



DETERMINATION OF THE WAIST CIRCUMFERENCE THRESHOLD FOR TYPE 2 DIABETES RISK IN PERUVIAN ADULTS

DETERMINACIÓN DEL PUNTO REFERENCIAL DE PERÍMETRO ABDOMINAL PARA RIESGO DE DIABETES MELLITUS TIPO 2 EN ADULTOS PERUANOS

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ABSTRACT

Introduction: Waist circumference (WC) increases the risk of type 2 diabetes mellitus (T2DM). **Objectives:** To determine WC cutoff points associated with T2DM risk in Peruvian adults. **Methods:** Analytical cross-sectional study using data from the 2022 Demographic and Family Health Survey (ENDES-22, by its Spanish acronym). Adults aged ≥ 18 years with complete data on WC, weight, height, and blood pressure and without a prior diagnosis of T2DM were included. T2DM risk was assessed using a validated questionnaire. The receiver operating characteristic (ROC) curve was used to identify the optimal WC cutoff based on sensitivity, specificity, and area under the curve (AUC). Results were validated using the 2023 ENDES database. Cramér's V (V), Cohen's Kappa (K), and prevalence ratio (PR) were also used. **Results:** In women, the AUC was 0.688 (CI: 0.678–0.699; $p < 0.001$) with a WC cutoff of 91 cm for T2DM risk. In men, AUC=0.821 (CI: 0.814–0.828; $p < 0.001$) with a cutoff of 88 cm. For men, the international cutoff (95 cm) and the ROC-based cutoff (88 cm) showed $V=0.519$; 0.489, $K=0.507$; 0.496, sensitivity=64%; 82% and specificity=87%; 61%, respectively. In women, using 82 cm and 91 cm as cutoffs yielded $V=0.115$; 0.240, $K=0.060$; 0.203, sensitivity=88%; 71% and specificity=23%; 57%, respectively. Results were replicated in ENDES-2023, with similar values. **Conclusion:** WC is effective for T2DM screening in men but limited in women.

Keywords: Diabetes mellitus, Type 2; Waist circumference; Anthropometry; Epidemiologic measurements; Population characteristics. (Source: MESH-NLM)

RESUMEN

Introducción: El perímetro abdominal (PA) aumenta el riesgo de diabetes mellitus tipo 2 (DM-2). **Objetivos:** Determinar puntos de corte del PA asociados al riesgo de DM-2 en adultos peruanos. **Métodos:** Estudio transversal analítico con datos de la Encuesta Demográfica y de Salud Familiar 2022 (ENDES-22). Se incluyeron adultos ≥ 18 años con datos completos de PA, peso, talla y presión arterial; sin diagnóstico previo de DM-2. El riesgo de DM-2 se evaluó mediante un cuestionario validado. Se utilizó la curva característica operativa del receptor (COR) para identificar el punto de corte óptimo del PA según sensibilidad, especificidad y área bajo la curva (AUC). Los resultados se validaron con la base de datos ENDES-2023. Además, se emplearon V de Cramer (V), prueba Kappa de Cohen (K) y razón de prevalencias (RP). **Resultados:** En mujeres, el AUC fue 0,688 (IC: 0,678–0,699; $p < 0,001$) con punto de corte de PA para riesgo de DM-2 de 91 cm. En hombres, AUC=0,821 (IC: 0,814–0,828; $p < 0,001$) con punto de corte de 88 cm. Para los hombres, el punto internacional (95 cm) y el de la COR (88 cm) mostraron $V=0,519$; 0,489, $K=0,507$; 0,496, sensibilidad=64 %; 82 % y especificidad=87 %; 61 %, respectivamente. En mujeres, con puntos de 82 cm y 91 cm, $V=0,115$; 0,240, $K=0,060$; 0,203, sensibilidad=88 %; 71 % y especificidad=23 %; 57 %, respectivamente. Los resultados se replicaron en la ENDES-2023, con valores similares. **Conclusión:** El PA es efectivo en hombres para cribado de DM-2, pero limitado en mujeres.

Palabras clave: Diabetes mellitus tipo 2; Circunferencia de la cintura; Antropometría; Mediciones epidemiológicas; Características de la población. (Fuente: DeCS- BIREME)

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INTRODUCTION

Diabetes mellitus (DM) is a chronic metabolic disorder characterized by persistent hyperglycemia which, in the case of type 2 diabetes mellitus (T2DM), is due to peripheral resistance to insulin actions⁽¹⁾. It affects approximately 422 million people worldwide (62 million in the Americas), and this number is expected to increase by 200 million by the year 2040⁽²⁾. In Peru, it affects approximately four individuals per 100,000 inhabitants⁽³⁾. Systemic organ damage is attributed to the synergy between chronic hyperglycemia and metabolic abnormalities, primarily affecting the microvasculature in early stages, and later the macrovasculature, which increases the risk of cardiovascular disease by two to four times⁽⁴⁾.

T2DM is a disease of multifactorial etiology, with environmental and lifestyle components manifesting in anthropometric characteristics detrimental to health, such as overweight or obesity, high blood pressure, and metabolic dysfunction⁽⁵⁾. Regarding overweight or obesity, the predominance of abdominal fat is a strong predictor of T2DM, as it promotes insulin resistance through complex metabolic mechanisms, such as the action of dipeptidyl peptidase-4 secreted by hepatocytes, which promotes inflammation of abdominal adipose tissue⁽⁶⁾.

Moreover, excess abdominal fat acts as an endocrine organ, releasing inflammatory cytokines such as tumor necrosis factor alpha, reduced adiponectin, and non-esterified fatty acids, among others⁽⁷⁾. The association between abdominal obesity and T2DM has been widely

established in international studies and meta-analyses, which suggest that reducing waist circumference lowers the risk of developing T2DM⁽⁸⁾. However, international study guidelines to assess this risk are primarily based on body mass index (BMI), and waist circumference is measured only in cases of overweight or obesity. This is a limitation, as BMI does not account for the distribution of body fat⁽⁹⁾.

Furthermore, guidelines and recommendations on waist circumference for assessing T2DM risk are based on studies conducted in countries with different anthropometric characteristics than the Peruvian population. Therefore, the aim of this study was to determine a reference cutoff point for waist circumference associated with the risk of T2DM in Peruvian adults. The results will provide a screening tool with potential for improvement and application in rapid and large-scale assessments for estimating the risk of this endocrinopathy.

METHODS

Study Design and Area

An analytical cross-sectional study was conducted using data from the 2022 Demographic and Family Health Survey (ENDES-22, by its Spanish acronym). ENDES is a population-based survey with a complex, probabilistic, two-stage, and independent sampling design⁽¹⁰⁾. The analyzed population consisted of adults aged 18 years or older who had complete measurements of weight, height, waist circumference, and blood pressure.

Table 1. Characteristics of the studied population.

		N	Percentage
Sex	Female	17522	56.8
	Male	13337	43.2
Age group (years)	>40	11492	39.6
	18-39	17548	60.4
Mother tongue	Indigenous	7824	25.4
	Spanish	22981	74.6





Table 1. Continuation

		N	Percentage
Ethnic identification	Non-mestizo	14.795	51.0
	Mestizo	14.243	49.0
Alcohol consumption	Yes	28.105	91.1
	No	2.749	8.9
Marital status	With partner	20.742	67.2
	Without partner	10.112	32.8
Educational level	Up to high school	20.995	70.5
	Higher education	8.784	29.5
T2DM risk	Yes	10.047	33.8
	No	19.690	66.2
		Mean	DE
WC (women)		91.15 cm	11.94
WC (men)		91.31 cm	11.68
Systolic blood pressure (SBP)		115.71 mmHg	16.85
Diastolic blood pressure (DBP)		74.18 mmHg	10.44
Mean arterial pressure (MAP)		88.02 mmHg	11.66

T2DM: Type 2 Diabetes Mellitus. WC: Waist circumference. SBP: Systolic blood pressure.
DBP: Diastolic blood pressure. MAP: Mean arterial pressure. cm: centimeters. mmHg: millimeters of mercury. SD: standard deviation.

Population and Sample

The sample included the entire target population (N=28,407) with complete data within the 2022 ENDES database, derived from a total of 34,301 individuals (Table 1). No additional sampling procedures were conducted. Individuals with a prior diagnosis of T2DM were excluded from the analysis, as this condition causes changes in body weight⁽¹¹⁾ and leads to

macrovascular and microvascular complications that affect systemic blood pressure⁽¹²⁾. For external validation of the waist circumference cutoff points determined in ENDES-2022, the adult population from ENDES-2023 (N=30,782) was used. The selected population is shown in Figure 1.



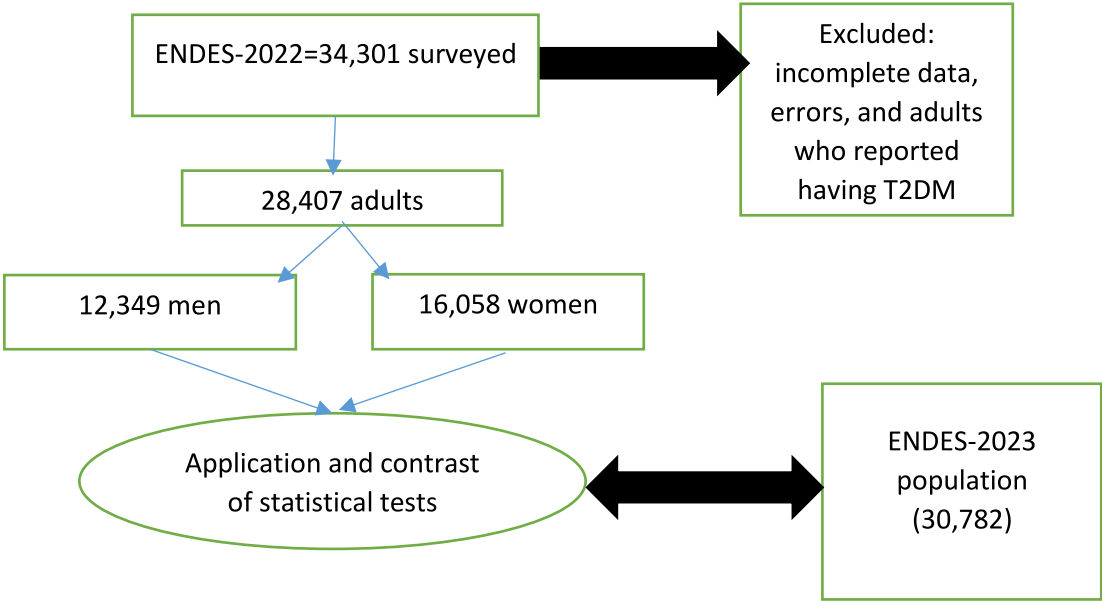


Figure 1. Selected and excluded population for the study.

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Variables and Instruments

The variables included sex (female/male) and waist circumference (WC), considered a cardiovascular risk indicator. The WC scale varied by sex: in men, it was defined as normal if less than 95 cm, elevated risk between 95 and 101 cm, and high risk if greater than or equal to 102 cm. In women, it was considered normal if less than 82 cm, elevated risk between 82 and 87 cm, and high risk if greater than or equal to 88 cm⁽¹³⁾. For the analysis, WC was dichotomized into two categories: normal and elevated (from 95 cm). According to the ENDES-2022 technical specifications, the measurement was taken with a tape measure placed between the costal margin and the iliac crest, perpendicular to the body's longitudinal axis, with the person standing⁽¹⁴⁾.

T2DM risk was determined using the diabetes risk questionnaire developed by Bang et al., validated by the American Diabetes Association (ADA)⁽¹⁵⁾. This instrument was chosen instead of the FINDRISC test because the available items in the database were more compatible with the Bang et al. test, as it does not include the frequency of fruit and vegetable consumption, an item missing in ENDES. The applied

formulas were as follows⁽¹⁶⁾:

$$\text{BMI Score} = (\text{weight} / 2.205) / (\text{height} / 39.37)^2$$
$$\text{Total diabetes risk score} = \text{BMI score} + \text{age} + \text{sex} + \text{family history of DM} + \text{physical activity} + \text{hypertension (HTN)}$$

Mean arterial pressure (MAP), calculated from the systolic blood pressure (SBP) and diastolic blood pressure (DBP) values obtained from the second measurement, was used as a reference to define the presence of HTN, following the formula⁽¹⁷⁾:

$$\text{MAP} = [(2 \times \text{DBP}) + \text{SBP}] / 3.$$

The use of MAP was justified because it more adequately represents tissue perfusion throughout the cardiac cycle⁽¹⁸⁾. The total score was constructed by assigning values to the variables: age (<40 years = 0; 40–49 = 1; 50–59 = 2; ≥60 = 3), sex (female = 0; male = 1), physical activity (subtracts 1 point), hypertension (adds 1 point), family history of DM (adds 1 point), and BMI score (continuous value). T2DM risk was dichotomized: scores ≥4 indicated the presence of risk; scores <4 indicated the absence of risk.

Procedures

Data were grouped according to defined categories, and the proposed WC cutoff points were applied to the ENDES-2022 population. These cutoff points were then validated on the ENDES-2023 population to assess their diagnostic accuracy for estimating T2DM risk according to the Bang et al. questionnaire ⁽¹⁶⁾. Additionally, significant differences between the findings in both databases were evaluated.

Statistical Analysis

Descriptive analysis was conducted using frequencies and percentages. To evaluate the strength of association between WC and T2DM risk, Cramer's V coefficient was used. Cohen's Kappa test was employed to estimate the agreement between WC categories (normal/elevated) and T2DM risk (present/absent). Prevalence ratios (PRs) with their respective 95% confidence intervals (95% CI) were calculated to determine the risk magnitude. A receiver operating characteristic (ROC) curve analysis was applied to establish the WC cutoff point with the highest sensitivity and specificity. The area under the curve (AUC) was interpreted as follows: 0.6–0.7 (low diagnostic ability), 0.7–0.8 (acceptable), 0.8–0.9 (excellent), and >0.9 (outstanding) ⁽¹⁹⁾. Sensitivity, specificity, and positive and negative predictive values

were calculated using an online tool (<http://araw.mede.uic.edu/cgi-bin/testcalc.pl>). Results with a p-value <0.05 were considered statistically significant.

Aspects

Authorization for the use of open data was obtained in accordance with Memorandum No. 001-2023-UDT-OTIC-INS issued by the Ministry of Health of Peru (MINSA, by its Spanish acronym), through the National Institute of Health (INS, by its Spanish acronym). The participants' information was anonymized and numerically coded to ensure their confidentiality. The study was conducted respecting the ethical principles of the Declaration of Helsinki. Supplementary information, including research protocols, is available at: <https://www.gob.pe/institucion/inei/informes-publicaciones/4233597-peru-encuesta-demografica-y-de-salud-familiar-endes-2022>

RESULTS

In women, the AUC was 0.688 (95% CI: 0.678–0.699; p-value < 0.001), with a waist circumference cutoff point associated with the risk of T2DM set at 91 cm (Figure 2A). In men, the AUC was 0.821 (95% CI: 0.814–0.828; p-value < 0.001), with a waist circumference cutoff point for the risk of T2DM set at 88 cm (Figure 2B).

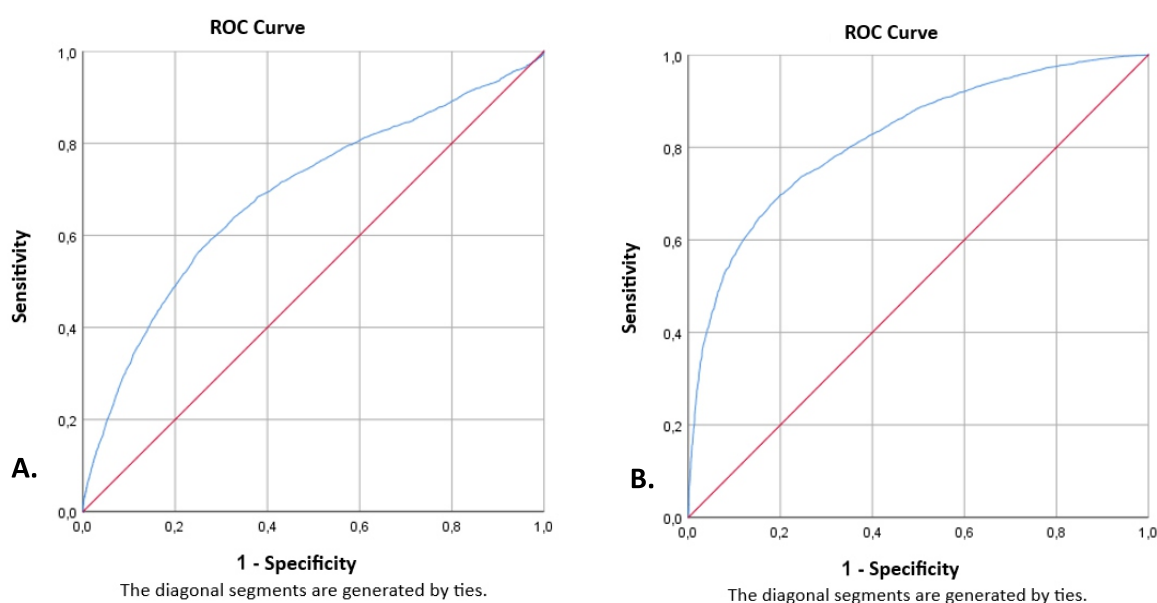


Figure 2. ROC Curve for waist circumference cutoff point adjusted to T2DM risk according to ENDES 2022.



A bivariate comparison of frequencies was conducted between adults with waist circumference and T2DM risk according to the Bang et al. questionnaire⁽¹⁶⁾. In men, on the left side of the table, using the international cutoff point of 95 cm, 63.3% of adults at risk of T2DM had elevated waist circumference.

On the right side, after applying the ROC curve analysis and establishing a new cutoff point of 88 cm, the frequency of T2DM risk was 82.3%. In women, with the international cutoff point of 82 cm, the frequency was 87.5%, while with the new cutoff point of 91 cm, it was 71.5% (Table 2).

Table 2. Frequency of men and women at risk of type 2 diabetes mellitus according to waist circumference reference before and after the application of the receiver operating characteristic curve.

Men (12,349)					
Cutoff point = 95 cm			Cutoff point = 88 cm (ROC curve)		
Circumference	T2DM Risk	No T2DM Risk	Circumference	T2DM Risk	No T2DM Risk
At risk (4662)	3825 (63.6%)	837 (13.2%)	At risk (7681)	5145 (82.3%)	2536 (39.0%)
Normal (6220)	2190 (36.4%)	5497 (86.8%)	Normal (5081)	1108 (17.7%)	3973 (61.0%)
Total	6015	634	Total	6253	6509

Women (16 058)					
Cutoff point = 82 cm			Cutoff point = 91 cm (ROC curve)		
Circumference	T2DM Risk	No T2DM Risk	Circumference	T2DM Risk	No T2DM Risk
At risk (12699)	3251 (87.6%)	9448 (76.5%)	At risk (12699)	2686 (71.5%)	5435 (42.8%)
Normal (3359)	459 (12.4%)	2900 (23.5%)	Normal (3359)	1073 (28.5%)	7250 (57.2%)
Total	3710	12348	Total	3710	12348

ROC: Receiver Operating Characteristic Curve; T2DM: Type 2 Diabetes Mellitus.

In men, both in the group evaluated with the international cutoff of 95 cm and in the group where the new cutoff of 88 cm determined by the ROC curve was applied, the association strength was relatively strong ($V=0.519$ and $V=0.489$, respectively), with moderate agreement ($K=0.507$; $K=0.496$).

Sensitivity was 64% and 82%; specificity was 87% and 61%; positive predictive value (PPV) was 82% and 67%; and negative predictive value (NPV) was 72% and 78%.

The prevalence ratio (PR) was 2.88 (95% CI: 2.77–2.99) and 3.07 (95% CI: 2.90–3.24), respectively. In women, with a cutoff based on international parameters (82 cm) and with the new cutoff of 91 cm, the association strength was $V=0.115$ and $V=0.240$; agreement was $K=0.060$ and $K=0.203$. Sensitivity was 88% and 71%; specificity was 23% and 57%; PPV was 25% and 33%; and NPV was 86% and 87%. The PR was 1.87 (95% CI: 1.71–2.05) and 2.56 (95% CI: 2.40–2.73), respectively (Table 3).

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Table 3. Measures of association and diagnostic tests for the normal waist circumference cutoff point according to the risk of type 2 diabetes mellitus.

Cutoff point of WC in Men			Cutoff point of WC in Women	
	Previous ROC curve	ROC curve	Previous ROC curve	ROC curve
	95 cm	88 cm (ROC curve)	82 cm	91 cm
V	0.519	0.489	0.115	0.240
K	0.507	0.496	0.060	0.203
S	64	82	88	71
E	87	61	23	57
PPV	82	67	25	33
NPV	72	78	86	87
PR(95% CI)	2.88(2.77-2.99)	3.07(2.90-3.24)	1.87(1.71-2.05)	2.56(2.40-2.73)

WC: Waist Circumference. ROC: Receiver Operating Characteristic Curve.
V: Cramér's V coefficient. K: Cohen's Kappa coefficient. S: Sensitivity. E: Specificity. PPV: Positive Predictive Value.
NPV: Negative Predictive Value. PR: Prevalence Ratio. 95% CI: 95% Confidence Interval.

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The cutoff points established in ENDES-2022 were evaluated by applying them to a different population corresponding to ENDES-2023. A bivariate table was used to compare the frequency of adults with elevated waist circumference and T2DM risk according to the Bang et al.⁽¹⁶⁾ questionnaire. In men, on the left side of the table, using the international cutoff point of 95 cm,

57.90% of adults at risk of T2DM had elevated waist circumference, while on the right side, with the new cutoff point of 88 cm, the frequency was 79.60%. In women, with the international cutoff point of 82 cm, the frequency was 85.90%, while with the new cutoff point of 91 cm, it was 67.80% (Table 4).

Table 4. Frequency of men and women at risk of type 2 diabetes mellitus according to waist circumference reference before and after the application of the receiver operating characteristic curve ENDES 2023.

Men (n=13.126)					
Cutoff point = 95 cm			Cutoff point = 88 cm (ROC curve)		
Circumference	T2DM Risk	No T2DM Risk	Circumference	T2DM Risk	No T2DM Risk
At risk (4516)	3500 (57.9%)	1016 (14.3%)	At risk (7549)	4814 (79.6%)	2735 (38.6%)
Normal (8610)	2545 (42.1%)	6065 (85.7%)	Normal (5577)	1231 (20.4%)	4346 (61.4%)
Total	6045	7081		6045	7081
Women (n=17.656)					
Cutoff point = 82 cm			Cutoff point = 91 cm (ROC curve)		
Circumference	T2DM Risk	No T2DM Risk	Circumference	T2DM Risk	No T2DM Risk
At risk (13447)	3333 (85.9%)	10114 (73.4%)	At risk (8556)	2632 (67.8%)	5924 (4.0%)
Normal (4209)	548 (14.1%)	3661 (26.6%)	Normal (9100)	1249 (32.2%)	7851 (6.0%)
Total	3881	13775	Total	3881	13775

ROC: Receiver Operating Characteristic Curve; T2DM: Type 2 Diabetes Mellitus.





When applying the cutoff points to the ENDES-2023 population, it was observed that in men, both with the international cutoff (95 cm) and the new cutoff derived from the ROC curve (88 cm), the association strength was relatively strong ($V=0.457$ and $V=0.424$), with moderate agreement ($K=0.444$; $K=0.403$). Sensitivity was 60% and 81%; specificity was 86% and 61%; PPV was 77% and 64%; and NPV was 72% and 78%. PR was 2.62 (95% CI: 2.52–2.71) and 2.89 (95% CI: 2.74–3.01),

respectively. In women, with a cutoff based on international parameters (82 cm) and with the new cutoff of 91 cm, the association strength was $V=0.121$ and $V=0.206$; agreement was $K=0.066$ and $K=0.173$. Sensitivity was 86% and 68%; specificity was 27% and 57%; PPV was 24% and 31%; and NPV was 87% and 86%. PR was 1.90 (95% CI: 1.75–2.07) and 2.24 (95% CI: 2.10–2.38), respectively (Table 5).

Table 5. Measures of association and diagnostic tests for the normal waist circumference cutoff point according to the risk of T2DM applied to ENDES 2023.

	Cutoff point of WC in Men		Cutoff point of WC in Women	
	Previous ROC curve	ROC curve	Previous ROC	ROC curve
	95 cm	88 cm	82 cm	91 cm
V	0.457	0.424	0.121	0.206
K	0.444	0.403	0.066	0.173
S	60	81	86	68
E	86	61	27	57
PPV	77	64	24	31
NPV	70	78	87	86
PR(95% CI)	2.62 (2.52-2.71)	2.89 (2.74-3.01)	1.90 (1.75-2.069)	2.24 (2.1-2.38)

WC: Waist Circumference. ROC: Receiver Operating Characteristic Curve. V: Cramér's V coefficient.
K: Cohen's Kappa coefficient. S: Sensitivity. E: Specificity. PPV: Positive Predictive Value.
NPV: Negative Predictive Value. PR: Prevalence Ratio. 95% CI: 95% Confidence Interval.

DISCUSSION

It was observed that the waist circumference cutoff points after the ROC curve had greater sensitivity in detecting adults at risk of T2DM compared to the use of reference points based on international studies. This aligns with the anthropometric characteristics of the Peruvian population, which has a tendency toward overweight and obesity, primarily in men of all ages, and in women except for older adults, being strongly related to socioeconomic status⁽²⁰⁾. Additionally, the average heights of 1.66 in men and 1.54 in women are influenced by genetic and nutritional factors from childhood⁽²¹⁾.

Therefore, it is suggested that anthropometric parameters should not be based on international ranges but rather adjusted to the characteristics of the

Peruvian population, given the biological and sociocultural heterogeneity that may influence the underestimation of populations at cardio-metabolic risk⁽²⁴⁾. The results of our study, which show higher sensitivity in the cutoff points based on local ROC curves to detect the risk of T2DM in Peruvian adults, align with recent research highlighting the importance of adjusting these cutoff points to the characteristics of each population. Bello-Chavolla et al.⁽²⁵⁾ and Lopez-Lopez et al.⁽²⁶⁾ noted that the use of local indices, such as waist circumference, offers superior performance compared to international criteria, which may be less sensitive in specific contexts. This approach emphasizes the need to adapt anthropometric parameters to the unique characteristics of the Peruvian population to improve diagnostic accuracy for cardio-metabolic risk. However, the adjustment of the cutoff point through





the ROC curve resulted in favorable changes for higher sensitivity only in men, decreasing in women, where the association between WC and T2DM risk was very low and poorly concordant before and after the ROC curve, while in men, the association and concordance were moderate in both cases.

This can be attributed to the fact that body fat distribution differs by sex, where white adipose tissue (lipid storage) in men is predominantly abdominal (visceral fat) due to androgens promoting fat accumulation in the splenic and visceral region, whereas, in women, white adipose tissue is mainly stored in the hips and thighs (subcutaneous fat)⁽²²⁾, influenced by estrogens, to which they are more exposed and are more sensitive in alpha and beta receptors at the nuclear level, affecting adipose tissue signaling, storage, and distribution⁽²³⁾. Therefore, using waist circumference measurement to determine the risk of T2DM, while feasible for both sexes, performs better as a screening tool in men, and may be used in women but considering the research of other anthropometric parameters such as the waist-to-hip ratio in women.

The use of the cutoff point of 88 cm in men and 91 cm in women was employed in another population group (ENDES-2023), observing similar results, so the use of these new reference points has remained consistent in the Peruvian population over both years, confirming that the 91 cm cutoff in women is not suitable as it loses sensitivity and specificity, so it is recommended that for T2DM risk screening, the new cutoff of 88 cm be used in men and the previous reference value of 82 cm in women as a screening method for T2DM risk at the national level in Peru.

The limitations of the study included the possible bias in waist circumference measurement since measurements were taken from over 30,000 adults, and before processing and analyzing the data, inconsistent

and poorly recorded data, such as 999 cm heights or 1 kg weights, were removed. Another limitation was the fact that basal glucose or hemoglobin A1c measurements were not used, which is logistically and economically unfeasible for the territorial extension covered by ENDES. However, the quantification of diabetes risk through the Bang et al.⁽¹⁶⁾ questionnaire provides an opportunity to measure T2DM risk based on more easily accessible measurement characteristics, being a highly reproducible tool in different populations. Additionally, the new cutoff points are not fixed; they need to be adjusted in future studies, which could also represent an opportunity to develop anthropometric measurement tools that are updatable based on the health, socio-economic, and demographic development of the population. This approach will allow for a more accurate assessment of risk, contributing to more effective public health strategies adapted to the changing needs of the population.

CONCLUSION

The waist circumference reference point for T2DM risk in men was 88 cm, and in women, it was 82 cm. Waist circumference measurement for screening is an effective tool for men, but less efficient for women, who may require instruments based on measurements related to the gynoid fat distribution. The advantages of waist circumference measurement, which only requires a tape measure, compared to BMI formulas or risk questionnaires, make it a useful tool for T2DM risk screening in large epidemiological studies, with the possibility of individualized clinical use in men, while being less recommended for individualized studies in women.

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