

Hypertensive patients show higher heart rate response during incremental exercise and elevated arterial age estimation than normotensive adult peers: VASCU-HEALTH PROJECT

Pacientes hipertensos muestran una mayor respuesta de la frecuencia cardíaca durante el ejercicio progresivo en relación con pares adultos normotensos: PROYECTO VASCU-HEALTH

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Abstract. There is limited information regarding heart rate (HR) response from predictive formulae and actual exercise tests between arterial hypertension (HTN) and normotensive adults, as well as about vascular similarities or differences between samples of different blood pressure control. This study aimed 1) to describe and compare the HR during exercise between HTN and normotensive adults and 2) to describe the endothelial function and related vascular parameters in both groups. A descriptive clinical study was conducted with 64 adults (men and women) who were divided into three groups: arterial hypertension (HTN $n=26$), elevated blood pressure (Ele $n=16$), or normotensive control (CG $n=22$). The participants underwent an incremental cycling exercise test of 5 stages, where HR (primary outcome) was measured, and secondary vascular outcomes (percentile classification of the pulse wave velocity (%ILE_{PWV_{ba}}), maximum carotid intima-media thickness (cIMT_{max}), and arterial age among others) were measured. In stage 2 of the test (50-100 watts), the HTN group showed significantly higher HR vs. CG (+14 beats/min; $p<0.05$) and vs. Ele group (+15 beats/min; $p<0.05$), and in stage 5 (125-250 watts), HTN group showed higher HR vs. CG (+22 beats/min; $p<0.05$). HTN group showed a higher arterial stiffness by %ILE_{PWV_{ba}} classification and arterial age estimation than the CG group. In conclusion, HTN patients reported a higher HR response only in two out of five (monitored) stages of the Astrand cycling exercise test than normotensive peers. Moreover, all groups showed a higher HR_{predicted} than real HR_{peak} obtained from the exercise test. These results are displayed with more altered vascular parameters in the HTN group.

Keywords: Arterial hypertension; Endothelial dysfunction; Overweight; Obesity; Vasculature.

Resumen. Existe información limitada respecto a la respuesta de la frecuencia cardíaca (FC) a partir de fórmulas predictivas y prueba de ejercicio real entre adultos con hipertensión arterial (HTA) y normotensos, así como sobre las similitudes o diferencias vasculares entre muestras de diferente control de la presión arterial. El objetivo de este estudio fue describir y comparar la frecuencia cardíaca durante el ejercicio entre adultos con HTN y normotensos, así como describir parámetros de función endotelial y vasculares. Se realizó un estudio clínico descriptivo con 64 adultos (hombres y mujeres) que fueron divididos en tres grupos: hipertensión arterial (HTN $n=26$), presión arterial elevada (Ele $n=16$), o normotensos control (CG $n=22$). Los participantes se sometieron a una prueba de ejercicio, en la que se midió la FC (variable principal) y parámetros vasculares secundarios (clasificación percentil de la velocidad de la onda del pulso (%ILE_{PWV_{ba}}), grosor máximo de la íntima-media carotídea (cIMT_{max}) y edad arterial entre otras. En la etapa 2 del test (50-100 vatios), el grupo HTN mostró una FC significativamente mayor vs. el grupo GC (+14 latidos/min), y vs. el grupo Ele (+15 latidos/min), ambos $p<0,05$; y en la etapa 5 (125-250 vatios) vs. el grupo GC (+22 latidos/min; $p<0,05$). El grupo HTN mostró una clasificación mayor de rigidez arterial %ILE_{PWV_{ba}}, y de edad arterial que el grupo NT. En conclusión, los sujetos con HTA presentan una mayor respuesta de la FC durante el ejercicio que los normotensos. Sin embargo, todos los grupos mostraron una mayor HR_{predicted} en relación con la HR_{peak} real. Estos resultados se muestran con una clasificación en percentiles superiores de rigidez arterial y una mayor estimación de la edad arterial con relación a adultos normotensos.

Palabras claves: Hipertensión arterial; Disfunción endotelial; Sobrepeso; Obesidad; Vasculatura

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Introduction

Arterial hypertension (HTN) is a common risk factor for cardiovascular disease (CVD) (Whelton et al., 2018). HTN has been linked to various functional and structural disorders, including endothelial dysfunction (EDys), atherosclerosis, dyslipidemia, micro- and macro-vascular damage in vessels, and the development of arterial atherosclerosis (Lobato et al., 2012). EDys is characterized by inflammation of the endothelial cells and decreased arterial vasodilation, which can be measured using gold standard methods such as flow-mediated dilation (FMD) measurement (Heiss et al., 2022; Thijssen et al., 2019), pulse wave velocity of the brachial artery (PWV_{ba}), which is a marker of arterial

stiffness, and carotid intima-media thickness (cIMT). PWV_{ba} is a well-reported outcome that detects functional and structural changes in the vascular wall (Kim, Rhee, & Kim, 2022; Yan et al., 2022). Similarly, maximum (cIMT_{max}) and average (cIMT_{av}) are suitable parameters for detecting structural changes in the arterial endothelial wall (Itoh et al., 2019).

Exercise training has been increasingly prescribed as a therapy for HTN patients because it improves blood pressure and vascular parameters (Oviedo, Niño, Bellomío, González, & Guerra, 2015; Pescatello et al., 2019; Román et al., 2019). In this sense, the American College of Sports Medicine (ACSM) (Garber et al., 2011) and the American Diabetes Association (ADA) recommend exercise in

populations with cardiometabolic risk factors, where the heart rate (HR) is a helpful parameter to regulate the exercise 'intensity' (Colberg et al., 2016). Previous studies have shown that monitoring the HR in exercise tests could be helpful for exercise prescription in HTN and cardiometabolic diseases (Andrade-Mayorga, Mancilla, Díaz, & Alvarez, 2020; Mancilla et al., 2014). Several electronic devices, such as telemetric HR monitors frequently used in exercise interventions, usually include the theoretically predicted maximum heart rate ($HR_{\text{predicted}}$) in their operating system that is calculated using age-related equations. However, previous cardiometabolic studies have shown that $HR_{\text{predicted}}$ may be supra-estimated (i.e., in physically inactive populations) or, by contrast, under-estimated (i.e., in highly trained populations) in comparison to the actual HR maximum of a subject (Miyai et al., 2002). Additionally, with the aims of exercise prescription, the $HR_{\text{predicted}}$ use is attractive considering that its value (heart rate maximum) can be easily obtained through formulas, such as the Karvonen formulae, to calculate an aimed exercise intensity (e.g., 60, 70, 80%) considering the correlation of HR with the percentage of maximum oxygen consumption (Karvonen, 1988). Therefore, it is essential to compare and describe the HR response to exercise between HTN and normotensive adults and compare vascular parameters between HTN and normotensive peers.

Previous findings showed that type 2 diabetes patients (T2DM) versus normoglycemic or hyperglycemic adult peers did not exhibit differences in HR during a similar incremental cycling test, as well as during interval exercise (Andrade-Mayorga et al., 2020), and other studies have shown that T2DM patients cannot increase their HR proportionally with increased exercise effort (Brubaker & Kitzman, 2011; Keytsman, Dendale, & Hansen, 2015). However, evidence about HR behavior during incremental exercise in HTN subjects is scarce. Thus, this study aimed 1) to describe and compare the HR during exercise between HTN and normotensive adults and 2) to describe the endothelial function and related vascular parameters in both groups.

Material and methods

A preliminary descriptive study was conducted as part of the VASCU-HEALTH randomized controlled clinical trial. Sixty-four ($n=64$) adult men and women participated in an initial evaluation of their cardiometabolic health and physical condition. All these participants, after this descriptive study, will have the possibility to be invited to a future exercise training intervention.

Participants

At the first enrollment stage, participants were adult citizens, members of a University staff (i.e., academics/faculties, students, and employees), and adults nearby residents of neighborhoods/areas invited by different public media. As the study included recruiting healthy normotensive, elevated BP, or HTN, the sample

size was intentionally distributed immediately after blood pressure categorization into one out of three blood pressure groups (normotensive, elevated blood pressure, or arterial hypertension) based on the American Heart Association's blood pressure categorization (Whelton et al., 2018). The study was conducted from September 2022 to January 2023 and is registered under the clinical trials.gov scientific platform NCT05710653.

Experimental procedures

The eligibility criteria for participants included: a) arterial hypertension, b) elevated blood pressure (treated with pharmacotherapy) or normotensive, c) normal weight, overweight, or obesity (as determined by body mass index [BMI]), and d) normoglycaemic, hyperglycemic or diagnosed with T2DM and treated with pharmacotherapy. Exclusion criteria were as follows: a) self-reporting to be 'insufficiently active' (i.e., participants who do not declare at least 150 to 300 min of low to moderate physical activity per week or at least 75 min of vigorous physical activity per week) (Álvarez et al., 2021), b) abnormal ECG, cardiovascular disease (CVD), heart disease, or vasculopathy, c) uncontrolled hypertension (systolic blood pressure [SBP] ≥ 169 mmHg or diastolic blood pressure [DBP] > 95 mmHg), d) morbid obesity (BMI ≥ 40 kg/m²), e) type 1 diabetes mellitus with insulin dependence, f) diabetes complications such as varicose ulcers, nephropathies, or muscle-skeletal disorders (e.g., osteoarthritis), g) recent participation in weight loss treatment or exercise training programs (or within the past three months), and h) use of pharmacotherapy that can influence body composition or weight loss. All participants provided written consent, and the study was conducted by the Declaration of Helsinki and was approved by the Ethics Committee of Universidad Andres Bello, Chile (Approval N° 026/2022).

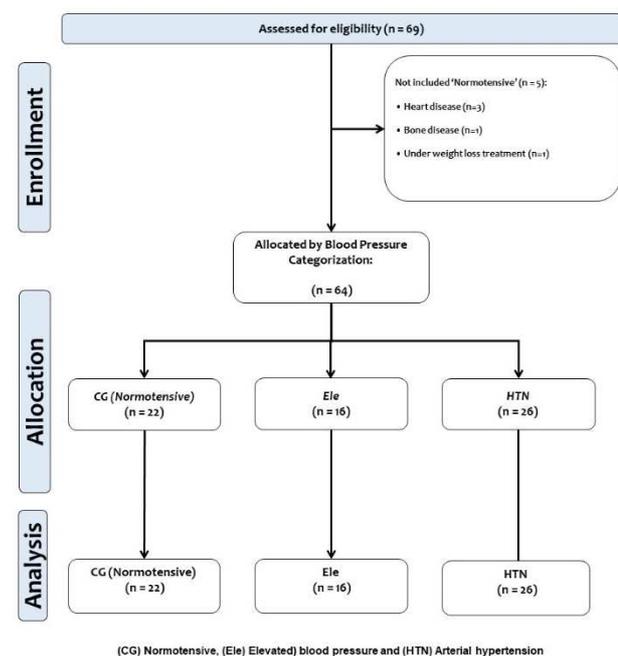


Figure 1. Study design

In the first stage of enrollment, ($n=69$) participants were initially recruited, where ($n=3$) subjects were excluded due to cardiovascular disease, ($n=1$) was excluded due to arthrosis, and ($n=1$) due to undergoing weight loss therapy with pharmacological treatment. The final sample size was as follows; normotensive control group (CG, $n=22$; SBP 110.4 and [95%CI]; [107.4; 113.4], DBP 73.8 [70.8; 76.8]), elevated blood pressure group (Ele, $n=16$; SBP 124.9 [123.5; 126.3], DBP 83.3 [79.1; 87.6]), or hypertension group (HTN, $n=26$; SBP 143.2 [139.1; 147.2], DBP 87.3 [82.5; 92.0] all values in mmHg). The study design can be found in (Fig. 1).

Measurements

Exercise test and HR

The Astrand cycling test was applied to evaluate the HR and power output (PO) in watts of the participant belonging to the normotensive control group (CG), elevated blood pressure group (Ele), and hypertension group (HTN) (Astrand & Stromme, 2003; Mancilla et al., 2014). The test consisted of five stages for men (stage 1: 50w, stage 2: 100w, stage 3: 150w, stage 4: 200w, or \geq stage 5: 250w) and women (stage 1: 25w, stage 2: 50w, stage 3: 75w, stage 4: 100w, or \geq stage 5: 125w; however to this study we reported only five stages in which all participant finished this 5th stage and showed the average data of men and women) with incremental increases in power output, and HR was measured during each stage using an electromagnetic cycle ergometer (Ergoselect 200, ERGOLINE™, Germany) and a heart rate monitor (A370, Polar™, Finland). This test was designed to assess the HR response during an incremental exercise, which was the study's primary outcome.

Blood pressure categorization

The systolic blood pressure (SBP) and diastolic blood pressure (DBP) of participants were classified according to the American Heart Association guidelines (Whelton et al., 2018). Normal blood pressure was defined as SBP/DBP less than 120/80 mmHg, elevated blood pressure (Ele) as SBP/DBP between 120-129/80 mmHg, and stage 1 hypertension as SBP/DBP between 130-139/80-89 mmHg, and stage 2 hypertension as SBP/DBP greater than or equal to 140/90 mmHg (Whelton et al., 2018). The readings were taken twice using an automatic monitor (OMRON™, model HEM 71 14, United States) with a pneumatic cuff positioned on the participant's left arm in a seated position for at least 10 minutes.

Percentile classification of pulse wave velocity

All subjects were positioned supine during 20 minutes of resting, where an electronic device with an inflation/deflation pneumatic cuff for the left arm was used for the PWV_{ba} measurement (Arteriograph, TENSIO MED™, Hungary). The device automatically inflated or deflated the cuff, maintaining occlusion in the left arm for 5 minutes. The information was then analysed using the Arteriograph Software (v.1.9.9.2; TensioMed, Budapest, Hungary),

from which a PDF information sheet was downloaded from the device. The percentile classification of pulse wave velocity (%ILE_{PWV_{ba}}) was obtained and registered. The Arteriograph has been validated against gold-standard equipment (Ring, Eriksson, Zierath, & Caidahl, 2014).

Endothelial dysfunction measurement

To measure cIMT_{max}, we used an ultrasound imaging 7–12 MHz linear-array transducer (GE Medical Systems, Model LOGIQ-E PRO, Milwaukee, United States). The subjects were asked to lie in a supine position for 20 minutes. When the carotid bulb was identified, an image was obtained in B mode for the right longitudinal orientation of the common carotid artery by an automatic ultrasound function. The scan was focused on 1 cm far from the bifurcation on the far wall of the common carotid artery of the right side. The ultrasound software recorded the image and later was analysed offline for average and cIMT_{max} values. All measurements were recorded at the end-diastolic stage (Coll & Feinstein, 2008). Given that the average of carotid intima-media thickness >0.9 mm has been used as previous cut-off points to denote high cardiovascular risk, to our cIMT_{max} outcome, we used this value similarly, following the European Society of Hypertension and European Society of Cardiology (Mancia et al., 2013).

Anthropometric and body composition

The anthropometry/body composition was measured using various methods. To anthropometry, body mass (in kilograms), waist circumference (in centimeters), and to body composition as body fat (as a percentage of total weight), and skeletal muscle mass (as a percentage of total weight) were measured using a digital bio-impedance scale (OMRON™ model HBF-514C, United States). Height (in meters) was measured using a stadiometer (SECA model 214, United States). Participants were asked to wear light clothing and remove their shoes for accurate measurements. Body mass index (BMI) was then calculated using body mass and height measurements, and the degree of obesity was determined based on standard criteria for underweight, normal weight, overweight, or obesity [37]. Table 1 shows the baseline characteristics of the participants.

Secondary Vascular parameters

Besides the cIMT_{max}, and %ILE_{PWV} measurement obtained in a supine position with 20 min resting, we measured other secondary vascular parameters such as aortic (Aix_{ao}) and brachial artery (Aix_{ba}) augmentation indexes, diastolic reflection area (DRA), and the estimated arterial age expressed in years that is a previously estimated vascular parameter obtained from a population of 10 thousand participants (Ring et al., 2014). All these parameters were obtained using the same electronic device (Arteriograph, TENSIO MED™, Hungary), and the information was analysed using the previously mentioned corresponding software (Ring et al., 2014).

Table 1.

Baseline characteristics of participants.

Outcomes	CG (n=22)	Ele (n=16)	HTN (n=26)	Baseline p-value
Age (y)	39.9 (33.3; 46.4)	38.3 (31.2; 45.5)	42.2 (36.8; 47.6)	p=0.702†
Weight (kg)	67.3 (63.1; 71.6)	79.7 (72.9; 86.6)*	84.1 (77.4; 90.8)*	p<0.0001†
Height (m)	1.59 (1.57; 1.62)	1.63 (1.59; 1.67)*	1.70 (1.65; 1.75)*	p<0.0001†
<i>Body mass index</i>				
Underweight (n=/%)	0 (0.0)	0 (0.0)	0 (0)	p<0.0001#
Normal weight (n=/%)	4 (18.1)	1 (6.2)	9 (34.6)	
Overweight (n=/%)	8 (36.3)	7 (43.7)	14 (53.8)	
Obesity (n=/%)	10 (45.4)	8 (50.0)	3 (11.5)	
Heart rate rest (beats/min)	75.5 (70.6; 80.3)	75.6 (70.0; 81.3)	73.3 (69.4; 77.3)	p=0.402
SpO ₂ (%)	97.2 (97.3; 98.5)	98.1 (97.4; 98.7)	97.8 (97.2; 98.3)	p=0.712
<i>Blood pressure</i>				
Systolic BP (mmHg)	110.4 (107.4; 113.4)	124.9 (123.5; 126.3)**	143.2 (139.1; 147.2)**	p<0.0001†
Diastolic BP (mmHg)	73.8 (70.8; 76.8)	83.3 (79.1; 87.6)**	87.3 (82.5; 92.0)**	p<0.0001†
<i>Pharmacotherapy</i>				
Angiotensin-converting enzyme inhibitors (n= / total)	-	-	2/26	
Beta blocker (n= / total)	-	-	2/26	
Metformin (n= / total)	-	1/18	-	

Data are shown as mean and 95%CI to continuous outcomes and as (n =) and percentage to ordinal outcomes. (*) Denotes significantly different versus CG at p<0.05. (**) Denotes significantly different versus CG at p<0.001. (***) Denotes significantly different versus CG at p<0.0001. (†) Analyzed by One-way ANOVA at p<0.05. (#) Analyzed by χ^2 test at p<0.05.

Statistical analysis

The sample size for the study was determined using the G*Power 3.1.9.7 sample size calculator. A minimum of ten subjects per group was determined to have a statistical power of $\geq 80\%$ with a 95% confidence interval and an alpha error of 5%. Data are presented as the mean and (95%CI) in Tables and as mean and \pm SD in Figures. The normality and homoscedasticity assumptions were tested by the Shapiro-Wilk test and Levene's test (F), respectively. The Wilcoxon test was used for non-parametric data. One-way ANOVA (groups x time) was used to test differences in HR among CG, Ele, and HTN groups. When an F value was significant, Sidack's *post hoc* test was applied to establish comparisons (CG vs. Ele, CG vs. HTN, and Ele vs. HTN group). A trend analysis [ptrend] was applied to test the potential (linear) tendency to increase or decrease a particular primary/secondary outcome through blood pressure categories. Statistical analyses were performed using Graph Pad Prism 8.0 software (Graph Pad Software, San Diego, CA, United States). The alpha level was fixed at (p \leq 0.05) for all statistical significance.

Results

Baseline characteristics

There were no significant differences in age, HR rest, and SpO₂ among groups (Table 1). There were significant baseline differences in weight, height, BMI categorization, and by design, in SBP and DBP outcomes (Table 1).

Endothelial dysfunction and vascular parameters (secondary outcomes)

There were no significant differences among CG, Ele, and HTN groups in outcomes cIMT_{max}, aortic augmentation index, brachial artery augmentation index, and diastolic reflection area (Fig. 2, panels A-D). A significant difference in the percentile categorization between CG vs. HTN group (CG %ILE_{PWVba} ~50th vs. HTN ~75th, p=0.028) was found (Fig. 2, panel E). A significant trend was detected to

increase the 'percentile categorization' from CG to Ele, and HTN group (%ILE_{PWVba} 25th, and 75th to each Ele and HTN, ptrend p=0.026) (Fig. 2, panel E). The arterial age estimation showed significant differences between CG vs. HTN group (CG 36.6 years vs. HTN 47.7 years, p=0.020) (Fig. 2, panel F). A significant trend was detected to increase the 'Arterial Age' from CG to Ele, and HTN group (CG 36.6 years, Ele 45.4 years, and HTN 47.7 years, ptrend p<0.01) (Fig. 2, panel F).

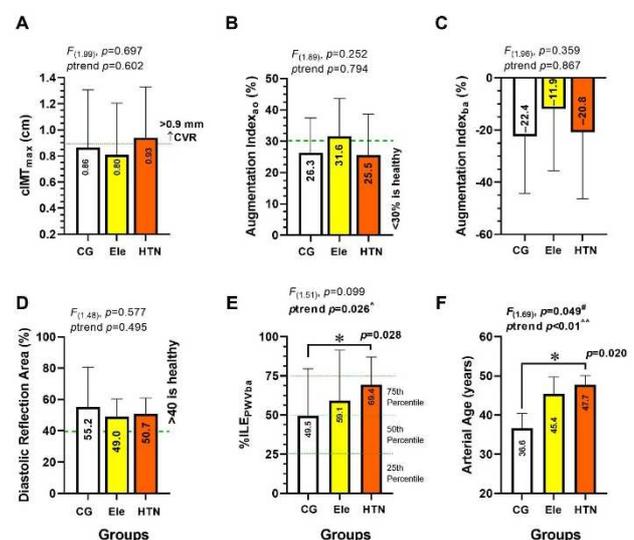


Figure 2. Endothelial function marker maximum carotid intima-media thickness and vascular parameters in normotensive (CG), elevated blood pressure (Ele), and hypertensive patients (HTN). (cIMT_{max}) maximum carotid intima-media thickness, (%ILE_{PWVba}) percentile classification on CG, Ele, and HTN subjects. (#) Denotes significant group interaction by One-way ANOVA at p<0.05. (*) Denotes significant group x group differences by Sidack's *post hoc* at p<0.05. Significant ptrend is shown at p<0.05 (*) and (**) p<0.01 in bold.

Heart rate during the incremental cycling exercise and comparing HTN vs. normotensive adults

There were significant differences in stage 2 of 50-100 watt of the Astrand test in the HR of CG vs. HTN group (105 vs. 119 beats/min, p<0.05), and between Ele vs. HTN

group (104 vs. 119 beats/min), as well as in the 125-250 watt stage between CG vs. HTN group (147 vs. 166 beats/min, $p < 0.05$) (Fig. 3, panel A). There was a significant $ptrend$ for increasing HR in the 125-250 watt stage of the Astrand test from CG, Ele, and HTN group (147, 163, 166 beats/min, $ptrend p = 0.035$) respectively to each group (Fig. 3, panel A). In stage 2; 50-100 watt, the HTN group shows +14 beats/min vs. CG, and +15 beats/min vs. Ele group, both $p < 0.05$ (Fig. 3, panel A). In stage 5; 125-250 watt, the HTN group showed +22 beats/min vs. CG with $p < 0.05$ (Fig. 3, panel A).

Significant differences were detected comparing $HR_{predicted}$ vs. HR_{peak} resulting from the exercise test in each group; CG (180 vs. 146, $p < 0.0001$), Ele (182 vs. 156, $p < 0.0001$), and HTN group (178 vs. 160, $p < 0.0001$) (Fig. 3, panel B). There was a significant $ptrend$ for eliciting a higher HR_{peak} in each CG, Ele, and HTN group (146, 156, and 160 beats/min, $ptrend p = 0.048$), showing Ele group +10 beats/min vs. CG, and HTN group showed +14 beats/min vs. CG group (Fig. 3, panel B).

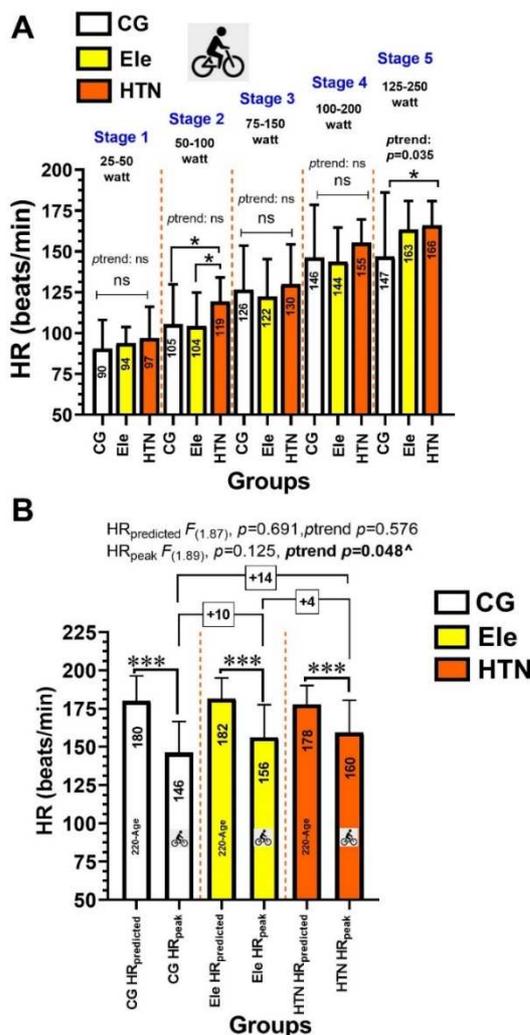


Figure 3. Heart rate during progressing cycling exercise into five stages of the Astrand exercise test. Groups are shown as (CG) normotensive, (Ele) Elevated blood pressure, and (HTN) hypertensive adults. (*) Denotes significant group x group differences by Sidack's *post hoc* at $p < 0.05$. Significant $ptrend$ is shown at $p < 0.05$ (^) (panel A). (***) Denotes the differences between heart rate predicted vs. heart rate peak by the Student *t-test* at $p < 0.05$. Significant $ptrend$ is shown at $p < 0.05$ (^) (panel B).

Discussion

The main findings showed that i) HTN patients had a higher HR during some stages of an incremental cycling exercise test than CG normotensive peers (Figure 2, panel A) and ii) vascular parameters such as the arterial stiffness indicator by $\%ILE_{PWV_{ba}}$ and arterial age estimation were similarly higher in HTN than CG peers (Fig. 2, panels E and F). Additionally, other results included that the HR_{peak} obtained from the incremental cycling test was significantly lower than the $HR_{predicted}$ in each HTN, Ele, and CG (normotensive) adult subj (Fig. 2, panel B).

The exercise test showed that HR was progressively increased from the first to the end of the exercise test in CG (normotensive), Ele, and HTN groups but revealed significant differences in the second (50-100 watts) and the fifth stage (125-250 watts) between the CG (normotensive) and HTN groups (Fig. 3 panel A). This increase in HR response was similar to previous studies about HR during a high-intensity interval training (HIIT) exercise, where T2DM patients also showed a progressive increase in HR (Andrade-Mayorga et al., 2020; Little et al., 2011). The response of HR during incremental exercise can be attributed to the increase in sympathetic tone and reduction in vagal activity, which plays a critical role in the cardiovascular adjustments needed to meet the increased metabolic demands of the active muscles (Fisher, Young, & Fadel, 2015). However, these differences between CG normotensive vs. HTN patients in some exercise stages (stages 2 and 5) revealed a lower capacity of the artery to apply adjustments in the HTN condition.

On the other hand, the findings that HR_{peak} obtained from an actual exercise test was significantly lower than $HR_{predicted}$ in the three HTN, Ele, and CG groups are not surprising. Previous studies have reported that HTN patients do not express their theoretical $HR_{predicted}$. For example, (Miyai et al., 2002) found that in physically inactive subjects with elevated blood pressure aged 20 to 59 years, none of these groups with higher blood pressure achieved their $HR_{predicted}$ when these were under an actual exercise test condition, being this $HR_{predicted}$ 'supra-estimated' than the real HR capacity. In other studies, (Andrade-Mayorga et al., 2020) showed that comparing T2DM vs. hyperglycemic and vs. normoglycemic control subjects, there were no differences in the HR at rest and during HIIT exercise between both groups, where more than 'during exercise test' or 'during HIIT-exercise, the differences in HR were mainly expressed in the beats/min of 'recovery' between each HIIT-interval (i.e., HR recovery) that was superior in normoglycaemic vs. T2DM, and hyperglycaemic subjects (Andrade-Mayorga et al., 2020). By contrast, (García-Flores et al., 2023) reported that adult sedentary subjects, when performing an exercise test, were able to reach their $HR_{predicted}$ during a real exercise test; however, this sample was ~10 years lower (~33.3 y) than our present sample.

The findings of altered EDys vascular parameters (i.e., $\%ILE_{PWV_{ba}}$ and cMT_{max}) in HTN subjects are consistent

with the literature. Previous studies have shown that individuals with HTN and multiple risk factors, including modifiable and non-modifiable, have higher PWV_{ba} values than healthy peers. For example, adult populations with risk factors also have a higher $cIMT_{av}$ than healthy individuals. However, the exact mechanisms behind the altered HR response to exercise remain unclear. Studies have suggested that comorbidities, such as abnormal blood catecholamine levels during exercise, structural heart changes, impaired baroreflex sensitivity, cardiovascular autonomic neuropathy, and ventricular or arterial stiffness may contribute to the higher HR and blood pressure seen during exercise in individuals with T2DM (Keysman et al., 2015; Miyai et al., 2002). PWV_{ba} is a marker of arterial stiffness, which tends to be higher in individuals with HTN, as was observed in this study. On the other hand, the estimated arterial age was higher in Ele and HTN groups (+7.1 years and +5.5 years, respectively) and surprisingly lower in the normotensive CG (-3.3 years). It is important to note that none of the participants was physically active, did not follow the international physical activity guidelines (i.e., by self-report), and considering those HTN participants, only one was under pharmacotherapy treatment.

The cardiovascular response to exercise is crucial before starting exercise training in HTN patients. This study describes the progressive changes (increases) in HR response between HTN, Ele, and normotensive adults during an exercise test, emphasizing the importance of direct measurement of HR in populations with HTN for future exercise prescription, where particularly $HR_{predicted}$ is not expressed in a real incremental exercise test, being supra-estimated than the actual HR condition by HR_{peak} .

Strengths and limitations

Some strengths were that *i*) we used a standardized cycling incremental exercise test like the Astrand test, *ii*) we applied standardized $cIMT_{max}$ measurement and reported additional vascular measurements. As limitations, we recognize that *i*) in the exercise cycling test, we reported only five stages of the Astrand test, as well as we described only the average data between men and women, *ii*) future studies should increase the sample size and could include other modalities of exercise more than incremental cycling, and *iii*) the physical activity patterns were screened empirically by questions of the amount of time involving in light, moderate or vigorous intensities physical activities (in min/week); however, we did not apply any standardized international questionnaire to check it.

Conclusion

HTN patients reported a higher HR response only in two out of five stages of the Astrand cycling exercise test than normotensive peers. Moreover, all groups showed a higher $HR_{predicted}$ than real HR_{peak} obtained from the exercise test. These results are displayed with more altered vascular

parameters in the HTN group. Further studies with larger sample sizes are necessary to confirm these results.

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Statement of ethics

The study was conducted by the Declaration of Helsinki and approved by the Institutional Review Board of the BIOETHICAL COMMITTEE OF UNIVERSIDAD ANDRES BELLO (Approval 026/2022 of September 22nd).

Conflicts of interest statement

C.A., C.C.J., E.G.C., G.V.G., O.A.M., J.C.M., D.C.A., P.D.F., A.A.M., M.I. and I.C. declare no conflict of interest.

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Author contributions

C.A. and C.C.J. designed the study. C.A. performed the experiments. C.A., E.G.C., G.V.G., analyzed the data. C.A., O.A.M., J.C.M., D.C.A., P.D.F interpreted the data and wrote the first manuscript. C.A., G.V.G., E.G.C., A.A.M., M.I. and I.C. reviewed, revised, and approved the final manuscript.

Informed consent statement

“Informed consent was obtained from all subjects involved in the study.”

Data availability statement

The current study's datasets are available from the corresponding author on reasonable request.

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