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Sex and Racial Differences in Exercise-induced Cardiac Remodeling

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Exercise induced cardiac remodeling

- Long-lasting athletic training leads to alteration in cardiac structure and function
- Remodeling allows the generation of a large stroke volume to the body with effective energy consumption
- After some degree of physiologic adaptation, it becomes an arrhythmia prone substrate that can progress to pathologic conditions.

Shim JY. Korean Circ J. 2021 May;51(5):439-440

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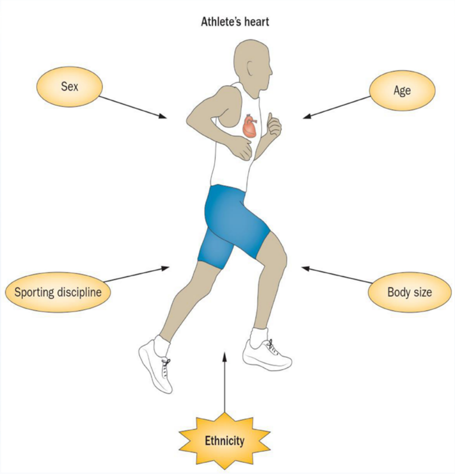
Exercise induced cardiac remodeling



- Degree and characteristics of cardiac remodeling varies according to
  - Type of sport
  - Frequency and intensity of athletic training
  - Gender
  - Age
  - Race

Sheikh N, et al. Nat. Rev. Cardiol. advance online publication 25 February 2014; Shim JY. Korean Circ J. 2021 May;51(5):439-440

Exercise induced cardiac remodeling

- Traditionally, left ventricle (LV) is the major concern for the athletic changes of cardiac structure and function
- LV hypertrophy or chamber enlargement has been the most commonly described cardiac abnormality
- Recent studies, however, have demonstrated that cardiac structural and functional changes can be developed not only in the LV, but also in the left atrium (LA) and right ventricle (RV)

Yoon HJ. Korean Circ J. 2021 May;51(5):426-438

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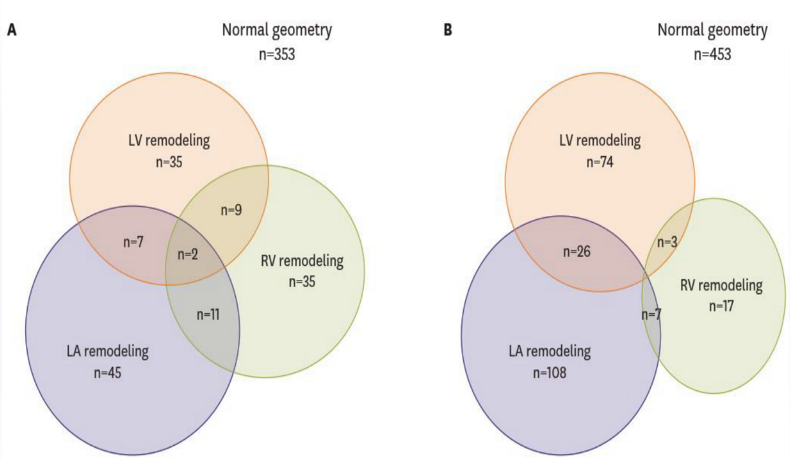
Gender specific exercise induced cardiac remodeling

Table 4. Patterns of exercise induced cardiac remodeling

Cardiac geometry	Total (n=1,185)	Female (n=497)	Male (n=688)	p value
LV remodeling	156 (13.2)	53 (10.7)	103 (15.0)	0.065
Normal geometry	1,018 (86.8)	445 (89.5)	584 (84.9)	0.065
Concentric remodeling	73 (6.2)	26 (5.2)	47 (6.8)	0.272
Concentric hypertrophy	25 (2.1)	5 (1.0)	20 (2.9)	0.025
Eccentric hypertrophy	58 (4.9)	22 (4.4)	36 (5.2)	0.586
LA remodeling	206 (17.4)	65 (13.1)	141 (20.5)	0.001
RV remodeling	82 (6.9)	57 (11.4)	27 (3.9)	<0.001
LV & LA remodeling	35 (3.0)	9 (1.8)	26 (3.8)	0.055
LV & RV remodeling	14 (1.2)	11 (2.2)	3 (0.4)	0.011
LA & RV remodeling	20 (1.7)	13 (2.6)	7 (1.0)	0.041
LV, LA & RV remodeling	2 (0.2)	2 (0.4)	0 (0.0)	0.176
Any remodeling	379 (31.9)	144 (30.0)	235 (34.2)	0.058

Yoon HJ. Korean Circ J. 2021 May;51(5):426-438

Gender specific exercise induced cardiac remodeling



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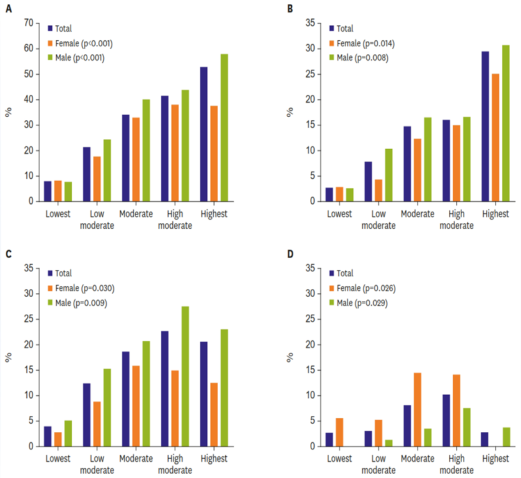
Gender specific exercise induced cardiac remodeling



- (A) Any remodeling
- (B) LV remodeling
- (C) LA remodeling
- (D) RV remodeling

Yoon HJ. Korean Circ J. 2021 May;51(5):426-438

Gender specific exercise induced cardiac remodeling

- Any remodeling in cardiac chambers was relatively common in both female and male athletes.
- About a third of university athletes experienced any remodeling in cardiac chambers, and any remodeling was more prevalent in male athletes than in female athletes.
- LV and LA remodeling were more common in male than female athletes,
- RV remodeling was more common in female than in male athletes.
- Concentric LVH was significantly frequent in male than in female athletes

Yoon HJ. Korean Circ J. 2021 May;51(5):426-438

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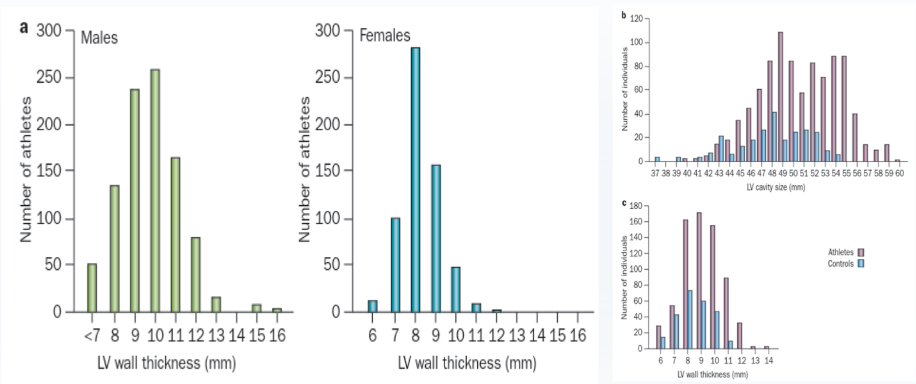
Gender specific exercise induced cardiac remodeling

- The exact mechanism for higher RV remodeling in female than in male university athletes is unclear and needed to be clarified.
- Data from an animal study hypothesized that sex hormone might be a modulator of the development and progression of cardiac adaptation.
- Exercise-induced increases in plasma FFA level are closely linked to a decrease in cardiac glucose uptake in the female.
- Sympathetic adrenergic response during exercise affected differently in female athletes.
- Body composition such as fat mass, volume sensitivity, and metabolic preference may affect the difference of EICR according to sex.

Yoon HJ. Korean Circ J. 2021 May;51(5):426-438

Gender specific exercise induced cardiac remodeling



Sheikh N, et al. Nat. Rev. Cardiol. advance online publication 25 February 2014;

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Racial difference

Association Between Cardiac Dimensions and Athlete Lineup Position: Analysis Using Echocardiography in NCAA Football Team Players

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Abstract: In determining what is "abnormal"—in terms of cardiac electrical and morphologic remodeling in athletes—it is important to identify what is "normal" or expected. With specialization for each position in a football team lineup, we attempted to describe the association between the position played and the physiologic cardiac changes of designated players. We evaluated data

Uberoi A, et al. The Physician and Sportsmedicine, 2011 Sep;41(3):58

Racial difference: ECG

Table 2. Comparison of Athlete ECG Variables Based on Field Position Type, Stratified by Race[a]

ECG Variables	Linemen[b] (n = 34)	Mobility/Power[b] (n = 13)	Skill[b] (n = 38)	*P* Value[c]
Heart rate, BPM	65 ± 11 (65 vs 65)	67 ± 12 (66 vs 67)	67 ± 10 (68 vs 67)	0.63
PQ interval, ms	176 ± 53 (149 vs 181)	186 ± 64 (222 vs 170)	165 ± 52 (159 vs 169)	0.43
QRS duration, ms	102 ± 10 (100 vs 103)	101 ± 7 (97 vs 103)	96 ± 7 **(94 vs 98; *P* < 0.05)**[c]	< 0.007
QTc interval, ms	400 ± 22 (401 vs 400)	389 ± 24 (391 vs 388)	390 ± 20 (394 vs 387)	0.08
LVH, %	59 (80 vs 55)	69 (75 vs 67)	71 (87.5 vs 59)	0.53
LVH voltage score	27.7 ± 6.5 (31.8 vs 27.0)	28.8 ± 7.0 (27.5 vs 29.4)	31.8 ± 7.6 (33.9 vs 30.4)	< 0.05
Right ventricular hypertrophy, %	0	0	2.6	0.53
Left atrial abnormality, %	0	0	0	N/A
Right atrial abnormality, %	0	0	5.3	0.28
ST segment depression present, %	0	0	2.6	0.53
Right axis deviation, %	5.9 (0 vs 6.9)	30.8 (0 vs 44.4)	10.5 (6.2 vs 13.6)	0.06
Abnormal Q waves, %	0	0	0	N/A
Lateral ST segment elevation, mm	0.7 ± 0.6 (0.60 vs 0.72)	0.9 ± 0.6 (0.68 vs 0.94)	1.0 ± 0.8 **(1.29 vs 0.77; *P* = 0.04)**[c]	0.22
Anterior ST segment elevation, mm	2.0 ± 0.8 (2.30 vs 1.97)	2.0 ± 1.0 (1.88 vs 2.11)	2.1 ± 0.9 (2.06 vs 2.11)	0.93
Brugada, %	0	0	0	N/A
Arrhythmogenic right ventricular dysplasia/cardiomyopathy, %	0	15.4 (25 vs 11)	2.6	< 0.04
Anterior T-wave inversion, %	0	0	0	N/A
Lateral T-wave inversion, %	0	0	0	N/A
Inferior T-wave inversion, %	2.9	0	2.6	0.83

[a]AA vs White/Other.
[b]Overall values presented ± SEM with racial substratification shown in parenthesis (AA vs White/Other, respectively).
[c]Comparisons of 3 groups using ANOVA for *P* value. Unpaired *t* test or χ^2 analysis and a significant value noted in boldface type; only presented for race when significant.
Data presented as mean ± SD.
Abbreviations: AA, African American; BPM, beats per minute; EEG, electrocardiographic; LVH, left ventricular hypertrophy; SEM, standard error of the mean.

- Racial difference in the ECG
- In the Skilled group
  - QRSd: slightly shorter in AA subgroup (94 vs. 98)
  - Lateral ST elevation: greater in AA subgroup

Uberoi A, et al. The Physician and Sportsmedicine, 2011 Sep;41(3):58

Memo

Racial difference: Echo

Table 3. Comparison of Athlete ECHO Variables Based on Player Position Type, Stratified by Race[a]

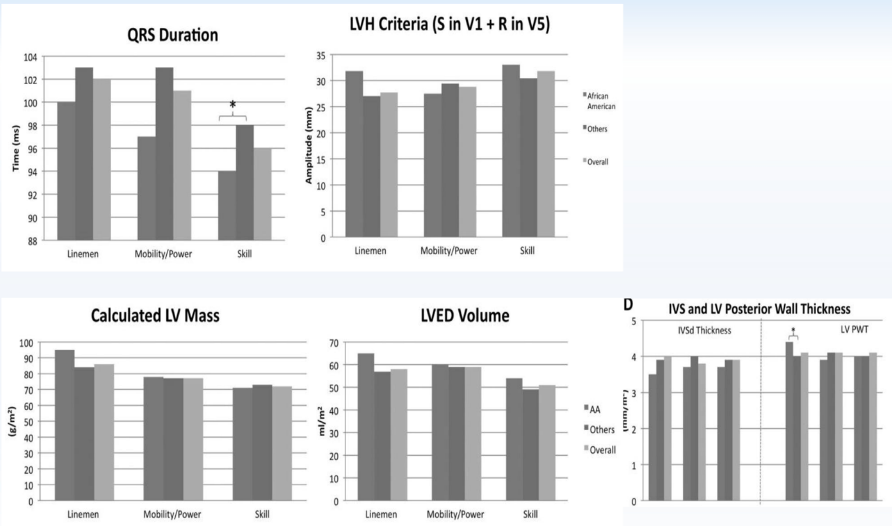
ECHO Variables	Linemen[b] (n = 34)	Mobility/Power[b] (n = 13)	Skill[b] (n = 38)	P Value[c]
Calculated LVM, g	220 ± 40	175 ± 29	154 ± 24	< 0.0001
Calculated LVM adjusted for BSA, g/m²	86 ± 15 (95 vs 84)	77 ± 12 (78 vs 77)	72 ± 9 (71 vs 73)	< 0.0002
LVED diameter, mm	57 ± 5	53 ± 4	51 ± 4	< 0.0001
LVED diameter adjusted for BSA, mm/m²	22 ± 2 (22 vs 22)	23 ± 2 (24 vs 23)	24 ± 2 (24 vs 24)	< 0.0005
LVES diameter, mm	35 ± 6	34 ± 3	32 ± 4	0.07
LVES diameter adjusted for BSA, mm/m²	14 ± 3 (14 vs 13)	15 ± 2 (15 vs 15)	15 ± 2 (15 vs 15)	< 0.03
Interventricular septal thickness diastole, mm	9.5 ± 1.5	8.9 ± 1.7	8.2 ± 0.9	< 0.002
Interventricular septal thickness diastole adjusted for BSA, mm/m²	3.7 ± 0.6 (3.5 vs 3.7)	3.9 ± 0.8 (3.9 vs 4.0)	3.9 ± 0.4 (4.0 vs 3.8)	0.32
LV posterior wall thickness diastole, mm	10.3 ± 1.2	9.1 ± 1.1	8.8 ± 1.1	< 0.0001
LV posterior wall thickness diastole adjusted for BSA, mm/m²	4.0 ± 0.4 **(4.4 vs 3.9; P = 0.03)**[c]	4.0 ± 0.5 (4.0 vs 4.1)	4.1 ± 0.5 (4.1 vs 4.1)	0.44
LVED volume, mL	149 ± 28	135 ± 38	109 ± 24	< 0.0001
LVED volume adjusted for BSA, mL/m²	58 ± 12 (65 vs 57)	59 ± 16 (60 vs 59)	51 ± 11 (54 vs 49)	0.06
LVES volume, mL	55 ± 14	53 ± 15	42 ± 11	< 0.0005
LVES volume adjusted for BSA, mL/m²	22 ± 5 (23 vs 22)	23 ± 6 (23 vs 23)	20 ± 5 **(22 vs 18; P = 0.008)**[c]	0.18
LVEF, %	62 ± 8	61 ± 7	61 ± 6	0.96
Fractional shortening, %	37 ± 7	37 ± 4	38 ± 5	0.75
LA major axis, mm	58 ± 6	55 ± 6	54 ± 9	0.08
LA major axis adjusted for BSA, mm/m²	23 ± 1 (22.0 vs 23)	24 ± 1 (23 vs 25)	25 ± 1 (27 vs 25)	< 0.02
LA minor axis, mm	45 ± 5	45 ± 5	43 ± 4	0.12
LA minor axis adjusted for BSA, mm/m²	18 ± 1 (17 vs 18)	20 ± 1 (20 vs 19)	20 ± 1 (21 vs 20)	< 0.0001
LA volume 4 chamber, mL	64 ± 19	54 ± 17	52 ± 13	< 0.02
LA volume 4 chamber adjusted for BSA, mL/m²	25 ± 1 (26 vs 25)	24 ± 2 (25 vs 23)	25 ± 1 (25 vs 24)	0.84
Aortic Root diameter, mm	31 ± 2	30 ± 3	27 ± 4	< 0.003
Aortic Root diameter adjusted for BSA, mm/m²	11.9 ± 1.2 (11.2 vs 12.0)	13.2 ± 1.3 (13.1 vs 13.3)	12.9 ± 1.5 (13.3 vs 12.6)	< 0.02
LVOT diameter, mm	26 ± 2	25 ± 2	23 ± 2	< 0.0001
LVOT diameter adjusted for BSA, mm/m²	10.2 ± 1.0 (10.1 vs 10.2)	11.2 ± 0.5 (11.1 vs 11.2)	10.8 ± 0.8 (11.0 vs 10.6)	< 0.009

[a] AA vs White/Other.
[b] Overall values presented ± SEM with racial substratification shown in parenthesis (AA vs White/Other, respectively).
[c] Comparisons of 3 groups using ANOVA for P value. Unpaired t test or χ^2 analysis and a significant value noted in boldface type; only presented for race when significant.
Data presented as mean ± SD.
Abbreviations: AA, African American; BSA, body surface area; ECHO, echocardiographic; LA, left atrial; LV, left ventricular; LVED, left ventricular end diastolic; LVEF, left ventricular ejection fraction; LVES, left ventricular end systolic; LVOT, left ventricular outflow tract.

- Racial difference in the Echo
- In the Linemen group
  - LVPW thickness/BSA: thicker in AA subgroup (4.4 vs. 3.9mm/m^2)
- In the Skill players group
  - LVESV/BSA: larger in AA subgroup (22 vs. 18 mL/ m^2)

Uberoi A, et al. The Physician and Sportsmedicine, 2011 Sep;41(3):58

Comparison of ECG and Echo



Uberoi A, et al. The Physician and Sportsmedicine, 2011 Sep;41(3):58

Memo

Racial difference

Impact of ethnicity on cardiac adaptation to exercise

Nabeel Sheikh and Sanjay Sharma

Abstract | The increasing globalization of sport has resulted in athletes from a wide range of ethnicities emerging onto the world stage. Fuelled by the untimely death of a number of young professional athletes, data generated from the parallel increase in preparticipation cardiovascular evaluation has indicated that ethnicity has a substantial influence on cardiac adaptation to exercise. From this perspective, the group most intensively studied comprises athletes of African or Afro-Caribbean ethnicity (black athletes), an ever-increasing number of whom are competing at the highest levels of sport and who often exhibit profound electrical and structural cardiac changes in response to exercise. Data on other ethnic cohorts are emerging, but remain incomplete. This Review describes our current knowledge on the impact of ethnicity on cardiac adaptation to exercise, starting with white athletes in whom the physiological electrical and structural changes—collectively termed the 'athlete's heart'—were first described. Discussion of the differences in the cardiac changes between ethnicities, with a focus on black athletes, and of the challenges that these variations can produce for the evaluating physician is also provided. The impact of ethnically mediated changes on preparticipation cardiovascular evaluation is highlighted, particularly with respect to false positive results, and potential genetic mechanisms underlying racial differences in cardiac adaptation to exercise are described.

Sheikh, N. & Sharma, S. *Nat. Rev. Cardiol.* advance online publication 25 February 2014; corrected online 28 February 2014; doi:10.1038/nrcardio.2014.15

Sheikh N, et al. Nat. Rev. Cardiol. advance online publication 25 February 2014;

Racial difference

- African-American individuals represent 13.1% of the US population, but comprise >75% of athletes competing in the National Basketball Association.
- Current diagnostic algorithms to differentiate physiological adaptation from pathology are derived almost exclusively from **white athletes**, concerns have been raised that the extrapolation of current recommendations to athletes of other ethnicities might result in erroneous diagnoses.

Sheikh N, et al. Nat. Rev. Cardiol. advance online publication 25 February 2014;

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LVEDD and LV wall thickness in athletes

Table 3 | Upper limits of normal for LV end-diastolic diameters and maximal wall thickness in athletes

Cohort	Sex	LV end-diastolic diameter				LV wall thickness			
		Study	Mean age (years) ± SD	Mean ± SD (mm)	Upper limit (mean + 2 SD) (mm)	Study	Mean age (years) ± SD	Mean ± SD (mm)	Upper limit (mean + 2 SD) (mm)
Adult white	Male	Pelliccia *et al.*[79]	24.3±6.0	55.±4.3	≤64	Pelliccia *et al.*[77]	22.4±3.1	10.1±1.1	≤12
	Female	Pelliccia *et al.*[78]	21.1±5.0	48.9±3.8	≤57	Pelliccia *et al.*[78]	21.1±5.0	8.2±1.2	≤11
Adolescent white	Male	Makan *et al.*[81]	15.7±1.2	51.6±3.3	≤58	Sharma *et al.*[80]	15.6±1.2	9.8±1.2	≤12
	Female		15.7±1.2	47.7±3.3	≤54		15.4±1.1	8.4±1.1	≤11
Adult black	Male	Basavarajaiah *et al.*[135]	20.5±5.8	53.0±4.4	≤62	Basavarajaiah *et al.*[135]	20.5±5.8	11.3±1.6	≤15
	Female	Rawlins *et al.*[129]	21±4.6	48.6±3.9	≤56	Rawlins *et al.*[129]	21±4.6	9.2±1.2	≤12
Adolescent black	Male	Sheikh *et al.*[134]	16.4±1.3	52.3±5.0	≤62	Sheikh *et al.*[134]	16.4±1.3	10.3±1.6	≤14
	Female		16.0±1.3	48.7±4.2	≤57		16.0±1.3	9.2±1.1	≤11
Adult Middle-Eastern	Male	Riding *et al.*[149]	22.7±5.9	52.7±4.2	≤61	Riding *et al.*[149]	22.7±5.9	8.9±0.9	≤11
	Female	NA	NA	NA	NA	NA	NA	NA	NA
Adult East Asian	Male	Ma *et al.*[155]	23.0±3.8	NR	NA	Ma *et al.*[155]	23.0±3.8	NR	NA
	Female		20.7±4.1				20.7±4.1		
Adolescent East Asian	Male Female	NA	NA	NA	NA	NA	NA	NA	NA
Adult South Asian	Male Female	NA	NA	NA	NA	NA	NA	NA	NA
Adolescent South Asian	Male Female	NA	NA	NA	NA	NA	NA	NA	NA

*Derived from means and SDs reported in studies. This Table highlights the paucity of data available for Middle-Eastern and Asian athletes. Abbreviations: LV, left ventricular; NA, data not available; NR, data not reported.

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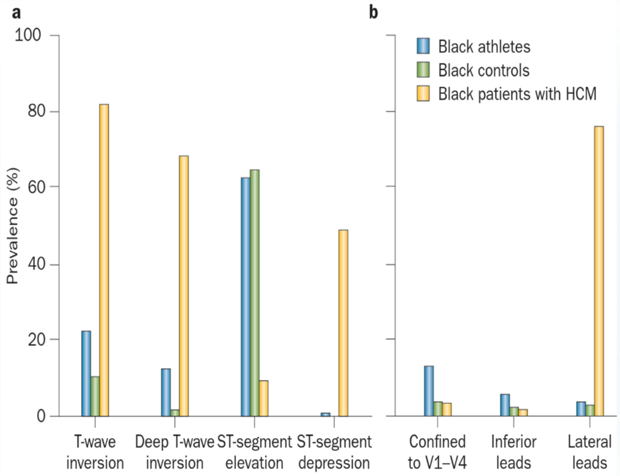
Prevalence of ECG changes in black athletes, black controls, and black patients with HCM.



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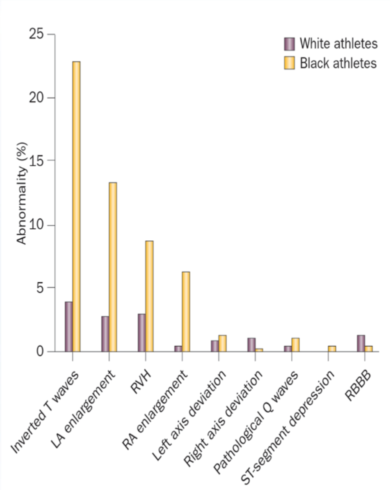
Prevalence of abnormal ECG patterns other than T-wave inversions



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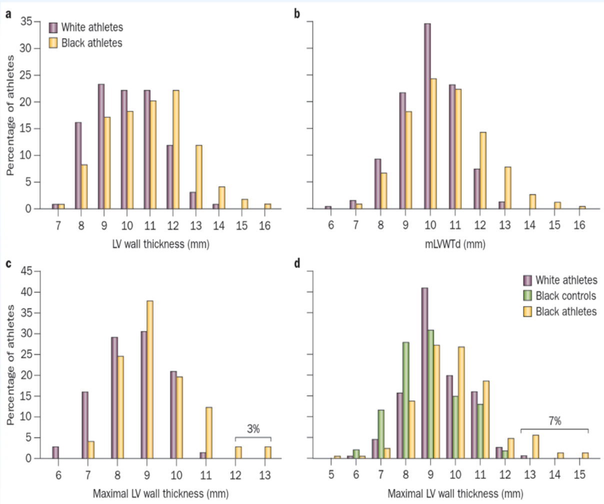
Differences in LVH between the ethnicities



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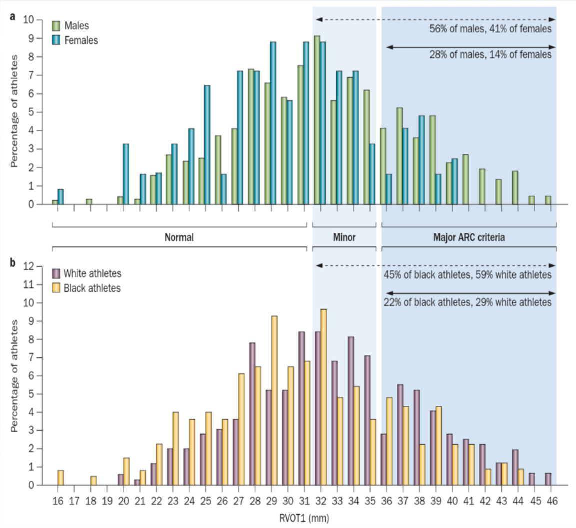
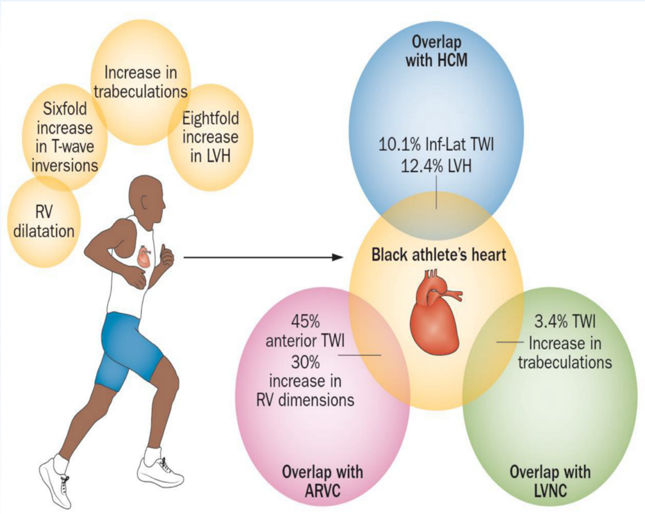
Distribution of values for parasternal short-axis proximal RVOT



Sheikh N, et al. Nat. Rev. Cardiol. advance online publication 25 February 2014;

Grey zones in Black Athlete



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Racial difference

- Ethnicity is an important determinant of cardiovascular adaptation to exercise and should be considered during interpretation of the ECG and Echo in athletes
- Black athletes reveal profound electrical and structural alterations in response to exercise; 23% exhibit T-wave inversion and 13% left ventricular hypertrophy
- Application of current ECG interpretation criteria derived from white athletes would result in >40% of black athletes being diagnosed with an abnormal electrocardiogram

Sheikh N, et al. Nat. Rev. Cardiol. advance online publication 25 February 2014;

Racial difference

- In the absence of symptoms or family history of CMP, T-wave inversion confined to leads V1–V4 is likely to physiological response to exercise in black athletes
- Middle-Eastern athletes seem to exhibit similar electrical and structural changes in response to exercise as white athletes
- More data are required for athletes from East and South Asia before conclusions can be made regarding cardiac adaptation to exercise in these ethnicities

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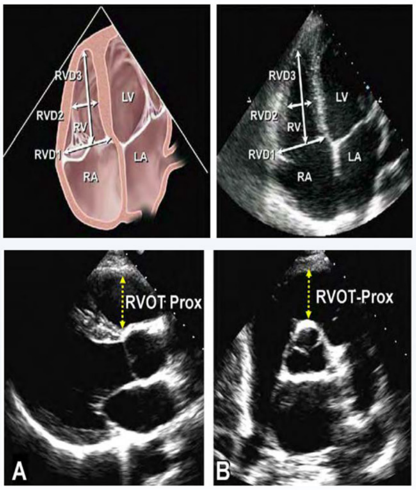
Current Recommendation for RV evaluation by 2DE

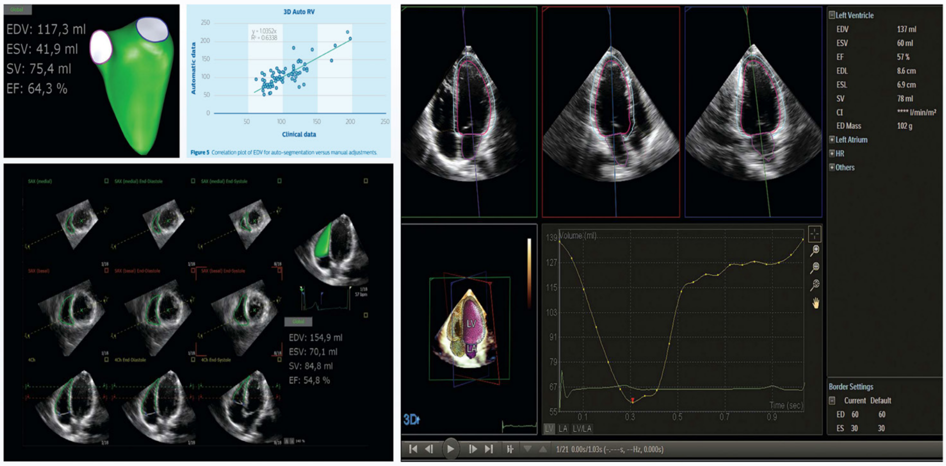


MAJOR ECHOCARDIOGRAPHIC CRITERIA FOR ARVC
Regional RV Dyskinesia or Aneurysm
And one of the following
PLAX RVOT ≥ 32mm (corrected for body size [PLAX/BSA] ≥ 19mm/m2)
PSAX RVOT ≥ 36mm (corrected for body size [PLAX/BSA] ≥ 21mm/m2)
Or
Fractional Area Change ≤ 33%

MINOR ECHOCARDIOGRAPHIC CRITERIA FOR ARVC
Regional RV Akinesia or Dyskinesia
And one of the following
PLAX RVOT ≥ 29 to < 32mm (corrected for body size [PLAX/BSA] ≥ 16 to < 19mm/m2)
PSAX RVOT ≥ 32 to < 36mm (corrected for body size [PLAX/BSA] ≥ 18 to 21mm/m2)
Or
Fractional Area Change > 33 to < 40%

2010 ASE Recommendation for Right Heart

3D Echo for RV and LV evaluation



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