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The impact of using sagittal abdominal diameter to predict major cardiovascular events in European patients with type 2 diabetes

K. Rådholm [a,*], A. Tengblad [a], E. Dahlén [a], T. Länne [b], J. Engvall [c], F.H. Nystrom [b], C.J. Östgren [a]

[a] *Division of Community Medicine, Primary Care, Department of Medicine and Health Sciences, Faculty of Medicine and Health Sciences, Linköping University, Department of Local Care West, County Council of Östergötland, SE-581 83 Linköping, Sweden*
[b] *Division of Cardiovascular Medicine, Department of Medical and Health Sciences, Faculty of Medicine and Health Sciences, Linköping University, SE-58185 Linköping, Sweden*
[c] *Department of Clinical Physiology, Faculty of Medicine and Health Sciences, Linköping University, Linköping, SE-58183, Sweden*

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Abstract *Background and aims:* Obesity is associated with diabetes type 2 and one of the most important risk factors for cardiovascular disease. We explored if sagittal abdominal diameter (SAD) is a better predictor of major cardiovascular events than waist circumference (WC) and body mass index (BMI) in type 2 diabetes.
Methods and results: The CARDIPP study consists of a cohort of patients with type 2 diabetes. In this study we used data from 635 participants with no previous myocardial infarction or stroke, with a mean follow-up time of 7.1 years. SAD, WC and BMI were measured at baseline and the end-point was first cardiovascular event, measured as a composite of ICD-10 codes for acute myocardial infarction, stroke or cardiovascular mortality. SAD was significantly higher in the major cardiovascular event group compared to participants that did not suffer a major cardiovascular event during follow-up ($p < 0.001$). SAD >25 cm was the only anthropometric measurement that remained associated with major cardiovascular events when adjusted for modifiable and non-modifiable factors (hazard ratio 2.81, 95% confidence interval 1.37–5.76, $p = 0.005$).
Conclusion: SAD with the cut off level of >25 cm, if confirmed in larger studies, may be used as a more independent risk-assessment tool compared with WC in clinical practice, to identify persons with type 2 diabetes at high cardiovascular risk. ClinicalTrials.gov: NCT01049737.

Background

Obesity has emerged as one of the most important risk factors for cardiovascular disease (CVD). Deteriorating metabolic health is due to worsening glycemic health and not to blood lipids or blood pressure, which have improved over the last 25 years [1]. Anthropometric measurements are inexpensive and serve to evaluate nutritional status as well as the health risks associated with overweight and obesity [2,3]. Body mass index (BMI, weight/height^2) is commonly recommended in guidelines to evaluate overweight and obesity [4–6]. However, BMI does not distinguish lean body mass from adiposity [7,8], and thus, cannot target central obesity which is particularly associated to an increased risk for cardiovascular disease, type 2 diabetes and mortality compared to fat deposits elsewhere [8–11]. Abdominal, truncal adipose tissue may be described as intra-abdominal where the fat is accumulated in the viscera which is particularly dangerous from a cardiometabolic perspective. If the truncal adipose tissue is subcutaneous, it is less associated to increased

* Corresponding author. Fax: +46 10 103 4020.
E-mail address: karin.radholm@liu.se (K. Rådholm).

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cardiometabolic risk [12]. Waist circumference (WC) and sagittal abdominal height (SAD) reflect central obesity [13] better than waist hip ratio (WHR), because a high WHR can be the result of a larger waist as well as a smaller hip [8]. WC is a more established anthropometric measure than SAD, although SAD, with the patient in supine position that aims to evaluate visceral adipose tissue, may be superior compared to other anthropometrics for CVD risk prediction [8] as well as a possible surrogate marker for insulin resistance [14]. However, consensus about SAD cut-offs for predicting CVD risk is lacking [15].

We have previously shown that sagittal abdominal diameter is a more independent measure compared with waist circumference to predict arterial stiffness in patients with type 2 diabetes [16]. Our aim in this study was to explore if SAD is a better predictor of major cardiovascular events than WC and BMI in patients with type 2 diabetes.

Methods

The design of the Cardiovascular Risk factors in Patients with Diabetes – a Prospective study in Primary care (CARDIPP) has been described previously [16,17]. In brief, CARDIPP was launched in 2005 with the aim of identifying markers for cardiovascular disease to facilitate earlier and individually adjusted intervention in middle aged patients with type 2 diabetes. Patients aged 55–65 years were consecutively recruited during their usual annual follow-ups at 22 primary healthcare centers in the counties of Östergötland and Jönköping, Sweden. Data from 635 study participants with no previous myocardial infarction or stroke (84% of the total cohort) were analyzed. Participants lacking anthropometric measurements were also excluded. The primary endpoint was a composite of the first non-fatal or fatal event of hospitalization for acute myocardial infarction (ICD-10 code I21), stroke (ICD-10 codes I60, I61, I63.0–I63.5, I63.8–I63.9, I64) or cardiovascular mortality (ICD-10 codes I00–99). Patients were followed until a primary outcome event occurred, or until December 31st, 2014, by linkage to the Swedish Cause of Death and Inpatient registries (The National Board of Health and Welfare, Stockholm, Sweden) using the national personal identification number of each individual patient, thus ensuring coverage of the entire population. The median follow-up time was 7.1 years. There was no loss to follow-up.

Data on BMI, WC and blood pressure were obtained by specially trained nurses at the primary health care centers. Height (to the nearest cm) and weight (to the nearest 0.1 kg) were measured with the participants wearing light indoor clothing. Waist circumference (WC) was measured according to the World Health Organization (WHO) recommendations: with the participant standing, after a regular expiration, to the nearest cm and midway between the lowest rib and the iliac crest [9]. Sagittal abdominal diameter (SAD) was recorded at the Departments of Clinical Physiology at Linköping University Hospital, Linköping, Sweden and at the County Hospital Ryhov, Jönköping, Sweden. The participants were in a supine position with bent knees. A standardized sliding beam caliper was applied at the highest point of the abdomen [18]. Cut-offs for WC were set according to the International Diabetes Federation Criteria, Europid specific values $\geq$94 cm for men and $\geq$80 cm for women [19], and to the NIH Practical guide to obesity which states $\geq$102 cm for men and $\geq$88 cm for women [20]. BMI was dichotomized to $\geq$25 kg/m^2 (pre-obesity and above), $\geq$30 kg/m^2 (obesity class I–III) and $\geq$35 kg/m^2 (obesity class II–III) according to the World Health Organization (WHO) classifications [21]. SAD was dichotomized to either >22 cm for men and >20 cm for women [22] or >25 cm for both men and women [23]. A standardized protocol was used to obtain medical history; data on diabetes duration, previous cardiovascular events and ongoing medication. A questionnaire was used to provide information on lifestyle habits including smoking status and alcohol consumption. Blood pressure was calculated as the average of three sitting measurements recorded with a 1 min interval between the measurements and after 5 min rest.

Laboratory analyses

Blood samples were collected at the health care centers after a 10 h overnight fast. The Swedish standard high-performance liquid chromatography (HPCL) Mono-S method was used to measure HbA1c and the results were converted to Diabetes Control and Complications Trial (DCCT) standards (%) and International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) units (mmol/mol). Levels of cholesterol, HDL and triglycerides were measured with enzymatic methodology and spectrophotometry, Selectra E, Vital Scientific, the Netherlands/Triolab. LDL was calculated by the Friedewald formula: LDL = cholesterol − HDL − 0.45 × fS/P-triglycerides. Serum creatinine was measured by use of an IDMS calibrated modified Jaffe method on an Advia 1800 analyzer (Siemens Healthcare Diagnostics). Coefficients of variation (CV) for the creatinine method was 4.3% at 90 μmol/L and 3.1% at 380 μmol/L. Glomerular filtration rate (eGFR) was estimated with the CKD-EPI formula [24]. Urine albumin was analyzed on the same instrument as creatinine using reagents from Siemens Healthcare Diagnostics. C-reactive protein (CRP) was measured by use of a high sensitive latex-enhanced turbidimetric immunoassay (Roche Diagnostics, Mannheim, Germany) with a lower limit of detection of 0.03 mg/L.

Ethics

The study was approved by the regional ethical review board in Linköping. All participants provided informed consent in writing.

Statistics

Differences in categorical variables were analyzed with the Pearson's chi-square test. Continuous variables were examined with the Student's t-test or the Mann–Whitney U test if their distribution was skewed. Cox regression analysis was used to estimate HRs and 95% CIs for