

Association between relative fat mass and the risk of hypertension in Peruvian adults: A longitudinal analytical study

Asociación entre la masa grasa relativa y el riesgo de hipertensión en adultos peruanos: un estudio analítico longitudinal

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ABSTRACT

Objectives: To estimate the incidence rate of hypertension and assess the association between relative fat mass (RFM) index and five-year hypertension incidence in a Peruvian adult cohort.

Methods: A longitudinal analytical study was conducted using secondary data from the PERU MIGRANT study (n = 731 adults at baseline, n = 647 adults with information on hypertension status at 5 years). RFM was calculated from height and waist circumference, with obesity defined as $\geq 30\%$ for men and $\geq 40\%$ for women. The outcome was 5-year incident hypertension (systolic blood pressure ≥ 140 mmHg, diastolic blood pressure ≥ 90 mmHg, or antihypertensive use). Incidence rates per 100 person-years and 95% confidence intervals (95% CI) were calculated using individual follow-up time. Relative risks (RR) with 95% CI were estimated using Poisson regression with robust variance for the binary outcome assessed at five-year follow-up, adjusted for sociodemographic and lifestyle covariates. A sensitivity analysis using propensity score matching (PSM) was performed to estimate the ATET (average treatment effect on the treated).

Results: Of the participants, 50.6% were women, with a mean age of 45.6 years (standard deviation [SD]: 10.6). RFM-defined obesity prevalence was 36.4%. The incidence of hypertension was higher in participants with RFM-defined obesity (1.87 per 100 person-years) than in those without (1.01 per 100 person-years). In the fully adjusted model, obesity was associated with a 2.43-fold higher risk of hypertension (RR: 2.43; 95% CI: 1.32-4.50; p = 0.004). The use of PSM further reinforced the robustness of our findings (ATET: 6.6%, 95% CI: 2.7-10.4%; p = 0.001).

Conclusion: RFM-defined obesity was statistically significantly associated with a higher risk of developing hypertension over five years in this Peruvian cohort. The RFM index is a practical tool that could be useful for identifying individuals at increased cardiometabolic risk in clinical and public health settings.

Keywords: Body Composition; Obesity; Waist Circumference; Body Mass Index; Adipose Tissue; Hypertension; Cardiometabolic Risk Factors; Cohort Studies; Transients and Migrants; Peru (source: MeSH NLM).

RESUMEN

Objetivos: Estimar la tasa de incidencia de hipertensión y evaluar la asociación entre el índice de masa grasa relativa (RFM) y la incidencia de hipertensión a cinco años en una cohorte de adultos peruanos. **Materiales y métodos:** Se realizó un estudio analítico longitudinal utilizando datos secundarios del estudio PERU MIGRANT (n = 731 adultos al inicio, n = 647 adultos con información sobre el estado de hipertensión a los cinco años). El RFM se calculó a partir de la talla y la circunferencia de cintura, definiéndose obesidad como $\geq 30\%$ en hombres y $\geq 40\%$ en mujeres. El desenlace fue la hipertensión incidente a cinco años (presión arterial sistólica ≥ 140 mmHg, presión arterial diastólica ≥ 90 mmHg o uso de antihipertensivos). Las tasas de incidencia por 100 persona-año y los intervalos de confianza al 95% (IC 95%) se calcularon utilizando el tiempo de seguimiento individual. Se estimaron los riesgos relativos (RR) con IC 95% mediante regresión de Poisson con varianza robusta para el desenlace binario evaluado a los cinco años, ajustado por covariables sociodemográficas y de estilo de vida. Se realizó un análisis de sensibilidad utilizando *propensity score matching* (PSM) para estimar el ATET (efecto promedio del tratamiento en los tratados). **Resultados:** El 50,6% de los participantes fueron mujeres, con una edad media de 45,6 años (desviación estándar [DE]: 10,6). La prevalencia de obesidad según el RFM fue de 36,4%. La incidencia de hipertensión fue mayor en los participantes con obesidad definida por RFM (1,87 por 100 persona-año) que en aquellos sin obesidad (1,01 por 100 persona-año). En el modelo completamente ajustado, la obesidad se asoció con un riesgo 2,43 veces mayor de hipertensión (RR: 2,43; IC 95%: 1,32-4,50; p = 0,004). El uso de PSM reforzó aún más la solidez de los hallazgos (ATET: 6,6%, IC 95%: 2,7-10,4%; p = 0,001).

Conclusión: La obesidad definida por RFM se asoció de manera estadísticamente significativa con un mayor riesgo de desarrollar hipertensión en cinco años en esta cohorte peruana. El índice RFM es una herramienta práctica que podría ser útil para identificar a personas con mayor riesgo cardiometabólico en entornos clínicos y de salud pública.

Palabras clave: Composición Corporal; Obesidad; Circunferencia de la Cintura; Índice de Masa Corporal; Tejido Adiposo; Hipertensión; Factores de Riesgo Cardiometabólico; Estudios de Cohortes; Migrantes; Perú (fuente: DeCS Bireme).

INTRODUCTION

Hypertension is one of the leading risk factors for ischemic heart disease, stroke, and other cardiovascular diseases worldwide [1]. Between 1990 and 2019, the number of adults aged 30-79 years living with hypertension doubled globally [2]. In 2019, more than one billion people with hypertension, representing 82% of the global total, lived in low- and middle-income countries (LMICs) [2], highlighting the substantial challenges faced by health systems in these settings [2,3].

Obesity is a well-established associated factor for hypertension, acting through multiple interrelated mechanisms. Excess adiposity promotes sympathetic nervous system activation, renin-angiotensin system activity, insulin resistance, low-grade inflammation, and endothelial dysfunction, all of which converge to increase blood pressure [4]. Beyond these pathophysiological links, evidence from prospective cohort studies has consistently shown that higher adiposity strongly predicts incident hypertension. A large dose-response meta-analysis of 57 prospective cohort studies including more than 2.3 million participants found graded positive associations between anthropometric adiposity measures such as body mass index, waist circumference, waist-to-hip ratio, and waist-to-height ratio with hypertension risk, supporting a continuous relationship between excess body fat and elevated blood pressure [5].

In clinical practice and population research, obesity has most often been assessed using body mass index (BMI) due to its simplicity and wide availability [6]. However, BMI has important limitations as it does not differentiate between fat and lean mass, fails to reflect fat distribution [6], and may misclassify individuals across populations with different body compositions [7]. To address these shortcomings, Woolcott et al. proposed the Relative Fat Mass (RFM) index in 2018, a simple sex-specific equation based on waist circumference and height that provides an estimate of body fat percentage and demonstrated better agreement with dual-energy X-ray absorptiometry (DXA) than BMI [8]. More recently, the Lancet Commission on Clinical Obesity has reinforced these concerns, emphasizing the need to complement BMI with additional indicators of adiposity or fat distribution in both research and clinical settings [7].

Recent studies have examined the relationship between RFM and blood pressure [9,10]. A large Chinese study reported strong positive associations between higher RFM values and hypertension [10], while research in Brazil found consistent correlations of RFM with systolic and diastolic blood pressure, although without clear superiority over traditional indices [9]. Nevertheless, no empirical evidence has been reported in Peruvian adults, a population characterized by high ethnic admixture [11] and a high prevalence of obesity and hypertension. Therefore, the

present study aimed to assess the association between RFM and five-year incidence of hypertension in a Peruvian adult cohort.

METHODS

Study design and data

A longitudinal analytical study was conducted using secondary data from the PERU MIGRANT study, a study originally designed to investigate differences in cardiovascular risk profiles between rural dwellers, rural-to-urban migrants, and urban dwellers in Peru [12]. For this analysis, only data on baseline measurements collected between 2007-2008 and the five-year follow-up conducted in 2012-2013 were used, as only these two time points were available.

The original PERU MIGRANT study (PERU's Rural to Urban MIGRANTS Study) was carried out in two geographic areas: the rural village of San José de Secce in Ayacucho (located at 3,239 meters above sea level), and the peri-urban shantytown of Pampas de San Juan de Miraflores in Lima [12]. Three population groups were recruited: 1) rural dwellers: individuals born and permanently residing in San José de Secce; 2) rural-to-urban migrants: individuals born in Ayacucho who migrated to Lima and were permanently residing in Pampas de San Juan de Miraflores; and 3) urban dwellers: individuals born and permanently residing in Lima. The baseline PERU MIGRANT Study was designed to recruit approximately 1,000 participants with the following distribution: 200 rural residents, 600 rural-to-urban migrants, and 200 urban residents. This sampling strategy intentionally oversampled migrants to enable more detailed analyses within this group, including stratification by migration-related variables such as length of urban residence and age at migration. These groups were selected to allow comparisons of cardiovascular risk profiles according to migration status. Detailed information was collected through structured interviews, clinical examinations, and standardized anthropometric measurements was collected from all study participants. Further methodological details of the PERU MIGRANT Study have been reported elsewhere [12-14].

Study participants

The PERU MIGRANT study included adults aged 30 years and older recruited at baseline using a single-stage random sampling method stratified by population group (rural, rural-to-urban migrant, and urban), sex, and age. The five-year follow-up re-contacted participants originally enrolled at baseline. Participants with prevalent hypertension at baseline ($n = 207$), defined as self-reported diagnosis, current use of antihypertensive

medication, or elevated blood pressure measurements (systolic blood pressure [SBP] ≥ 140 mmHg and/or diastolic blood pressure [DBP] ≥ 90 mmHg), were excluded from the analysis to avoid misclassification of prevalent cases as incident hypertension. In addition, individuals with baseline diabetes mellitus (defined as self-reported physician diagnosis, current use of antidiabetic medication, fasting plasma glucose ≥ 126 mg/dL, or HbA1c $\geq 6.5\%$) were excluded ($n = 38$). This exclusion criterion was applied to minimize potential confounding and reverse causation bias, as pre-existing diabetes can alter cardiovascular pathophysiology and is a strong mediator in the pathway between adiposity and hypertension [15]. Finally, participants with missing data on any of the main variables were excluded to prevent information bias ($n = 13$). The final analytic sample comprised 361 men and 370 women after applying these criteria.

Study variables

The exposure variable was obesity, assessed using the RFM index, calculated according to the formula validated by Woolcott *et al.* [8]:

$$RFM = 64 - \left(20 \times \frac{\text{Height}}{\text{Waist circumference}} \right) + (12 \times \text{sex})$$

where sex was coded as 0 for men and 1 for women, height was measured in meters, and waist circumference in meters. Continuous RFM values were subsequently categorized into a dichotomous variable for obesity (0 = No, 1 = Yes), using cut-off points of $\geq 40\%$ for women and $\geq 30\%$ for men, consistent with thresholds proposed by Woolcott and subsequently used in analyses of the Peruvian population [16,17].

Anthropometric measurements for the RFM calculation included waist circumference, measured in triplicate measured at the midpoint between the lower rib and the iliac crest using a non-stretchable tape, and height, measured to the nearest 0.1 cm with a portable stadiometer and standard stools. The average of the three waist circumference measurements was used for the analysis.

The outcome variable was hypertension at five-year follow-up (Yes / No), defined according to the JNC 7 criteria as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg, or current use of antihypertensive medication. Information on self-reported diagnosis was not available at follow-up. SBP and DBP were measured using calibrated devices (OMRON M5-I, and OMRON HEM-780, Omron, Japan) and standardized protocols, with participants seated and the right arm supported at chest level. Blood pressure was measured in triplicate with at least 5 minutes between readings, and the average of the last two measurements was used for analysis.

Covariates included in the adjusted models were selected based on an epidemiological approach and previous evidence [5,18-20]. These variables were: sex (female/male), age (30-44, 45-59, ≥ 60 years), educational level (none/some primary school, complete primary, secondary or higher), migration status (rural resident, rural-to-urban migrant, urban resident), asset index in tertiles (constructed using principal component analysis), physical activity level assessed with the International Physical Activity Questionnaire (IPAQ) protocol (low, moderate, high, based defined) [21], and alcohol consumption [low/high], and tobacco use (Yes / No), both assessed with an adapted version of the World Health Organization (WHO) STEPS questionnaire [22].

Statistical analysis

A descriptive analysis of sample characteristics was performed, presenting means and standard deviations (SD) for continuous variables and frequencies and percentages for categorical variables. Individual follow-up time was calculated as the difference between the baseline and the five-year follow-up interview dates, expressed in years. Incidence rates per 100 person-years and 95% confidence intervals (95% CI) were calculated. To evaluate the association between RFM and hypertension, relative risks (RR) with 95% CI were estimated using robust Poisson regression models, a method selected due to the binary outcome assessment at a fixed five-year interval. Three models were constructed: a crude model, a model adjusted for sex, age, education level, migration status, and asset index, and a multivariable model adjusted for all selected covariates (sex, age, education level, migration status, asset index, physical activity level, alcohol consumption and tobacco).

To assess the robustness of the results, two sensitivity analyses were conducted. First, RFM was categorized into tertiles to evaluate dose-response patterns. Second, propensity score matching (PSM) was used. The propensity score was estimated with a logistic regression model that included the same covariates as in the main epidemiological model: sex, age, education level, migration status, asset index, physical activity level, alcohol consumption and tobacco. Based on this score, a matching algorithm was applied to balance the probability of belonging to different RFM categories, generating groups that were more comparable in their baseline characteristics. This analysis allowed the estimation of the average treatment effect on the treated (ATET), interpreted as the average difference in the risk of hypertension among obese individuals compared with the risk they would have had if they had not been obese, after accounting for the covariate distribution.

Statistical significance was set at $p < 0.05$. Analyses were performed in R version 4.5.1 and sensitivity analysis was conducted in Stata version 18 (StataCorp, College Station, TX, USA) using the *teffects* command.

Ethical considerations

The baseline evaluation of the PERU MIGRANT Study was approved by the Ethics Committees of Universidad Peruana Cayetano Heredia (UPCH) and the London School of Hygiene and Tropical Medicine (LSHTM). Follow-up evaluations were approved by the Ethics Committee of Universidad Peruana Cayetano Heredia (approval number 60014). All participants provided written informed consent. For the present analysis, anonymized data were used from the publicly available database (https://figshare.com/articles/dataset/PERU_MIGRANT_Study_Baseline_and_5yr_follow-up_dataset/4832612?file=31171291), therefore, no additional consent from participants or approval from an ethics committee was required. At no point did the authors have access to identifiable information from PERU MIGRANT participants.

RESULTS

A total of 731 participants were included, of whom 50.6% were women. The mean age was 45.6 years (SD: 10.6). The prevalence of RFM-defined obesity was higher among women (73.6%) than men (26.5%). Most participants were between 30 and 44 years of age, while 39.0% were between 45 and 59 years, and 9.7% were 60 years or older. Regarding educational level, more than half reported at least some secondary education (54.6%). Rural-to-urban migrants predominated (62.4%), with a higher frequency among participants with obesity (72.1%) compared with non-obese participants (56.5%). By contrast, rural residents represented 21.2% of the sample but were less frequent in the obese group (6.5%). Regarding physical activity, 46.5% of participants reported high activity, which was more common among non-obese individuals (54.1%), whereas low activity was more frequent among those with obesity (29.4% vs. 21.1%) (Table 1).

The mean follow-up time was 5.1 years (SD: 0.5 years), totaling 3,309 person-years of observation. During follow-up, 44 incident cases of hypertension were identified, yielding an overall incidence rate of 1.33 per 100 person-years (95% CI: 0.97-1.80). Incidence rates of hypertension according to sample characteristics are presented in Table 2. Overall incidence (per 100 person-years) was higher among participants with RFM-defined obesity (1.87; 95% CI: 1.19-2.81) compared with those without obesity (1.01; 95% CI: 0.63-1.54). Stratification by sex, showed that

Table 1. Baseline characteristics of the study population

Characteristics	Total (n = 731)		Non-obese (RFM) (n = 455)		Obese (RFM) (n = 276)	
	n	%	n	%	n	%
Sex						
Female	370	50.6	167	36.7	203	73.6
Male	361	49.4	288	63.3	73	26.5
Age, mean (SD)	45.6	10.6	45	10.9	47.2	10.0
BMI (kg/m ²), mean (SD)	26.1	4.2	23.8	2.4	29.9	3.8
WC (cm), mean (SD)	85.6	10.8	80.0	7.7	94.7	8.6
RFM (%), mean (SD)	33.4	8.1	29.1	5.9	40.6	5.8
Age group						
30 to 44	375	51.3	257	56.5	131	47.5
45 to 59	285	39.0	154	33.9	118	42.8
60 or more	71	9.7	44	9.7	27	9.8
Educational level						
None / Incomplete primary	221	30.2	128	28.1	93	33.7
Complete primary	111	15.2	65	14.3	46	16.7
Secondary or higher	399	54.6	262	57.6	137	49.6
Migration status						
Rural resident	155	21.2	137	30.1	18	6.5
Rural-to-urban migrant	456	62.4	257	56.5	199	72.1
Urban resident	120	16.4	61	13.4	59	21.4
Asset index (tertiles)						
Lowest	253	34.6	193	42.4	60	21.7
Middle	248	33.9	134	29.5	114	41.3
Highest	230	31.5	128	28.1	102	37.0
Physical Activity						
Low	177	24.2	96	21.1	81	29.4
Middle	214	29.3	113	24.8	101	36.6
High	340	46.5	246	54.1	94	34.1
Alcohol consumption						
Low	667	91.2	406	89.2	261	94.6
High	64	8.8	49	10.8	15	5.4
Tobacco use						
No	652	89.2	400	87.9	252	91.3
Yes	79	10.8	55	12.1	24	8.7

SD: Standard deviation, BMI: Body Mass Index, WC: Waist Circumference, RFM: Relative Fat Mass.

Obesity was defined using Relative Fat Mass (RFM) cut-offs: $\geq 40\%$ for women and $\geq 30\%$ for men.

incidence was higher in women with obesity (2.03; 95% CI: 1.22-3.17) than in women without obesity (0.88; 95% CI: 0.36-1.82), whereas differences among men were smaller. Across age groups, incidence increased with age, reaching 3.51 (95% CI: 0.96-8.98) in obese participants aged 60 years or older. Rural residents with RFM-defined obesity also showed particularly elevated rates (4.20;

95% CI: 1.14-10.75). Finally, incidence was higher among participants with obesity and moderate physical activity (2.32; 95% CI: 1.11-4.27), as well as among non-smokers with obesity (1.77; 95% CI: 1.08-2.73) compared to their non-obese counterparts.

Table 3 shows the association between RFM-defined obesity and hypertension. In the crude model, obesity was associated with a RR of 1.75 (95% CI: 0.99-3.10; $p = 0.054$). In model 1, adjusted for potential confounders (sex, age, education, migration status, and asset index), the RR increased to 2.43 (95% CI: 1.31-4.48; $p = 0.004$), remaining similar in model 2, which additionally included physical activity, alcohol consumption, and tobacco use (RR: 2.43; 95% CI: 1.32-4.50; $p = 0.004$).

Table 2. Hypertension incidence rates per 100 person-years of follow-up by sample characteristics ($n = 646^*$)

Characteristics	Non-obese (RFM)	Obese (RFM)
	Incidence rate (95% CI)	Incidence rate (95% CI)
Total	1.01 (0.63–1.54)	1.87 (1.19–2.81)
Sex		
Female	0.88 (0.36–1.82)	2.03 (1.22–3.17)
Male	1.09 (0.59–1.82)	1.36 (0.37–3.49)
Age group		
30 to 44	0.59 (0.24–1.21)	1.45 (0.63–2.86)
45 to 59	1.25 (0.57–2.38)	1.95 (0.97–3.49)
60 or more	2.87 (0.93–6.71)	3.51 (0.96–8.98)
Educational level		
None/Incomplete primary	1.14 (0.46–2.36)	2.37 (1.14–4.36)
Complete primary	0.97 (0.20–2.83)	1.55 (0.32–4.54)
Secondary or higher	0.95 (0.47–1.70)	1.62 (0.78–2.99)
Migration status		
Rural resident	1.81 (0.96–3.09)	4.20 (1.14–10.75)
Rural-to-urban migrant	0.73 (0.32–1.44)	1.62 (0.89–2.72)
Urban resident	NC	1.85 (0.60–4.31)
Asset index (tertiles)		
Lowest	1.28 (0.66–2.24)	2.14 (0.79–4.66)
Middle	1.22 (0.49–2.51)	2.20 (1.10–3.93)
Highest	0.35 (0.04–1.27)	1.34 (0.49–2.91)
Physical Activity		
Low	0.23 (0.01–1.29)	1.36 (0.44–3.17)
Middle	0.64 (0.13–1.88)	2.32 (1.11–4.27)
High	1.44 (0.84–2.30)	1.85 (0.80–3.65)
Alcohol consumption		
Low	0.97 (0.57–1.53)	1.88 (1.18–2.85)
High	1.36 (0.28–3.98)	1.65 (0.04–9.19)
Tobacco use		
No	0.98 (0.58–1.54)	1.77 (1.08–2.73)
Yes	1.27 (0.26–3.70)	2.99 (0.62–8.75)

NC: not calculated due to the absence of hypertension cases in that subgroup, RFM: Relative Fat Mass, CI: confidence interval.

* As one observation was missing the follow-up time, incidence rates were calculated using 646 participants.

Table 3. Association between relative fat mass and hypertension ($n = 647$)

Characteristic	Crude model		Adjusted model 1		Adjusted model 2	
	RR (95% CI)	P	RR (95% CI)	P	RR (95% CI)	P
Obese (RFM)						
No	Reference		Reference		Reference	
Yes	1.75 (0.99–3.10)	0.054	2.43 (1.31–4.48)	0.004	2.43 (1.32–4.50)	0.004
Sensitivity analysis 1						
Low	Reference		Reference		Reference	
Middle	1.10 (0.49–2.43)	0.821	1.75 (0.76–4.05)	0.190	1.71 (0.70–4.17)	0.241
High	1.78 (0.88–3.61)	0.108	6.72 (2.27–19.89)	0.001	6.67 (2.19–20.31)	0.001
Sensitivity analysis 2*						
Obese vs. non-obese						
(based on RFM)						
ATET 0.066 (0.027 – 0.104) $p = 0.001$						

RR: Relative risk, CI: confidence interval, RFM: Relative Fat Mass, ATET: average treatment effect on the treated.

Adjusted model 1: sex, age, education level, migration status, and asset index were included as covariates.

Adjusted model 2: sex, age, education level, migration status, asset index, physical activity level, alcohol consumption and tobacco use were included as covariates.

* Sensitivity analysis performed with the *teffects* command with sex, age, education level, migration status, asset index, physical activity level, alcohol consumption and tobacco as covariates.

In the sensitivity analysis using RFM tertiles (Table 3, Sensitivity analysis 1), participants in the highest tertile showed a higher risk of developing hypertension compared to those in the lowest tertile (RR: 6.72; 95% CI: 2.27-20.31; $p = 0.001$ in Adjusted model 2). In the second sensitivity analysis using PSM (Table 3, Sensitivity analysis 2), the absolute difference was 6.6% (95% CI: 2.7-10.4%; $p = 0.001$), corresponding to the ATET; that is, the average difference in the risk of hypertension observed among participants with obesity compared with the hypothetical risk they would have had if they had not been obese. Supplementary material (Supplementary Table S1 and S2; Figure S1 and S2) provides a summary of covariate balance before and after matching, as well as the distribution of propensity scores in participants with and without obesity, supporting the validity of the sensitivity analysis.

DISCUSSION

Despite the growing interest in RFM as a practical alternative for assessing adiposity, no empirical evidence on its association with incident hypertension has been reported in Latin American populations. Our data showed that RFM-defined obesity was associated with

an increased risk of developing hypertension over a five-year period in a Peruvian adult cohort. Moreover, the observed associations remained robust after adjustment for multiple covariates and were further corroborated in the sensitivity analysis, underscoring both the statistical robustness and the public health relevance of our findings.

In line with previous research, our findings reinforce the strong association between adiposity and the development of hypertension. A large dose-response meta-analysis including more than 2.3 million participants found graded positive associations between increments in anthropometric adiposity indicators such as the BMI, waist circumference, waist-to-hip ratio, and waist-to-height ratio and the risk of incident hypertension, supporting a continuous relationship between excess body fat and elevated blood pressure [5]. Similarly, an 8-year community-based cohort from Korea stratified participants according to quartiles of change in body fat percentage measured by bioelectrical impedance and reported that those in the highest quartile had almost twice the risk of developing hypertension compared with those in the lowest quartile [23]. Although the approach differed as it focused on adiposity changes rather than baseline status, the magnitude of association is consistent with our findings, suggesting robustness of the adiposity-hypertension association across different measurement strategies. Importantly, while that study relied on bioimpedance [23], RFM has been validated against dual-energy X-ray absorptiometry (DXA) [8], considered the gold standard for body composition assessment [24], which may provide a more accurate estimation of body fat and an advantage for its use in population studies.

Evidence on the association between RFM and hypertension remains limited, yet both cross-sectional and longitudinal studies have reported positive associations between RFM and hypertension risk [9,10,25,26], which are in line with our findings. A cross-sectional study in Brazilian university students (18-40 years) from a private institution found that a high RFM, defined as $\geq 25\%$ in men and $\geq 35\%$ in women, was associated with greater odds of hypertension after adjustment for age (Odds ratio [OR]: 2.44; 95% CI: 1.56-3.83) in men, and (OR: 3.67; 95% CI: 1.92-7.00 in women) [9]. It should be noted that different studies have used varying RFM cut-offs to define obesity, reflecting the lack of international standardized thresholds. While the Brazilian study used $\geq 25\%$ (men) and $\geq 35\%$ (women), we employed $\geq 30\%$ (men) and $\geq 40\%$ (women) based on cut-offs specifically applied in Peruvian adults [16], ensuring consistency with local epidemiological context and facilitating comparability with other Peruvian studies. Prospective studies have also confirmed the association between RFM and hypertension. In Chinese adults, higher quartiles of RFM values were associated with nearly a twofold

increase in the odds of developing hypertension over a six-year follow-up compared with the lowest quartile [10]. Similarly, a longitudinal analysis of the U.S. NHANES survey, including more than 26,000 participants and almost 14 years of follow-up, found that individuals in the highest quintile of RFM had substantially greater odds of hypertension compared with those in the lowest quintile (OR 3.43; 95% CI: 2.82-4.17 in men, and OR: 2.06; 95% CI: 1.72-2.46 in women) [26]. Importantly, the aforementioned longitudinal studies have relied on odds ratios, which may overestimate the strength of association when outcomes are common, and none excluded individuals with diabetes at baseline. Given the strong links of diabetes with both adiposity and hypertension, not accounting for this factor may have introduced residual confounding [15,27]. By contrast, our analysis estimated relative risks and risk differences, and explicitly excluded participants with diabetes at baseline, thereby providing a more precise assessment of the independent association between RFM-defined obesity and incident hypertension. These considerations highlight the contribution of our study in providing the first longitudinal evidence from a Latin American population on the role of RFM in hypertension risk, thereby strengthening the external validity of this index across diverse populations. The consistency of our results with established biological mechanisms further supports their plausibility, as excess adiposity, particularly central fat accumulation, has been shown to impair vascular function through neurohormonal activation, metabolic dysregulation, and inflammatory pathways that contribute to elevated blood pressure [4]. By integrating waist circumference relative to height, RFM directly captures central adiposity, which is particularly harmful for vascular function and blood pressure regulation [28,29], thereby providing a physiologically plausible explanation for its predictive capacity in our cohort.

Our findings have important clinical and public health implications. While BMI remains the most widely used and practical indicator for assessing adiposity in both clinical practice and population-based screening due to its simplicity and standardization, RFM offers a complementary approach by incorporating waist circumference relative to height [8]. This feature allows RFM to better capture central adiposity patterns, which may be particularly relevant in populations where body fat distribution varies substantially. However, RFM requires waist circumference measurement, which demands greater standardization and training compared to the simple weight and height measurements needed for BMI, making it less practical for large-scale screening in low-resource settings [24]. By generating longitudinal evidence from a Peruvian cohort, this study underscores the potential of RFM to enhance the early identification of individuals at increased risk of hypertension and other cardiometabolic conditions, thereby supporting

its inclusion in preventive strategies and public health programs. Moreover, our results are in line with the recommendations of the Lancet Commission on Clinical Obesity [7], which emphasize that the diagnosis of obesity should be confirmed through direct assessment of excess adiposity, either with anthropometric indicators such as BMI, waist circumference, waist-to-height ratio, or waist-to-hip ratio. In this context, RFM may provide an additional option for adiposity assessment, as it integrates waist circumference relative to height to approximate body fat percentage. However, our study did not directly compare the predictive performance of RFM with other anthropometric indicators such as BMI or waist circumference. Future research should conduct individual comparisons to determine the relative utility of RFM versus established indicators for predicting hypertension and other cardiometabolic outcomes. Nevertheless, specific cut-offs for defining obesity through RFM should be further validated across diverse populations before routine implementation. This aligns with recent nationally representative evidence from Peru showing that the prevalence of clinically relevant obesity is highly sensitive to both the indicator used and the cut-offs applied, and that reliance on BMI alone underestimates clinically relevant cases [30]. Together, these findings reinforce that not only the choice of indicator (such as RFM) but also the definition of appropriate cut-offs are essential for accurate identification, surveillance, and prevention strategies.

This study has several strengths. It was based on a prospective cohort design with five years of follow-up, which allowed us to establish temporality between RFM-defined obesity and incident hypertension. Participants with diabetes were excluded at baseline, reducing potential confounding from this important comorbidity. The use of PSM further reinforced the robustness of our findings. After baseline covariates balance an absolute difference of 6.6% found, thus confirming the consistency of the association.

This prospective cohort study has several limitations that should be acknowledged, particularly given its observational nature, which precludes causal inference and leaves residual confounding from unmeasured or imperfectly controlled variables as an inherent concern. First, there is the possibility of exposure misclassification, given that RFM is an anthropometric estimator (not a direct measurement of body fat) subject to measurement error, as well as outcome misclassification due to potential variability in blood pressure assessments. Second, selection bias may have arisen from the exclusion of participants with diabetes mellitus or missing data, which could limit the extrapolation of the findings and yield a final sample more specific than the source population. Third, residual confounding cannot be ruled out due to unmeasured variables such as sodium or caloric intake, or imperfectly controlled ones. Fourth, to

our knowledge, there is no specific validation of RFM in populations comparable to PERU MIGRANT, and the cohort is not representative of the Peruvian population as a whole. An additional limitation is that the RFM formula and the cut-off points used ($\geq 40\%$ for women and $\geq 30\%$ for men) were not specifically validated in the Peruvian population for predicting hypertension risk. While these thresholds have been used in previous analyses with Peruvian data, they were originally derived from studies in other populations. Finally, it is important to note that data were collected more than ten years ago, and the current epidemiological landscape may differ; however, national statistics indicate an increasing prevalence of chronic non-communicable diseases, making it plausible that the observed associations represent an underestimation of the current magnitude of risk. Accordingly, the results should be interpreted with caution and considered in light of the methodological limitations described and the temporal context of data collection.

In conclusion, RFM-defined obesity was associated with a higher risk of developing hypertension over five years in the PERU MIGRANT study. Despite the temporal gap since data collection, the prospective design of this analysis strengthens the validity of these findings across diverse Latin American populations. RFM emerges as a useful indicator in both clinical practice and epidemiological surveillance for the identification of cardiometabolic risk.

Author contributions

JGV and AHV conceived the research idea, designed the study, and collected and processed the data. JGV and AHV analyzed the data. NCB critically reviewed the manuscript. All authors contributed to the interpretation of the data, drafting of the manuscript, and approved the final version.

Conflicts of interest statement

The authors declare no conflicts of interest.

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Data availability statement

The data supporting the findings of this study are publicly available in the following link: https://figshare.com/articles/dataset/PERU_MIGRANT_Study_Baseline_and_5yr_follow-up_dataset/4832612?file=31171291.

Artificial Intelligence use statement

During the preparation of this work, the authors used DeepL for the purpose of assisting with the translation of key terms from English. After using this tool, the authors reviewed and carefully edited the content as needed and take full responsibility for the content of the publication.

Supplementary material

The supplementary material can be accessed at the following link: <https://revistas.cientifica.edu.pe/index.php/mecp/article/view/2842/1631>.

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