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Waist-to-height ratio as a predictor of cardiovascular risk in patients with Type 2 Diabetes Mellitus

Inês Maria Pinto Lima dos Santos

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Dissertação de candidatura ao grau de Mestre em Medicina, submetida ao Instituto de Ciências Biomédicas Abel Salazar, Universidade do Porto.

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Porto, junho de 2026

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Declaration of Scientific Integrity

I, Inês Maria Pinto Lima dos Santos, student of Integrated Master's Degree in Medicine at the Institute of Biomedical Sciences Abel Salazar, with the mechanographic number 202004191, declare to have acted in accordance with the principles of academic integrity set by the University of Porto in the creation of this dissertation.

Thus, I confirm that throughout the entirety of this work, I did not engage in plagiarism, data falsification, or manipulation of results and acted with due care regarding the individuals included in this study.

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Portuguese Abstract (Resumo)

Introdução: A obesidade abdominal é um determinante crítico das complicações vasculares na Diabetes mellitus tipo 2 (DM2). As limitações do índice de massa corporal (IMC) em avaliar a distribuição da gordura visceral tornam imperativa a utilização de métricas de adiposidade central que permitam uma estratificação de risco rigorosa.

Objetivo: Avaliar a associação entre a relação perímetro da cintura/altura e o risco de doença cardiovascular em adultos de nacionalidade portuguesa com DM2 e comparar o desempenho preditivo desta relação com o IMC no risco cardiovascular e nas complicações macro e microvasculares.

Métodos: Foi conduzido um estudo transversal que incluiu 213 adultos com DM2 (idade mediana de 62 anos [IQR: 56-66], 56,8% do sexo masculino). As complicações vasculares foram classificadas em macrovasculares (doença arterial coronária, doença cerebrovascular e doença arterial periférica) e microvasculares (nefropatia diabética, retinopatia e neuropatia). Foram realizadas análises de regressão logística binária utilizando três modelos sequenciais: Modelo 1 (não ajustado), Modelo 2 (ajustado para idade, sexo e duração da diabetes) e Modelo 3 (ajustado para as mesmas variáveis incluídas no Modelo 2, adicionando-se hemoglobina glicada (HbA1c), hábitos tabágicos, pressão arterial sistólica e apolipoproteína B (apoB)). Foram conduzidas análises paralelas para a relação perímetro da cintura/altura e o IMC de forma a permitir uma comparação direta. A área sob a curva ROC (AUROC) foi calculada para avaliar o desempenho preditivo.

Resultados: A relação perímetro da cintura/altura média foi de 0,62±0,09 e a mediana do IMC foi de 28,0 kg/m² [IQR: 25,1-32,0]. As complicações macrovasculares estavam presentes em 30,0% dos participantes e as microvasculares em 37,1%. Em todos os modelos, a relação perímetro da cintura/altura demonstrou associações significativas com nefropatia diabética (Modelo 1: OR 1,65, IC 95% 1,06-2,56; p=0,027; Modelo 2: OR 1,68, IC 95% 1,06-2,65; p=0,026; Modelo 3: OR 1,65, IC 95% 1,03-2,62; p=0,037) e retinopatia diabética (Modelo 1: OR 1,60, IC 95% 1,05-2,42; p=0,027; Modelo 2: OR 1,86, IC 95% 1,16-2,98; p=0,010; Modelo 3: OR 1,85, IC 95% 1,14-3,01; p=0,013). Pelo contrário, o IMC não demonstrou significância estatística para nenhum dos eventos vasculares analisados, incluindo nefropatia, retinopatia, neuropatia ou complicações macrovasculares em nenhum dos modelos (p>0,05). Nenhuma das variáveis demonstrou associações significativas com doença macrovascular ou risco cardiovascular global. Nos modelos ajustados, a idade, o sexo masculino e a duração da diabetes surgiram como determinantes independentes do risco cardiovascular global, enquanto a duração da diabetes foi independentemente associada à retinopatia e à doença macrovascular.

Conclusões: A relação perímetro da cintura/altura demonstra associações independentes com complicações microvasculares específicas (como a nefropatia e retinopatia) em adultos com DM2, enquanto o IMC não evidencia associação com qualquer um dos eventos avaliados.

Palavras-chave: Diabetes mellitus tipo 2; relação perímetro da cintura/altura; índice de massa corporal;

obesidade abdominal; doença cardiovascular; complicações microvasculares; nefropatia diabética; retinopatia diabética

Abstract

Introduction: Abdominal obesity is a key determinant of vascular complications in Type 2 Diabetes Mellitus (T2DM). Given the inability of body mass index's (BMI) to assess visceral fat distribution, alternative central adiposity metrics are imperative for accurate risk stratification.

Objective: The aim of the study was to evaluate the association between waist-to-height ratio (WHtR) and cardiovascular disease risk in Portuguese adults with T2DM and to compare the predictive performance of WHtR versus BMI in assessing cardiovascular risk, micro and macrovascular complications within this population.

Methods: A cross-sectional study of 213 adults with T2DM (median age of 62 years [IQR: 56-66], 56.8% male) was conducted. Vascular complications were classified as macrovascular (coronary artery disease, cerebrovascular disease and peripheral arterial disease) and microvascular (diabetic nephropathy, retinopathy and neuropathy). Binary logistic regression analyses were performed using three sequential models: Model 1 (unadjusted), Model 2 (adjusted for age, sex, diabetes duration), and Model 3 (additionally adjusted for HbA1c, smoking status, systolic blood pressure and apoB). Parallel analyses were conducted for WHtR and BMI to enable direct comparison. The area under the receiver operating characteristic (AUROC) curve was calculated to assess predictive performance.

Results: The mean WHtR was 0.62±0.09 and median BMI was 28.0 kg/m² [IQR 25.1-32.0]. Macrovascular complications were identified in 30.0% of participants, while microvascular complications were observed in 37.1%. WHtR demonstrated significant independent associations across all models with diabetic nephropathy (Model 1: OR 1.65, 95% CI 1.06-2.56; p=0.027; Model 2: OR 1.68, 95% CI 1.06-2.65; p=0.026; Model 3: OR 1.65, 95% CI 1.03-2.62; p=0.037) and diabetic retinopathy (Model 1: OR 1.60, 95% CI 1.05-2.42; p=0.027; Model 2: OR 1.86, 95% CI 1.16-2.98; p=0.010; Model 3: OR 1.85, 95% CI 1.14-3.01; p=0.013). In contrast, BMI failed to achieve statistical significance for any vascular outcome examined, including nephropathy, retinopathy, neuropathy or macrovascular complications across all models (all p>0.05). Neither WHtR nor BMI demonstrated significant associations with macrovascular disease or overall cardiovascular risk. In adjusted models, age, male sex, and diabetes duration emerged as independent determinants of overall cardiovascular risk, while diabetes duration was independently associated with retinopathy and macrovascular disease.

Conclusions: WHtR exhibits independent associations with specific microvascular complications (nephropathy and retinopathy) in adults with T2DM, whereas BMI demonstrates no association with any vascular outcome.

Keywords: Type 2 Diabetes Mellitus; waist-to-height ratio; body mass index; abdominal obesity; cardiovascular disease; microvascular complications; diabetic nephropathy; diabetic retinopathy

Abbreviations/Acronyms

ABI: Ankle-Brachial index

AHA: American Heart Association

ApoB: Apolipoprotein B

ASCVD: Established Atherosclerotic Cardiovascular Disease

AUC: Area Under the Curve

BMI: Body Mass Index

CAD**:** Coronary Artery Disease

CI: Confidence Interval

CVD: Cardiovascular Disease

DPP4i: Dipeptidyl Peptidase-4 inhibitors

eGFR**:** Estimated Glomerular Filtration Rate

EP: Events per variable

FPG: Fasting Plasma Glucose

GLP-1 RA: Glucagon-like Peptide-1 Receptor Agonists

HbA1c: Glycated haemoglobin

HDL: High-density Lipoprotein

IQR**:** Interquartile range

LDL: Low-density lipoprotein

Lp(a): Lipoprotein(a)

MESA**:** Multi-Ethnic Study of Atherosclerosis

OGTT: Oral Glucose Tolerance Test

OR: Odds ratios

PAD: Peripheral Artery Disease

ROC: Receiver Operating Characteristic

SGLT2i**:** Sodium-Glucose Cotransporter 2 inhibitors

SD**:** Standard Deviation

T2DM: Type 2 Diabetes Mellitus

TIA: Transient Ischemic Attack

WC: Waist Circumference

WHR: Waist-to-Hip ratio

WHtR: Waist-to-Height ratio

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Introduction

Cardiovascular disease (CVD) has emerged as a major public health challenge, driven by an ageing global population[1]. It is a group of heart and blood vessel-related conditions that includes coronary artery disease (CAD), congestive heart failure (CHF), peripheral artery disease (PAD), and stroke [2, 3]. The Global Burden of Disease 2023 Study estimated that CVD were responsible for 19.2 million deaths worldwide in 2023, representing the leading cause of global mortality and disability. Its global prevalence exceeds 626 million individuals [4].

Obesity constitutes a major risk factor for the development of CVD and CVD mortality independently of other cardiovascular risk factors. It plays a direct role in the pathogenesis of several cardiovascular risk factors, including dyslipidaemia, type 2 diabetes mellitus (T2DM), hypertension, and sleep disorders [5, 6]. However, its major impact is in its contribution to the epidemic of T2DM [7-9]. Individuals diagnosed with T2DM exhibit a substantially elevated risk of developing CVD relative to the general population, and CVD constitutes the leading cause of mortality within this patient group [2, 8].

Obesity is characterised by the excessive accumulation of fat, which can disrupt normal metabolic homeostasis of the body [10]. However, it is increasingly documented as a heterogeneous condition, such that individuals with similar body mass index (BMI) values may present with markedly distinct metabolic and CVD risk profiles. As emphasised by the American Heart Association (AHA), the risk of obesity-related cardiovascular complications is not determined merely by total body fat mass; rather, it is largely modulated by individual differences in regional fat distribution, particularly the accumulation of visceral and ectopic adipose tissue, which exerts harmful effects on cardiac structure and function [5]. Visceral adiposity is a key driver of both systemic and vascular inflammation, which is essential to all aspects of the atherosclerotic process, from the initial formation of fatty streaks to the development of atherothrombosis. Inflammation associated with obesity increases the propensity for low-density lipoprotein (LDL) oxidation, thereby facilitating the progression of atherosclerotic lesions. Obesity-induced insulin resistance is closely linked to a dyslipidaemia profile characterised by elevated triglycerides, reduced high-density lipoprotein (HDL) cholesterol, and the predominance of small, dense LDL particles. Obesity-induced insulin resistance is also associated with metabolic syndrome, which encompasses abdominal obesity, atherogenic dyslipidaemia, hypertension, insulin resistance (with or without glucose intolerance), and proinflammatory and prothrombotic states, contributing substantially to the pathogenesis of atherosclerosis [5]. Endothelial dysfunction is central in atherosclerotic plaque formation, primarily resulting from diminished nitric oxide bioavailability in the context of chronic inflammation and oxidative stress. This impairment of endothelial function promotes leukocyte adhesion, vascular smooth muscle proliferation, and thrombosis [5, 10]. Collectively, these mechanisms, associated with obesity and particularly with visceral adiposity, are determinant factors linked to the initiation and

progression of atherosclerotic CVD [5].

Anthropometric indices, including BMI, waist-to-hip ratio (WHR), waist circumference (WC) and waist-to-height ratio (WHtR) constitute the most practical and cost-efficient modalities for assessing adiposity in both clinical and epidemiological contexts [1]. Although BMI is widely recognised as a straightforward and frequently employed metric for categorising obesity, it fails to accurately assess body composition, i.e. quantity, quality, and distribution of fat and lean mass, all of which are important components of cardiometabolic risk [6]. Consequently, it doesn't provide information on the role of adipose tissue distribution and function in disease severity and overlooks the distinct contributions of muscle and fat mass [6]. For instance, the accumulation of abdominal visceral fat constitutes a significant risk factor for health deterioration, even among individuals with low BMI [11]. Hence, BMI cannot encompass the entire spectrum of adiposity, like normal-weight central obesity and metabolically healthy obesity [12]. Also, the proportion of body fat displays significant discrepancy across ethnic groups, sexes, and age categories. For example, individuals of South Asian descent generally possess a higher percentage of body fat compared to Caucasians at an equivalent BMI [9].

The Multi-Ethnic Study of Atherosclerosis (MESA) found that WHtR and WC were significantly associated with incident coronary heart disease events, while BMI was not, highlighting the importance of central adiposity over general adiposity [6]. In this context, metrics reflecting central adiposity, such as WHR, WC and WHtR, may offer superior predictive value [5, 6]. The evaluation of WHR is limited, as reductions in body weight typically result in proportional decreases in both waist and hip circumferences, leaving the ratio unchanged and diminishing its utility for monitoring changes in adiposity over time. WC, when measured without accounting for height, may overestimate adiposity in taller individuals and underestimate it in shorter individuals. Unlike WC, which requires population-specific thresholds, WHtR provides a more standardised and cross-culturally applicable assessment of central adiposity [12]. WHtR is the ratio of waist circumference (in centimetres) and the individual's height (in centimetres), which remains largely constant, so WHtR will change only when the waist measurement changes [12]. Thus, this metric adjusts for individual body size, and it is not affected by usual factors such as age, sex, and ethnicity [12, 13]. Furthermore, the European Association for the Study of Obesity advocates for the utilisation of the WHtR in clinical evaluation considering it has demonstrated superior efficacy compared to WC alone in identifying individuals at increased risk for cardiometabolic disease [6, 11]. The most recent large-scale studies and meta-analyses consistently demonstrate that WHtR is a superior predictor of cardiovascular events compared to BMI and WC [13]. In a 2025 prospective U.S. cohort study of over 94,000 adults, WHtR was independently associated with all-cause and cardiovascular mortality, with predictive strength similar to or greater than BMI and WC, especially in individuals under 70 years of age [14].

Despite the evidence from international cohorts, demonstrating that WHtR had the strongest association with CVD events when compared with WHR, WC, and BMI in individuals with T2DM, these

findings have not yet been validated in Portuguese populations with T2DM. Considering that WHtR is a metric largely independent of age, sex, and ethnicity, it is imperative to establish its specific predictive value and clinical utility within the Portuguese healthcare context to optimize cardiovascular risk stratification [6]. Existing Portuguese data, such as the PORMETS study, have evaluated adiposity measures for metabolic syndrome and cardiometabolic risk in a representative Portuguese adult population. Nevertheless, this study did not assess incident cardiovascular events in patients with T2DM, nor did it establish direct associations between these anthropometric indices and cardiovascular outcomes in this subgroup [15].

Thus, identifying which anthropometric index, among BMI and WHtR, most accurately predicts incident CVD in adults with T2DM remains a clinically relevant question, particularly in populations where this association has not yet been directly evaluated, such as the Portuguese diabetic population. Clarifying this relationship may contribute to more effective cardiovascular risk stratification and support the integration of simple, cost-efficient adiposity measures into routine clinical practice.

Objectives

This original article seeks to elucidate the association between abdominal obesity, as measured by the WHtR, and the risk of CVD in individuals with T2DM. Additionally, it aims to compare the predictive performance of the WHtR versus BMI in assessing cardiovascular risk, as well as their associations with specific microvascular and macrovascular complications within this population.

Methods

This retrospective study included patients referred to an initial multidisciplinary appointment for therapeutic education in T2DM between January 2021 and December 2024, in a tertiary hospital in Porto, Portugal.

Inclusion criteria included individuals aged 18 years or older diagnosed with T2DM. Exclusion criteria consisted of patients younger than 18 years or those diagnosed with forms of diabetes other than T2DM.

Data for this study were obtained from a previously authorised institutional database containing demographic, clinical, and laboratory information from patients' first diabetes education appointment. Data were extracted from electronic medical records (SClínico, PCE, and RSE). As all data were collected during routine clinical practice, no additional procedures or resources were required for data collection or analysis. Variables collected included age, weight, BMI, blood pressure, current medication, duration of diabetes, and the presence of retinopathy, diabetic kidney disease, neuropathy and known CAD, cerebrovascular disease or PAD, HbA1c, total cholesterol, LDL cholesterol, n-HDL cholesterol, HDL cholesterol, triglycerides, Lp(a) and apoB.

All diagnoses were ascertained through review of medical records at the time of the first clinical appointment.

Diagnosis of T2DM was established by the presence of at least two of the following criteria, or the same criterion confirmed on two separate occasions: 1) fasting plasma glucose (FPG) level ≥ 126 mg/dL; 2) blood HbA1c concentration ≥ 6.5%; 3) 2-hour oral glucose tolerance test (OGTT) ≥ 200 mg/dL. Patients with evidence of other forms of diabetes, including those with beta-cell autoimmunity markers or a prior history of exocrine pancreatic disease, were excluded. Blood pressure was measured on a single occasion, using a standard mercury sphygmomanometer with the cuff applied to the right upper arm, following a 10-minute rest period.

Body weight was measured to 0.1 kg using a digital scale, and height to the nearest centimetre using a wall stadiometer with participants in the standing position. WC was measured in centimetres to the nearest 0.1 cm, at the narrowest part of the trunk, during exhalation. WHtR was calculated by dividing WC by height. BMI was calculated as weight, in kilograms, divided by the square of height, in meters.

HbA1c, total cholesterol, LDL cholesterol, non-HDL cholesterol, HDL cholesterol, triglycerides and apoB duration of diabetes were analysed at a central laboratory.

Participants were considered current smokers if they smoked daily or occasionally in the last 6 months, former smokers if they had stopped smoking for at least 6 months, and non-smokers if they had never smoked.

Established atherosclerotic cardiovascular disease (ASCVD) was defined as the presence of known CAD, cerebrovascular disease, or PAD at the first appointment. CAD was defined as a history of acute coronary syndrome (including myocardial infarction and unstable angina), stable angina, or prior coronary revascularization (percutaneous coronary intervention or coronary artery bypass grafting). Cerebrovascular disease was defined as a documented history of ischemic stroke or transient ischemic attack (TIA). PAD was defined as a history of intermittent claudication with an ankle-brachial index (ABI) <0.90, prior lower-extremity revascularization, or non-traumatic lower-limb amputation.

Diabetic retinopathy was confirmed via fundoscopy. Diabetic kidney disease was defined by an estimated glomerular filtration rate (eGFR) of <60 mL/min/1.73 m^2 and/or the presence of urinary albumin-creatinine ratio ≥ 30mg/g in an occasional sample. Diabetic neuropathy was assessed through clinical evaluation comprising symptom history and neurological examination of the lower extremities, including assessment of vibration perception using a 128-Hz tuning fork, pressure sensation using a 10-g Semmes-Weinstein monofilament, pinprick sensation, temperature discrimination, and ankle reflexes.

The primary outcome was the association of WHtR with ASCVD. Secondary outcomes included association of WHtR with each individual macrovascular and microvascular diabetes complication/target-organ damage and the comparative predictive performance of WHtR versus BMI.

This study was approved by the Ethics Committee of Centro Hospitalar Universitário de Santo

António (authorised on 21st January 2026). Additionally, authorization was provided by the Clinical Director of Medicine Department. Informed consent was waived.

Statistical Analysis

SPSS software version 30.0 was used to analyse all data. A two-sided p-value <0.05 was considered statistically significant. Confidence intervals (CI) were set at 95%.

Data normality was evaluated using the Shapiro-Wilk test alongside visual inspection of histograms and Q-Q plots. Continuous variables were described as the mean and standard deviation (SD) for normally distributed data or as median and corresponding 25 and 75th percentiles [interquartile range (IQR)] for non-normally distributed variables. Categorical variables were expressed as absolute frequencies and percentages. Continuous variables were compared using Student's t-test or the Mann-Whitney U test for normally and non-normally distributed data, respectively. To yield clinically interpretable odds ratios (OR), the WHtR was multiplied by 10. Consequently, the calculated OR reflect the risk associated with each 0.1-unit increase in the original ratio.

Multivariable logistic regression models were used to estimate the cross-sectional associations between anthropometric indices (WHtR and BMI) and the clinical outcomes of interest. To minimize the risk of overfitting and respect the events-per-variable (EPV) criteria within a cross-sectional design utilizing a fixed sample size, multivariable analyses were conducted using three sequential modelling approaches. First, an unadjusted baseline model (Model 1) was applied, followed by a second model (Model 2) adjusted for age, sex and time since diabetes diagnosis. And a third model incorporating additional metabolic covariates (HbA1c, smoking status, systolic blood pressure and apoB) was tested. The maximum number of concurrent covariates introduced into the fully adjusted models was strictly restricted to ensure a minimum threshold of 5 to 10 events per predictor variable, ensuring statistical stability and robust model parsimony. To prevent multicollinearity and overfitting due to these sample size constraints, apoB was pre-specified and prioritised as the sole lipid metric in the final multivariable models. To allow for a direct comparison, this identical modelling approach was repeated using BMI as the primary independent variable. Results were reported as OR with 95% CIs.

Receiver operating characteristic (ROC) curves were constructed to evaluate WHtR and BMI as individual cross-sectional predictors. The area under the curve (AUC) with 95% CI was calculated for each index, and the respective AUCs were compared using the DeLong test.

Results

A total of 213 adult patients with T2DM were included in this study, with an average age of 62 [IQR: 56-66 years], including 121 males (56.8%). The clinical characteristics of the subjects are demonstrated in Table I.

Regarding the presence of overall vascular disease (CAD, cerebrovascular disease and/or PAD), the Independent-Samples Mann-Whitney U test revealed no statistically significant difference in BMI between the study groups (p=0.921). Diabetic patients with overall vascular complications presented a median BMI of 28.0 kg/m^2 [IQR: 25.3-31.6 kg/m^2] whereas those without global vascular involvement showed a similar median BMI of 27.7 kg/m^2 [IQR: 24.9-32.1 kg/m^2].

In the univariable analysis, BMI was not significantly associated with the presence of macrovascular disease (p=0.473). Patients with macrovascular complications presented a median BMI of 27.7 kg/m^2 [IQR: 24.5-31.5 kg/m^2], which closely mirrored the 27.9 kg/m^2 [IQR: 25.1-32.1 kg/m^2] observed in those without such complications. No significant differences in BMI were observed across individual macrovascular complications. Median BMI values were statistically comparable between patients with and without CAD (27.7 kg/m^2 [IQR: 24.4–31.5] vs. 28.0 kg/m^2 [IQR: 25.2-32.1]; p=0.460), cerebrovascular disease (26.2 kg/m^2 [IQR: 24.6–31.0] vs. 27.9 kg/m^2 [IQR: 25.1-32.0]; p=0.376), and PAD (30.3 kg/m^2 [IQR: 25.8–31.6] vs. 27.7 kg/m^2 [IQR: 24.9-32.0]; p=0.417).

The median BMI of patients with microvascular disease (29.1 kg/m^2 [IQR: 26.1-32.2 kg/m^2]) did not differ significantly from that of patients without microvascular involvement (27.4 kg/m^2 [IQR: 24.5-31.5 kg/m^2]), as was confirmed by the Mann-Whitney U test (p=0.106). When assessing for individual microvascular manifestations, a significant difference in BMI was observed exclusively for diabetic neuropathy, with a higher median value in the affected group (30.7 kg/m^2 [IQR: 27.2–32.7] vs. 27.4 kg/m^2 [IQR: 24.9-31.5]; p=0.048). In contrast, no statistically significant associations were observed between BMI and the presence of either nephropathy (30.6 kg/m^2 [IQR: 24.9–33.7] vs. 27.6 kg/m^2 [IQR: 25.0-31.5]; p=0.116), or diabetic retinopathy (28.6 kg/m^2 [IQR: 26.6–31.5] vs. 27.7 kg/m^2 [IQR: 24.7-32.1]; p=0.400).

Univariable analysis indicated that WHtR was not significantly associated with global vascular disease (p=0.139). Mean WHtR values were statistically similar between diabetic patients with overall vascular complications (0.63 ± 0.09) and their counterparts without known CVD (0.61 ± 0.09).

The mean WHtR did not differ significantly between patients with and without macrovascular disease (0.62 ± 0.09 vs. 0.62 ± 0.09, respectively; p = 0.833).

When analysing individual macrovascular manifestations, univariable analysis revealed no statistically significant differences in the WHtR across the evaluated territories. Specifically, the mean WHtR values were statistically comparable between patients with and without CAD (0.61 ± 0.08 vs. 0.62 ± 0.09; p=0.503), cerebrovascular disease (0.63 ± 0.09 vs. 0.62 ± 0.09; p=0.592) and PAD (0.65 ± 0.09 vs. 0.62 ± 0.09; p=0.238).

Regarding the WHtR, an Independent-Samples t-test demonstrated a statistically significant difference between the groups when evaluating microvascular disease (p=0.012). Specifically, patients with microvascular complications presented a significantly higher mean WHtR of 0.64 ± 0.09 compared to the 0.61 ± 0.09 observed in those free from microvascular events.

Significant differences in WHtR values were identified across individual microvascular complications for nephropathy (0.65 ± 0.09 vs. 0.61 ± 0.09; p=0.024) and diabetic retinopathy (0.65 ± 0.09 vs. 0.61 ± 0.08; p=0.025). However, the ratio was not significantly associated with the presence of diabetic neuropathy (0.64 ± 0.08 vs. 0.62 ± 0.09; p=0.227).

Regarding the lipid profile, univariable logistic regression analyses revealed that most conventional lipid metrics displayed no statistically significant association with the primary clinical outcome (Table II). Similarly, Lipoprotein(a), failed to demonstrate predictive value during this initial univariable screening. On the contrary, HDL-cholesterol showed a statistically significant association, displaying a protective effect against the clinical outcomes.

Regarding global CV risk, Model 1 showed no statistically significant association for WHtR (OR=1.29, 95% CI: 0.92-1.80; p=0.140). When adjusting for baseline demographic and clinical confounders in Model 2, WHtR remained statistically non-significant, despite a decrease in its p-value (OR=1.39, 95% CI: 0.96-2.01; p=0.081). In this adjusted framework, biological sex emerged as an independent predictor, with male patients exhibiting more than a two-fold increase in the odds of global CV risk compared to females (OR=2.49, 95% CI: 1.30-4.78; p=0.006). Additionally, both age (OR=1.05, 95% CI: 1.01-1.10; p=0.022) and diabetes duration (OR=1.05, 95% CI: 1.01-1.09; p=0.015) were confirmed as independent risk factors. In Model 3, WHtR retained a non-significant independent effect (OR=1.35, 95% CI: 0.93-1.98; p=0.118). Within this final framework, age (OR=1.06, 95% CI: 1.02-1.12; p=0.010), male sex (OR=2.11, 95% CI: 1.05-4.24; p=0.035) and duration of diabetes (OR=1.05, 95% CI: 1.01-1.10; p=0.010) persisted as the only independent determinants of overall cardiovascular risk. Parallel analyses were performed to evaluate the predictive capacity of BMI on global CV risk across three identical sequential models. In Model 1, BMI exhibited no statistical association with the outcome (OR=0.99, 95% CI: 0.94-1.05; p=0.789). Upon adjusting, in Model 2, BMI remained fundamentally neutral (OR=1.00, 95% CI: 0.95-1.06; p=0.950), whereas diabetes duration (OR=1.06, 95% CI: 1.02-1.09; p=0.003), male sex (OR=2.00, 95% CI: 1.11-3.60; p=0.022) and age (OR=1.04, 95% CI: 1.00-1.08; p=0.035) stood as significant independent risk factors. In the fully adjusted model, BMI remained non-significant (OR=1.00, 95% CI: 0.95-1.06; p=0.884). Within this model, only age (OR=1.06, 95% CI: 1.01-1.12; p=0.011) and diabetes duration (OR=1.06, 95% CI: 1.02-1.10; p=0.003) maintained robust independent predictive values for global cardiovascular risk.

Regarding nephropathy, in Model 1, WHtR was associated with renal involvement (OR=1.65, 95% CI: 1.06-2.56; p=0.027). This significant association persisted in Model 2 (OR=1.68, 95% CI: 1.06-2.65; p=0.026) after adjusting for chronological age, biological sex and diabetes duration, none of which

reached statistical significance. Finally, in Model 3 WHtR remained a powerful independent determinant of diabetic nephropathy (OR=1.65, 95% CI: 1.03-2.62; p=0.037), whereas all other incorporated covariates failed to achieve independent statistical significance. In contrast to the robust findings obtained for WHtR, BMI failed to achieve statistical significance across all models regarding nephropathy. In Model 1, the association for BMI was non-significant (OR=1.05, 95% CI: 0.98-1.12; p=0.170). This lack of independent predictive value persisted in Model 2 (OR=1.05, 95% CI: 0.98-1.13; p=0.175). In Model 3, BMI remained non-significant (OR=1.05, 95% CI: 0.98-1.13; p=0.193), with no other covariates emerging as independent risk factors.

For diabetic retinopathy, Model 1 demonstrated that WHtR was associated with retinal involvement (OR=1.60, 95% CI: 1.05-2.42; p=0.027). Upon adjustment in Model 2, the independent association for WHtR strengthened considerably (OR=1.86, 95% CI: 1.16-2.98; p=0.010), alongside a strong independent effect of diabetes duration (OR=1.08, 95% CI: 1.04-1.13; p<0.001). Finally, in Model 3, WHtR successfully sustained its independent statistical significance (OR=1.85, 95% CI: 1.14-3.01; p=0.013). In this last model, only the duration of diabetes persisted as a concurrent independent risk predictor (OR=1.08, 95% CI: 1.04-1.13; p<0.001). Mirroring the previous findings, BMI did not demonstrate a statistically significant association with the outcome in any of the models. Model 1 yielded a non-significant association (OR=1.02, 95% CI: 0.96-1.08; p=0.573), just as Model 2 (OR=1.05, 95% CI: 0.98-1.12; p=0.210) and Model 3 (OR=1.04, 95% CI: 0.97-1.12; p=0.234). Only the duration of diabetes persisted as an independent risk determinant in Model 2 (OR=1.09, 95% CI: 1.05-1.14; p<0.001) and Model 3 (OR=1.09, 95% CI: 1.05-1.14; p<0.001).

For diabetic neuropathy, WHtR did not demonstrate a statistically significant independent association across any of the evaluated models. In Model 1, the effect of WHtR was non-significant (OR=1.33, 95% CI: 0.84-2.11; p=0.227), a profile that persisted in Model 2 (OR=1.50, 95% CI: 0.91-2.47; p=0.110). However, within Model 3, poor glycaemic control (OR=1.35, 95% CI: 1.05-1.73; p=0.017) and smoking status (OR=1.05, 95% CI: 0.98-1.12; p=0.045) emerged as independent risk determinants, while WHtR remained non-significant (OR=1.45, 95% CI: 0.86-2.45; p=0.169). In Model 1, BMI remained non-significant (OR=1.07, 95% CI: 0.99-1.14; p=0.079). This lack of independent predictive value persisted in Model 2 (OR=1.07, 95% CI: 0.99-1.15; p=0.085) and Model 3 (OR=1.08, 95% CI: 1.00-1.16; p=0.062). Furthermore, no other covariates achieved independent statistical significance within these models.

In the present cohort, among the 64 participants with macrovascular disease, 29.7% (*n*=19) were classified as overweight, 42.2% (*n*=27) presented with obesity, and 28.1% (*n*=18) had normal BMI.

For macrovascular complications, WHtR showed no significant association across all models, Model 1 (p=0.832), Model 2 (p=0.505) and Model 3 (p=0.500). In Model 2, male sex (OR=2.50, 95% CI: 1.23-5.09; p=0.011) and diabetes duration (OR=1.04, 95% CI: 1.01-1.08; p=0.026) were independent risk predictors. In the final Model, only diabetes duration remained an independent determinant (OR=1.05, 95% CI: 1.01-

1.09; p=0.012). BMI was not a significant predictor of macrovascular complications across any model, Model 1 (p=0.415), Model 2 (p=0.590) and Model 3 (p=0.614). In Model 2, male sex independently doubled the odds of events (OR=2.25, 95% CI: 1.18-4.27; p=0.013).

WHtR demonstrated a statistically valid discriminative capacity in diabetic nephropathy, yielding an Area Under the Curve (AUC) of 0.62 (95% CI: 0.51-0.73; p=0.028). Conversely, BMI exhibited a non-significant classification performance, failing to perform better than chance (AUC=0.57, 95% CI: 0.46-0.68; p=0.229) (Figure 1). The direct paired comparison of the two areas didn't reach statistical significance but revealed a trend toward significance (DeLong's test, AUC difference=0.054; p=0.077).

For diabetic retinopathy, WHtR demonstrated a statistically validated classification capacity, achieving an AUC of 0.60 (95% CI: 0.51-0.70; p=0.035). In contrast, BMI displayed a non-significant discriminative performance (AUC=0.56, 95% CI: 0.47-0.65; p=0.214) (Figure 2). The direct paired-sample difference between the two receiver operating curves trended toward a borderline threshold without reaching strict statistical significance (DeLong's test, AUC difference=0.045; p=0.096).

Discussion

The principal findings demonstrate that WHtR exhibits significant independent associations with specific microvascular complications, particularly diabetic nephropathy and retinopathy, even after comprehensive adjustment for potential confounders. In contrast, BMI fails to demonstrate predictive value for any vascular outcome examined. These findings contribute to the growing body of evidence suggesting that central adiposity measures may be superior in risk stratification compared to traditional BMI-based assessments in diabetic populations. Neither anthropometric index achieved statistical significance in predicting macrovascular disease or overall cardiovascular risk in this cohort.

WHtR and Microvascular Complications

The association between WHtR and diabetic nephropathy persisted across all three sequential models, with OR ranging from 1.65 to 1.68, even after correction for metabolic covariates including HbA1c, smoking status, systolic blood pressure and apoB. This finding aligns with previous research demonstrating that WHtR demonstrates stronger associations with microalbuminuria and diabetic kidney disease compared to other anthropometric indices [16, 17]. Additional studies confirm that WHtR represents a superior anthropometric predictor of cardiorenal outcomes in T2DM, where WHtR was the only anthropometric index significantly associated with combined cardiorenal disease risk among traditional obesity measures, outperforming BMI in multivariate analysis [18]. The mechanistic basis for this association likely reflects the pathophysiological role of visceral adiposity in promoting insulin resistance, systemic inflammation, endothelial dysfunction, and activation of the renin-angiotensin-aldosterone system, all of which contribute to progressive renal injury in diabetes [19-21]. The predictive superiority of WHtR in this cohort suggests that visceral fat related factors, like low-grade inflammation and local activation of the renin-angiotensin-aldosterone system, are earlier determinants of microvascular injury than the global adiposity captured by BMI. Similarly, WHtR demonstrated a robust independent association with diabetic retinopathy, with the effect strengthening upon adjustment for confounders (OR 1.60 in Model 1; 1.86 in Model 2 and 1.85 in Model 3). The association between central obesity and retinopathy may be mediated through multiple pathways, including chronic low-grade inflammation, oxidative stress, and dysregulation of adipokines such as leptin and adiponectin, which have been implicated in retinal vascular dysfunction [20, 25, 26]. The robust association of WHtR with nephropathy and retinopathy, which persisted after adjusting for apoB and HbA1c, suggests that central adiposity exerts a pathogenic effect on the microvasculature that is independent of traditional lipid and glycaemic markers. Diabetes duration emerged as a simultaneous independent predictor in these models, consistent with established understanding that prolonged glycaemic exposure drives microvascular pathology [22-24].

In contrast, WHtR did not achieve statistical significance for diabetic neuropathy across any model. Within Model 3, HbA1c and smoking status emerged as the primary independent determinants of

neuropathy risk. This finding appears to contradict emerging evidence demonstrating that visceral adiposity represents an independent risk factor for diabetic peripheral neuropathy [27]. While visceral adiposity is a known driver of systemic inflammation, the lack of statistical significance for diabetic neuropathy in this cohort likely reflects the limited power of the small subgroup (n=30) rather than a lack of biological plausibility. Furthermore, this result may be influenced by an underdiagnosis bias, as screening for diabetic neuropathy is not always performed systematically in clinical practice, unlike nephropathy and retinopathy, which benefit from well-established and routinely implemented screening protocols. Additionally, the cross-sectional design and high prevalence of glucose-lowering therapies may have attenuated the metabolic perturbations typically associated with visceral adiposity.

BMI and Vascular Complications

The consistent incapacity of BMI to predict any vascular outcome in this cohort, including microvascular and macrovascular complications, contrasts with some prior literature but aligns with emerging evidence questioning the value of BMI in diabetic populations [28]. While large-scale studies such as the UK Biobank analysis demonstrated associations between BMI and diabetic microvascular complications, these relationships were substantially weaker than those observed for WC [20], and this study's null findings may reflect several important considerations. First, BMI does not distinguish between lean mass and adipose tissue, nor does it capture fat distribution patterns [29]. Individuals with identical BMI values may have markedly different visceral adiposity patterns, which represent the metabolically active component driving cardiovascular and renal risk [5]. Second, the present cohort exhibited a median BMI of 28.0 kg/m². Our findings reinforce the 'diagnostic insufficiency' of BMI in the overweight range, where it fails to account for the metabolically active visceral fat that drives microvascular damage. Third, the high prevalence of cardioprotective therapies in our cohort, specifically SGLT2 inhibitors (70.4%) and GLP-1 receptor agonists (33.8%), may have attenuated the observable impact of elevated BMI on prevalent macrovascular disease.

Macrovascular Disease and Overall Cardiovascular Risk

Neither WHtR nor BMI demonstrated significant associations with macrovascular disease or overall cardiovascular risk in the present cohort. This finding diverges from multiple large-scale studies demonstrating robust associations between WHtR and cardiovascular events in diabetic populations. A recent analysis of 7 000 diabetic patients from NHANES demonstrated that WHtR exhibited significant positive linear relationships with CVD, CHF, CAD, and stroke, with fully adjusted OR ranging from 1.43 to 2.35 for the highest versus lowest quartile [2]. Similarly, a Chinese cohort of 3 108 individuals with T2DM found that WHtR was the only anthropometric measure independently associated with cardio-cerebrovascular events when all four indices (WHtR, WC, WHR and BMI) were modelled simultaneously[30].

Furthermore, prospective data from the ADVANCE-ON study demonstrated that WHtR was superior to BMI and WHR in predicting major macrovascular events over extended follow-up in patients with T2DM and high cardiovascular risk[13].

Several methodological and population-specific factors may explain the discordance between the present findings and prior literature. First, the cross-sectional design precludes assessment of incident events and relies on prevalent disease, which introduces survival bias. Patients with severe macrovascular disease and poor metabolic control may have been underrepresented due to premature mortality or inability to attend clinic visits. Therefore, the observed 30% prevalence of macrovascular disease is likely an underestimate of the true population burden and may reflect a 'survivor' subgroup in whom the relationship between adiposity indices and CVD is inherently attenuated. Second, the substantial prevalence of ASCVD in this cohort (30%) may itself limit the discriminatory capacity of anthropometric measures. The well-documented obesity paradox suggests that BMI and other body composition parameters are not consistent cardiovascular risk factors once atherosclerotic disease is established [5]. In patients with T2DM and prevalent CVD, overweight and mild obesity have been associated with better short-to moderate-term prognosis compared to normal weight individuals, a phenomenon attributed to reverse causation (disease-related weight loss), differences in cardiorespiratory fitness, lead-time bias (earlier diagnosis and treatment in patients with obesity), and potential metabolic reserve in the setting of cardiac cachexia [5, 31]. Data from the TECOS trial demonstrated that among patients with T2DM and ASCVD, those with overweight or class I obesity had lower cardiovascular risk than those with normal weight, suggesting that the obesity paradox may obscure the relationship between adiposity and cardiovascular outcomes in populations with prevalent disease [31]. In the present cohort, among the 64 participants with macrovascular disease, 29.7% (*n*=19) were classified as overweight and 28.1% (*n*=18) had normal BMI, a distribution consistent with the obesity paradox phenomenon and potentially contributing to the attenuated associations observed between anthropometric indices and cardiovascular outcomes. Also, this paradox is particularly pronounced in cross-sectional analyses and may be further amplified by smoking status and sex, with stronger effects observed in current smokers and men [32]. In the present cohort, with a predominantly male population (56.8%) and a substantial proportion of current (14.1%) and former smokers (28.2%), these demographic characteristics may have contributed to the attenuation of the relationship between adiposity indices and prevalent macrovascular disease, particularly given the cross-sectional design which is known to amplify paradoxical findings. Third, the high prevalence of cardioprotective therapies used in this cohort, including statins (77.0%), SGLT2 inhibitors (70.4%), and GLP-1 RA (33.8%), constitutes a central biological confounder. These agents confer robust cardiorenal protection through hemodynamic and anti-inflammatory mechanisms that transcend adiposity reduction, thereby potentially attenuating the statistical association between WHtR and prevalent macrovascular events. Fourth, the relatively small sample size (n=213) may have limited

statistical power to detect associations with macrovascular disease, particularly when stratified by individual manifestations such as CAD (n=45, 21.1%), cerebrovascular disease (n=14, 6.6%), and PAD (n=20, 9.4%). The low event rates for cerebrovascular and PAD constrain the statistical power of logistic regression models. Large-scale studies demonstrating associations between WHtR and cardiovascular outcomes have typically included thousands of participants, providing substantially greater power to detect modest effect sizes.

The emergence of male sex, age, and diabetes duration as independent predictors of overall cardiovascular risk in adjusted models aligns with established epidemiological patterns and reinforces the predominance of non-modifiable and time-dependent risk factors in this cross-sectional analysis [33, 34].

Comparative Performance of WHtR Versus BMI

The differential performance of WHtR and BMI observed in this study supports the hypothesis that central adiposity measures provide superior risk stratification for specific diabetic complications. When both indices were evaluated in parallel models, WHtR consistently demonstrated associations with nephropathy and retinopathy, whereas BMI remained non-significant across all outcomes. This pattern suggests that visceral fat accumulation, approximated by WHtR, captures pathophysiological relevant adiposity that BMI, as a measure of overall body mass, fails to detect. The theoretical advantage of WHtR lies in its ability to normalize WC for height, thereby accounting for body frame size and providing a more standardised assessment of central adiposity across individuals of varying stature. The threshold of WHtR ≥0.5 has been proposed as a simple screening tool for cardiometabolic risk [35]. In the present cohort, the mean WHtR of 0.62 substantially exceeded this threshold, indicating widespread central obesity despite a median BMI in the overweight rather than obese range. This discordance underscores the limitation of BMI-based obesity classification and supports the integration of central adiposity measures into routine diabetic care.

Clinical Implications

The present findings suggest that WHtR may serve as a valuable tool for identifying individuals with T2DM at elevated risk for specific microvascular complications, particularly nephropathy and retinopathy. Given the high prevalence of central obesity in this cohort (mean WHtR 0.62) and the independent associations observed after adjustment for glycaemic control, blood pressure, and lipid parameters, WHtR assessment could complement traditional risk factor monitoring in diabetic care. The failure of BMI to predict any vascular outcome in this cohort challenges the reliance on BMI-based obesity classification for cardiovascular risk stratification in diabetes and supports the incorporation of WHtR measurements into routine assessment protocols.

The observation that neither WHtR nor BMI predicted macrovascular disease in this cohort, despite robust associations in prior literature, warrants cautious interpretation. The cross-sectional design, high prevalence of cardioprotective medication use and potential survival bias limit the ability to draw definitive conclusions regarding the utility of these measures for macrovascular risk prediction. Future studies should evaluate whether longitudinal reduction in WHtR, independent of BMI variation, translates into regression of albuminuria or stabilization of diabetic retinopathy progression in patients under combined therapy with SGLT2i and GLP-1 RA.

Strengths and Limitations

The present study benefits from comprehensive assessment of both microvascular and macrovascular complications, detailed characterization of metabolic parameters including apoB and Lp(a), and systematic evaluation of multiple anthropometric indices using standardised sequential modelling approaches. The high rate of contemporary glucose-lowering and cardioprotective medication use reflects real-world diabetic care and enhances external validity.

However, several limitations merit consideration. The cross-sectional design precludes causal inference and assessment of incident complications. The relatively modest sample size (n=213) may have limited statistical power to detect associations with macrovascular disease and restricted robust subgroup analyses by sex, age, or diabetes duration. The single-centre recruitment from a Portuguese cohort may limit applicability of these results to broader diabetic populations and other ethnic groups. Furthermore, individuals aged 80 years and older were poorly represented in our study population. Residual confounding from unmeasured variables, including dietary patterns, physical activity levels and medication adherence, cannot be excluded. The reliance on clinical diagnosis of vascular complications rather than standardised screening protocols may have introduced misclassification bias. Finally, the lack of direct visceral adiposity measurement through imaging modalities such as computed tomography or magnetic resonance imaging limits the ability to validate WHtR as a surrogate for visceral fat burden.

Future perspectives

Prospective cohort studies with longitudinal follow-up are needed to establish whether WHtR predicts incident microvascular and macrovascular complications in T2DM and whether it provides incremental predictive value beyond established risk scores. Investigation of sex-specific associations, given emerging evidence of differential effects in women versus men, would inform targeted screening strategies [36]. Finally, intervention studies examining whether reduction in WHtR through lifestyle modification or pharmacotherapy translates to reduced microvascular complication rates would establish the clinical utility of WHtR-guided risk stratification and treatment intensification.

Conclusion

In conclusion, this study demonstrates that WHtR exhibits independent associations with diabetic nephropathy and retinopathy in Portuguese adults with T2DM, whereas BMI fails to predict any vascular outcome investigated. These findings support the integration of central adiposity assessment into diabetic care and suggest that WHtR may provide superior risk stratification compared to BMI for specific microvascular complications. The lack of associations between both indices and macrovascular complications in this cross-sectional cohort warrants further investigation in prospective studies.

Appendix

1. Tables

Table I. Characteristics of subjects

**Data for BMI were missing for 1 patient.*

Variables	
Male (n,%)	121 (56.8%)
Female (n,%)	92 (43.2%)
Black (n, %)	2 (0.9%)
Age (years)	62 [56-66]
Duration of T2DM (years)	13 [8-21]
Smoking (n,%)	30 (14.1%)
Former smokers (n,%)	60 (28.2%)
Never smoked (n,%)	123 (57.7%)
Antidiabetic medications (n,%)	212 (99.5%)
Insulin (n,%)	122 (57.3%)
SGLT2i (n,%)	150 (70.4%)
Metformin (n,%)	175 (82.2%)
GLP1a (n,%)	72 (33.8%)
DPP4i (n,%)	61 (28.6%)
Sulfonylureas (n,%)	22 (10.3%)
Glitazones (n,%)	1 (0.5%)
Acarboses (n,%)	1 (0.5%)
Dyslipidaemia (n,%)	177 (83.1%)
Lipid-Lowering Drugs (n,%)	165 (77.5%)
Statins (n,%)	164 (77.0%)
Ezetimib (n,%)	53 (24.9%)
Hypertension (n,%)	149 (70.0%)
Antihypertensive Agents (n,%)	144 (67.6%)
Microvascular complications (n,%)	79 (37.1%)
Diabetic Nephropathy (n,%)	33 (15.5%)
Retinopathy (n,%)	46 (21.6%)
Neuropathy (n,%)	30 (14.1%)
Macrovascular complications (n,%)	64 (30.0%)
Ischemic Heart Disease (n,%)	45 (21.1%)
Cerebrovascular Disease (n,%)	14 (6.6%)
Peripheral Artery Disease (n,%)	20 (9.4%)
SBP (mmHg)	134 ±18
WC (cm)	102.5 ± 13.3
WHtR	0.62 ±0.09
BMI (kg/m^2)	28.0 [25.1 - 32.0]
Normal weight (n,%)	53 (25.0%)
Overweight (n,%)	74 (34.9%)
Obesity (n,%)	85 (40.1%)
Weight (kg)	78.0 [68.6 – 90.4]
Height (cm)	166 [158 – 172]
HbA1C (%)	8.3 [7.3 – 9.6]
Total cholesterol (mg/dL)	149 [127 – 179]
HDL-C (mg/dL)	43 [36 – 52]
LDL-C (mg/dL)	74 [51 – 101]
Non-HDL (mg/dL)	104 [80 – 134]
TG (mg/dL)	157 [110 – 247]
ApoB (mg/dL)	81 [65 – 102]
GFR ($ml/min/1.73\ m^2$)	96 [77 – 104]

Table II. Lipid profile

Variables	Odds Ratio	95% Confidence Interval	p-value	Status for Multivariable Model
Total Cholesterol	0.997	0.992–1.002	0.271	Excluded
LDL Cholesterol	0.997	0.991–1.004	0.401	Excluded
HDL Cholesterol	0.975	0.954–0.996	0.022	Excluded
Non-HDL Cholesterol	0.999	0.994–1.004	0.700	Excluded
Triglycerides	1.000	0.998–1.002	0.787	Excluded
Lipoprotein(a)	1.001	0.999–1.003	0.362	Excluded
Apolipoprotein B	0.999	0.991–1.007	0.860	Pre-specified Clinical Criterion

Table III. Results

Outcome and Predictive Models	p-value	OR (95% CI)	Covariates Included
NEPHROPATHY			
Model 1			
WHtR	**0.027**	1.65 (1.06 – 2.56)	None
BMI	0.170	1.05 (0.98 – 1.12)	None
Model 2			
WHtR	**0.026**	1.68 (1.06 – 2.65)	Age. Sex. Diabetes duration
BMI	0.175	1.05 (0.98 – 1.13)	Age. Sex. Diabetes duration
Model 3			
WHtR	**0.037**	1.65 (1.03 – 2.62)	Model 2 + Smoking. HbA1c. ApoB. Systolic BP
BMI	0.193	1.05 (0.98 – 1.13)	Model 2 + Smoking. HbA1c. ApoB. Systolic BP
RETINOPATHY			
Model 1			
WHtR	**0.027**	1.60 (1.05 – 2.42)	None
BMI	0.573	1.02 (0.96 – 1.08)	None
Model 2			
WHtR	**0.010**	1.86 (1.16 – 2.98)	Diabetes duration (p<0.001). Age. Sex
BMI	0.210	1.05 (0.98 – 1.12)	Diabetes duration (p<0.001). Age. Sex
Model 3			
WHtR	**0.013**	1.85 (1.14 – 3.01)	Diabetes duration (p<0.001). Model 2 + Smoking. HbA1c. ApoB. Systolic BP
BMI	0.234	1.04 (0.97 – 1.12)	Diabetes duration (p<0.001); Model 2 + Smoking. HbA1c. ApoB. Systolic BP
NEUROPATHY			
Model 1			
WHtR	0.227	1.33 (0.84 – 2.11)	None
BMI	0.079	1.07 (0.99 – 1.14)	None
Model 2			
WHtR	0.110	1.50 (0.91 – 2.47)	Age. Sex. Diabetes duration
BMI	0.085	1.07 (0.99 – 1.15)	Age. Sex. Diabetes duration
Model 3			
WHtR	0.169	1.45 (0.86 – 2.45)	Model 2 + Smoking (p=0.045). HbA1c (p=0.017). ApoB. Systolic BP
BMI	0.062	1.08 (1.00 – 1.16)	Model 2 + Smoking. HbA1c. ApoB. Systolic BP
MACROVASCULAR			
Model 1			
WHtR	0.832	1.04 (0.73 – 1.49)	None
BMI	0.415	0.98 (0.92 – 1.03)	None
Model 2			
WHtR	0.505	1.14 (0.77 – 1.69)	Age. Male sex (p=0.011). Diabetes duration (p=0.026).
BMI	0.590	0.98 (0.93 – 1.04)	Age. Male sex (p=0.013); Diabetes duration.
Model 3			
WHtR	0.500	1.14 (0.77 – 1.69)	Model 2 [Diabetes duration (p=0.012)] + Smoking. HbA1c. ApoB. Systolic BP
BMI	0.614	0.98 (0.93 – 1.05)	Model 2 + Smoking. HbA1c. ApoB. Systolic BP
GLOBAL CV			
Model 1			
WHtR	0.140	1.29 (0.92 – 1.80)	None
BMI	0.789	0.99 (0.94 – 1.05)	None
Model 2			
WHtR	0.081	1.39 (0.96 – 2.01)	Age (p=0.022). Male sex (p=0.006). Diabetes duration (p=0.015)
BMI	0.950	1.00 (0.95 – 1.06)	Age (p=0.035). Male sex (p=0.022). Diabetes duration (p=0.003).
Model 3			
WHtR	0.118	1.35 (0.93 – 1.98)	Model 2 [Age (p=0.010). Male sex (p=0.035). Diabetes duration (p=0.010] + Smoking. HbA1c. ApoB. Systolic BP
BMI	0.884	1.00 (0.95 – 1.06)	Model 2 [Age (p=0.011). Diabetes duration (p=0.003)] + Smoking. HbA1c. ApoB. Systolic BP

2. Figures/Charts

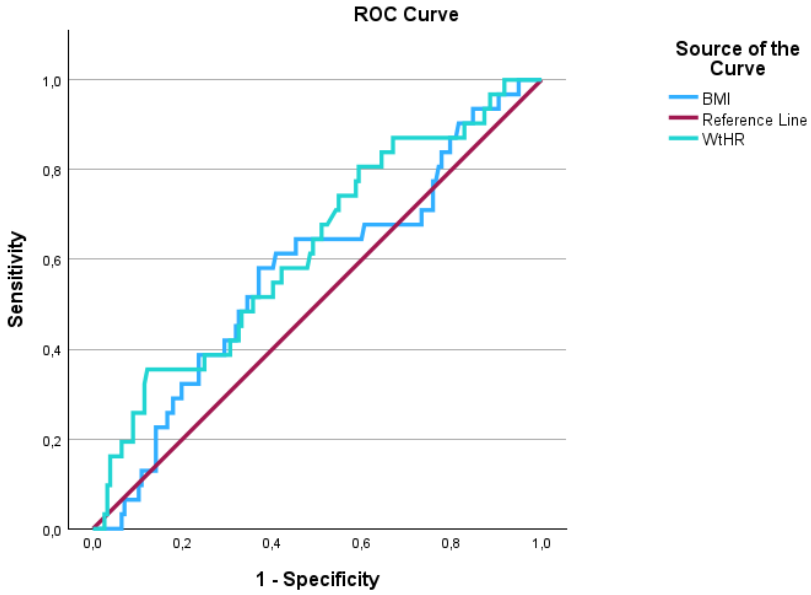

Figure 1. ROC Curve Nephropathy

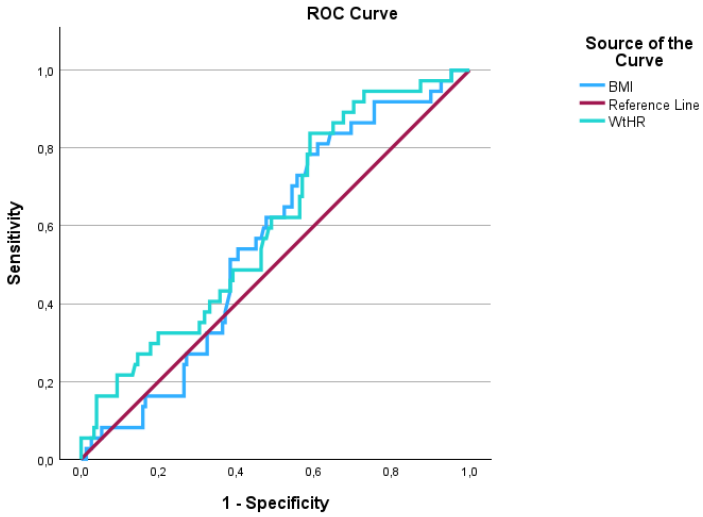

Figure 2. ROC Curve Retinopathy

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