Is there a Benefit to Use Calculated Percent Body Fat or Age- and Gender-adjusted BMI-SDS_{LMS} to Predict Risk Factors for Cardiovascular Disease? A German/Austrian Multicenter DPV-Wiss Analysis on 42 048 Type 2 Diabetic Patients

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Key words

- body mass index
- body fat percentage
- body mass index standard deviation score
- hypertension
- dyslipidemia

Abstract

Objective: In clinical practice Body Mass Index is generally used to evaluate overweight status in adults. The present multicenter study examines whether Body Mass Index (BMI), age- and gender-adjusted Body Mass Index Standard Deviation Score, or calculated \%body fat is a better predictor for cardiovascular disease risk factors, specifically hypertension and dyslipidemia, in a high-risk population.

Methods: Data of 42 048 adult type 2 diabetic patients (median age: 67.1 years) from 161 centers in Germany (n = 158) and Austria (n = 3) registered in a standardized, prospective, computer-based documentation program, were included in the study. For each patient body weight, height, blood pressure and blood lipids were documented. Spearman correlation analyses as well as multivariable logistic regression models were used to examine the relationship between anthropometric measurements and cardiovascular disease risk factors.

Results: Correlation and regression analyses revealed minor, non significant differences between the 3 anthropometric measurements (all p > 0.05). In both genders, relationships between anthropometric measurements and hypertension or reduced HDL-cholesterol were nearly identical. Only for increased triglycerides, the relations with the 3 anthropometric measurements were significantly stronger in males than in females (p < 0.0001, respectively). With increasing age, associations between anthropometric measurements and hypertension, reduced HDL-cholesterol or increased triglycerides became weaker. Spearman correlation coefficients for total cholesterol and LDL-cholesterol revealed weak associations with the 3 anthropometric measurements.

Conclusion: Compared to Body Mass Index, age- and gender-adjusted Body Mass Index Standard Deviation Score, or calculation of \%body fat, has no further benefit to predict cardiovascular disease risk factors in adult type 2 diabetic patients.

Introduction

Cardiovascular diseases (CVDs) are the leading cause of death worldwide [1]. The World Health Organization (WHO) assumes that by 2030 CVD will lead to nearly 23.6 million deaths [1]. Therefore adequate screening methods are necessary to estimate cardiovascular risk. According to the Adult Treatment Panel III (ATP III) of the National Cholesterol Education Program, elevated LDL-cholesterol, high levels of triglycerides, low HDL-cholesterol, hypertension, diabetes and overweight/obesity are major CVD risk factors [2]. They are established risk factors and can be determined in routine clinical practice, where specialized cardiovascular risk assessment methods like body fat estimation by dual energy X-ray absorptiometry or bioelectrical impedance are not always practicable. The present investigation focused on the estimation of overweight and obesity by anthropometric measurements and their associations to hypertension and dysliipidemia.

Overweight and obesity in adults are commonly defined by Body Mass Index (BMI) according to WHO cut-offs [3], even though limitations are present. For instance, a person with a high proportion of muscle mass may have the same BMI as a person with a high proportion of body fat. Furthermore, age- and gender-specific differences are usually not considered. Thus, Hemmelmann et al. [4], based on the Second German National Nutrition Survey, established age- and gender-dependent percentile
curves for BMI, similar to BMI percentiles for children and adolescents. The authors hypothesized that with this BMI classification, health risks for the individual will be assessed more precisely [4].

Another recent publication by Gómez-Ambrosi et al. [5] proposed the calculation of %body fat (%BF) as a clinical tool to detect patients with elevated cardiovascular risk. %BF was calculated by a validated formula that includes BMI, age and gender [6].

Until now, several studies examined the association between different anthropometric measurements and CVD risk factors like hypertension or dyslipidemia [5, 7–14]. However, few studies address type 2 diabetic patients, who are at increased risk for CVD [2, 10, 15]. Therefore the purpose of this study was to examine the relationship of BMI, age- and gender-adjusted Body Mass Index Standard Deviation Score (BMI-SDS<sub>LMS</sub>) and calculated %BF with CVD risk factors in a cohort of 42 048 adult patients with type 2 diabetes mellitus (T2DM). Furthermore, to our knowledge, this investigation is the first to analyze the relationship of age- and gender-adjusted BMI-SDS<sub>LMS</sub> with CVD risk factors in adults.

### Materials and Methods

**Standardized documentation**

The DPV-Wiss-database is based on a standardized, computer-based, prospective, multicenter documentation and was developed at the Institute of Epidemiology and Medical Biometry, Ulm, Germany. In this database, diagnosis and follow-up of T2DM patients are documented by participating centers. Every half-year data entered locally are anonymized and transferred to Ulm, Germany for central analyses. If necessary, participating centers are requested to correct inconsistent data.

The DPV Initiative is approved by the Ethic Committee of the University of Ulm, Germany.

**Patients**

Until March 2012, data of 171 442 adult type 2 diabetic patients (≥18 years) were registered in DPV-Wiss. For the present investigation, data of 42 048 type 2 diabetic patients (42 022 German; 26 Austrian) from 161 specialized centers in Germany (n = 158) and Austria (n = 3) were included (Fig. 1). Patients with missing values of either body weight, height or blood pressure and with no blood lipid value (total cholesterol or LDL-cholesterol or HDL-cholesterol or triglycerides) were excluded (n = 51 003, Fig. 1). Further exclusion criteria were antihypertensive medication, lipid lowering medication, use of antidepressants or...
antipsychotics, bariatric surgery or systemic steroid therapy (n = 78 391, Fig. 1).

For each included patient, datasets were aggregated over the first year of care. HbA1c values were standardized to the DCCT norm (4.05–6.05%) based on local reference ranges by the multiple of the mean (MOM) method.

Hypertension was defined as elevated systolic blood pressure > 140 mmHg or diastolic blood pressure > 90 mmHg [16] at repeated measurements during the year of observation. According to the ATP III criteria [2], median HDL-cholesterol values of  150 mg/dl were considered elevated [2].

Calculation of anthropometric measurements
BMI was calculated as body weight in kilograms divided by the square of the height in meters (kg/m²).

For each included patient, datasets were aggregated over the first year of care. HbA1c values were standardized to the DCCT norm (4.05–6.05%) based on local reference ranges by the multiple of the mean (MOM) method.

Statistical analysis
Firstly, descriptive statistics for the study population and the patients excluded were carried out. Baseline characteristics are presented as medians with lower (Q₁) and upper quartiles (Q₃), if not indicated otherwise. Correlation and regression analyses were performed for the whole study population. Furthermore, regression analyses were carried out after categorization of the study population by gender and age (18–<40 years; 40–<60 years; 60–<80 years; ≥80 years).

Spearman correlation coefficients were calculated for detecting positive or negative relationships between BMI, age- and gender-adjusted BMI-SDSₐₜ, calculated %BF and systolic, diastolic blood pressure, total cholesterol, LDL-cholesterol, HDL-cholesterol or triglycerides, respectively. To further analyze relationships between these anthropometric measurements and CVD risk factors, receiver operating characteristic (ROC) curves based on logistic regression were created. Logistic regression models were adjusted for age, gender and diabetes duration in analyses of the whole study population as well as in age-specific analyses. In gender-specific analyses, models were adjusted for age and diabetes duration. Areas under the curve (AUC) were compared between BMI, age- and gender-adjusted BMI-SDSₐₜ and calculated %BF, respectively. All statistical analyses were implemented with SAS 9.2 (Statistical Analysis Software, SAS Institute, NC, USA). A p-value of < 0.05 was considered statistically significant.

Results

Study population
Baseline characteristics of the study population and the patients excluded are presented in Table 1. The study population was slightly younger than the patients excluded (median age [Q₁; Q₃]: 67.1 [56.8; 74.9] years vs. 69.2 [60.1; 76.8] years). Other differences in baseline characteristics between included and excluded patients were without clinical relevance. Exclusion of patients was mostly due to the use of antihypertensive drugs, missing blood lipid values and missing height measurements in older adults (Fig. 1).

Table 1  Baseline characteristics of the whole study population, for males and females separately, and for patients excluded.

<table>
<thead>
<tr>
<th></th>
<th>All (n = 42 048)</th>
<th>Study population</th>
<th>All (n = 129 394)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men (n = 22 035)</td>
<td>Women (n = 20 013)</td>
<td>Patients excluded</td>
</tr>
<tr>
<td>sex [%male/%female]</td>
<td>52.4/47.6</td>
<td>–</td>
<td>50.6/49.4</td>
</tr>
<tr>
<td>age [a]</td>
<td>67.1 [56.8; 74.9]</td>
<td>65.4 [55.4; 73.0]</td>
<td>69.2 [60.1; 76.8]</td>
</tr>
<tr>
<td>169.0 [162.0; 176.0]</td>
<td>175.0 [170.0; 180.0]</td>
<td>163.0 [158.0; 167.0]</td>
<td>168.0 [162.0; 175.0]</td>
</tr>
<tr>
<td>BMI [kg/m²]</td>
<td>29.2 [25.8; 33.3]</td>
<td>28.9 [26.0; 32.5]</td>
<td>29.6 [25.8; 34.3]</td>
</tr>
<tr>
<td>BMI-SDSₐₜ</td>
<td>+0.4 [−0.4; +1.2]</td>
<td>+0.3 [−0.5; +1.1]</td>
<td>+0.5 [−0.4; +1.3]</td>
</tr>
<tr>
<td>%BF</td>
<td>37.8 [31.1; 44.4]</td>
<td>31.5 [28.1; 35.4]</td>
<td>44.4 [40.6; 48.5]</td>
</tr>
<tr>
<td>HbA1c [%]</td>
<td>7.1 [6.2; 8.4]</td>
<td>7.1 [6.2; 8.5]</td>
<td>7.0 [6.2; 8.3]</td>
</tr>
<tr>
<td>blood pressure [mmHg]</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>systolic</td>
<td>130.0 [120.0; 140.0]</td>
<td>130.0 [120.0; 140.0]</td>
<td>135.0 [120.0; 145.0]</td>
</tr>
<tr>
<td>diastolic</td>
<td>80.0 [70.0; 80.0]</td>
<td>80.0 [70.0; 80.0]</td>
<td>80.0 [70.0; 81.0]</td>
</tr>
<tr>
<td>total cholesterol [mg/dl]</td>
<td>193.0 [162.0; 225.0]</td>
<td>187.0 [156.0; 220.0]</td>
<td>200.0 [170.1; 231.0]</td>
</tr>
<tr>
<td>LDL-cholesterol [mg/dl]</td>
<td>111.0 [83.5; 139.0]</td>
<td>107.0 [80.0; 135.3]</td>
<td>115.0 [87.0; 143.0]</td>
</tr>
<tr>
<td>HDL-cholesterol [mg/dl]</td>
<td>45.0 [36.0; 55.0]</td>
<td>42.0 [34.0; 51.0]</td>
<td>48.0 [39.0; 59.0]</td>
</tr>
<tr>
<td>triglycerides [mg/dl]</td>
<td>155.0 [110.0; 224.0]</td>
<td>155.0 [109.0; 229.0]</td>
<td>156.0 [112.0; 219.0]</td>
</tr>
</tbody>
</table>

Data are presented as median with lower and upper quartile (median [Q₁; Q₃]).
Baseline characteristics of the study population separated by gender are also shown in Table 1. 52.4% were male and 47.6% were female. In general, minor differences between genders existed. However, medians of body weight, height, calculated %BF, total cholesterol, LDL- and HDL-cholesterol differed significantly between men and women (all p < 0.0001). In detail, males were heavier than females (88.0 kg vs. 78.0 kg), but median BMI was nearly the same (28.9 kg/m² vs. 29.6 kg/m²). Women presented higher median values for calculated %BF (44.4% vs. 31.5%), total cholesterol (200.0 mg/dl vs. 187.0 mg/dl), LDL-cholesterol (115.0 mg/dl vs. 107.0 mg/dl) and HDL-cholesterol (48.0 mg/dl vs. 42.0 mg/dl) than men.

According to WHO, 15,305 T2DM patients had a BMI between 25.0 kg/m² and 29.9 kg/m² and were classified as normal weight. Women presented higher median values for calculated %BF (44.4% vs. 42.0% for men). According to WHO, 15,305 T2DM patients had a BMI between 25.0 kg/m² and 29.9 kg/m² and were classified as normal weight. Women presented higher median values for calculated %BF (44.4% vs. 42.0% for men). In each case, this difference was statistically significant (BMI: p < 0.05, BMI-SDS < 3a and calculated %BF: p < 0.10). Between 40 and < 80 years the relation of the 3 anthropometric measurements with elevated triglycerides was not significantly different (p > 0.05, respectively; Fig. 4b). For total cholesterol and LDL-cholesterol, ROC-AUCs were not calculated, because these risk factors showed only very weak correlations with the 3 anthropometric measurements.

**Correlation analyses**

Spearman correlation between anthropometric measurements showed a strong and significant relation between BMI and age and gender-adjusted BMI-SDS < 3a (r = 0.98; p < 0.0001). The association between calculated %BF and BMI or age- and gender-adjusted BMI-SDS < 3a was less tight (r = 0.67, r = 0.65; p < 0.0001, respectively). Consequently, in the whole study population no nameable differences could be found between the 3 anthropometric measurements regarding their correlations with blood pressure and blood lipids. In detail, correlation coefficients for systolic blood pressure with BMI, age- and gender-adjusted BMI-SDS < 3a and calculated %BF were +0.14, +0.12 and +0.12, respectively. For diastolic blood pressure: +0.16, +0.17 and +0.06. For triglycerides: +0.22, +0.23 and +0.13. For HDL-cholesterol: −0.10, −0.10 and +0.09. For total cholesterol: +0.06, +0.08 and +0.11. For LDL-cholesterol: +0.04, +0.05 and +0.07. All correlations were statistically significant (p < 0.0001).

**Logistic regression analyses**

The comparison of AUCs of ROC curves (ROC-AUCs) also showed minor, non significant differences between BMI, age- and gender-adjusted BMI-SDS < 3a and calculated %BF to predict hypertension, reduced HDL-cholesterol or elevated triglycerides (all p > 0.05). In the whole study population, age-, gender- and diabetes duration-adjusted ROC-AUC was equal within the 3 anthropometric measurements for the model with hypertension as dependent variable (0.58). For reduced HDL-cholesterol and elevated triglycerides, minor differences could be observed (ROC-AUCs for BMI, BMI-SDS < 3a and calculated %BF: HDL-cholesterol: 0.57 vs. 0.56 vs. 0.57, triglycerides: 0.61 vs. 0.61 vs. 0.62).

Fig. 2–4 present age- and gender-specific ROC-AUCs with standard error for hypertension (Fig. 2), reduced HDL-cholesterol (Fig. 3) and elevated triglycerides (Fig. 4) as dependent variables. P-values are shown for the comparisons between gender and the youngest and oldest age group (18–<40 years vs. ≥80 years). For both genders, all 3 anthropometric measurements had nearly the same relationship with hypertension and reduced HDL-cholesterol (Fig. 2a, 3a). No significant differences between gender could be found (all p > 0.05). However, relationships decreased continuously with increasing age and were significantly different between the youngest and oldest age group (p < 0.0001, respectively; Fig. 2b, 3b). For elevated triglycerides, the relation with anthropometric measurements was significantly stronger in males than in females (p < 0.0001; Fig. 4a).

**Discussion**

Before data analysis, we hypothesized that age- and gender-adjusted BMI-SDS < 3a or calculated %BF will be more adequate predictors for CVD risk factors than BMI, because they take age and gender into consideration. However, the present investigation showed that all 3 anthropometric measurements were comparable screening tools because they had nearly the same associations with hypertension and dyslipidemia, only the degree of association varied between age classes and partly dependencies between variables.


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**Fig. 2** AUC of ROC curves (ROC-AUC) for demographic variables only, or combined with BMI, BMI-SDS < 3a or calculated %BF to predict hypertension: a stratified by gender, adjusted for age and diabetes duration, b stratified by age groups, adjusted for age, sex and diabetes duration; data are presented as ROC-AUC with standard error, p-values for the comparison between gender and the youngest and oldest age group (ns = not significant).
between genders. Overall, associations were rather weak. These results lead to the assumption that other measurements – maybe more specialized – are necessary for detailed analyses of body composition and therefore presumably of cardiovascular risk. For example: bioelectrical impedance analysis, dual energy X-ray absorptiometry, hydro-densitometry or magnet resonance tomography. However, in populations already at increased CVD risk, the question appears whether these specialized measures are still relevant. Despite of their impracticability in routine care and their questionable validity in extremely obese patients, we think that these specialized measures should not be fully eliminated because in obesity therapy they can improve patients’ adherence, therapy success and reduction of CVD risk. Nevertheless, in high-risk, obese populations, a major focus should be direct monitoring of established cardiovascular risk factors (e.g. dyslipidemia, hypertension).

To date, as reported in the review of Huxley et al. 2010 [19], there is no consensus in the literature whether BMI or other anthropometric measurements are more strongly related to CVD risk factors. The association between BMI and CVD risk factors was examined in multiple studies all over the world [5, 7–14, 19–22]. Because BMI clearly has limitations as a measure of body composition, several studies have proposed additional anthropometric measurements like waist circumference [8, 10, 13, 14, 19, 20], waist:height ratio [7, 10, 19], waist:hip ratio [19] or %body fat [5, 9, 23] as more accurate predictors for CVD risk factors. In our investigation on T2DM patients, BMI as well as age- and gender-adjusted BMI-SDS and calculated %BF seemed to be rather imperfect screening tools for CVD risk factors, specifically hypertension and dyslipidemia.

A comparison of our results with the current literature is difficult, because previous studies that correlated anthropometric measurements and CVD risk factors especially in T2DM patients are scarce and not always consistent [21–23]. Our results are in line with the studies of Arora et al. [23] and Albu et al. [21]. Arora et al. [23] reported in 40 Indian type 2 diabetic patients a positive correlation between triglycerides and measured percentage body fat. Albu et al. [21] showed in the Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) Trial on 2,273 subjects with T2DM and coronary artery disease that BMI was associated with blood pressure, HDL-cholesterol and triglycerides.

Other studies, not limited on T2DM patients, further confirm our results [9, 13, 24]. A supplement of the Canadian heart health surveys [13] also found a stronger relationship between BMI and blood pressure, HDL-cholesterol or triglycerides in younger subjects compared to older participants. In accordance with our investigation, Dervaux et al. [9] showed positive correlations of blood pressure and triglycerides with BMI or %BF assessed by bioelectrical impedance. Furthermore, the authors reported a significantly negative correlation of HDL-cholesterol with BMI, no association with total cholesterol, and no differences between body fat mass and BMI in their relationships with CVD risk factors [9]. The lack of association between total cholesterol and

**Fig. 3** AUC of ROC curves (ROC-AUC) for demographic variables only, or combined with BMI, BMI-SDS or calculated %BF to predict reduced HDL-cholesterol: a stratified by gender, adjusted for age and diabetes duration, b stratified by age groups, adjusted for age, sex and diabetes duration; data are presented as ROC-AUC with standard error, p-values for the comparison between gender and the youngest and oldest age group (ns = not significant).

**Fig. 4** AUC of ROC curves (ROC-AUC) for demographic variables only, or combined with BMI, BMI-SDS or calculated %BF to predict elevated triglycerides: a stratified by gender, adjusted for age and diabetes duration, b stratified by age groups, adjusted for age, sex and diabetes duration; data are presented as ROC-AUC with standard error, p-values for the comparison between gender and the youngest and oldest age group (ns = not significant).
BMI or %BF was explained by the transport of cholesterol within atherogenic and non-atherogenic lipoproteins in blood [9]. Another publication of our research group in obese adolescents from Holl et al. [24] further confirm the weak correlations between BMI and total cholesterol or LDL-cholesterol in the present study. Consequently, the studies by Dervaux et al. [9] and Holl et al. [24] as well as the present study lead to the assumption that total cholesterol and LDL-cholesterol seem to be determined by genes rather than by body weight or body fat. In the current literature, studies on correlation analyses between calculated %BF and hypertension or dyslipidemia are scarce [5]. The unexpected slightly positive correlation between calculated %BF and HDL-cholesterol in the present investigation can be explained by the histogram for calculated %BF (Fig. 5a). There are 2 peaks: one for females and one for males. This can be attributed to the fact that the calculation formula for %BF considers gender differences. In contrast, the histograms for each gender separately show only one frequency peak (Fig. 5b) and with gender-specific analysis coefficients were negative as expected (data not shown).

Finally, there exist studies in the general population that reported nearly similar relations between BMI, waist:height ratio, waist:hip ratio, waist circumference and CVD risk factors [7,11,19]. Differences were small [7,11], in general not statistically significant [11] and probably not of clinical relevance [11]. These studies underline our results which indicate that compared to BMI other anthropometric measurements like age- and gender-adjusted BMI-SDS \textsubscript{LMS} or calculated %BF have no additional benefit to predict CVD risk factors in T2DM patients. A major strength of this analysis is its large number of included subjects. However, due to the multicenter nature of data collection, variability in the measured values can occur, even though assessment of blood pressure was standardized according to the guidelines of the German Hypertension League [25], laboratory measurements of blood lipids were carried out based on the Rilibak guidelines [26] and measurements of body height and weight (and therefore BMI) were also standardized: patient’s height was measured in a standing position without shoes using a wall-mounted stadiometer. Body weight was assessed in light clothes on a calibrated scale.

The large number of patients excluded due to missing BMI documentation can be explained by the significantly higher age of this patient cohort compared to the study population (72.7 [63.3; 80.5] years vs. 67.1 [56.8; 74.9] years; \( p < 0.0001 \)). Due to immobility, curved spine and being bed-ridden, measurements of height and body weight become more difficult with increasing age, so that calculation of BMI in older subjects is often not possible. However, the comparison of further baseline characteristics between the study population and patients excluded due to missing BMI showed no clinically relevant differences (data not shown). Therefore, the findings of the present investigation are not biased by the exclusion of patients with missing BMI. Furthermore, exclusion of Austrian patients from study population did not alter the results of the present study (data not shown).

**Conclusion**

In conclusion, the current study showed that compared to raw BMI age- and gender-adjusted BMI-SDS \textsubscript{LMS} as proposed by Hemmelmann et al. [4] carried no relevant additional benefit to predict CVD risk factors in adult T2DM patients. The same can be said for calculated %BF as proposed by Gómez-Ambrosi et al. [5] for detecting patients with increased cardiovascular risk. Furthermore, all 3 anthropometric measurements seemed to be insufficient predictors for CVD risk factors in adult T2DM patients.

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**Fig. 5** Histograms for calculated %BF: a whole study population, b separate for males and females.
Conflict of interest: The authors report no conflicts of interest.

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