SUPPLEMENTAL MATERIAL TO

Exercise-induced Cardiac Troponin Elevations: *from underlying mechanisms to clinical relevance*

RUNNING TITLE: Exercise and Cardiac Troponins

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Supplemental Table 1: Overview of studies that sampled cTnT ≥3 times between 0-72h following exercise. Median cTnT concentrations are reported, with the maximal median value of each study highlighted in bold text.

Author, year	Study population	Type of exercise	Assay	cTnT pre-exercise	cTnT +0h	cTnT +1h	cTnT +2-4h	cTnT +5-6h	cTnT +7-23h	cTnT +24-47h	cTnT +48-72h
Tian, 2006[95]	N=10 100% male 16.2±0.6 yrs CVD/CVRF na Junior long-distance runners at national level	21-km treadmiss exercise	cTnT (3. generation, Roche Diagnostics) URL 30 ng/L	5			**75**	70		6	
Middleton, 2006[96]	N=14 93 % male 29±5 yrs 0% self-reported CVD CVRF na Marathon runners with 0-16 previous marathon competitions	Marathon	cTnT (3. generation, Roche Diagnostics) URL 10 ng/L	0	0	0	0	0	10	**20**	
Frassl, 2008[97]	N=15 0% male 37 (28-39) yrs 0% self-reported CVD CVRF na Marathon runners with 0-10 previous marathon competitions	Marathon	cTnT (3. generation, Roche Diagnostics) URL 10 ng/L	0	**32**					0	0
Nie, 2008[98]	N=10 100% male 15.0±0.7 yrs 0% CVD by clinical assessment CVRF na Junior basketball players, 14h training per week	Basketball game	cTnT (3. generation, Roche Diagnostics) URL 30 ng/L	5	5		**5**			5	
Lippi, 2010[99]	N=9 100% male 25±3 yYrs 0% CVD (method of assessment na)	Downhill walking 40 min	cTnT (Roche Diagnostics) URL 14 ng/L	5.1	**5.8**					5.2	5.1

	Previous training characteristics na									
Scherr, 2011[100]	N=102 100% male 42±9.5 yrs CVRF: 45 % had family history of CVD, 15 % had hypercholesterolemia, 16% had hypertension, 3% current smokers Marathon runners, 0-66 previous marathon competitions	Marathon, 2009	cTnT (Roche diagnostics) URL 14 ng/L	3.3	**31.1**				9.3	3.6
Nie, 2011[101]	N=12 100% male 16.2±0.6 yrs 0% CVD by clinical assessment CVRF na National level long-distance junior runners, VO2 max 59.5±5.3 mL/kg/min	Half-marathon	cTnT (3. generation, Roche Diagnostics) URL 10 ng/L	5			65	**100**	5	
Tian, 2012[102]	N=13 100% male 24.0±3.6 yrs 0% CVD by clinical assessment CVRF na Recreational runners, VO2 max 54.7±3.0 mL/kg/min	90 min treadmill run (adults)	cTnT (Roche Diagnostics) URL 14 ng/L	5	9.30	13.30	**19.10**	16.70	4.0	
	N=13 100% male 14.1±1.1 yrs 0% CVD by clinical assessment CVRF na Recreational runners, VO2 max 57.5 mL/kg/min	90 min treadmill run (adolescents)	cTnT (Roche Diagnostics) URL 14 ng/L	3	18.4	81	**211**	141	24.7	
Ma, 2014[103]	N=28 100% male children 7.2±1.1 yrs	Table tennis	cTnT (3. generation, Roche Diagnostics) URL 30 ng/L	5	23		**26**		021	

	0% self-reported CVD/CVRF Amateur table tennis players with 0.5-1yr training experience									
Legaz-Arrese, 2015[33]	N=15 100% male 35±9 yrs 0% CVD by clinical assessment CVRF na Triathletes with mean 8h training per week	60 min swimming	cTnT (Roche Diagnostics) URL 14 ng/L	4.2	7.2	11.1	**18.9**	16.5	9.7	6.0
	N=15 100% male 35±9 yrs 0% CVD by clinical assessment CVRF na Triathletes with mean 8h training pr week	60 min cycling	cTnT (Roche Diagnostics) URL 14 ng/L	4.3	6.0	10.1	**16.8**	10.6	8.2	5.6
	N=15 100% male 35±9 yrs 0% CVD by clinical assessment CVRF na Triathletes with mean 8h training pr week	60 min running	cTnT (Roche Diagnostics) URL 14 ng/L	4.1	6.9	10.4	**19.1**	16.7	9.5	6.3
Li, 2016[104]	N=10 100% male 22.1±2.6 yrs 0% self-reported CVD/CVRF Marathon runners, VO2 max 64.7±5.6 mL/kg/min	Normoxic, intermittent exercise	cTnT (Roche Diagnostics) URL 14 ng/L	5.2	9.8		20.3	**21.0**		6.4
Li, 2016[105]	N=9 100% male 21.7±2.3 yrs 0% CVD, CVRF na VO2 max 64.3±6.7 mL/kg/min Marathon runners, training volume of 51.1±3.3 km/week	Normoxic, intermittent exercise	cTnT (Roche Diagnostics) URL 14 ng/L	5.44	9.8		23.6	**23.8**		6.6

Klinkenberg, 2016[106]	N=25 76% male 40±13 yrs 0% self-reported CVD CVRF na 56% had prior marathon or ultra-marathon experience, median training volume of 7h pr week	30-km run	cTnT (Roche Diagnostics) URL 14 ng/L	6.0	37.0		**45.0**	40.0			
Legaz-Arrese, 2017[107]	N=16 44% males 31.1±7.9 yrs 0% CVD by clinical assessemnt CVRF na Swimmers, training volume: 14.6±9.5 h/week	High-intensity swimming exercise (adults)	cTnT (Roche Diagnostics) URL 14 ng/L	3.0	3.0	6.0	**12.5**	7.1	3.5	3.0	
Li, 2017[108]	N=21 Sex distribution na 22.9±4.5 yrs 0% CVD/CVRF by clinical assessment Experienced marathon runners, VO2 max 63.3±5.6 mL/kg/min	High-intensity interval exercise	cTnT (Roche Diagnostics) URL 14 ng/L	5.0	10.0		**25.6**			6.6	
Vassalle, 2018[109]	N=18 83% male 46±6 yrs 0% self-reported CVD CVRF na Training volume of 3-7 sessions pr week	21-km run	cTnT (Roche Diagnostics) URL 14 ng/L	5.0	**11.0**					6.0	4.0
Broz, 2018[110]	N=19 100% male 37 (24-48) yrs 0% self-reported CVD/CVRF Marathon runners, VO2 max 59.7 (36.9-75.3) mL/kg/min	2h treadmill run	cTnT (Roche Diagnositcs) URL 14 ng/L	7.2	14.8	**18.5**				8.7	
Skadberg, 2018[111]	N=97	91-km cycling event	cTnT (Roche Diagnostics)	4.1	**40.9**		37.4			12.2	

	76% male 42.8±9.6 yrs 0% self-reported CVD, CVRF: 36% with fam history of CVD, 4% smokers, 40 % prior smokers. Recreational cyclists, 7 (5-10) hours of training/wk		URL 14 ng/L							
Martinez-Navarro, 2020[112]	N=98 85% male 38.7±3.6 yrs 0% CVD (assessment strategy na) CVRF na Previous marathon experience, VO2 max: 54.5±5.6 mL/kg/min	Marathon	cTnT (Roche Diagnostics) URL 14 ng/L	5.7	**50.4**				15.6	11.5
Li, 2020[113]	N=12 92% male 23.5±5.5 yrs 0% self-reported CVD/CVRF Endurance runners, VO2 max 62.4±5.4 mL/kg/min	Intermittent exercise for 92 min	cTnT (Roche Diagnostics) URL 14 ng/L	5.0	14.0	23.0	**36.0**		7.5	6.0
	N=12 92% male 23.5±5.5 yrs 0% self-reported CVD/CVRF Endurance runners, VO2 max 62.4±5.4 mL/kg/min	Continuous exercise for 92 min	cTnT (Roche Diagnostics) URL 14 ng/L	4.0	9.0	18.5	**34.5**		7.0	6.5
Nie, 2020[114]	N=17 0% male Age na CVD/CVRF na Training experience na	Moderate intensity continous exercise (follicular phase)	cTnT (Roche Diagnostics) URL 14 ng/L	3.0	3.1	4.1	**4.3**			
	N=17 0% male Age na CVD/CVRF na Training experience na	Moderate intensity continous exercise (luteal phase)	cTnT (Roche Diagnostics) URL 14 ng/L	2.7	2.8	3.7	**3.8**			

	N=17 0% male Age na CVD/CVRF na Training experience na	High-intensity interval exercise (follicular phase)	cTnT (Roche Diagnostics) URL 14 ng/L	3.0	3.5	6.0	**8.2**			
	N=17 0% male Age na CVD/CVRF na Training experience na	High-intensity interval exercise (luteal phase)	cTnT (Roche Diagnostics) URL 14 ng/L	2.4	2.9	4.7	**6.5**			
Huang, 2020[115]	N=14 0% male Age na CVD/CVRF na	High-intensity interval exercise	cTnT (Roche Diagnostics) URL 14 ng/L	1.5	3.8		**7.0**		7.2	
	N=14 0% male Age na CVD/CVRF na	Moderate-intensity continous exercise	cTnT (Roche Diagnostics) URL 14 ng/L	1.5	2.6		**13.8**		4.2	
Bernat-Adell, 2021[116]	N=86 86% male 38.6±3.6 yrs 0% self-reported CVD CVRF na Previous marathon completed at <4/4.5hrs for male/female subjects	Marathon	cTnT (Roche Diagnostics) URL 14 ng/L	5.6	**48.4**				15.4	11.3
Aengevaeren, 2021[117]	N=11 100% males 51 (50-56) Yrs 0% CVD/CVRF by clinical assessment Previous marathon experience (2-25 marathons), 22 [16-38] average lifelong Metabolic Equivalent of Task-hours/week.	Marathon	cTnT (Roche Diagnostics) URL 14 ng/L	5.5		31.5	**36.4**	9.4		

cTnT, cardiac troponin T; na, not available from publication.

Supplemental Table 2: Overview of studies that sampled cTnI ≥3 times between 0-72h following exercise. Median cTnI concentrations are reported, with the maximal median value of each study highlighted in bold text.

Author, year	N	Type of exercise	Assay	cTnI pre-exercise	cTnI +0h	cTnI +1h	cTnI +2-4h	cTnI +5-6h	cTnI +7-23h	cTnI +24-47h	cTnI +48-72h
Tian, 2006[95]	N=10 100% male 16.2±0.6 yrs CVRF na Junior long-distance runners at national level	21-km treadmill exercise	cTnI (AccuTnI, Beckman Coulter) URL 80 ng/L	23			117	**184**		44	
Frassl, 2008[97]	N=15 0% male 37 (28-39) yrs 0% self-reported CVD CVRF na Marathon-runners with 0-10 previous marathon competitions	Marathon	cTnI (ADVIA centaur assay, BayerHealthcare) URL 100 ng/L	0	**98**					0	0
Lippi, 2008[118]	N=10 47 (range: 38-52) yrs 0% CVD (assessment strategy na) CVRF na Engaged in specific endurance training > 5 yrs, VO2 max 58±4 mL/kg/min	Half-marathon	cTnI (Evidence Investigators, Randox Laboratories) URL na	0	0		0	0		0	
Nie, 2008[98]	N=10 100% male 15.0±0.7 yrs 0% CVD by clinical assessment CVRF na Junior basketball players, 14h training pr week	Basketball game	cTnI (AccuTnI, Beckman Coulter) URL 60 ng/L	12	18		**24**			24	
Lippi, 2010[99]	N=9 100% male 25±3 yrs 0% CVD (assessment strategy na) Previous training characteristics na	Downhill walking 40 min	cTnI (ADVIA Centaur immunoassay system, Siemens) URL 40 ng/L	5.6	**5.8**					5.7	5.2

Nie, 2011[101]	N=12 100% male 16.2±0.6 yrs 0% CVD by clinical assessment CVRF na National level long-distance junior runners, VO2 max 59.5±5.3 mL/kg/min	Half-marathon	cTnI (AccuTnI, Beckman Coulter) URL na ng/L	20			130	**195**		45
Carranza-Garcia, 2011[119]	N=18 24±3 yrs CVD/CVRF na 3 weight-lifting session pr week	Weithlifting session	cTnI (AccuTnI, Beckman Coulter) URL 40 ng/L	24	12	14	19	18	18	**20**
	N=12 100% male 24±4 yrs CVD/CVRF na Soccer players, VO2 max 56.3±4.0 mL/kg/min	Indoor soccer match	cTnI (AccuTnI, Beckman Coulter) URL 40 ng/L	38	36	31	37	**42**	35	33
	N=12 0% male 24±4 yrs CVD/CVRF na Soccer players, VO2 max 47.6±3.3 mL/kg/min	Indoor soccer match	cTnI (AccuTnI, Beckman Coulter) URL 40 ng/L	12	8	9	**15**	13	14	11
Lippi, 2012[120]	N=17 100% male 47 (range: 37-64) yrs 0% CVD (method of assessment na) CVRF na Experience with endurance training, VO2 max 65±5 mL/kg/min	Half-marathon	cTnI (HS-AccuTnI) URL 8.6 ng/L	2.90	4.8		9.0	**12.3**		4.5
Ma, 2014[103]	N=28 100% male children 7.2±1.1 yrs 0% self-reported CVD/CVRF Amateur table tennis players with 0.6-1yr training experience	Table tennis	cTnI (AccuTnI, Beckman Coulter) URL 60 ng/L	20	**55**		54			55

Carmona, 2015[121]	N=17, however only 8 subjects completed the study 88% of finishers were male Age na CVD/CVRF na Experienced nonprofessional endurance runners	85-km running	cTnI (Siemens Healthcare Diagnostics) URL na	18	**67**					0
Li, 2016[105]	N=9 100% male 21.7±2.3 yrs 0% CVD by clinical assessment CVRF na Marathon runners, training volume of 51.1±3.3 km/week; VO2 max 64.3±6.7 mL/kg/min	Intermittent exercise (normoxic condition)	cTnI (AccuTnI, Beckman Coulter) URL 40 ng/L	10	10		20	**30**		10
Klinkenberg, 2016[106]	N=25 76% male 40±13 yrs 0% self-reported CVD CVRF na 56% had prior marathon or ultra-marathon experience, median training volume of 7h per week	30-km run	cTnI (STAT high-sensitiv assay, Abbott Diagnostics) URL 26.2 ng/L	6.0	30.0		49.0	**67.0**		
	N=25 76% male 40±13 yrs 0% self-reported CVD CVRF na 56% had prior marathon or ultra-marathon experience, median training volume of 7h pr week	30-km run	cTnI (Access AccuTnI+3, Beckman Coulter) URL 40 ng/L	5.0	37.0		60.0	**80.0**		
Lopez-Laval, 2016[122]	N=12 100% male 37.3±4.1 yrs 0% CVD by clinical assessment CVRF na Adult elite athletes, VO2 max 58±3 mL/kg/min	Basketball game	cTnI (Access AccuTnI, Beckmann Coulter) URL 40 ng/L	9	18	30	45	**47**	33	13

	N=12 100% male 29.6±2.9 yrs 0% CVD by clinical assessment CVRF na Adult amateur athletes, VO2 max 56±7 mL/kg/min	Basketball game	cTnI (Access AccuTnI, Beckmann Coulter) URL 40 ng/L	3	4	7	13	**16**	7	4	
	N=12 100% male 16.6±0.9 yrs 0% CVD by clinical assessment CVRF na Junior elite athletes, VO2 max 58±3 mL/kg/min	Basketball game	cTnI (Access AccuTnI, Beckmann Coulter) URL 40 ng/L	11	12	23	39	**52**	45	29	
Skadberg, 2017[123]	N=97 76% male 42.8±9.6 yrs 0% self-reported CVD CVRF: 36 % with family history of CVD, 4 % current smokers, 40 % prior smokers Recreational cyclists, 7 (5-10) hours of training pr week prior to race	91-km cycling event	cTnI (STAT assay, Abbott Diagnostics) URL 30 ng/L	3.4	50.5		**69.3**			14.2	
Vassalle, 2018[109]	N=18 83% male 46±6 yrs 0% self-reported CVD CVRF na Training volume of 3-7 sessions per week	21-km run	cTnI (STAT High Sensitive, Abbott Diagnostics) URL 26.2 ng/L	6.0	**7.0**					7.0	4.0
Broz, 2018[110]	N=19 100% male 37 (24-48) yrs 0% self-reported CVD/CVRF Marathon runners, VO2 max 59.7 (36.9-75.3) mL/kg/min	2h treadmill run	cTnI (STAT High Sensitive, Abott Diagnostics) URL 19.3 ng/L	3.4	5.6	**8.0**				4.7	
Park, 2018[124]	N=11 100% male 51.7±4.4 yrs CVD/CVRF na	100-km run	cTnI (ADVIA Centaur, Siemens Healthcare) URL 78 ng/L	6	**10**					5	6

	Completed at least one 100km ultramarathon, VO2 max 51.0±4.7 mL/kg/min	(normotensive participants)								
Rubio-Arias, 2019[125]	N=10 100% male 37.0±5.7 yrs CVD/CVRF na Experienced ultramarathon runners	54-km run	Troponin I (assay na) URL na	10	**56**				10	10
	N=6 100% male 30.5±8.0 yrs CVD/CVRF na Experienced ultramarathon runners	111-km run	Troponin I (assay na) URL na	10	**15**				10	10
Sierra, 2019[126]	N=81 100% male 39±1 yrs CVD/CVRF na Training volume 56±2.1 km/week of running	Marathon	TnI (assay na) URL na ng/L	20	**90**				30	20
Marshall, 2020[28]	N=10 70% male 34±7 yrs 0% CVD self-reported and clinical assessment CVRF na Exercise experience na	Low-intensity cycling, 60min	cTnI (Abbot Laboratories) URL 34 ng/L in men, 15 ng/L in women	1.8		1.7	**3.2**		1.9	1.8
	N=10 70% male 34±7 yrs 0% CVD self-reported and clinical assessment CVRF na Exercise experience na	High-intensity cycling, 60min	cTnI (Abbot Laboratories) URL 34 ng/L in men, 15 ng/L in women	1.6		2.3	**13.0**		6.1	2.8
	N=10 70% male 34±7 yrs 0% CVD self-reported and clinical assessment CVRF na	Moderate-intensity cycling, 4 hours	cTnI (Abbot Laboratories) URL 34 ng/L in men, 15 ng/L in women	2.8		3.5	6.9	**8.1**	3.8	1.6

	Exercise experience na										
Li, 2020[113]	N=12 92% male 23.5±5.5 yrs 0% self-reported CVD/CVRF Endurance runners, VO2 max 62.4±5.4 mL/kg/min	Intermittent exercise, 92min	cTnI (STAT assay from Abbott Diagnostics) URL 26 ng/L	4.2	13.7	38.4	**72.6**		11.6	6.25
	N=12 92% male 23.5±5.5 yrs 0% self-reported CVD/CVRF Endurance runners, VO2 max 62.4±5.4 mL/kg/min	Continuous exercise, 92min	cTnI (STAT assay from Abbott Diagnostics) URL 26 ng/L	4.5	15.9	36.6	**94.9**		21.1	15.5
Aengevaeren, 2021[117]	N=11 100% males 51 (50-56) Yrs 0% CVD/CVRF by clinical assessment Previous marathon experience (2-25 marathons), 22 [16-38] average lifelong Metabolic Equivalent of Task-hours/week.	Marathon	cTnI (Singulex Clarity cTnI system) URL 8.97 ng/L	2.7		14.5	**23.6**	8.4		
	N=11 100% males 51 (50-56) Yrs 0% CVD/CVRF by clinical assessment Previous marathon experience (2-25 marathons), 22 [16-38] average lifelong Metabolic Equivalent of Task-hours/week.	Marathon	cTnI (Siemens ADVIA Centaur TnI-Ultra) URL 40 ng/L	0		43.5	**57.0**	3.0		

cTnI, cardiac troponin I; na, not available from publication.

Supplemental Table 3. Studies investigating associations between cardiac troponin and changes in right ventricular cardiac function following exercise, ordered by race duration.

Study	Study Population	Type of exercise	Functional indices	cTn	Association between cTn and cardiac function
Weippert et al 2016[29]	13 males, 26±3 years; no CVD.	1hr running (at 70% peak HR) and 17.5 min intermittent sprint exercise (90% peak HR)	TTE: no change in RV systolic function 30 min post-exercise. No strain analyses were reported.	cTnI; 1hr post-exercise: no significant change 4hrs post-exercise: ↑	No change in RV systolic function
Neilan et al 2006[25]	41 males, 19 females, 41±11 years; no CVD.	Marathon (average time 245 min)	TTE: RV systolic function ↓ using strain analysis.	cTnT; Directly post-exercise: ↑	Reduction in RV endocardial velocities and strain correlated with the increase in cTnT (RV basal, *r*=.68; mid, *r*=.70; and apical, *r*=.72; *P*<0.001 for all).
Mousavi et al. 2009[68]	8 males, 6 females, 33±6 years; no CVRF, CVD or family history	Marathon (average time 245±68 minutes)	TTE/CMR: RV systolic function ↓. No strain analyses were reported.	cTnT; directly and <3 days post-exercise: ↑	No association analyses were done

	of coronary artery disease				
O´ Hanlon et al. 2010[69]	17 males, 34±7 years; no CVD, hypertension or diabetes.	Marathon (average time 209±19 min)	TTE/CMR: No change in RV systolic function. No strain analyses were reported.	cTnI; immediately post-exercise: ↑, 6 hrs post-exercise at time of CMR: ↑↑	No change in RV systolic function.
Gaudreault et al. 2013[127]	14 males, 6 females, 45±8 years; no CVD and no drug therapy	Marathon (average time 232±40 min)	CMR: RVEF ↓. No strain analyses were reported.	cTnT; immediately post-exercise ↑, 6-48 hrs post-exercise at time of CMR not significantly different from baseline.	Association with RV not reported.
Aengevaeren et al. 2020[8]	11 males, 51 [50-56] years; no CVD or CVRF	Marathon (median time 223 [208-274] min)	CMR: no change in RVEF. No RV strain analyses were reported.	cTnI; ±1 hrs post-exercise: ↑, and 4±2 hrs post-exercise at time of CMR: ↑	No change in RV systolic function.
Tahir et al. 2019[93]	30 males, 45±10 years; no CVD, no CV medication	Triathlon, multiple distances (average 3.3±2.7 hrs)	CMR: no change in RVEF. No strain analyses were done.	cTnT; 2.4±1.1 (range 1–5) hrs post-exercise at time of CMR: ↑	No change in RV systolic function.

La Gerche et al. 2012[83]	36 males, 4 females, 37±8 years; no CVD, CVRF or symptoms.	Marathon (7, 179±30 min), Endurance triathlon (11, 324±25 min), Alpine cycling (9, 485±42 min), Ultra triathlon (13, 652±76 min)	TTE: RV systolic function ↓, both EF and strain analysis.	cTnI; immediately post-exercise at time of TTE: ↑	Correlation between change in RVEF and post-race troponin (r=.49, P=.002)

↑ means elevation. CVD, cardiovascular diseases; CVRF, cardiovascular risk factors; TTE, transthoracic echocardiogram; CMR, cardiovascular magnetic resonance; RV, right ventricular; EF, ejection fraction.