cardiac function and fibrosis

One controlled trial showed a between-group effect in tricuspid annular plane systolic excursion (TAPSE) owing to its increase after soccer training (Table 8) [32], and one RCT showed no between-group effect on the integrated backscatter, despite its reduction within the exercise group (Supplement 4: Table 3) [37].

Effects of exercise on the markers of heart failure with preserved ejection fraction

HF with preserved ejection fraction (HFPEF) comprises 75% of all HF diagnoses in T2D [7], and it can be diagnosed invasively and non-invasively. The invasive investigation involves hemodynamic exercise testing for obtaining LV end-diastolic pressure (LVEDP), pulmonary capillary wedge pressure (PCWP) [20, 41] and pulmonary capillary wedge pressure by cardiac output slope (PCWP/CO slope) [41, 42]. The non-invasive imaging includes E, E/A, e', E/e', LA volume index (LAVI), and tricuspid regurgitation peak velocity (TRV) at rest [43, 44], and s', E/e' and mean pulmonary artery pressure by cardiac output slope (mPAP/COslope) during exercise [45]. The probability scores H2FPEF [46] and HFAPEFF [47] additionally focus on systolic pulmonary artery pressure (sPAP) [46, 47], global longitudinal strain [47], LVMi [47], relative wall thickness [47] and LV wall thickness (LVWd) [47] to estimate the risk of HFPEF. From these HFPEF markers, exercise interventions can affect global strain [18, 32], E [29, 30], e' [29, 30, 32], E/A [29, 30, 32] and LVMi [34], but not systolic [34] and diastolic posterior LVWd [33, 34] in T2D. The effects of exercise interventions on LAVi, TRV, sPAP, RWT, LVEDP, PCWP, E/e', s', PCPW/COslope, and HFPEF probability scores remain unknown.

Exercise intervention-specific cardiac effects in T2D: intensity and duration

In healthy adults, cardiac adaptations to exercise interventions are intervention- [48] and person-specific [49]. In

Table 2 Intervention description: frequency, intensity, time and type of exercise

Study	Group	Time (months)	Frequency (t/week)	Intensity	Time(min/training)	Type	Adherence(%trainings)	Supervised
McGavock 2004(39)	MICT+RT	≈2.5	3	ET: 65-75%HRR, RT: 50-65%1RM	ET: 30-50RT: 3x10-15rep	ET: cyclingRT: 7 exercises	92±3	/
	CON	≈2.5	/	Usual care	/	/	/	/
Van Ryckeghem 2022(23)	MICT	≈6	3	70-80%HRpeak	35	Cycling	/	yes
	HIIT	≈6	3	Part1: 70-80%HRpeakPart2: 90-100%Wpeak+70%HRpeakPart3: 90-100%Wpeak+70%HRpeakPart4: 90-100%Wpeak+70%Hrpeak	35Phase2: 6x1+6x4Phase3: 7x1+7x4Phase4: 8x1+8x4	Cycling	/	yes
Brassard 2007(33)	MICT	3	3	60-70% VO2peak	30-60	Cycling	/	yes
	CON	3	/	Usual care	/	/	/	/
Loimaala 2007(40)	MICT+RT	12	4ET: 2RT: 2	ET: HR at 65-75%VO2peakRT: 70-80%1RM, 3x12rep	ET: ≤30	ET: walking or joggingRT: 8 exercises for arms, legs and trunk	/	semi
	CON	12	/	usual care	/	/	/	/
Hordern 2014 & Hare 2011(28,31)	MICT+RT+Diet	12	Month 1: 3Months 2-12:/	ET: BORG 12-13/20RT: 3x12-15RM	150min/week	Month 1: gym ET+RTMonth 2-12: HomeET: walking, jogging, cycling, swimmingRT: gym machines, thera-bands, free weights	/	semi
	CON	12	/	Usual care	/	/	/	/
Schrauwen-Hinderling 2011(35)	MICT+RT	≈3m	ET: 2RT: 1	ET: 55%WmaxRT: 1x8rep, 55%MVC2x8rep, 75%MVC	ET: 30	ET: cyclingRT: chest press, leg extension, lat pull-down, leg press, triceps curls, biceps curls, abdominal crunches, horizontal row	/	yes
Schmidt 2013(32)	SOCCER	≈6m	2	Soccer: 43±22% training time >85%HRpeak	5x10=502min breaks	Indoor soccer	60%	yes
	CON	≈6m	/	usual care	/	/	/	/
Gulsin 2020(22)	MIT	≈3m	/	HR at ≈60% VO2peak	≤50	Walking and/or cycling	/	yes

Table 2 (continued)

Study	Group	Time (m)	Frequency (n/week)	Intensity	Time(min/training)	Type	Adherence(%trainings)	Supervised
Wilson 2019(24)	HIIT	≈3	3	≥10min at ≥90%HRmax-Month 1: 1 min intervals, 1 min rest Month 2: 2 min intervals, 2 min restMonth 3: 3 min intervals, 2 min rest	20	/	78±4	/
	CON	≈3	/	usual care	/	/	/	/
Suryanegara 2019(25)	HIIT	≈3	3	Part 1: Borg 9-13/20Part 2: 5x2min, 80rpm, Borg 16-17/20 with 3 min breaks (90s active cycling, 90 s passive). Progress: +10s/week till 3min50s	<40	Cycling	/	no
	CON	≈3	/	usual care	/	/	/	/
Cassidy 2016(34)	HIIT	≈3	3	Part 1: 5 min, Borg 9-13/20Part 2: 5x2min, 80rpm, Borg 16-17/20 with 3 min breaks (90s active cycling, 60 s band-resisted upper body exercise, 30 s passive) Progress: +10s/week to 3min50s	<40	/	100±3	no
	CON	≈3	/	usual care		/	/	/

Table 2 (continued)

Study	Group	Time (m)	Frequency (n/week)	Intensity	Time(min/training)	Type	Adherence(%trainings)	Supervised
Heiskanen 2017(38)	SIT	0.5	0-6	4-6x30s all-out cycling at 10% fat-free mass, 4 min rest in-between	<27	Cycling	/	yes
	MICT	0.5	0-6	60%Wmax	40-60	Cycling	/	/
Sacre 2014(37)	MIT+RT+HOME	6	Gym: 2Home:/	Moderate-vigorous: by RPE and HR	150 min/week ET:20-40RT: 6-12exercises	/	/	semi
	CON	6	/	usual care	/	/	/	/
Hollekim-Strand 2014 & 2016(29,30)	Home MIT (sham)	3	/	/	≥10min/bout; 210min/week	/	94	yes
	HIIT	3	3	Part 1: 10 min at 70%HRmax- Part 2: 4†4min at 90%–95% HRmax 3 min rest between bouts at 70%HRmax- Part 3: 5 min cool-down	404x4min	Walking/jogging (inclined treadmill)	/	yes
Cugusi 2015(36)	AQUATIC	12	3	50-75% VO2max	50	Pool exercises	96	
Jonker 2013(16)	MIT+RT+Trekking	≈7	MIT: 1RT: 2Trekking: 7	/	3.5-4h/weekTrekking= 4-7h/d	MIT:/ RT:/ Trek-king:/	/	/

MICT-moderate-intense continuous training, HIIT-high-intense interval training, RT-resistance training, CON-control group, ET-endurance training, "/"-not reported, Rep-repetitions, HR-heart rate, W-workload, VO2-oxygen consumption, 1RM-one maximal repetition, MVC-maximal voluntary contraction, semi-semisupervised.MICT-moderate-intensity continuous training, HIIT-high-intense interval training, MIT-moderate intense training, RT-resistance training, CON-control group, ET-endurance training, "/"-not reported, Rep-repetitions, HR-heart rate, W-workload, VO2-oxygen consumption, 1RM-one maximal repetition, MVC-maximal voluntary contraction

Table 3 Effects of exercise interventions on the cardiac structure and function at rest in type 2 diabetes– summary of controlled trials

Cardiac structure	MIT	HIIT	MIT+RT	Systolic function	MIT	HIIT	MIT+RT	Diastolic function	MIT	HIIT	MIT+RT
IVSd	-	?	?	s'	-	+/-	-	E	-	+/-	-
LVPWd diastolic	-	-	?	LVEF	-	-	-	e'	+	+/-	-
LVPWd systolic	-	-	?	LVSV	?	-	?	E/e'	-	-	-
LVDd	+/-	?	-	LVSV(BSA or FFM)	?	+	?	A	-	-	-
LVSd	-	?	-	LVCO	?	-	?	Early LV filling rate	?	+	?
Eccentricity ratio	?	-	?	LVCO(BSA or FFM)	?	-	?	Late LV filling rate	?	-	?
LVEDV	+/-	+/-	?	Stroke work	?	-	?	E/A	+/-	+/-	-
LVEDV/(BSA or FFM)	-	+/-	?	LVdisplacement	-	?	?	E-deceleration time	+/-	?	-
LVESV	?	-	?	Global strain	-	+/-	-	IVRT	-	?	?
LVESV/(BSA or FFM)	?	-	?	Strain rate	-	+	-	LVPEDSR	+	?	?
LVM	-	+/-	?	Circumferential strain	?	-	?	Perfusion reserve	-	?	?
LVMi	+/-	-	?	Peak twist	?	+/-	?	Aortic distensibility	-	?	?
LAV	-	?	?	LV basal rotation	?	-	?	Pva	?	?	-
Integrated backscatter	?	?	-	LV basal twist rate	?	-	?	Pvs/Pvd	?	?	-
				LV basal untwist rate	?	-	?				
				Time to LV basal untwist	?	-	?				
				LV apical rotation	?	-	?				
				LV apical twist rate	?	-	?				
				LV apical untwist rate	?	-	?				
				Time to LV basal untwist	?	-	?				
				Peak LV twist rate	?	-	?				
				Peak LV untwist rate	?	-	?				
				Time to peak untwist rate	?	-	?				

"+" all CTs favor intervention over control, "+/-" some CTs do and some do not favor intervention over control, "-"CTs do not favor intervention vs control, "?" - no CT has ever examined intervention vs control, MIT-moderate-intense training, HIIT-high-intense interval training, SIT-sprint interval training, MIT+RT-moderate intense+resistance training; IVSd-interventricular septal diameter diastolic, LVPWd-left ventricle posterior wall diameter, LVDd/s-left ventricle diastolic/systolic diameter, LVEDV-left ventricle end-diastolic volume, LVEDV/(BSA or FFM)-LVEDV per body surface area or fat-free mass, LVESV-left ventricle end-systolic volume, LVESV/(BSA or FFM)-LVESV per body surface area or fat-free mass, LVM-left ventricle mass, LVMi-LVM per body surface area/volume,, LAV-left atrial volume, s'- mitral annulus systolic velocity via pulsed wave (pwTDI) or colored(cTDI) tissue doppler imaging, LVEF-left ventricle ejection fraction, LVSV-left ventricle stroke volume, LVSV/(BSA or FFM - LVSV per body surface area or fat-free mass, LVCO-left ventricle cardiac output, LVCO/(BSA or FFM) - LVCO per body surface area or fat-free mass, LVdis-left ventricle displacement, E and A-early and late inflow velocity at mitral annulus, e'pwTDI or e'colorTDI-early tissue velocity at mitral annulus via pulsed wave or colored tissue doppler imaging, E/e'-early inflow velocity by early tissue velocity at mitral annulus, E/A-early by late inflow velocity at mitral annulus, IVRT-isovolumetric relaxation time, LVPEDSR-left ventricle peak early diastolic strain rate, Pva and Pvs/Pvd -pulmonary venous flow during atrial systole by diastole

T2D, only two non-controlled studies compared the effects of different exercise interventions on cardiac variables (Table 3) [23, 38]. In the first study, moderate-intense continuous training (MCIT) was superior to high-intense interval training (HIIT) in increasing left ventricle outflow tract diameter (LVOT), but there were no between-group differences in other parameters of cardiac structure and diastolic function at rest (IVSd, LVPWd, LVDd, s', IVCT, ET, E, e', E/e', A, a', E/A, E-deceleration time and IVRT), and systolic and diastolic function at peak exercise (LV cardiac output (LVCO), cardiac index (CI), and global strain, E, e', E/e' and ejection time (ET)). However, E/e' did reduce within the HIIT group, and ET increased within the MICT group [23].

In the second study, the MICT was superior to sprint interval training (SIT) in increasing LVSV/BSA, the absolute and relative right ventricular mass (RVmass and RVmass/BSA), and right ventricular end-diastolic volumes (RVEDV and RVEDV/BSA), but not right ventricular end-systolic volumes (RVESV and RVESV/BSA) [38] (Supplement 4: Table 3). There were also no between-group differences in the right ventricular systolic function (RVSV, RVSV/BSA, RVCO, RVCO/BSA, RVEF), and left ventricular structure and systolic function (left ventricular work, work index, LVEF, LVSV, LVCO, LVCO/(BSA or FFM), LVESV, LVESV/(BSA or FFM), LVM and LVMi) [38]. Despite this, time effects for the latest six left ventricular variables were primarily driven by changes in the MICT group, which might lead to significant differences on a bigger sample [38]. To conclude, these non-controlled studies indicate that MICT is more effective than SIT, but probably similar to HIIT in improving cardiac structure and function in T2D.

Although RCTs directly comparing exercise groups are lacking, two author groups hypothesized which exercise intensity and duration might induce the greatest diastolic improvements in T2D. Brassard et al. first showed that

exercise intervention can improve diastolic strain rate in patients with T2D and mild, but not severe diastolic dysfunction, and hypothesized that exercise interventions longer than three months might maximize cardiac benefits [33]. And secondly, Hordern et al. hypothesized that exercise intensity, and not just the duration [33], might maximize benefits, as T2D patients with the biggest increases in moderate and vigorous physical activity, had the greatest improvements in diastolic cardiac function [28].

Methodological shortcomings of previous studies

Prospective studies from this review received a modest average TESTEX score of 6.25/15 points for quality of study and reporting (Supplement 4). Studies adequately reported the inclusion criteria, between-group p-values for primary outcomes, and baseline glycemic values, but not randomization, concealment, between-group point estimates, adherence, attendance, and adverse events (Supplement 4).

Moreover, the included studies did not report the inter-rater reliability for the cardiac imaging outcomes, which might limit their clinical usability. Furthermore, only two studies had > 25 participants per group, and only three studies based sample size on cardiac outcomes, thereby risking obtaining false negative findings [50]. Conversely, the absence of corrections for multiple comparisons elevated the risk of false positive findings [51].

Next, participants were not included in the studies by following the same diagnostic criteria, although prognosis [52], and possibly cardiac effects, depend on it. The risk of the new onset cardiovascular disease differs > 25% between T2D phenotypes [10], and equalizing the between-group risk at baseline is desirable. The confounders of prognosis are outlined in the ESC's 2023 risk stratification tool "SCORE2-Diabetes" [10], and include: age, sex, smoking status, geographic region, systolic blood pressure, total and HDL cholesterol, diabetes duration, HbA1c, and kidney function (eGFR). In this review, however, only one prospective study reported kidney function via eGFR [37].

Furthermore, only one study accounted for between-group differences in medication intake [22]. Antidiabetic medications sodium-glucose cotransporter-2 (SGLT2) inhibitors, and glucagon-like peptide-1 receptor agonists (GLP-1 RA), reduce major adverse cardiovascular events in T2D [13, 14], while dipeptidyl peptidase IV (DPP4) inhibitor saxagliptin increases the risk of HF [53]. Finally, dyspnea during daily life might influence exercise-induced cardiac changes, as dyspneic T2D patients have worse cardiac function than non-dyspneic ones [54], and exercise interventions longer than three months might therefore be needed to reverse this dysfunction [33].

Despite the known sex differences in cardiac structure and function in patients with T2D [54] and non-diabetic adults [55], studies did not report sex-specific analyses, exclusive one study in women [39]. Stratification by sex is desirable due to the known sex-specific cardiac changes in aging, pressure and volume overload, and after acute ischemia in healthy adults [56]. Further, changes in cardiac function in athletes seem to be exercise dose-dependent [57]. Yet, two-thirds of the studies did not report exercise adherence (Table 2). Finally, overweight and obese patients with T2D [58] are prone to weight loss after an exercise intervention [11], which can independently affect cardiac function and mask the effects of exercise [15, 59–61].

Future directions

The effects of exercise interventions on HFPEF markers LAVi, TRpV, sPAP, relative wall thickness, $PCWP^{48}$, PCWP/CO, and left and right atrial function inclusive right ventricular structure and function are unknown. Secondly, only one study examined cardiac changes at peak exercise [23], but cardiac imaging during exercise improves the detection of HFPEF [20, 21] and could be more sensitive than imaging at rest in capturing cardiac improvements. As outlined herein and previously [17], an absence of controlled trials with multiple exercise groups precludes knowing which exercise frequency, intensity, duration and volume improve cardiac structure and function the most in T2D. Finally, it is unknown whether cardiac changes translate to a better prognosis.

Conclusion

Exercise interventions can improve left ventricular structure and function at rest and during exercise and right ventricular systolic function at rest in patients with T2D. Future studies should investigate sex- and phenotype-specific effects of exercise on the right heart during rest and peak exercise, determine the optimal exercise intensity, duration and volume for inducing cardiac changes, and the translation of cardiac changes into long-term prognosis.

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Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate Not applicable.

Consent for publication Not applicable.

Competing interests The authors declare no competing interests.

Additional materials Supplements 1–3. Methods, flowchart, lipid profile, and inclusion criteria of individual studies.
Supplement 4. Tables 1–13: The effects of exercise on cardiac structure and function in T2D.
Supplement 5. Study quality assessment.

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