Erectile dysfunction, microangiopathy and UKPDS risk in type 2 diabetes

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Abstract

Background. – Erectile dysfunction (ED) is a frequent comorbidity in patients with type 2 diabetes mellitus (T2DM), and is now increasingly considered a surrogate marker of endothelial dysfunction as well as a sentinel predictor of new-onset macroangiopathic events. Less attention, however, has been directed at the potential association of ED and microangiopathy in hyperglycaemic states.

Methods. – We analyzed 221 consecutive male T2DM outpatients in whom ED was assessed by the International Index of Erectile Function (IIEF-5) questionnaire. ED(+) patients (IIEF-5 1–20; n = 83) were compared with an age-matched ED(−) cohort (IIEF-5 21–25; n = 51), with similar diabetes duration, in terms of cardiovascular (CV) risk factors, micro-/macroangiopathy and the United Kingdom Prospective Diabetes Study (UKPDS) risk score.

Results. – Mean age and diabetes duration were 58 and 10 years, respectively. IIEF-5 score (1 S.D) was 23 (1) in ED(−) vs 11 (6) in ED(+). Anamnestic impotence and erectogenic drug use were reported by 52% and 36%, respectively, of ED(+) vs 12% and 8%, respectively, of ED(−) (P<0.0002 and P<0.0001, respectively). The metabolic syndrome prevalence (88% vs 64%; P = 0.002) and central adiposity markers (waist, waist/height and visceral fat) were all significantly higher in ED(+). HbA1c was similar in both groups: 7.5% (1.3%), and there were also no significant differences in smoking, blood pressure, HOMA insulin sensitivity, cholesterol and glomerular filtration rate. However, prevalences of retinopathy, polyneuropathy and elevated albuminuria, and the composite endpoint of peripheral artery disease, transient ischaemic attacks and/or stroke, were markedly increased in ED(+) (all P < 0.05). No differences were observed in coronary artery disease prevalence or in the UKPDS 10-year CV risk between the two ED groups.

Conclusion. – IIEF-5-defined ED in men with T2DM is associated with a marked increase in the metabolic syndrome, central adiposity and microangiopathy. These data suggest that diagnosing ED in T2DM warrants detailed screening and monitoring for microangiopathy in target organs.

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Keywords: Erectile dysfunction; Diabetes; Retinopathy; Stroke; Coronary artery disease; Albuminuria

Résumé

Dysfonction érectile, microangiopathie et risque selon le modèle UKPDS dans le diabète de type 2.

But. – La dysfonction érectile (DE), comorbidité fréquente dans le diabète de type 2, est de plus en plus considérée comme marqueur ancillaire de dysfonction endothéliale ainsi que comme facteur prédictif d’événements macroangiopathiques. L’association potentielle entre la DE et la microangiopathie en situation d’hyperglycémie est mal documentée.

Méthodes. – Nous avons relevé le score de DE chez 221 diabétiques de type 2 à l’aide du questionnaire international index of erectile function-5 (IIEF-5). Les patients ont été répartis en deux groupes : ceux avec DE (DE(+)) ; IIEF-5 1–20 ; n = 83 ont été comparés à une cohorte de diabétiques sans DE, d’âge et de durée moyenne de diabète identiques : DE(−) ; IIEF-5 21–25 ; n = 51. Nous avons comparé leurs facteurs de risque cardiovasculaire, la présence de micro-/macroangiopathies, et le risque cardiovasculaire estimé par l’algorithme United Kingdom prospective diabetes study (UKPDS).

Résultats. – L’âge moyen et la durée du diabète étaient de 58 et dix ans. Le score IIEF-5 valait (1 écart-type) 23 (1) chez les patients DE(−) versus 11 (6) dans le groupe DE(+). Une impuissance anamnestique et le recours à des médication(s) érectogène(s) étaient mentionnés par 52–36 % des DE(+) versus 12–8 % des DE(−) (P < 0.0002 et < 0.0001, respectivement). La prévalence de syndrome métabolique (88 versus 64 % ; P = 0.002) et les mesures d’adiposité centrale (tour de taille, tour de taille/hauteur et graisse viscérale) étaient significativement plus élevées dans le groupe DE(+).
Erectile dysfunction (ED) is a frequent comorbidity in patients with cardiometabolic risk (CMR) factors such as type 2 diabetes mellitus (T2DM) and, yet, is frequently overlooked in routine clinical evaluation. Obtaining normal erections requires a complex and harmonious interplay between psychosexual, endocrine, vascular, neural and endothelial functions. In addition to chronic hyperglycaemia, numerous causal or pharmacological agents of CMR states (such as smoking, dyslipidaemia, high blood pressure, sedentarity, obstructive sleep apnoea syndrome, hypogonadism, β-blockers, diuretics and central-acting hypotensive agents) can result in ED [1–6]. The association between ED and macroangiopathy is so close that ED is now increasingly considered a surrogate marker of endothelial dysfunction as well as a sentinel predictor of new-onset macroangiopathic events. In the specific setting of T2DM and the metabolic syndrome (MetS), endothelial dysfunction markedly overlaps with insulin resistance (IR) and/or hyperinsulinaemia, given the reciprocal relationship between IR and endothelial dysfunction. Whereas local imbalances between vasoconstrictor and nitric oxide (NO) production can impair insulin action in glucose-homoeostasis organs, IR/hyperinsulinaemia can negatively affect vasodilation in erectile tissue [7–9]. While recent studies have focused on the relationship between ED and macroangiopathy, considerably less attention has been directed at the association between ED and microangiopathy in hyperglycaemic states. For this reason, we analyzed a large cohort of Caucasian patients with T2DM (> 18 years; > 90% Caucasian) followed at the outpatient clinic of the Saint-Luc Academic Hospital (Brussels). T2DM was diagnosed according to the report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [13]. The prevalence/severity of self-assessed ED was evaluated from the patient’s anamnestic history combined with a screening questionnaire (the 5-item, abridged International Index of Erectile Function, or IIEF-5) [10]. Patients with a history of prostate surgery and/or treated with androgen-suppression therapy were not included. To rule out the confounding effects of age and diabetes duration on micro- and macrovascular complications, the ED(−) cohort (IIEF-5 scores 21–25) was compared with a subgroup of the ED(+) cohort (IIEF-5 scores 1–20; n = 83) that represented the 1–49th percentiles of ED(+) age distribution (n = 170).

ED(+) patients were compared with ED(−) in terms of sociodemographic and clinical variables, CV risk profiles, micro- and/or macroangiopathy prevalence, and UKPDS risk [11,12]. The following data were also collected: age; achieved level of education; family history (diabetes, CV disease); known diabetes duration; current medications (oral antidiabetic drugs [OADs], insulin, blood pressure [BP]-lowering drugs, aspirin or lipid-lowering drugs); weight; height; body mass index (BMI); relative total and visceral fat (bioelectrical impedancemetry; Omron BF500 body-fat analyzer); and waist-to-height ratio as an additional surrogate of central adiposity [14,15]. Hypertension was defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg and/or current treatment with BP-lowering drug(s) prescribed for treating high BP.

The presence of the MetS was defined according to American Heart Association/National Heart, Lung and Blood Institute (AHA/NHLBI) criteria [16]. The prevalence of micro- and macroangiopathic complications was obtained by reviewing the medical history and the diabetes clinic database. As for microangiopathy, the prevalence of peripheral neuropathy was based on clinical examination (knee and ankle reflexes, and the Semmes–Weinstein 5.07/10 monofilament test) and/or electromyography. Eye examination by an experienced ophthalmologist and/or fluorescein angiography was used to diagnose retinopathy. For macroangiopathy, coronary artery disease (CAD) was determined by a well-documented medical history of myocardial infarction, angioplasty, stents, revascularization surgery and/or significant coronary stenosis confirmed by angiography. Peripheral artery disease (PAD) was confirmed by the presence of imaging and/or clinical signs of carotid, aortic and/or lower-limb arterial constrictions. Stroke was defined as any neurological deficit with symptoms or signs lasting > 1 month, with no distinctions made between ischaemic, embolic and haemorrhagic strokes. In patients who had suffered multiple strokes, only the first was used for the prevalence data.

**1. Introduction**

Erectile dysfunction (ED) is a frequent comorbidity in patients with cardiometabolic risk (CMR) factors such as type 2 diabetes mellitus (T2DM) and, yet, is frequently overlooked in routine clinical evaluation. Obtaining normal erections requires a complex and harmonious interplay between psychosexual, endocrine, vascular, neural and endothelial functions. In addition to chronic hyperglycaemia, numerous causal or pharmacological agents of CMR states (such as smoking, dyslipidaemia, high blood pressure, sedentarity, obstructive sleep apnoea syndrome, hypogonadism, β-blockers, diuretics and central-acting hypotensive agents) can result in ED [1–6]. The association between ED and macroangiopathy is so close that ED is now increasingly considered a surrogate marker of endothelial dysfunction as well as a sentinel predictor of new-onset macroangiopathic events. In the specific setting of T2DM and the metabolic syndrome (MetS), endothelial dysfunction markedly overlaps with insulin resistance (IR) and/or hyperinsulinaemia, given the reciprocal relationship between IR and endothelial dysfunction. Whereas local imbalances between vasoconstrictor and nitric oxide (NO) production can impair insulin action in glucose-homoeostasis organs, IR/hyperinsulinaemia can negatively affect vasodilation in erectile tissue [7–9]. While recent studies have focused on the relationship between ED and macroangiopathy, considerably less attention has been directed at the association between ED and microangiopathy in hyperglycaemic states. For this reason, we analyzed a large cohort of Caucasian patients with T2DM (> 18 years; > 90% Caucasian) followed at the outpatient clinic of the Saint-Luc Academic Hospital (Brussels). T2DM was diagnosed according to the report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [13]. The prevalence/severity of self-assessed ED was evaluated from the patient’s anamnestic history combined with a screening questionnaire (the 5-item, abridged International Index of Erectile Function, or IIEF-5) [10]. Patients with a history of prostate surgery and/or treated with androgen-suppression therapy were not included. To rule out the confounding effects of age and diabetes duration on micro- and macrovascular complications, the ED(−) cohort (IIEF-5 scores 21–25) was compared with a subgroup of the ED(+) cohort (IIEF-5 scores 1–20; n = 83) that represented the 1–49th percentiles of ED(+) age distribution (n = 170).

ED(+) patients were compared with ED(−) in terms of sociodemographic and clinical variables, CV risk profiles, micro- and/or macroangiopathy prevalence, and UKPDS risk [11,12]. The following data were also collected: age; achieved level of education; family history (diabetes, CV disease); known diabetes duration; current medications (oral antidiabetic drugs [OADs], insulin, blood pressure [BP]-lowering drugs, aspirin or lipid-lowering drugs); weight; height; body mass index (BMI); relative total and visceral fat (bioelectrical impedancemetry; Omron BF500 body-fat analyzer); and waist-to-height ratio as an additional surrogate of central adiposity [14,15]. Hypertension was defined as systolic BP ≥ 140 mmHg and/or diastolic BP ≥ 90 mmHg and/or current treatment with BP-lowering drug(s) prescribed for treating high BP.

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**2. Patients and methods**

The present study design was cross-sectional and included 221 consecutive male patients with T2DM (> 18 years; > 90% Caucasian) followed at the outpatient clinic of the Saint-Luc Academic Hospital (Brussels). T2DM was diagnosed according to the report of the Expert Committee on the Diagnosis and Classification of Diabetes Mellitus [13]. The prevalence/severity of self-assessed ED was evaluated from the patient’s anamnestic history combined with a screening questionnaire (the 5-item, abridged International Index of Erectile Function, or IIEF-5) [10]. Patients with a history of prostate surgery and/or treated with androgen-suppression therapy were not included. To rule out the confounding effects of age and diabetes duration on micro- and macrovascular complications, the ED(−) cohort (IIEF-5 scores 21–25) was compared with a subgroup of the ED(+) cohort (IIEF-5 scores 1–20; n = 83) that represented the 1–49th percentiles of ED(+) age distribution (n = 170).

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In addition, the following biological variables were recorded: current HbA1c; fasting lipids and apolipoproteins A1 and B100; total cholesterol (C); HDL C; triglycerides; LDL C (Friedewald’s formula); non-HDL-C (total C minus HDL C); high-sensitivity C-reactive protein (hsCRP); serum total and free testosterone; sex hormone-binding globulin (SHBG); homocysteine; and (micro)albuminuria (urinary albumin concentrations 20–200 mg/L). For computer-based homoeostasis model assessment of insulin sensitivity (HOMA-S) and β-cell function (HOMA-B), triplicate measures of fasting plasma glucose and specific serum insulin were taken at 5-min intervals by arterialized venous sampling, following the withdrawal of all pharmacological agents for the treatment of diabetes, including insulin, as recommended (http://www.dtu.ox.ac.uk) [17,18]. Values of HOMA-B (%) were plotted as a function of HOMA-S (%), defining a hyperbolic product area (B × S; unit: %²). 100%, corresponding to 10 × 10 (2), representing true, underlying β-cell function [14,19,20].

UKPDS Risk Engine equations were used to provide 10-year CV risk estimates in primary-prevention T2DM patients for non-fatal and fatal CAD, fatal CAD, non-fatal and fatal stroke, and fatal stroke. These were calculated from the following variables: known T2DM duration; age; gender; ethnicity; smoking status; atrial fibrillation; HbA1c value; systolic BP; and total and HDL C [11,12]. Each patient gave his informed consent to participate in the present study, and the protocol approved by the local institutional review board.

2.1. Statistical methods

Results are presented as means ± 1 standard deviation (S.D.) or as proportions (%). The significance of differences between means was assessed by Student’s t test or by the Welch test for datasets with Gaussian distributions, but significant differences between S.D., and by Fisher’s exact test for differences in proportions. Results were considered significant with P < 0.05 and non-significant (NS) with P > 0.05.

3. Results

For the whole of the study cohort (n = 221), mean age ± S.D. was 64 ± 11 years, known diabetes duration was 13 ± 8 years, the MetS phenotype was present in 78% and ED in 23%. As for micro- and/or macroangiopathic complications, diabetic retinopathy was diagnosed in 24% of the men, distal polyneuropathy in 37%, (micro)albuminuria in 45%, CAD in 29%, PAD in 18% and transient ischaemic attacks (TIAs) and/or stroke in 7%. Age and diabetes duration were 57 ± 11 years and 10 ± 7 years, respectively, in ED(−) men (n = 51) vs 66 ± 10 years and 14 ± 9 years, respectively, in ED(+) men (n = 170) (P < 0.0001 and P < 0.0001, respectively).

On comparing the ED(−) cohort with the age- and diabetes-duration-matched ED(+) subgroup (n = 83), there were no significant differences in terms of diabetes and CV family histories, past/present exposure to tobacco smoke, socioeconomic status, hypertension prevalence, BP values, HOMA scores and MetS score distributions. Also, insulin sensitivity was not significantly lower in the ED(+) men (Table 1). However, the ED(+) group had markedly different clinical features, including greater BMI scores, waist circumference, relative and visceral fat indices, waist-to-height ratios and MetS prevalence (all P < 0.05).

There were no significant differences between the ED(−) and ED(+) groups in terms of β-cell secretagogues, metformin, thiazolidinedione and insulin dosages or in the proportion of patients receiving insulin monotherapy. Angiotensin-converting enzyme (ACE) inhibitor, calcium-channel blocker, diuretic, benzodiazepine, statin or oestrogen usage also did not differ between groups. However, the ED(+) were more often prescribed insulin, especially in combination with OADs, angiotensin receptor blockers, β-blockers, aspirin and antidepressant drugs (all P < 0.05; Table 2). Both groups were comparable for HbA1c, estimated glomerular filtration rate (GFR), homocysteine and lipid values (including non-HDL cholesterol and apolipoproteins A1 and B100). Levels of hsCRP were higher in ED(+), although the difference was not statistically significant. Triglycerides were significantly higher (by 50%; P < 0.001) in ED(+), and their total testosterone levels was lower (P = 0.017), however, free testosterone and SHBG levels did not differ from those of the ED(−) (Table 3).

Erectile function parameters are presented in Table 4. Complaints related to anamnestic impotence were 4.3-fold more frequent in ED(+). Mean IIEF-5 scores were 23 ± 1 in ED(−) and 11 ± 6 in ED(+), with anamnestic impotence and erectogenic drug use reported by 12 and 8%, respectively, in ED(−) vs 52 and 36%, respectively, in ED(+) patients (P = 0.0002 and P < 0.0001, respectively). The prevalences of micro- and macroangiopathic complications in the two groups are shown in Fig. 1. The ED(+) had significantly higher

Table 1

<table>
<thead>
<tr>
<th>Patients’ characteristics.</th>
<th>ED (−)</th>
<th>ED (+)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>51</td>
<td>83</td>
<td>~</td>
</tr>
<tr>
<td>Age (years)</td>
<td>58 (11)</td>
<td>58 (7)</td>
<td>~</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>10 (7)</td>
<td>10 (6)</td>
<td>~</td>
</tr>
<tr>
<td>Smoking (never/former/current)</td>
<td>37 - 47 - 16</td>
<td>30 - 49 - 21</td>
<td>NS</td>
</tr>
<tr>
<td>Hypertension (%)</td>
<td>65</td>
<td>75</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg m⁻²)</td>
<td>28 (6)</td>
<td>30 (5)</td>
<td>0.027</td>
</tr>
<tr>
<td>Waist circumference (cm)</td>
<td>101 (14)</td>
<td>106 (13)</td>
<td>0.023</td>
</tr>
<tr>
<td>Relative fat mass (%)</td>
<td>26 (7)</td>
<td>29 (6)</td>
<td>0.017</td>
</tr>
<tr>
<td>Waist (cm)height (cm⁻¹)</td>
<td>0.57 (0.08)</td>
<td>0.61 (0.08)</td>
<td>0.006</td>
</tr>
<tr>
<td>Visceral fat (0–30 score)</td>
<td>12 (4)</td>
<td>15 (5)</td>
<td>0.0002</td>
</tr>
<tr>
<td>HOMA S (%)</td>
<td>54 (36)</td>
<td>44 (28)</td>
<td>NS</td>
</tr>
<tr>
<td>HOMA Product (B × S) (%)²</td>
<td>24 (12)</td>
<td>22 (14)</td>
<td>NS</td>
</tr>
<tr>
<td>Metabolic syndrome (%)</td>
<td>64</td>
<td>88</td>
<td>0.002</td>
</tr>
<tr>
<td>3 - 4 - 5 / 5 score (%)</td>
<td>25 - 34 - 41</td>
<td>22 - 41 - 37</td>
<td>NS</td>
</tr>
</tbody>
</table>

Results are expressed as means (1 S.D.) or proportions (%). Differences between means were assessed by z or t test for unmatched samples, and between proportions by Fisher’s exact test. Differences were considered statistically significant at P values < 0.05. BMI: body mass (Queuele’s) index; BP: blood pressure; CVD: cardiovascular disease; ED: erectile dysfunction, diagnosed using International Index of Erectile Function questionnaire; NS: non significant; HOMA: homeostatic model assessment; HOMA-S: insulin sensitivity.
rates of retinopathy, polyneuropathy, albuminuria, PAD, TIAs and/or stroke (all P < 0.05). However, no significant differences were noted for either CAD prevalence or UKPDS Risk Engine 10-year estimated risks for developing non-fatal and fatal CAD, fatal CAD, non-fatal and fatal stroke, and fatal stroke in patients with or without ED in primary CV prevention (Fig. 2).

![Image](354x193 to 604x302)

![Image](354x397 to 604x564)

![Image](637x596 to 657x696)

![Image](637x696 to 657x796)

![Image](637x796 to 657x896)

![Image](637x896 to 657x996)

![Image](637x996 to 657x1096)

![Image](637x1096 to 657x1196)

![Image](637x1196 to 657x1296)

![Image](637x1296 to 657x1396)

![Image](637x1396 to 657x1496)

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![Image](637x1596 to 657x1696)

![Image](637x1696 to 657x1796)

![Image](637x1796 to 657x1896)

![Image](637x1896 to 657x1996)

![Image](637x1996 to 657x2096)

![Image](637x2096 to 657x2196)

![Image](637x2196 to 657x2296)

![Image](637x2296 to 657x2396)

![Image](637x2396 to 657x2496)

![Image](637x2496 to 657x2596)

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![Image](637x2896 to 657x2996)

![Image](637x2996 to 657x3096)

![Image](637x3096 to 657x3196)

![Image](637x3196 to 657x3296)

![Image](637x3296 to 657x3396)

![Image](637x3396 to 657x3496)

![Image](637x3496 to 657x3596)

![Image](637x3596 to 657x3696)

Results are expressed as means (1 S.D.) or proportions (%). Differences between means were assessed by $z$ or $t$ test for unmatched samples, and between proportions by Fisher’s exact test. Differences were considered statistically significant at $P$ values < 0.05. NS: non significant; ACE-I: angiotensin-converting enzyme inhibitor; ARB: angiotensin receptor blocker; ASA: acetylsalicylic acid; βS: beta-cell stimulant; CCB: calcium-channel blocker; ED: erectile dysfunction, diagnosed using International Index of Erectile Function questionnaire; TZD: thiazolidinedione.
4. Discussion

The major finding of the present study is that ED in T2DM men is associated with a marked increase in adiposity, MetS, PAD and microangiopathy in target organs (retina, nerves and kidneys). Results revealed that ED(+) patients had significantly higher values for BMI, waist circumference, waist-to-height ratio, and relative and visceral fat than ED(−) subjects, and that the anthropometric phenotype of ED(+) bears the hallmark of greater adiposity in a central/truncal distribution. While the underlying causal relationship between obesity per se and ED remains a subject of continuing debate [1], it is noteworthy that four of the five defining components used to score the MetS, as well as IR, are also established risk factors for both endothelial dysfunction and ED [2]. States characterized by decreased insulin sensitivity and portal hyperinsulinaemia may promote adiposity through a hypogonadal–obesity self-reinforcing cycle. Although total testosterone was lower in the ED(+), free testosterone and SHBG levels were similar in both study groups, suggesting that the divergent anthropometrics observed cannot be ascribed to relative hypogonadism in the ED(+) [15].

Endothelial dysfunction is an early marker and factor predisposing to micro- and macroangiopathic complications. In addition to penile arterial macroangiopathy and nonvascular ED aetiologies, human reproductive erectile tissue is largely composed of specialized endotheliocytes that are most likely vulnerable to local and systemic deleterious factors that are known to affect other endothelial tissues, and poised to compromise penile microcirculation. In addition, there is now growing evidence that the association between endothelial dysfunction and ED is neither fortuitous nor coincidental, with some authors suggesting that ED may even be a surrogate of endothelial damage. ED has also been proposed as a low-grade marker of systemic inflammation in endothelial-dysfunction states, the hallmark of which is endothelin-1 (ET-1)/NO imbalance. These states include obesity, IR and/or hyperinsulinaemia, hypertension, atherogenic dyslipidaemia and T2DM [1–5,7,9].

IR is a common finding in centrally obese/overweight subjects, in whom BMI reflects both global adiposity and sarcopenia, when present. Fat-tissue expansion is causally related to abnormal adipokine secretion, lipotoxicity and systemic inflammation. We also observed higher hsCRP and lower insulin sensitivity in ED(+) subjects, although these differences did not reach statistical significance. As for confounders affecting microangiopathy, the two cohorts had similar degrees of metabolic control. Free testosterone levels were also similar in both groups, making a confounding effect of age-related decline in androgen production unlikely [21]. We have previously reported that the MetS phenotype is associated with raised circulating ET-1 in T2DM, which is in keeping with the current understanding of the wider glucometabolic effects of insulin and selective impairment in IR states, as insulin is an endogenous vasodilatory peptide that modulates key regulators of vascular tone, including ET-1 and NO production [9].

Our present data reveal no differences between the ED(−) and ED(+) groups in 10-year predicted UKPDS risk. This was not unexpected, as most of the main input variables were comparable in the two groups, including age, gender and ethnicity. Of greater relevance was the observation that the ED(+) group had significantly higher rates of retinopathy, polyneuropathy (another organ-specific small-vessel disease), albuminuria, PAD and TIAs/stroke. Triglyceride levels were the only biological variable that significantly differed between the groups. Elevated triglyceridaemia — fasting or postprandial — is increasingly being recognized as a non-traditional risk factor for both micro- and macrovascular disease [22].

The present study had several limitations. ED was established from medical history combined with an abridged screening questionnaire, with neither tumescence studies nor extensive workups carried out in a specialized sex-health clinic. Nevertheless, the screening approach used, although likely to lead to ED underdiagnosis, is nevertheless suitable for routine clinical assessments. However, more stringent screening for ED might have reinforced the associations found between ED and the high-vascular-risk phenotype. As for potential confounders of ED, there was a significantly higher use of drugs with potential side-effects on erectile function, such as β-blockers and antidepressants, in the ED(+) group. Finally, the cross-sectional study design does not allow inferences to be made on the directionality of the observed associations.

In conclusion, our data show that diagnosing ED in men with T2DM warrants a detailed search for established microangiopathy in target organs and subclinical atherosclerosis in peripheral vessels in addition to the recommended screening for CAD. Such a search should encompass the earliest stages of atherosclerosis and, in particular, endothelial dysfunction and small-vessel subclinical disease.

5. Conflicts of interest

The authors have no conflicts of interest with this report. The research was not supported by any external grants or funding.

References


