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Cardiorespiratory fitness in relation to cardiometabolic health in adult Mexican Rarámuri

Relación entre la aptitud cardiorrespiratoria y la salud cardiometabólica en adultos rarámuris mexicanos

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Abstract

Objective: *In indigenous people of Mexico, there is a scarcity of information on the relationship between cardiorespiratory fitness (CRF) and clinical cardiometabolic health. The objective was to study the relationship between CRF and cardiometabolic health in adult Mexican Rarámuri (also known as Tarahumara), and to study cardiac health and physiological adaptations to ultradistance running in a subgroup of Rarámuri.* **Methods:** *In rural Rarámuri (n = 66) living at moderate altitude (1150-2400 m above sea level), we carried out measurements of anthropometry, hemodynamics (sitting blood pressure and heart rate), plasma glucose, electrocardiogram and echocardiography, and estimated CRF using a sub-maximal steptest.* **Results:** *Mean age of the studied population was 36.1 (standard deviation 11.6) years. Two participants (3%) were underweight, and ~47% were overweight/obese. Hypertension was found in ~24% of the participants. Mean CRF was moderately high to moderately low at 49 and 34 mLO_2/min/kg in men and women, respectively, and CRF was significantly and inversely associated with hemodynamic and biochemistry measures except for blood glucose ($p < 0.05$). In a sub-group of runners, three men had mildly increased relative ventricular mass (range 118-128 g/m^2).* **Conclusion:** *We found a relatively high proportion of overweight/obesity as well as hypertension. The expected inverse relationship between CRF and cardiometabolic measurements was observed. Abnormal physiological myocardial adaptation to ultradistance running was minimal.*

Keywords: *Cardiorespiratory fitness. Cardiometabolic health. Rarámuri. Indigenous people.*

Resumen

Objetivo: *En poblaciones indígenas de México existe escasa información sobre la relación entre la aptitud cardiorrespiratoria (ACR) y la salud clínica cardiometabólica. El objetivo fue estudiar la relación entre la ACR y la salud cardiometabólica en población indígena rarámuri adulta de México (conocidos también como tarahumaras) y estudiar la salud cardiaca y las adaptaciones fisiológicas a la carrera de ultradistancia en un subgrupo de rarámuris.* **Método:** *De una población rural rarámuri (n = 66) localizada a una altitud moderada (1150-2400 m sobre el nivel del mar) se tomaron mediciones antropométricas, hemodinámicas (presión arterial y frecuencia cardiaca en posición sentada), glucosa en plasma, electrocardiograma y eco-*

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cardiografía, y se estimó la ACR usando una prueba submáxima (steptest). **Resultados:** *La edad media de la población estudiada fue de 36.1 años (DE: 11.6). Dos participantes (3%) mostraron bajo peso, mientras que cerca del 47% tuvo sobrepeso u obesidad. Se encontró hipertensión en aproximadamente el 24% de los participantes. Se halló que la ACR media fue moderadamente elevada a moderadamente baja, de 49 a 34 mlO_2/min/g en hombres y mujeres, respectivamente. Así mismo, se observó una asociación significativa e inversa entre el valor de la ACR y los resultados hemodinámicos y bioquímicos, a excepción de la glucosa ($p < 0.05$). En un subgrupo de corredores, tres hombres tuvieron un leve incremento de la masa ventricular relativa (rango: 118-128 g/m^2).* **Conclusión:** *Encontramos una proporción relativamente alta de sobrepeso/obesidad e hipertensión. Se observó una relación inversa entre la ACR y los resultados hemodinámicos y bioquímicos. Se encontró una mínima adaptación fisiológica cardiaca anormal a la carrera de ultradistancia.*

Palabras clave: *Aptitud cardiorrespiratoria. Salud cardiometabólica. Rarámuri. Gente indígena.*

Introduction

Cardiorespiratory fitness (CRF) is a powerful predictor of all-cause and cause-specific mortality[1,2] and morbidity[3,4]. While directly measured oxygen uptake – the gold standard measure of CRF – is rarely carried out in public health-related studies, especially in indigenous people[5], sub-maximal tests using heart rate as a proxy for oxygen uptake are more common, especially in low- and middle-income countries[6-8].

In northern Mexico, the Rarámuri (also known as Tarahumara) are known for their high habitual physical activity level[7,9] beyond occasional participation in traditional and in recent decades “modern” ultradistance running races[10,11]. Nonetheless, CRF does not necessarily reflect the high habitual physical activity level in the Rarámuri population, which could be due to low activity intensity as walking at low to moderate intensity is the most common form of physical activity[7,9,12].

Studies on CRF in relation to cardiovascular or metabolic health measures in the Rarámuri are few[7,13,14] with the most recent publications focusing on adolescents. The Rarámuri are an indigenous population of approximately 91,500 people (self-identified and > 2 years of age) primarily residing in the so-called Sierra Tarahumara mountains in the state of Chihuahua[15] and they are undergoing an epidemiological transition[16]. Therefore, capturing the range of CRF will give an indication of the impact of fitness on cardiometabolic health.

Furthermore, in studies of small groups of ultradistance runners with a highly heterogenous CRF profile, we have been able to investigate cardiac-specific adaptation to extreme exercise in Rarámuri athletes. Therefore, we aim to give a better understanding of the relationship between CRF, cardiometabolic health, and myocardiac adaptation to ultradistance running activities in adult Rarámuri.

Methods

Participants

Participants of the current study consist of three groups of rural Rarámuri individuals recruited for different studies conducted during the period 2010-12[7,11,17,18]. Initially, we recruited 94 participants, but 11 participants were excluded as they either did not identify as Rarámuri (n = 7), were pregnant (n = 1), or had known hypertension or diabetes (n = 3). Another 17 participants were excluded, as they either did not do or did not finish a valid CRF test, except if they underwent echocardiography measurements (n = 3). Therefore, the final number of participants was n = 66. All participants were recruited in the Sierra Madre Occidental region, Chihuahua, Mexico where they resided, during the months of July (n = 13), September (n = 40), and November (n = 13). For this study, we defined runners as having participated in a race in relation to their recruitment for one of the three original studies on which this study was based[7,11,17,18]. We compared the cardiometabolic profile for men versus women, as well as for runners versus non-runners, among men only due to a small sample size for female runners (n = 3). The study sites are situated between ~1150 m and 2400 m above sea level. During the three periods of data collection, we set up makeshift laboratories in schools, private homes, or local hospitals. All participants gave written and oral informed consent. In case of illiteracy, the consent form was signed with a thumbprint. Ethical approval was given by the Ethical Committee of Science in Chihuahua, Mexico (no. 0003925).

Anthropometry

Participants had their weight, height, and waist circumference measured to the nearest 0.1 kg and nearest 0.1 cm, respectively, with the participants wearing minimal clothing. The body mass index (BMI, kg/m^2) was derived. Underweight, overweight, and obesity were defined as BMI < 18.5, BMI ≥ 25.0-29.9, and BMI ≥ 30.0 kg/m^2, respectively[19]. Waist circumference was measured twice according to standard procedures[20], and body fat percentage was measured using bioimpedance (Tanita Pro Body Composition Analyzer TBF-310-GS, Tokyo, Japan).

Blood pressure and heart rate

Sitting systolic and diastolic blood pressures (SBP and DBP, respectively, mmHg) as well as sitting heart rate (SHR beats/min) were measured with a full-automatic monitor (Omron M8 RC, Kyoto, Japan). Blood pressure was measured 3 times on the right upper arm with the participant seated and following 15 min of rest, and with 2 min between each measurement. Hypertension was defined as SBP ≥ 135 and/or DBP ≥ 85 mmHg, respectively[21].

Blood samples

Random capillary blood glucose test was determined by the glucose dehydrogenase method (HemoCue B-Glucose 2011, Ängelholm, Sweden) in some of the participants (n = 40), while the remaining participants (n = 26) had a capillary glycated hemoglobin (HbA_{1c}) test using an automated boronate affinity assay (Afinion AS100 Analyzer (Afinion AS100 Analyzer [Axis Shield PoC, Oslo, Norway]). The latter was converted to estimated average blood glucose before statistical analysis by using the formula ($28.7*HbA_{1c}$) - 46.7[22] to present plasma glucose results for all participants. Diabetes mellitus was defined as plasma glucose ≥ 200 mg/dL according to World Health Organization guidelines[23]. In runners only (n = 25), hemoglobin (Hb) was analyzed by a modified azide-methemoglobin reaction[24] using a Hb 2011 device (HemoCue AB, Ängelholm, Sweden). Anemia was defined as Hb below 13 and 12 mg/dL for men and women, respectively, adjusted to the participants' altitude of living (meters above sea level) to avoid false high Hb levels[25]. Furthermore, in runners, 10 mL blood was collected in lithium heparin-containing BD-Vacutainer VR tubes for the analyses of high-sensitivity C-reactive protein (hs-CRP) and other plasma markers. However, for this study, only hs-CRP is presented.

Fitness and physical activity measurements

CRF was derived as a VO_{2max} estimate using a standardized, incremental, 8-min step test as described by[26] using an Actiheart®, a combined heart rate and accelerometry device. Twenty potential participants were either unavailable for the test, unable to follow the rhythm of the standardized incremental test, or they discontinued the test before 4 min, which was the minimum amount of time accepted for estimating VO_{2max}. Physical activity energy expenditure (PAEE) was measured using an Actiheart® over 3 days and nights in a sub-sample (n = 12) not differing significantly from the larger sample by age, sex, BMI, plasma glucose, or blood pressure measures.

Electrocardiography

In runners (n = 25), a 12-lead electrocardiogram (ECG) was performed using a Medi Trace, ver. 5.2 (Medi Core, Mexico City). Different PR intervals, QRS intervals, heart rate, QT interval and corrected QT interval, R wave voltages, T wave, and ST segment variations were measured. The presence of left and right ventricular hypertrophy, as well as atrial enlargement data, was analyzed in a targeted manner. The ECG results were read by two experienced cardiologists, blinded to participant demographic data.

Echocardiography

In a sub-group of runners (n = 13), transthoracic echocardiogram was performed using the Philips Excelera version R3.3L1 and Qlab software version 9.1, applying the Quasi-Monte Carlo solution for deformation analysis. Thorough studies were performed using two-dimensional images, pulsed and continuous Doppler, with parasternal long-axis, 4-chamber apical, 2-chamber, short-axis, and subcostal views performed by an expert in this technique. Left ventricular (LV) mass was calculated according to the formula: 0.8*{1.04*([LV internal dimension-diastole+posterior wall thickness at end diastole+superior wall thickness at end diastole]^3-[LV internal dimension-diastole]^3)}, and then indexed to body surface area[27].

Statistics

Normally distributed descriptive results are given as mean standard deviation (SD). If skewed, data were log-transformed to find p-value and presented as geometric mean (95% confidence interval [CI]). To establish differences between men and women and runners and non-runners, respectively, Student's *t*-test without and with log-transformed numbers, respectively, was performed. Linear regression analyses were performed to establish the association with exposure variables (mainly CRF), and clinical outcome variables. Log-transformed data for the regression analyses were back-transformed to give a coefficient e^B, which should be interpreted as a ratio. If the dependent variable was skewed, it was log-transformed to determine the p-value and subsequently back-transformed to determine a ratio (%) using the formula (exp[X]-1)*100. Regression analyses are presented as univariate results but adjusted for age and sex to establish potential confounding of the univariate results. Clinical variables (BMI, blood pressure, plasma glucose, Hb, and hs-CRP) were categorized according to standard risk cut offs, and differences between categories were assessed by doing Fisher's exact test. All analyses were done with Stata 18.0 Intercooled version (Stata Corp, College Station, TX). P < 0.05 was considered significant.

Results

Mean age was 36.1 (SD 11.6) years, with 40.9% being women. Sex differences were significant in height, weight, fat mass, SHR, and CRF (Table 1 for background characteristics). For BMI categories, two participants (3.0%) were underweight, 20 (30.3%) participants were overweight, and 11 (16.7%) participants were obese, with no difference between the sexes (p = 0.16). Hypertension was found in nine men and six women (23.1 vs. 22.2 %), respectively (p = 0.59), and two participants (one man, one woman) had diabetes mellitus. Mean Hb was 15.2 (SD 1.6) g/dL, and three runners had anemia. For hs-CRP levels, geometric mean was 4.1 (95% CI: 1.8;9.3) mg/L, and 10 runners had very high-risk levels for cardiovascular disease (CVD)[28].

For the runners, no presence of left and right ventricular hypertrophy, as well as no evidence of left and right atrial enlargement, was observed based on electrocardiographic criteria. Complete right bundle branch block was diagnosed in three individuals (all men), without clinical manifestations. ECG neither showed atrioventricular blocks nor specific signs of ischemia. Acuminate T waves were observed in four participants with a maximum voltage of 8 mm, as well as non-specific changes, including ST segment elevation or non-ST segment elevation > 1.5 mm. See table 2 for mean (SD) and range of ECG analyses.

Table 1. Background characteristics (mean ± standard deviation) of rural Rarámuri (n = 66)

Variable	Men (n = 39)	Women (n = 27)	p
Age (years)	36.0 (10.9)	36.1 (12.7)	0.98
Height (m)	1.65 (0.1)	1.50 (0.1)	< 0.001
Weight (kg)[1]	65.2 (61.0;69.7)	58.8 (55.1;62.8)	0.04
Body mass index (kg/m^2)	24.5 (4.2)	26.4 (4.2)	0.07
Waist circumference (cm)	81.7 (16.5)	80.6 (11.9)	0.78
Fat mass, n (%)	21 (12;28)	35 (26;37)	< 0.001
Systolic blood pressure (mmHg)[2]	117 (14)	115 (18)	0.63
Diastolic blood pressure (mmHg)[2]	74 (12)	76 (11)	0.41
Heart rate (beats min^{-1})[2]	60 (11)	71 (8)	< 0.001
Plasma glucose (mg/dL)[1,2]	117 (110;124)	127 (117;138)	0.11
Cardiorespiratory fitness (mLO_2/min/kg)[3]	48.9 (12.7)	33.8 (7.7)	< 0.001
Physical activity energy expenditure (kJ/day/kg)[1,4]	67.5 (42.1;108.0)	73.7 (53.8;100.8)	0.69

[1]Geometric mean (95% confidence interval).
[2]Includes mix of random plasma glucose and converted HbA1c
[3]Estimated heart rate following an 8-min, incremental sub-maximal steptest, n = 63.
[4]Physical activity energy expenditure using combined accelerometry and heart rate monitor following 3-days continuous monitoring, n = 12.

Based on echocardiographic criteria, the different structural and functional parameters of the left ventricle were within normal limits (wall thicknesses, diameters, volume, and systolic function). Mean echocardiography-derived relative to body LV mass was 100 (SD 20) g/m^2, with the majority being within the reference range of 49-115 g/m^2 according to[27] except for three participants, who had mildly increased relative LV mass (118, 121, and 128 g/m^2, respectively). Of these, one participant was competing in a 63 km race, and two participants were competing in a 100 km race. For the whole sub-group (n = 13), the volume of the atrium was normal, and indirect estimation of pulmonary pressure by tricuspid regurgitation velocity was also within normal limits. No valve anomalies were observed. See table 2 for mean (SD) and range of echocardiographic analyses.

Table 2. Electrocardiographic (n = 26) and echocardiographic findings (n = 13) in adult Rarámuri

Electrocardiographic findings	Mean ± SD	Range
PQ interval (ms)	156.5 ± 17.7	120-200
QRS complex (ms)	81.2 ± 10	60-100
QT interval (ms)	436 ± 45	360-500
QTc interval (ms)	429 ± 48	382-482
RR interval (ms)	1046 ± 164	740-1320
Ventricular frequency at rest (bts/min)	59 ± 9	45-81
Right bundle branch block	3	
Echocardiographic findings	**Mean ± SD**	**Range**
RV diastolic diameter (> 4.2 cm abnormal)	3.14 ± 0.25	2.8-3.6
LV AP diameter end-systole	3.15 ± 0.29	2.5-3.5
LV AP diameter end diastole (4.2-5.9 cm)	4.68 ± 0.34	4-5.1
LV Interventricular septum thickness (0.6-1.0 cm)	0.83 ± 0.09	0.68-1
LV Posterior wall thickness (0.6-1.0 cm)	0.77 ± 0.12	0.56-0.93
LV mass (96-200 g)	123 ± 25	67-161
Relative LV mass (49-115 g/m^2)	100.6 ± 20	84-128
LV ejection fraction (> 54%)	64 ± 4	55-71
Left atrial diameter (3.0-4.8 cm)	3 ± 0.3	2.6-3.5
Left atrial volume (18-58 mL)	38 ± 10	24-57
LV volume (mL) end systole (67-155 mL)	70 ± 10	46-88
E wave	87 ± 13	67-116
A wave	48 ± 10	34-61
Ao vel. max (< 2.0 m/s)	128 ± 12	116-162
Ao valve area	2.73 ± 0.23	2.3-3.1
Tricuspide regurgitation velocity	218 ± 23	130-247

LV: left ventricular; RV: right ventricle; AP: anteroposterior; SD: standard deviation.

Figure 1 shows a panel of linear correlations between exposure (X-axis) and outcome (Y-axis) variables. Correlation between CRF and LV mass (n = 10) was $\beta = 0.54$ (95% CI: −0.96;2.04, p = 0.43), and correlation between BMI and hs-CRP (n = 21) was $e^{\beta} = 32.1$ (95% CI: −4.6;82.8, p = 0.09). All linear correlation results were largely sustained when independently adjusted for age and sex, respectively (results not shown).

When comparing male runners (n = 22) versus non-runners (n = 17), there was a significantly better cardiometabolic profile in the runners with the notable exception of plasma glucose (Table 3).

Table 3. Background characteristics (mean ± standard deviation) of male Rarámuri runners versus non-runners (n = 39)

Variable	Runners (n = 22)	Non-runners (n = 17)	p
Age (years)	33.3 (10.6)	39.5 (12.7)	0.078
Height (m)[1]	1.61 (1.58;1.66)	1.65 (1.65;1.70)	0.022
Weight (kg)[1]	56.8 (51.2;61.0)	81.6 (72.6;87.8)	< 0.001
Body mass index (kg/m^2)	21.5 (2.2)	28.3 (2.8)	< 0.001
Waist circumference (cm)	68.6 (10.1)	96.3 (7.1)	< 0.001
Fat mass, n (%)[1]	12 (10;20)	27 (24;30)	< 0.001
Systolic blood pressure (mmHg)[2]	110 (12)	126 (9)	< 0.001
Diastolic blood pressure (mmHg)[2]	67 (10)	83 (6)	< 0.001
Heart rate (beats min^{-1})[2]	56 (2)	64 (8)	0.035
Plasma glucose (mg/dL)[1,3]	113 (108;120)	115 (114;123)	0.15
Cardiorespiratory fitness (mLO_2/min/kg)[1,4]	59.9 (51.7;63.4)	40.9 (36.5;42.7)	0.001

[1]Geometric mean (95% confidence interval).
[2]Measured in the seated position.
[3]Includes mix of random plasma glucose and converted HbA_{1c}.
[4]Estimated heart rate following an 8-min, incremental sub-maximal steptest, n = 63.

Discussion

In a compiled group of rural Rarámuri, we observed inverse relationships between estimated CRF and several cardiometabolic traits. The results were based on univariate regression analyses but were largely sustained by independent age and sex adjustments.

Hemodynamic traits, SBP, DBP, and SHR, were all inversely associated with CRF, but the relatively high proportion (~23%) of Rarámuri with hypertension in this study population is of concern, even if potential white coat hypertension is considered. We used the revised clinic-based cut off for hypertension (135/85 mmHg)[21], which increases the proportion of hypertension as per definition compared to the still widely used definition (140/90 mmHg)[29]. Interestingly, the geographically and supposedly genetically closely related Pima of

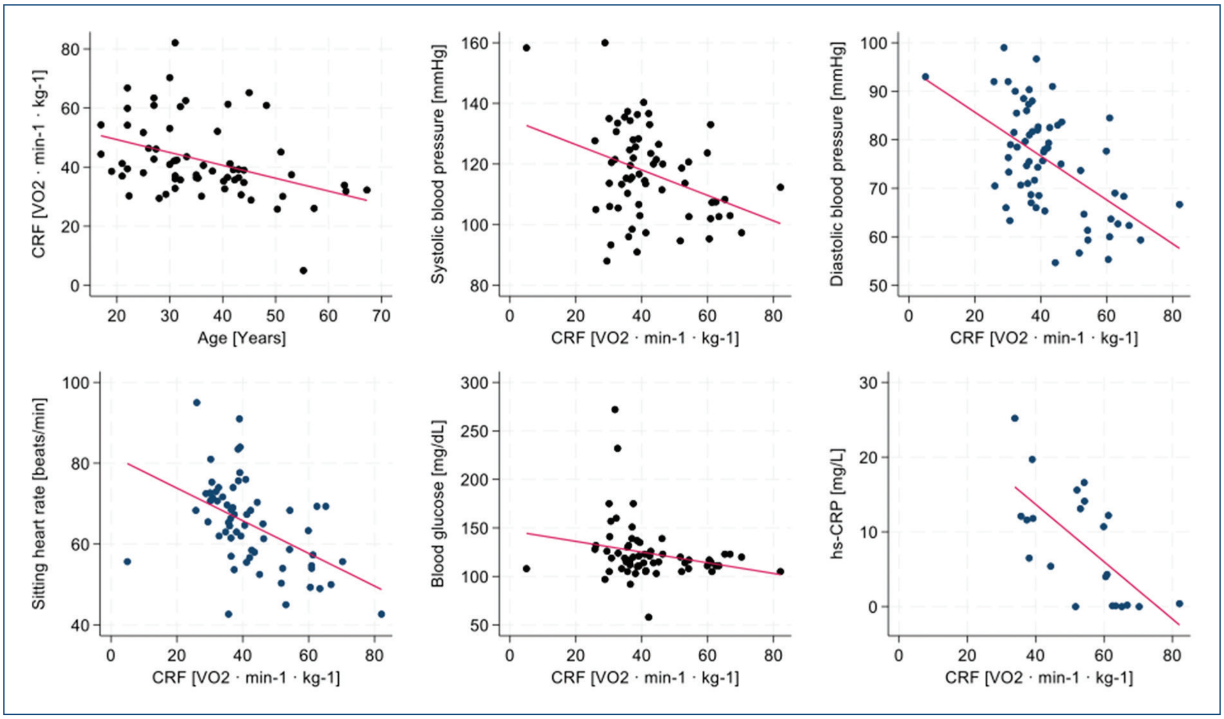

Figure 1. Associations between exposure variables (X-axis) and outcome variables (Y-axis) in rural Rarámuri. Cardiorespiratory fitness (CRF), high-sensitivity C-reactive protein (hs-CRP), and sitting heart rate (SHR). For all associations n = 63 except for CRF and hs-CRP, n = 19 (runners only). The correlations were, respectively, between age and CRF $\beta = -0.4$ (95% confidence interval [CI]: −0.7; −0.2, $p = 0.002$), CRF and systolic blood pressure $\beta = -0.4$ (95% CI: −0.7; −0.1, $p = 0.004$), CRF and diastolic blood pressures $\beta = -0.5$ (−0.6; −0.3, $p < 0.001$), CRF and SHR $\beta = -0.3$ (95% CI: −0.5; −0.1, $p = 0.016$), CRF and blood glucose e^{β} −0.36 (95% CI: −0.75; 0.03, $p = 0.07$), as well as CRF and hs-CRP $e^{\beta} = -8.7$ (95% CI: −13.6, −3.6, $p = 0.002$).

Chihuahua and Sonora (Mexico) as well as Arizona (USA), seem to have lower risk of hypertension compared to Caucasian populations due to lower beta-adrenergic sensitivity, including when adjusted for body fat percentage[30], and lower muscle sympathetic nervous system activity[31]. If similar physiological mechanisms apply to the Rarámuri, this could explain why the proportion of overweight and obesity was twice as high as the proportion of hypertension. Future carefully designed clinical and epidemiological studies need to be implemented in the Rarámuri to address these seemingly ethnic-specific physiological mechanisms.

We observed moderately high (~49 mLO_2/min/kg) to moderately low (~34 mLO_2/min/kg) mean CRF levels in men and women, respectively, considering their average age (36 years). There was substantial variation in individual CRF values, especially among the men (~32-82 mLO_2/min/kg). These results may reveal a mixture of lifestyle factors and selection bias among the study participants. As for lifestyle factors, the main daily movement pattern is walking rather than running[9], which by definition entails low intensity, and thereby has a higher impact on peripheral or metabolic fitness than central fitness or CRF; for an overview see[32].

The very high daily PAEE (68 and 74 [kJ/day/kg for men and women, respectively]) in relation to CRF was not statistically significant, but the results indicate that activity volume and fitness are not necessarily associated, even though firm conclusions cannot be drawn due to the small sample size (n = 12). In support of the high PAEE we measured, Shave et al. demonstrated a high daily step count (average 18,800) based on accelerometer measurements, which equals approximately 15 km of daily walking over 14 consecutive days in 21 Rarámuri men (mean age 35 years) during a period with no running activities and outside the physically demanding harvest season. All physical activity was performed within light and moderate intensity strata[12]. Furthermore, we have previously reported physical activity at such high levels in comparable populations such as the East African Maasai, an agro-pastoralist people with a similar relatively low activity intensity pattern reflecting walking rather than running as the main physical activity domain. Furthermore, we found similar moderately high to moderately low CRF levels in Maasai men and women, respectively[8].

Regarding bias in relation to CRF, 23 out of the 39 men (59%) in the study were selected in relation to ultradistance running events, while this was only the case for three out of 27 women (11%). While not all participants were ultradistance athletes based on their individual CRF levels and running times, especially in 78 and 52 km races performed by men and women, respectively[17], mean CRF may have been "inflated" in the men when compared to women, as the former had higher training status. On average, we showed 30% higher fitness levels in men, as opposed to ~15-25% difference in CRF, which has previously been found when comparing healthy young men and women matched for physical activity[33]. In males only, we did show that except for plasma glucose, CRF and cardiometabolic profile were significantly better in runners versus non-runners. This demonstrates that despite considerable heterogeneity in CRF levels, participating in races is a valid indicator of a healthy, cardiometabolic profile in the Rarámuri.

Ultradistance running competition has historically been part of the culture of the Rarámuri, whether performed as traditional events (rarájipari for men and ariwete for women) or in more recent decades as part of running events organized outside the traditional culture of the Rarámuri[9,11]. Therefore, cardiac adaptation to running extremely long distances and more recently possible acute organ (specifically the heart and kidneys) damage has been a research focus in the Rarámuri[11,17]. None of the early studies[10] or personal observations[34] showed cardiac enlargement in Rarámuri runners. However, these results could be biased by sub-optimal technology used for these kinds of measurements, that is, usage of X-ray. In the current study, we used more sophisticated ultrasound technology and found three runners with mildly increased LV mass, but no significant relationship between CRF and LV mass in the 10 runners in whom we carried out both measurements. Thus, while LV hypertrophy does exist in Rarámuri runners, it seems to be of a mild nature. A larger sample size is needed to determine whether LV mass is connected to CRF and thereby exercise and physical activity intensity.

ECG results were within the normal range. We did find three runners who had right bundle branch block, but without clinical symptoms, including chest pain, dizziness, or fainting.

In runners (n = 25) with hs-CRP analysis, the proportion of elevated hs-CRP levels was high, which is not uncommon in indigenous populations living in rural areas under constrained conditions[35]. The highest level measured was 25.2 mg/L, a moderately elevated level, and thus reflecting potentially high risk of CVD rather than acute bacterial or fungal infections[36]. Even though the correlation between BMI and hs-CRP was not significant, we cannot rule out the possibility that part of the elevated hs-CRP levels was mediated by obesity.

Furthermore, in the group of runners included in this study, only three Rarámuri males had mild anemia. The burden of anemia is generally high in indigenous populations, but in the Rarámuri population, it has only previously been systematically reported in women and children[37]. These results have shown that compared to national data in Mexico, lower estimates were reported in relatively small studies in Rarámuri children (n = 331, 13%) and non-pregnant women (n = 446, 12%)[38,39]. As CRF was 33.9, 39.0, and 60.9 mLO_2/min/kg, respectively in the three men with anemia, possible "sports anemia" – a phenomenon characterized by high plasma volume expansion[40] – may only explain one of the cases. Overall, the results are indicative of a diet sufficient in micronutrients in the current study population.

Strengths of the study were the collection of data in a difficult-to-access population, especially the echo scans, which were conducted for the 1st time in the Rarámuri. We acknowledge several weaknesses of the study. First, the sample size was small, and any firm conclusions cannot be made based on any of the results and group comparisons presented. Second, the compilation of participants from three different studies does create some methodological deficiencies, such as a lack of measurements of several parameters in all participants, including echo scans, ECG, Hb, hs-CRP, and PAEE.

Conclusion

We found an inverse relationship between CRF and cardiometabolic risk factors in a study population of 66 rural living, adult Rarámuri men and women (mix of non-runners and runners). The results were similar when comparing male runners versus non-runners. The proportion of overweight/obesity was high, while the proportion of hypertension was substantially lower. Among Rarámuri ultramarathon runners, three had mildly elevated LV mass. The results warrant larger studies in the Rarámuri population in which fitness and physical activity levels are systematically and carefully recorded along with cardiovascular and metabolic variables to determine cardiometabolic health at the population level, and especially comparing runners versus non-runners. Furthermore, possible social determinants for the high proportion of overweight/obesity in the rural Rarámuri population indicated here should be considered in future studies.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from all patients, and secured approval from the Ethics Committee. SAGER guidelines have been followed as applicable to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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