*Rev Port Endocrinol Diabetes Metab. 2023;***18(3-4)**

Revista Portuguesa
de Endocrinologia, Diabetes e Metabolismo

www.spedmjournal.com

Artigo Original

Metabolic Control and Cardiovascular Risk in Men and Women with Type 2 Diabetes Mellitus Living in a Low-Income Country

Luciana Corrêa Rodrigues [a], Ângela Cristine Bersch-Ferreira [b], Aline Marcadenti [a,c,*]

[a] *Graduate Program in Health Sciences (Cardiology) / Instituto de Cardiologia/Fundação Universitária de Cardiologia do Rio Grande do Sul, Brasil*
[b] *Department of Research / BP - A Beneficência Portuguesa de São Paulo, São Paulo, Brasil*
[c] *Hcor Research Institute, São Paulo, Brasil*

INFORMAÇÃO SOBRE O ARTIGO

Historial do artigo:
Received/ Recebido: 2024-03-13
Accepted/Aceite: 2024-07-26
Publicado / Published: 2024-09-13

Keywords:
Cardiovascular Diseases;
Diabetes Mellitus Tipo 2;
Metabolic Syndrome.

A B S T R A C T

Introduction: As data on cardiovascular risk and metabolic control by sex in multiethnic populations with type 2 diabetes mellitus living in low-income countries are scarce, this study aimed to evaluate these indicators in a sample of men and women with type 2 diabetes mellitus who use the Brazilian public health system.
Methods: This was a cross-sectional analysis of a national, multicenter, randomized clinical trial that included participants with type 2 diabetes mellitus aged >30 years. Sociodemographic, clinical, biochemical, anthropometric, and food intake data were collected. Logistic regression models adjusted for confounding factors were used to determine the association between metabolic control and sex.
Results: The study included 225 women and 146 men with a mean age of 60.6 ± 9.8 years and mean time since type 2 diabetes mellitus diagnosis of 11.48± 9.1 years. Men had a higher prevalence of a high cardiovascular risk than women (82.3% *vs* 45.9%, $p < 0.001$). After adjusting for age and physical activity levels, men had a reduced chance of having low-density lipoprotein cholesterol and blood pressure levels within the normal range according to cardiovascular risk stratification (odds ratio [OR] 0.88, CI 95%: 0.82–0.95; $p < 0.01$ and OR 0.88, CI 95%: 0.79–0.97; p=0.01). Women were more likely to have increased waist circumference than men (OR 1.13, CI 95% 1.07–1.19; $p < 0.01$).
Conclusion: This study revealed a difference in cardiovascular risk and metabolic control between the sexes in a multiethnic population with type 2 diabetes mellitus.

Palavras-chave:
Diabetes *Mellitus*, Type 2;
Doenças Cardiovasculares;
Síndrome Metabólica.

Controle Metabólico e Risco Cardiovascular em Homens e Mulheres com Diabetes Mellitus Tipo 2 Residentes em um País de Baixa Renda

R E S U M O

Introdução: Considerando que os dados referentes a risco cardiovascular e controle metabólico de acordo com o sexo em populações multiétnicas com diabetes *mellitus* tipo 2 residentes em países de baixa renda são escassos, este estudo teve como objetivo avaliar esses indicadores em uma amostra de homens e mulheres com diabetes *mellitus* tipo 2 usuários do sistema público de saúde brasileiro.
Métodos: Esta foi uma análise transversal com dados da linha de base de um ensaio clínico randomizado multicêntrico que incluiu participantes com diabetes *mellitus* tipo 2 e com idade >30 anos. Foram coletados dados sociodemográficos, clínicos, bioquímicos, antropométricos e de consumo alimentar. Modelos de regressão logística ajustados para fatores de confusão foram utilizados para determinar a associação entre controle metabólico e sexo.

* Autor Correspondente / Corresponding Author.
E-Mail: marcadenti.aline@gmail.com (Aline Marcadenti)
200 Desembargador Eliseu Guilherme Street, 8th floor
Vila Mariana, São Paulo - SP, Brazil, Zip code 04004-030

https://doi.org/10.26497/ao240009

Resultados: O estudo incluiu 225 mulheres e 146 homens com idade média de 60,6 ± 9,8 anos e tempo médio desde o diagnóstico de diabetes *mellitus* tipo 2 de 11,48 ± 9,1 anos. Os homens apresentaram maior prevalência de risco cardiovascular elevado em comparação às mulheres (82,3% *vs* 45,9%, $p < 0,001$). Após ajuste para idade e níveis de atividade física, os homens tiveram uma chance reduzida de ter colesterol da lipoproteína de baixa densidade e níveis de pressão arterial dentro da faixa de normalidade de acordo com a estratificação de risco cardiovascular (*odds ratio* [OR] 0,88, IC 95%: 0,82–0,95; $p < 0,01$ e OR 0,88, IC 95%: 0,79–0,97; $p=0,01$). As mulheres foram mais propensas a ter circunferência da cintura aumentada do que os homens (OR 1,13, IC 95% 1,07–1,19; $p < 0,01$).
Conclusão: Este estudo revelou diferença no risco cardiovascular e no controle metabólico entre os sexos em uma população multiétnica com diabetes *mellitus* tipo 2.

Introduction

According to the International Diabetes Federation, the prevalence of type 2 diabetes mellitus (T2DM) has been exponentially increasing, specialty in low-income countries and among individuals from lower socioeconomic backgrounds.[1] This disease is closely associated with a sedentary lifestyle and poor dietary habits, resulting in a spectrum of cardiometabolic changes related to overweight/obesity, hypertension, and dyslipidemia.[2] Consequently, the risk of cardiovascular events in individuals with T2DM is two–three times greater than that in individuals without the disease, irrespective of sex.[1,3]

Although the overall risk of cardiovascular disease is higher in individuals with T2DM in the general population, this risk varies between men and women. Some studies indicate that women with T2DM have a significantly higher risk of cardiovascular events and mortality than men with T2DM.[4-6] However, the factors contributing to this phenomenon are not yet fully understood,[7] suggesting that they may be linked to different insulin sensitivities between sexes.[8] Furthermore, women with T2DM appear to be more sensitive to coagulation and systemic inflammatory disorders than men with T2DM.[9]

In addition to sex-specific biological factors, environmental and modifiable risk factors have also been investigated.[10] Access to healthcare services can be a determining factor,[11] as can considerations of race and ethnicity.[12] Women have a higher prevalence of suboptimal drug treatment for cardiovascular risk factors,[13,14] leading to poorer glycemic, blood pressure, and lipid control,[13,15] and a tendency towards a sedentary lifestyle.[16] In contrast, they maintain a better diet quality[17] and exhibit a lower prevalence of smoking than men.[18] Furthermore, metabolic responses to certain drug classes seem to differ between sexes.[19]

Although the literature consistently highlights differences between men and women with T2DM in terms of cardiovascular risk and metabolic control, there are limited data on diverse mixed-race populations living in low-income countries and users of large public health systems, such as those in Brazil. Besides, most focusing only on glycemic control[20] and data about differences between men and women with T2DM regarding quality of diet are scarce. Therefore, considering the rich sociocultural diversity of Brazil, as well as the high racial miscegenation and different levels of access to healthcare, this study aimed primarily to evaluate the distribution of cardiovascular risk and prevalence of metabolic control in men and women diagnosed with T2DM users of the Brazilian Unified Health System across different regions of the country.

Material and Methods

Study Design and Participants

A cross-sectional study utilizing baseline data from a national multicenter randomized clinical trial (the NUGLIC study, Clinical Trials ID NCT03793855) was conducted across three distinct regions of Brazil: the northeast, southeast, and south. The participants were recruited from endocrinology, cardiology, and nutrition outpatient clinics between May 2019 and September 2021.

Eligibility Criteria

The inclusion criteria were individuals who voluntarily participated, were diagnosed with T2DM in accordance with established guidelines,[2] exhibited a glycated hemoglobin (HbA1c) level of ≥ 7% at the screening stage, and had not received nutritional counseling for a minimum of six months before the clinical trial. The exclusion criteria included type 1 diabetes mellitus; adult latent autoimmune diabetes mellitus; HbA1c ≥ 12%; severe neuropathy (evaluated according to medical records); chronic kidney disease requiring dialysis; diagnosed cancer with a life expectancy of less than 6 months; chemical dependency/alcoholism or use of antipsychotic drugs; autoimmune disease or chronic steroid use; gastroparesis; pregnancy; lactation; gestational diabetes; acute coronary syndrome events within the preceding 60 days; wheelchair dependence; extreme obesity (body mass index [BMI] ≥ 40 kg/m^2); cognitive, neurological, or psychiatric conditions impeding study participation (at the discretion of the researcher); and concurrent participation in other clinical intervention studies. A convenience (non-probability) sampling method was used in the NUGLIC study.

Ethical Approval

The study protocol was approved by the Research Ethics Committee (REC) of the Instituto de Cardiologia do Rio Grande do Sul (CAEE number 53749321.5.0000.5333). All participants provided informed consent before participating in the study, which was conducted in strict adherence to the ethical principles outlined in the Declaration of Helsinki and Resolution 466/12 of the National Health Council of Brazil.

Procedures and Variables Evaluated

Following the execution of informed consent forms, the participants completed a standardized questionnaire that collected demographic, clinical, and lifestyle information. Socioeconomic and educational data were assessed according to the Brazilian Economic Classification Criteria.[21] Physical activity levels were categorized using the short version of the International Physical Activity Questionnaire (IPAQ) validated for the Brazilian population.[22]

Body weight (kg) was measured with the participants barefoot and wearing minimal clothing. Height (in cm) was measured in the supine position, with both arms hanging freely at the sides of the body and palm-facing thighs. BMI (kg/m^2) was calculated by dividing body weight by the square of height in meters. Waist circumference (cm) was measured with a precision of 0.1 cm, using a measuring tape

composed of resistant, inelastic, and flexible material, positioned at the midpoint between the lower edge of the costal arch and iliac crest in the midaxillary line. Systolic and diastolic blood pressures (SBP and DBP) were assessed according to established guidelines[23] using an Omron HEM-705CP automatic blood pressure monitor (Kyoto Head Office, Japan). Laboratory tests were conducted according to techniques standardized by the reference clinical analysis laboratory of each research center or computed using specific mathematical formulas. The participants fasted for 12 h and refrained from alcohol consumption for 72 h prior to all analyses.

Food intake was evaluated using two 24-hour dietary recalls (24HR) administered during the initial visit and 15 days after inclusion in the study. Diet quality was assessed using the Modified Alternative Healthy Eating Index (mAHEI)[24] and all dietary data were recorded using dedicated software (Sistema Vivanda de Alimentação®, São Paulo, Brazil).

The American Heart Association (AHA) calculator[25] was used to determine cardiovascular risk. Participants were stratified into the following 10-year risk categories for atherosclerotic cardiovascular disease: low risk (< 5%), borderline risk (5.0%–7.4%), moderate risk (7.5%–19.9%), and high risk (≥ 20%). Metabolic control targets were identified as follows: HbA1c < 7%; BMI < 25 kg/m^2; waist circumference < 90 cm for men and < 80 cm for women; total cholesterol < 200 mg/dL; serum triglycerides < 150 mg/dL; SBP/DBP < 140/90 mmHg for low, borderline, and moderate cardiovascular risk; <130/80 mmHg for high cardiovascular risk; low-density lipoprotein (LDL)-cholesterol < 100 mg/dL for low and borderline cardiovascular risk; < 70 mg/dL for moderate risk; and < 50 mg/dL for high cardiovascular risk; and high-density lipoprotein (HDL)-cholesterol > 50 mg/dL for women and > 40 mg/dL for men. Individuals with previous cardiovascular disease were automatically stratified at high risk.

Sample Calculation

In accordance with a study by Wright,[14] wherein approximately 43% of women and 39% of men with T2DM exhibited at least one controlled cardiovascular risk factor (HbA1c, blood pressure, and lipid profile), approximately 380 participants were required to identify sex-related variations in this study.

Statistical Analysis

Participant characteristics, laboratory results, medication type, nutritional data, and metabolic control were presented as absolute and relative frequencies for categorical variables and as mean and standard deviation or median and quartiles for continuous variables. Fisher's exact test was used for comparisons between sexes and categorical variables. The t-test or Mann-Whitney test was used to compare continuous variables by sex, considering the data distribution. Logistic regression models were adjusted for comparisons between sexes and metabolic control data with *p*-values < 0.05 (LDL-cholesterol, waist circumference, and blood pressure), considering sex, age, and physical activity as explanatory variables. The significance level was set at 5%, and all statistical tests were conducted using the R software (R Core Team, 2021).

Results

The study included a total of 371 participants, consisting of 225 women and 146 men, with a mean age of 60.6 ± 9.8 years and a mean time since T2DM diagnosis of 11.4 ± 9.1 years. Table 1 shows the characteristics of the volunteers. This indicates that approximately 70% of women were classified as having lower socioeconomic strata and demonstrated higher physical activity levels. Moreover, women exhibit a higher prevalence of abdominal obesity and a lower prevalence of previous acute myocardial infarction (AMI) than men.

Tables 2 and 3 provide descriptions of the biometric and chemical variables, blood pressure, and medications used according to sex, respectively. Women displayed higher total cholesterol (p = 0.02) and HDL-cholesterol levels ($p < 0.001$) than men, whereas they had lower SBP (p = 0.003). Additionally, the proportion of women using antithrombotic medications was lower than that of men ($p < 0.001$), with no significant difference in the use of hypoglycemic agents by sex. Regarding diet quality, there was no discrepancy in the total mAHEI score between the two sexes (25.8 ± 7.9 for women, 26.5 ± 7.7 for men, p = 0.45). However, when assessing the individual components of the index, women exhibited a higher consumption of whole grains and a lower consumption of nuts/soy protein and alcohol (Table 4).

Table 5 presents the prevalence of metabolic control and cardiovascular risk according to sex. Men had a higher prevalence of high cardiovascular risk than women (82.3% *vs* 45.9%, $p < 0.001$). Furthermore, the proportion of women with LDL-cholesterol and blood pressure within the normal range, as per the cardiovascular risk stratification, was greater than that of men. Nevertheless, men had a higher prevalence of adequate waist circumference than women. After adjusting for age and physical activity levels, it was observed that men had a reduced likelihood of having LDL-cholesterol and blood pressure levels within the normal range, as per cardiovascular risk stratification (odds ratio [OR], 0.88, 95% confidence interval [CI] 95%: 0.82–0.95; $p < 0.01$; OR, 0.88, CI 95%: 0.79–0.97; p=0.01). Conversely, women were more likely to have an increased waist circumference than men (OR, 1.13, CI 95%: 1.07–1.19; $p < 0.01$).

Discussion

The present study highlights significant disparities between sexes in the control of cardiovascular risk factors among Brazilian patients with T2DM. Our principal finding points to a higher risk of cardiovascular disease in men than in women, primarily because of the increased prevalence of prior AMI among men. Men also exhibited poorer management of SBP and LDL-cholesterol levels irrespective of age and physical activity level. This outcome aligns with expectations, as achieving the target levels for LDL-cholesterol and blood pressure is notably challenging for individuals categorized as having a high or very high cardiovascular risk. Failure to control these two risk factors translates to increased susceptibility to cardiovascular events.[26]

Several factors may have accounted for these results. Limited access to medications and medical care in countries with lower socioeconomic development[27,28] may contribute to these sex-based discrepancies. Additionally, men may exhibit inferior self-care management and adherence to treatment regimens compared with women.[29] Furthermore, AMI tends to be underdiagnosed in women with T2DM compared to their male counterparts,[30] which may have contributed to the significantly lower prevalence of prior cardiovascular disease among women in our study. This under-diagnosis also affects the mathematical estimation of cardiovascular risk.

The differences in insulin sensitivity between men and women may also play a role. Adult women are generally more insulin-sensitive than men and often require a greater adipose mass to develop T2DM, especially at younger ages.[31] Dietary choices

Table 1. Baseline characteristics of study participants.

Variables	Women (n = 225)	Men (n = 146)	*p*-value
Age, in years, mean ± SD	59.76 ± 9.88 (n=225)	61.77 ± 9.46 (n=146)	0.05
Marital status, n/N (%)			
Single	55/225 (24.44%)	12/146 (8.22%)	<0.001
Common-law marriage	2/225 (0.89%)	12/146 (8.22%)	
Married	110/225 (48.89%)	105/146 (71.92%)	
Divorced	16/225 (7.11%)	11/146 (7.53%)	
Widower/widow	42/225 (18.67%)	6/146 (4.11%)	
Race; n/N (%)			
Asian	3/225 (1.33%)	2/146 (1.37%)	0.55
White	106/225 (47.11%)	74/146 (50.68%)	
Indigenous	3/225 (1.33%)	0/146 (0%)	
Black	56/225 (24.89%)	29/146 (19.86%)	
Pardo	57/225 (25.33%)	41/146 (28.08%)	
Average monthly family income (USD), n./N (%) *			
4245.00	1/225 (0.44%)	3/145 (2.07%)	<0.001
1889.00	2/225 (0.89%)	4/145 (2.76%)	
975.00	20/225 (8.89%)	22/145 (15.17%)	
540.00	45/225 (20%)	45/145 (31.03%)	
358.00	78/225 (34.67%)	47/145 (32.41%)	
129.00	79/225 (35.11%)	24/145 (16.55%)	
Education, n/N (%)			
Illiterate/ Incomplete elementary school	66/225 (29.33%)	36/145 (24.83%)	0.68
Complete elementary/Incomplete middle school	47/225 (20.89%)	30/145 (20.69%)	
Complete middle/Incomplete high school	41/225 (18.22%)	23/145 (15.86%)	
Complete high school/Incomplete higher education	55/225 (24.44%)	42/145 (28.97%)	
Complete higher education	16/225 (7.11%)	14/145 (9.66%)	
Smoking, n/N (%)			
Current smoker	15/225 (6.67%)	10/145 (6.9%)	<0.001
Past smoker	68/225 (30.22%)	73/145 (50.34%)	
Never smoked	142/225 (63.11%)	62/145 (42.76%)	
Excessive alcohol consumption, n/N (%)			
No	224/225 (99.56%)	135/145 (93.1%)	0.001
Yes	1/225 (0.44%)	10/145 (6.9%)	
Physical activity, n/N (%)			
Sedentary/Low activity level	177/225 (78.67%)	114/145 (78.62%)	0.044
Moderate activity level	34/225 (15.11%)	29/145 (20%)	
High activity level	14/225 (6.22%)	2/145 (1.38%)	
Time since diabetes mellitus diagnosis, in years, mean ± SD	11.45 ± 9.75 (n=225)	11.26 ± 8.04 (n=145)	0.54
Body mass index, in kg/m², mean ± SD	30.83 ± 4.83 (n=225)	29.56 ± 4.22 (n=145)	0.01
Waist circumference, in cm, mean ± SD	101.38 ± 11.37 (n=223)	105.75 ± 11.51 (n=143)	<0.001
Comorbidities, n/N (%)			
General obesity	127/225 (56.44%)	70/145 (48.28%)	0.14
Central obesity	217/223 (97.31%)	121/143 (84.62%)	<0.001
Hypertension	185/225 (82.22%)	117/145 (80.69%)	0.78
Dyslipidemia	134/225 (59.56%)	92/145 (63.45%)	0.51
Retinopathy	35/225 (15.56%)	17/145 (11.72%)	0.36
Amputation	1/225 (0.44%)	5/145 (3.45%)	0.036
Previous cardiovascular disease, n/N (%)			
Acute myocardial infarction	20/225 (8.89%)	49/145 (33.79%)	<0.001
Angina	15/225 (6.67%)	9/145 (6.21%)	1
Stroke	10/225 (4.44%)	10/145 (6.9%)	0.35
Heart failure	11/225 (4.89%)	6/145 (4.14%)	0.81

* 1 US$ = 5.50 Brazilian Reais.

Table 2. Biometric and clinical variables of study participants according to sex.

Variables, mean ± SD	Women (n = 225)	Men (n = 146)	*p*-value
Total cholesterol, mg/dL	181.86 ± 40.74 (n=220)	173.19 ± 51.32 (n=142)	0.017
LDL-cholesterol, mg/dL	96.57 ± 34.82 (n=218)	90.39 ± 39.77 (n=139)	0.06
HDL-cholesterol, mg/dL	53.47 ± 16.7 (n=220)	46.3 ± 13.39 (n=141)	<0.001
VLDL-cholesterol, mg/dL	31.71 ± 17.7 (n=218)	37.62 ± 31.66 (n=141)	0.44
Non-HDL cholesterol, mg/dL	128.4 ± 39.16 (n=220)	126.52 ± 48.93 (n=141)	0.10
Serum triglycerides, mg/dL	158.57 ± 88.48 (n=218)	188.09 ± 158.28 (n=141)	0.55
Fasting glucose, mg/dL	163.77 ± 60.29 (n=220)	170.93 ± 56.6 (n=143)	<0.001
Glycated hemoglobin, %	8.69 ± 1.51 (n=222)	8.79 ± 1.46 (n=142)	0.79
Creatinine, mg/dL	0.88 ± 0.6 (n=220)	1.07 ± 0.28 (n=142)	0.35
Glomerular filtration rate, mL/min/1.73 m2	78.32 ± 22.93 (n=220)	78.3 ± 22.84 (n=142)	0.47
Serum sodium, mEq/L	140.39 ± 2.67 (n=213)	140.19 ± 2.74 (n=136)	0.018
Urine sodium, mEq/L	101.18 ± 52.27 (n=192)	108.41 ± 57.74 (n=125)	0.47
Serum potassium, mEq/L	4.53 ± 0.42 (n=211)	5.02 ± 3.53 (n=134)	0.12
Urine potassium, mEq/L	46.79 ± 28.42 (n=184)	44.48 ± 27.52 (n=123)	0.44
Albuminuria, mg/g	23.4 ± 123.37 (n=184)	14.47 ± 50.02 (n=120)	0.27
Systolic blood pressure, mmHg	129.25 ± 20.68 (n=224)	135.74 ± 20.35 (n=145)	0.003
Diastolic blood pressure, mmHg	80.4 ± 11.38 (n=224)	80.9 ± 10.88 (n=145)	0.82

LDL: low-density lipoprotein; HDL: high-density lipoprotein; VLDL: very low-density lipoprotein.

Table 3. Drugs in use according to sex.

Variables, mean ± SD	Women (n = 225)	Men (n = 146)	*p*-value
Medication, n/N (%)			
Lipid-lowering	133/225 (59.11%)	99/145 (68.28%)	0.08
Antihypertensive	184/225 (81.78%)	123/145 (84.83%)	0.48
Antithrombotic	65/225 (28.89%)	73/145 (50.34%)	<0.001
Hypoglycemic	221/225 (98.22%)	142/145 (97.93%)	1
Number of hypoglycemic medications			0.97
0	4/225 (1.78%)	3/145 (2.07%)	
1	64/225 (28.44%)	38/145 (26.21%)	
2	106/225 (47.11%)	71/145 (48.97%)	
≥ 3	51/225 (22.67%)	33/145 (22.76%)	
Type of hypoglycemic medications			
Sulfonylurea	76/225 (33.78%)	62/145 (42.76%)	0.10
Mitiglinide	4/225 (1.78%)	1/145 (0.69%)	0.65
Biguanide	192/225 (85.33%)	126/145 (86.9%)	0.76
Alpha-glucosidase inhibitors	1/225 (0.44%)	1/145 (0.69%)	1
Glitazone	7/225 (3.11%)	2/145 (1.38%)	0.49
Gliptins (DPP-4 inhibitors)	14/225 (6.22%)	10/145 (6.9%)	0.83
GLP-1 receptor analog	2/225 (0.89%)	0/145 (0%)	0.52
SGLT2 inhibitor	36/225 (16%)	20/145 (13.79%)	0.66
Insulin	102/225 (45.33%)	57/145 (39.31%)	0.28

DPP-4: dipeptidyl peptidase 4; GLP-1: glucagon-like peptide-1; SGLT2: sodium/glucose cotransporter 2.

Table 4. Diet quality assessment according to sex among study participants.

Variables, mean ± SD	Women (n = 225)	Men (n = 146)	*p*-value
Total mAHEI score	25.77 ± 7.92 (n=221)	26.48 ± 7.65 (n=143)	0.45
Ratio of fish/(meat + eggs)	0.3 ± 1.53 (n=221)	0.24 ± 1.44 (n=143)	0.54
Vegetables	2.8 ± 2.83 (n=221)	3.12 ± 3.14 (n=143)	0.55
Fried foods	8.63 ± 3.07 (n=221)	8.38 ± 3.05 (n=143)	0.09
Fruit	3.88 ± 3.24 (n=221)	4.2 ± 3.74 (n=143)	0.66
Whole grains	3.34 ± 3.93 (n=221)	2.48 ± 3.74 (n=143)	0.01
Nuts and soy protein	6.72 ± 4.36 (n=221)	7.7 ± 3.93 (n=143)	0.015
Alcohol	0.09 ± 0.95 (n=221)	0.36 ± 1.6 (n=143)	0.004

mAHEI: modified Alternative Healthy Eating Index.

Table 5. Prevalence of metabolic control and cardiovascular risk according to sex.

Variables	Women (n = 225)	Men (n = 146)	*p*-value
Glycemic control, n/N (%)	23/222 (10.36%)	11/142 (7.75%)	0.46
Lipid control, n/N (%)			
Total cholesterol	155/220 (70.45%)	104/142 (73.24%)	0.63
LDL-cholesterol	43/219 (19.63%)	7/141 (4.96%)	<0.001
HDL-cholesterol	118/220 (53.64%)	88/141 (62.41%)	0.10
Serum triglycerides	218/220 (99.09%)	142/142 (100%)	0.52
Anthropometric control, n/N (%)			
Body mass index	26/225 (11.56%)	16/145 (11.03%)	1
Waist circumference	6/223 (2.69%)	22/143 (15.38%)	<0.001
Blood pressure control, n/N (%)	119/222 (53.6%)	57/144 (39.58%)	0.01
Cardiovascular risk (n/N (%)			
Low	31/220 (14.09%)	1/141 (0.71%)	<0.001
Borderline	9/220 (4.09%)	7/141 (4.96%)	
Moderate	79/220 (35.91%)	17/141 (12.06%)	
High	101/220 (45.91%)	116/141 (82.27%)	

LDL: low-density lipoprotein; HDL: high-density lipoprotein.

may contribute to obesity differences between sexes, with women tending to consume higher-calorie foods, while men are more inclined to consume higher amounts of alcohol.[32] Socioeconomic status is another contributing factor, particularly the relationship between lower socioeconomic classes (a predominant profile in our study sample) and abdominal obesity in women, which does not hold true for men.[33] Physically demanding, low-income jobs that expend higher energy levels may explain this phenomenon.[34]

Estrogen, a key hormone, influences fat accumulation patterns, especially in the visceral adipose tissue. Estrogen exerts inhibitory effects on lipoprotein lipase activity and lipogenic gene expression.[35] It also suppresses lipolytic activity in gluteus-femoral subcutaneous adipose tissue and stimulates the expression of antilipolytic α2A adrenergic receptors.[36] In our study, the mean age of women corresponded to the postmenopausal stage, during which lower estrogen levels contributed to greater accumulation of visceral fat.[37] This shift in fat distribution, coupled with lower estrogen levels, is independently associated with increased blood pressure, LDL-cholesterol levels, and elevated fasting glucose.[38] Additionally, a decrease in lean body mass linked to postmenopausal estrogen decline contributes to worsened metabolic control.[39]

Our study has some limitations. We did not assess subclinical coronary disease using imaging methods, which could have led to an underestimation of asymptomatic AMI cases and classification of cardiovascular risk. Women-specific cardiovascular risk factors, such as preeclampsia and gestational diabetes, along with emerging factors, such as sleep apnea and low-grade inflammation, were not considered. Our methods for assessing dietary consumption relied on the participants' memories, introducing a potential recall bias. Furthermore, the original NUGLIC trial, from which our sample was drawn for this sub analysis, was not initially designed to address the specific research question proposed in this study. And finally, due to the convenience sampling method used in the NUGLIC study, our population might not be representative.

Conclusion

Differences in cardiovascular risk and metabolic control between sexes in this multiethnic population of patients with T2DM indicate a higher prevalence of elevated cardiovascular risk and a lower probability of achieving LDL-cholesterol and SBP targets in men. Additional studies are warranted to confirm whether sociocultural, ethnic, and behavioral variables and access to health services could also account for our findings.

Contributorship Statement / Declaração de Contribuição:

LCR, ACB-F and AM: Designed the study protocol.
LCR: Collected the data.
LCR, ACB-F and AM: Analyzed the data.
All authors contributed to the drafting and revision of the manuscript. All authors have approved the final manuscript.

LCR, ACB-F e AM: Conceberam o protocolo do estudo.
LCR: Recolheu os dados.
LCR, ACB-F e AM: Analisaram os dados.
Todos os autores contribuíram para a redação e revisão do manuscrito. Todos os autores aprovaram o manuscrito final.

Responsabilidades Éticas

Conflitos de Interesse: Os autores declaram a inexistência de conflitos de interesse na realização do presente trabalho.
Fontes de Financiamento: Este trabalho foi financiado pelo Hcor como parte dos "Hospitais de Excelência a Serviço do SUS" em parceria com o "Programa de Apoio ao Desenvolvimento Institucional do Sistema Único de Saúde" (PROADI-SUS) (NUPs: 25000.019226/2018-42 e 25000.182629/2020-41), e pela "Coordenação de Aperfeiçoamento de Pessoal de Nível Superior" (CAPES).
Confidencialidade dos Dados: Os autores declaram ter seguido os protocolos da sua instituição acerca da publicação dos dados de doentes.
Proteção de Pessoas e Animais: Os autores declaram que os procedimentos seguidos estavam de acordo com os regulamentos estabelecidos pela Comissão de Ética responsável e de acordo com a Declaração de Helsínquia revista em 2013 e da Associação Médica Mundial.
Proveniência e Revisão por Pares: Não comissionado; revisão externa por pares.

Ethical Disclosures

Conflicts of Interest: The authors have no conflicts of interest to declare.

Financing Support: This work was supported by Hcor as part of the "Hospitais de Excelência a Serviço do SUS," in partnership with the "Programa de Apoio ao Desenvolvimento Institucional do Sistema Único de Saúde" (PROADI-SUS) (NUPs: 25000.019226/2018-42 and 25000.182629/2020-41), and by the "Coordenação de Aperfeiçoamento de Pessoal de Nível Superior" (CAPES).

Confidentiality of Data: The authors declare that they have followed the protocols of their work center on the publication of data from patients.

Protection of Human and Animal Subjects: The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki as revised in 2013).

Provenance and Peer Review: Not commissioned; externally peer reviewed.

References / Referências

1. International Diabetes Federation. IDF Diabetes Atlas. Brussels: International Diabetes Federation;2021.
2. American Diabetes Association. Standards of Medical Care in Diabetes 2023. Diabetes Care. 2023;46:S1–284.
3. Prospective Studies Collaboration and Asia Pacific Cohort Studies Collaboration. Sex-specific relevance of diabetes to occlusive vascular and other mortality: a collaborative meta-analysis of individual data from 980 793 adults from 68 prospective studies. Lancet Diabetes Endocrinol. 2018;6:538–46.
4. Toedebusch R, Belenchia A, Pulakat L. Diabetic cardiomyopathy: impact of biological sex on disease development and molecular signatures. Front Physiol. 2018; 9:453. doi: 10.3389/fphys.2018.00453
5. Huxley R, Barzi F, Woodward M. Excessive risk of fatal coronary heart disease associated with diabetes in men and women: Meta-analysis of 37 prospective cohort studies. BMJ. 2006;332:73–78.
6. Heald AH, Stedman M, Laing I, Gibson M, Whyte M. Type 2 diabetes and mortality in females versus males in England: the Salford diabetes cohort. Cardiovasc Endocrinol Metab. 2023;12:e0276.
7. Tramunt B, Smati S, Grandgeorge N, Lenfant F, Arnal JF, Montagner A, et al. Sex differences in metabolic regulation and diabetes susceptibility. Diabetologia. 2020;63:453-61.
8. de Ritter R, de Jong M, Vos RC, et al. Sex differences in the risk of vascular disease associated with diabetes. Biol Sex Differ. 2020;11:1.
9. Ranucci M, Aloisio T, Di Dedda U, et al. Gender-based differences in platelet function and platelet reactivity to P2Y12 inhibitors. PLoS One. 2019; 14:e0225771. doi: 10.1371/ journal.pone.0225771
10. Zhao E, Crimmins EM. Mortality and morbidity in ageing men: Biology, lifestyle and environment. Rev Endocr Metab Disord. 2022;23:1285-1304. 1
11. Shaikh M, Peters SA, Woodward M, Norton R, Jha V. Sex differences in utilisation of hospital care in a state sponsored health insurance programme providing access to free services in South India. BMJ Glob Health. 2018;3:e000859. doi: 10.1136/bmjgh-2018-000859.
12. Hassan S, Gujral UP, Quarells RC, Rhodes EC, Shah MK, Obi J, et al. Disparities in diabetes prevalence and management by race and ethnicity in the USA: defining a path forward. Lancet Diabetes Endocrinol. 2023;11:509-24. doi: 10.1016/S2213-8587(23)00129-8.
13. Wright AK, Kontopantelis E, Emsley R, Buchan I, Mamas MA, Sattar N, et al. Cardiovascular risk and risk factor management in type 2 diabetes: a population-based cohort study assessing sex disparities. Circulation. 2019;139:2742–53.
14. Newman JD, Berger JS, Ladapo JA. Underuse of medications and lifestyle counseling to prevent cardiovascular disease in patients with diabetes. Diabetes Care. 2019;42:e75-e76.
15. Yoshida Y, Chen Z, Baudier RL, Krousel-Wood M, Anderson AH, Fonseca VA, et al. Sex differences in the progression of metabolic risk factors in diabetes development. JAMA Netw Open. 2022;5:e2222070.
16. Brugnara L, Murillo S, Novials A, Rojo-Martínez G, Soriguer F, Goday A, et al. Low physical activity and its association with diabetes and other cardiovascular risk factors: a nationwide, population-based study. PLoS One. 2016;11:e0160959.
17. Hiza HAB, Casavale KO, Guenther PM, Davis CA. Diet quality of Americans differs by age, sex, race/ethnicity, income, and education level. J Acad Nutr Diet. 2013;113:297-306. doi: 10.1016/j.jand.2012.08.011.
18. Millett ERC, Peters SA, Woodward M. Sex differences in risk factors for myocardial infarction: cohort study of UK Biobank participants. BMJ. 2018;363:k4247.
19. Raparelli V, Elharram M, Moura CS, Abrahamowicz M, Bernatsky S, Behlouli H, et al. Sex differences in cardiovascular effectiveness of newer glucose-lowering drugs added to metformin in type 2 diabetes mellitus. J Am Heart Assoc. 2020;9:e012940.
20. Duarte F, da Silva Moreira S, Almeida MD, de Souza Teles CA, Andrade CS, et al. Sex differences and correlates of poor glycaemic control in type 2 diabetes: a cross-sectional study in Brazil and Venezuela. BMJ Open. 2019;9:e023401. doi: 10.1136/bmjopen-2018-023401.
21. Associação Brasileira de Empresas de Pesquisa (ABEP). Brazilian Economic Classification Criteria. [Accessed: 12/02/2022] Available at: http://www.abep.org/criterio-brasil.
22. Matsudo S, Araújo T, Matsudo V. Questionário internacional de atividade física (ipaq): estudo de validade e reprodutibilidade no Brasil. Rev Bras Ativ Fís Saúde. 2012;6:5-18.
23. Barroso WKS, Rodrigues CIS, Bortolotto LA, Mota-Gomes MA, Brandão AA, Feitosa AD, et al. Brazilian Guidelines of Hypertension - 2020. Arq Bras Cardiol. 2021;116:516-658. doi: 10.36660/abc.20201238.
24. Dehghan M, Mente A, Teo KK, Gao P, Sleight P, Dagenais G, et al. Relationship between healthy diet and risk of cardiovascular disease among patients on drug therapies for secondary prevention: a prospective cohort study of 31 546 high-risk individuals from 40 countries. Circulation. 2012;126:2705-12. doi: 10.1161/CIRCULATION AHA.112.103234.
25. Goff DC Jr, Lloyd-Jones DM, Bennett G, Coady S, D'Agostino RB Sr, Gibbons R, et al. 2013 ACC/AHA guideline on the assessment of cardiovascular risk: a report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. Circulation. 2014;129:S49-73.
26. Joseph JJ, Deedwania P, Aguilar D, Bhatt DL, Chyun DA, et al. Comprehensive management of cardiovascular risk factors for adults with type 2 diabetes: a scientific statement from the American Heart Association. Circulation. 2022;145:e722–e759
27. Ozawa S, Shankar R, Leopold C, Orubu S. Access to medicines through health systems in low and middle income countries. Health Policy Plan. 2019;34:3.
28. Cobo B, Cruz C, Dick PC. Gender and racial inequalities in the access to and the use of Brazilian health services. Cien Saude Colet. 2021;26:4021-32.
29. Mahmoodi H, Jalalizad Nahand F, Shaghaghi A, Shooshtari S, Jafarabadi MA, Allahverdipour H. Gender based cognitive determinants of medication adherence in older adults with chronic conditions. Patient Prefer Adherence. 2019:13:1733–1744.
30. Martínez-Nadal G, Miro O, Matas A, Cepas P. An analysis based on sex & gender in the chest pain unit of an emergency department during the last 12 years. Eur Heart J Acute Cardiovasc Care. 2021;10:zuab020.122.
31. Sattar N. Gender aspects in type 2 diabetes mellitus and cardiometabolic risk. Best Pract Res Clin Endocrinol Metab 2013;27:501–7.
32. Kanter R, Caballero B, Global gender disparities in obesity: a review. Adv Nutr. 2012;3: 491–8.
33. Anekwe CV, Jarrell AR, Townsend MJ, Gaudier GI, Hiserodt JM, Stanford FC. Socioeconomics of obesity. Curr Obes Rep. 2020;9:272-9.
34. Devaux M, Sassi F. Social inequalities in obesity and overweight in 11 OECD countries. Eur J Public Health. 2013;23:464-9.
35. Steiner BM, Berry DC. The regulation of adipose tissue health by estrogens. Front Endocrinol. 2022;13:889923.
36. Pedersen SB, Kristensen K, Hermann PA, Katzenellenbogen JA, Richelsen B. Estrogen controls lipolysis by up-regulating alpha2A-adrenergic receptors directly in human adipose tissue through the estrogen receptor alpha: implications for the female fat distribution. J Clin Endocrinol Metab. 2004;89:1869-78.
37. Kodoth V, Scaccia S, Aggarwal B. Adverse Changes in body composition during the menopausal transition and relation to cardiovascular risk: a contemporary review. Women's Health Rep. 2022; 3: 573-581.
38. El Khoudary SR. Gaps, limitations and new insights on endogenous estrogen and follicle stimulating hormone as related to risk of cardiovascular disease in women traversing the menopause: A narrative review. Maturitas. 2017;104:44-53.
39. Alabadi B, Civera M, De la Rosa A, Martinez-Hervas S, Gomez-Cabrera MC, Real JT. Low muscle mass is associated with poorer glycemic control and higher oxidative stress in older patients with type 2 diabetes. Nutrients. 2023;15:3167.